TJ | Tumori Journal

Abstract Book

Guest Editor: Giordano Beretta

Abstract Book of the
22th National Congress of Italian Association of Medical Oncology (AIOM)

30th October – 1st November, 2020

Guest Editor

Giordano Beretta
Director of Medical Oncology Humanitas Gavazzeni, Bergamo; President, Italian Association of Medical Oncology (AIOM)

Volume 106, 2020 Issue 2S

22th National Congress of Italian Association of Medical Oncology (AIOM)
30th October – 1st November, 2020

Please note that Abstracts marked with an asterisk "*" are Oral Communications.

Giordano Beretta
Director of Medical Oncology Humanitas Gavazzeni, Bergamo

Dear Colleagues,

On behalf of the Scientific Board, it is a great pleasure for me to introduce the proceedings of the XXII (virtual meeting) National Congress of Italian Association of Medical Oncology (AIOM).

The abstracts are published in a special issue of "Tumori Journal". The number of submitted abstracts has continuously increased over years suggesting, once again, the presence of a widespread research activity in spite of the shortage of public funds and lack of interest of public authorities. Many and many young oncologists are coauthors of the abstracts and several of them are first authors. This should be an encouragement for all of us: there is a present and also a future for AIOM.
In this Covid Era the Scientific Committee introduce a special oral session about Cancer and Covid19.

As you can realize by reading this issue, the abstracts cover all topics of medical oncology, including prevention, screening, diagnosis, treatment, follow-up, simultaneous care, patients and media communication always with a multidisciplinary approach. These topics will be debated in several educational and scientific sessions co-organized with other scientific societies and also National and regional health agencies. We would like to highlight as the innovations in the field of immunotherapy and targeted therapy and all the results of Italian research are a relevant part of the program of the meeting. As clinicians involved in the care of the patients, we have to keep in mind that research activity improves the care of cancer patients. The ability to conjugate these two aspects is the only way to improve the chance of cure for our patients.

Finally, I'd like to thank the Scientific Committee and all the reviewers for their invaluable work and I hope that the meeting could be the occasion of sharing knowledge and experiences, in order to enrich our skills.
Enjoy the virtual meeting!

TJ | Tumori
     | Journal

The Board of Directors for the years 2019-2021 includes:

This abstracts book will be available on-line and will also be freely available to subscribers to the following website congresso.aiom.it from November 2nd, 2020

Plenary Session

LBA01*

INFLUENZA VACCINE INDICATION DURING THERAPY WITH IMMUNE CHECKPOINT INHIBITORS: A TRANSVERSAL CHALLENGE. THE MULTICENTER, PROSPECTIVE, OBSERVATIONAL INVIDIA-2 STUDY (A FICOG STUDY)

Bersanelli M.[1], Giannarelli D.[2], Verzoni E.[3], Procopio G.[3], Clemente A.[4], Signorelli D.[3], Costanzo R.[5], De Vivo R.[6], Zara D.[7], Zacheo A.[8], Scotti V.[9], Guglielmini P.F.[10], Giusti R.[11], Bimbatti D.[12], Rossi E.[13], Rijavec E.[14], Tiseo M.[1], Pignata S.[5], Di Maio M.[15], Buti S.[1], De Giorgi U.[4]

[1]Azienda Ospedaliero-Universitaria di Parma, Parma; [2]Istituto Nazionale Tumori Regina Elena, Roma; [3]IRCCS Istituto Nazionale Tumori di Milano, Milano; [4]Istituto Scientifico Romagnolo per lo Studio e la Cura de Tumori (IRST) IRCCS, Meldola; [5]IRCCS Istituto Nazionale Tumori G. Pascale, Napoli; [6]Ospedale San Bortolo Azienda ULSS8 Berica - Distretto Est, Vicenza; [7]Azienda Sanitaria Universitaria Friuli Centrale, Udine; [8]IRCCS Istituto Tumori "Giovanni Paolo II", Bari; [9]Azienda Ospedaliero Universitaria Careggi, Firenze; [10]Azienda Ospedaliera di Alessandria, Firenze; [11]Azienda Ospedaliero-Universitaria Sant'Andrea, Roma; [12]Istituto Oncologico Veneto IOV - IRCCS, Padova; [13]Policlinico Gemelli - Università La Sapienza, Roma; [14]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano; [15]Ospedale Mauriziano - Università degli Studi di Torino, Torino

Background: The susceptibility of advanced cancer patients treated with immune checkpoint inhibitors (ICI) for viral infections has not been investigated. Currently, there are no robust data supporting the efficacy, safety and recommendation for influenza vaccination in cancer patients receiving ICI. The retrospective INVIDIa study suggested that flu vaccine could be ineffective in these patients.

Methods: The prospective, multicenter, observational INVIDIa-2 study investigated the clinical efficacy of influenza vaccination in advanced cancer patients receiving ICI between October 2019 and January 2020. The primary endpoint was the incidence of influenza-like illness (ILI) until April 30, 2020. Secondary endpoints regarded ILI severity and lethality and flu vaccine safety.

Results: The study enrolled 1279 patients; 1177 patients were evaluable for the primary endpoint analysis. Of them, 48.8% (574) received flu vaccination. The ILI incidence was 7.7% (91 patients). Patients receiving the flu vaccine were significantly more frequently elderly (p<0.0001), former or active smokers (p<0.0001), affected by lung cancer (p=0.017) and by non-cancer comorbidities (p<0.0001) when compared to unvaccinated patients. The ILI incidence was not different according to influenza vaccination: the incidence of ILI was 8.2% in vaccinated vs 7.3% in unvaccinated patients (p=0.57). The time-adjusted ILI incidence, in terms of influenza-free survival (IFS), was similar in vaccinated and unvaccinated patients (6-months IFS 91.4% vs 89.7% respectively, p=0.92). Nevertheless, the vaccine administration was related to significantly lower rate of ILI complications: 12.8% vs 40.9%, p=0.002. Hospitalization was infrequent among vaccinated patients (only 3 of 10 patients requiring hospital admission due to ILI were vaccinated) and ILI lethality was 0%, whilst it was 4.5% in unvaccinated patients. Among vaccinated patients, those receiving adjuvated vaccines had lower incidence of ILI (4.8% vs 9.9%, p=0.046). No difference has been found between trivalent and quadrivalent vaccines (p=0.09). Adverse events (AEs) to flu vaccine were rare and mild (1.6%, grade 1-2).

Conclusions: The flu vaccine administration was not correlated with ILI incidence, but it significantly reduced ILI complications, with no ILI-related deaths in vaccinated patients. Influenza vaccination should be recommended in ICI-treated cancer patients; adjuvated vaccines may be preferred in this patient population.

01*

NEOADJUVANT IPILIMUMAB/ NIVOLUMAB FOLLOWED BY ADJUVANT NIVOLUMAB IN LOCALLY ADVANCED OR OLIGOMETASTATIC MELANOMA

Ferrucci P.F.[1], Pala L.[1], Nezi L.[1], Manzo T.[1], Mazzarella L.[1], Lotti F.[1], Gandini S.[1], Conforti F.[1], Mazzarol G.[1], Orsolini G.M.[1], Queirolo P.[1], Pennacchioli E.[1], Fierro M.T.[2], Ribero S.[2], Senetta R.[2], Fava P.[2], Picciotto F.[2], Caliendo V.[2], Quaglino P.[2], Cocorocchio E.[1]

[1]*European Institute of Oncology, IRCCS, Milan;* [2]*University of Turin, Turin*

Background: Neo-adjuvant approaches in locally advanced melanoma have been shown to improve outcomes and facilitate translational research in order to identify biomarkers of response and resistance. In particular, pathological responses at surgery seem to work as a surrogate of survival. We investigated the efficacy and safety of Ipilimumab/Nivolumab combination as primary treatment of locally advanced or oligometastatic (stage IIIB-IV) melanoma patients (pts), within an open label, single arm, two centers study.
Patients and Methods: 35 pts will be enrolled in the study receiving 4 neoadjuvant cycles of Ipilimumab 1 mg/kg and Nivolumab 3 mg/kg every 3 weeks, followed by surgery and adjuvant Nivolumab 480 mg every 4 weeks for 6 cycles. Primary objective is pathological complete remission (pCR) rate. Secondary objectives are: efficacy, safety, feasibility; identification of molecular and immunological biomarkers of response and resistance (somatic genetic drivers, tumor mutational burden, mutational signatures, predicted neoantigens, germline HLA typing, somatic HLA mutations and liquid biopsy); quality of immune activation; evaluation of microbioma and microbiota and their variation in time; health related quality of life.
Results: 26/35 pts were enrolled starting from March 2019. 4 pts were screening failure. In the ITT population (22 pts), 21 pts were stage III and 1 stage IV-M1b cutaneous melanoma; 17 pts concluded neoadjuvant therapy and received surgery; 4 pts concluded the adjuvant treatment. pCR was reached in 9/17 (52%), pathological partial remission in 4/17 (pPR = 24%) and pathological no response in 4/15 (pNR = 26%) pts. With a median follow-up of 5 months, all pts are alive; one, with pNR at surgery, relapsed during adjuvant phase. In the neoadjuvant phase, 4 pts (18%) developed G3-4 adverse events (AE): 2 G3 transaminitis, 1 myocarditis and 1 asyntomatic CPK increase. All pts, but one, performed surgery. So far, no G3-4 AEs were observed in the adjuvant phase.
Conclusions: Neoadjuvant Ipilimumab/Nivolumab inverted dose is effective and feasible. pCR rate is high. Toxicity with is superimposable to the expected one. Correlation between pathological response and survival will be evaluated after a longer follow-up. Translational data will be available and discussed at AIOM.

02*

FINAL RESULTS OF DEPATUXIZUMAB MAFODOTIN (DEPATUX-M) PLUS TEMOZOLOMIDE (TMZ) IN RECURRENT GLIOBLASTOMA PATIENTS: REAL-WORLD EXPERIENCE FROM A MULTICENTER STUDY OF ITALIAN ASSOCIATION OF NEURO-ONCOLOGY (AINO)

Padovan M.[1], Eoli M.[2], Pellerino A.[3], Rizzato S.[4], Caserta C.[5], Simonelli M.[6], Michiara M.[7], Caccese M.[1], Anghileri E.[2], Finocchiaro G.[2], Zagonel V.[1], Rudà R.[3], Lombardi G.[1]

[1]*Department Oncology, Oncology 1, Veneto Institute of Oncology - IRCCS, Padova;* [2]*Unit of Molecular Neuro-Oncology, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano;* [3]*Department of Neuro-Oncology, University of Turin and City of Health and Science Hospital, Torino;* [4]*Department of Oncology, Azienda Sanitaria Universitaria Friuli Centrale, Udine;* [5]*Medical Oncology Unit, Azienda Ospedaliera S. Maria, Terni;* [6]*Humanitas University, Department of Biomedical Sciences, Milano;* [7]*Medical Oncology Unit, University Hospital of Parma, Parma*

Background: Precision medicine is a promising tool in oncology. Depatux-M is a new antibody-drug conjugate, consisting of a specific antibody against activated EGFR and a cytotoxic agent with antimicrotubule activity. The Intellance2/EORTC 1410 phase II trial, showed interesting results for Depatux-M and TMZ combination in EGFR-amplified glioblastoma (GBM) patients (PTS) at first recurrence after RT and TMZ. In our study, we investigated clinical outcome and safety of this combination used in recurrent GBM PTS as "compassionate use".
Methods: PTS were enrolled from 7 centres of AINO and followed prospectively. Major inclusion criteria were: histologically confirmed diagnosis of GBM, 1 or more prior systemic therapies, ECOG PS $\leq$ 2 and EGFR-amplified (analyzed by FISH). According to original schedule, patients received Depatux-M 1.25 mg/kg every two weeks combined with TMZ until disease progression or unacceptable toxicity. Kaplan-Meier method was used to estimate the survival curves, RANO criteria for radiological assessment, CTCAE v5.0 for drug related adverse events
Result: From October 2018 to June 2019, we enrolled 36 PTS: median age was 57, ECOG PS 0-1 in 88% of PTS, MGMTmet in 64%, 42% received the treatment as second-line therapy and 27% underwent further chemotherapy at progression. At the time of analysis, 24 PTS (67%) had died and 31 PTS (86%) had progressed. Median OS was 8.04ms (95%CI 5.3-10.7), 12m-OS was 37%; median PFS was 2.1ms (95% CI 1.7-2.4), 6ms-PFS was 38%. All PTS were evaluable for response: disease control rate was 47%: stable disease was reported in 36%, partial response in 11% and complete response in 3% of PTS. Drug-related adverse events led to dose reductions of Depatux-M in

17% of PTS, in 28% was delayed and in 5% was permanently discontinued. Grade 3 ocular toxicity occurred in 11% of patients, no grade 4 ocular toxicity was reported; no death was considered drug-related.

Conclusions: We report the first "real world" experience of Depatux-M plus TMZ in recurrent GBM. We showed encouraging clinical benefit, despite most patients were treated beyond the second-line of therapy. Overall, the results are closed to those reported in previous phase II trial. Toxicity was moderate and manageable. This combination would be re-considered as a potential treatment for this setting of patients.

03*

MAINTENANCE VERSUS DISCONTINUATION OF ANDROGEN DEPRIVATION THERAPY DURING DOCETAXEL ADMINISTRATION WITH A CONTINUOUS OR AN INTERMITTENT SCHEDULE IN METASTATIC, CASTRATION RESISTANT, PROSTATE CANCER PATIENTS. A MULTICENTER RANDOMIZED PHASE III STUDY OF THE PIEMONTE ONCOLOGY NETWORK

Bianchi S.[1], Alessandra M.[2], Prati V.[2], Ortega C.[3], Buttigliero C.[4], Fea E.[5], Vanella P.[5], Valcamonico F.[6], Ciccone G.[7], Sirotova Z.[8], Chiappino I.[9], Dal Canton O.[10], Masini C.[11], Sacco† C.[12], Amoroso D.[13], Leone F.[14], Comandone A.[15], Gennari A.[16], Berruti A.[6], Tucci M.[17]

[1]ASST Spedali Civili di Brescia - Università degli studi di Brescia, Brescia; [2]Candiolo Cancer Institute, FPO-IRCCS, Candiolo; [3]ASL CN2, Alba; [4]A.O.U. San Luigi Gonzaga, Orbassano; [5]A.O.S.Croce e Carle, Cuneo; [6]ASST Spedali Civili di Brescia - Università di Brescia, Brescia; [7]CPO Piemonte, Torino; [8]Azienda USL della Valle d'Aosta, Aosta; [9]AOU Città della Salute e della Scienza di Torino, Torino; [10]ASL TO4, Ciriè, Chivasso, Ivrea; [11]AUSL-IRCCS di Reggio Emilia, Reggio Emilia; [12]Azienda Sanitaria Universitaria Integrata, Udine; [13]Azienda USL 12, Viareggio; [14]ASL Biella, Biella; [15]San Giovanni Bosco, Torino; [16]Ospedale Maggiore della Carità, Novara; [17]ASL AT, Asti

Background: The maintenance of androgen deprivation therapy (ADT) is the current standard of care in metastatic castration resistant prostate cancer (mCRPC) patients (pts) eligible to docetaxel (D). However, no randomized clinical trials have been conducted to support its efficacy. Furthermore, limited data are available on head-to-head comparison of intermittent versus continuous D schedule.

Methods: In this multicenter, open-label, phase 3 randomized trial, 198 pts were enrolled between 2010 and 2014. The study was early interrupted due to insufficient accrual. In the first randomization, 96 pts received D 75 mg/m2 every 3 weeks with maintenance of LHRH-A (DL+), while 102 pts received D 75 mg/m2 every 3 weeks with suspension of LHRH-A (DL-). Pts with progression-free disease after 4 D cycles underwent second randomization to receive continuous (35 pts) vs intermittent (42 pts) D therapy. ADT in the DL- arm was restored upon D discontinuation due to disease progression.

Results: PSA response was observed in 43.8% and 38.2% of DL+ and DL- pts. Median progression free survival (PFS) was 10.3 months in DL+ and 10.8 months in DL- pts (Hazard Ratio [HR] 1.02, 95% confidence interval (CI): 0.76-1.36, p=0.9), the corresponding median overall survival (OS) was 23.3 and 24.8 months, respectively (HR 1.02, 95% CI: 0.75-1.38, p=0.91). Toxicity did not differ in the 2 treatment arms. After six months of therapy, serum testosterone levels raised above the castration range in 23 (22.8%) DL- pts, while in 6 (5.9%) DL- pts testosterone attained normal levels. No difference in terms of PSA response, PFS and OS was observed comparing pts randomized to continuous versus intermittent D administration.

Conclusions: The efficacy of docetaxel in mCRPC pts is not influenced by the maintenance or suspension of ADT nor by the continuous or intermittent schedule of administration. Quality of life data will be available at the meeting.

A - Thoracic Cancers

A01*

SELPERCATINIB (LOXO-292) IN PATIENTS WITH RET-FUSION+ NON-SMALL-CELL LUNG CANCER

Goto K.[1], Oxnard G.R.[2], Tan D.S.[3], Loong H.H.[4], Bauer T.M.[5], Gainor J.F.[6], McCoach C.E.[7], Gautschi O.[8], Besse B.[9], Cho B.C.[10], Peled N.[11], Weiss J.[12], Kim Y.[13], Ohe Y.[14], Horiike A.[15], Park K.[16], Huang X.[17], Olek E.[17], Subbiah V.[18], Drilon A.E.[19], Cappuzzo F.O.[20]

[1]National Cancer Center Hospital East, Kashiwa; [2]Dana-Farber Cancer Institute, Boston; [3]National Cancer Centre Singapore, Singapore; [4]The Chinese University of Hong Kong, Shatin; [5]Sarah Cannon Research Institute, Nashville; [6]Massachusetts General Hospital Cancer Center, Boston; [7]University of California, San Francisco; [8]University of Berne and Cantonal Hospital of Lucerne, Lucerne; [9]Gustave Roussy Université Paris Sud, Villejuif; [10]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul; [11]Soroka Medical Center, Beer Sheva; [12]University of North Carolina, Chapel Hill; [13]Seoul National University Bundang Hospital, Gyeonggido; [14]National Cancer Center Hospital, Tokyo; [15]The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo; [16]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul; [17]Loxo Oncology Inc., a wholly owned subsidiary of Eli Lilly and Company, Stamford; [18]MD Anderson Cancer Center, Houston; [19]Memorial Sloan Kettering Cancer Center, New York; [20]Hematology and Oncology Department, AUSL della Romagna, Ravenna

Background: Selpercatinib (LOXO-292) is a highly selective and potent small molecule RET kinase inhibitor. Here we report an update on the efficacy and safety of

selpercatinib in *RET*-fusion+ non-small-cell lung cancer (NSCLC).

Patients and methods: Patients with *RET*-fusion+ NSCLC were enrolled to the Phase 1/2 LIBRETTO-001 trial (NCT03157128), a global, multicenter trial (16 countries, 89 sites). Following the Phase 1 dose escalation portion of the trial, patients received the recommended dose of 160 mg orally twice daily. Each cycle was 28 days. The primary endpoint was objective response rate (ORR) per RECIST 1.1. Secondary endpoints included duration of response (DoR) and safety. Per health authority agreement, the primary analysis set was defined as the first 105 consecutively enrolled patients previously treated with platinum-based chemotherapy. Treatment-naïve patients were analyzed separately. All analyses were based on a 16-Dec-2019 data cutoff date.

Results: In the primary analysis set of platinum-treated patients (median of 3 prior systemic regimens; range 1-15), the ORR by investigator assessment was 70% (95% CI 59.8–78.1, n = 73/105). Responses did not differ by fusion partner or number or type of prior therapies, including anti-PD-1/PD-L1 agents and off-label multikinase inhibitor use. The median DoR was 20.3 months (95% CI 15.6–24.0) with 45 of 73 (62%) responders censored at a median follow-up of 14.8 months. Among 39 treatment-naïve patients, the ORR by investigator assessment was 90% (95% CI 75.8–97.1, n = 35/39, including 2 responses pending confirmation). Median DoR was not reached with 27 of 33 (82%) confirmed responses ongoing at a median follow-up of 7.4 months. In the safety analysis set consisting of all selpercatinib dosed patients (N = 702), the most common treatment-related adverse events (TRAEs) that occurred in ≥15% of patients were dry mouth (33.3%), increased AST (24.5%), increased ALT (23.8%), hypertension (23.2%), diarrhea (19.7%), and fatigue (16.8%). Only 2% (14 of 702) of patients discontinued selpercatinib for TRAEs.

Conclusions: Selpercatinib achieved marked and durable antitumor activity in patients with *RET*-fusion+ NSCLC. Selpercatinib was well tolerated. Efficacy data assessed by independent review committee based on the 16-Dec-2019 data cutoff date will be presented. ©2020 ASCO, Inc. Reused with permission.

A02*

RAMES TRIAL: A MULTICENTRE, DOUBLE-BLIND, RANDOMIZED, PHASE II STUDY ON GEMCITABINE PLUS RAMUCIRUMAB VERSUS GEMCITABINE ALONE AS SECOND-LINE TREATMENT FOR ADVANCED MALIGNANT PLEURAL MESOTHELIOMA (MPM)

Pagano M.[1], Ceresoli G.L[2], Paolo Andrea Z.[3], Pasello G.[4], Garassino M.[5], Grosso F.[6], Tiseo M.[7], Soto Parra H.[8], Zanelli F.[9], Cappuzzo F.[10], Grossi F.[11], De Marinis F.[12], Paolo P.[13], Berselli A.[14], Bonelli C.[14], Boni L.[15], Normanno N.[16], Pinto C.[17]

[1]*Oncology Unit, Clinical Cancer Centrer, Azienda Unità Sanitaria Locale (AUSL)-IRCCS, Reggio Emilia, Italy, Reggio Emilia;* [2]*Medical Oncology, Cliniche Humanitas Gavazzeni Bergamo, Italy, Bergamo, Italy;* [3]*Humanitas Cancer Center, Humanitas Clinical and Research Center, Rozzano, Italy;* [4]*Istituto Oncologico Veneto IOV IRCCS, Padova, Italy;* [5]*Department of Medical Oncology Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy;* [6]*SS Antonio e Biagio Hospital, Department of Oncology, Alessandria Italy;* [7]*Medical Oncology Unit, University Hospital of Parma, Italy, Parma, Italy;* [8]*Medical Oncology, University Hospital Policlinico, Vittorio Emanuele Catania, Italy, Catania, Italy;* [9]*Oncology Unit, Clinical Cancer Centre, Azienda Unità Sanitaria Locale (AUSL)-IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy;* [10]*Clinical Cancer Centrer, Ravenna, Italy;* [11]*Istituto Toscano Tumori-Ospedale Civile Livorno, Italy, Livorno, Italy;* [12] *European Institute of Oncology, Milan,Italy;* [13]*UOC Oncologia Medica Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan,Italy;* [14]*Oncology Unit, Clinical Cancer Centrer, Azienda Unità Sanitaria Locale (AUSL)-IRCCS,, Reggio Emilia,Italy;* [15]*Clinical Epidemiology Unit, IRCCS San Martino Hospital, Genoa, Italy;* [16]*Cell Biology and Biotherapy Unit, Istituto Nazionale Tumori, Fondazione Pascale Naples, Italy, Naples, Italy;* [17]*Oncology Unit, Clinical Cancer Centrer, Azienda Unità Sanitaria Locale (AUSL)-IRCCS, Reggio Emilia, Italy*

Background: Malignant pleural mesothelioma (MPM) is a rare, highly aggressive malignancy of the mesothelium that is usually diagnosed at an advanced stage. Chemotherapy, which is the only available therapeutic option in the clinical setting, is modestly effective in MPM.The RAMES Trial (EudraCT number 2016-001132-36) is a multicenter, double-blind, randomized Phase II trial exploring the efficacy and the safety of the addition of ramucirumab to gemcitabine as the 2°line treatment in patients with MPM.

Methods: The pts were assigned (1:1) to receive Gemcitabine 1000 mg/m^2 iv on days 1 and 8 every 21 days with Placebo (Arm A) or Ramucirumab 10 mg/kg iv on day 1, of a 21-day cycle (Arm B), until tolerability or progressive disease. Pts randomised was stratified by ECOG/PS (0-1 vs 2), age (= 70 vs > 70 yrs), histology (epithelioid vs non-epithelioid) and time to progression (TTP) after 1°line therapy. The primary endpoint was overall survival (OS). Assuming a proportion of OS equal to 40% at 1 years in arm A, a 12% absolute improvement in OS at 1 years was expected in Arm B (hazard ratio = 0.70). 114 events (156 subjects) are required for a one-sided log-rank test with alfa = 0.15 to have 80% power.

Results: From December 2016 to July 2018, 164 pts were randomized, 81 pts in Arm A and 80 Arm B; 3 pts were randomized but not treated. Characteristics of pts were: median age 69 yrs (44-81), males 119 (73.9%), females 42 (26.1%); ECOG/PS0 96 (59.6%); histotype epithelioid 132 (81.9%), non-epithelioid 29 (18.1%); stage III 98 (60.7%), stage IV 60 (37.3%), 3 (2.0%) missing; asbestos exposure assessed 80 (49.7%). Median of courses was 3.50 in Arm A and 7.50 in Arm B. OS was significantly longer in Arm B with median 13.8 mths (70% CI

12.7-14.4) vs Arm A with 7.5 mths (70% CI 6.9-8.9), HR 0.71 (70% CI 0.59-0.85, p=0.057). OS at 6 and 12 mths was in Arm A 63.9% and 33.9%, and in Arm B 74.7% and 56.5%, respectively. In Arm B OS was not correlated to TTP at first-line therapy (13.6 mths in TTP =6 mths and 13.9 mths in TTP >6 mths) and histotypes (13.8 months in the epithelioid and 13.0 months in non-epithelioid). No significant differences in thromboembolism G3-4 events were observed between Arm A and Arm B (p=0.64). None hypertension G3-4 was reported in Arm A vs 5 pts (6.3%) in Arm B (p=0.022).

Conclusions: In the RAMES Study the addition of Ramucirumab to Gemcitabine significantly improved OS and can be considered a manageable regimen in 2°line treatment of MPM pts.

A03*

SAFETY AND ACTIVITY OF COMBINED AVELUMAB WITH AXITINIB IN UNRESECTABLE OR METASTATIC THYMOMAS B3 AND THYMIC CARCINOMAS: THE CAVEATT STUDY

Conforti F.[1], Pala L.[1], Zucali P.[2], Catania C.[1], Della Vigna P.[1], Pirola S.[1], Di Venosa B.[1], Zagami P.[1], Stucchi S.[1], Pennacchioli E.[1], Queirolo P.[1], De Pas T.[1]

[1]Istituto Europeo di Oncologia, Milano; [2]Humanitas, Milano

Background: Patients (pts) with advanced B3 thymoma (B3T) and thymic carcinoma (TC) resistant to chemotherapy have limited treatment options.

Treatment with Anti-PD1 showed not negligible toxicity and limited activity, and anti-angiogenic drugs obtained short lasting antitumor responses.

No data on combined anti-PD1/PD-L1 with antiangiogenic drugs are available in B3T/TC.

We report preliminary results on safety and activity of avelumab-axitinib combination in this pts population.

Methods: The CAVEATT is a multicentric, phase II trial in immunotherapy-naive pts with advanced B3T-TC, progressing after at least one line of platinum-based chemotherapy.

Prior therapy with antiangiogenic drugs is allowed. Pts received Avelumab 10 mg/kg iv every 2 weeks and Axitinib 5 mg twice a day until progression or toxicity.

The primary endpoint of the study is overall response rate (ORR) by RECIST 1.1; secondary endpoints include ORR by irRC and ITMIG, and QoL by EORTC QLQ-C30.

An interim futility analysis is planned after the enrollment of the first 18 patients. If at least 5 out of 18 patients obtain a PR, the accrual continues to reach the total number of 33 pts, according with a Simon's minimax design.

Tumor and blood samples are collected at baseline and whenever feasible at disease progression, to identify predictive biomarkers of response and mechanisms of resistance to treatment.

Results: 16 pts (15 TC/1 B3T) were enrolled from April 2019 to May 2020. Median age was 62 years (range 33-80). 10 pts received =2 previous line of therapies, and 6 pts were pretreated with an anti-angiogenic drug. The median follow-up was 7.2 months.

Out of 13 pts evaluable for response (3 pts: too early), 38% (95% CI 17%–64%) achieved a partial response and 62% (95% CI 35%–83%) a stable disease. The median PFS was 7.3 months (95% CI 4.2–NA).

Treatment-related adverse events (AE) of grade 1 or 2 occurred in 10 out of 16 (62%) evaluable pts, and the most common was diarrhea. Grade ≥3 AEs occurred in 2 (17%) pts: G3 hyperthension leading to axitinib drug reduction and G2 immune-related psoriasis form dermatitis, resolved with corticosteroids treatment.

No patient stopped treatment for toxicity, 6 pts stopped for progressive disease, 10 pts are still on treatment.

Conclusions: Preliminary results suggest promising antitumor activity and a good toxicity profile of the combination of axitinib and avelumab in pts with advanced B3T and TC. Accrual is ongoing to reach the target of 33 pts.

A04*

BE-PACIFIC (ITALIAN OBSERVATIONAL STUDY ON PATIENT MANAGEMENT STRATEGIES IN REAL-WORLD CLINICAL PRACTICE FOR PATIENTS WITH LOCALLY ADVANCED (STAGE III) NSCLC: FIRST INTERIM ANALYSIS ON THE DIAGNOSTIC WORK-UP

Silipigni S.[1], Olmetto E.[2], Leonetti A.[3], Adamo V.[4], Romano G.[5], Montrone M.[6], Gridelli C.[7], Morabito A.[8], Tagliaferri P.[9], Tonda L.[10], Ciuffreda L.[11], Borghetti P.[12], Allegrini G.[13], Cortinovis D.[14], Rossi S.[15], Scognamiglio F.[16], Roncari B.[17], Novello S.[2], Ramella S.[1]

[1]Università Campus Bio-Medico, Roma; [2]S.S.D Oncologia Toracica, AOU S.Luigi Gonzaga, Orbassano; [3]A.O.U di Parma, Parma; [4]A.O.Papardo, Messina; [5]Ospedale Vito Fazzi, Lecce; [6]Ospedale Oncologico Giovanni Paolo II, Bari; [7]A.O.S.G. Moscati, Avellino; [8]IRCCS G. Pascale, Napoli; [9]A.O.U Mater Domini, Catanzaro; [10]Ospedale S. Giovanni Bosco, Torino; [11]AOU Città della Salute e della Scienza PO Molinette, Torino; [12]ASST Spedali Civili, Brescia; [13]Ospedali Riuniti, Livorno; [14]ASST San Gerardo, Monza; [15]Humanitas Research Hospital, Rozzano; [16]AstraZeneca S.p.A, Basiglio (MI); [17]MediNEOS S.U.R.L, Modena

Background: Locally advanced (Stage III) disease is an important yet controversial diagnostic subgroup, representing 25-30% of all NSCLC diagnoses, and encompasses patients with significantly different prognosis.

Given its complexity, both staging and optimal treatment of stage III NSCLC require an experienced multidisciplinary team. The locally advanced setting is rapidly evolving the treatment paradigm for unresectable disease changed with the results from PACIFIC trial. In this scenario, the BE-PACIFIC observational study has been designed to describe the management of patients with stage III NSCLC in the Italian real-life setting.

Patients and methods: BE-PACIFIC is an observational multicenter retrospective-prospective cohort study on stage III NSCLC patients. It includes patients with confirmed diagnosis of Stage III NSCLC at enrollment or within the prior 6 months. The study is conducted in 48 Italian oncology centers. A total number of 300 patients will be enrolled in a 12-month period. Results of a preplanned interim analysis, aimed at describing the diagnostic pattern in clinical practice for Stage III NSCLC, are here reported descriptively.

Results: 138 patients were eligible. The mean duration of the diagnostic work-up was 47.4 days. Diagnostic process was entirely performed in the center where the patient was initially admitted in 44.9% of cases and largely involved (89.1%) a multidisciplinary team. The diagnostic procedures mainly comprised clinical evaluation, radiological/imaging examinations for clinical staging, and cyto/histopathologic analyses for pathological confirmation. A 18F-FDG PET scan has been carried out in 77.5% of patients. A bronchoscopy was performed in 53.6% of cases. 83.3% of patients were tested for PD-L1 expression. Particularly, PD-L1 expression was assessed on cytological samples in 16.5% of cases and on histological specimens in 80.9% (2.6% unknown). In 66.1% of cases, =1% of tumor cells expressed PD-L1, with median level of PD-L1 expression of 50% (12.5-60%).

Conclusions: The BE-PACIFIC study will draw a detailed portrait of the current standard practices in locally advanced NSCLC and this interim analysis offers interesting insights on the diagnostic patterns across Italy.

A05*

REGISTRATIONAL DATASET FROM THE PHASE 1/2 ARROW TRIAL OF PRALSETINIB (BLU-667) IN PATIENTS (PTS) WITH ADVANCED RET FUSION+ NON-SMALL-CELL LUNG CANCER (NSCLC)

Curigliano G.[1], Cappuzzo F.[2], Siena S.[3], Marchetti P.[4], Gainor J.F.[5], Kim D.[6], Lee D.H.[7], Besse B.[8], Baik C.S.[9], Doebele R.C.[10], Cassier P.[11], Lopes G.[12], Shao-Weng Tan D.[13], Garralda E.[14], Paz-Ares L.[15], Cho B.C.[16], Gadgeel S.M.[17], Thomas M.[18], Liu S.V.[19], Turner C.D.[20], Subbiah V.[21]

[1]European Institute of Oncology, IRCCS, and University of Milan, Milan; [2]Azienda Unità Sanitaria Locale della Romagna, Ravenna; [3]Niguarda Cancer Center and Università degli Studi di Milano, Milan; [4]Sant' Andrea Hospital and Sapienza University, Rome; [5]Massachusetts General Hospital, Boston; [6]Seoul National University Hospital, Seoul; [7]Asan Medical Center, University of Ulsaarn College of Medicine, Seoul; [8]Gustave Roussy Cancer Centre, Paris-Saclay University, Orsay; [9]University of Washington, Seattle; [10]University of Colorado School of Medicine, Aurora; [11]Centre Léon Bérard, Lyon; [12]Miller School of Medicine and Sylvester Comprehensive Cancer Center, Miami; [13]National Cancer Centre Singapore, Singapore; [14]Vall d'Hebron Institute of Oncology and Vall d'Hebron University Hospital, Barcelona; [15]University Hospital 12 de Octubre and Spanish National Cancer Research Center, Madrid; [16]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul; [17]University of Michigan, Ann Arbor; [18]Thoracic Oncology and Translational Lung Research Center Heidelberg and Heidelberg University Hospital, Heidelberg; [19]Lombardi Comprehensive Cancer Center, Georgetown University, Washington; [20]Blueprint Medicines Corporation, Cambridge; [21]University of Texas MD Anderson Cancer Center, Houston

Background: Pralsetinib is an investigational, highly potent, selective RET kinase inhibitor targeting oncogenic RET alterations. We present the registrational dataset for pts with RET fusion+ NSCLC with and without prior treatment from the global ARROW study.

Material and methods: ARROW (75 sites in 11 countries; NCT03037385) consists of a phase 1 dose escalation to establish recommended phase 2 dose (400 mg once daily [QD] orally) and phase 2 expansion cohorts defined by tumor type and/or RET alteration. Primary objectives were overall response rate (ORR; blinded independent central review per RECIST v1.1) and safety. Efficacy analyses are shown for response-evaluable pts (REP) with RET fusion+ NSCLC who initiated pralsetinib 400 mg QD by 11 July 2019 and safety for all pts (regardless of diagnosis) treated with 400 mg QD.

Results: As of 18 November 2019, 354 pts with advanced solid tumors had received pralsetinib at 400 mg QD; median follow-up 8.8 months. ORR, disease control rate (DCR), and% of pts with tumor size reduction are shown in the table for pts with metastatic RET fusion+ NSCLC (n=116; 72% KIF5B; 16% CCDC6; 12% other/fusion type unknown) and with prior platinum treatment (n=80) or no prior systemic treatment (n=26). ORR was similar regardless of RET fusion partner, prior therapies, or central nervous system involvement. Overall there were 7 (6%) complete responses, 4 (5%) in prior platinum pts and 3 (12%) in treatment naïve pts; median time to response overall was 1.8 months and median duration of response was not reached (95% CI, 11.3–NR). In the safety population (n=354), most treatment-related adverse events (TRAEs) were grade 1-2, and included increased aspartate aminotransferase (31%), anemia (22%), increased alanine aminotransferase (21%), constipation (21%) and hypertension (20%); 4% of pts discontinued treatment due to TRAEs.

Conclusions: Updated, registrational, centrally reviewed data demonstrate that pralsetinib has rapid, potent, and durable clinical activity in pts with advanced RET fusion+ NSCLC regardless of RET fusion genotype or prior therapies, and QD oral dosing is well-tolerated.

	Overall (n=116)[a]	Prior platinum treatment (n=80)	No prior systemic treatment (n=26)
RR, % (95% CI)	65 (55–73)[b]	61 (50–72)[b]	73 (52–88)
DCR, % (95% CI)	93 (87–97)	95 (88–99)	88 (70–98)
Tumor size reduction, %	96	95	100

[a]Including n=10 with prior non-platinum treatment; [b]Including n=2 with partial response pending confirmation

A06

A PHASE III STUDY COMPARING SB8, A PROPOSED BEVACIZUMAB BIOSIMILAR, AND REFERENCE BEVACIZUMAB IN PATIENTS WITH METASTATIC OR RECURRENT NON-SQUAMOUS NSCLC

Loupakis F.[1], Reck M.[2], Luft A.[3], Bondarenko I.[4], Shevnia S.[5], Trukhin D.[6], Kovalenko N.[7], Vacharadze K.[8], Fülöp A.[9], Hontsa A.[10], Choi J.[11], Shin D.[12]

[1]Department of Oncology, Istituto Oncologico Veneto, IRCCS, Padova; [2]Department of Thoracic Oncology, Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Lung Clinic, Grosshansdorf, Germany; [3]Department of Thoracic Surgery, Leningrad Regional Clinical Hospital, St. Petersburg, Russian Federation; [4]Oncology and Medical Radiology Department, Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [5]Department of Chemotherapy, Podillia Regional Oncology Center, Vinnytsia, Ukraine; [6]Oncology Department, Odessa Regional Oncology Center, Odessa, Ukraine; [7]Oncology, Volgograd Regional Clinical Oncology Dispensary, Volgograd, Russian Federation; [8]Department of Phthisiatry, Research Institute of Clinical Medicine, Tbilisi, Georgia; [9]Department of Pulmonary Class and Bronchology, Országos Korányi TBC és Pulmonológiai Intézet, Budapest, Hungary; [10]Day Staing Department, Chernivtsi Regional Oncology Center, Chernivtsi, Ukraine; [11]Biometrics, Samsung Bioepis Co., Ltd., Suwon, Republic of Korea; [12]Clinical Development, Samsung Bioepis Co., Ltd., Suwon, Republic of Korea

Background: SB8 is a proposed biosimilar of the reference bevacizumab (BEV). This study compared the efficacy, safety, pharmacokinetics (PK), and immunogenicity of SB8 to BEV in patients with metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC).
Methods: In this randomised, double-blind, multicentre study, patients were randomised (1:1) to receive SB8 or BEV with paclitaxel and carboplatin Q3W followed by SB8 or BEV maintenance therapy until disease progression, unacceptable toxicity, death, or 1 year from the randomisation of the last patient. The primary endpoint was the best overall response rate (ORR) by 24 weeks of chemotherapy; risk ratio was analyzed in the full analysis set (FAS) and risk difference was analyzed in the per-protocol set (PPS). Secondary endpoints were progression free survival (PFS), overall survival (OS), duration of response (DOR), safety, PK, and immunogenicity.
Results: A total of 763 patients (SB8, n=379; BEV, n=384) were randomized. Baseline characteristics were balanced between SB8 and BEV. In the FAS, the best ORR was 47.6% in SB8 and 42.8% in BEV; the risk ratio was 1.11 and its 90% CI was [0.975, 1.269], which was within the pre-defined equivalence margin of [0.737, 1.357]. In the PPS, the best ORR was 50.1% in SB8 and 44.8% in BEV; the risk difference was 5.3% and its 95% CI was [−2.2%, 12.9%], of which the lower margin was contained within and the upper margin was outside the pre-defined equivalence margin of [−12.5%, 12.5%]. The secondary efficacy endpoints in the FAS were comparable between SB8 vs BEV: median PFS (8.50 vs 7.90 months), median OS (14.90 vs 15.80 months), and median DOR (5.60 vs 5.85 months). The overall incidence of treatment-emergent adverse events (TEAEs) was comparable between SB8 vs BEV (92.1% vs 91.1%). The most frequently occurring TEAEs were alopecia, anaemia, and nausea. PK parameters (Ctrough and Cmax) and the incidence of overall anti-drug antibodies (16.1% vs 11.0%) were comparable between SB8 vs BEV.
Conclusions: This study demonstrated equivalence between SB8 and BEV in terms of best ORR risk ratio. Other efficacy endpoints, safety, PK, and immunogenicity were comparable between SB8 and BEV. Previously presented at ESMO Congress 2019, "FPN:1565P", "Martin Reck et al." - Reused with permission.

A07

LOW-DOSE ORAL ETOPOSIDE IS AN ACTIVE OPTION FOR PATIENTS WITH HEAVILY PRE-TREATED THYMIC EPITHELIAL TUMORS

Palmieri G.[1], Ottaviano M.[2], Tortora M.[1], Terracciano D.[3], Dolce P.[4], Di Lauro V.[5], Picozzi F.[5], Parola S.[5], Riccio V.[5], De Placido P.[5], Pietroluongo E.[5], Liotti A.[3], La Civita E.[3], Guggino G.[6], Cicalese M.[7], Curcio C.[8], Longo M.[3], Botti G.[9], Daniele B.[2], De Placido S.[10], Giuliano M.[10]

[1]CRCTR Rare Tumors Reference Center of Campania region, Naples, Italy, Napoli; [2]Oncology Unit, Ospedale del Mare, Naples, Italy, Napoli; [3]Università degli Studi di Napoli "Federico II", Department of Translational Medical Sciences, Napoli; [4]Università degli Studi di Napoli "Federico II", Department of Public Health, Napoli; [5]Università degli Studi di Napoli "Federico II", Department of Clinical Medicine and Surgery, Napoli; [6]Thoracic Surgery Unit, Antonio Cardarelli Hospital Naples, Italy, Napoli; [7]Azienda Ospedaliera dei Colli Naples, Italy, Napoli; [8]Division of Thoracic Surgery, Monaldi Hospital Naples, Italy, Napoli; [9]Istituto Nazionale Tumori IRCCS Fondazione "G. Pascale", Naples, Italy, Napoli; [10]Università degli Studi di Napoli "Federico II", Department of Clinical Medicine and Surgery and CRCTR Rare Tumors Reference Center of Campania region, Naples, Italy, Napoli

Background: Platinum based regimens are used in the first line setting for advanced Thymic Epithelial Tumors (TETs). Angiogenesis plays an important role in TETs: VEGF is overexpressed in TETs, and associated with aggressiveness and advanced stage. Etoposide inhibits angiogenesis *in vitro* and *in vivo* by decreasing VEGF production and microvessel density. The aim of this study is to assess the activity of metronomic oral etoposide, with identification of circulating and pharmacodynamics biomarkers.

Methods: Platinum pretreated TET referred from 2014 to 2019 at Rare Tumors Reference Center of Naples, were enrolled in this study. Oral etoposide 50 mg daily for 3 weeks on and 1 week off every 28 days, has been delivered until progression of disease, complete response or unacceptable toxicity. Response rate (RR), progression free survival (PFS), toxicity and ratio between time to etoposide progression (TTPe) and time to previous best treatment progression (TTPp) were evaluated. Serum samples were obtained from ten patients with simultaneously radiological assessment. cfDNA quantification was assessed using Qubit Fluorometric Quantitation.

Results: 21 patients were enrolled: median age 59 years range (41 - 88); 70% male, 60% T (4 B1, 3 B2, 4 B3, 1 B1-B2); 40% had TC. A median of 5 (range 1-9) prior therapy regimens had been administered. Median follow-up since etoposide was 5 years (range 0.5-5). An overall response rate of 85%, 3 patients achieved complete response and 15 partial response. Median PFS was 16 months [95%CI 3-60] with respectively a median PFS of 12 for T (95%CI 3-38) and 19 for TC (95%CI 6-60). No grade 3-4 related events occurred, G1-2 myelotoxicity has been registered in 20% of patients. Therapy is still ongoing for 15 patients and all are still alive. Median TTPe was 16 months, TTPp was 9 months and TTPe / TTPp ratio equal to 1.7. The median cfDNA of 8 responder patients, before starting therapy, was 2.2 ng/μl (0.178-5.24), dropping dramatically at radiological response to 0.5 ng/μl (0.323-2.56). 2 out of 3 non-responder patients had a median baseline value of 2.49 ng/μl, increasing to 4.6 ng/μl at progression. Variation of circulating VEGF correlates with radiological response.

Conclusions: Taking into account that other antiangiogenic drugs, showing some activity in second and further lines treatment, are associated with several side effects, we suggest that low dose oral etoposide might become the preferred treatment option in pretreated TETs

A08

AN EXOSOMAL MIRNA SIGNATURE TO PREDICT OUTCOMES OF NON-SMALL CELL LUNG CANCER PATIENTS DURING TREATMENT WITH NIVOLUMAB

Genova C.[1], Rossi G.[1], Coco S.[1], Longo L.[1], Chiorino G.[2], Ostano P.[2], Guana F.[2], Metro G.[3], Baglivo S.[3], Ludovini V.[3], Vanni I.[4], Rijavec E.[5], Biello F.[6], Dal Bello M.G.[1], Tagliamento M.[1], Dellepiane C.[1], Alama A.[1], Bennicelli E.[1], Chiari R.[7], Grossi F.[5]

[1]IRCCS Ospedale Policlinico San Martino, Genova; [2]Fondazione Edo ed Elvo Tempia, Biella; [3]Ospedale Santa Maria della Misericordia, Perugia; [4]Dipartimento di Medicina Interna (DIMI), Università di Genova, Genova; [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano; [6]AOU Ospedale Maggiore della Carità, Novara; [7]Ospedali Riuniti Padova Sud "M. Teresa di Calcutta", Padova

Background: While immune checkpoint inhibitors (ICIs) have revolutionized the management of advanced non-small cell lung cancer (NSCLC), the identification of reliable predictive factors is still a partially unmet need. Numerous studies have shown the potential of miRNAs as biomarkers for diagnosis, prognosis, and prediction of response to therapy. Tumor-derived miRNAs have been identified in several body fluids and within extracellular vesicles such as exosomes (Exo), which can mediate intercellular cross-talk. Here, we aimed at identifying a prognostic signature of Exo-miRNAs in NSCLC patients treated with nivolumab.

Material and methods: We included 174 advanced NSCLC patients who received nivolumab in second or subsequent lines. For each, a plasma sample was collected at baseline to isolate Exo-miRNAs that were profiled using the agilent microarray platform, containing 2,549 miRNAs. Raw data were analyzed by the LIMMA package applying background subtraction and between array normalization. Patients were then randomly divided for 10 times into a training (n=125) and a validation (n=49) set, and 10 penalized Cox regression models using the LASSO method were built on each different training set and applied to the corresponding validation sets.

Results: The median age of patients was 67 years, mainly men (69.6%) with non-squamous histotype (71.7%) and smokers (87.5%). Overall, 82 patients (47.3%) underwent at least two treatment lines before nivolumab. The miR-Nome profile identified two miRNAs (miR-208a-5p and miR-574-5p) overexpressed in patients with a survival time lower than 9 months (adjusted p-value=0.03) that were consistently retained by the penalized Cox regression models and were positively associated with poor survival in each validation set. Notably, by dividing the total cohort of patients into two groups according to the median value of the combined expression of the two Exo-miRNAs, the overall survival Kaplan-Meier curves were significantly different (p-value=0.0001). The in-silico prediction of the genes targeted by the two miRNAs suggested two main pathways already described in ICI resistance mechanisms: the TGF beta and the antigen processing and presentation pathways.

Conclusions: Our miRNome profile identified 2 miRNAs that could serve as a signature to identify NSCLC patient

subgroups with different benefits from nivolumab. This study was supported by Bristol Myers Squibb (CA209-828-BMS) and the Italian Ministry of Health (CO-2016-02361470).

A09

GUSTAVE ROUSSY IMMUNO SCORE (GRIM-SCORE) VARIATIONS AS EARLY PREDICTOR OF PROGNOSIS IN NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH IMMUNE CHECK-POINT INHIBITORS

Lenci E.[1], Cantini L.[1], Rinaldi S.[1], Cognigni V.[1], Lupi A.[1], Agostinelli V.[1], Mentrasti G.[1], Pecci F.[1], Ranallo N.[1], Copparoni C.[1], Paoloni F.[1], Mazzanti P.[1], Di Pietro Paolo M.[1], Berardi R.[1]

[1]Clinica Oncologica, Università Politecnica delle Marche, Azienda Ospedaliero-Universitaria Ospedali Riuniti Umberto I – GM Lancisi – G Salesi, Ancona, Ancona

Background: The Gustave Roussy Immune Score (GRIm-score) takes into account neutrophil-to-lymphocyte ratio (NLR), serum albumin concentration and lactate dehydrogenase (LDH) and represents a validated prognostic score. We aimed to assess the prognostic value of GRIm-score both at baseline (GRImT0) and 45 days since treatment initiation (GRImT1) in a cohort of metastatic NSCLC treated with immune checkpoint inhibitors (ICIs). Furthermore, we investigated whether GRIm-score variations (GRIm?) between the two time points may predict clinical outcomes.

Methods: We retrospectively evaluated 91 metastatic NSCLC patients treated with ICIs monotherapy. NLR, serum albumin and LDH concentrations were assessed at T0 and at T1 (corresponding to 45 days since treatment initiation). Patients were assigned 1 point if they had NLR > 6, LDH > upper limit normal or albumin < 35 g/l, for a total of 3 points (GRIm-score <1 was considered as a low score). Median overall survival (OS) and progression free survival (PFS) were estimated by Kaplan-Meier method and log-rank test was used to assess differences by subgroups. The independent prognostic role of the scores was further analysed by multivariate Cox proportional hazard analyses.

Results: At a median follow up of 35.2 months, median OS and PFS were 14.6 months and 5.7 months, respectively. In the group with low score GRImT0, compared to the one with high score, we observed a significant difference in terms of OS (low vs. high: median OS 13.4 vs. 3.24 months, p<0.001), but not in term of PFS (low vs. high: median PFS 8.6 vs. 3.6 months, p=0.09). Conversely, both median OS and PFS of the low Score group were significantly longer than those of the high Score group at T1 (low vs. high: median OS 35.5 vs. 3.5 months, p<0.001 and median PFS 13.3 vs. 3.4 months, p<0.001). The outcome of patients with no decrease in the GRIm-score between the two time points (GRImΔ) was better than that of patients with decrease (median OS 18.7 vs. 3.7 months, p<0.001 and median PFS 12.0 vs. 3.2 months, p<0.001). The prognostic role of GRImT1 and of GRImΔ was further confirmed at multivariate analyses, after adjusting for PD-L1 status and line of therapy.

Conclusions: Our data suggest that GRImT1 and GRImΔ are more reliable predictors of outcome compared to GRImT0. Both GRImT1 and GRImΔ might be useful as early indicators of treatment response and prognosis for advanced NSCLC patients treated with ICIs in routine clinical practice.

A10

DETECTION OF KRAS MUTATION IN NON-SMALL CELL LUNG CANCER (NSCLC): RESULTS FROM AN ITALIAN SURVEY

Malapelle U.[1], Passiglia F.[2], Del Re M.[3], Righi L.[2], Pagni F.[4], Furlan D.[5], Danesi R.[3], Troncone G.[1], Novello S.[2]

[1]Università degli Studi di Napoli Federico II, Napoli; [2]Università di Torino, Torino; [3]Università di Pisa, Pisa; [4]Università di Milano-Bicocca, Monza; [5]Università dell'Insubria, Varese

Background: To date, for NSCLC patients, KRAS has not been endorsed yet as predictive biomarkers for treatment selection. Thus, it is not recommended by the current AIOM Guidelines. However, data from early clinical trials have recently shown the predictive role of KRAS p.G12C mutation for target treatments. In this scenario, this survey aimed to describe the current status of KRAS mutations detection in the Italian real-word practice.

Methods: A 10-questions survey focusing on KRAS real-word detection practice was sent to 75 Italian centers specialized in thoracic malignancies. A 5-questions survey was separately sent to 4 referral molecular pathology units (University of Turin, University Federico II of Naples, University Bicocca of Milan and University of Varese).

Results: From November 21th to December 6th, 53 responses (70.6%) were received. The 68% of respondents declared to perform KRAS mutation testing in metastatic NSCLC patients, without any significant differences between geographical areas (69% north versus 63% south). Reflex KRAS molecular testing by pathologists was routinely done in about half of the centers, while in the remaining cases it was conducted upon request by medical oncologist. KRAS mutational analysis was performed concomitantly to the EGFR testing (89%), and a detailed molecular report including exon, codon, and the specific mutation was produced (93%). The most frequent testing platform adopted was NGS (54%), followed by Sanger Sequencing (27%) and RT-PCR (19%). Of note, KRAS

molecular analysis was regularly reimbursed among the majority (84%) of evaluated centers. KRAS mutations were detected in 212/766 (27.6%) patients with a newly diagnosed metastatic lung ADC within the 2019. The KRAS p.G12C and p.G12V were the most frequent mutations found in 92/766 (12%) and 37/766 (4.8%) of evaluated patients, thus representing about 43% and 17% of the overall KRAS mutations, respectively. The other mutations found in the tested population included KRAS p.G12D (2.9%), p.G12A (2.2%), p.G13C (1.2%), p.G13D (0.9%), p.Q61H (0.9%), p.G12R (0.5%), p.G12S (0.4%), and p.Q61L (0.3%).

Conclusions: These data revealed that the current status of KRAS detection in advanced NSCLC patients is quite heterogeneous in Italy, leading to a different mutation rate and specific variant distribution. The standardization of diagnostic molecular approaches across the different Italian regions represents a major challenges to be adequately addressed.

A11

MACHINE LEARNING AND PROGNOSIS IN LUNG CANCERS: A PROOF OF CONCEPT

Ponzetti A.[1], Zilich R.[2], Pisani F.[2], Cristiano C.[1], Bustreo S.[1], Milanesi E.[1], Filippi R.[1], Laface R.[1], Galliano R.[1], Ciuffreda L.[1]

[1]*S.C. Oncologia Medica 1, Presidio Molinette, A.O.U. "Città della Salute e della Scienza", Torino;* [2]*Mix-x S.r.l. - Rulex® Logic Learning Machine, Ivrea*

Background: Prognostication is a complex but fundamental part of clinical practice for aggressive tumors of elderly or frail patients like lung cancers. Unfortunately, in this setting only few independent prognostic factors have been clearly identified: stage at diagnosis, performance status (PS) and target-gene alterations. Moreover, especially in the advanced disease, the relative role of these factors is not well defined.

Artificial Intelligence (AI)-Machine Learning (ML) techniques, are able to deeply analyze the interactions of multiple clinical variables. This observational, longitudinal, retrospective study evaluated the ability of ML to identify the absolute and relative prognostic role of multiple clinical variables in patients affected from lung cancers and treated in a tertiary care center.

Methods: A clinical database of 592 consecutive patients diagnosed in 2014-2019 *with* NSCLC or SCLC was analyzed using a unique ML algorithm: the Rulex 'clear box' Logic Learning Machine. The absolute and relative prognostic role of 53 variables was assessed. Then the rules generated by the system were used to identify the most relevant prognostic variables together with their threshold values. Afterwards the system generated a predictive model of 1-year survival from diagnosis,

explaining, for each individual, the reason of the prediction (which rule was applied by the model).

Results: Mean age of patients was 67.2 years and 90% were affected by NSCLC (67.4% adenocarcinoma); about 60% had a stage IV disease at diagnosis, 15% a stage IIIA. Nearly 22% had a PS 2 or higher and 12% had a mutations of EGFR or an ALK amplification. Globally the prognostic algorithm had an accuracy of 92% with sensitivity and specificity of 0.88 and 0.95. AUC, NPV and PPV were respectively 0.92 (IC95% 0.90-0.94), 0.90 and 0.94.

Regarding the identification of prognostic factors, 17 rules have been generated by the system and main prognostic variables were identified. When escluding stage, PS and molecular alterations, time to treatment initiation (TTI) and progression-free survival (PFS) had the strongest impact.

In advanced NSCLC, the impact of PS at diagnosis was strongest than age's impact. A predictive model of 1-year survival was created and 21 specific "rules" were identified.

Conclusions: When applying AI/ML techiques to prognostication in lung cancers, high accuracy can be reached with a subsequent possibile strong clinical impact and it would be worth confirming it with prospective studies.

A12

LIQUID BIOPSY AND PET PARAMETERS AS PREDICTIVE FACTORS OF OSIMERTINIB TREATMENT IN ADVANCED EGFR-MUTATED NSCLC

Leonetti A.[1], Bola S.[2], Minari R.[1], Scarlattei M.[2], Buti S.[1], Bordi P.[1], Baldari G.[2], Gnetti L.[3], Sammartano A.[2], Migliari S.[2], Cosenza A.[1], Ferri L.[1], Bonatti F.[1], Mastrodomenico L.[4], Ruffini L.[2], Tiseo M.[4]

[1]*Medical Oncology Unit, University Hospital of Parma, Parma;* [2]*Nuclear Medicine Unit, University Hospital of Parma, Parma;* [3]*Pathology Unit, University Hospital of Parma, Parma;* [4]*Department of Medicine and Surgery, University of Parma, Parma*

Background: Osimertinib resistance constitutes a major challenge for the management of advanced *EGFR*-mutated (adv-*EGFR*+) NSCLC and the identification of predictive factors is largely needed. We aimed to investigate a putative role of liquid biopsy (LB) and metabolic parameters in predicting response to osimertinib.

Methods: We prospectively enrolled adv-*EGFR*+ NSCLC patients (pts) who were treated with osimertinib both in first- (1L) and second-line (2L). Pts underwent LB before starting of osimertinib and *EGFR* activating mutation (*EGFRact*) allele frequency (AF) was assessed on circulating free DNA (cfDNA) by ddPCR. Pts with *EGFRact* AF > 0 were defined as *shedders*. FDG-PET was performed at baseline and after 1 month of treatment; metabolic response (MR) was assessed as per PERCIST 1.0 criteria. Tumor

response was assessed by CT-scan after 2-3 months (mos) as per RECIST 1.1 criteria. FDG-PET parameters (maximum standardized uptake value [SUVmax], SUVpeak, lean body mass corrected SUV [SULpeak], total lesion glycolysis [TLG]) cut-offs were calculated using ROC curve analysis.

Results: 23 pts with adv-*EGFR*+ NSCLC (1L=15; 2L=8) were enrolled at the time of data cut-off (April 21th, 2020). Overall, mPFS was 7.1 mos (95% CI, 0.3-13.9) and mOS was not reached (Range, 1.1-17.9). Basal *shedders* had a significantly shorter mPFS compared to *non-shedders* (mPFS: 3.6 vs 17.0 mos, $p<0.05$). Among all FDG-PET parameters, basal TLG (bTLG) was significantly related to basal *EGFRact* AF (Spearman r: 0.57, 95%CI 0.17-0.81, $p<0.05$). Pts who had a high bTLG had a significantly shorter mPFS vs pts with a low bTLG (mPFS: 3.6 vs 14.2 mos, $p<0.05$). Pts who had a high bTLG and were *shedders* had a significantly shorter mPFS vs pts who had only 1 of the 2 features and who had none (mPFS: 3.0 vs 7.1 vs 17.0 mos, respectively, $p<0.05$). Mean SUVmax, SUVpeak, SULpeak and median TLG of the entire population were significantly decreased after 1 month of osimertinib (all $p<0.05$), similarly to median *EGFRact* AF. Among basal *shedders* (n=12), the clearance of *EGFRact* after 1 month was significantly associated with MR ($p<0.05$). Pts who achieved a MR at the 1-month FDG-PET had a significantly longer mPFS vs pts who did not (mPFS: 14.2 vs 5.5 mos, $p<0.05$).

Conclusions: *EGFRact* shedding and high bTLG identified a poor responder group to osimertinib. Integration of basal and early cfDNA analysis and metabolic parameters might be a promising not-invasive approach to predict benefit to osimertinib.

A13

DETECTION OF KRAS MUTATIONAL STATUS BY NEXT-GENERATION SEQUENCING (NGS) OF CELL-FREE CIRCULATING TUMOR DNA (CTDNA) IN NON-SMALL CELL LUNG CANCER (NSCLC) IN THE BASAL SETTING

Gristina V.[1], Malapelle U.[2], Galvano A.[1], Bazan V.[3], Troncone G.[2], Russo A.[4]

[1]Department of Section of Medical Oncology, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo; [2]Department of Public Health, University Federico II of Naples, Naples; [3]Department of Experimental Biomedicine and Clinical Neurosciences, School of Medicine, University of Palermo, Palermo; [4]Department of Section of Medical Oncology, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo

Background: In advanced Non-Small Cell Lung Cancer (NSCLC) patients, Kirsten Rat Sarcoma Viral Oncogene Homolog (*KRAS*) testing may soon acquire a predictive significance to select patients for AMG510 treatment. Since obtaining tissue biopsies for molecular analysis has resulted to be challenging and/or tissue specimens are often rejected for insufficient cellularity, liquid biopsy may represent a viable option for *KRAS* testing.

Methods: We retrospectively analyzed the last three years clinical practice performed on 194 plasma-based liquid biopsies by a customized next-generation sequencing (NGS) narrow panel. In addition to automatic variant calling analysis, we took into account several run metric parameters while Binary Alignment Map (BAM) files were visually inspected to assess the robustness and the reliability of this NGS panel on blood.

Results: Namely, 36 (18.6%) *KRAS*-mutated cases were identified, with an overall median allelic frequency of 5.0% (ranging between 0.2% and 46.8%). No concomitant mutations were observed in the other NSCLC clinically relevant genes included in the NGS panel, such as epidermal growth factor receptor (*EGFR*) and v-Raf murine sarcoma viral oncogene homolog B (*BRAF*). Exon 2 p.G12C was the most common detected mutation (13/36, 36.1%).

Conclusions: This is the first study demonstrating the technical feasibility of assessing KRAS mutational status (and particularly the exon 2 p.G12C point mutation) by using an NGS approach on plasma samples of treatment-naïve advanced NSCLC patients. Further investigation is required to design more cost-effective diagnostic algorithms to harmonize clinically relevant biomarker testing on tissue and blood in advanced NSCLC clinical practice.

A14

SMOKING HABIT AND NGS-BASED MOLECULAR PROFILING IN 'TRIPLE-NEGATIVE' (EGFR/ALK/ROS1) ADVANCED NON-SMALL-CELL LUNG CANCER (ANSCLC)

Simionato F.[1], Calvetti L.[2], Pancheri F.[2], Scarparo S.[3], Frugoni P.[3], Cosci M.[4], Andrea Giovanni M.[5], Ave S.[6], Lupi A.[6], Aprile G.[2]

[1]Oncologia - Ospedale San Bortolo, AULSS8 Berica, Vicenza; [2]Oncologia Ospedale San Bortolo, AULSS8 Berica, Vicenza, Vicenza; [3]Pneumologia Ospedale San Bortolo, AULSS8 Berica, Vicenza, Vicenza; [4]Chirurgia Ospedale San Bortolo, AULSS8 Berica, Vicenza, Vicenza; [5]Anatomia Patologica Ospedale San Bortolo, AULSS8 Berica, Vicenza, Vicenza; [6]Medicina Nucleare Ospedale San Bortolo, AULSS8 Berica, Vicenza, Vicenza

Background: Although promising, the impact in the clinical practice of upfront multi-gene profiling in advanced non-small-cell lung cancer (aNSCLC) is not yet well defined.

Methods: From July 2018 to December 2019, NGS analyses were conducted on "triple negative" (EGFR/ALK/ROS1) aNSCLC patients. The analyses were conducted on

FFPE tumor blocks and/or liquid biopsies in a multicenter compassionate program using Foundation 1 Medicine (FM1) platform or Guardant 360 test. The aim of our analysis was to investigate the presence of potential druggable alterations and their correlation ù with baseline clinical factors.

Results: Overall, thirty-four aNSCLC patients were gathered. Median age was 64 years with 53% of male versus 47% of female. Never smokers were 11 patients (32%) versus 23 patients former/current smokers (68%). 95% had an ECOG Performance Status of 0-1. 74% were metastatic at diagnosis with 88% of adenocarcinoma, 6% of squamous carcinoma and 6% not otherwise specified (NOS) cancers. Complete molecular results were available in 30 patients (88%), as test failed in 4 patients (12%) due to inadequate materials (tissue for 3 patients and liquid biopsy for 1 patient). Among 30 patients with available results, a targetable alteration was detected in 5 patients (17%). Among these, 1 was EML4/ALK fusion (local ICH test was negative), 1 KIF5B-RET fusion, 1 BRAFV600E mutation, 1 MET exon 14 skipping alteration, 1 EGFR exon 18 E709_T710>D mutation. For all these patients a target treatment was started. No targetable alterations were found in smoker patients, as all targetable alterations were found in non-smokers patients in which molecular test was available (10/11). Smoking status demonstrated a significant differential effect (Chi-square test, p=0.009) in predicting the presence of druggable alterations. Among no targetable alterations of interest, KRAS was mutated in 30% (9/30) of the patients (4 of them had concomitant STK11 mutations), both ERBB2 alterations (A730T and P780–Y781insGSP) and FGFR family alterations in 7% (2/30). Incidence of targetable alterations among KRAS wild-type patients was not statistically different from the overall population (24% versus 17%, chi-square p=0.731).

Conclusions: Our analysis suggests that NGS analyses may provide useful results in aNSCLC patients. Since clinically significant results were obtained only in non-smoker patients, we suggest considering smoking status as a possible driver for NGS analyses in aNSCLC.

Background: Currently, predictive factors for recurrence risk of resected, early stage non-small cell lung cancer (NSCLC) are limited to post-surgical stage, and novel predictors might improve patient selection for adjuvant chemotherapy. Recently, circulating tumor-derived exosome (Exo) miRNAs have emerged as highly specific non-invasive biomarkers for early NSCLC diagnosis. In this study, we aimed at identifying an Exo-miRNA signature to select resected NSCLC patients at higher risk of disease recurrence.

Material and methods: The expression profiles of 2,549 miRNAs were screened by microarray in the plasma ExomiRNome isolated from 67 patients, who underwent resection for NSCLC and had a follow-up of at least 5 years. The plasma for Exo-miRNome analysis was collected before surgery. To build a predictive score, we applied penalized Cox regression analysis, with the LASSO method, to a subset of miRNAs with mean logIntensity higher than 5, age, sex and stage. Finally, we plotted the Kaplan-Meier curves of patients divided according to the median predictive score and tested their difference using the Log Rank test.

Results: The median age of patients was 68 years, of whom 76% were men. The disease stages were classified as follows: stage I (42%), stage II (46%), stage III (12%). Disease recurrence (interval: 4-75 months) was observed in 36/67 (54%) patients. A patient "risk score" was built by combining the stage with 5 (miR-4481, miR-4436b-3p, let-7b-3p, let-7e-5p, miR-3620-3p) and 3 (miR-4716-5p, miR-1249-3p, miR-6766-3p) Exo-miRNAs, which were either positively or negatively associated with disease recurrence, respectively. Differences of both recurrence-free survival and overall survival of patients' groups were statistically significant (p< 0.0001 for both) according to the predictive risk score. In particular, high risk patients had median recurrence-free survival 4 times lower than low risk patients.

Conclusions: The risk score we found, which include 8 Exo-miRNAs and disease stage, can predict early stage NSCLC patients, who are more likely to relapse after initial surgery. Such patients may eventually be eligible for personalized protocols involving post-operative chemo/radiotherapy.

A15

PREDICTION OF RECURRENCE IN RESECTED NON-SMALL CELL LUNG CANCER BY MEANS OF AN EXOSOMAL MIRNA-BASED RISK SCORE

Rossi G.[1], Coco S.[1], Longo L.[1], Chiorino G.[2], Ostano P.[2], Dal Bello M.G.[1], Grassi M.[1], Venturi C.[1], Mastracci L.[3], Tagliamento M.[1], Dellepiane C.[1], Zullo L.[1], Beshiri K.[1], Alama A.[1], Bennicelli E.[1], Bottini A.[1], Pronzato P.[1], Genova C.[1]

[1]IRCCS Ospedale Policlinico San Martino, Genova; [2]Fondazione Edo ed Elvo Tempia, Biella; [3]Università degli Studi di Genova, Genova

A16

RELAY, ERLOTINIB PLUS RAMUCIRUMAB OR PLACEBO IN UNTREATED EGFR-MUTATED METASTATIC NSCLC: OUTCOMES BY EGFR MUTATION TYPE

Nakagawa K.[1], Nadal E.[2], Garon E.[3], Nishio M.[4], Seto T.[5], Yamamoto N.[6], Park K.[7], Shih J.[8], Frimodt-Moller B.[9], Zimmerman A.[10], Visseren-Grul C.[11], Reck M.[12], Pasello G.P.[13]

[1]Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka; [2]Department of Medical Oncology, Catalan Institute of Oncology, L'Hospitalet de Llobregat, Barcelona; [3]David Geffen School of Medicine at

University of California Los Angeles/TRIO-US Network, Los Angeles; [4]The Cancer Institute Hospital of JFCR, Tokyo; [5]National Kyushu Cancer Center, Fukuoka; [6]Wakayama Medical University Hospital, Wakayama; [7]Samsung Medical Center, Seoul; [8]Department of Internal Medicine, National Taiwan University Hospital, Taipei City; [9]Eli Lilly and Company, Copenhagen; [10]Eli Lilly and Company, Indianapolis; [11]Lilly Oncology, Utrecht; [12]LungenClinic, Airway Research Center North (ARCN), German Center for Lung Research (DZL), Grosshansdorf; [13]Second Medical Oncology Unit, Istituto Oncologico Veneto, Padua

Background: In *EGFR* mutated, metastatic (met) NSCLC, outcomes from EGFR tyrosine kinase inhibitors (TKIs) have differed historically by mutation (mut) type present, with lower benefit reported in pts with an exon 21 L858R (ex21) versus (v) an exon 19 deletion (ex19). In the phase 3 RELAY trial, RAM+ERL provided a superior PFS v PBO+ERL (Nakagawa K, et al, *Lancet Oncol.* 2019.20:1655-69). Additional efficacy and safety by mut type are reported here for the first time.

Patients and methods: Pts with untreated met NSCLC, an *EGFR* ex19 or ex21 mut, and no CNS mets were randomized (1:1) to receive erlotinib (150 mg/day) with either ramucirumab (10 mg/kg) (RAM+ERL) or placebo (PBO+ERL), Q2W, until RECIST1.1-defined progression or unacceptable toxicity. Stratification factors included mut type (ex19/ex21) and region (East Asia/Other). The primary endpoint was PFS. Secondary and exploratory endpoints included ORR, DCR, DOR, safety, PFS2, and biomarker analyses. Statistical analyses included Cox regression and Kaplan-Meier estimation. Adverse events were evaluated using NCI-CTCAE 4.0.

Results: More pts with ex21 v ex19 (83% v 72%) were of Asian race. PFS, ORR, and DCR showed consistent improvements across mut types for RAM+ERL v PBO+ERL (Table). The safety profile (Grade ≥3, serious AEs, dose adjustments) was similar between the mut types. Exploratory data are forthcoming.

Conclusions: RAM+ERL-treated pts with ex21 mut had similar treatment benefit as pts with ex19 mut, which was consistent with that of the ITT. The safety profiles were as expected. These results support RAM+ERL as a first-line therapy for both ex19 and ex21-positive met NSCLC. Previously submitted at ESMO (2020), Nakagawa et al. Reused with permission.

	Ex19		Ex21	
	RAM+ERL (n=123)	PBO+ERL (n=120)	RAM+ERL (n=99)	PBO+ERL (n=105)
PFS				
Median, months	19.6	12.5	19.4	11.2
HR* (95% CI)*; Log-rank p-value*	0.651 (0.469-0.903); p=0.01		0.618 (0.437-0.874); p=0.006	
1yr PFS rate, %	74	54	70	47
ORR, %	79	83	74	66
DCR, %	96	96	95	95
DOR n responders	97	99	73	69
Median, months	18.2	11.0	16.2	11.1
HR (95% CI)*	0.542 (0.380-0.772)		0.731 (0.493-1.083)	

PFS, progression free survival; ORR, objective response rate; DCR, disease control rate; DOR, duration of response; HR, hazard ratio.
Median follow-up time = 20.7 mo (range, 0.1-35.4).
*unstratified.

A17

PRETREATMENT LUNG IMMUNE PROGNOSTIC INDEX (LIPI) AS BIOMARKER IN PATIENTS (PTS) WITH ADVANCED NON-SMALL CELL LUNG CANCER (ANSCLC) TREATED WITH FIRST LINE PEMBROLIZUMAB: PRELIMINARY RESULTS FROM A RETROSPECTIVE MULTICENTER ANALYSIS

Veccia A.[1], Sforza V.[2], Vattemi E.[3], Inno A.[4], Kinspergher S.[1], Dipasquale M.[1], Gori S.[4], Morabito A.[2], Caffo O.[1]

[1]Medical Oncology, Santa Chiara Hospital, Trento; [2]Thoracic Medical Oncology, Istituto Nazionale Tumori, 'Fondazione G Pascale', IRCCS, Napoli; [3]Medical Oncology, Central Hospital, Bolzano; [4]Medical Oncology, IRCCS Ospedale Sacro Cuore Don Calabria, Negrar di Valpolicella, Verona

Background: Although immunotherapy represents a milestone in the treatment of aNSCLC, the clinicians need predictive biomarkers to better select pts most likely to benefit from immune checkpoint inhibitors (ICIs). Recently, the pretreatment LIPI was reported as an inflammatory biomarker associated with survival and response outcomes in pts treated with ICIs.

Patients and methods: We retrospectively reviewed the clinical records of aNSCLC pts with PDL1 ≥ 50% expression who received pembrolizumab as first line treatment from August 2017 to December 2019 at four Italian oncology departments. Pretreatment derived neutrophils/(leucocytes minus neutrophils) ratio (dNLR) and lactate dehydrogenase (LDH) values were evaluated in order to calculate LIPI. The score was based on dNLR (ratio ≤ 3 and > 3 were scored 0 and 1, respectively), and LDH

(score 0 and 1 indicated values ⩽ and > upper limit of normality, respectively). The LIPI score defined 3 prognostic groups: good (0 factors), intermediate (1 factor) and poor (2 factors). For each pt we evaluated the overall survival (OS), the progression-free survival (PFS) and the disease control rate (DCR).

Results: We identified a consecutive series of 111 pts, most of them were male (67.6%), with adenocarcinoma (62.2%), and an ECOG performance status of 0 (59.5%). The median age at diagnosis was 69 (range 45-81) years. LIPI score was 0, 1 and 2 in 63 (56.8%), 34 (30.6%) and 14 pts (12.6%), respectively. After a median follow-up of 11.2 months (mos), the median OS was 23.5 mos in the overall population: it was significantly shorter in the poor group (2.1 mos) compared to good (23.5 mos) and intermediate (median not reached) groups (p<0.0001). Median PFS was 11, 5 and 2.4 mos in LIPI 0, 1 and 2 groups, respectively (p<0.008).

In 89 pts evaluable for response, the overall DCR was 81.1%, 71.4% and 50% in LIPI 0, 1 and 2, respectively.

Conclusions: Our data confirmed that higher LIPI score is related to worse survival and response outcomes in aNSCLC pts treated with first-line pembrolizumab, suggesting that LIPI might be a useful tool to select pts for ICIs treatment.

A18

IMPACT OF MULTIDISCIPLINARY BASELINE EVALUATION FOR THYMIC EPITHELIAL TUMORS: EXPERIENCE FROM AN ITALIAN REFERENCE CENTER

Brambilla M.[1], Abatedaga L.[2], Bosisio M.[3], Borreani C.[3], Eigenmann M.[3], MAnglaviti S.[2], Nichetti F.[2], Lobefaro R.[2], Labianca A.[2], Occhipinti M.[2], De Toma A.[2], Viscardi G.[2], Prelaj A.[2], Ferrara R.[2], Signorelli D.[2], Proto C.[2], Lo Russo G.[2], Zilembo N.[2], De Braud F.[2], Garassino M.C.[2], Galli G.[2]

[1]*Fondazione IRCCS Istituto Nazionale dei Tumori, Milano;* [2]*Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano;* [3]*Psycho-oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano*

Background: Thymic Epithelial Tumors (TETs) are rare malignancies frequently associated with comorbidities such as myasthenia gravis (MG) and autoimmune diseases (ADs), which add further difficulties in patients' (pts) care. We aimed to assess potential impact of comprehensive baseline evaluation on TETs management.

Material: All pts diagnosed with TETs and presented at first access at Istituto Nazionale dei Tumori, Milan, between 7th August 2019 and 19th February 2020 were evaluated through a multidisciplinary assessment. The first evaluation included serologic screening for MG (anti-AchR antibodies) and ADs (reticulocyte count, anti-nuclear antibodies, serum immunoglobulin concentration, lymphocyte immunophenotype), unless already known. Furthermore, all pts were addressed to psychological evaluation and compiled a quality of life questionnaire (distress management scale). At the end, a pathological, neurological and reumatological consults were carried out at physicians' discretion.

Results: Among 26 pts evaluable, 16 (61.54%) came for second opinions, 8 (30.77%) were taken in charge for cancer treatment and 4 (15.38%) for follow up. Seven pts (26.92%) underwent pathological revision, resulting in change in histological diagnosis in 5 (19.23%) cases. Previous diagnoses of MG, ADs and psychological disorders were present in 7, 5 and 1 pts (26.92%, 19.23% and 3.85%) respectively. None of 12 pts (46.15%) who were screened for MG was positive for specific antibodies. Six pts (23,08%) were addressed to a neurological consult due to pre-existent MG or clinical suspicion of neurologic disease; one (3.85%) of them was diagnosed with a non-MG neurologic condition (autoimmune peripheral neuropathy), the other one received consult to optimize MG treatment with symptom improvement. Eight (30.77%) of 17 pts (65.38%) showed abnormalities at autoimmunity laboratory assessment. Among them, 5 pts (19.23%) performed a reumatological consult and 1 (3.85%) started a specific treatment. Moreover, 3 (11.54%) of the 22 pts who performed psychological assessment were addressed to support due to mental distress.

Conclusions: A multidisciplinary baseline assessment, including laboratory, pathological and psychological evaluations, performed in Cancer Centers with specific expertise, could be a key strategy to manage both malignancy and autoimmune comorbidities in TETs pts. Indeed, such a comprehensive evaluation could advantage TET pts in better dealing with their disease.

A19

CLINICAL MANAGEMENT OF PATIENTS WITH UNRESECTABLE STAGE III NON-SMALL CELL LUNG CANCER (NSCLC) IN THE REAL WORLD CLINICAL PRACTICE: RESULTS FROM AN ITALIAN SURVEY

Passiglia F.[1], Bironzo P.[1], Bertaglia V.[1], Palesandro E.[1], Olmetto E.[1], Artusio E.[1], Carnio S.[1], Napoli V.[1], Reale M.L.[1], Tabbò F.[1], Rapetti S.[1], Capelletto E.[1], Novello S.[1]

[1]*Department of Oncology, University of Turin, S. Luigi Gonzaga Hospital, Orbassano (TO), Italy, Torino*

Background: Consolidation therapy with durvalumb is currently recommended as treatment of choice for patients with unresectable stage III NSCLC, who had disease control after chemoradiation, and tumor PD-L1 expression ⩾ 1%. Although a significant survival benefit for durvalumab consolidation has been observed in the PACIFIC trial, disease progression occurred in about 50% of patients between the 12th and 18th month of therapy, with lack of published evidence regarding post-durvalumab progression strategies. This survey aimed to investigate the current management of

stage III unresectable NSCLC patients in the Italian real-word scenario.

Methods: A 15-questions survey focusing on the clinical management of patients with stage III NSCLC was sent to 75 oncology/pathology centers specialized in the field of thoracic malignancies across the different Italian regions.

Results: From January 15th to January 30th 2020, 45 responses (60%) were collected, with a total of 251 patients receiving durvalumab therapy for stage III unresectable NSCLC. The 63% of patients undergone previous concurrent chemoradiation, with carboplatin-paclitaxel and platinum-etoposide, emerging as the most common regimen associated to radiotherapy in 61% and 39% of cases, respectively. In almost all cases the expression level of PD-L1 was assessed at the time of histological diagnosis (pre-chemoradiation), upon request of medical oncologists. Consolidation therapy with Durvalumab was initiated between the 14th day and the 6th week, and between the 6th and the 8th week from the last day of radiotherapy in 68% and 25% of cases, respectively. Among the 250 included patients, a significant subgroup discontinued durvalumab because of early disease progression (12%) or high grade toxicities (8%) occurrence, while 27% of them completed 1-year consolidation treatment, as established by current guidelines. The remaining population was still on treatment at the time of data collection. Finally, among those patients who completed 1-year durvalumab consolidation, 7% experienced disease progression and all of them were candidate to platinum-doublets chemotherapy.

Conclusions: This survey provides a reliable picture of the current clinical management for unresectable stage III NSCLC patients in the Italian real-word scenario, and highlight the urgent need for post-durvalumab progression treatment strategies in this setting.

A20

CORRELATION BETWEEN TOXICITY AND RESPONSE RATES IN NSCLC TREATED WITH NIVOLUMAB ACCORDING TO NEUTROPHIL TO LYMPHOCYTES RATIO (NLR) AND PLATELETS TO LYMPHOCYTES RATIO (PLR)

Rossi L.[1], Gozzi E.[2], Raimondi L.[2], D'Assisi Cardillo F.[3], Verrico M.[3], Cimino G.[4], Angelini F.[5], Conte D.[5], Lo Russo V.[5], Tomao S.[6]

[1]Università Sapienza di Roma, Aprilia; [2]Università la Sapienza di Roma, Aprilia; [3]ASL Latina, Formia; [4]Università la Sapienza di Roma, Latina; [5]Ospedale Regina Apostolorum Albano Iaziale, Albano; [6]Università la Sapienza di Roma, Roma

Background: Elevated pre-treatment NLR and PLR are associated with worse overall survival (OS) in several tumors treated with immunotherapy.

The aim of our study was to correlate NLR and PLR to response rates and safety of Nivolumab in NSCLC.

Patients and methods: We enrolled 75 patients (pts) (37 men and 38 women) with metastatic NSCLC treated with Nivolumab after failure of first line chemotherapy.

Pre-treatment NLR and PLR were calculated by division of neutrophils and platelets by lymphocytes measured in peripheral blood.

Pts were divided into groups based on the NLR (NLR<3 and NLR ≥3) and PLR value (PLR< 170 and PLR ≥170). We examined several immunorelated toxicities such as: endocrine, hepatic, hematological, cardiovascular, hypertension, fever, fatigue, diarrhea/colitis, pneumonitis, dyspnea, myalgia, hypomagnesemia, oedema.

We correlated the number of toxicities found with treatment effectiveness according to NLR and PLR.

Response rate: complete response (RC), partial response (RP), stable disease (SD), clinical benefit (CB) (RC+RP+SD), progression disease (PD).

Results: All pts had toxicity grade (G)1,G2 and G3. We did not observe toxicity G4.

Regarding NLR, 36 pts (48%) had high NLR and 39 (52%) pts had low NLR.

At the first instrumental evaluation, 12 pts (33.3%) with high NLR had CB and 24 pts (66.6%) had PD.

In pts with low NLR, 25 (64.1%) had CB and 14 (35.8%) PD.

In subgroup with high NLR, pts with CB had an average number of toxicity of 3.9 VS 5.5 in pts with PD.

In subgroup with low, pts with CB had an average number of toxicity of 2.6, VS 4.9 in pts with PD.

Regarding PLR, 35 pts (46.6%) had high PLR and 40 pts (53.3%) had low PLR.

10 pts (28.5%) with high PLR had CB while 25 (71.4%) had PD.

27 pts (67.5%) with low PLR had CB and 13 pts (32.5%) had PD.

In subgroup with high PLR, pts with CB had an average number of toxicity of 3.4 VS 5.2 in pts with PD.

In subgroup with low PLR, pts with and CB had an average number of toxicity of 2.9, VS 5.5 in pts with PD.

Conclusions: Our study showed that in high NRL and PRL there is a higher incidence of immuno-related toxicity in patients with worse prognosis: they could be considered prognostic and safety markers.

A21

PROGNOSTIC VALUE AND SAFETY OF EOSINOPHILIA (EO) IN NON-SMALL-CELL LUNG CANCER (NSCLC) TREATED WITH NIVOLUMAB: OUR EXPERIENCE

Colonna M.[1], Gozzi E.[2], Rossi L.[2], Mannino A.[2], Verrico M.[3], Cimino G.[4], Tomao S.[5]

[1]Ospedale Fiorini, Terracina; [2]Università la Sapienza di Roma, Aprilia; [3]ASL Latina, Formia; [4]Università la Sapienza di Roma, Latina; [5]Università la Sapienza di Roma, Roma

Background: Eosinophilia (EO) is defined as an absolute eosinophil count (EC) of more than 500 cells/μL.

The prognostic role of eosinophils in cancer is controversial: in some cancers such as Hodgkin's lymphoma, EO is associated with a worse prognosis, while in gastrointestinal tumors it is associated with a better survival.

About EO and immunotherapy there are few scientific evidence: EO has been associated with better responses in some patients with melanoma, but this has not been investigated in NSCLC.

In our study, we aimed to investigate the prognostic value and safety of EO in NSCLC treated with Nivolumab.

Patients and methods: We enrolled 69 patients (pts) (44 men and 25 women) with advanced NSCLC treated with Nivolumab.

Mean age was 70 years (range 48-82).

Squamous and non squamous histologies were diagnosed in 33 and 36 pts, respectively.

We defined EO as an absolute EC of more than 500 cells/μL. Pts were divided into two groups based on EC ($<$ 500 cells/ μL or $>$ 500 cells/ μL).

We evaluated response to treatment and safety in relation to EC.

Results: 44/69 pts (63.7%) had low EC while 25/69 (36.3%) had high EC.

At the first instrumental evaluation, 18 pts with low EC had progression disease (PD) (41%), 13 pts stable disease (SD) (29.5%), 11 showed partial response (RP) (25%) and 2 complete response (RC) (4.5%) with a clinical benefit (CB) (RC+RP+SD) of 59%.

Pts with high EC, 18 had PD (72%), 6 SD (24%) and 1 RP (4%) with a CB of 28%.

We examined several immune-related toxicities and for some of these we found differences between the groups examined:

Low EC versus (VS) high EC: Diarrhea/Colitis(18%VS32 %);Rash(15.9%VS48%); Itching(25%VS36%),

Conclusions: Our results suggest that high pre-treatment EC is associated with lower response rate and greater incidence of immune-related toxicities such as Diarrhea/Colitis, rash and itching in NSCLC treated with Nivolumab.

A22

IDENTIFICATION OF PREDICTIVE BIOMARKERS OF CLINICAL BENEFIT TO IMMUNOTHERAPY IN PRETREATED ADVANCED NON-SMALL CELL LUNG CANCER: A PROSPECTIVE OBSERVATIONAL STUDY

Mazzoni F.[1], Caliman E.[1], Liotta F.[2], Maggi L.[2], Pillozzi S.[1], Lavacchi D.[1], Cosmi L.[2], Annunziato F.[2], Antonuzzo L.[1]

[1]*Oncology Department, Careggi University Hospital, Firenze;* [2]*Department of Experimental and Clinical Medicine, University of Florence, Firenze*

Background: The anti-programmed death 1 (anti-PD-1) agent, nivolumab, has demonstrated remarkable clinical activity in patients with advanced non-small cell lung cancer (NSCLC). Thus far, few clinically-available biomarkers of response to immune checkpoint inhibitors (ICIs) have been identified.

Methods: The aim of the present monocentric prospective observational study was to identify predictive biomarkers in peripheral blood (PB) that correlate with clinical responses to nivolumab in NSCLC patients. PB samples from 30 patients who received nivolumab in second-line setting, from February 2016 to May 2018 at Clinical Oncology Unit, Careggi University Hospital, were subjected to immunological assessments. The following parameters were evaluated and compared with healthy donors cohort: lymphocyte subpopulations, inhibitory and cytotoxic molecules on lymphocyte subpopulations and cytokines production profile after in vitro polyclonal stimulation. The Cox model was used to correlate biomarkers values and patients' survival outcomes.

Results: The expression of PD-1 in circulating immune cells of the study population was higher in CD4+ cells and CD16+ cells when compared to healthy donors (22.86 ± 2.31 vs 17.07 ± 1.36 (p=0.038) and 4.74 ± 1.00 vs 2.33 ± 0.51 (p=0.039), respectively). The cytotoxic molecules granzyme A and perforine have a lower expression in CD16+ cells from PB of NSCLC patients compared to controls (77.13 ± 3.28 vs 89.55 ± 1.03 (p$<$0.001) and 72.03 ± 4.01 vs 86.84 ± 1.30 (p=0.001), respectively), while they are higher expressed in CD8+ cells of patients than CD8+ cells of healthy donors (65.13 ± 4.19 vs 56.19 ± 2.66 (p=0.076) and 58.43 ± 4.64 vs 37.93 ± 3.01 (p$<$0.001), respectively). The cytokines IL-2 and TNF-alfa are significantly higher in CD4+ from patients' samples than in control group (63.39 ± 2.68 vs 40.64 ± 1.99 (p$<$0.001) and 32.67 ± 3.31 vs 24.10 ± 2.36 (p=0.039), respectively). Finally, PD-L1 expression on CD4+ cells negatively correlated with PFS (p=0.0379) and OS (p=0.0152) and PD-L1 expression on CD16+ cells negatively correlated with OS (p=0.0302).

Conclusions: NSCLC patients have a peculiar subpopulation of lymphocytes and express molecules and cytokines other than healthy controls. A better understanding of this immunological profile can lead to the identification of predictive biomarkers of response to ICIs.

A23

OVERALL SURVIVAL PREDICTION IN NON-SMALL CELL LUNG CANCER: A RADIOMIC APPROACH WITH A MULTI-VOI ANALYSIS

Ippolito E.[1], Fiore M.[2], Greco C.[2], D'Amico N.C.[3], Sicilia R.[4], Cordelli E.[4], Gentile S.[2], Miele M.[2], Iannello G.[5], Soda P.[6], Ramella S.[7]

[1]Radioterapia Oncologica Università Campus Bio-Medico, Roma;
[2]Radioterapia Oncologica, Università Campus Bio-Medico, Roma; [3]Centro
Diagnostico Italiano Spa, Milano; [4]Sistemi di Elaborazione ed Informatica,
Facoltà di Ingegneria Biomedica, Università Campus Bio-Medico, Roma;
[5]Facoltà di Ingegneria, Università Campus Bio-Medico, Roma; [6]Sistemi di
Elaborazione ed Informatica, Facoltà di Ingegneria Biomedica, Università
Campus Bio-Medico, Roma; [7]Radioterapia Oncologica, Università Campus
Bio-Medico, Roma

Background: This study aims to predict the Overall
Survival (OS) of patients with lung cancer who underwent
a chemoradiotherapy treatment using a radiomic approach.
Moreover, we evaluate how an accurate segmentation
impacts the results using three incremental segmentations
of the same lesion.

Material and methods: For this retrospective study 97
CT images of patients with NSCLC lung cancer treated
with chemoradiotherapy were included. Images were
acquired with a Siemens Somatom Emotion, with 140
Kv, 80 mAs, and 3mm slice thickness. Patients were
divided into two classes according to their OS (53 patients
died, 44 survived after median follow-up of 18.55
months. For each patient three segmentations were con-
sidered: the Gross Tumor Volume (GTV), the Clinical
Target Volume (CTV) and the Planning Target Volume
(PTV). All volumes were manually segmented by a radia-
tion oncologist who included in the GTV all the macro-
scopic disease seen at CT, in the CTV the GTV plus a
margin for sub-clinical disease and in the PTV, the CTV
plus of a 0.5 cm safety margin. Totally 242 radiomic fea-
tures: First order, 3D Gray Level Co-occurrence Matrix
and Three Orthogonal Planes-Local Binary Patterns,
were extracted with an inhouse developed MATLAB
code. For features selection, we ran a wrapper based
approach using three machine learning (ML) algorithms;
AdaBoost (Ada), Decision Tree (DT) and Random
Forest(RF). In the classification stage, the same ML algo-
rithms were used.

Results: Totally 9 different experiment were performed,
combining three ML algorithms and three segmentations
for each patient. Performance was evaluated through accu-
racy and AUC. We obtained the following results: Ada-
GTV:70.1%,70.1%, Ada-CTV:83.5%,82.8%,Ada-PTV:
71.1%,70.1%, DT-GTV:70.1%,70.1%, DT-CTV:60.8%,
61.1%, DT-PTV:63.9%,64.1%, RF-GTV:73.2%,71.8%,
RF-CTV:78.4%,77.3%, RF-PTV:77.3%,76.6%.

Conclusions: Results reported an accuracy of 83.5% and
an AUC of 82.8% in predicting the OS for stage III
patients undergoing chemoradiation. The best result was
obtained with the intermediate segmentation, which
includes margin for sub-clinical disease and increases the
prediction accuracy. This result could be the first try to
change the knowledge about the segmentation step in
radiomics.

A24

ATEZOLIZUMAB TREATMENT OF NSCLC PATIENTS IS ASSOCIATED WITH ANTINUCLEAR ANTIBODY INCREASE AND OCCURRENCE OF ABERRANT NK CELLS ASSOCIATED TO ADCC

*Fameli A.[1], Bianco G.[1], Monoriti M.[1], Calandruccio N.D.[1], Iuliano E.[1],
Oliva B.M.[1], Giannicola R.[1], Correale P.[1]*

[1]Grande Ospedale Metropolitano, Reggio Calabria

Background: Peripheral PD-1/PDL1-immunecheckpoint
blockade is an innovative treatment for NSCLC.
Atezolizumab, is a mAb to PDL1 which is expressed in
cancer cells and tumor infiltrating inflammatory cells that
may account for additional ADCC-activity. This mAb has
been recently approved for the treatment of metastatic-
NSCLC patients and few information is available concern-
ing its effects on either hematochemical or lymphocyte
subsets change. We have therefore evaluated possible
change in these parameters.

Material (patients) and methods: This is a retrospective
observational study on 14 NSCLC patients (3 with squa-
mous and 11 with non squamous histology). We evaluated
baseline and post treatment changes in inflammatory
markers (LDH, CRP, ESR), autoantibodies and then we
performed a flow cytometric study of peripheral lympho-
cyte subsets involving T, B and natural killer (NK) cells in
patients' PBMCs. NK subsets were studied in
CD56^{bright}CD16+/-, CD56^{dim}CD16^{bright} and CD56$^-$CD16$^+$
NK cell compartments.

Results: Our monitoring revealed no change in inflamma-
tory markers as well as WBC with the exception of neutro-
phils to lymphocytes ratio (Baseline vs. third cycle =
4.38±3.06 vs. 3.5±1.65; p=0.09) that showed a trend to
decline and of a significant increase in antinuclear-anti-
bodies (ANA) (Baseline vs. third cycle = 28% vs.64%,
P<0.0005). Flow cytometric analysis did not show
changes in CD4+ and CD8+ T cells, even though a sig-
nificant post-treatment decline in CD4+/CD8+ T cell
ratio was recorded (Baseline vs. third cycle = 2.22±1.24
vs. 2.02±1.20, p=0.01). Similarly, there was no significant
change in CD56^{bright}, CD56^{dim} NK cells with the exception
of the CD56$^-$CD16$^+$ subset that showed a significant post-
treatment increase (Baseline vs. third cycle = 3.76±0.8
vs. 4.68±0.81; p<0.036).

Conclusions: Anti-PDL-1 blockade by atezolizumab is
associated to a significant increase in auto-antibodies and
CD56-CD16+ NKs a particular aberrant subset that usu-
ally is expanded in patients with chronic viral infections or
autoimmune disorders and which is associated with
NK-mediated ADCC. A phenomenon that could play an
additional therapeutic effect for this mAb. We believe that

Auto-antibody, Lymphocyte subsets monitoring and flow cytometry analysis of NK cells in patients receiving Atezolizumab deserve to be investigated as a potential biomarker of response and immunerelated adverse events in patients with NSCLC receiving PD-1/PDL1 immune-checkpoint blockade.

A25

PROGNOSTIC IMPLICATION OF SOLUBLE PROGRAMMED DEATH-LIGAND 1 IN PATIENTS WITH NON-SMALL CELL LUNG CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS

Dellepiane C.[1], Coco S.[1], Dal Bello M.G.[1], Rossi G.[1], Rijavec E.[2], Biello F.[3], Tagliamento M.[1], Longo L.[1], Mora M.[1], Anselmi G.[1], Alama A.[1], Bennicelli E.[1], Grossi F.[2], Zullo L.[1], Beshiri K.[1], Bottini A.[1], Pronzato P.[1], Genova C.[1]

[1]IRCCS Ospedale Policlinico San Martino, Genova; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano; [3]AOU Maggiore della Carità, Novara

Background: Immune checkpoints inhibitors (ICIs) have revolutionized the treatment of advanced non-small cell lung cancer (NSCLC). PD-L1 expression on tumor specimens is the only approved predictive biomarker (tissue PD-L1, tPD-L1). However, the outcome of patients treated with ICIs is frequently independent from tPD-L1 status; thus, more suitable biomarkers are needed. In this study, we analyzed the role of soluble PD-L1 (sPD-L1) collected from the peripheral blood of patients with advanced NSCLC treated with nivolumab (Nivo) or pembrolizumab (Pembro).

Patients and methods: We evaluated sPD-L1 in baseline plasma samples withdrawn from 196 advanced NSCLC patients, including 118 patients treated with Nivo in second or further lines (range: 1-6 previous lines), 56 patients with high tissue PD-L1 expression (tPD-L1≥50%) treated with Pembro in first line, and 22 patients with low tissue PD-L1 expression (tPD-L1<50%) treated with chemotherapy (Chemo); additionally, we evaluated sPD-L1 from 88 healthy donors. sPD-L1 was analyzed with enzyme linked immunosorbent assay (ELISA), by using Dako PD-L1 28-8 pharmDx assay. We explored correlations between sPD-L1 and clinical outcomes of Pembro cohort and Nivo cohort. In addition, we compared sPD-L1 with tPD-L1 in previously untreated patients (Pembro cohort and Chemo cohort).

Results: The sPD-L1 median concentration of 23.92 pg/ml was used as cut- off. sPD-L1 level was higher in patients with advanced NSCLC compared to healthy controls (p<0.0001). Moreover, we found higher concentration of sPD-L1 in previously untreated patients with tPD-L1≥50% versus patients with tPD-L1<50% (p= 0.033).

In Pembro cohort, median overall survival in low and high sPD-L1 level groups were 16.0 and 10.9 months, respectively (p=0.045). No difference in progression-free survival or objective response was observed. In Nivo cohort, sPD-L1 was not associated with clinical outcomes.

Conclusions: Our study shows that baseline sPD-L1 is associated with poor prognosis in advanced NSCLC patients treated with Pembro in first line. sPD-L1 was not prognostic for pre-treated patients receiving Nivo. Additional analyses on longitudinal sPD-L1 assessments are ongoing.

A26

PROGNOSTIC VALUE AND SAFETY OF NEUTROPHIL TO LYMPHOCYTES RATIO (NLR) AND PLATELETS TO LYMPHOCYTES RATIO (PLR) IN NSCLC TREATED WITH NIVOLUMAB

Gozzi E.[1], Rossi L.[1], Raimondi L.[1], Cimino G.[2], Angelini F.[3], Conte D.[3], Lo Russo V.[3], Tomao S.[4]

[1]Università La Sapienza di Roma, Aprilia; [2]Università La Sapienza di Roma, Latina; [3]Ospedale Regina Apostolorum Albano Laziale, Albano; [4]Università La Sapienza di Roma, Roma

Background: NLR and PLR are inflammation-associated indexes.

Pre- treatment high NLR and PLR suggest worse prognosis with lower response rates in patients with NSCLC treated with immunotherapy.

In our study, we aimed to investigate the prognostic value of NLR and PLR and their correlation with immunotherapy toxicity in NSCLC treated with Nivolumab.

Patients and methods: We enrolled 65 patients (pts) (35 men and 30 women) with advanced NSCLC treated with Nivolumab. Mean age was 70 years (range 48-82).

Squamous and non squamous histologies were diagnosed in 35 (53,8%) and 30 (46,1%) pts, respectively.

Pre-treatment NLR and PLR were calculated by division of neutrophils and platelets by lymphocytes measured in peripheral blood

Pts were divided into groups based on the NLR value (NLR <3 and NLR ≥3) and PLR value (PLR< 170 and PLR ≥170).

We evaluated response and safety of the treatment in relation to NLR and PLR value.

Results: Regarding NLR, 30/65 pts (46,1%) had high value, 35/65 (53.9%) had low value.

At the fist instrumental evaluation, 21 pts with high NLR had disease progression (PD) (70%) while 2 pts (6.6%) showed partial response (RP) and 7 (23.3%) stable disease (SD), with a clinical benefit (CB) (RC+RP+SD) of 29.9%.

Pts with a low NLR, 13 had PD (37%), 9 (25,7%) RP, 1 (2,8%) RC (complete response) and 12 (34,2%) SD, with a CB of 62,7%.

Regarding PLR, 29/65 pts (44,6%) had high value, 36/65 (55,4%) had low value.

21 pts with high PLR had PD (72,41%) while 1 (3,4%) RP and 7 (24,1%) SD, with a CB of 27.5%.

13 pts with low PLR had PD (36,1%), 10 (27,7%) RP, 1 (2,7%) RC and 12 (33.3%) SD, with CB of 63,7%.

We examined several immunocorrelated toxicities and for some of these we found differences between the groups examined: High NRL versus (VS) low NLR: Fatigue (66.6%VS45,7%); Diarrhea/Colitis (33.3%VS20%); Rash (46,6%VS14,2%); Dyspnea (70%VS31,4%); Hematological toxicity (26.6%VS2,8%); Itching (30%VS8,5%); High PLR VS low PLR: Fatigue (75,8%VS 55.5%); Hematological toxicity (24.1VS13.8%); Itching(20.6%VS13.8%).

Conclusions: Our results suggest that high pre-treatment NLR and PLR are associated with lower response rate and greater incidence of toxicity patients treated with Nivolumab. They could be considered prognostic and safety markers.

A27

ITALIAN SURVEY ON UNMET MEDICAL NEEDS IN SMALL CELL LUNG CANCER (ULYSSES)

Paratore C.[1], Vallone S.[2], Bungaro M.[1], Pacchiana M.V.[1], Conte P.[3], Cortinovis D.[4], Galetta D.[5], Lo Russo G.[6], Mantini G.[7], Mantovani C.[8], Martelli O.[9], Mencoboni M.[10], Menis J.[11], Mortellaro G.[12], Nardone A.[13], Pinto C.[14], Rapetti S.[1], Russo A.[12], Sepulcri M.[15], Novello S.[1]

[1]Department of Oncology, University of Turin, San Luigi Hospital, Orbassano, Turin; [2]Women Against Lung Cancer in Europe, Orbassano, Turin; [3]Department of Surgery, Oncology and Gastroenterology, University of Padua and Medical Oncology2, Veneto Institute of Oncology IOV-IRCCS, Padua; [4]UO Medical Oncology, ASST San Gerardo Hospital, Monza; [5]Medical Thoracic Oncology Unit, IRCCS Istituto Tumori "Giovanni Paolo II", Bari; [6]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [7]Radiation Oncology Department Gemelli-ART, Fondazione Policlinico Agostino Gemelli, Università Cattolica del S. Cuore, Rome; [8]Radiation Oncology Department, AOU Città della Salute, University of Turin, Turin; [9]U.O Medical Oncology, ASL Frosinone, Frosinone; [10]Oncology Unit, Villa Scassi Hospital, Genova; [11]Department of Surgery, Oncology and Gastroenterology, University of Padua and Medical Oncology2, Veneto Institute of Oncology IOV-IRCCS, Padua; [12]University Hospital Paolo Giaccone, University of Palermo, Palermo; [13]Radiotherapy Unit IRCCS Oncologico Giovanni Paolo II, Bari; [14]Medical Oncology Unit, Clinical Cancer Centre, AUSL-IRCCS di Reggio Emilia, Reggio Emilia; [15]Radiation Oncology Department, Veneto Institute of Oncology IOV-IRCCS, Padua

Background: Small cell lung cancer (SCLC) is an aggressive tumor, with high rate of recurrence and metastatic progression. About 90% of SCLC patients have extensive disease. As there was no significant breakthrough, the current standard of care has remained unchanged for the past 20 years. The aim of this survey is to identify and gather the unmet needs of patients and stakeholders involved in the journey, to improve their outcomes and quality of life.

Methods: The study consisted of three steps: a first desk analysis on the state of the art of SCLC, a second step of qualitative research with individual interviews to clinicians and caregivers and monitoring the online conversations and, finally, a quantitative research through web interviews to size the data collected. 110 subjects were recruited: 50 oncologists, 30 radiotherapists and 30 caregivers from 11 Italian centers.

Results: More than half of caregivers reported delays in health care system, mainly due to multiple visits with specialists and to the several diagnostic procedures required. The average delay between the onset of symptoms and diagnosis is 10-12 weeks. Some patients do not notice any symptoms, and diagnosis of SCLC is incidental in around 12% of them.

More than 75% of clinicians consider SCLC to be complex, which requires a multidisciplinary approach, so 80% discuss new cases in weekly meeting. The majority of clinicians have low satisfaction with current standards of care, as in this area, there are no new therapies currently approved. People interviewed believe that the therapeutic options are limited and ineffective.

70% of clinicians and 90% of caregivers consider palliative care at home the best resources to manage the end of life. According to clinicians, home assistance palliative care is available in only 70% of cases.

Conclusions: These data reflect the urgent need to ensure early diagnosis and novel treatment strategies for SCLC. Education campaigns on populations and training to primary care doctors could improve awareness of SCLC and facilitate early access to healthcare. Multidisciplinary approach, including palliative care and psychological support, could lead to an early diagnosis and treatment and improve quality of life of SCLC patients.

A28

INTEGRATING MOLECULAR ANALYSIS AND RADIOMIC FEATURES TO SURVEIL CLONAL HETEROGENEITY OF EGFR-MUTATED NSCLC

Cucchiara F.[1], Del Re M.[1], Valleggi S.[2], Romei C.[2], Petrini I.[2], Lucchesi M.[2], Crucitta S.[1], Rofi E.[1], De Liperi A.[2], Chella A.[2], Russo A.[3], Danesi R.[1]

[1]A.O.U.P. "Santa Chiara" University Hospital, Pisa; [2]A.O.U.P. "Cisanello" University Hospital, Pisa; [3]A.O.U.P., Palermo

Background: EGFR-mutated NSCLC is a dynamic entity and tumor progression and resistance to treatment arises from the accumulation over time and across different disease sites of subclonal genetic mutations. The concept of a single-site biopsy to monitor disease dynamics is practically unfeasible since it is invasive and may result in underestimation of such heterogeneity. Instead, a combined approach

of radiomics and liquid biopsy data may result in a better understanding of such dynamic. Moreover, these methods are both minimally invasive, easy to perform and to repeat on patient follow-up visits.

Methods: This is a case series of 7 patients with metastatic EGFR mutant NSCLC, monitored during EGFR-TKI treatment. Plasma derived circulating free DNA was analysed by a ddPCR, while the LifeX® software allowed to perform radiomic analyses from multiple basal CT-images. Liquid biopsy sampling was concordant with radiographical assessment. EGFR dynamics in plasma were compared with radiomic ones and three signatures were developed on the sum of the top ranked radiomic features referring to tumor molecular data, weighted by their corresponding regression coefficients for the LASSO model. ROC curve analysis were computed to estimate diagnostic performance of such signatures.

Results: The dynamics of activating EGFR (ex19del/L858R), T790M and the total copies/ml of mutations in patients progressed to TKIs (ex19del/L858R, T790M and C797S) were related to specific changes in radiomic features highlighting spherical disproportion and texture heterogeneity, over time (p<0.05), while three signatures integrating selected radiomic features were assessed in predicting the presence of EGFR mutations (R2 = 0.447, p<0.001 for activating EGFR copies/ml; R2 = 0.301, p=0.003 for T790M copies/ml; and R2 = 0.354, p=0.001 for the total copies/ml), as confirmed by ROC analysis (AUC of 0.90, 0.84 and 0.98, respectively). No correlation emerged for C797S.

Conclusions: Get a multi-parametric (radiogenomic) signature of clonal heterogeneity may represent a promising and clinically relevant strategy to monitor targeted drug therapies in NSCLC and identify those patients which are at risk to progress during treatment, due to the appearance of new mutations. With the availability of big data and cutting-edge analysis strategies, information coming from tumor genotype and phenotype decoded via imaging, may predict treatment failures suggesting a change in treatment strategy earlier than with conventional methods.

A29

THE NEUTROPHIL/LYMPHOCYTE RATIO (NLR) IN ADVANCED NON-SMALL LUNG CANCER (NSCLC) PATIENTS TREATED WITH CHECK POINT INHIBITORS (CPI): ANALYSIS OF PATIENTS WITH LONG-TERM CLINICAL BENEFIT

Alessio M.[1], Zai S.[2], Piovano P.[2], Laquatra C.[3], De Martino I.[4], Rossi M.[2], Traverso E.[2], Blengio F.[2], Fusco V.[2], Vincenti M.[2], Manfredi R.[2], Guglielmini P.F.[2], Bellotti G.[2], Numico G.[2]

[1]I.R.F.I. - Azienda Ospedaliera SS. Antonio e Biagio e C. Arrigo, Alessandria; [2]S.C. Oncologia - Azienda Ospedaliera SS Antonio e Biagio e C. Arrigo, Alessandria; [3]Università degli Studi del Piemonte Orientale "Amedeo Avogadro", Alessandria; [4]I.R.F.I. - Azienda Ospedaliera SS Antonio e Biagio e C. Arrigo, Alessandria

Background: We still do not have reliable pre-treatment tools to predict the efficacy of treatment with CPI. The NLR could be a useful tool in this respect and, in retrospective series, has been shown to have a potential role, being values<5 predictive of response. We aimed at assessing the basal NLR value and its change in a group of patients with long term response to CPI.

Patients and methods: Among a population of 122 NSCLC pts treated with CPI we selected the 47 (38,5%) pts with disease control and treatment continuation for at least 6 months. We examined the basal, at the third cycle and at 6 months NLR value.

Results: The 47 selected pts had a mean age of 70,0 (range 42-86); Males were 35 (74,4%). 14 (29,7%) had squamous-cell while 33 (70,2%) had non-squamous cell lung cancer. Treatment consisted in single agent Nivolumab (25 pts) or Atezolizumab (4 pts) as second or further treatment line, Pembrolizumab (14 pts, of whom 8 as first line), Durvalumab (4 pts) as maintenance treatment after chemo-radiotherapy for stage III disease. The median treatment duration was 13,3 months (range 6,2 – 52,3). Best response, as measured through RECIST criteria was: PR 28/47 (59,5%) and SD 19/47 (40,5%). At the time of analysis 21 pts had a disease progression and 15 died. Of the dead pts 10 had a PD and 5 died for an intercurrent event. Median PFS was 14,4 months, and median Survival was 16,5 months. The mean basal NLR value was 4,6. 35 pts (74,4%) had a basal NLR <5. All the 12 pts with a basal NLR =5 had a 50% reduction of NLR at the control before the third cycle, although 6 of them had still a value =5. At 6 months 8 pts had an increasing NLR value with respect to the 3rd month value. Of them 5 had a PD and 1 a severe treatment related pneumonia and had to be given steroids. Of the 75 pts with a treatment duration <6 months, 4 were on treatment. Among the remaining 71, the mean basal NLR value was 8,4 and was <5 in 27 (38,0%). 44 pts (61,9%) had a NLR >5. Of them 29 reached the third course and only 8 had a NLR reduction compared with the basal value. Overall, 19 pts (26,7%) had a basal value <5 or a reduction at the third administration that could predict a long treatment duration.

Conclusions: A basal NLR value <5 or a decrease at the third administration is highly predictive of long treatment duration (the false negative rate being extremely low). However, the false positive rate is quite high. An increasing value at 6 months seems to be strictly related with PD.

A30

THYROID DISFUNCTION (TD) IN NON-SMALL CELL LUNG CANCER TREATED WITH IMMUNE CHECKPOINT INHIBITORS PD1/PD-L1

Chilelli M.G.[1], Signorelli C.[1], Giron Berrios J.R.[1], Nelli F.[1], Fabbri M.A.[1], Marrucci E.[1], Virtuoso A.[1], Primi F.[1], Padalino D.[1], Ruggeri E.M.[1]

[1]Ospedale Belcolle, Viterbo

Background: Immune-related thyroid dysfunction (irTD) is common and occurs in 10-20% of patients treated with immune checkpoint blockade and it seems to correlate with improved outcomes. The proportion of the patients who needs therapy for irTD, as well as the need to delay, omit or interruption is not well known.

Patients and methods: We reviewed the data of 85pts with metastatic NSCLC treated with PD1/PD-L1 blockade at our institution from July 2015 to April 2020. The incidence of immune-related thyroid disfunction (irTD), requiring delay, omission, or permanent discontinuation, and the need for hormonal replacement or antithyroidal drugs were assessed. Patients with pre-existent thyroid disease, patients who did not receive at least two immunotherapy courses or who did not perform at least two dosages of thyroid hormones (TSH, FT3, FT4) were excluded from the analysis. The severity of adverse events is graded using CTCAE v. 4.03.

Results: 75 pts were enrolled (M/F = 49/26), median age 69 years (range 37-82), ECOG PS 0-1 in 70 pts and PS 2 in 5 pts. 10 pts were excluded for pre-existent TD. At the time of analysis, the median number of administered courses was 8 (range 2-75), 55 pts received nivolumab, 12 pts pembrolizumab and 8 pts atezolizumab. Primary TD was found in 19 patients (25.3%), which is similar to that reported in previous studies, after a median of 5 cycles of therapy (range 1-42). 5 pts developed hypothyroidism (G2 in 4 pts and G3 in 1 pts) and needed hormone replacement, 4 pts experienced G2 hyperthyroidism and were treated with metimazole. 1 pt had G2 hyperthyroidism, followed by G2 hypothyroidism due to thyroiditis. Other TD were subclinical hyperthyroidism in 6 pts and subclinical hypothyroidism in 4 pts. 3 pts delayed immunotherapy due to TD, 2 pts omitted an immunotherapy course and 1 pt permanently discontinued treatment due to hypothyroidism. Approximately, 50% of these pts required hormonal replacement or antithyroidal drugs. ORR was 14.7% (11 PR + 0 CR) and the DCR was 48% (25 SD + 11 PR). The median PFS was 4.9 months, the 6-month PFS rate was 39.7% and the 12-month PFS rate was 24.7%. In patients who developed irTD the median PFS was 15.7 months vs 3.6 months in those who did not (p<0.001).

Conclusions: Accordingly, with other studies, our data confirms that the development of irTD relates with better outcomes and that thyroid function monitoring must be routinely tested during therapy with immune checkpoint inhibitors (PD1/PD-L1).

A31

OPTIONS OF FIRST LINE MONOCHEMOTHERAPY IN METASTATIC NSCLC ELDERLY PATIENTS: A REAL-LIFE EXPERIENCE

Meletani T.[1], Rinaldi S.[1], Marcantognini G.[1], Lenci E.[1], Fiordoliva I.[1], Cantini L.[1], Di Pietro Paolo M.[1], Mazzanti P.[1], Burattini L.[1], Berardi R.[1]

[1]Clinica Oncologica, Università Politecnica delle Marche, Azienda Ospedaliero-Universitaria Ospedali Riuniti Umberto I – GM Lancisi – G Salesi, Ancona/Italy, Ancona

Background: Due to frail clinical conditions and comorbidities, the management of NSCLC in elderly patient is still controversial. In several studies, first-line double chemotherapy demonstrated to improve survival compared to mono-chemotherapy, despite of important toxicity. However, these data emerge from randomized controlled trials (RCTs), in which this setting of patients is underrepresented and often selected according comorbidity. In clinical practice, most patients are unfit for a platinum-based chemotherapy. We report our experience with monochemotherapy in metastatic NSCLC elderly patients.

Methods: We retrospectively analyzed data about consecutive ≥ 75 years old patients who started a first line mono-chemotherapy treatment at our Institution (Università Politecnica Marche, Italy) and Evangelische Lungenklinik (ELK) of Berlin for advanced NSCLC, between September 2003 and August 2017. Tumor response was assessed using the Response Evaluation Criteria In Solid Tumors (RECIST). Progression free survival (PFS) and overall survival (OS) were estimated using Kaplan-Meier method. A Cox regression model was carried out for univariate and multivariate analyses.

Results: Eighty-eight patients were enrolled, males 75 (85%) and females 13 (15%). Median age was 86 (range 76-96). 32 (36%) received carboplatin and 56 (64%) other mono-chemotherapy regimens (mainly vinorelbine and gemcitabine). 20% of them had a poor Performance Status (PS) at the start of first line treatment, according to the Eastern Cooperative Oncology Group (ECOG) system (ECOG >2). Median Overall Survival (mOS) was 11.4 months (m), median follow-up was 35.2 m. A statistically significant difference between carboplatin and other single agents was not found in terms of OS (11.4 m vs 13.0 m respectively, p= 0.2) and PFS (6.5 m vs 4.0 m respectively, p= 0.5). At multivariate analysis sex, smoking history, histology, did not result as prognostic and predictive factors.

Conclusions: Currently only 30% of patients with PD-L1 >50% can be treated first-line with immunotherapy alone. Platinum-based chemotherapy or chemo-immunotherapy for patients with non-squamous histology represent the standard in case of PD-L1 < 50%. This study suggests that carboplatin mono-chemotherapy might represent a valid option as first line treatment in elderly and very elderly patients in real life, not eligible for a first line double platinum-based chemotherapy.

A32

IMPACT OF BASELINE SYSTEMIC INFLAMMATION SCORES IN PATIENTS WITH NSCLC TREATED WITH IMMUNOTHERAPY: A PROPENSITY MATCHED SCORE ANALISYS

Borrelli A.[1], Di Lisa F.S.[1], Cristofani L.[1], Sorace C.[1], Arcuri T.[1],
Speranza I.[2], Bianco V.[2], Fuccillo F.[1], Santamaria F.[1], Resuli B.[1],
Vivona L.[1], Fusco F.[1], Astorino V.[1], Verrico M.[1], Tomao S.[1]

[1]Università Sapienza, Roma; [2]Oncologia Policlinico Umberto 1, Roma

Background: Immunotherapy has demonstrated to improve overall survival (OS) and progression-free survival (PFS) in a subset of patients with metastatic or locally advanced non-small cell lung cancer (NSCLC). Recently, there has been an increasing interest in the prognostic role of systemic inflammation. According to many studies an increase of neutrophil-to-lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR) is associated with poor prognosis. In this study, we evaluated the prediction role of all these systemic inflammation scores at baseline in NSCLC patients treated for at least six months with immunotherapy.

Material and methods: We retrospectively reviewed 85 patients with advanced NSCLC treated with anti-PD-1 antibodies at Policlinico Umberto I between 2015 and 2020. Propensity score, based on age, sex and BMI as clinical features, selected 50 patients for matching. Mean value of NLR, MLR, PLR at baseline was used to determine the cut-off values, 5.26, 5.8 and 213.6 respectively. Patients with high NLR ($\geq$ 5,26), MLR ($\geq$ 5,8) and PLR ($\geq$ 213,6) were given a score of 3. Patients with two of three high values were given a score of 2. Patients without either abnormality were scored 0. Based on the total score that patient received, we divided them in two main groups; GROUP A including patients with total score between 0-1 and GROUP B including patients with total score between 2-3.

Results: We analyzed the response to immunotherapy in the Group A and B with Kruskal-Wallis test: GROUP B with higher inflammatory score at baseline correlated with worse clinical outcomes. A baseline high inflammatory score had a significantly increased risk of progression disease and lower response to treatment (4/25; 16%) (p<0,05) compared with patients of the GROUP A with lower inflammatory ratio in which a significative number of patients had stability or partial remission of disease 17/25 (68%) (p<0,05).

Conclusions: Increased baseline of inflammatory score before initiation of anti-PD1 antibodies is associated with lower response to treatment in advanced NSCLC patients. The potential predictive value of these representative index might help with risk stratification. We acknowledge to this study obvious limitations including the relatively small sample size, the retrospective and not-randomized nature of the analysis, and the short observational period. These findings should be investigated in a larger and prospective study.

A33

THE ROLE OF DISTRESS THERMOMETER ON CLINICAL OUTCOMES IN LUNG CANCER PATIENTS: A MONO-INSTITUTIONAL EXPERIENCE

Lauro S.[1], Mazzotta M.[2], Rossi A.[1], Marinelli D.[1], Argentieri F.[3], De Meo S.[3], Krasniqi E.[2], Marchetti P.[1], Rendina E.A.[4], Costantini A.[3]

[1]Department of Molecular and Clinical Medicine, "Sapienza" University, Oncology Unit, Sant'Andrea Hospital, Rome, Italy, Roma; [2]Division of Medical Oncology 2, IRCCS Regina Elena National Cancer Institute, Rome, Italy, Roma; [3]Psychoncology Unit, Faculty of Medicine and Psychology, Sant'Andrea Hospital, Sapienza University, Rome, Italy, Roma; [4]Department of Thoracic Surgery, Sapienza University, Sant'Andrea Hospital, Rome, Italy, Roma

Background: In lung cancer (LC) patients, psychological and emotional aspects deserve a primary attention in clinical management, as depression and anxiety are strictly linked to survival. Emotional distress can be assessed with the Distress Thermometer (DT). Our study aims to evaluate whether the DT score can be useful to predict clinical outcomes in a cohort of LC patients.

Patients and methods: Patients with histological diagnosis of LC admitted at Sant'Andrea Hospital of Rome that completed the DT were retrospectively investigated. The DT is a visual analogue scale that ranges from 0 (no distress) to 10 (extreme distress). Furthermore, patients are invited to complete a problem list that comprises 47 items (addressing practical, social, emotional, spiritual, and physical problems).

Results: From Jan 2018 to Jul 2019, 243 patients were enrolled. The clinical characteristics of population are summarized in Table 1. At the end of the follow-up period (13 months, median), 214 patients were still alive (88.0%). DT was completed by all patients: the median score was 4.25 (range 0-10). High DT score was correlated with Sex (female vs male, *p=0.011*) and stage at diagnosis (IV vs other, *p=0.023*). In whole population, the DT score as continuous variable and the Performance Status (PS) were prognostic for overall survival (OS) in univariate analysis. DT score confirms significantly for OS in multivariate analysis. Furthermore, in metastatic patients, DT score was correlated with the type of treatment received at the time of the test (anova test, *p=0.037*): patients receiving target-therapy have the lower median DT score (3.21), followed by immunotherapy (4.30) and chemotherapy (4.77). In Kaplan-Meier analysis, OS was significantly lower in subjects that declared issues in the emotional (*p=0.040*) and physical (*p=0.007*) items.

Conclusions: These results suggest that the DT score can be linked to clinical outcomes of LC patients and confirm the usefulness of this tool in oncology practice.

Table 1. Characteristics of LC patients enrolled in the study (N=243).

Characteristics	N (%)
Age at diagnosis	
Median [DS]	67.3 [±9.0]
Gender	
Male	153 (63.0)
Female	90 (37.0)
Histology	
Adenocarcinoma	174 (71.6)
Squamous carcinoma	54 (22.2)
Other	15 (6.2)
Stage at diagnosis	
IV	106 (43.6)
I-III	137 (56.4)
Performance Status (ECOG)	
0	132 (54.3)
1-2	111 (46.7)
Metastatic at study enrollment	
Yes	127 (52.3)
No	116 (47.7)
Treatment for metastatic disease	
Chemotherapy	68 (53.5)
Immunotherapy	26 (20.5)
Target Therapy	33 (26.0)

A34

MAIN GENETIC ALTERATIONS IN A SERIES OF ABOUT 1500 SARDINIAN PATIENTS WITH LUNG ADENOCARCINOMA

Colombino M.[1], Paliogiannis P.[2], Doneddu V.[2], Cossu A.[2], Sardinian Lung Cancer (SLC) S.G.[2], Casula M.[1], Sini M.C.[1], Palomba G.[1], Pisano M.[3], Manca A.[3], Rozzo C.[3], Palmieri G.[3]

[1]ICB-CNR, Sassari; [2]AOU, Sassari; [3]IRGB-CNR, Sassari

Background: Lung cancer is one of the most incident neoplastic disease, and a leading cause of death for cancer worldwide. Knowledge of the incidence of genetic alterations, their correlation with clinical and pathological features of the disease, as well as their interplay in cases of co-occurrence is crucial for selecting the best clinical management of patients with lung cancer. In this real-life study, we describe the molecular epidemiology of genetic alterations in five driver genes, and their correlations with the demographic and clinical characteristics of Sardinian patients with lung adenocarcinoma.

Methods: 1,440 consecutive Sardinian patients with a histologically proven diagnosis of lung adenocarcinoma made from January 2011 through July 2016 were included in the study. EGFR mutation analysis was performed for all of them, while KRAS and BRAF mutations were searched in 1,047 cases; ALK alterations were determined with fluorescence in situ hybridization in 899 cases, and

cMET amplifications in 788 cases. Testing was dictated by the gradual introduction of the single analyses in clinical practice, and the availability of sample tissues for testing.

Results: KRAS mutations were the most common genetic alterations involving 22.1% of the cases and being mutually exclusive with the EGFR mutations, which were found in 12.6% of them. BRAF mutations, ALK rearrangements, and cMET amplifications were detected in 3.2%, 5.3%, and 2.1% of the cases, respectively. Concomitant mutations were detected only in a few cases.

Conclusions: Almost all the genetic alterations studied showed a slightly lower incidence in comparison with other Caucasian populations. Concomitant mutations were rare, and they probably have a scarce impact on the clinical management of Sardinians with lung adenocarcinoma. The low incidence of concomitant cMET amplifications at diagnosis suggests that these alterations are acquired in subsequent phases of the disease, often during treatment with TKIs.

A35

STATINS AND IMMUNOTHERAPY: TOGETHERNESS MAKES STRENGTH. THE POTENTIAL EFFECT OF STATINS ON IMMUNOTHERAPY FOR NSCLC

Rossi A.[1], Filetti M.[2], Mazzotta M.[2], Piras M.[2], Taurelli Salimbeni B.[2], Rizzo F.[2], Marchetti P.[2], Giusti R.[2]

[1]AO Sant'Andrea-Sapienza Univeristà di Roma, Roma; [2]AO Sant'Andrea-Sapienza Università di Roma, Roma

Background: Statins are commonly used agents in primary and secondary prevention of cardiovascular disease, but recent studies suggested that they can display pleiotropic effects on several cancer-related cellular processes, such as proliferation, apoptosis, angiogenesis, and metastasis. Even though the promising molecular features, results of randomized clinical trials investigating the combinations between statins and anticancer treatments have been controversial so far. A recent meta-analysis of observational studies and randomized clinical trials suggested that statins could positively affect the risk of all-cause mortality and improve OS in lung cancer patients; conversely, no influence on PFS and overall response rate was observed. Preclinical studies suggested that these drugs could synergize with immunotherapy in the treatment of lung cancer. However, a large cohort study that could help validate these findings is still lacking in clinical practice. Given the encouraging in vitro and in vivo results of available evidence, we analyzed the data collected from 162 patients treated with immunotherapy for Non-small Cell Lung Cancer (NSCLC) in I and II line setting.

Materials and methods: In this observational study, we enrolled 162 Lung cancer patients who were treated at our

institution between October 2015 and April 2020. All patients were candidate for immunotherapy, according to the tumor molecular profile. Descriptive statistics were used to analyze patients' baseline features. Tumor response was evaluated using RECIST version 1.1 guidelines. Uni and multivariate analysis were conducted to investigate the relationship between statin use and response to immunotherapy, using the χ2–test. Kaplan-Meier curves were used to estimate both OS and PFS in statin and non-statin users.
Results: Among all 162 screened patients, 122 met the requested criteria (52 in the non-statin group, 70 in the statin group) and were included in the final analysis. Median PFS was 17,57 months in the statin group and 9,57 months in the non-statin group, with a p=<0.001. Also median OS was superior in the statin-users group, with a statistically significant difference (19,94 vs 10,94 months, p=<0.001).
Conclusions: In our study, we demonstrated a significant relationship between improved PFS and OS and statin use when compared to those achieved in non-statin users. Although interesting, this result needs to be validated with randomized clinical trials and larger cohorts.

A36

IS A SYSTEMIC TREATMENT FOR METASTATIC LUNG CANCER IN PATIENTS WITH DIAGNOSIS OF IDIOPATHIC PULMONARY FIBROSIS DETRIMENTAL?

Della Torre S.[1], Zannier F.[2], Di Bella S.[2], Cozzi C.[2], Bollina R.[2]

[1]*ASST-Rhodense- U.O. di Oncologia Medica, Rho, Milano;* [2]*ASST-Rhodense-UO di Oncologia Medica, Rho, Milano*

Background: Despite Lung Cancer (LC) is often associated with Idiopathic Pulmonary Fibrosis (IPF), it is still debated if it is useful to treat patients with metastatic disease with systemic chemotherapy. We present 3 similar cases of Lung Adenocarcinoma and their outcome during systemic treatment for metastatic disease.
Patients and methods: Among 75 pts with metastatic Lung Cancer treated in our hospital in 2018 and 2019, 3 pts had diagnosis of IPF other than metastatic Lung Adenocarcinoma. They developed metastatic disease during follow-up after surgery approach for primary tumors.
Results: All patients were male, median age 69yrs, with smoke history (median 20.2 pack-years). Low disease burden and asymptomatic metastatic lesions characterized all cases. The disease's sites were not bulky mediastinic nodes, oligo-metastases in bone and lung. Because of EGFR, ALK and PDL-1 negativity, they were candidated to systemic first line chemotherapy with CDDP and Pemetrexed. During systemic therapy all patients experienced a respiratory failure for IPF's worsening in two cases and for lung complications and cancer progression in

the other one, with hospital admissions. The treatment was stopped respectively after 5, 4 and 6 cycles and median survival was 6 months.
Conclusions: Our cases confirm the systemic chemotherapy might induce the IPF's worsening and increase the risk of pulmonary adverse events. The poor survival is similar to that reported in previously studies. Above all in oligo-metastatic and asymptomatic disease the choice to not treat with chemotherapy pts with metastatic lung cancer and IPF should be considered.

A37

BODY COMPOSITION AND INFLAMMATORY STATUS IMPACT IN NON-SMALL CELL LUNG CANCER PATIENTS TREATED BY FIRST LINE IMMUNOTHERAPY. A MONOCENTRIC EXPERIENCE

Baldessari C.[1], Guaitoli G.[1], Valoriani F.[1], Bonacini R.[1], Marcheselli R.[1], Linda R.[1], Pecchi A.[1], Menozzi R.[1], Torricelli P.[1], Bertolini F.[1], Dominici M.[1], Barbieri F.[1]

[1]*University Hospital of Modena, Modena*

Background: Immunotherapy (IT) changed the landscape of NSCLC. Several efforts were made to understand and implement its action. Body composition and balance of nutrition and inflammatory status are important factors for immune system function and IT effectiveness. This study aims to evaluate the correlation of muscle mass (MM) and adipose tissue (AT) parameters, BMI, weight loss (WL), blood exams (BE) and nutritional and inflammatory scores with outcome, response and toxicities in NSCLC patients (pts) treated by first line IT.
Patients and methods: We analysed 44 consecutively pts who received at least two doses of pembrolizumab between 07.2017 and 12.2018. MM and AT were studied from L3 sections in CT scans routinely performed. Kaplan-Meier method was used to calculate survival curves, log-rank test to compare groups based on literature cut-off or normal values, Cox proportional hazard model for uni and multivariate analysis and Fisher exact test to examine differences between categorical variables.
Results: mOS was 9.2 months (mo) (95% CI 6.1-24.2), mPFS 6 mo (95% CI 4-11.5) and overall response rate 56%. 50% of pts experienced G1-2 toxicities, 10% G3-4. Sex, age, smoking status, baseline CNS metastases, BMI, WL, MM and AT parameters, C-reactive protein, NLR and PLR were not significantly related with OS, although sometimes a trend was seen. Pts with higher MM or muscle density have a trend for better OS. Better OS was confirmed by ECOG 0-1 (p=0.032), normal WBC (p= 0.023), normal albumin (p=0.03) and low Prognostic Index (p=0.008), a trend was showed for Advance lung cancer

inflammation index (ALI) and modified ALI (p=0.056 and p=0.071). In multivariate model, only the development of toxicities maintained a positive Hazard Ratio for OS (p=0.0003). No significant correlation were found between selected MM, AT and BE baseline parameters and response or toxicities to IT. During IT, only a major decrease of psoas muscle area in pts with PD (p=0.036) was significant.

Conclusions: In our small, retrospective, but homogeneous casuistry, MM, AT and BMI did not show impact on OS or relation with toxicities or response. Significant results were observed with ECOG, some BE and scores. Probably a combination of clinical and biological factors will be necessary to guide treatment choice and care of pts. More studies with multidimensional approach are warranted.

A38

GENDER MATTERS. A RETROSPECTIVE ANALYSIS ON PATIENTS AFFECTED BY ADVANCED NON SMALL CELL LUNG CANCER EVALUATING THE IMPACT OF SEX DIFFERENCES IN THE OUTCOME OF IMMUNOTHERAPY

Rossi V.[1], Petrella M.C.[1], Brugia M.[1], Pillozzi S.[1], Mazzoni F.[1], Grosso A.M.[2], Modesti M.[1], Botteri C.[1], Paderi A.[1], Antonuzzo L.[1]

[1]SODc Oncologia Medica - Azienda Ospedaliero Universitaria Careggi, Firenze; [2]SODc Fisiopatologia toraco-polmonare - Azienda Ospedaliero Universitaria Careggi, Firenze

Background: Lung cancer remains the most common malignancy and the leading cause of cancer-related mortality worldwide. Currently, for the non oncogene-addicted disease, the use of immune-checkpoint inhibitors (ICIs) has radically changed the prognosis of these patients. First demonstrated to improve outcomes in second-line or later therapy of advanced disease, ICIs were shown to improve overall survival compared with chemotherapy in first-line therapy for patients whose tumors express PD-L1 on at least 50% of cells. More recently, combining ICIs with chemotherapy has been shown to improve survival in patients with both squamous and non-squamous NSCLC, regardless of PD-L1 expression. As reported in literature the magnitude of benefit of ICIs treatments is sex-linked. This could be related to the central involvement of the immune response, strongly influenced from complex interactions between genes, hormones and the environment, to the sex dimorphism in cancer biology and also to the sex-hormone modulation of the PD-1–PD-L1 pathway.

Patients and Methods: We retrospectively analysed clinical data of 99 patients diagnosed with advanced NSCLC and treated with ICIs (Pembrolizumab and Nivolumab) at Clinical Oncology Unit, AOU Careggi-Firenze (Italy), between April 2014 and August 2019.

Results: From the data analysis, considering overall the responses to the treatments, 24 partial responses were obtained (PR) of which 16 in men and 8 in women and 21 disease stability (SD) of which 15 in men and 6 in women. In 54 patients we achieved disease progression (PD), 32 were males and 22 females. The disease control rate (DCR) was 49% in males and 39% in females.

Conclusions: The better DCR in men compared to women affected by NSCLC and treated with ICIs registered in our study agrees with the literature. It has been not possible to date to highlight any statistically significant difference in PFS and OS due to the immaturity of the data.

A39

ASSOCIATION BETWEEN INFLAMMATION INDEX AND NUTRITIONAL STATUS AND THE EFFECTIVENESS OF IMMUNOTHERAPY IN NSCLC TREATMENT

Tolu S.[1], Liscia N.[1], Balconi F.[1], Donisi C.[1], Persano M.[1], Stefano M.[1], Impera V.[1], Pretta A.[1], Marco D.[1], Migliari M.[1], Spanu D.[1], Musio F.[1], Saba G.[1], Pireddu A.[1], Pinna G.[1], Piredda R.[1], Massa E.[1], Demurtas L.[1], Astara G.[1], Scartozzi M.[1], Madeddu C.[1]

[1]AOU Cagliari, Cagliari

Background: Immunotherapy is an important therapeutic strategy for NSCLC, but only about 20% of patients had benefit. To identify predictive markers is crucial for a proper patient selection. Few trials assessed the correlation between nutritional/inflammation status and the effectiveness of immunotherapy.

Material (patients) and methods: A retrospective trial included patients (pts) with metastatic lung adenocarcinoma treated with immunotherapy from June 2017 to October 2019. We evaluated the following parameters: body mass index, weight loss, body composition by BIVA and computed tomography (CT) at L3-L4, C-reactive protein (CRP), albumin, hemoglobin, absolute lymphocytes count, patient performance status (PS), anorexia and quality of life (by miniCASCO questionnaire). Clinical response (CR) according iRECIST crtiteria, overall survival and progression-free survival (PFS) were assessed. All pts were evaluated every 4-6 months.

Results: We included 18 patients. CR significantly correlated with CRP (r = 0.4943;CI95% 0.05164-0.7746; p=0.0315) and muscle mass index (MMI) calculated by CT at baseline (r = 0.4955; CI95% 0.05328- 0.7752; p=0.031). We also found a significant correlation between PFS and CRP (r = -0.7304; CI95% -0, 8928 to -0.3999; p = 0.0006), MMI (r = 0.8229; CI95% 0.2119-0.6623; p = 0.0255) and PS at baseline (r = -0.5101; CI95% -0.7890 to -0.05667; p = 0.0306). Additionally, OS correlated significantly with baseline CRP (r = -0.6637; CI95% -0.8631 to -0.2851; p = 0.0027) and MMI at CT (r = 0.584; CI95%

-0.2370-0.6472; p = 0.0304). At multivariate analysis CRP was an independent predictive factor of clinical response (p = 0.0213), PFS (p = 0.0006) and OS (p = 0.0027). The miniCASCO correlated positively with PS (r = 0.567; p = 0.036) and negatively with CR (r = -0.438; p = 0.010). Moreover, patients with partial response and stable disease had a significant decrease of CRP and a significant increase of MMI and hemoglobin compared to pts with progressive disease.

Conclusions: Our results showed, even in a limited sample size, the negative correlation of inflammation and poor nutritional status with clinical response and survival in NSCLC pts treated with immunotherapy. Blocking inflammation and the related nutritional impairment may be crucial in improving efficacy of immunotherapy in advanced lung cancer pts.

A40

PNEUMONIA ASSOCIATED WITH IMMUNE CHECKPOINT INHIBITORS IN NON-SMALL-CELL LUNG CANCER

Sorace C.[1], Di Lisa F.S.[1], Borrelli A.[1], Speranza I.[2], Bianco V.[2], Cristofani L.[1], Arcuri T.[1], Fuccillo F.[1], Singarj M.[1], Gozzi E.[1], Santamaria F.[1], Resuli B.[1], Vivona L.[1], Fusco F.[1], Astorino V.[1], Rossi L.[3], Verrico M.[1], Tomao S.[1]

[1]*Università Sapienza, Roma; [2]Policlinico Umberto 1, Roma; [3]ASL Latina, Presidio Aprilia, Roma*

Backgrund: Immunotherapy has transformed cancer treatment. However, increasing use of immune-based therapies, including the class of agents known as immune checkpoint inhibitors, has exposed a discrete group of immune-related adverse events (irAEs), different from that related totraditional chemotherapeutic agents and molecularly target therapies. Skin, gut, endocrine, lung and musculoskeletal are relatively common, whereas cardiovascular, hematologic, renal, neurologic and ophthalmologic occur much less frequently. In particular lung toxicity is infrequent but potentially fatal. According to Common Terminology Criteria for Adverse Events (CTCAE) lung toxicity is divided in G1 in asymptomatic patient, G2 in symptomatic patients with drug intervention, G3 in severely symptomatic patients who need oxygen, G4 as risk to life.

Methods: We retrospectively reviewed the records of 126 patients with non-small-cell lung cancer (NSCLC) treated with Nivolumab and Pembrolizumab at Policlinico Umberto 1 between 2015-2019. We evaluated the association of immunotherapy toxicity with age, gender and histological types of lung cancer.

Results: We identified 42 women and 84 men; 94 with non-small-cell lung cancer and 32 with squamous cell cancer. 56% of the patients were under 70 years old and 44%

were over 70. Immunotherapy related pneumonia occurred in 7 patients with nonsquamous histology and in 6patients with squamous histology. Among nonsquamous patients, four developed pneumonia G1(4/96) (4,3%), two had pneumonia G2 (2/96) (2,2%) and one pneumonia G3 (1/96) (1,1%). All six squamous patients developed pneumonia G1 (19,4%). In this sample, risk of pneumonia was increased and statistically significant (p<0,048) for squamous histology compared with patients with nonsquamous histology.

Conclusions: The risk of pneumonia associated with Immunotherapy was increased in squamous patients. However the success of immunotherapy is related to ongoing evaluation/identification and treatment of these immunerelated side effects.

A41

EFFICACY AND TOLERABILITY OF IMMUNE CHECKPOINT INHIBITORS IN NSCLC: OUR EXPERIENCE OF A SINGLE INSTITUTION

Cristofani L.[1], Di Lisa F.S.[1], Borrelli A.[1], Astorino V.[1], Sorace C.[1], Fuccillo F.[1], Speranza I.[2], Bianco V.[2], Santamaria F.[1], Fusco F.[1], Sinjari M.[1], Gozzi E.[1], Resuli B.[1], Arcuri T.[1], Vivona L.[1], Rossi L.[3], Verrico M.[1], Tomao S.[4]

[1]*Università Sapienza, Roma; [2]Policlinico Umberto I, Roma; [3]ASL Latina, Aprilia; [4]Università Sapienza Policlinico Umberto I, Roma*

Background: Immunotherapy is one of the most interesting and innovative treatment strategy in oncology and it has proven to be potentially effective in several cancers by showing prolonged disease control in a significant percentage of patients. The main pathway studied is the PD1 / PDL1 checkpoint which leads to inhibition of the immune response. Several antibodies are used to contrast this mechanism, including Nivolumab and Pembrolizumab. These drugs cause immune-mediated side effects, such as pneumonia, hepatitis, colitis, thyroiditis.

Methods: The aim of our study was to assess toxicity and the response to therapy in NSCLC patients treated by nivolumab and pembrolizumab by dividing them into groups by age, gender and tumor histotype. We retrospectively analyzed 126 patients treated for NSCLC with immunotherapy at Sapienza University of Rome during the period 2015-2019: 103 treated with nivolumab and 23 with pembrolizumab. 84 were men and 42 women with an average age of 68 years (range 46-86).

Results: At a median follow-up of 12 months 25.4% of the patients presented a partial or complete response; this value reaches 41.9% in squamous histology which represented 24.6% of the total patients. About 80% of the total patients reported adverse events of all grades, most frequent were fatigue, pain and diarrhea; 22% had grade G3-4

toxicity with only 3 G4 events which led to the definitive discontinuation of treatment. Toxicities were mostly found in male subjects <70 years of age.

Conclusions: Immune checkpoint inhibitors are drugs with enormous potential efficacy could change the prognosis of several highly inauspicious oncological diseases. Toxicity profile usually appears manageable and differs from traditional chemotherapy. The increasingly frequent and prolonged use in clinical practice will lead to greater knowledge and investigation of possible toxicities. To date, there are no direct comparison studies between the various immunotherapics in terms of efficacy and side effects, therefore they all represent valid therapeutic alternatives.

A42

REAL WORLD DATA ON IMMUNOTHERAPY (IT) IN METASTATIC NSCLC: A GENERAL HOSPITAL, SINGLE INSTITUTION, RETROSPECTIVE ANALYSIS

Beshiri K.[1], Sogno G.[1], Ponzanelli A.[2], Benasso M.[1]

[1]*San Paolo Hospital, Savona;* [2]*Santa Corona Hospital, Pietra Ligure*

Background: IT has become the cornerstone in the treatment of advanced NSCLC. Data from real world are still incomplete. This is an observational retrospective analysis on patients (pts) treated with IT in clinical practice in the Oncology Unit of the San Paolo Hospital, Savona and Santa Corona Hospital, Pietra Ligure.

Methods: Eligibility criteria included stage IV histologically confirmed NSCLC treated with IT as first or second line therapy in our Unit from May 2016 to November 2019. The aim of the analysis was to assess the outcomes and safety of IT in these subsets of pts in our daily clinical practice compared to the pivotal trials.

Results: We retrospectively collected data on 57 patients: 43 pts (24 adenocarcinoma and 19 SCC) received Nivolumab (NIVO) as second line treatment, while 15 pts (11 adenocarcinoma and 4 SCC) received Pembrolizumab (PEMBRO) alone as first line. The median age was 72 years (range: 52-85) in NIVO group, and 80 years (range: 52-83) in PEMBRO group. On December 2019, pts evaluable for response were 39 in NIVO group and 15 in PEMBRO group. Responses in NIVO group were 12/39 (ORR: 30.7%). One of these pts with adenocarcinoma had a complete response. Responses in PEMBRO group were 9/15 (ORR: 60%). 13 pts (30.2%) in NIVO group and 7 pts (46.6%) were alive at 12 months. The most common adverse events were asthenia, diarrhea and thyroiditis. No grade III-IV toxicities were reported.

Conclusions: In our daily clinical practice the ORRs of pts treated with IT were higher than in pivotal trials despite the higher median age of the pts treated. Updated data will be presented at the congress.

A43

IS GASTRO-INTESTINAL TOXICITY RELATED WITH PROLONGED CLINICAL BENEFIT IN NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH IMMUNOTHERAPY?

Guaitoli G.[1], Baldessari C.[1], Trudu L.[1], Di Emidio K.[1], Dominici M.[1], Bertolini F.[1], Barbieri F.[1]

[1]*Azienda Ospedaliero - Universitaria Policlinico di Modena, Modena*

Background: Immune checkpoint inhibitors (ICIs) are widely used in the treatment of NSCLC. Despite immunotherapy (IT) is generally well tolerated, immune-related adverse events occur in about one third of patients, and gastro-intestinal (GI) toxicity is one of the most common. Here, we describe a small subgroup of NSCLC patients that discontinued IT due to GI toxicity and experienced prolonged clinical benefit after discontinuation.

Material and methods: We performed a retrospective review of NSCLC patients who started IT at Modena University Hospital between August 2015 and December 2018 and we selected patients who experienced grade ≥2 diarrhea and underwent colonoscopy with histological examination.

Results: A total of 6 Caucasian patients were included (2 males and 4 females). Median age at diagnosis was 68.5 years (range 46-77). Three patients were treated with pembrolizumab as first line treatment and 3 with nivolumab in second or third line. Median duration of treatment was 10 months (95% CI 2.2–18.8). GI toxicity appeared after a median time of 4.5 months (95% CI 1.2–14). All patients were treated with steroids without significant benefit and in all cases stool culture was performed to exclude infectious causes. Endoscopic findings were normal in 2/6 cases, while in the remaining hyperemia and edema were detected, with mucosal erosions in one case. The most common histologic findings were chronic inflammation of the lamina propria (67%) and eosinophils infiltration (67%). Given the absence of benefit with steroids, in four cases mesalazine was started with clinical benefit. Four patients had partial response as best response to IT, and 1 patient achieved complete metabolic response, that is still maintained after one year from nivolumab discontinuation. After a median follow up of 28 months, 5 patients are currently alive and 1 was lost at follow up. In 3 cases (50%) disease progressed and a subsequent treatment was administered. Median time between the end of ICIs treatment and the beginning of new treatment or last observation was 14.5 months (95% CI 3.5–27.8).

Conclusions: In this case series, GI toxicity presented as reported in literature. We found of interest, even if in a very small group, the apparent correlation between GI toxicity and prolonged clinical benefit of IT. GI toxicity seems to be a "marker" of immune system activation. Pathophysiology of toxicity and its possible relationship with outcome should be studied in larger population.

B - Gastrointestinal (Colorectal) Cancers

B01*

ADJUVANT THERAPY IN STAGE III AND ELDERLY PATIENTS WITH COLON CANCER: SUBGROUP ANALYSIS OF THE TOSCA TRIAL

Rosati G.[1], Galli F.[2], Carlomagno C.[3], Bidoli P.[4], Amoroso D.[5], Bochicchio A.M.[6], Ciarlo A.[7], Maiello E.[8], Frassineti L.[9], Corsi D.[10], Buonadonna A.[11], Turci D.[12], Cortesi E.[13], Zaniboni A.[14], Marchetti P.[15], Rebuzzi S.E.[16], Galli F.[2], Silvestri N.[17], Bernardini I.[18], Labianca R.[19]

[1]Ospedale San Carlo, Potenza; [2]Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano; [3]Università degli studi Federico II, Napoli; [4]Azienda Ospedaliera S. Gerardo, Monza; [5]Ospedale Versilia, Lido di Camaiore; [6]Ospedale Oncologico Regionale CROB, Rionero in Vulture; [7]Azienda USL4, Prato; [8]Casa Sollievo della Sofferenza, San Giovanni Rotondo; [9]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola; [10]Ospedale S. Giovanni Calibita Fatebenefratelli, Roma; [11]Centro Riferimento Oncologico, Aviano; [12]Ospedale Santa Maria delle Croci, Ravenna; [13]Policlinico Umberto I, Roma; [14]Fondazione Poliambulanza Istituto Ospedaliero, Brescia; [15]Ospedale IDI IRCCS, Roma; [16]IRCCS Ospedale Policlinico San Martino, Genova; [17]IRCCS Istituto Tumori "Giovanni Paolo II", Bari; [18]Ospedale Ramazzini, Carpi; [19]Cancer Center ASST Papa Giovanni XXIII, Bergamo

Background: Previous studies stating the oxaliplatin-based chemotherapy as the standard of care for the adjuvant therapy of stage III colon cancer (CC) patients (pts) obtained controversial results and a reduced benefit for those over the age of 70 years.

Methods: Our group assessed the impact of age (categorized as $<$ or $>$ 70 years) on relapse free interval (RFI), defined as time from random to relapse or last disease assessment, in stage III CC pts randomized to receive 3 or 6 months of FOLFOX (fluorouracil, leucovorin plus oxaliplatin) or CAPOX (capecitabine plus oxaliplatin) in the Italian, multicenter, phase III, TOSCA study (clinicaltrials.gov NCT0064660).

Results: 3,759 pts were enrolled from 130 sites. Overall, 2,360 of them had stage III disease, including 1,667 aged under 70 and 693 aged 70 or over. The elderly had an ECOG performance status (PS) more often equal to 1 (10.5% vs 3.3%, p $<$0.001), fewer women (40.8% vs 45.1, p=0.057), more T3/T4 tumors (90.9% vs 84.3%, p<0.001), a greater number of poorly differentiated (G3)

tumors (28.3% vs 24.2%, p=0.039) and located on the right (40.9% vs 26.6%, p $<$0.001). No variation for type and treatment arm (p=0.965) was observed. The median follow-up was 62.5 and 60.6 months for the under 70 and the over 70, respectively. In pts over 70, we found a greater proportion of dose reductions (46.7% vs 41.4%, p=0.018), treatment interruptions (26.1% vs 19.3%, p<0.001) and a higher proportion of recurrences (24.2% vs 20.3%, p=0.033). The multivariable analysis of the RFI, corrected for sex, ECOG PS, tumor site, stage, grade, treatment, treatment duration and dose reduction, does not indicate a statistically significant effect of age (HR 1.19, 95% CI 0.98-1.44, p=0.082), although the point estimate is not negligible. Only a stage III high risk CC had a significant impact on RFI (HR [vs low risk] 2.05, 95% CI 1.71-2.46, p<0.001).

Conclusions: Comparing to younger pts, in elderly stage III CC pts treated with an oxaliplatin-based adjuvant therapy, a different treatment tolerability and a potential reduction of benefit was highlighted. Considerations should be made about the patient's general health status, his comorbidities and the management of the expected side effects. Disease free survival and overall survival data will be provided at the meeting.

B02*

CONSENSUS MOLECULAR SUBTYPES AND CRCASSIGNER CLASSIFICATIONS IN METASTATIC COLORECTAL CANCER (MCRC): PROGNOSTIC AND PREDICTIVE IMPACT IN THE TRIBE2 STUDY

Borelli B.[1], Fontana E.[2], Giordano M.[3], Antoniotti C.[1], Bergamo F.[4], Murgioni S.[4], Pietrantonio F.[5], Morano F.[5], Tamburini E.[6], Boccaccino A.[1], Santini D.[7], Conca V.[1], Pella N.[8], Maiello E.[9], Ugolini C.[10], Fontanini G.[3], Falcone A.[1], Nyamundanda G.[2], Sadanandam A.[2], Cremolini C.[1]

[1]Department of Translational Research and New Technologies in Medicine and Surgery, Unit of Medical Oncology 2, Azienda Ospedaliera Universitaria Pisana, Pisa; [2]Division of Molecular Pathology, The Institute of Cancer Research, London; [3]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa; [4]Unit of Medical Oncology 1, Department of Oncology, Istituto Oncologico Veneto, IRCCS, Padua; [5]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan; [6]Oncology Unit, Ospedale degli Infermi, Rimini; [7]Department of Medical Oncology, University Campus Biomedico, Rome; [8]Department of Oncology, University and General Hospital, Udine; [9]Oncology Unit, Foundation IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo; [10]Unit of Pathological Anatomy, Azienda Ospedaliero-Universitaria Pisana, Pisa

Background: The TRIBE2 study (NCT02339116) recently demonstrated the superiority of upfront FOLFOXIRI plus bevacizumab (bev) when compared to a pre-planned strategy of doublets plus bev in molecularly unselected but mostly (74%) RAS/BRAF mutant mCRC patients. The Consensus

Molecular Subtypes (CMS) and CRCAssigner (CRCA) demonstrated prognostic value in multiple studies, but their predictive role has not been established so far. Given the poor prognosis associated with early stage mesenchymal/ stem-like subtypes, we hypothesized that the CMS and CRCA classifiers could predict benefit from the upfront intensified strategy in patients included in the TRIBE2 study.

Methods: Untreated formalin-fixed paraffin-embedded samples were classified into CMS and CRCA subtypes using a custom nCounter assay (NanoString Technologies). The impact of subtypes on progression free survival (PFS), progression free survival 2 (PFS2, defined as the time from randomization until the second evidence of disease progression) or overall survival (OS) was evaluated in the profiled population.

Results: 426 and 428 (63%) patients enrolled in the TRIBE2 study were profiled according to CMS and CRCA classifications, respectively. The distribution of CMS and CRCA subtypes differed according to primary tumour site (both p<0.001 for CMS/CRCA) and RAS/BRAF mutational status (both p<0.001 for CMS/CRCA). Significant associations of both CMS and CRCA classifiers with PFS, PFS2 and OS were demonstrated (Table). The effect of treatment intensification was independent of CMS subtypes (p for interaction for PFS/PFS2/OS: ns). Significant interaction effect between CRCA subtypes and treatment arm was reported in terms of PFS (p=0.017), PFS2 (p=0.010) and OS (p=0.008). The benefit from the intensification of the upfront chemotherapy seemed more relevant in the stem-like (PFS, HR=0.60; p=0.03) and mixed subtypes (HR=0.44; p=0.002).

Conclusions: CMS subtypes have a prognostic role in mCRC independently of RAS/BRAF status. CRCA classification may help identifying subgroups of patients who may derive a more substantial benefit from upfront FOLFOXIRI plus bev.

	CMS1	CMS2	CMS3	CMS4	Enterocyte	Goblet-like	Inflammatory	Stem-like	Transit-amplifying	Mixed
Median PFS (months)	5.4	12.9	8.3	10.7	10.0	9.9	7.9	14.6	11.2	9.9
P unadj/adj		**0.0001** / 0.01					**0.04** / 0.36			
Median PFS2 (months)	12.3	19.2	13.7	18.1	15.7	16.0	12.2	24.0	18.1	16.5
P unadj/adj		**0.0004** /0.09					**0.04** / 0.37			
Median OS (months)	13.7	27.0	18.3	26.2	22.3	24.9	19.8	31.3	25.6	21.0
P unadj/adj		**0.0003** / 0.08					**0.02** / 0.55			

B03

THE ROLE OF PRIMARY TUMOR (PT) SITE AS PROGNOSTIC FACTOR AFTER RESECTION OF COLORECTAL (CRC) LIVER METASTASES (LM): A MONO-INSTITUTIONAL COHORT STUDY

Bensi M.[1], Ardito F.[2], Di Stefano B.[1], Vellone M.[2], Vivolo R.[1], Mele C.[2], Ribelli M.[1], Panettieri E.[2], Camarda F.[1], Frascarelli A.[2], Calegari M.A.[1], Basso M.[1], Pozzo C.[1], Giuliante F.[2], Tortora G.[1], Salvatore L.[1]

[1]Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli – IRCCS. Università Cattolica del Sacro Cuore, Roma; [2]Chirurgia Epato-biliare, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli – IRCCS. Università Cattolica del Sacro Cuore, Roma

Background: Radical resection of LM is the only chance of cure for liver-only mCRC pts. Besides the evaluation of technical resectability, several factors must be taken into account for the evaluation of recurrence risk. Among them we should consider the Fong Risk Score and its modified version, including RAS/BRAF status (Brudvik's score). Tumor sidedness is an important prognostic factor in CRC. The impact of PT site on the outcome of LM resection is still debated. We retrospectively analysed mCRC pts, underwent to radical LM resection at our Institution, investigating the impact of PT site on DFS and OS.

Methods: Liver-only mCRC pts underwent to radical LM resection were included. The association of PT site with DFS and OS was evaluated. The following variables were collected: gender; age; ECOG PS; CEA baseline level; PT site; RAS and BRAF status; mucinous histology; grading; RECIST response during preoperative treatment; resected PT; synchronous vs metachronous; number of LM; bilobar vs unilobar LM; LM diameter; R0 vs R1 resection. Univariate and multivariate analyses for DFS and OS were performed.

Results: A total of 463 liver-only mCRC pts underwent to radical LM resection were included. Seventy (15%) pts had a right-sided (r-s) tumor and 393 (85%) pts a left-sided (l-s) tumor. R-s CRC pts more often had RAS/BRAF mutations in comparison to l-s tumors (76% vs 37%; p < 0.0001). Median DFS and OS was 13.1 and 41.6 months in r-s CRC vs 16.0 (p=0.65) and 62.2 months (p=0.033) in l-s tumors. At the multivariate analysis no significant association with survival parameters was shown for tumor sidedness. At the multivariate analysis, R0 resection was independently associated both with better DFS and OS; RAS/BRAF wt CRC and resected PT were significantly associated with improved OS. Considering all wt CRC pts

(N=237), 14 (6%) pts had r-s tumor and 223 (94%) l-s tumor. No significant association of tumor sidedness with survival was shown (DFS r=10.0 vs l=16.0 month, p=0.62; OS r=40.3 vs l=66.2 months, p=0.12).

Conclusions: Our results showed that a significant smaller proportion of r-s CRC underwent to radical LM rection, indirectly confirming its worse prognosis. Among radically resected pts, r-s CRC was associated to a shorter OS (significant) and DFS (not significant) compared to l-s CRC, but it was not confirmed at the multivariate analysis. We can conclude that right PT site should not be considered as a contraindication for radical LM surgery, when feasible.

B04

MONOCYTE-TO-LYMPHOCYTE RATIO TO BETTER DEFINE SURVIVAL OUTCOMES AND METASTATIC SPREAD IN STAGE III COLON CANCER

Buriolla S.[1], Basile D.[1], Polano M.[2], Gallois C.[3], Corvaja C.[4], Andreotti V.J.[4], Parnofiello A.[1], De Scordilli M.[1], Michelotti A.[1], Ongaro E.[5], Cinausero M.[6], Foltran L.[5], Toffoli G.[2], Pella N.[7], Buonadonna A.[5], Zaanan A.[3], Fasola G.[7], Aprile G.[8], Taieb J.[3], Puglisi F.[1]

[1]*Department of medical oncology and cancer prevention, IRCCS National Cancer Institute, Aviano (IT); Department of Medicine (DAME), University of Udine, Udine (IT) - Aviano, Aviano;* [2]*Experimental and Clinical Pharmacology Unit, IRCCS National Cancer Institute, Aviano (IT); Aviano;* [3]*Hôpital Européen Georges-Pompidou, Paris;* [4]*Department of Oncology, ASUIUD Santa Maria della Misericordia, Udine, (IT); Department of Medicine (DAME), University of Udine, Udine - Udine, Udine;* [5]*Department of medical oncology and cancer prevention, IRCCS National Cancer Institute, Aviano (IT);, Aviano;* [6]*Department of Oncology, ASUIUD Santa Maria della Misericordia, Udine, (IT);, Udine;* [7]*Department of Oncology, ASUIUD Santa Maria della Misericordia, Udine, (IT) - Udine, Udine;* [8]*Department of Oncology, San Bortolo General Hospital, Vicenza, Vicenza*

Background: Circulating monocytes are recruited in the tumor site to differentiate into tumor-associated macrophages, acquiring pro-tumor functions and suppressing adaptive immune response. This study aims at investigating a prognostic tool based on lymphocytes ratio (LR) to better classify stage III colon cancer (CC) patients (pts).

Material and Methods: This is a multicentric study conducted on 653 consecutive CC pts treated between 2008-2019 at the Centres of Aviano, Pordenone, Udine and Paris (HEGP). A Cox regression model was used to determine the prognostic impact in terms of overall survival (OS) and disease-free survival (DFS). The performance of the prognostic model was evaluated using the Harrell's C statistic (HCS). Random Forrest (RF) to predict pattern of metastasis was implemented on python using h2oai.

Results: Overall, 70% had stage IIIB, 75% G1-2 tumors and 57% CEA>5. Notably, 50%, 41% and 14% had a lymphatic (LI), vascular (VI) and perinervouse infiltration (PI), respectively. Regarding the molecular profile, 45/263 pts had MSI status, 94/212 and 28/199 were KRAS and

BRAF mutated. At median follow-up of 59 mo, median DFS and OS were not reached, 32% of pts relapsed and 24% died. At 3y-DFS 24% relapsed. By multivariate analysis, including potential confounders, significantly shorter DFS (HR 1.84, 95%CI 1.13-3.00, p=0.014) and OS (HR 2.32, 95%CI 1.27-4.25) were observed among high monocyte-to-LR (MLR >0.45) patients compared to low. MLR was associated also with 3y-DFS (p=0.02). The addition of MLR improved the performance of the prognostic model (from 0.69 to 0.87 HCS). RF showed that BRAF, LR, sidedness, KRAS, CEA, and LDH were the main features linked with liver (ACC 0.67) and node (0.68) organotropism. LDH, PI, LR, KRAS, pT, pN with lung (0.77), while LR, sidedness, KRAS, BRAF, MMR and VI with bone (ACC 0.55). Factors linked with peritoneum were LR, CEA, BRAF, pT, pN (ACC 0.57).

Conclusions: A prognostic model including MLR results more accurate in predicting survival and metastatic process in stage III CC, allowing a more tailored monitoring. These findings pave the way at developing a potential nomogram based on MLR and macrophages immune-score to more accurately define stage III CC.

B05

EFFICACY OF THIRD-LINE ANTI-EGFR-BASED TREATMENT (TX) VERSUS (VS) REGORAFENIB/TAS-102 (R/T) ACCORDING TO PRIMARY TUMOR SITE IN RAS/BRAF WILD-TYPE (WT) METASTATIC COLORECTAL CANCER (MCRC) PATIENTS (PTS)

Vivolo R.[1], Bria E.[1], Zurlo I.V.[2], Bensi M.[1], Dell'Aquila E.[3], Anghelone A.[1], Corsi D.C.[4], Caira G.[5], Santini D.[3], Ingrosso D.[6], Emiliani A.[4], Calegari M.A.[1], Citarella F.[3], Pozzo C.[1], Grande R.[7], Basso M.[1], Tortora G.[1], Salvatore L.[1]

[1]*Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Roma;* [2]*Università cattolica del Sacro Cuore-Oncologia Medica San Giovanni Calibita, Fatebenefratelli, Roma;* [3]*Oncologia Medica, Policlinico Universitario Campus Bio-Medico, Roma;* [4]*Oncologia Medica San Giovanni Calibita, Fatebenefratelli, Roma;* [5]*Università Cattolica del Sacro Cuore, Roma;* [6]*Università Cattolica del Sacro Cuore, Roma;* [7]*Oncologia Medica, Ospedale Fabrizio Spaziani, Frosinone*

Background: Right (R) and left-sided (L) mCRCs exhibit different clinical and molecular features. Several retrospective analyses showed that the survival benefit of anti-EGFR-based tx is limited to *RAS/BRAF* wt L-sided mCRC pts, which a larger effect in the first-line setting. Few data are available concerning the anti-EGFR efficacy according to primary tumor site in third line.

Methods: Pts affected by *RAS/BRAF* wt mCRC treated with third-line anti-EGFR-based tx or R/T were retrospectively collected. The objective of the analysis was to

compare tx activity and efficacy according to tumor site. Primary endpoint was PFS; secondary endpoints were OS and RR. PFS and OS analyses were performed using Kaplan-Meier method, and survival curves were compared using the log-rank test. RR was evaluated according to RECIST criteria and it was compared in the two groups using Fisher's exact test. Statistical significance was set at $p = 0.05$ for a bilateral test. Univariate and multivariate analyses for PFS and OS were performed.

Results: A total of 76 *RAS/BRAF* wt mCRC pts, treated with third-line anti-EGFR-based tx or R/T, were enrolled.

Of those, 19 (25%) pts had R-sided tumor (9 pts received anti-EGFR tx and 10 pts received R/T) and 57 (75%) pts had L-sided tumor (30 pts received anti-EGFR tx and 27 pts received R/T). As shown in the table, a significant PFS and OS benefit in favor of anti-EGFR tx vs R/T was observed in L-sided pts, while no difference both in PFS and OS was observed in R-sided pts. RR was significantly higher in L-sided pts treated with anti-EGFR vs R/T, no difference was shown in R-sided pts. At the multivariate analysis, tx regimen was independently associated with PFS in L-sided pts, but not in R-sided pts.

	R-sided		L-sided	
	Anti-EGFR (N=9)	R/T (N=10)	Anti-EGFR (N=30)	R/T (N=27)
Median PFS (months)	3.5	3.8	7.3	3.6
	HR=1.4 (95%CI 0.53-3.75), p=0.49		HR=0.47 (95%CI 0.26-0.85), p=0.0028	
Median OS (months)	9.3	9.2	15.2	11.0
	HR=0.83 (95%CI 0.30-2.26), p=0.696		HR=0.58 (95%CI 0.31-1.08), p=0.0428	
RR	11%	10%	43%	0%
	p=0.99		p<0.0001	

Conclusions: Our study confirmed the results deriving from the retrospective analysis of the phase III study 20020408. Our results demonstrated a different benefit from third-line anti-EGFR tx according to primary tumor site, confirming the role of L-sided tumor in predicting benefit from third-line anti-EGFR vs R/T, while no difference was observed in R-sided tumors.

B06

TUMOR MUTATIONAL LOAD, MICROSATELLITE INSTABILITY, BRCANESS AND ACTIONABLE ALTERATIONS IN METASTATIC COLORECTAL CANCER: RESULTS FROM THE TRIBE2 STUDY

Rossini D.[1], Antoniotti C.[1], Marmorino F.[1], Lonardi S.[2], Corti F.[3], Moretto R.[4], Ugolini C.[5], Latiano T.P.[6], Giordano M.[7], Tamburini E.[8], Passardi A.[9], Santini D.[10], Zaniboni A.[11], Aprile G.[12], Bordonaro R.[13], Fontanini G.[7], Lenz H.[14], Falcone A.[1], Korn M.[15], Cremolini C.[1]

[1]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa; [2]Medical Oncology Unit 1, Department of Clinical and Experimental Oncology, Istituto Oncologico Veneto (IOV) – IRCCS, Padua; [3]Fondazione IRCCS Istituto Nazionale Tumori, Milano; [4]Department of Oncology, University Hospital of Pisa, Pisa; [5]Unit of Pathological Anatomy, Azienda Ospedaliero-Universitaria Pisana, Pisa; [6]Division of Medical Oncology, Fondazione IRCCS "Casa Sollievo della Sofferenza",, San Giovanni Rotondo (FG); [7]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa; [8]Oncology Unit, Ospedale degli Infermi, Rimini; [9]Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola (Forlì-Cesena); [10]Department of Medical Oncology, University Campus Biomedico, Roma; [11]Medical Oncology Unit, Poliambulanza Foundation, Brescia; [12]Department of Oncology, University and General Hospital, Udine; [13]Medical Oncology Unit, ARNAS Garibaldi, Catania; [14]University of Southern California, Los Angeles (California); [15]Caris Life Sciences, Phoenix (Arizona)

Background: We performed a comprehensive NGS analysis of samples from randomized mCRC patients in TRIBE-2 trial in order to investigate the prognostic impact of tumor mutational load (TML), its additional value with respect to the assessment of microsatellite instability (MSI), and the overall prevalence of potentially actionable alterations. We also investigated the prevalence and the prognostic impact of the so-called "BRCAness" alterations.

Methods: Tumor DNA was obtained from formalin-fixed, paraffin-embedded blocks from primary tumors of 296 (44%) of 679 randomized patients, and underwent NGS analysis using the Caris MI TumorSeek panel, assessing 592 genes. TML was defined as low, intermediate, or high based on finding <7, 7-16, or >16 mutations/Mb. MSI status was determined both by NGS and by IHC. BRCAness group was defined by the presence of pathogenic alterations in at least one of the following genes: BRCA1/2, PALB2, RAD50, RAD51, ATM, ATR, FANC(A-C- D2-E-F-G-L), EMSY, BARD1, BRIP1, CHEK1, CHEK2, MRE11, BLM, NBN, or WNR.

Results: TML and MSI were determined by NGS in 224 (76%) cases. NGS and IHC results were concordant in 221 (99%) cases. TML was low, intermediate, or high in 56 (25%), 157 (70%), and 11 (5%) cases, respectively. TML-high tumors were MSI-high or MSS in 8 (73%) and 3 (27%) cases, respectively. Two of 3 TML-high and MSS

tumors showed a pathogenic POLE mutation (p.S459F and p.P286R). The other TML-high, MSS, and POLE wt tumor was dMMR at IHC (loss of MSH6 expression) and showed a pathogenic MSH6 mutation (p.F1040fs). As compared with low and intermediate TML, high TML was associated with longer PFS (median PFS: 17.3 vs 10.6; HR: 0.54 [95% CI: 0.35- 1.09], P = .098) and OS (median OS: not reached vs 23.7; HR :0.45 [95% CI: 0-28-1.13], P = .106). At least one BRCAness alteration was reported in 40 (14%) of 296 patients. In all, 56 different BRCAness alterations were found, with ATM (21/56, 38%) and BRCA1/2 (13/56, 23%) being the most frequently mutated genes. Longer PFS (13.4 vs 10.6 months; HR: 0.67 [95% CI: 0.48-0.93], P = .032) and OS (30.1 vs 23.9, HR: 0.66 [95% CI: 0.43-1.02], P = .062) were observed in the BRCAness group.

Conclusions: TML-high tumors are not limited to MSI-high, but may also present POLE or MSH6 somatic mutation and show improved outcomes. BRCAness alterations are associated with better prognosis. Molecular alterations predictive of benefit from targeted strategies are detectable in a small percentage of mCRCs.

B07

ITALIAN RESULTS OF THE PHASE 3B PRECONNECT STUDY: SAFETY, TOLERABILITY AND EFFICACY OF TRIFLURIDINE/TIPIRACIL IN PREVIOUSLY TREATED METASTATIC COLORECTAL CANCER

Zaniboni A.[1], Barone C.A.[2], Banzi M.C.[3], Bergamo F.[4], Blasi L.[5], Bordonaro R.[6], Di Bartolomeo M.[7], Di Costanzo F.[8], Frassineti G.L.[9], Garufi C.[10], Giuliani F.[11], Latiano T.P.[12], Martinelli E.[13], Personeni N.[14], Racca P.[15], Tamburini E.[16], Tonini G.[17], Besse M.[18], Spione M.[18], Falcone A.[19]

[1]Fondazione Poliambulanza, Istituto Ospedaliero, Brescia; [2]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma; [3]IRCCS - Azienda Ospedaliera Arcispedale S. Maria Nuova, Reggio Emilia; [4]Istituto Oncologico Veneto - IRCCS, Padova; [5]Azienda Ospedaliera "Civico-Di Cristina-Benfratelli", Palermo; [6]Azienda Ospedaliera Garibaldi - Nesima, Catania; [7]Fondazione IRCCS - Istituto Nazionale dei Tumori, Milano; [8]Azienda Ospedaliero-Universitaria Careggi, Firenze; [9]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (I.R.S.T.), Meldola (FC); [10]Azienda Ospedaliera San Camillo Forlanini, Roma; [11]IRCCS Ospedale Oncologico di Bari, Bari; [12]Ospedale IRCSS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG); [13] Università degli Studi della Campania "Luigi Vanvitelli", Napoli; [14]Humanitas Clinical and Research Center – IRCCS, Milano; [15]A.O.U. Città della Salute e della Scienza di Torino, Torino; [16]Ospedale Infermi, Rimini; [17]Policlinico Universitario Campus Biomedico, Roma; [18]Medical Affairs, Servier Italia, Roma; [19]Azienda Ospedaliero Universitaria Pisana, Pisa

Background: The international PRECONNECT early access study demonstrated safety and efficacy of trifluridine/tipiracil (FTD/TPI) in the management of patients with metastatic colorectal cancer (mCRC) who had progressed on standard therapies. Post-hoc analyses in a

national context are important due to the differences in the disease management across countries.

Patients and methods: PRECONNECT is an international phase 3b, open-label, prospective, single-arm study (NCT03306394). The Italian patient subset was extracted. Safety and efficacy analyses were conducted in all patients who received at least one dose of the study drugs. Patients' quality of life (QoL) was assessed from baseline to end of treatment (EOT).

Results: The Italian study cohort consisted of 161 patients enrolled in 18 clinical centers. The median age at treatment was 64 years (range 30-82). Ninety-eight patients (60.9%) were males and 112 (69.5%) had an ECOG performance status (PS) score of 0. The median number of previous lines of therapy was 3 and 59 (36.6%) of the patients received at least 4 previous lines. Median treatment duration was 3.2 months (range 0.4-14.7), with 108 (67.1%) patients having 3 or more cycles. The most common hematological adverse events (AE) were neutropenia (41.0% > grade 3) and anemia (13.7% > grade 3). Febrile neutropenia was reported in 3 patients (1.9%). The frequency of non-hematological grade 3 AEs was less than 5% for each of them, except for asthenia/fatigue (6.8%). Eleven (6.8%) and 14 (8.7%) patients discontinued the drug and reduced the dose due to AEs, respectively. The median progression free survival (PFS) was reached at 3.0 months (95% confidence interval [CI] 2.7-3.4), with a disease control rate of 28.6% (95% CI 21.7-36.2).

The median PFS was higher in patients who received at least 3 cycles of FTD/TPI than in those who did not (4.0 *versus* 1.8 months, respectively). The median time to ECOG PS = 2 was not reached, with only 15 patients (10.1%) showing an ECOG PS > 2 at FTD/TPI treatment discontinuation. Overall, there were no clinically relevant changes in QoL, although the QLQ-C30 score improved in 25.4% of patients from baseline to EOT.

Conclusions: These are the first prospective data on the clinical use of FTD/TPI in Italy. These results, in line with those reported in the RECOURSE trial, confirm FTD/TPI as a feasible and favorable treatment option for pretreated mCRC patients.

B08

TP53 MUTATIONAL STATUS IMPACTS ON SURVIVAL OUTCOMES OF PATIENTS (PTS) WITH METASTATIC COLORECTAL CANCER (MCRC) TREATED WITH CHEMOTHERAPY (CT) PLUS BEVACIZUMAB (BEV). AN ANALYSIS IN THE PROSPECTIVE, RANDOMIZED, PHASE III TRIBE-2 TRIAL

Graziano F.[1], Cremolini C.[2], Lonardi S.[3], Aprile G.[4], Santini D.[5], Conca V.[2], Tamburini E.[6], Latiano T.P.[7], Pietrantonio F.[8], Passardi A.[9], Germani M.M.[10], Zaniboni A.[11], Antoniotti C.[10], Rossini D.[10], Falcone A.[10], Ruzzo A.[12]

[1]*Azienda Ospedali Riuniti Marche Nord - Unità di oncologia Medica, Pesaro;*
[2]*Università di Pisa, Pisa;* [3]*Istituto Oncologico Veneto IOV - IRCCS, Pisa;*
[4]*San Bortolo General Hospital, Vicenza;* [5]*Università Campus Bio-Medico,
Roma;* [6]*Card. G. Panico Hospital, Tricase;* [7]*IRCCS Casa Sollievo della
Sofferenza, San Giovanni Rotondo;* [8]*Università degli Studi di Milano, Milano;*
[9]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola;*
[10]*Università di Pisa, Pisa;* [11]*Fondazione Poliambulanza, Brescia;* [12]*Universita
degli Studi di Urbino Carlo Bo, Fano*

Background: Loss of p53 tumor suppressor function has been associated with chemoresistance and poor prognosis in cancer pts. New experimental and clinical data have identified p53 as a master regulator in tumor angiogenesis. A highly conserved functional p53-binding site has been identified within the VEGF promoter and p53 down-regulates vascular endothelial growth factor (VEGF) expression. Disruptive *TP53* mutations impair p53 tumor suppressor functions and increase VEGF expression levels in human cancer tissues. This background prompted us to analyze the clinical impact of TP53 in mCRC patients (pts) enrolled in the TRIBE-2 trial.

Methods: TRIBE-2 is a prospective phase III trial in which untreated mCRC pts were randomized to receive first-line FOLFOX or FOLFOXIRI plus Bev followed by FOLFIRI or FOLFOXIRI re-introduction plus Bev after first disease progression. *TP53* mutations were identified by next-generation sequencing in primary tumors. Each *TP53* missense mutation was assigned a residual transcriptional activity score ($TP53_{RTAS}$) according to the results of a site-directed mutagenesis technique and yeast-based functional assay. Overall survival (OS) and first progression-free survival (PFS1) times were correlated with *TP53* status: A) wild-type; B) $TP53_{RTAS}$=10% missense mutation; C) $TP53_{RTAS}$<10% missense mutations or truncating non-missense mutations (nonsense and frameshift).

Results: Tumor samples for *TP53* analysis were collected from 278 pts (arm A/B 152/126) out of 679 pts enrolled in the TRIBE-2 study. RAS/RAF mutations were found in 177/38 pts. According to *TP53* analysis, groups A, B and C pts were 51 (18%), 31 (11%) and 196 (71%), respectively. Median OS times in groups A, B and C were 30.4 months (95%CI 25.7-38.6 months), 29.8 months (95%CI 28.3-35 months) and 21.2 months (p5%CI 18.7-24.4 months), respectively (p=0.003). Median PFS1 times in groups A, B and C were 15.8 months (95%CI 11.9-19.6 months), 12.1 months (95%CI 9.5-16.3 months) and 10 months (95%CI 8.4-11.1 months), respectively (p=0.006). The detrimental effect of the *TP53* group C status was retained in OS/PFS1 multivariate models. Tumor response analysis did not show significant association with *TP53* mutations.

***Conclusions*:** In mCRC pts treated with CT plus Bev, the *TP53* mutational status including deleterious missense and truncating non-missense mutations negatively impacts on survival outcomes. Alternative therapeutics should be explored in this clinically unfavorable group of mCRC pts.

B09

STATINS INCREASE PATHOLOGICAL RESPONSE IN LOCALLY ADVANCED RECTAL CANCER (LARC) TREATED WITH CHEMO-RADIATION (CRT): A MULTICENTRIC EXPERIENCE

*Caputo F.[1], Santini C.[1], Casadei-Gardini A.[1], Cerma K.[1], Bardasi C.[1],
Garajovà I.[2], Lattanzi E.[3], Passardi A.[4], Rapposelli I.G.[4], Spallanzani
A.[1], Reggiani Bonetti L.[5], Gelmini R.[6], Meduri B.[7], Piccoli M.[8], Pecchi
A.[9], Benatti S.[1], Dominici M.[1], Luppi G.[1], Gelsomino F.[1]*

[1]*University Hospital of Modena, Division of Oncology, Modena., Modena;*
[2]*University Hospital of Parma, Medical Oncology Unit, Parma., Parma;*
[3]*University Hospital of Parma, Radiotherapy Unit, Parma., Parma;*
[4]*Department of Medical Oncology, Istituto Scientifico Romagnolo per lo
Studio e la Cura dei Tumori (IRST) IRRCS, Meldola, Meldola;* [5]*University
Hospital of Modena, Section of Pathology, Modena., Modena;* [6]*University
Hospital of Modena, Department of Surgery, Modena., Modena;* [7]*University
Hospital of Modena, Radiotherapy Unit, Modena., Modena;* [8]*Azienda
Ospedaliero-Universitaria of Modena, Department of Surgery, OCB
(Ospedale Civile Baggiovara), Modena., Modena;* [9]*University Hospital of
Modena, Department of Radiology, Modena., Modena*

Background: Complete tumor response to neoadjuvant chemo-radiation (CRT) for locally advanced rectal cancer (LARC) is associated with better outcomes. Unfortunately, it is achieved in only 20-30% of patients (pts). Many studies evaluated the potential role of concomitant medications in addition to CRT to enhance response rate, but data are not definitive. In this multicentric, retrospective study, we investigated the influence of various concomitant medications on outcomes of pts undergoing CRT for LARC.

Material and methods: 246 pts treated at Azienda Ospedaliero-Universitaria of Modena, University of Parma, and Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori between 2003 and 2018 were retrospectively identified. Demographical and clinicopathological data of potential interest were collected. The association between the use of concomitant drugs and outcomes (Dworak tumor regression grade [TRG] and disease-free survival [DFS]) was assessed by Odds Ratio (OR).

Results: Globally, 246 pts received neoadjuvant CRT. Of them, 15.8% were taking antihypertensive drugs, 3.7% statins, 1.2% antiplatelet drugs, and 1.6% antidiabetic drugs. Furthermore, 30.5% of pts were taking ≥ 2 of these drugs simultaneously. 40% of pts have experienced CRT-related toxicity, leading to a dose reduction or treatment discontinuation in 27% of cases. Of the 221 surgical specimens available, a Dworak TRG score of 3-4 was found in 68 (30.7%) pts. At both univariate and multivariate analysis, an association between statins and a Dworak grade 3-4 was found (OR 8.78, 95% CI 1.57-49.15, p=0.01). Moreover, statins were significantly associated with more frequently CRT-related toxicity (OR 2.39, 95% CI 1.23-4.64, p=0.0098) and a more frequent chemotherapy dose reduction or discontinuation (OR 2.26, 95% CI 1.06-4.80, p=0.03). No correlations were found between the use of the evaluated drugs and the DFS.

Conclusions: Despite a higher frequency of chemotherapy interruption or dose reduction and radiotherapy interruption, in this series of pts with LARC treated with neoadjuvant CRT, the concomitant use of statins proved to be associated with better tumor regression, according to the Dworak system. This hypothesis deserves further confirmation in larger prospective trials.

B10

THE ADDITION OF OXALIPLATIN TO NEOADJUVANT CHEMO-RADIOTHERAPY IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER: INDIVIDUAL PATIENT DATA META-ANALYSIS OF THREE RANDOMISED CONTROLLED TRIALS WITH SUBGROUP ANALYSES OF AGE AND STAGE COHORTS

Zichi C.[1], Fontana E.[2], Smyth E.[3], Mauer M.[4], Roedel C.[5], Fokas E.[6], Hofheinz R.[7], Arnold D.[8], Schmoll H.J.[9], Van Cutsem E.[10], Haustermans K.[10], Stein A.[11], Gerard J.[12], Conroy T.[13], Jouffroy-Zeller C.[14], Moehler M.[15], Lordick F.[16], Ben-Aharon I.[17], Di Maio M.[1]

[1]Division of Medical Oncology, University of Turin, Ordine Mauriziano Hospital, Turin, Italy; [2]Sarah Cannon Research Institute, London, United Kingdom; [3]Addenbrookes Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [4]EORTC, Brussels, Belgium; [5]Department of Radiation Oncology, University Hospital Frankfurt, Goethe-Universität Frankfurt, Frankfurt, Germany; [6]German Cancer Consortium (DKTK) Core Center Heidelberg and DKTK Partner Site Frankfurt, Oxford, United Kingdom; [7]University Medical Center Mannheim, Tagestherapiezentrum am ITM, Mannheim, Germany; [8]Asklepios Tumorzentrum Hamburg AK Altona, Hamburg, Germany; [9]Martin Luther University, Halle, Germany; [10]University Hospitals Gasthuisberg Leuven, KU Leuven, Leuven, Belgium; [11]University Medical Center Hamburg-Eppendorf, Department of Oncology, Haematology, Stem Cell Transplantation and Pneumology, Hamburg, Germany; [12]Centre Antoine Lacassagne, Nice, France; [13]Institut de Cancérologie de Lorraine, Vandoeuvre-Les-Nancy, France; [14]Unicancer, Paris, France; [15]University Medical Center Mainz, I. Dept. of Internal Medicine, Mainz, Germany; [16]University Cancer Center Leipzig, Leipzig, Germany; [17]Division of Oncology, Rambam Health Care Center, Haifa, Israel

Background: Neoadjuvant chemo-radiotherapy (CRT) with fluoropyrimidine (FP) is the current standard of treatment for locally advanced rectal cancer (LARC). Most randomised controlled trials (RCTs) examining the addition of Oxaliplatin (OX) were negative, but a post hoc analysis of the CAO/ARO/AIO-04 trial showed significant benefit adding OX in patients (pts) <60y. We hypothesized that OX-CRT might improve outcomes in younger pts with LARC.

Methods: We performed a systematic review and individual patient data (IPD) meta-analysis. RCTs testing the addition of OX to standard FP-based CRT in LARC were eligible. Primary endpoint: disease-free survival (DFS), secondary endpoints: pathologic complete response (ypCR) and overall survival (OS). Analyses were by intention to treat (ITT), stratified by trial. Age cut-offs were 60y and 50y.

Results: Data from 3 of 9 identified RCTs were available (CAO/ARO/AIO-04, ACCORD-12, PETACC-6), corresponding to 2914 pts (48.5% of available literature). Median age was 63y, 40% were <60y, 12% were <50y, 72% were stage ≥III. No significant improvement in DFS was observed with OX in ITT (Hazard Ratio [HR] 0.88, 95%CI 0.77-1.01, p=0.06). OX significantly improved DFS in <60y (n=1166 - HR 0.77, 95%CI 0.62-0.96, p=0.02), whereas the improvement was not statistically significant in <50y (n=350 - HR 0.73, 95%CI 0.49-1.08, p=0.12). There was no significant interaction with age (60y p=0.11; 50y p=0.44). Stratifying the DFS analysis by stage (I-II vs. ≥III) no difference was found in all age subgroups (Table 1). OX increased ypCR in ITT from 13% to 16% (Odds Ratio [OR] 1.28, 95%CI 1.04-1.57, p=0.024). There was no OS benefit (HR 0.97, 95%CI 0.82-1.15, p=0.75).

Conclusions: This IPD meta-analysis evaluating the addition of OX to CRT did not show significant interaction of OX with age. However, data showed a signal for DFS benefit in pts <60y, with a non-significant increment in DFS in <50y, although this analysis may be underpowered.

Stage	Age	PFS - HR	95%CI	p-value
I/II	<60	0.64	0.39-1.03	0.06
I/II	<50	0.67	0.30-1.51	0.34
I/II	>60	0.89	0.66-1.25	0.46
I/II	>50	0.81	0.62-1.06	0.12
≥III	<60	0.81	0.63-1.04	0.10
≥III	<50	0.72	0.46-1.14	0.16
≥III	>60	0.97	0.80-1.19	0.78
≥III	>50	0.93	0.79-1.10	0.38

B11

CARDIOVASCULAR EVENTS IN COLORECTAL CANCER PATIENTS TREATED WITH FLUOROPYRIMIDINES: INTERIM ANALYSIS OF THE PROSPECTIVE CHECKPOINT TRIAL (NCT02665312)

Aimar G.[1], Lombardi P.[1], Filippi R.[2], Quarà V.[1], Milanesio M.C.[1], Crespi V.[1], Farinea G.[1], Bonzano A.[3], Cavalloni G.[4], Peraldo Neia C.[4], Basiricò M.[4], Depetris I.[5], Ferraris R.[6], Leone F.[7], Aglietta M.[1], Fenocchio E.[6]

[1]Department of Oncology, University of Turin; Department of Medical Oncology, Candiolo Cancer Institute, FPO - IRCCS, Torino; [2]Centro Oncologico Ematologico Subalpino, Azienda Universitaria Ospedaliera Città della Salute e della Scienza di Torino Department of Oncology 10126, Torino Italy, Torino; [3]Department of Cardiology, Candiolo Cancer Institute, FPO, IRCCS, Candiolo, Italy., Torino; [4]Clinical Research Office, Candiolo Cancer Institute, FPO - IRCCS - Candiolo, Torino; [5]Ospedale di Ivrea Department of Medical Oncology 10015, Ivrea, Italy, Torino; [6]Multidisciplinary Outpatient Oncology Clinic, Candiolo Cancer Institute FPO-IRCCS, Candiolo Torino, Italy, Torino; [7]Dipartimento di Oncologia, Ospedale degli Infermi, Biella, Italy, Biella

Background: Cardiotoxicity represents an unexpected and potentially life-threatening toxicity in colorectal (CRC) patients (pts) treated with fluoropyrimidines (FP). Currently, there are no predictive factors of FP-induced cardiotoxicity (FIC), moreover the correlation between FIC and known cardiovascular (CV) risk factors remains controversial.

Methods: Colorectal (CRC) FP naïve pts have been enrolled at Candiolo Cancer Institute since January 2016 to February 2020. Before the start of FP-regimen, all patients were screened for CV comorbidities and risk factors with an optimization of the cardiological treatment. During the first 3 chemotherapy (CT) cycles, seriated electrocardiograms and questionnaires on CV symptoms were administered, as well as brain natriuretic peptide (BNP) levels assessment and plasma samples storing for the validation of circulating microRNAs (c-miRNAs) were performed. Primary objective was to determine the incidence rate of FIC in our colorectal cancer patients treated with FP. A secondary endpoint was to determine any predictive factors for FIC.

Results: An interim analysis was conducted at 135 pts (60.7% men, median age 66 years). We recordered CV risk factor in 48.7% of enrolled pts. During the treatment period 20 pts (15,38%) experienced FIC: 1 acute coronary syndrome, 1 coronary vasospasm, 1 paroxysmal supraventricular tachycardia, 1 complete left bundle branch block, 3 syncope, 4 typical chest pain, 6 sudden wheezing and 3 sudden palpitations. Unfortunately, none of clinical or laboratories index was able to suggest an increased risk of FIC. Instead, we found a higher incidence of FIC in women (p. 0.048). The onset of FIC is not related to age ($</>$ 75 years), cardiovascular risk (high / low), type of FP (5-fluorouracil / capecitabine) and disease status (adjuvant / metastatic). BNP levels increased significantly more in patients treated with infusion-based 5-FU CT (p. 0.003) in the first 3 days of therapy, however no correlation was observed with FIC.

Conclusions: Although FIC was observed in a not negligible percentage of patients, no relationship with CV risk factors or laboratory data was found. A more precise correlation of cardiac events with c-miRNAs will be available at completed recruitment (200 pts).

B12

IMPACT OF EARLY TUMOR SHRINKAGE (ETS) AND DEPTH OF RESPONSE (DOR) ON THE OUTCOMES OF PANITUMUMAB(PAN)-BASED MAINTENANCE THERAPY IN PATIENTS (PTS) WITH RAS WILD-TYPE METASTATIC COLORECTAL CANCER (MCRC) AND ENROLLED IN THE VALENTINO STUDY

Manca P.[1], Corallo S.[1], Calareso G.[1], Lonardi S.[2], Cremolini C.[3], Rimassa L.[4], Racca P.[5], Murialdo R.[6], Clavarezza M.[7], Zaniboni A.[8], Tomasello G.[9], Adamo V.[10], Antonuzzo L.[11], Vaiani M.[1], Cinieri S.[12], Di Bartolomeo M.[1], Niger M.[1], Morano F.[1], De Braud F.[1], Pietrantonio F.[1]

[1]*IRCCS Istituto Nazionale dei Tumori, Milano;* [2]*Istituto Oncologico Veneto, Padova;* [3]*AOU Pisana, Pisa;* [4]*Humanitas Cancer Center, Milano;* [5]*AOU Città della Salute e della Scienza, Torino;* [6]*IRCCS AOU San Martino-IST, Genova;* [7]*Ente Ospedaliero Ospedali Galliera, Torino;* [8]*Fondazione Poliambulanza, Brescia;* [9]*Niguarda Cancer Center, Milano;* [10]*A.O. Papardo, Messina;* [11]*AOU Careggi, Firenze;* [12]*Ospedale Antonio Perrino, Brindisi*

Background: The prognostic role of ETS and DoR in mCRC pts receiving first-line therapy is well established. However, these parameters were not collected in maintenance trials and their impact on maintenance tx is unknown.

Methods: VALENTINO showed that maintenance tx with pan (arm B) achieved inferior PFS compared to 5-FU/LV+pan (arm A) after FOLFOX/pan induction in 229 pts with *RAS*wt mCRC. CT scans performed every 8 weeks were centrally reviewed to determine ETS and DoR (defined as 20% reduction of the sum of target lesions at 8 weeks and their best % reduction) and their correlation with outcomes. Uni and multivariate cox regressions were used to investigate factors associated with PFS and OS.

Results: Out of 196 evaluable pts, 132 (67%) had ETS and median DoR was -44.1%. ETS frequency did not differ by main baseline features, except for liver limited disease (p=0.025) and *in-situ* primary tumors (0.004). ETS was associated with longer mPFS (12.5 vs 8.8 m; HR=0.66 [0.48-0.91]; p=0.010) and mOS (32.5 vs 23.1 m; HR=0.60 [0.41-0.86]; p=0.006). Maximization of log-rank statistics identified the optimal DoR cut-off as -34% for both PFS and OS. DoR$>$34% was associated with longer mPFS (13.2 vs 7.3 m; HR=0.51 [0.37-0.70]; p$<$0.001) and mOS (38.4 vs 19.4 m; HR=0.44 [0.31-0.64]; p$<$0.001). Notably, ETS and DoR were highly associated (p$<$0.001) and 89% of pts with ETS achieved a DoR$>$34%. In multivariable models, DoR was independently associated with PFS (p=0.024) and OS (p=0.027). In the predictive analyses (table), the PFS benefit of adding 5-FU/LV to pan was independent from both ETS and DoR (interaction p values ns). However, pts with no-ETS and poorer DoR treated with maintenance pan alone achieved extremely poor PFS compared to other subgroups. For ETS, such detrimental effect was evident also for OS.

	arm B	arm A	arm B	arm A
	no-ETS		ETS	
mPFS	7.7	9.5	11.1	13.2
mOS	18.7	24.7	33.1	30.6
	DoR$\leq$34%		DoR$>$34%	
mPFS	6.5	8.0	11.4	14.6
mOS	18.0	19.7	33.1	38.0

Conclusion: ETS and DoR are relevant prognostic factors in an extended-*RAS* wt population. No-ETS and poorer DoR are associated with unfavourable outcomes after maintenance tx, with particular regard to pan alone.

B13

BASELINE RADIOMICS FEATURES (RF) IN METASTATIC COLORECTAL CANCER (MCRC): CORRELATION WITH M SITE AND CLINICAL-PATHOLOGICAL CHARACTERISTICS

Camarda F.[1], Boldrini L.[2], Lenkowicz J.[3], Caliolo G.[4], Vivolo R.[1], Anghelone A.[1], Di Stefano B.[1], Calegari M.A.[1], Pozzo C.[1], Basso M.[1], Liguori C.[1], De Gaetano A.M.[2], Dinapoli N.[2], Manfredi R.[2], Valentini V.[2], Tortora G.[1], Salvatore L.[1]

[1]Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli IRCCS Università Cattolica del Sacro Cuore, Roma; [2]Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario, Roma; [3]Istituto di Radiologia, Università Cattolica del Sacro Cuore, Roma; [4]Istituto di Radiologia, Università Cattolica del Sacro Cuore, Roma

Background: R is an emerging field of research based on extraction of a large amount of F from biomedical images and on computed analysis algorithms of tumor architecture. Few data regarding mCRC are available and no correlation of baseline RF both with m sites and clinical-pathological characteristics was so far investigated.

Methods: Baseline chest-abdomen CT scans of mCRC patients (pts) were retrospectively analysed. RF were extracted from Regions of Interest (ROI) delineated on CT scan from each m sites, including primary tumor, when on site. The association of specific F and disease site (liver, lung, nodes, peritoneum and on-site primary tumor) was investigated. Sites similarity was assessed with Principal Component Analysis, an unsupervised learning technique to identify patterns and clusters. Then RFs were tested individually for correlation with clinical-pathological covariates of interest (gender, CEA level, synchronous disease, RAS/BRAF status, mucinous histology, grading, number of m site, primary tumor site). Wilcoxon-Mann-Whitney test was used for this purpose (significance level set at 0.05).

Results: After RF extraction from different ROIs, dataset was composed of 433 observations of 236 variables. Observations referred to the number (N) of pts = 89 and the N of ROIs = 18. RF classes were divided in statistical F (grey-level histogram) (N of F=10); morphological F (N=14); texture F GLCM (grey level co-occurrence matrix) (N=100); texture F GLRLM (grey level run length matrix) (N=66); texture F GLSZM (grey level size zone matrix) (N=32). Regarding the association of RF with m sites, a homogenous distribution with liver, nodes, peritoneum and primary tumor was detected, while lung metastases showed a different pattern for all the RF classes. A significant correlation of specific RF with clinical-pathologic characteristics was shown, particularly with gender, CEA level, synchronous disease, mucinous histology, RAS/BRAF status.

Conclusions: Despite its retrospective nature and the limited number of pts, this is the first experience demonstrating a different pattern of RF for lung m versus a homogeneous

RF distribution for the other m sites; and a significant association of specific RF with few clinical-pathologic characteristics. Our results, if confirmed in a prospective validation set, may represent an hypothesis generator regarding the different behavior of lung m and a possible R signature able to identify different prognostic subgroups of pts.

B14

LONG TERM SURVIVAL WITH REGORAFENIB: REALITY (REAL LIFE IN ITALY) TRIAL - A GISCAD STUDY

Lai E.[1], Cremolini C.[2], Puzzoni M.[1], Bergamo F.[3], Zucchelli G.[2], Libertini M.[4], Dettori M.[5], Banzi M.[6], Boccaccino A.[2], Pusceddu V.[1], Cinieri S.[7], Cavo A.[8], Piacentini G.[9], Andreozzi F.[10], Banna G.L.[11], Pellino A.[12], Iachetta F.[6], Rota S.[13], Conca V.[2], Zaniboni A.[4], Scartozzi M.[1]

[1]Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari; [2]U.O. Oncologia Medica 2 Universitaria Ospedale S. Chiara - Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy, Pisa; [3]Unit of Medical Oncology 1, Department of Clinical and Experimental Oncology, Veneto Institute of Oncology IOV - IRCCS, Padua, Italy, Padova; [4]U.O. Oncologia, Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy, Brescia; [5]Medical Oncology Unit, Azienda Ospedaliera Brotzu, Ospedale Businco, Cagliari, Italy, Cagliari; [6]SS "Sperimentazioni cliniche" U.O. Oncologia Medica - Clinical Cancer Centre USL-IRCCS Reggio Emilia, Reggio Emilia, Italy, Reggio Emilia; [7]Medical Oncology Division & Breast Unit, Senatore Antonio Perrino Hospital, ASL Brindisi, Brindisi, Italy, Brindisi; [8]Oncology Unit, Villa Scassi Hospital, Sampierdarena, Genova, Italy, Genova; [9]Oncologia Medica, ASST Papa Giovanni XXIII, Bergamo, Italy, Bergamo; [10]U.O.C. Oncologia, A.O.R.N. dei Colli Ospedali Monaldi-Cotugno-CTO, Napoli, Italy, Napoli; [11]Haematology/Oncology, Queen Alexandra & St Mary's Hospitals, Portsmouth & IOW, UK, Portsmouth & IOW; [12]Department of Oncology, Veneto Institute of Oncology IOV – IRCCS, Padua, Italy; Department of Surgery, Oncology and Gastroenterology, University of Padua, Padua, Italy, Padova; [13]Fondazione GISCAD – Gruppo Italiano per lo Studio dei Carcinomi dell'Apparato Digerente, Vanzago, Milano

Background: Regorafenib is a key agent for metastatic colorectal cancer (mCRC) treatment but no validated factors predicting longer survival are available.

Material (patients) and methods: REALITY was a retrospective multicentric trial in Italian refractory mCRC patients (pts) reaching OS= 6 months (m) with regorafenib. We aimed to assess the association between clinical parameters and outcome in the study population to define a panel identifying long term survivors among regorafenib candidates. Primary and secondary endpoints were OS and PFS, respectively. Statistical analysis was performed with MedCalc (survival distribution: Kaplan-Meier method; survival curves comparison: log-rank test).

Results: 100 regorafenib-treated mCRC pts from January 2014 to December 2015 with OS≥6 m were enrolled. Median OS was 11.5 m (95%CI 9,60-12,96). OS was longer in moderately differentiated (G2) mCRC (12,4 versus [vs] 7,4 vs 9,1 m G1 vs G3; p=0,0026) and for LDH levels ≤217 U/l (12,1 vs 8,7 m, p=0,0470). OS was improved with 160 mg starting dose at cycle 2 (12,4 vs

10,9 m 120 mg vs 9,1 m 80 mg, p=0,0325) and 4 (17,7 vs 12,1 m 120 mg vs 14,5 m 80 mg, p=0,0288), and in absence of adverse events (AE) over the first 4 cycles (22,5 vs 10,2 m, p=0,0018), cycle 1 (14,7 vs 10,7 m, p=0,0410) and 2 (15,6 vs 10,9 m, p=0,0474). OS was longer in absence of dose/schedule changes overall during the first 4 cycles (17,7 vs 10 m, p=0,0012), cycle 3 (14,7 vs 9,7 m, p=0,0031), and 4 (15,4 vs 10,9 m, p=0,0351), for single site PD (12,9 vs 10,7 m, p=0,0349), non-liver single site PD (15,6 vs 8,1 m, p=0,0066), no liver PD (13,6 vs 10 m, p=0,0043). Median PFS was 4.2 m (95%CI 3,43-43,03). PFS was longer in G2 mCRC (4,5 m vs 2,2 G1 vs 3,3 G3, p<0,0001), in absence of AE over the first 4 cycles (6,53 vs 3,9 m, p=0,0047), cycle 1 (6,1 vs 3,8 m, p=0,0056) and 2 (6,1 vs 3,9 m, p=0,0244) and of dose/schedule changes globally during the first 4 cycles (11,3 vs 3,4 m, p=0,0020), cycle 2 (4,5 vs 3,7 m, p=0,0298), 3 (6,5 vs 3,3 m, p=0,0008) and 4 (6,5 vs 4,2 m, p=0,0080). PFS was improved for single site PD (4,5 vs 3,7 m, p=0,0138), non-liver single site PD (6,5 vs 3 m, p=0,0090), no lung (4,8 vs 3,9 m, p=0,0338) and no liver PD (6,3 vs 3,3 m, p<0,0001).

Conclusions: In our study G2 mCRC, low LDH, single site PD, absence of AE, treatment changes and of liver/lung PD were associated with better outcome in pre-treated long term mCRC survivors receiving regorafenib.

B15

CLINICAL UTILITY OF PLASMA REAL TIME PCR FOR RAS/BRAF MUTATIONS IN METASTATIC COLORECTAL CANCER (MCRC) PATIENTS. THE IMPORTANCE OF DISCORDANT CASES

Lucchetti J.[1], Doldo E.[1], Riondino S.[1], Formica V.[1], Morelli C.[1], Renzi N.[1], Nitti D.[1], Palmieri G.[1], Orlandi A.[1], Roselli M.[1]

[1]Policlinico Tor Vergata, Roma

Background: Tissue (T) mutational analysis is the standard for mCRC however liquid biopsy can better represent tumor heterogeneity. Highly sensitive methods (as ddPCR) with a limit of detection (LoD) of <0.01% detects rare RAS/BRAF mutations with uncertain clinical meaning. Conversely, real-timePCR (RTPCR) techniques have a lower LoD (0.5-0.1%) with possible higher clinical utility

Patients and methods: Consecutive mCRC pts candidate for a firstline chemotherapy with known T-KRAS/NRAS/BRAF status, were enrolled. Progression free survival (PFS) was defined according to RECIST 1.1 and considered as primary prognostic endpoint. The total number of tumor lesions (TNL) and the sum of maximum diameters of all lesions (SMD) were calculated as measures of tumor burden. Data on routine biochemical variables and CEA and CA19.9 were also collected. DNA-binding magnetic beads (MagCore® Plasma DNA Extraction Kit) and selective detections of exons 2, 3 and 4 of KRAS and NRAS and exon 15 of BRAF mutations by qualitative Real-Time PCR (EasyPGX®) were used to assess PL mutational status. Cox-regression hazard model and Kaplan Meier method were used for survival analysis. Logistic regression analysis (LRA) was used to identify predictors of T vs PL discordant cases.

Results: 45 mCRC pts were enrolled. All BRAF MUT cases were concordant between PL and T; 10 pts were concordant for RAS mutation in PL and T (RAS MUT concordant); 20 pts were RAS WT in both PL and T (RAS WT concordant); 9 RAS discordant cases were recorded: 4 WT in T and MUT in PL (RAS WT-T/MUT-PL) and 5 pts MUT in T and WT in PL (RAS MUT-T/WT-PL). RAS plasma mutational assessment was significantly associated with PFS: RAS WT-T/MUT-PL had similar PFS to RAS MUT concordant pts and RAS MUT-T/WT-P had similar PFS to RAS WT concordant pts (table). SMD was found to be a significant predictor of discordant cases among RAS MUT-T pts (p=0.02). RAS MUT-T pts with a SMD<140 mm had a 80% chance to be RAS WT in PL vs 10% of pts with SMD>140 mm (OR 36; 95% CI 1.78- 731.6). TNL was of borderline significance as predictor of discordant cases among RAS WT-T pts (p=0.07). RAS WT-T pts with >10 TNL had a 50% chance of being MUT in PL vs 10% of pts with TNL<10(OR 9).

Conclusions: PL mutational status assessed by RTPCR allows a better prognostication than T analysis alone. Large sample size and further investigations are required to corroborate these findings.

Mutations	PFS (months)	HR	p value
BRAF MUT	4.5	1	
RAS MUT concordant	7.9	0.33	0.06
RAS WT-T/MUT-PL	9.6	0.22	0.04
RAS MUT-T/WT-PL	24.4	0.02	0.0001
RAS WT concordant	23.3	0.04	0.0002

B16

CENTRAL NERVOUS SYSTEM AS POSSIBLE SANCTUARY OF RELAPSE IN HER2-POSITIVE METASTATIC COLORECTAL CANCER

Tosi F.[1], Sartore Bianchi A.[2], Rizzato M.D.[3], Amatu A.[1], Ghezzi S.[1], Martino C.[4], Bonazzina E.[1], Bencardino K.[1], Fenocchio E.[4], Patanè D.[1], Ardizzoni A.[5], Torri V.[6], Valtorta E.[1], Bonoldi E.[1], Vanzulli A.[2], Regge D.[4], Ciardiello F.[7], Lonardi S.[3], Marsoni S.[8], Siena S.[2]

[1]Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milano; [2]Dipartimento di Oncologia ed Emato-Oncologia, Università degli Studi di Milano, Milano; [3]Oncologia Medica 1, Istituto Oncologico Veneto - IRCCS, Padova; [4]Istituto di Candiolo, Fondazione del Piemonte per l'Oncologia-IRCCS, Candiolo; [5]UOC Oncologia Medica, Policlinico S. Orsola,

Dipartimento di Medicina Specialistica, di Laboratorio e Sperimentale, Università Alma Mater, Bologna; [6]Dipartimento di Oncologia - Istituto Mario Negri - IRCCS, Milano; [7]Università della Campania "L. Vanvitelli", Napoli; [8]Precision Oncology, IFOM-FIRC Institute of Molecular Oncology, Milano

Background: Central nervous system (CNS) metastases rarely occur in metastatic colorectal cancer (mCRC) patients (1-4%). HER2 amplification can be detected in 5% of *RAS* WT mCRC and has been recognized as a therapeutic target for trastuzumab in combination with lapatinib or pertuzumab. We recently reported a high rate of CNS recurrences (19%) among HER2-positive mCRC treated with trastuzumab and lapatinib (Sartore-Bianchi et al. *JAMA Oncol* 2020). Here we describe the prevalence, timing of onset and characteristics in a larger cohort of patients.

Patients and Methods: Consecutive patients with HER2-positive mCRC by immunohistochemistry and *in-situ* hybridization, treated with both anti-HER2 regimens within the multi-center HERACLES clinical program and *per* institutional protocols at Niguarda Cancer Center were included in the analysis.

Results: Between August 2012 and April 2020, 92 patients have been treated with an anti-HER2 regimen: 42 patients received trastuzumab and lapatinib, 31 patients pertuzumab and T-DM1 and 19 patients other treatments in clinical trials. Progression in CNS was clinically evident in 10/92 (11%). Clinical characteristics are provided in Table 1. In one patient, who underwent surgical removal of a cerebellum metastases, maintenance of HER2-positivity in CNS was demonstrated.

Conclusions: Present data indicate a high prevalence of CNS recurrences in HER2 positive mCRC, suggesting that the CNS may represent a sanctuary of relapse, and brain imaging for staging and tumor assessment is warranted. Further studies are needed to understand the mechanisms underlying this observed tropism.

Table 1.

Patient	Anti-Her2 Treatment	ORR to anti-HER2 treatment	Brain PFS (months)[§]	Timing of CNS progression*	Brain metastases treatment	OS (months)[§]
1	T+L	SD	59.8	Off-treatment	Surgery	77.9
2	T+L	PR	51.0	On-treatment	None	51.3
3	T+L	SD	32.9	On-treatment	-	36.5
4	T+L	PR	57.8	Off-treatment	None	62.6
5	T+L	PD	33.9	On-treatment	SRS	36.8
6	T+L	SD	13.7	On-treatment	SRS	21.4
7	T+L	PD	26.3	Off-treatment	SRS	29.0
8	P+T-D	PD	38.7	Off-treatment	SRS	45.7
9	P+T-D –> O	SD; PD	18.6	On-treatment	None	19.8
10	O –> T+L	PR; PD	84.9	Off-treatment	Surgery	85.4+

[§]=from diagnosis of stage IV.
*= 2 pre-existing and stable after SRS, 5 documented under and 3 after anti-HER2 treatment.
ORR=Objective Response Rate; PFS=Progression Free Survival; OS=Overall Survival; PD=Progressive Disease; PR=Partial Response; SD=Stable Disease; T=trastuzumab; L=lapatinib; P=pertuzumab; T-D=T-DM1; O=other anti-Her2 in clinical trial; SRS=Stereotactic radiosurgery; +=ongoing.

B17

PREOPERATIVE CHEMORADIOTHERAPY OF LOCALLY ADVANCED RECTAL CANCER AND TUMOR-INFILTRATING LYMPHOCYTE RESPONSE RELATED: THE SMART-STAR STUDY

Negri F.[1], Bottarelli L.[1], Gnetti L.[1], Campanini N.[1], Negru E.[2], Bergamo F.[3], Siena S.[4], Frisinghelli M.[5], Petric M.[6], Chiaulon G.[7], Mosconi S.[8], Gelsomino F.[9], Azzoni C.[1], Silini E.M.[1], Valentini S.[10], Gaiani F.[1], De'Angelis G.L.[1], Leonardi F.[1], Pedrazzi G.[11], Aschele C.[2]

[1]Azienda Ospedaliero-Universitaria di Parma, Parma; [2]ASL5, La Spezia; [3]Istituto Oncologico Veneto IOV - IRCCS, Padova; [4]Ospedale Niguarda, Milano; [5]Ospedale Civile Santa Chiara, Trento; [6]Azienda Sanitaria dell'Alto Adige, Bolzano; [7]Azienda Sanitaria Universitaria Integrata di Udine, Udine; [8]Ospedale Papa Giovanni XXIII, Bergamo; [9]Azienda Ospedaliero-Universitaria di Modena, Modena; [10]Ospedale Borgomanero, Novara; [11]Università degli Studi di Parma, Parma

Background: Preoperative chemoradiotherapy can enhance antitumor immunity through increasing T-cell activation and tumor infiltration. These effects could potentially sensitize tumors to immunotherapies, including checkpoint inhibitors. We explored whether preoperative therapy for locally advanced rectal cancer induces immunologic changes.

Materials and Methods: We analyzed by immunohistochemistry 55 cases, of whom 25 paired pre- and postoperative specimens of locally advanced rectal cancer from the STAR-01 cohort. The multicenter study enrolled patients treated with preoperative chemoradiation with or without oxaliplatin. The immunoistochemical analysis was performed with a panel of immune cells and associated factors as CD3, CD20, CD4/CD8, PD1 and FoxP3. The pattern of tumor infiltrating lymphocytes (TILs) and related infiltrating lymphocytes (RILs) was also evaluated.

Response to preoperative chemoradiotherapy was assessed according to tumor regression grade (TRG sec. Ryan –AJCC Eight ed.)

Results: The expression level of CD3+, CD20+, FoxP3+ and PD-1+ cells were not significantly different after therapy. The TILs and RILs immunosuppressive cells were higher in better responder (TRG0), although we did not find any statistical significance given the small sample size. Decreasing CD4/CD8 ratio on postoperative samples was significantly associate with TRG 0 (p <0.01). The increase of lymphocyte CD8+ was related to a good pathological response after chemoradiotherapy.

Conclusions: Our data suggest that chemoradiotherapy may induce an enrichment of lymphocytes T CD8+ in good responders. The new frontier of best treatment could be the use of specific immune cells (T lymphocytes) to activate the system's response immune against disease.

B18

CIRCULATING TUMOUR DNA ANALYSIS FOR MONITORING RAS/BRAF STATUS UNDER EGFR BLOCKADE AS A GUIDE FOR RECHALLENGE STRATEGY IN METASTATIC COLORECTAL CANCER PATIENTS IN CLINICAL PRACTICE

Mariani S.[1], Liscia N.[2], Puzzoni M.[1], Lai E.[1], Ziranu P.[1], Pretta A.[2], Impera V.[2], Musio F.[1], Persano M.[1], Migliari M.[1], Dubois M.[1], Tolu S.[2], Donisi C.[1], Pireddu A.[2], Camera S.[2], Demurtas L.[1], Pusceddu V.[1], Palomba G.[3], Pisano M.[3], Palmieri G.[3], Scartozzi M.[1]

[1]Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari; [2]Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari, Italy, Cagliari; [3]Istituto di Ricerca Genetica e Biomedica (IRGB), Consiglio Nazionale delle Ricerche (CNR), Sassari, Italy, Sassari

Background: The dynamic nature of tumour biology and the genetic heterogeneity of colorectal cancer (CRC) has long been known. Liquid biopsy and circulating tumour DNA (ct-DNA) extraction allow us to follow the trend of RAS mutational status, which is crucial in EGFR-blockade acquired resistance. In parallel, data from several studies suggest the option of rechallenge with EGFR-inhibitors in pre-treated RAS wild type (WT) metastatic CRC (mCRC) patients (pts).

Material (patients) and methods: Our study aim was to retrospectively evaluate the pulsatile behaviour of RAS clones under EGFR-blockade along with the anti-EGFR rechallenge effectiveness in clinical practice. ct-DNA from RAS/BRAF WT mCRC pts was analysed for RAS/BRAF mutations. The analysis was performed with Pyrosequencing assay (PyroMark Q24 MDx Workstation) and Sanger-based automated sequencing approach (ABI3130 Genetic Analyzer). Real-time PCR was performed to confirm RAS/BRAF mutations. CEA and CA 19.9 behaviour

under rechallenge with anti-EGFR was analysed as surrogate endpoint biomarker.

Results: Globally, seventeen pts treated with anti-EGFR containing therapy were included in the study, 13 males and 4 females. Thirteen (76%) pts received anti-EGFR containing therapy as first-line treatment, whereas 4 (23%) as third-line treatment. All pts were tested for RAS/BRAF mutations in ct-DNA; fourteen pts (82%) had a RAS/BRAF WT molecular profile whereas three pts (18%) had a KRAS-G12V mutation. Among RAS/BRAF WT ct-DNA pts, 8 (57%) underwent rechallenge with anti-EGFR: 7 pts received irinotecan+ cetuximab, and 1 underwent single agent panitumumab; six (75%) were eligible for response evaluation at the date of the present analysis. Two (33%) pts had a partial response whereas 4 (66%) pts had disease progression according to RECIST criteria. The Ca19.9 and the CEA level under rechallenge treatment decreased after 1 month in 5 (62%) patients and 7 (87%) patients, with a median percentage of reduction of 76,8% (95% IC:69.6-79.6) and 53.15% (95% IC :43.0-68.1%), respectively. No grade 3 toxicities occurred.

Conclusions: Despite the small sample size and the retrospective nature, our study suggests that liquid biopsy might be a useful tool to follow the trend of RAS mutational status and consequently for the decision making in this setting. Rechallenge with anti-EGFR was feasible and well tolerated in the study population. Results from prospective trials are awaited to better understand this exciting perspective.

B19

NOVEL EPIGENETIC 12-GENE SIGNATURE PREDICTIVE OF POOR PROGNOSIS AND MSI-LIKE PHENOTYPE IN HUMAN METASTATIC COLORECTAL CARCINOMAS

Condelli V.[1], Calice G.[2], Cassano A.[3], Basso M.[3], Rodriquenz M.G.[2], Zupa A.[2], Maddalena F.[2], Crispo F.[2], Pietrafesa M.[2], Aieta M.[2], Sgambato A.[2], Tortota G.[3], Zoppoli P.[2], Landriscina M.[4]

[1]Centro di Riferimento Oncologico della Basilicata, Rionero in Vulture, Potenza; [2]Centro di Riferimento Oncologico della Basilicata, Rionero in Vulture; [3]Policlinico Universitario Agostino Gemelli, Roma; [4]Università di Foggia, Foggia

Background: Epigenetic remodeling is responsible for tumor progression and drug resistance in human colorectal carcinoma (CRC). This study addressed the hypothesis that DNA methylation profiling may identify metastatic CRC (mCRC) subtypes with different clinical behavior.

Material and methods: Global methylation profile was comparatively analyzed between 24 first-line primary-resistant and 12 drug-sensitive mCRCs, two subgroups with significantly different outcome. Gene expression and methylation data from the COAD TCGA mCRCs cohort were

used to identify, among differentially methylated genes, a prognostic signature of functionally methylated genes.

Results: Noteworthy, twelve functionally methylated genes yielded a hierarchical clustering of patients in two well-defined clusters with hypermethylated tumors characterized by a significantly worse relapse-free and overall survival compared to hypomethylated cancers. Interestingly, the poor prognosis cluster was enriched of CIMP-high and MSI-like cases. Furthermore, methylation events were enriched in genes located on q-arm of chromosomes 13 and 20, two chromosomal regions with gain/loss alterations strongly associated with adenoma-to-carcinoma progression. Finally, the expression of the 12-genes signature and MSI-enriching genes was confirmed in two independent oxaliplatin- and irinotecan-resistant CRC cell lines.

Conclusions: These data represent the proof of concept that the hypermethylation of specific sets of genes may provide prognostic information being able to identify a subgroup of mCRCs with poor prognosis.

B20

EFFICACY AND SAFETY OF REGORAFENIB (REG)-TO-TRIFLURIDINE/ TIPIRACIL (FTD/TPI) SEQUENCING AND VICE VERSA IN REFRACTORY METASTATIC COLORECTAL CANCER (MCRC): A MULTICENTER REAL-LIFE EXPERIENCE

Signorelli C.[1], Chilelli M.G.[1], Morandi M.G.[2], Grande R.[3], Spinelli G.P.[4], De Marco S.[5], Sperduti I.[6], Ceribelli A.[2], Ruggeri E.M.[1]

[1]*Medical Oncology Unit, Belcolle Hospital, Viterbo;* [2]*Medical Oncology Unit, San Camillo de Lellis Hospital, Rieti;* [3]*Medical Oncology Unit, ASL Frosinone, Frosinone;* [4]*UOC Oncology, University of Rome "La Sapienza", ASL Latina, Aprilia (LT);* [5]*Medical Oncology Unit, San Camillo Forlanini Hospital, Roma;* [6]*Biostatistics Unit, IRCCS Regina Elena National Cancer Institute, Roma*

Background: REG and FTD/TPI have demonstrated significant improvements in overall survival (OS) in patients (pts) with refractory mCRC. The aim of our study was to evaluate the efficacy and safety profiles of both agents administered in sequence in the real world practice.

Materials and methods: Clinical data of pts treated beyond the 2°line with REG or FTD/TPI between October 2015 and May 2020, were retrospectively collected in 5 institutes in the Lazio Region.

Results: Overall, we included 62 pts but we focused our attention on the 2 groups of pts treated with sequencing: 13 pts (21%) with FTD/TPI-to-REG and 11 pts (17.7%) with REG-to-FTD/TPI. M/F=15/9; median age was 70 years (ys) (45-80); median duration of follow-up was 10 months (ms) (4-50); median duration of sequence treatment was 9.5 ms (5-17); median number of cycles was 8.5 (4-25). A median of 9.6 cycles per pt were administered. Performance Status ECOG ranged between 0 (29.1%) and 2 (8.3%). 13

pts (54.1%) received active 3 lines of treatment, 10 pts (41.6%) 2 lines and 1 pt (4.1%) 4 lines before the sequences above. 11 pts (45.8%) experienced g3-4 toxicities (36.3% in FTD/TPI-to-REG vs 63.6% in REG-to-FTD/TPI). Toxicities, such as neutropenia (g4 23.07%), anemia (g3 7.6%) and leucopenia (g3 7.6%) occurred more with FTD/ TPI-to-REG, while events such as hand-foot skin reaction (g3 36.3%) and fatigue (g3 9.09%) were reported with REG-to-FTD/TPI. No therapy related death was reported. Median OS for all patients was 16.7 ms (95% CI=7,6-25,7) regardless of therapy administered; in particular, 20.8 ms in REG-to-FTD/TPI sequence (95% CI=1,8-39,8, p=0.62), not estimable in the FTD/TPI-to-REG group. Best 1-y survival rate was 46.1% with FTD/TPI-to-REG sequence vs 36.3% of REG-to-FTD/TPI group. No differences were found for median progression free survival: 5 ms with FTD/TPI-to-REG (95% CI=2,7-7,4) vs 4.1 ms with REG-to-FTD/TPI (95% CI=2,5-5,7) (p=0.78). Partial response was achieved only in 1 out of 11 pts (9.09%) for REG-to-FTD/TPI. Disease control was greater with REG-to-FTD/TPI (54.5%) vs 23.1% of FTD/TPI-REG.

Conclusions: With the limit of the sample size, we conclude that in our real-world experience, both sequences REG-to-FTD/TPI and vice versa could extend survival while only REG-to-FTD/TPI stabilizes cancer growth. Prevalent toxicities seem dependent from the first drug of the sequencing. So it could be important to decide which agent in the sequence should be administered in the beginning.

B21

DRUG-DRUG INTERACTIONS AND PHARMACOGENOMIC EVALUATIONS IN COLORECTAL CANCER PATIENT: THE NEW DRUG-PIN® SYSTEM COMPREHENSIVE APPROACH

Roberto M.[1], Rossi A.[2], Panebianco M.[2], Pomes L.M.[3], Simmaco M.[4], Mazzuca F.[5], Marchetti P.[5]

[1]*Dipartimento di Medicina Clinica e Molecolare, Università "La Sapienza", AOU Sant'Andrea, Roma;* [2]*UOC Oncologia Medica, AOU Sant'Andrea, Roma;* [3]*Department of Neuroscience, Mental Health, and Sensory Organs (NESMOS), Sapienza University; UOD Diagnostica Molecolare avanzata, AOU Sant'Andrea, Roma;* [4]*UOD Diagnostica Molecolare avanzata, AOU Sant'Andrea, Roma;* [5]*Dipartimento di Medicina Clinica e Molecolare, UOC Oncologia, AOU Sant'Andrea, Roma*

Background: Polypharmacotherapy is a relevant issue in cancer patients, since a Drug-Drug Interaction (DDI) condition may affect both treatment efficacy and toxicity. The combination of DDIs and individual genetic polymorphisms, called Drug-Drug-Gene Interaction (DDGI), is a new fascinating concept of personalized medicine. Thus, we present the use of Drug-PIN® (Personalized Interactions Network) software in Patients treated for colorectal cancer (CRC) at our institution.

Material and Methods: From January 2018 we enrolled Patients with i) stage III-IV CRC, ii) ECOG PS ≤ 2, iii)taking at least 5 concomitant drugs, and iv)adequate renal, hepatic, and bone marrow function. Informed consent for DNA extraction and pharmacogenomic analysis was provided before chemotherapy. Toxicity was graded according to Common Terminology Criteria for Adverse Event v4.03. Drug-PIN® is the first intelligent system that recognizes the critical role of multiple interactions between active and/or pro-drug forms by integrating biochemical, demographic, and genomic data of 110 SNPs from each patient. The result of the DDGI analysis is represented by a numerical score: the greater the associated number, the more dangerous drugs cocktail will be. We selected the following scores: i) DDI, resulted from concomitant medications interactions, ii) DrugPin1, resulted from concomitant medications and SNPs profile; iii) DrugPin2, called as global score, resulted from DrugPin1 added to chemotherapy drugs.

Results: Eighteen patients, with a median age of 74 years (range 60-79), 61% male, 56% with a Charlson comorbidity index >8, and taking a median number of 7 concomitant medications (range 5-9) were included in this study. Overall, the median value of DrugPin1 and DrugPin2 was 43 (range 11-180) and 78 (range 17-200), respectively. In 6 (33%) patients the DrugPin2 score was 2-fold higher than DrugPin1 score. Four out of these 6 patients reported severe toxicity that required hospitalization: two for cardiotoxicity, one for profuse diarrhea, and the other one for an allergic reaction to oxaliplatin. At chi-2 test for any toxicity, thyroid hormone replacement therapy (P = 0.034) and a doubled Drugpin2 score (P = 0.001) were significantly related to G3-4 toxicity.

Conclusions: Drug-PIN® could be very useful in the new era of personalized medicine in order to prevent severe adverse events, decrease hospitalizations, and improve survival in cancer Patients. Further confirmatory analyses will be done.

B22

THE SITE OF PRIMARY COLORECTAL CANCER: IMPACT ON SURVIVAL OF LIVER METASTASIS RESECTION AFTER INDUCTION CHEMOTHERAPY

Mancarella S.[1], Poti' O.[2], De Giorgi D.[3], Rizzo A.[4], De Maria G.[5]

[1]PO Santa Caterina Novella ASL Lecce UO Oncologia Medica, Galatina; [2]PO San Giuseppe da Copertino UO Chirurgia, Copertino; [3]PO San Giuseppe da Copertino UO Ghirurgia, Copertino; [4]PO Santa Caterina Novella UO Radiologia, Galatina; [5]PO Santa Caterina Novella UO Oncologia, Galatina

Background: The primary tumor site is currently being evaluated as a prognostic factor in liver metastases of colorectal cancer. In this work we wanted to see the survival between right and left tumors (including the rectum) with liver metastases.

Materials and methods : We evaluated 70 patients with liver metastases over an 8-year period with a minimum follow-up of 24 months. We have included patients with synchronous, methachronic R0 liver resection after induction chemotherapy, and patients with primitive colorectal cancer resection without or partial treatment on liver metastases, R2, and patients with palliative surgery, pulmonary metastases, peritoneal carcinosis (except minimum peritumoral spread). We performed an overall survival analysis on all patients.

Results: We had 34 patients who underwent synchronous and metachronous liver resection. 36 patients underwent resection of primitive with R2 on metastases. We had 12 rectal cancers 14 right colon cancers and 8 left colon cancers in the group of resected R0. We had 8 rectal cancers 10 right colon cancers, 18 left colon colon cancer in the R2 patient group. The mean survival for tumors with R0 liver resection was 32 months for the rectum, 25 months for the right colon, 47 months for the left colon. The mean survival for R2 resections was 18 months for the rectum, 12 months for the right colon, 20 months for the left colon. Analyzing Kaplan Meier curves we see a worse survival of metastatic resected tumors of the rectum compared to the left colon even if not statistically significant p = 0.2. There is instead a survival curve superimposable with tumors of the right colon p = 0.93. The left colon with liver resection R0 has a better survival than the right colon even if not statistically significant p = 0.38. Analyzing the survival between the rectum with hepatic resection R0 vs the rectum with resection R2, the survival in pz with R0 is statistically significant superior p = 0.02., Similarly it occurs in the left colon with high significance p = 0.007. On the right instead, in the comparison between radical surgery and R2 the advantage is obviously for radical surgery p = 0.2 but it does not reach the statistical significance of the rectal / colon left group.

Conclusions: Rectal tumors with liver metastases with R0 resection after induction chemotherapy have a lower survival than left colon cancers resected R0. They have a survival comparable to the cancers of the right colon with resected liver metastasis.

B23

A RETROSPECTIVE STUDY OF SHORTER ADJUVANT OXALIPLATIN-BASED CHEMOTHERAPY FOR HIGH RISK STAGE II AND STAGE III COLON CANCER

Cogoni A.A.[1], Pazzola A.[1], Scotto T.[1], Cuccu A.S.[1], Fadda G.M.[1], Contu M.[2], Erbetta E.[3]

[1]UO Oncologia AOU Sassari, Sassari; [2]CPDI ASSL Sassari ATS Sardegna, Sassari; [3]Medicina e Chirurgia Università di Sassari, Sassari

Background: 6 months adjuvant chemotherapy (CT) with oxaliplatin (OXA) plus fluoropyrimidines (FP) is regarded as the standard treatment for high risk stage II or stage III

resected colon cancer, with the major issue of OXA-related neuropathy. The IDEA metanalysis showed a clear reduction in neuropathy incidence when CT is shortened from 6 to 3 months, but formally failed in demonstrating the non-inferiority of the short regimen versus the standard. Although the loss in 3-years DFS has been only 0.9%, it generated a great debate and many professionals and opinion leaders didn't welcome the 3 months regimen as a new standard. The aim of this retrospective trial is to explore how the reduction of OXA exposure impacts on survival outcomes in clinical practice.

Material and methods: Records of patients treated with OXA-based adjuvant CT for high risk stage II (pT4N0) or stage III (any pT N+) colon cancer at our institution from 2011 to 2015 were collected. Patients were divided into 3 different groups based on the total amount of OXA cycles received: low exposure (A: 1-2 CAPOX cycles or 1-4 FOLFOX cycles); intermediate (B: 3-6 CAPOX cycles or 4-9 FOLFOX cycles); high (C: 7-8 CAPOX cycles or 10-12 FOLFOX cycles). OXA could have been withdrawn for any reason and FP monotherapy withheld. The primary endpoint was to prove the non-inferiority of DFS for B over C, with maximum Δ set to -20%.

Results: The search retrieved full data for 50 patients (60% males, mean age 65 y). The mean dose of OXA delivered was 72,6% of the full dose. The first cause of OXA withdrawal was toxicity, mainly neuropathy. Patient division by OXA exposure was: A = 7 (14%), B = 17 (34%), C = 26 (52%). 3-y DFS for B was 80,7% vs 58,4% for C (Non-inferiority HR 0.41; 90% C.I. 0.14-1.19; p=0.049). OS HR was 0.4 (90% C.I. 0.11-1.46, p=0.21). Multivariate analysis did not show any subgroup significantly associated with survival. The most frequent G3-4 adverse events were diarrhea (4%), neutropenia (4%) and neuropathy (42%). Neuropathy was higher in B than in C (p=0.014).

Conclusions: This study confirmed that adjuvant OXA therapy for high risk stage II/stage III resected colon cancer may be shortened without affecting survival outcomes. The role of FP monotherapy beyond oxaliplatin withdrawal remains unclear.

B24

LYMPH NODE STATUS AFTER PERSONALIZED NEOADJUVANT CHEMO RADIOTHERAPY: COMPARATIVE ANALYSIS ON A MONOINSTITUTIONAL RETROSPECTIVE SERIES WITH FOLLOW-UP AT 2 YEARS

Poti' O.[1], De Giorgi D.[2], Ingrosso D.[3], Marcucci G.[4], Mancarella S.[5]

[1] U.O Chirurgia P.O San Giuseppe Da Copertino ASL Lecce, Copertino, Lecce; [2]U.O. Chirurgia P.O. San Giuseppe Da Copertino ASL Lecce, Copertino; [3]U.O. Chirurgia P.O. Sacro Cuore Gallipoli ASL Lecce, Gallipoli; [4]U.O. Chirurgia P.O. San Giuseppe Da Copertino ASL Lecce, Copertino; [5]U.O. Oncologia Medica P.O. Santa Caterina Novella Galatina ASL Lecce, Galatina

Background: One of the topics of major discussion in conservative surgery of the rectum subjected to neoadjuvant chemo-radiotherapy is the status of the lymph nodes that cannot be performed for the omitted lymphectomy.

Materials and methods: In this work we studied two cases retrospectively over a period of 3 years (2015-2018), concerning the surgery of the rectum subjected to neoadjuvant chemo-radiotherapy. We included in the group A pz cT3, cT4, with each N, M0 who performed a complete cycle of personalized CHRT and who underwent rectal resection with standard lymphectomy and complete excision of the mesorect. In addition, we included patients who had a complete response highlighted on T as a complete pathological response on TEM (transanal resection), with negative lymph node metastasis. in the group B we included patients with middle / high and high rectal neoplasia pT3, T4 with any N and M0 not subjected to neoadjuvant treatments, who performed a standard rectal resection with complete excision of the mesorectum and surgical R0.

Results: In group A we treated 20 patients, obtaining 6 (30%) complete pathological response (3 pCR with resection, 3 pCR with TEM). In 3 (15%) patients in this group there were lymph node metastases, the total number of lymph nodes involved was 4. In three pz with N +, the average ratio (LN ratio) between pathological and LN removed was 2 / 9.2 / 18.1 / 14 (ln ratio 0.2.0.1.0.07 with average 0.12). Regarding tumour (T) it was downstaging in 16 patients, from ypT2 to ypT0,end metastatic lymph nodes were found in 2 pz with ypT3 and 1ypT2. In group B out of 12 patients we had 4 patients with lymph node metastases (equal to 33%), The total number of lymph nodes involved was 18 in the four pz N +. The relationship between pathological and removed lymph nodes (LN ratio) was 15 / 18.1 / 9.1 / 6.1 / 8 (LN ratio, 0.8,0.1,0.6,0.12 with average 0.40) Comparing the two groups, the neoadjuvant CHRT statistically reduced the incidence of lymph node metastases in the population under examination, but also the number of lymph nodes involved in the metastatic process.

Conclusions: Personalized neo-adjuvant therapy allows a significant reduction of lymph node metastases, determining in selected cases a conservative approach to surgical therapy of the rectum. From our evidence, an extension of the neaodiuvamte therapy may also appear indicated even in selected patients with intraperitoneal rectum.

B25

TAS-102 WITH BEVACIZUMAB IN PATIENTS WITH CHEMOREFRACTORY METASTATIC COLORECTAL CANCER. REAL FIFE STUDY

Miano S.[1], Francini G.[2], Petrioli R.[1], Francini E.[3], Martellucci I.[1], Marsili S.[1], Vannini A.[1], Pascucci A.[1]

[1]UOC Oncologia Medica AOUS, Siena; [2]Università degli Studi, Siena; [3]Università degli Studi, Firenze

Background: TAS-102 (trifluridine-tipiracil) has shown a significant overall survival benefit in patients with chemore-fractory metastatic colorectal cancer. According preliminar data of a several studies about the combination of TAS-102 plus bevacizumab in patients with chemorefractory meta-static colorectal cancer, we aimed to evaluate the efficacy of TAS-102 plus bevacizumab in patients in III line therapy for metastatic colorectal cancer in our institution.

Methods: This is a single-arm, open-label, prospective on going trial conducted in UOC Oncologia Medica AOUS. The study regimen comprised 28-day cycles with biweekly oral administration of TAS-102 (35 mg/m^2 twice daily on days 1-5 and 15-19 of every 28-day cycle) and bevaci-zumab (5.0 mg/kg on days 1 and 15). The primary end point is the PFS; secondary end points include response rate (RR), OS, and grade $\geqslant 3$ neutropenia.

The main inclusion criteria were histopathologically con-firmed metastatic colorectal cancer refractory or intolerant to a fluoropyrimidine, irinotecan, oxaliplatin, and cetuxi-mab or panitumumab (only for RAS wild-type), and WHO performance status of 0 or 1. Previous therapy with beva-cizumab, aflibercept, ramucirumab, or regorafenib was allowed but not mandatory.

Findings: From July 24, 2017 15 patients were assigned to TAS-102 plus bevacizumab (n=15). After a median follow-up of 100 months (IQR 6,8 -14,0) median progression-free survival was 4.75 months (3,0-6,5), (hazard ratio 0,45 [95% CI 0,29-0,72]; p=0,0015). The most frequent grade 3 or worse adverse event was neutropenia 10 [67%] of 15 patients treated. No deaths were deemed treatment related.

Interpretation: In patients with chemorefractory meta-static colorectal cancer, TAS-102 plus bevacizumab, was associated with a significant and relevant improvement in progression-free survival with tolerable toxicity. These results are encouraging, we aim to treat more patients to confirm these data. The combination of TAS-102 plus bev-acizumab could be a new treatment option for patients with refractory metastatic colorectal cancer.

B26

BEVACIZUMAB PLUS FOLFOX-4 COMBINED WITH DEEP REGIONAL HYPERTHERMIA AS FIRST-LINE THERAPY IN METASTATIC COLON CANCER: A PILOT STUDY

Gadaleta C.D.[1], Laface C.[1], Laforgia M.[2], De Summa S.[3], Porcelli M.[1], Macina F.[1], Molinari P.[1], Alessandra D.P.[4], Ferrari C.[4], Rubini G.[4], Ammendola M.[5], Ranieri G.[1]

[1]Interventional and Medical Oncology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy; [2]Pharmacology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy; [3]Molecular and Medical Oncology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy; [4]Nuclear Medicine Unit, D.I.M, University of Bari, Bari, Italy; [5]Department of Health Science, Digestive Surgery Unit, University "Magna Graecia" Medical School, Catanzaro, Italy

Background: Bevacizumab plus FOLFOX-4 regimen represents the first-line therapy in patients affected by met-astatic colorectal cancer (mCRC). Hyperthermia has been considered an effective ancillary treatment for cancer ther-apy through several anti-tumour mechanisms, sharing with Bevacizumab the inhibition of angiogenesis. Up to now, scientific literature offers very few clinical data on the combination of bevacizumab plus oxaliplatin-based chem-otherapy with deep regional hyperthermia (DRHT) for metastatic colon cancer (mCC) patients. Therefore, we aimed at evaluating the efficacy of this combination based on the possible interaction between the DRHT and Bevacizumab anti-tumour mechanisms.

Patients and Methods: We conducted a retrospective analysis on 40 patients affected by mCC treated with the combination of Bevacizumab plus FOLFOX-4 (fluoroura-cil/folinic acid plus oxaliplatin) and DRHT (EHY2000), between January 2017 and May 2020. DRHT treatment was performed weekly, with capacitive electrodes at 80-110W for 50 min, during and between subsequent bev-acizumab administrations. Treatment response assessment was performed, according to the Response Evaluation Criteria for Solid Tumors (RECIST). The primary end-points were disease control rate (DCR) and progression-free survival (PFS). The secondary endpoint was overall survival (OS). DCR, counted as the percentage of patients who had the best response rating [complete response (CR), partial response (PR), or stable disease (SD)], was assessed at 90 days (timepoint-1) and at 180 days (timepoint-2).

Results: DCR was 95% and 89,5% at timepoint-1 and timepoint-2, respectively. The median PFS was 12,1 months, whereas the median OS was 21,4 months. No major toxicity related to DRHT was registered; overall, this combination regimen was safe.

Conclusions: Our results suggest that the combined treatment of DHRT with Bevacizumab plus FOLFOX-4 as first-line therapy in mCC is feasible and effective with a favourable dis-ease control, prolonging PFS of 2,7 months with respect to standard treatment without DRHT for mCC patients. Further studies will be required to prove its merit and explore its potentiality especially if compared to conventional treatment.

B27

IRINOTECAN MONOTHERAPY IN PATIENTS WITH HEAVILY PRETREATED MCRC AND POLYMORPHISM OF UGT1A: A SINGLE INSTITUTION CASE SERIES OF MAGNIFICENT BENEFIT

Cito P.[1], Cafiero C.[2], Brunetti A.E.[1], Lasigna M.B.[1], Rinaldi A.[1], Silvano G.[2], Lazzari G.[2], Pisconti S.[2]

[1]Struttura Complessa di Oncologia ASL-Taranto (Po San Pio), Castellaneta (TA); [2]Struttura Complessa di Oncologia ASL-Taranto (Po San Giuseppe Moscati), Taranto

Background: Genetic polymorphism of genes encoding drug-metabolizing enzymes constitutes individual's susceptibility to drugs. UDP-glucuronosyltransferase (UGT) is an enzyme encoded by polymorphic UGT1A and UGT2B genes. The incidence of genetic polymorphisms and associated altered gene functions results in inter-individual variability in metabolic clearance and elimination of drugs. Mutations in the UGT1A1 gene are very common in the south of Italy and have been implicated in Gilbert syndrome and a more aggressive childhood subtype Crigler–Najjar syndrome. Based on the high incidence in our region of subclinical Gilbert syndrome we have decided to look for the presence of UGT polymorphism in patients with heavily pretreated metastatic colon cancer (mCRC) and to administer lower dose of irinotecan as a single-agent for patients known to be homozygous for the UGT1A1*28 allele. Our strategy was designed to investigate the relationship between UGT1A1 polymorphisms and the incidence of adverse events or the therapeutic effect in mCRC patients who received irinotecan.

Material (patients) and methods: In our center three of ten mCRC patients tested for UGT1A polymorphism were homozygous carriers of the UGT1A1*28 allele. In base of FDA recommendations these patients could be treated by reduced dosage of irinotecan based chemotherapy. We started with 70% of the standard dose of be-weekly irinotecan. If the patient didn't tolerate this initial dose, the dose could be decreased.

Results: From November 2017 to January 2019 three patients received lower doses of single agent irinotecan treatment. The median PFS was 14 months. The best radiological response evaluated by CT scan was partial response and the all patients reported great clinical benefit. The incidence rates of typical side effects of irinotecan regimes were very low. The main side effect of asinthomatic neutropenia (grade ≥ 3) and sporadic diarrhea occurred in two of these patients were resolved by exclusive support care without hospitalization.

Conclusions: Although the presence of variants of UGT increase hypothetical risk of irinotecan toxicity, we observed in our clinical practice magnificent clinical benefit and minimal side effects in patients with heavily pretreated metastatic colon cancer receiving a low dose of be-weekly irinotecan regimen. This therapy appears to be effective and seems to be a reasonable option for this setting of patients.

B28

KRAS AND BRAF CONCOMITANT MUTATIONS IN PATIENTS WITH METASTATIC COLON ADENOCARCINOMA

Pisconti S.[1], Cito P.[2], Friscini A.[3], Luccarelli G.[4], Lazzari G.[5], Modoni G.[4], Russo F.[4], Fanelli F.[4], Nenna C.[4], D'alessandro A.R.[4], Pastore C.[4], Galeano T.[4], Broussard C.[4], Nisi C.[4], Bruno M.[4], Silvano G.[5], Leone M.F.[6], Brunetti A.E.[2], Lasigna M.B.[2], Cafiero C.[7]

[1]*Struttura Complessa di Oncologia ASL TA, Ospedale S.G. Moscati, Taranto;* [2]*Struttura Semplice Terapie Oncologiche ASL TA, Ospedale San Pio, Castellaneta; Taranto;* [3]*Struttura Complessa di Oncologia ASL TA, Ospedale S.G. Moscati, Taranto;* [4]*Struttura Complessa di Oncologia ASL TA, Ospedale S.G. Moscati, Taranto;* [5]*Struttura Complessa di Radioterapia Oncologica ASL TA, Ospedale S.G. Moscati, Taranto;* [6]*Direzione Medica Presidio Centrale ASL TA, Ospedale S.S. Annunziata, Taranto;* [7]*Struttura Complessa di Oncoematologia ASL TA, Ospedale S.G. Moscati, Taranto*

Background: Colorectal cancer (CRC) is characterized by several critical genes mutation and altered signaling pathways (e.s WNT, RAS, MAPK, PI3K) important in the initiation and tumor progression. The most frequent mutations in CRC are missense with gain of function in KRAS and BRAF. Of note, about 50-60% of colorectal cancers are mutated in the KRAS gene, indicating that up to 40% of patients with colorectal cancer (CRC) could respond to antibody therapy with the anti-epidermal growth factor receptor (EGFR). However, 40% of patients with wild-type KRAS primary tumors do not respond to this therapy. In these patients, data suggest that the mutated BRAF gene, occur in 5-10% of tumors, may influences responsiveness to the therapy. Herein we investigated the presence of BRAF mutation in addition to KRAS analysis.

Materials and Methods: We describe three cases of metastatic colorectal cancer (mCRC) with rapid progression of disease: patients (1M/2F, age range 60-70 years old) were admitted to the " S.G. Moscati Hospital" of Taranto. After obtaining informed consent, patients were subjected to liver biopsy. The EGFR immunohistochemical expression was investigated by immunohistochemistry (anti-EGFR monoclonal antibody) and by molecular analysis of KRAS and BRAF mutations.

Results: Hematoxylin and eosin slides were reviewed by the pathologist to confirm the diagnosis (mCRC) and select the best representative area of tumor for DNA extraction. The molecular analysis showed the coexistence of KRAS and BRAF mutations in hepatic metastases and the presence of the BRAF V600E mutation alone in the primary tumor of our patients.

Conclusions: Patients affected by mCRC, as considered for therapy with anti-EGFR antibodies, should be tested for the presence of KRAS mutation prior to therapy. It is unclear whether the lack of response in wild-type KRAS CRC is due to BRAF mutations, but the data suggest that mutated BRAF confers resistance to anti-EGFR therapy administered beyond first-line treatment. In our patients the BRAF mutation in primary tumor turned out to be a negative prognostic factor. Additional studies are required to determine the clinical-pathological effect of KRAS and BRAF simultaneous mutations on the CRC disease course and treatment outcome, and for better management of these patients.

C - Gastrointestinal (non-Colorectal) Cancers

C01*

UPDATED RESULTS FROM THE RANDOMIZED PHASE 2 TRIAL OF AVELUMAB ALONE OR WITH CETUXIMAB FOR UNRESECTABLE, LOCALLY ADVANCED OR METASTATIC SQUAMOUS CELL ANAL CARCINOMA PROGRESSED TO AT LEAST ONE LINE OF TREATMENT: THE CARACAS STUDY

Prete A.A.[1], Pietrantonio F.[2], Messina M.[3], Formica V.[4], Corsi D.C.[5], Cortesi E.[6], Frassineti G.L.[7], Zampino M.G.[8], Ronzoni M.[9], Scartozzi M.[10], Casagrande M.[11], Conca V.[12], Bergamo F.[1], Prisciandaro M.[2], Daniel F.[1], Pagani F.[2], Magni G.[1], Vettore V.[1], Zagonel V.[1], Lonardi S.[1]

[1]Veneto Institute of Oncology IOV – IRCCS, Padua; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; [3]Fondazione Istituto G. Giglio, Cefalù; [4]Tor Vergata University Hospital of Rome, Rome; [5]San Giovanni Calibita Fatebenefratelli, Rome; [6]Sapienza University of Rome, Rome; [7]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [8]European Institute of Oncology IRCCS, Milan; [9]Ospedale San Raffaele, Milan; [10]University Hospital, University of Cagliari, Cagliari; [11]Azienda Sanitaria Universitaria Integrata di Udine, Udine; [12]Azienda Ospedaliera Universitaria Pisana, Pisa

Background: Advanced squamous cell anal carcinoma (advSCAC) is a rare disease and no standard therapies beyond first line are currently available.

Data from retrospective case series and phase I and II prospective studies respectively suggest activity of the anti-EGFR cetuximab (CET) and of immunotherapy in advSCAC after the first line.

In this study, we evaluated activity and safety of avelumab (AVE) alone or in combination with CET in pretreated advSCAC.

Material (patients) and methods: In this open-label, "pick the winner", prospective, multicenter randomized phase 2 trial (NCT03944252), patients (pts) with mSCAC with documented progressive disease after at least 1 line of treatment were randomized 1:1 to receive either AVE (arm A) or AVE plus CET (arm B). Primary endpoint was overall response rate (ORR). According to the Simon's two-stage Mini-Max design used, the null hypothesis that the true response rate was 5% (p = 0,05) was tested against the alternative of a true response rate of 20% (p1= 0,20) in each arm. Type I error rate was set at 0,05.

No formal comparison was allowed between the two arms. Secondary endpoints were PFS, OS and safety

Results: 30 pts were enrolled in each arm, for a total of 60. Median age was 63 years; M/F was 19/41. All baseline characteristics were well balanced between the arms.

At a median follow up of 11 months, ORR was 10% (95% CI 2.5 - 27) in arm A and 17% (95% CI 6.3 – 34,1) in arm B: with 5 patients achieving PR in arm B, the primary endpoint was reached in this arm. Disease control rate (DCR) was 50% (95% CI 35.3 – 71.3) in arm A and 57 (95% CI 42.4 – 77.6) in arm B.

Median PFS was 2.05 months (95% CI 1.84 – 5.52) in Arm A and 3.88 months (95% CI 2.07 – 6.14) in Arm B. Median OS data are not yet mature.

The most common treatment related adverse event (TRAE) was fatigue in Arm A (17% of patients) and skin toxicity in arm B (87% of patients); no permanent interruptions due to TRAE were observed in arm A while 2 patients (7%) in arm B permanently interrupted the treatment due to TRAE

Conclusions: The CARACAS study met its primary endpoint in the arm B, documenting promising activity of EGFR and PD-L1 blockade in advSCAC; this strategy deserves further investigation. Favorable safety profile was observed in both the arm.

C02*

REAL-LIFE ITALIAN EXPERIENCE WITH PERIOPERATIVE FLOT FOR RESECTABLE GASTRIC CANCER: RESULTS OF PROSPECTIVE OBSERVATIONAL REALFLOT STUDY

Giommoni E.[1], Lavacchi D.[1], Tirino G.[2], Fornaro L.[3], Iachetta F.[4], Pozzo C.[5], Satolli M.A.[6], Spallanzani A.[7], Puzzoni M.[8], Stragliotto S.[9], Sisani M.[10], Formica V.[11], Giovanardi F.[12], Strippoli A.[5], Prisciandaro M.[13], Di Donato S.[14], Pecora I.[3], Romagnani A.[4], Pillozzi S.[1], De Vita F.[2], Antonuzzo L.[1]

[1]Clinical Oncology Unit, AOU Careggi, Firenze; [2]Division of Medical Oncology, Department of Precision Medicine, University of Study of Campania "L. Vanvitelli", Napoli; [3]Medical Oncology, Azienda Ospedaliero-Universitaria Pisana, Pisa; [4]Medical Oncology Unit, Clinical Cancer Center, AUSL-IRCCS, Reggio Emilia; [5]Medical Oncology, Fondazione Policlinico Universitario "A. Gemelli", IRCCS, Roma; [6]Department of Medical Oncology, University of Turin, Torino; [7]University Hospital of Modena, Modena; [8]Medical Oncology Department, University Hospital, University of Cagliari, Cagliari; [9]Oncology Unit - Dipartimento di Oncologia Clinica e Sperimentale Istituto Oncologico Veneto IOV-IRCCS, Padova; [10]Medical Oncology, Usl Toscana Sudest, Arezzo; [11]Internal Medicine Department, Roma; [12]Medical Oncology, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia; [13]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [14]Medical Oncology, Department Nuovo Ospedale-Santo Stefano Istituto Toscano Tumori, Prato

Background: Perioperative chemotherapy significantly improved survival in patients with resectable gastric cancer (GC), increasing 5-year overall survival (OS) from 23% with surgery alone to 45% with FLOT (5-fluorouracil, oxaliplatin, docetaxel) regimen.

Methods: RealFLOT is an Italian, multicentric observational study, designed to describe the feasibility and activity, in terms of pathological responses and survival, of perioperative FLOT in a real-world patient population with resectable gastric or gastro-oesophageal junction (GEJ) adenocarcinoma treated as clinical practice, and according to inclusion criteria of FLOT4-AIO trial. We also evaluated the prognostic role of microsatellite instability (MSI) status in a soubgroup of patients.

Results: Between September 2016 and September 2019, a total of 206 patients received perioperative FLOT at 15 Italian centers: of those, 24 (60.2%) received FLOT for at least 4 full-dose cycles, 190 (92.2%) underwent surgery, and 142 (68.9%) started the postoperative phase. Among patients who started the postoperative phase, 105 (51.0%) received FLOT, while 37 (18%) received de-intensified regimens (e.g. FOLFOX or 5FU/LV). The main reasons for de-intensifying postoperative treatment were mainly the deterioration of clinical conditions after surgery and the toxicities experienced in the preoperative phase. Pathological complete response (pCR) was obtained in 7.3% of patients. Safety profile was consistent with literature. Neutropenia was the most commonly reported G 3-4 adverse events (AE), affecting 19.9% of patients in the preoperative phase and 16.9% of those who started the postoperative phase. No toxic death was observed and 30-day postoperative mortality rate was 1.0%.Furthermore, FLOT regimen exhibited similar tolerability also in elderly patients (≥65 years). MSI status was available for 93 patients and 9.7% were MSI-H. A trend towards better disease-free survival (DFS) was observed among MSI-H patients.

Conclusions: Perioperative FLOT is standard of care in Italy for patients with resectable gastric or GEJ adenocarcinoma. These real-world data confirm the feasibility of perioperative FLOT in a less-selected population, representative of the clinical practice. Pathological CR rate was lower than expected, nevertheless we confirm pCR as a predictive parameter of survival. In addition, MSI-H status seems to be a positive prognostic marker also in patients treated with taxane-containing triplets.

C03*

GUIDELINE APPLICATION IN REAL WORLD: MULTI-INSTITUTIONAL BASED SURVEY OF ADJUVANT AND FIRST LINE PANCREATIC DUCTAL ADENOCARCINOMA TREATMENT IN ITALY: THE GARIBALDI TRIAL. PRELIMINARY RESULTS

Reni M.[1], Bergamo F.[2], Giommoni E.[3], Di Marco M.C.[4], Cordio S.[5], Bernardini I.[6], Cardellino G.G.[7], Spada M.[8], Milella M.[9], Luppi G.[10], Silvestris N.[11], Maiello E.[12], Bozzarelli S.[13], Giordano M.[14], Cavanna L.[15], Ghidini M.[16], Peretti U.[1], Valente M.M.[1], Torri V.[17], Porcu L.[17], Giugliano V.[17]

[1]IRCCS San Raffaele, Milano; [2]IRCCS Istituto Oncologico Veneto, Padova; [3]AOUC Azienda Ospedaliero-Universitaria Careggi, Firenze; [4]Ospedale Policlinico Sant'Orsola Malpighi, Bologna; [5]Ospedale Maria Paternò Arezzo, Ragusa; [6]Ospedale Ramazzini di Carpi e Mirandola, Carpi (MO); [7]Azienda Sanitaria Università Integrata di Udine, Udine; [8]Fondazione Istituto Giglio, Cefalù; [9]Azienda Ospedaliera Universitaria Integrata Verona, Verona; [10]Azienda Ospedaliera Universitaria di Modena, Modena; [11]IRCCS Istituto Tumori "Giovanni Paolo II", Bari; [12]Istituto Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG); [13]IRCCS Istituto Clinico Humanitas, Milano; [14]ASST-lariana, Como; [15]Azienda Ospedale Civile, Piacenza; [16]ASST Cremona, Cremona; [17]Istituto Mario Negri, Milano

Background: Limited prospective information is available about therapeutic management of patients (pts) with Pancreatic Ductal Adenocarcinoma (PDAC) and on adherence to Scientific Societies Guidelines in the 'real world' out of clinical trials. The aim of this national, observational, multicenter, prospective trial is to describe the therapeutic management for pts with PDAC and evaluate the agreement with recommendations provided by the Italian Association of Medical Oncology (AIOM 2017).

Methods: Participating institutions were selected to adequately represent different geographical and expertise areas (high-volume with >50 pts treated /year; medium-volume with 25-50 pts treated /year; low-volume with <25 pts treated /year). The attending physician indicated treatment without restrictions. Since December 2017, treatment-naïve consenting pts, > 17-year, with pathological diagnosis of PDAC were enrolled and grouped in 3 settings: 1) receiving adjuvant therapy after resection; 2) receiving primary chemotherapy; 3) metastatic.

Here we present the results of pts accrued until October 31st 2019.

Results: 659 eligible pts were enrolled in 43 Italian centers: Nord 494 (75%), Centre 84 (13%), South 81 (12%); high-volume 431 (66%); medium volume 121 (18%); low-volume 107 (16%). Home to hospital distance was ≤50 km for 88% of pts. Median age was 69 (range 36-89); 52% male; 93% ECOG PS 0-1; clinical stage: 8% I, 15% II, 25% III, and 52% IV.

Guidelines adherence was 74% for group 1 (N=148); 97% for group 2 (N=174); 98% for group 3 (N=337). The most frequently administered regimens were gemcitabine (G) 39%; nab-paclitaxel + G (AG) and FOLFIRINOX 21% each in group 1; AG 57%; FOLFIRINOX 26%; G 13% in group 2; AG 74%; G 16%; FOLFIRINOX 6% in group 3. The interval between symptoms and diagnosis was < 15 days in 85% of pts and > 1 month in 8%. The time between diagnosis and start of treatment was < 15 days in 67% of pts and > 1 month in 15%. The 1st physician involved by the pt was the general practitioner (32%), emergency doctor (20%), internal medicine (15%), surgeon (15%; in metastatic disease=14%), gastroenterologist (12%), oncologist 0.5%.

Conclusions: The data of our study, whose enrollment is ongoing, show a very high rate of adherence with some attrition in the adjuvant setting. Data on interval between symptoms-diagnosis-treatment start are reassuring. The oncologist is a neglected specialist in Italian culture of cancer.

C04

COMPARATIVE EFFICACY OF CABOZANTINIB AND REGORAFENIB FOR ADVANCED HEPATOCELLULAR CARCINOMA

Daniele B.[1], Kelley R.K.[2], Mollon P.[3], Blanc J.[4], Yau T.[5], Cheng A.[6], Valcheva V.[3], Marteau F.[3], Guerra I.[7], Abou-Alfa G.K.[8]

[1]Ospedale del Mare, Naples, Italy; [2]UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [3]Ipsen Pharma, Boulogne-Billancourt, France; [4]Hôpital Haut-Lévêque, CHU de Bordeaux, Bordeaux, France; [5]University of Hong Kong, Hong Kong; [6]National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan (Republic of China); [7]IQVIA Ltd, London, UK; [8]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Background: Cabozantinib and regorafenib are approved for the second-line treatment of advanced hepatocellular carcinoma (aHCC). As no trials have compared the drugs directly, this matching-adjusted indirect comparison (MAIC) evaluated the efficacy and safety of cabozantinib and regorafenib in patients with progressive aHCC after prior sorafenib.

Methods: The phase 3 CELESTIAL and RESORCE trials were used for the analysis. Population-level data were available for RESORCE, individual patient data (IPD) for CELESTIAL. To align with RESORCE, the CELESTIAL population was limited to patients who received first-line sorafenib only. To minimize potential effect-modifying population differences, the CELESTIAL IPD were weighted to balance the distribution of clinically relevant baseline characteristics with those of RESORCE. Overall survival (OS) and progression-free survival (PFS) were evaluated for the matching-adjusted second-line CELESTIAL population and compared to those for RESORCE using weighted Kaplan-Meier (KM) curves and parametric modelling. Grade 3/4 treatment-emergent adverse events affecting > 5% of patients in any trial arm were compared.

Results: The MAIC included 573 RESORCE patients and an effective sample size of 266 from CELESTIAL. Weighted KM estimates for median (95% confidence interval [CI]) OS were similar for the matching-adjusted cabozantinib and regorafenib populations (11.4 [8.9–17.0] vs. 10.6 [9.1–12.1] months; $p = 0.3474$, log-rank test). Estimated median (95% CI) PFS was longer for cabozantinib than regorafenib (5.6 [4.9–7.3] vs. 3.1 [2.8–4.2] months; $p = 0.0005$, log-rank test). As visual inspection of the log-cumulative hazard plots for OS and PFS revealed non-parallelism, and statistical tests confirmed that the proportional hazards assumption was not satisfied, anchored hazard ratios were not justified. Parametric models were therefore fitted, and generated survival estimates mirroring those of the weighted KM analysis. Comparative estimates for some grade 3/4 TEAEs were affected by low incidence; only rates of grade 3/4 diarrhea were significantly different, favouring regorafenib ($p \leq 0.001$).

Conclusions: Cabozantinib may achieve similar OS and prolonged PFS compared with regorafenib in patients with progressive aHCC after prior sorafenib; grade 3/4 diarrhea rates maybe lower with regorafenib. MAIC analyses cannot replace randomized clinical trials, but may help to guide decision making in the absence of direct trial evidence.

C05

PROGNOSTIC ROLE OF PECS2 INDEX IN ADVANCED BILIARY TRACT CANCER (BTC) PATIENTS TREATED WITH FIRST LINE CHEMOTHERAPY: TRAINING AND VALIDATION COHORTS

Rovesti G.[1], Leone F.[2], Brandi G.[3], Cesario S.[4], Scartozzi M.[5], Niger M.[6], Yoo C.[7], Caputo F.[1], Filippi R.[8], Casagrande M.[9], Silvestris N.[10], Santini D.[11], Faloppi L.[12], Aglietta M.[13], Cho H.[7], Lai E.[5], De Braud F.[6], Aprile G.[14], Orsi G.[15], Cascinu S.[15], Casadei Gardini A.[1]

[1]Department of Oncology and Hematology, Division of Oncology, University Hospital of Modena, Modena; [2]Division of Medical Oncology, Nuovo Ospedale degli Infermi, Ponderano (BI); [3]Oncology Unit, Sant'Orsola Malpighi Hospital, University of Bologna, Bologna; [4]Medical Oncology Unit, Pisa University Hospital, Pisa; [5]Medical Oncology, University Hospital of Cagliari, Cagliari; [6]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano; [7]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul (Republic of Korea); [8]Department of Oncology, Centro Oncologico Ematologico Subalpino, Azienda Universitaria Ospedaliera Citta` della Salute e della Scienza di Torino, Torino; [9]Medical Oncology Unit, Azienda Ospedaliero Universitaria Santa Maria della Misericordia, Udine; [10]Medical Oncology Unit, IRCCS Istituto Tumori "Giovanni Paolo II", Bari; [11]Medical Oncology Department, Campus Biomedico University, Roma; [12]Oncology Unit, Macerata Hospital, Macerata; [13]Department of Oncology, Candiolo Cancer Institute, FPO-IRCCS, Candiolo (TO); [14]Department of Clinical Oncology ULSS8 Berica, Vicenza; [15]Department of Medical Oncology, Universita` Vita- Salute, San Raffaele Hospital IRCCS, Milano

Background: Validated prognostic indexes are essential for BTC. We previously set up the PECS index(PsECogSii), made of PS ECOG and Systemic Inflammatory Index. To improve its risk-stratification power, we created the PECS2 index made of PECS, Prognostic Nutritional Index (PNI) and GOT. The aim of this study is to evaluate PECS2 index as prognostic factor in unresectable locally advanced or metastatic BTC patients treated with first-line chemotherapy.

Material and methods: The study was retrospectively conducted on a training cohort of 126 BTC patients from Modena CancerCenter. A first validation cohort of 457 patients was recruited by 13 Italian CancerCenters, a second one of 76 patients by University of Cagliari and Istituto Nazionale dei Tumori of Milan and a third one of 256 patients by ASAN medical Center in Republic of Korea. The PECS2 index was calculated as PECS+PNI+GOT (PECS:0=1point; PECS:1=1.4points; PECS:2=3.2points) + (PNI>36.7=1point; PNI<36.7=2points) + (GOT<100= 1point; GOT>100=2points). Patients were categorized into three groups: PECS2-0 (value<3.5 points), PECS2-1 (value>3.5points; <5.4points), PECS2-2 (value>5.4points). Event-time distributions were estimated using the Kaplan-Meier method and survival curves were compared using the log-rank test.

Results: In the training cohort, median overall survival (mOS) was 12.9 months,6.3 months and 2.8 months for PECS2-0,PECS2-1 and PECS2-2, respectively (PECS2-0:HR=1; PECS2-1:HR 2.11,95% IC 1.34-3.31; PECS2-2:HR 4.93,95% IC 1.85-13.12; p<0.0001). The Harrell's C

between PECS and PECS2 increased from 0.69 to 0.78 (95% CI:0.68–0.87) (p=0.001). In the first validation cohort, mOS was 11.5 months,7.3 months and 3.3 months for PECS2-0,PECS2-1 and PECS2-2, respectively (PECS2-0:ref HR=1; PECS2-1:HR 1.74,95% CI 1.36-2.22; PECS2-2:HR 3.41,95% CI 2.20-5.29; p<0.0001). In the second validation cohort, mOS was 25.2 months,12.5 months and 3.0 months for PECS2-0,PECS2-1 and PECS2-2, respectively (PECS2-0:ref HR=1; PECS2-1:HR 2.33, 95% CI 1.32-4.13; PECS2-2:HR 8.46, 95% CI 1.50-47.7; p<0.0001). In the third validation cohort, mOS was 11.8 months, 8.1 months and 4.6 months for PECS2-0,PECS2-1 and PECS2-2, respectively (PECS2-0:ref HR=1; PECS2-1:HR 1.47,95% CI 1.06-2.03; PECS2-2:HR 3.17, 95% CI 1.45-6.88; p<0.0001). Multivariate analysis in all cohorts confirmed the PECS2 index as an independent prognostic factor for OS.

Conclusions: The low cost, easy assessment, reproducibility and good risk-stratification performance make PECS2 index a promising tool to assess BTC patients' prognosis in future clinical practice.

C06

THE ROLE OF RESPONSE AS PREDICTOR OF IMPROVED OUTCOME IN ADVANCED PANCREATIC CANCER (APC) PATIENTS (PTS) TREATED WITH FIRST-LINE GEMCITABINE PLUS NAB-PACLITAXEL (GEMNAB)

Ribelli M.[1], Bensi M.[2], Di Stefano B.[2], Bagalà C.[2], Spring A.[2], Chiaravalli M.[2], Camarda F.[2], Maratta M.G.[2], Tortora G.[2], Salvatore L.[2]

[1]*Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Roma;* [2]*Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Rome*

Background: GemNab is one of the first-line standard treatment (tx) of APC. No predictive factors, both clinical and molecular, of benefit from this regimen exist. Two retrospective studies showed that early tumor shrinkage (ETS) can predict an improved outcome in APC pts receiving a first-line tx with FOLFIRINOX or GemNab. However, data regarding GemNab, limited to a small population of only 57 pts, seem to not confirm the association of ETS with a better outcome. We retrospectively analysed an homogeneous population of APC treated with first-line GemNab at our Institution, investigating the impact of several clinical factors, including response and ETS.

Methods: APC pts receiving a first-line tx with GemNab were included in the analysis. The association of RECIST response and ETS with PFS and OS was evaluated. The following variables were collected: gender; age (> vs = 55 years and = vs < 70 years); baseline ECOG PS; Ca 19.9

baseline level (= vs < 200); anamnesis of diabetes; site of primary tumor (head/uncinate process vs body/tail); locally A vs metastatic (m) PC; synchronous vs metachronous; number of m sites (1 vs >1); m sites (liver, peritoneum, lung, nodes); number of tx lines (1 vs >1). Univariate and multivariate analyses for PFS and OS were performed.

Results: A total of 184 APC pts receiving first-line GemNab at our Institution from February 2014 to May 2019 were included in the analysis. RR and ETS were assessed in 174 and 168 pts, respectively. RR was 30%, disease control rate (DCR) 63% and ETS was 24%. Responders had a significant better PFS (12.5 vs 5.7 months, p < 0.0001) and OS (25.1 vs 12.1 months, p < 0.0001). ETS was associated with improved PFS (12.3 vs 6.2 months, p < 0.0001) and OS (24.0 vs 12.8 months, p < 0.0001). At the multivariate analysis a significant association with survival parameters was confirmed for RECIST response, but not for ETS. At the multivariate analysis, also metachronous disease and number of tx lines >1 were independently associated with better OS.

Conclusions: Despite its retrospective nature, this is one of the largest series of APC pts treated with first-line GemNab investigating the role of RECIST response and ETS in predicting outcome. On the basis of our results, RECIST response may be considered a positive prognostic factor, whereas ETS does not. In conclusion, achieving tumor shrinkage, not necessarily early, significantly delays PC progression and prolongs survival in pts treated with first-line GemNab.

C07

MMR, PD-L1 AND EBV STATUS IN ADVANCED GASTRIC CANCER (AGC): PREVALENCE, CLINICOPATHOLOGIC FEATURES AND TREATMENT RESPONSE

Riggi M.L.[1], Salati M.[2], Bocconi A.[2], Rimini M.[2], Riccò B.[2], Santini C.[2], Canino F.[2], Rovesti G.[2], Caputo F.[2], Reggiani Bonetti L.[2], Benatti S.[2], Casade Gardini A.[2], Gelsomino F.[2], Luppi G.[2], Dominici M.[2], Spallanzani A.[2]

[1]*Azienda Ospedaliero-Universitaria di Modena, Modena;* [2]*Azienda Ospedaliero - Universitaria Modena, Modena*

Background: Recent reports provided initial evidence on the clinical exploitation of the TGCA classification, suggesting MSI-h and EBV-positive as predictors of response to immune checkpoint blockade (ICI). Moreover, incremental PD-L1 expression has been correlated to higher chance of benefit from ICI. However, the exact prevalence of these biomarkers as well as their association with clinicopathologic features and treatment response is largely unknown in the real-world setting.

Methods: Pretreatment tumour tissue of AGC followed at our Institution between January 2016 and April 2020 were

evaluated for: MMR, EBV, and PD-L1 status. HER-2 status was also tested according to guidelines. Pts treated with at least one line of chemotherapy (1L) and having at least one biomarker tested were eligible. Chi-square and t-student test were used to assess the association between categorial and continue variables of interest.

Results: A total of 87 AGC were included in the analysis The median age was 66 years and 62% (n=54) were males. 83% (n=72) presented with novo AGC and 84% (n=73) had an ECOG PS of 0-1. 18/87 (21%) had HER-2 positive AGC, all with pMMR status. dMMR was detected in 6/87 (6.8%) pts, showing an older median age at diagnosis (68 vs 64 years; p=0.04). While all dMMR pts had nodal involvement, no differences in number of metastatic sites nor in biochemical parameters were recorded (p=0.85) between dMMR and pMMR pts. All dMMR pts received 1L without achieving an objective response and 2/6 (33%) experienced early progression. 3/6 (50%) were treated with ICI in later lines and 2/3 (67%) achieved a durable and still ongoing benefit with a median duration of response of 10.5 months. EBV-positivity was detected in 4/87 (4.5%) of pts and all of them obtained a clinical benefit with chemotherapy (3 PR and 1 SD). PD-L1 CPS was available for 29/87 pts (33%), 65% (n=19) displaying CPS $\geq$ 1 and 19% (n=5) CPS $\geq$ 10. No pts in both EBV- and PD-L1 positive group were treated with ICI.

Conclusions: We reported one of the first real-world characterization of MMR, EBV and PD-L1 status in a well-annotated cohort of AGC receiving systemic treatment. While dMMR tumours confirmed to benefit from ICI and not from chemotherapy, EBV-positive AGC achieved a significant disease control with cytotoxics. Although limited by its small sample size, this study provided a piece of evidence on the clinical utility and feasibility of MMR, EBV and PD-L1 testing in daily practice.

C08

THE IMPACT OF CT-BASED BODY COMPOSITION PARAMETERS ON SURVIVAL OUTCOMES IN WESTERN PATIENTS (PTS) WITH RESECTED GASTRIC AND GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA (GEA) TREATED WITH ADJUVANT CHEMOTHERAPY

Santini C.[1], Salati M.[1], Pecchi A.[1], Prampolini F.[1], Kaleci S.[2], Canino F.[1], Benatti S.[1], Casadei Gardini A.[1], Gelsomino F.[1], Luppi G.[1], Torricelli P.[2], Dominici M.[2], Spallanzani A.[1]

[1]Azienda Ospedaliero-Universitaria di Modena, Modena; [2]Università degli Studi di Modena e Reggio Emilia, Modena

Background: Sarcopenia is a multifactorial syndrome defined by progressive and generalized loss of skeletal muscle mass, reduction of strength and physical performance which has been increasingly correlating with impaired cancer patient outcomes. High accuracy and reproducible results make CT one of the gold standard for body composition measurement. We aimed at assessing the impact of CT-based body composition parameters on the survival outcomes of resected GEA.

Methods: cT3-T4 and/or N-positive GEA pts undergoing curative-intent resection followed by adjuvant chemotherapy at our Institution between 2008-2018 were eligible. Presurgical clinicopathologic, biochemical, and antropometric data were retrospectively retrieved, while body composition parameters and its deltas were derived by CT scan using GE Healthcare AW VolumeShare 7 software. Univariate and multivariate analyses for DFS and OS were performed.

Results: A total of 107 pts were included in the analysis. Median age was 66.1 years (range 20-85), 61 (57%) were males. 45 pts (42.1%) had stage II, while 62 pts (57.9%) had stage III. Mean preoperative BMI was 23.9 kg/m^2. CT scans were performed presurgically and from 4 to 15 months after resection. In the whole population, the 3-year DFS and OS were 48% and 49%, respectively. Out of 27 tested covariates, baseline IntraMuscular Adipose tissue Content (IMAC), together with ECOG PS and disease stage, was significantly associated with DFS (HR 1,97; p=0.03) and OS (HR 1,77; p=0.04) at the multivariate analysis. Specifically, pts with high baseline IMAC ($\geq$ -0.42) had a shorter 3-year DFS (35% vs 62%, p<0,018) and 5-year OS (32% vs 55%, p=0,037).

Conclusions: We showed for the first time that presurgical IMAC, which reflects the quality of skeletal muscle, was an independent predictor of survival in resected GEA. This easy-to-calculate and largely available CT-derived parameter, may identify high-risk patients in need for a prompt and tailored nutritional intervention aimed at improving patients' outcome.

C09

REAL-LIFE CLINICAL DATA OF CABOZANTINIB FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA

Tovoli F.[1], Dadduzio V.[2], De Lorenzo S.[3], Garajovà I.[4], Marra F.[5], Trevisani F.[6], Pini S.[7], Granito A.[1], Zagonel V.[2], Brandi G.[3], Piscaglia F.[1]

[1]University of Bologna, Department of Medical and Surgical Sciences, Unit of Internal Medicine, Bologna; [2]Istituto Oncologico Veneto, Padova; [3]University of Bologna, Department of Experimental, Diagnostic and Specialty Medicine, Unit of Oncology, Bologna; [4]AOU Parma, Oncology Unit, Parma; [5]University of Florence, Firenze; [6]University of Bologna, Department of Medical and Surgical Sciences, Unit of Semiotics, Bologna; [7]AUSL Romagna, Rimini

Background: Cabozantinib (CABO) has been approved by the European Medicine Agency (EMA) as a second or third-line therapy for hepatocellular carcinoma (HCC) previously treated with sorafenib. CABO is also being tested

in combination with immune checkpoint inhibitors in the frontline setting. Real-life clinical data of CABO for HCC are lacking, as its approval by most national drugs agencies is still pending. In Italy, the manufacturing company can currently provide CABO for HCC patients with no therapeutic alternatives, after individual request by physicians, in the legal context of named patient use.

Patients and methods: We evaluated clinical data and outcome of HCC patients who received CABO in the mentioned context in different Italian centres.

Results: Fifty-two patients from 7 centres received CABO according to EMA recommendations (median follow-up: 7.1 months). All patients had preserved liver function (Child-Pugh A), mostly with an advanced HCC (80.8%) in a third-line setting (88.0%). Prevalence of performance status>0, macrovascular invasion, extrahepatic spread, and alfa-fetoprotein>400 ng/ml was 42.3, 34.6, 75.0, and 38.5%, respectively. Median overall survival was 12.9 months (95% CI 8.7-17.1). Median progression-free survival was 5.1 months (95% CI 2.7-7.5). Disease control rate was 59.2% with no objective responses. Most common treatment-related adverse events (AEs) were: fatigue (75.0%), diarrhoea (59.6%), anorexia (44.2%), HFSR (42.3%), weight loss (28.8%), hypertension (26.9%), abdominal pain (23.1%), dysphonia (17.3%), ALT increase (17.3%), hypothyroidism (13.5%), nausea (13.5%), mucositis (13.5%),thrombocytopenia (11.5%), skin rash (11.5%). Most common treatment-related Grade 3-4 AEs were: fatigue (9.6%), HFSR (7.7%), hypertension (5.8%), ALT increase (5.8%). No treatment-related deaths were observed. Serious AEs included: liver failure (n=1), pulmonary embolism (n=1), cerebral haemorrhage (n=1). Most patients (78.8%) required temporary drug stops. Permanent reduction to 40 or 20 mg/day was needed in 46.2% and 17.3% of patients, respectively. Rate of permanent discontinuation for intolerance was 17.3%.

Conclusions. In a real-life Western scenario (mostly in a third-line setting) CABO maintained efficacy data comparable with those reported in its registrative trial. Also, the safety profile was acceptable with no new signals.

C10

METASTATIC PANCREATIC CANCER: THE PROGNOSTIC ROLE OF CAVEOLIN-1

Pecci F.[1], Bittoni A.[1], Mentrasti G.[1], Pellei C.[1], Zizzi A.[2], Mandolesi A.[2], Piva F.[3], Murrone A.[1], Cantini L.[1], Crocetti S.[1], Meletani T.[1], Baleani M.G.[1], Copparoni C.[1], Lupi A.[1], Lenci E.[1], Giglio E.[1], Giampieri R.[1], Berardi R.[1]

[1]Clinica Oncologica, Università Politecnica delle Marche, AOU Ospedali Riuniti, Ancona; [2]Anatomia Patologica, Università Politecnica delle Marche, AOU Ospedali Riuniti, Ancona; [3] Università Politecnica delle Marche, Ancona

Background: Pancreatic cancer (PC) detains a dismal prognosis, showing a 5-year survival rate of 5%. The detection of potentially prognostic biomarkers is needed to better stratify patient risk in the palliative setting. Preclinical studies demonstrated Caveolin-1 (Cav-1) role as enhancer of tumour invasiveness, promoting epithelial-to-mesenchymal transition. We aim to investigate the impact of Cav-1 on outcome of metastatic PC patients (pts) treated with first-line chemotherapy.

Material and methods: Twenty-five tissue samples, both liver metastasis and primary PC, were collected retrospectively in our Institution. Tissue Caveolin-1 (Cav-1-T) evaluation was performed by immunohistochemistry (IHC). In the prospective cohort Cav-1 expression was assessed in circulating exosomes. Data concerning response to treatment, overall survival (OS) and progression free survival (PFS) were available for 16 pts and 8 pts of the retrospective and prospective cohorts respectively, and were calculated by Kaplan-Meier method. Survival differences were assessed by log-rank test. Association between categorical variables was performed by Chi-square test. Level of statistical significance alpha was set at 0.05.

Results: Median OS (mOS) and median PFS (mPSF) of the retrospective cohort were 11 and 4.5 months, whereas the mOS and mPFS of the prospective cohort were 11.04 and 6.16 months. Negative (grade 0-1) IHC Cav-1-T staining was observed in 12 primary tumors samples, intermediate (grade 2) in 5 metastases and 4 primary samples, high (grade 3) in 4 metastases. Differences in Cav-1-T staining between primary tumors and liver metastases were statistically significant (p=0.0001). Cav-1-T positive pts (9/16) had worse mOS compared to Cav-1-T negative ones (9.93 vs 31.92 months, p=0.09), but a statistically significant difference in mPFS was observed (3.68 vs 13.55 months; p=0.02). Positive Cav-1-T expression was also associated with greater risk of progression at the first radiological assessment (p=0.02). In the prospective cohort pts with higher exosomal Cav-1 concentration at baseline showed worse mOS (5.8 vs 16.45 months, p=0.045) and lower mPFS (3.47 vs 8 months; p=0.21).

Conclusions: Our study suggests Cav-1 as a poor prognostic biomarker for advanced PC pts, related to liver metastasis and higher tumor aggressiveness. Further studies are awaited to better clarify its role in promoting cancer progression in PC.

C11

A SYSTEMATIC REVIEW AND META-ANALYSIS ON THERAPEUTIC STRATEGIES IN RESECTED/RESECTABLE PANCREATIC CANCER PATIENTS

Ciliberto D.[1], Staropoli N.[1], Ierardi A.[1], Cuomo O.[1], Calandruccio N.D.[1], Caridà G.[1], Barbieri V.[1], Tassone P.[2], Tagliaferri P.[2]

[1]Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy;, Catanzaro; [2]Translational Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy

Background: To date, surgery represents the only potential curative treatment in pancreatic ductal adenocarcinoma (PDAC) patients despite the high relapse rate. The effectiveness of adjuvant (ADJ) chemotherapy was assessed in several randomized clinical trials (RCTs) showing a modest improvement on survival outcomes. However, these results are limited by the high peri and post-surgical morbidities. The role of radiotherapy (RT) and neoadjuvant chemotherapy (neoADJ) remains unclear. The aim of this work is to rank the therapeutic strategies, in order to indicate the most effective clinical management in patients with resected/resectable PDAC.

Patients and Methods: A systematic literature review of Pubmed and abstracts from major cancer meetings was carried out including all published prospective RCTs. We performed the pairwise comparisons based on the different chemotherapy with or without radiotherapy in patients with resecable/resected PDAC. Primary endpoints are overall survival (OS) and disease-free survival (DFS). Meta-analysis was conducted with pairwise comparisons by random effect model and the ranking inference was based on Bayesian approaches.

Results: Our analysis includes 28 RCTs (6603 patients), 19 studies on adjuvant, and 9 studies on neoadjuvant treatment. It was demonstrated a significant OS benefit with hazard ratio (HR) of 0.81 (CI 0.70-0.94) for the various combinatory approaches compared to gemcitabine alone and HR 0.84 (CI 0.73-0.98) vs untreated controls. Finally, stratifying different settings of treatment we reported: ADJ HR 0.81 (0.75-0.90), ADJ+RT HR 0.93 (CI 0.77-1.12), neoADJ+RT HR 0.88 (0.61-1.25), neoADJ 0.72 (0.55-0.94) as compared to gemcitabine or observation as control arm. The available data allowed DFS analysis for adjuvant setting only, confirming the OS advantage. Concerning Bayesian analysis, mFOLFIRINOX rankes as first option in terms of efficacy.

Conclusions: In the current scenario, ADJ polychemotherapy-based schedules, particularly mFOLFIRINOX, appear as the first choice. Conversely, the combination of capecitabine+gemcitabine or gemcitabine monotherapy represent valid alternatives for patients unfit for aggressive schedules. Considering the controversial and non-comparable literature data on neoADJ and RT approaches, new RCTs are eagerly awaited to define their potential role. Furthermore, innovative RT techniques and/or new targeted agents based on molecular portraits for PDAC could become changing practice in the next future.

C12

NUTRITIONAL INDEX FOR IMMUNE-CHECKPOINT INHIBITORS (ICI) (NUTRIICI) FOR PATIENTS (PTS) WITH METASTATIC GASTRO-ŒSOPHAGEAL JUNCTION (GOJ)/GASTRIC CANCER (GC)

Morelli C.[1], Formica V.[1], Lucchetti J.[1], Renzi N.[1], Nitti D.[1], Patrikidou A.[2], Shiu K.K.[3], Arkenau T.[2], Roselli M.[1]

[1]Policlinico Tor Vergata, Roma; [2]Sarah Cannon Research Institute, Londra; [3]University College Hospital, Londra

Background: Nutritional status is strongly related to the prognosis of mGOJ/GC pts. ICI improved the overall survival (OS) in heavily pre-treated mGOJ/GC pts. The aim of this retrospective study was to investigate the potential prognostic role of nutritional markers in ICI-treated mGOJ/GC pts.

Patients and methods: Twelve serum and anthropometric nutritional markers derived from blood and CT scans [weight, body mass Index (BMI), sagittal and waist diameter, waist to hip ratio (WHR), albumin, glucose, lymphocytes, albumin/globulin ratio (AGR), total serum proteins (PRO), Onodera's prognostic nutritional index] were retrospectively analyzed at baseline. All variables were categorized according to the MaxStat statistics and analyzed for their prognostic value with univariate (UVA) and multivariate (MVA) cox regression analyses.

Results: From June 2014 to December 2018, 57 mGOJ/GC pts (14 females, 43 males) (median (m) age 63 years) received ICI as second-line therapy (Pembrolizumab n=26, Nivolumab n=16, Avelumab n=15). The mfollow-up was 27 months (mo) (4 to 53 mo). mOS was 10.8 mo (0.2 to 52.2 mo). PRO and WHR were independent predictors for OS in the MVA (Hazard ratio (HR) 0.98, p 0.01 and HR 1.31, p 0.03, respectively) and used to build the NUTRICI. Pts with both PRO >60 g/l and WHR >1 had a mOS of 36 mo, vs. 12 mo of pts with one unfavourable factor (either PRO <60 g/l or WHR<1), vs. 4 mo of pts with both unfavorable factors (p 0.0006). Taking as reference pts with both favorable factors, HR was 4.16 and 10.08 for pts with one and two unfavourable factors, respectively.

Conclusions: NUTRIICI, combining PRO and WHR, is the first nutritional index with a significant prognostic value in mOGJ/GC pts receiving second-line ICIs. A prospective validation is currently under way.

C13

CA19-9 NORMALIZED BY THE CHOLESTASIS INDEXES DIRECT BILIRUBIN (BIL), ALKALINE PHOSPHATASE (ALP) AND GAMMA-GLUTAMYL TRANSFERASE (GGT). CA19-9/BIL, CA19-9/ALP AND CA19-9/GGT RATIOS AND OVERALL SURVIVAL IN METASTATIC PANCREATIC CANCER (MPC)

Formica V.[1], Nitti D.[1], Morelli C.[1], Lucchetti J.[1], Renzi N.[1], Del Vecchio Blanco G.[1], Anselmo A.[1], Argirò R.[1], Benassi M.[1], Doldo E.[1], D'angelillo R.M.[1], Palmieri G.[1], Tisone G.[1], Roselli M.[1]

[1]Policlinico Tor Vergata, Roma

Background: CA19-9 is the reference tumor marker for mPC, however it is subject to non-specific increase in presence of cholestasis. We investigated whether cholestasis-normalized values improved the prognostic performance of CA19-9

Methods: Consecutive mPC patients candidate for first-line chemotherapy were reviewed and baseline CA19-9/BIL, CA19-9/ALP and CA19-9/GGT ratios were calculated and compared to raw CA19-9 values for association with overall survival (OS). Cox-regression analysis with restricted cubic splines with 5 knots modelling and hazard ratio (HR) smoothed curves were used to account for non-linearity.

Results: 302 patients with complete data were included. Raw CA19-9 was predictive of OS only if very high values (>2000 U/ml) were recorded: median(m) OS for CA19-9 > 2000 vs <2000 3.7 months (mo) vs 9.9 mo, HR 2.91, p = 0.0004 (results comparable with data from the literature, e.g. Hess, Lancet Oncol, 2008). Among patients with CA19-9 <2000 (82%), none of the normalized indexes was able to improve the prognostic performance of CA19-9: cox regression p-values of CA19-9/BIL, CA19-9/ALP and CA19-9/GGT were 0.059, 0.275 and 0.309, respectively. Surprisingly, looking at HR smoothed curves, CA19-9/ALP ratio was inversely associated with survival. In fact higher CA19-9/ALP (> 6) was associated with significantly improved survival as compare to CA19-9/ALP < 6: 20.18 mo vs 8.1 mo (HR 0.39, p = 0,023). This finding is probably due to a direct adverse effect of increasing values of the denominator (ALP), thus suggesting that ALP might function in mPC more as proper tumor marker (it is known that ALP is produced by proliferating tumor cells) than as non-specific cholestatic marker.

Conclusions: the prognostic value of CA19-9 is not improved by normalization based on cholestasis indexes. CA19-9 is prognostically informative only for very high values (>2000). For patients with CA19-9 < 2000, other proper tumor markers need to be investigated to refine survival prediction.

C14

NEOADJUVANT CHEMORADIOTHERAPY AND SURGERY VERSUS SURGERY ALONE IN RESECTABLE PANCREATIC CANCER: LONG TERM FOLLOW-UP RESULTS FROM A SINGLE-CENTER PROSPECTIVE, RANDOMIZED, CONTROLLED TRIAL

Di Marco M.[1], Ricci C.[2], Brandi G.[1], De Lorenzo S.[1], Tovoli F.[3], Carloni R.[1], Palloni A.[1], Abbati F.[1], Grassi E.[4], Guido A.[5], Morganti A.G.[5], Nigro M.C.[5], Rizzo A.[5], Ricci A.D.[5], Alberici L.[6], D'Onofrio M.[7], Minni F.[6], Santini D.[8], Casadei R.[9]

[1]*Department of Experimental, Diagnostic, and Specialty Medicine - DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna;* [2]*Department of Internal Medicine and Surgery (DIMEC), Alma Mater Studiorum, S.Orsola-Malpighi Hospital, University of Bologna, Bologna;* [3]*Department of Medical and Surgical Sciences, University of Bologna, Bologna;* [4]*Medical Oncology, Ospedale degli Infermi, Faenza;* [5] *Department of Experimental, Diagnostic, and Specialty Medicine - DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna;* [6] *Department of Internal Medicine and Surgery (DIMEC), Alma Mater Studiorum, S.Orsola-Malpighi Hospital, University of Bologna, Bologna;* [7] *Department of Experimental, Diagnostic, and Specialty Medicine - DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna;* [8] *Department of Experimental, Diagnostic, and Specialty Medicine - DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna;* [9] *Department of Internal Medicine and Surgery (DIMEC), Alma Mater Studiorum, S.Orsola-Malpighi Hospital, University of Bologna, Bologna*

Background: Neoadjuvant chemoradiotherapy has shown benefits for locally advanced and borderline resectable pancreatic cancer and several studies seem to show a potential benefit also for resectable pancreatic cancer. Despite this, its role remains controversial.

Materials and methods: This study was a single-center RCT, patients with histologically proven resectable pancreatic adenocarcinoma were randomized between surgery alone (arm A) and neoadjuvant chemoradiation followed by surgery (arm B). Accrual was completed between May 2007 and July 2013 and results of our trial were published in 2015. Five year after we would like to assess the outcome in terms of overall survival (OS) and disease-free survival (DFS). We used the intention-to-treat approach and data were evaluated with Kaplan-Meyer method and compared using the log-rank test. In the original study patients with no clear fat planes around the celiac axis, hepatic artery, and superior mesenteric artery, as well as patients with more than 180° maximal involvement of the superior mesenteric and portal veins were excluded. The chemoradiation schedule consisted initially of chemotherapy with gemcitabine alone 1000 mg/m2 on days 1 and 8 every 21 days for two cycles (total of 6 weeks) followed by combined chemoradiotherapy for a total of 6 weeks (conventional radiotherapy with 45 Gy and a boost of 9 Gy on the pancreatic lesion; chemotherapy with gemcitabine 50 mg/m2 twice weekly).

Results: 38 patients were randomized: 20 in arm A and 18 in arm B. Median DFS was 8.53 months (95% CI, range 4.47-12.59) vs 18.03 months (95% CI, range 2.58-33.48) for arm A and B respectively (p=0.242), while median OS was 21.17 months (95% CI, range 8.37-33.96) for arm A and 24.35 months (95% CI, range 8.04-40.66) for arm B (p=0.174).

Conclusions: OS and DFS were not significantly different between the two groups even if, especially DFS, they were more favorable in the neoadjuvant group. The very low power of this study suggests that this result could be due to the underpowered data. Further multicenter RCTs with more effective chemoradiotherapy regimens are needed in order to better understand the real impact of chemoradiotherapy for resectable pancreatic cancer.

C15

SEQUENTIAL TREATMENT IN METASTATIC PANCREATIC CANCER: A RETROSPECTIVE MONO-INSTITUTIONAL COHORT STUDY

Santaniello A.[1], Napolitano F.[1], Foschini F.[1], Servetto A.[1], Marciano R.[1], Mozzillo E.[1], Carratù A.C.[1], De Placido P.[1], Cascetta P.[1], Formisano L.[1], De Placido S.[1], Bianco R.[1]

[1]AOU Federico II, Napoli

Bakground: Unresectable locally advanced (ULAPC) and metastatic pancreatic cancer (MPC) have a rising incidence, with a 5-year survival rate less than 5%. New combined treatment options, such as FOLFIRINOX (FFN) and Gemcitabine-nab-Paclitaxel (GnP), improved overall survival when compared to Gemcitabine alone. To date, no head-to-head comparison between these two regimens has ever been conducted, neither in first nor in the second line settings.

Methods: Between May 2011 and May 2020, a retrospective, mono-institutional, cohort study has been conducted: patients with ULAPC and MPC were eligible if treated with either FFN followed by GnP (sequence A) or *vice-versa* (sequence B). The patients were analyzed for clinical characteristics at baseline, survival outcomes, treatments' efficacy and tolerability.

Results: A total of 235 patients with ULAPC and MPC were evaluated in our institution: at the time of the analysis, 48 patients were included (31 in sequence A, 17 in sequence B). There were no significant differences between the two groups in terms of baseline characteristics (age, sex, performance status). The overall response rate and disease control rate were comparable between the two groups.

No significant differences in median overall survival (mOS) were observed: 60.6 weeks in sequence A vs 74.3 weeks in the sequence B (p=0.28). Likewise, progression free survival 1 (PFS1) and PFS2, defined as the time from start of first line to disease progression and as the time from start of second line to disease progression or death from any cause, respectively: the results were not statistically significant (PFS1 24.4 weeks vs 27 weeks, p=0.72, and PFS2 16.7 weeks vs 27.7 weeks, p=0.32).

Among grade 3–4 hematological toxicities, neutropenia was less frequent with GnP (17.6% vs 45%), while neurotoxicity and anemia were less frequent with FFN (29.4% vs 41% and 3.2% vs 11.8% respectively). No febrile neutropenia, or severe gastrointestinal toxicities were observed.

Conclusions: In our daily clinical practice, only 20% of patients with ULAPC and MPC were eligible for a sequential treatment (FFN followed by GnP or reverse sequence). Although this analysis has not provided evidence of a statistically significant benefit of one sequence or the other, we observed an interesting clinical benefit in OS in patients treated with GnP followed by FFN. The differences in the toxicity profile represent a key consideration for treatment decisions.

C136

IMMUNE PROFILING OF GASTRIC (GC) AND GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA (GEJC) PATIENTS (PTS) RECEIVING PERIOPERATIVE FLOT: PRELIMINARY REPORT FROM SINGLE-CENTRE EXPERIENCE

Pecora I.[1], Ugolini C.[2], Giordano M.[3], Giannini R.[3], Vivaldi C.[4], Lencioni M.[1], Santi S.[5], Massa V.[1], Pallabazzer G.[5], Catanese S.[1], Salani F.[1], Vasile E.[1], Falcone A.[6], Fontanini G.[3], Fornaro L.[1]

[1]Unit of Medical Oncology, Pisa University Hospital, Pisa; [2]Department of Laboratory Medicine, Section of pathology, Pisa University Hospital, Pisa; [3]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa; [4]Department of Translational Research and New Technologies in Medicine, University of Pisa, Pisa; [5]Esophageal Surgery Unit, Tuscany Regional Referral Center for the Diagnosis and Treatment of Esophageal Disease, Pisa University Hospital, Pisa; [6]Unit of Medical Oncology, Pisa University Hospital - Department of Translational Research and New Technologies in Medicine, University of Pisa, Pisa

Background: Perioperative FLOT is a standard of care for locally advanced, resectable GC/GEJC. Chemotherapy (CT) and immunotherapy (IO) combinations are under investigation, but data on the immune landscape are still scarce. Our aim is to explore the immune signature and its modification after FLOT therapy in this setting.

Material and methods: We retrospectively analysed both diagnostic biopsy (PRE) and surgical samples (POST) from pts treated with perioperative FLOT at our centre. Clinicopathologic and molecular data were collected. Gene expression profile was obtained on RNA samples from tumor microenvironment (TME) cells using NanoString nCounter® PanCancer Immune Profiling Panel.

Results: A pilot cohort of 14 cases, 9 GEJC and 5 GC, all in clinical TNM stage III (12 cT3-4 and 2 cT2, all with nodal positive status), was obtained. Three pts reported ypT0-2 (21.4%) and 2 pts ypN0 (14.3%). All cases were EBV negative and MSS, only one was HER2 3+.The unsupervised clustering method for data set analysis showed 2 groups according to different gene expression, "less activated" (N=13) and "more activated" (N=15), corresponding to PRE and POST samples respectively, except for 1 PRE sample already "more activated" before CT exposure. Several immune-related genes resulted differentially expressed by POST respect to PRE samples (p<0.05, see Table 1). Focusing on 3 cases with ypT regression, we found a statistically significant activation of TNF-superfamily genes in POST samples and cytotoxicity and T-cell functions related genes in both PRE and POST tissues, suggesting a baseline activation.

Conclusions: Despite small sample size, our experience confirmed CT influence on immune system. Of note, pathologic downstaging seems to occur preferentially in tumors with baseline activation of immune infiltrate in TME.

These initial results support the development of CT plus IO combinations in locally advanced GC/GEJC and could shed light on the identification of novel putative biomarkers. Further analyses are still ongoing.

Table 1.

mRNA-GENE	Log2 fold change POST versus PRE (confidence interval)	Benjamini-Yakutieli p-value (multiple test correction)	Gene set
C7	7.0 (6.0-7.9)	1.37E-14	Complement
C1S	1.9 (1.4-2.3)	6.55E-06	
C3	2.6 (1.9-3.3)	6.55E-06	Regulation
CD96	1.6 (0.9-2.3)	0.009	
CD8A	1.7 (1-2.4)	0.005	Antigen processing
IL6ST	1.1 (0.8-1.4)	3.63E-05	Chemokines
IL11RA	1.2 (0.8-1.7)	<0.001	
TNFRSF13C	2.3 (1.3-3.2)	0.006	Regulation, TNF Superfamily
CD1C	1.9 (1.3-2.5)	<0.001	T-cell functions
GZMK	2.7 (1.7-3.6)	<0.001	Cell functions

C17

FLUOROPYRIMIDINES-MONOTHERAPY (FUCT) VERSUS OXALIPLATIN-REGIMEN (OXCT) AS ADJUVANT CHEMOTHERAPY (ACT) IN GASTRIC CANCER (GC) NODE-POSITIVE PATIENTS (PTS): A RETROSPECTIVE BICENTRIC PROPENSITY SCORE (PS) ANALYSIS

Zurlo I.V.[1], Strippoli A.[2], Salati M.[3], Spallanzani A.[3], Di Stefano B.[4], Maratta M.G.[4], Astore S.[4], Gelsomino F.[3], Rimini M.[3], Vivolo R.[5], Bria E.[2], Giannarelli D.[6], Pozzo C.[2], Tortora G.[2]

[1]Oncologia Medica - Università Cattolica del Sacro Cuore, Roma; [2]Oncologia Medica - Fondazione Policlinico Universitario A. Gemelli IRCCS-Comprehensive Cancer Center, Roma; [3]Oncologia Medica - Universita' di Modena e Reggio Emilia, Modena; [4]Oncologia Medica - Universita' Cattolica del Sacro Cuore, Roma; [5]Oncologia Medica - Universita' Cattolica del Sacro Cuore, Roma; [6]Dipartimento di Biostatistica - IRCCS Regina Elena, Roma

Background: Surgery followed by aCT is one of the standard of care for resectable GC, mostly in Asia. Although meta-analyses reported a 6% absolute improvement in 5-year OS for fluoropyrimidine-based aCT, these were mainly inflated by Asian studies. Western trials failed to show a clear survival benefit for aCT, and the benefit of oxaliplatin-containing regimen is even more controversial. The aim of this retrospective analysis is to compare FuCT vs OxCT and to assess the impact on survival of clinico-pathologic features.

Method: 112 treated with FuCT were compared with 119 pts treated with OxCT between Jan-2009 to Jun 2019 at 2 Italian institutions. Kaplan-Meier curves and Cox regression method were used for survival analysis. Patients undergoing FuCT or OxCT were matched 1:1 using the propensity score matching (PSM) method, and a survival analysis was conducted on matched patients.

Results: Clinical data of 231 nodes positive GC pts underwent aCT (112 treated with FuCT and 119 with OxCT) were retrospectively collected. At multivariate analysis age, performance status (PS-ECOG), grading, LVI, positive resection margin (R1), tumor location, pathological stage (III vs II), T status independently correlated with DFS (p=0.001, 0.002, 0.006, <0.0001, <0.0001, <0.0001, 0.02). The median DFS was 95.6 m (95% CI: 50.5-140.7) and 77.3 m (95% CI: 60.4-94.2) for FuCT and OxCT respectively (log-rank *p*0.78) while mOS 120.4 m and 72.9 m (p=0.36), respectively. Seven variables were unbalanced in the two groups. After PSM, the indipendent variables significantly associated with survival were PS-ECOG, LVI and pathological stage. Even after PSM, no differences were observed in both mDFS and mOS between the two groups (p=0.36 and p=0.67 respectively).

Conclusions: In this retrospective study, we demonstrated that adding oxaliplatin to FuCT did not improve DFS or OS in a western population of resected GC. Using PSM to reduce treatment allocation bias and simulate randomization which is the main limitation of a retrospective study, we have confirmed the prognostic value of known clinico-pathological features and the crucial role of surgery in this tumor. Prospective randomized studies, including molecular biomarkers, are guaranteed to better stratify the risk points that could benefit from a more aggressive regimen and those to which only FuCT could be offered.

C18

THE IMPACT OF A MULTIDISCIPLINARY APPROACH (MA) IN THE MANAGEMENT OF PANCREATIC DISEASE (PD)

Di Stefano B.[1], Quero G.[2], Bagalà C.[1], Fiorillo C.[2], Bensi M.[1], Menghi R.[2], Cina C.[2], Mattiucci G.C.[3], Manfredi R.[3], Cellini F.[3], Brizi M.G.[3],

D'Aversa F.[4], Perri V.[5], Larghi A.[5], Attili F.[5], Inzani F.[6], Alfieri S.[2], Tortora G.[1], Salvatore L.[1]

[1]Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Roma; [2]Chirurgia Digestiva, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS. Università Cattolica del Sacro Cuore, Roma; [3]Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario "A. Gemelli" IRCCS. Istituto di Radiologia, Università Cattolica del Sacro Cuore, Roma; [4]Gastroenterologia, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli–IRCCS, Università Cattolica del Sacro Cuore, Roma; [5]Endoscopia Digestiva Chirurgica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli –IRCCS, Università Cattolica del Sacro Cuore, Roma; [6]Anatomia patologica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli – IRCCS. Università Cattolica del Sacro Cuore, Roma

Background: The management of PD is very insidious, due to the difficult differential diagnosis between benign and malignant diseases, and, in case of pancreatic ductal adenocarcinoma (PDCA), to the hard differentiation among resectable/borderline PDCA susceptible to upfront surgery, locally advanced PDCA susceptible to a neoadjuvant approach and never resectable or metastatic PDCA in which a palliative treatment is the only option. A correct PD evaluation and the subsequent choice of the most appropriate treatment strategy need a MA, involving surgeons, oncologists, radiologists, radiation oncologists, endoscopists, gastroenterologists and pathologists. We investigate the impact of the multidisciplinary meeting (MM) in the management of PD at our Institution.

Methods: We retrospectively evaluated all the cases discussed by surgeons at our MM. We collected data, both pre- and post-MM, regarding diagnosis (cyst vs pancreatitis vs IPMN vs PDCA), and, in case of PDCA, tumor burden at baseline (resectable vs border-line resectable vs locally advanced vs metastatic disease) and disease response to treatment (disease control vs progression). Primary endpoint was the overall rate of discrepancy in diagnosis and/or PD evaluation between pre- and post-MM.

Results: From October 2018 to December 2019, a total of 139 cases were presented by surgeons. After MM, a total of 38 diagnosis and/or PD evaluation were modified, for an overall discrepancy rate of 27%. In particular, of the 38 discordant cases, 9 (24%) were initial diagnosis, 24 (63%) baseline tumor burden assessments and 5 (13%) were PDCA response evaluations. Among the 24 cases of tumor burden evaluations, treatment strategy changed in 17 out of 24 cases. More specifically, of the 19 cases, evaluated as borderline/resectable before the MM, 15 were defined as locally-advanced or metastatic disease after the MM; of the 5 cases, evaluated as not resectable before the MM, 2 were considered border-line/resectable after the MM. Similarly, out of 9 cases of discrepant initial diagnosis, 5 cases, considered as malignant disease before MM, were assessed as benign after the MM.

Conclusions: Our analysis demonstrates a significant rate of discrepancy in diagnosis and/or PD evaluation between pre- and post-MM. Our results show that a MA allows a considerable modification in PD diagnosis and evaluation, maximizing the treatment strategy, in particular avoiding unnecessary and detrimental pancreatic surgery.

C19

THE IMPACT OF 2ND-LINE TREATMENT (TX) AFTER 1ST-LINE GEMCITABINE PLUS NAB-PACLITAXEL (GEMNAB) IN ADVANCED PANCREATIC CANCER (APC) PATIENTS (PTS)

Maratta M.G.[1], Di Stefano B.[2], Bensi M.[2], Bagalà C.[2], Spring A.[2], Chiaravalli M.[2], Ribelli M.[2], Tortora G.[2], Salvatore L.[2]

[1]Fondazione Policlinico A.Gemelli, Roma; [2]Fondazione Policlinico A. Gemelli, Roma

Background: Three main phase III randomized studies investigated the role of 2nd-line tx in APC pts. The PANCREOX study failed to demonstrate a survival advantage of mFOLFOX vs 5FU/LV. Conversely, the CONKO-003 and NAPOLI-1 trials demonstrated a significant survival improvement from the combination regimen, OFF and 5FU+Nal-IRI, in comparison to 5FU/LV alone. Final OS analysis from NAPOLI-1 demonstrated an association of specific characteristics (ECOG PS, age, Ca 19.9 baseline level, neutrophil-to-lymphocyte ratio, no liver metastases (m)) with OS > 1 year. The main limit of all these studies was due to the period they were carried out: no pts received 1st-line GemNab. We retrospectively analyzed a homogeneous population of APC treated with 1st-line GemNab at our Institution investigating the impact of 2nd-line tx.

Methods: APC pts receiving a 2nd-line tx after 1st-line GemNab were included in the analysis. The following variables were collected: gender; age (> vs = 55 years and = vs < 70 years); baseline ECOG PS (0-1 vs 2-3); Ca 19.9 baseline level (= vs < 200); anamnesis of diabetes; site of primary tumor (head/uncinate process vs body/tail); number of m sites (1 vs >1); m sites (liver, peritoneum, lung, nodes); RECIST response and ETS during 1-line GemNab. Univariate and multivariate analyses for PFS and OS were performed.

Results: Out of 167 APC pts progressed to 1st-line GemNab, 93 (56%) pts received a 2nd-line tx, specifically 58 received an oxa-based regimen, 11 FOLFIRINOX, 8 FOLFIRI and 16 other tx. Median 2nd-line PFS and OS were 3.3 and 5.6 months respectively. Out of 87 pts evaluable for response, 7 achieved a partial response and 27 a stable disease, with a RR and a disease control rate (DCR) of 8% and 39% respectively. Pts with baseline ECOG PS 0-1 had a significant better outcome in comparison to with PS 3-4 (PFS 4.2 vs 1.2 months, $p < 0.0001$; OS 7.2 vs 2.6 months, $p = 0.0001$). This significant association with survival parameters and ECOG PS was confirmed at the multivariate analysis.

Conclusions: Despite the limited number of pts evaluated and the restrospective nature of our analysis, our results are in line with previous evidences, confirming the importance of a 2nd-line combination tx, when feasible, as well in a homogeneous population of APC pts treated with 1st-line GemNab. On the basis of our results, ECOG PS may be considered a prognostic factor and the choice of 2nd-line tx should be guided in primis by the baseline general conditions of APC pts.

C20

BRCA1/2 GERMLINE ANALYSIS IN UNSELECTED PANCREATIC ADENOCARCINOMA: EXPERIENCE AT THE GROSSETO COMPREHENSIVE CANCER CENTER

Di Rocco R.[1], Orrico A.[2], Barucca V.[3], Messinese S.[4], Astorino M.[4], Bianchi P.P.[5], Formisano G.[5], Giuliani G.[5], Salaj A.[5], Salvischiani L.[5], Renieri A.[6], Bengala C.[4]

[1]*Departement of Oncology, Misericordia Hospital, Grosseto;* [2]*UOC Molecular Medicine and Genetics AOUS; Clinical Genetics Misericordia Hospital Grosseto, Grosseto;* [3]*UOC Oncology San Camillo Forlanini Hospital, Roma;* [4]*Departement of Oncology Misericordia Hospital, Grosseto;* [5]*Departement of Surgery Misericordia Hospital, Grosseto;* [6]*Departement of Medical Genetics University of Siena, Siena*

Background: Germline BRCA1/2 mutations are identified in about 4-7% of unselected patients with pancreatic AdenoCarcinoma. NCCN Guidelines recommends to offer genetic counseling and testing to all patients diagnosed with AdenoCa, regardless of family history. Moreover, patients with BRCA mutations may benefit from treatment with platinum compounds and PARP inhibitors. Here we report our clinical experience regarding germline BRCA1/2 testing from 2018 to date.

Materials and methods: Genetic testing was performed on unselected patients with pancreatic AdenoCa. DNAs, extracted from peripheral blood, were amplified by Ion AmpliSeq BRCA1/2 Panel and sequenced on an Ion Torrent PGM sequencer. Every pathogenic mutation detected was confirmed by Sanger sequencing. Testing results were discussed at genetic-oncology multidisciplinary groups. All BRCA1/2 negative AdenoCa with important personal or family history of BRCA related cancers will be tested for additional cancer susceptibility genes.

Results: 30 unselected patients were tested for BRCA1/2 mutations: 8 patients were diagnosed with resectable, 8 with locally advanced, 13 with metastatic disease and 1 with IPMN. Genetic tests are available on 28 patients. BRCA1/2 gene mutations were detected in 3 patients: 2 AdenoCa (7,1%; 1 BRCA1 and 1 BRCA2) and 1 IPMN (3.6%: BRCA2).1 BRCA2 VUS was identified. A BRCA1 mutated patient with locally advanced disease received platinum-based neoadjuvant treatment and achieved a pathological complete response. She is still disease-free after 3 years from diagnosis. All BRCA1/2 mutated AdenoCa patients had,additionally, personal history of breast and ovarian cancer. No BRCA1/2 mutations was observed in 25 patients: 7 had a family history of pancreatic and breast cancer, even at young age, and 4 had a personal history of prostate, skin and breast cancer.

Conclusions: In our series of unselected AdenoCa, the frequency of BRCA1/2 germline mutations was 7.1%, within the range reported in the literature. One BRCA1 mutated patients achieved a pathological complete response with platinum-based chemotherapy and a long term disease-free survival.Interestingly, 28% of BRCA1/2 negative patients had family history and 16% had personal history of BRCA related cancers. Our results confirm the importance of genetic testing in order to provide the most effective treatment and would support the literature data about involvement of multiple genes, beyond BRCA1/2, in the onset of hereditary pancreatic cancer.

C21

EARLY-ONSET GASTRIC CANCER: IS IT REALLY ON THE RISE? A REGISTRY-BASED ANALYSIS OF EPIDEMIOLOGY AND SURVIVAL

Laface R.[1], Filippi R.[2], Quarà V.[3], Rosso S.[4], Spadi R.[1], Bustreo S.[1], Chiappino I.[1], Satolli M.A.[1], Ciuffreda L.[1]

[1]*S.C. Oncologia Medica 1 - AOU Città della Salute e della Scienza di Torino, Torino;* [2]*S.C. Oncologia Medica 1 - AOU Città della Salute e della Scienza di Torino; Candiolo Cancer Institute, FPO- IRCCS-Candiolo, Torino;* [3]*Candiolo Cancer Institute, FPO- IRCCS-Candiolo; Department of Oncology, University of Turin, Torino;* [4]*Piedmont Cancer Registry - CPO Piemonte - AOU Città della Salute e della Scienza di Torino, Torino*

Background: Recent evidence suggests that early-onset (<50 years of age) gastric carcinoma (EOGC) is a genetically and clinically distinct disease from late-onset gastric carcinoma (LOGC). Available data on histopathology, incidence and risk factors of EOGC are still few and conflicting.

Patients and Methods: The Piedmont Cancer Registry (RTP) was retrospectively queried for cases of gastric and cardias carcinoma occurred in the city of Turin, Northern Italy, from 1985 to 2014. We present a characterization of EOGC as for temporal trend, overall survival (OS), prognosticators, as opposed to LOGC.

Results: Among 6402 unique cases of gastric and cardias carcinoma, diagnoses <50 years were 362 (5.7%); their incidence decreased by 67.0% over 20 years' time (from 103 cases in the 1985-'89 period to 34 in 2010-'14), as compared to -43.4% in LOGC. A gastric primary site could be definitely attributed to 2917 cases only; 5.9% were EOGC. EOGG was associated with diffuse Lauren's histology (diffuse/intestinal ratio 3.2:1 vs 1.0:1 in LOGC, p<0.001); however, rates of not retrievable histology were high in both

groups, and statistically higher in LOGC (63.1% vs 51.7% of EOGC, p 0.003). No difference in sex was observed (male sex 56.1% in EOGC vs 58.8% in LOGC, p 0.76). OS was significantly longer in EOGC compared with LOGC (HR 0.54, 95%CI 0.42-0.70, p<0.001). This favorable prognostic association was consistent across subgroups (sex and histologic subtype). EOGC (HR 0.54, 95%CI 0.41-0.72) and intestinal subtype (HR 0.82, 95%CI 0.72-0.95) retained a significant positive impact on OS on multivariate analysis. However, the intestinal subtype did not show its favorable prognostic association in EOGG (HR 0.99, p 0.96). Sex never correlated with OS, either in the whole cohort (HR 0.90, p 0.15) or in EOGC (HR 0.84, p 0.35).

Conclusions: In contrast with reports from other parts of the world, we observed a neat decline in incidence of EOGC, apparently steeper than that observed with LOGC. EOGC cases displayed a meaningfully better prognosis, as well as a differential prognostic impact of histology subtype. Limitations of this study include the lack of distinction between gastric and cardias site and the irretrievability of histology subtype for a conspicuous share of patients.

C22

ASSOCIATION OF REGION OF ORIGIN WITH EARLY-ONSET GASTRIC OR GASTROESOPHAGEAL JUNCTION CANCER IN A LARGE CITY OF NORTHERN ITALY

Filippi R.[1], Laface R.[2], Patriarca S.[3], Spadi R.[2], Satolli M.A.[2], Ponzetti A.[2], Cristiano C.[2], Aglietta M.[4], Ciuffreda L.[2]

[1]*S.C. Oncologia Medica 1 - AOU Città della Salute e della Scienza di Torino; Candiolo Cancer Institute, FPO - IRCCS Candiolo, Moncalieri;* [2]*S.C. Oncologia Medica 1 - AOU Città della Salute e della Scienza di Torino, Turin;* [3]*Piedmont Cancer Registry - CPO Piemonte - AOU Città della Salute e della Scienza di Torino, Turin;* [4]*Candiolo Cancer Institute, FPO - IRCCS - Str. Prov. 142, km. 3.95, Candiolo, Torino; Department of Oncology, University of Turin, Candiolo*

Background: The fourth largest Italian city, Turin is a historical destination of young workforce migration. Regional incidence rates of gastric cancer are similar between Piedmont and the most represented regions of immigration. However, early-onset (diagnosis <50 years of age) gastric or gastroesophageal junction cancer (EOGGEC) is a rare disease with distinct features and unequivocal epidemiological trends.

Methods: We present a registry analysis aimed to explore the epidemiology of EOGGEC in Turin. A subset of EOGGEC cases with histology clearly attributable to either Lauren subtype (diffuse or intestinal) was further explored with regard of parental origin. Diagnoses with ICD-9 code 151 occurred from 1985 to 2014 were extracted from the Piedmont Cancer Registry (RTP); data on patients (pts) and parental origin were extracted from population administrative files.

Results: Of 421 diagnoses of EOGGEC occurring in pts ever-resident in Turin, most occurred in pts born outside Piedmont region (64.4%, $CI_{95\%}$ 59.8-68.9). Particularly, 54.6% ($CI_{95\%}$ 49.9-59.4) of pts was born in Southern regions: Puglia and Calabria amounted together to a quarter of cases (24.7%). Of 174 cases with apt histological information, the primary was gastric in 50.0%, gastroesophageal junction in 2.3%, remaining undetermined in 47.5%. Diffuse subtype characterized 85.4% and 88.2% of cases of pts born in Southern and in Northern Italy, respectively (p 0.66). Forty-one pts with available geographic origin for both parents were born in Piedmont: 14 (34.1%) and 22 (53.7%) had at least one parent from Calabria or Puglia regions and from Southern Italy, respectively. The share of pts that had both parents from Southern Italy was similar to those who had both parents from Piedmont (29.3% and 34.1%, respectively).

Conclusions: Origin from specific regions from Southern Italy is over-represented among EOGGEC cases in Turin city. This effect appears maintained among second-generation immigrants. Possible contributing factors include: harsher working and living conditions; frequent provenance from small communities; lifestyle and dietary habits.

	Share of EOGGEC ($CI_{95\%}$)	Share of Turin residents (average of 1990 and 2011 distributions)	Delta (absolute, relative)
Piedmont	35.6% (31.1-40.2)	57.0%	-21.4% (-38%)
Puglia	13.8% (10.5-17.1)	7.8%	+6.0% (+77%)
Calabria	10.9% (7.9-13.9)	4.1%	+6.9% (+169%)
Sardinia	8.3% (5.7-11.0)	1.4%	+6.9% (+493%)
Campania	6.9% (4.5-9.3)	3.2%	+3.7% (+118%)
Southern Italy	54.6% (49.9-59.4)	25.0%	+29.7% (119%)

C23

ASSOCIATION BETWEEN NEUTROPENIA AND SURVIVAL TO NAB-PACLITAXEL AND GEMCITABINE IN PATIENTS WITH METASTATIC PANCREATIC CANCER

Catalano M.[1], Roviello G.[2], Mini E.[2], Nobili S.[2], Dreoni L.[1], Ramello M.[3], Ianza A.[3], Conca R.[4], Aieta M.[4], Gasperoni S.[5], Petrioli R.[6], D'Angelo A.[7]

[1]*School of Human Health Sciences, University of Florence, Firenze;* [2]*Department of Health Sciences, University of Florence, Firenze;* [3]*Oncology Unit, Department of Medical, Surgical, & Health Sciences, University*

of Trieste, Trieste; [4]Division of Medical Oncology, Department of Onco-Hematology, IRCCS-CROB, Referral Cancer Center of Basilicata, Potenza; [5]Translational Oncology Unit, University Hospital Careggi, Firenze, Firenze; [6]Department of Medicine, Surgery and Neurosciences, Medical Oncology Unit, University of Siena, Siena; [7]Department of Biology and Biochemistry, University of Bath, United Kingdom

Background: Neutropenia is a common side effect associated with nab-paclitaxel gemcitabine (Nab-Gem) therapy. We retrospectively investigated the association between neutropenia induced by first-line Nab-Gem and survival in metastatic pancreatic carcinoma patients Nab-Gem.

Patients and methods: Metastatic pancreatic patients treated with first-line Nab-Gem were included in this retrospective analysis. Neutropenia was categorized using the National Cancer Institute Common Toxicity Criteria toxicity scale. Outcome measures were overall survival (OS), progression-free survival (PFS) and response rate.

Results: 115 patients were analyzed. Median PFS was 7 months (95% CI 5-8) in patients with grade =3 neutropenia and 6 months (95% CI 5-6) for patients with grade <3 neutropenia (p=0.08; hazard ratio (HR: 0.68). Median OS was 13 months (95% CI 10-18) in patients with grade =3 neutropenia and 10 months (95% CI 8-13) for patients with grade < 3 neutropenia (p=0.04; HR: 0.44). In multivariate analysis, the occurrence of grade = 3 neutropenia showed a statistically significant association with OS (HR: 0.62; 95% CI, 0.09-0.86; P=0.05).

Conclusions: Nab-Gem-induced neutropenia is associated with longer survival in metastatic pancreatic cancer patients.

C24

NEUTROPHIL/LYMPHOCYTE RATIO AND ITS OPTIMAL CUT-OFF IS ASSOCIATED WITH LONG SURVIVAL IN METASTATIC PANCREATIC CANCER PATIENTS

Mauro E.[1], Carandina I.[2], Tiberi E.[2], Farina J.[2], Fasano A.R.[2], Cecchetto C.[2], Martella L.R.[2], Lancia F.[2], Toma I.[2], Frassoldati A.[2]

[1]Azienda Ospedaliera -Universitaria, Ferrara; [2]Azienda Ospedaliero - Universitaria, Ferrara

Background: Long survival is rare in pancreatic cancer, and limited information are available about determinants of favourable outcome. The NLR (neutrophils/lymphocytes ratio) has been reported as a prognostic factor in early stage pancreatic adenocarcinoma, due its relation to the dominant inflammatory or immune status of the patient, but data are lacking in the metastatic disease.

Patients and methods: To evaluate the possible prognostic role of NLR in stage IV pancreatic cancer, we retrospectively analyzed patients treated at our institution (Oncology Unit of Ferrara) between 2013 and 2019. We analyzed the prognostic effect on survival of clinical (like age, BMI, ECOG PS, tumor site, location of metastases, obstructive jaundice, diabetes, previous therapies) and biological parameters (like

CEA and CA19.9 tumor markers, NLR, PLR (platelets/lymphocytes ratio) and LMR (lymphocytes/ monocytes ratio). Published cut-off of these parameters, as well as optimal cut-off defined by ROC curves have been used to predict the long survival.

Results: 106 patients with stage IV pancreatic cancer were retrospectively collected. Median age was 65 years. ECOG PS was > 0 in 62% of the patients. A better mOS has been associated with baseline NLR, both using cut-off of ≤ 4 (8 m vs 4 m, p=0,006), and a cut-off of ≤ 2,5 (11 m vs 5 m di mOS, p=0,024). At this cut-off level, baseline NLR showed an independent prognostic value in multivariate analysis (HR= 1,940, IC 95% 1,230-3,061, p=0,010). Moreover, we evaluate the optimal cut-off by generating ROC curves for NLR. The NLR cut-off of ≤ 2,83, (AUC=0,648, p=0,022; sensibility 90%, specificity 54.26%) showed the best performance. Baseline CEA ≤5 resulted also a parameter associated with long survival (8 m vs 5 m, p= 0.005), with HR= 1,816, IC 95% 1,161-2,843, p=0,004 in multivariate analysis. The CEA optimal cut-off by ROC curves able to discriminate the long survivors was ≤3,9 (AUC=0,714, p=0,012, (sensibility 90%, specificity 52.58%). No significant results were observed for PLR, LMR, CA19.9, age, and disease characteristics at onset of metastases.

Conclusions: Two factors resulted associated to a different prognosis in terms of overall survival: NLR < 2,83 and CEA<3.9 at baseline. These simple parameters might be useful to estimate prognosis in advanced pancreatic cancer.

C25

CONTINUUM OF CARE FOR UNRESECTABLE HEPATOCARCINOMA (UHCC): A REFERRAL-CENTRE EXPERIENCE ON SEQUENTIAL STRATEGIES

Massa V.[1], Pecora I.[1], Salani F.[1], Vivaldi C.[1], Bargellini I.[2], Crocetti L.[2], Fornaro L.[1], Oliveri F.[3], Cesario S.[1], De Simone P.[4], Romagnoli V.[3], Catalano G.[4], Brunetto M.R.[3], Catanese S.[1], Caccese M.[1], Bernardini L.[1], Vasile E.[1], Lencioni M.[1], Falcone A.[1], Masi G.[1]

[1]Oncologia Medica, Università di Pisa, Pisa; [2]Radiologia Diagnostica ed Interventistica, AOUP, Pisa; [3]Epatologia, AOUP, Pisa; [4]Chirurgia Epatica e del Trapianto di fegato, AOUP, Pisa

Background: A wider accessibility to tyrosine-kinase inhibitors (TKI), antiangiogenics and immuno-oncological (IO) drugs, have pushed the therapeutic paradigm for uHCC toward sequential strategies. However, how to tailor them on patients (pts) is still unclear.

Methods: We retrospectively analysed data from uHCC pts treated with ≥2 lines at our Centre from January 2010. We aimed to describe different sequences' efficacy in terms of overall survival (OS) and progression-free survival (PFS) 1+2 -the time from first line beginning to progression of disease (PD) at second line.

Results: Four sequences were identified: Sorafenib (Sor) followed by either regorafenib or cabozantinib (Sor-TKI), or chemotherapy (CT, capecitabine and/or cyclophosphamide, Sor-CT) or anti-PD1 agents (Sor-IO) and IO succeeded by Sor (IO-Sor).

Among the 77 pts enrolled, 28 received Sor-TKI, 34 Sor-CT, 6 Sor-IO and 9 IO-Sor: all of them were homogeneous in terms of baseline performance status, BCLC stage, Child Pugh score, macrovascular invasion, disease's etiology and extent (all p>0.05).

PFS1+2 was significantly different according to sequences (p=0.01), with the highest value observed in Sor-TKI and the lowest in IO-Sor (17.2 and 7.8 months, respectively), while no differences were shown in OS (p=0.34).

Looking at baseline characteristics across the sequences, AFP>400 was associated with poorer PFS1+2 both in Sor-TKI (p=0.015) and Sor-CT (p<0.001), where it also acted as an independent negative prognostic factor for OS (p=0.002). Similarly, the extrahepatic spread of disease was related to worse PFS1+2 (p=0.03) and OS (p=0.01) both in Sor-CT (PFS1+2: p=0,04) and in Sor-IO (OS: p=0.03).

HCV etiology correlated with better PFS1+2 in all sequences but IO-Sor, as did a lower BCLC stage with respect to Sor-CT both in terms of PFS1+2 and OS (both Cox's p=0.01).

Conclusions: In our series, Sor-TKI performed as the best strategy, especially in low AFP and in HCV pts. A disease extent beyond the liver played a poor prognostic role in Sor-CT and Sor-IO. No predictive factors (not even HCV etiology, unlike all other sequences) were found for IO-Sor, likely due to its limited numerosity. Additional data are still warranted.

C26

TUMOR BURDEN SCORE: A USEFUL TOOL TO PREDICT IMMUNE-RELATED HEPATOTOXICITY DURING IMMUNOTHERAPY FOR HCC

D'Alessio A.[1], Personeni N.[2], Cammarota A.[2], Prete M.G.[2], Ferrillo G.[3], Pedicini V.[3], Pressiani T.[2], Smiroldo V.[2], Bozzarelli S.[2], Giordano L.[4], Santoro A.[2], Rimassa L.[2]

[1]Humanitas Clinical and Research Center - IRCCS, Rozzano; [2]Medical Oncology and Hematology Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center - IRCCS, Rozzano; [3]Department of Radiology, Humanitas Clinical and Research Center - IRCCS, Rozzano; [4]Biostatistics Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center - IRCCS, Rozzano

Background: Treatment with immune checkpoint inhibitors (ICI) is complicated by the development of hepatic immune-related adverse events (HIRAEs) in around 9-20% of cases. While the risk factors for such adverse events are largely unknown, we assessed the role of tumor burden as a determinant for development of HIRAEs.

Material and methods: Our analysis included 36 patients with HCC treated with a monoclonal antibody (mAb) targeting the programmed cell death receptor-1 or its ligand (PD-1/PD-L1) as single agent (16 patients, 44%) or in combination with a mAb against the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) (20 patients, 56%). The pretreatment Tumor Burden Score (TBS) was calculated considering both the total number of liver nodules (a) and the maximum diameter (b) according to the following formula: $TBS^2 = a^2 + b^2$. Furthermore, we used a ROC curve to set a TBS threshold which could be used to predict the onset of HIRAEs. HIRAEs were categorized according to the Common Terminology Criteria for Adverse Events (v. 5.0).

Results: 18 patients (50%) developed any grade HIRAEs, of whom 5 (18%) developed G3-G4 HIRAEs. No G5 toxicity was registered. No patient permanently discontinued treatment because of HIRAEs. Patients who developed any grade HIRAEs had significantly higher mean values of TBS compared to patients with no HIRAEs (13.4 [95% CI 8.3 - 18.5] vs 7.3 [95% CI 3.7 - 11.1], p = 0.048). We did not find a significant correlation between the mean baseline TBS value and the development of G3-G4 HIRAEs (12.0 vs 10.1, p = 0.70, in patients who developed G3-G4 HIRAEs vs those with a lower grade hepatotoxicity, respectively). From the analysis of the ROC curve, we chose a TBS threshold of 10, with an area under the curve of 0.70 (95% CI 0.52-0.87, p = 0.046).

Patients with a TBS of 10 or more had a significantly higher risk of developing any grade HIRAEs compared to patients with TBS < 10 (Odds ratio = 5 [95% CI 1.1-17.8], p = 0.041). Median overall survival did not significantly differ between patients with TBS<10 and patients with TBS≥10 (7.9 months vs 6.3 months, p = 0.60).

Conclusions: In HCC patients treated with ICI, hepatic tumor burden could be a risk factor for the development of any grade HIRAEs. TBS is a useful tool to measure hepatic tumor burden and it could be used to predict the risk of HIRAEs. The role of TBS in predicting HIRAEs needs to be confirmed and validated in larger cohorts of HCC patients.

C27

TARGETING OF MITOCHONDRIA AS A NOVEL THERAPEUTIC STRATEGY IN BILIARY TRACT CANCER

Salati M.[1], Barbato A.[2], Indrieri A.[2], Volpe M.[2], Quadrano P.[2], Brillante S.[2], Mirante L.[2], Riccardo S.[2], Cacchiarelli D.[2], Iuliano A.[2], Franco B.[3], Dominici M.[4], Reggiani Bonetti L.[5], Salatiello M.[6], Troncone G.[6], Pietro C.[2]

[1]Division of Oncology, Department of Oncology and Hematology, University Hospital of Modena, Modena; [2]Tigem - Telethon Institute of Genetics and Medicine, Pozzuoli; [3]Tigem - Telethon Institute of Genetics and Medicine, Modena; [4]Division of Oncology, Department of Oncology and Hematology, University Hospital of Modena, Modena; [5]Section of Pathology, Azienda

Ospedaliero - Universitaria Policlinico di Modena, Modena, Italy, Modena;
[6]Department of Public Health, University of Naples Federico II, Napoli

Background: Mitochondria (Mi) are fundamentally implicated in cancer biology, including initiation, growth, metastasis, relapse, and acquired drug resistance. Mi are considered as the target organelles for therapeutic strategies of several cancers including CCA. The project aims to dissect the novel MiPa, to identify all molecular players, to functional characterize their role in CCA, to identify novel targeted therapies, to develop a gene signature exhibiting consistent prognostic power and predictive value as potential biomarker.

Methods: HTS has been performed by using Prestwick Chemical Library (Prestwick) and siGENOME Druggable-Genome-Library (Dharmacon). CASP9 activity has measured using the ApoAlert CASP9 assay (Clontech). Cell viability was monitored by CellTiter-Blue assay (Promega). The patient cohort consists of 100 patients retrospectively identified by Univeristy of Modena, IT. Lentiviral-based shRNA and CRISPR/Cas9 systems were utilized to establish stable gene knockdown and knockout model. FFPE-RNA extraction, RNAseq, WES and bioinformatic analyses will beperformed using protocols and pipeline available at TIGEM (2).

Results: Molecular players of the novel MiPa, which triggers APAF1-independent CASP-9 activation have been identified using a proteomic approach combined to siRNA library screening. HTS allowed to identify compounds targeting the novel MiPa. Two compounds were found to inhibit tumour growth in vitro and their anti-tumour efficacy has been assessed. Experiments in HuCCT-1, KMCH, CCLP, SW1, EGI, TFK1 cell lines revealed their effect on autophagy inhibition and apoptosis and correlated the MiPa pathway with drug treatment response and drug resistance. Whole-genome analysis is ongoing to profile the novel MiPa gene signature in cell lines treated and not with standard therapeutic approach and in a cohort of 100 CCA patients.

Conclusions: A novel MiPa has been identified regulating the apoptosis in CCA. Implication of the novel MiPa in drug resistance and sensitivity to classical therapeutic treatment has been assessed. Whole-transcriptome and exome analysis are ongoing to evaluate the clinical value of the MiPa gene signature in CCA patients.

1.Indrieri, A., et al., EMBO Mol Med, 2013.

2.Cacchiarelli D, et al., Cell. 2015.

C28

IMMUNE-INFLAMMATORY INDEXES AND BMI AS PREDICTORS OF OUTCOME AND TREATMENT RESPONSE IN ADVANCED GASTRIC CANCER RECEIVING RAMUCIRUMAB-CONTAINING SECOND-LINE

Riccò B.[1], Salati M.[1], Bocconi A.[1], Rimini M.[1], Santini C.[1], Caputo F.[1], Rovesti G.[1], Canino F.[1], Riggi M.L.[1], Bardasi C.[1], Benatti S.[1], Casadei Gardini A.[1], Gelsomino F.[1], Dominici M.[1], Luppi G.[1], Spallanzani A.[1]

[1]Università degli Studi di Modena e Reggio Emilia, Modena

Background: The efficacy of Ramucirumab in the treatment of advanced gastric cancer was demonstrated in the two pivotal study REGARD and RAINBOW, which both demonstrated significant improvements in Overall Survival (OS) and Progression-Free Survival (PFS). However, data on validated clinical and biochemical predictive factors in a real-life setting are still lacking.

Matherial and methods Retrospective analysis of medical records of patients with advanced gastric cancers treated with ramucirumab or ramucirumab/paclitaxel from April 2015 to April 2020 at Modena Cancer Center was conducted. Clinicopathological and biochemical parameters deemed of interest were collected. The cut-off value for continuous variables was assessed at 75° percentile. Treatment effects were evaluated by univariate and multivariate Cox proportional hazards regression models for OS and logistic regression analysis.

Results: During the study period, 49 patients with advanced gastric cancers were treated with ramucirumab alone (6.1%) or in combination with paclitaxel (93.9%) as second line therapy. At the multivariate, only CEA showed to impact on the second-line PFS with statistical significance (p=0.013, 95% Confidence Interval [CI] 1.08-6.4). By performing a logistic regression analysis, Absolute Neutrophil Count (ANC), Neutrophil Lymphocyte Ratio (NLR), Systemic Inflammatory Index (SII), CEA, Body Mass Index (BMI), ECOG Performance Status and Clinical Benefit (defined as complete response, partial response and stable disease versus disease progression) showed to be correlate with a PFS of more than 6 months. ECOG 0 and BMI>25 were the main predictive factors associated with Clinical Benefit (p=0.018 and p= 0.0006, respectively).

Conclusions: Favorable inflammatory indexes, CEA, BMI and ECOG confer a better second-line PFS. ECOG and BMI seem to be strictly related to Clinical Benefit, thus making these two parameters predictive of response to Ramucirumab. In the future, it will be mandatory a validation of our results on a larger population by the use of more specific parameters for the sarcopenia assessment.

C29

RETROSPECTIVE ASSESSMENT OF THE PROGNOSTIC VALUE OF THE NEUTROPHIL/LYMPHOCYTE RATIO (NLR) IN ADVANCED PANCREATIC CANCER (APC) PATIENTS UNDERGOING PALLIATIVE CHEMOTHERAPY. INTERDISCIPLINARY GROUP INTERCOMPANY CARE (GIC) OF BILIO-PANCREATIC CANCERS, ALESSANDRIA-ASTI, RETE ONCOLOGICA DEL PIEMONTE E DELLA VALLE D'AOSTA, ITALY

Traverso E.S.[1], Alessio M.[2], Gabelli V.[3], Bellotti G.[4], Fusco V.[4], Amisano M.[5], Nada E.[5], Silvestri S.[5], Novi M.L.[6], Gemme C.[6], Barbero S.[7], Segreto A.L.[8], Pastorino A.[7], Varese P.[9], Erra S.[10], Mariani N.[11], Feyles E.[12], Muni A.[13], Numico G.[4]

[1]S.C. Oncologia - A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [2]A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [3]Università Piemonte Orientale. A. Avogrado, Alessandria; [4]S.C. Oncologia - A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [5]Chirurgia Generale- Ospedale Santo Spirito Casale Monferrato, Casale Monferrato; [6]Gastroenterologia - A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [7]SC Radiologia - A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [8]SC Chirurgia Generale - A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [9]Medicina Generale-Ospedale Civile di Ovada, Ovada; [10]Anatomia Patologia- Ospedale Santo Spirito Casale Monferrato, Casale Monferrato; [11]Anatomia Patologia- A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria; [12]Anatomia Patologia- Ospedale Cardinal Massaia, Asti; [13]S.C. Medicina Nucleare- A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria

Background: The NLR is a simple and universally available index whose prognostic value has been shown in other solid tumors. We aimed at assessing the role of NLR in a series of pts with APC consecutively treated in our center.

Patients and methods: All the pts with APC undergoing chemotherapy since October 2017 were consecutively included in our data base. Baseline demographic and clinical characteristics were recorded, together with chemotherapy regimen, objective response rate, date of disease progression and of last follow up or death. For the time-to-event analysis median follow up of surviving pts was 11,2 months.

Results: 74 pts were included: 40 males (54,1%) and 34 females (45,9%); median age 69 (range 38-82). Site of primary: pancreatic head in 50 (67,6%), body in 10 (13,1%), tail in 11 (14,9%). In two pts the tumor was originating from the Vater papilla and in one case the primary could not be detected. Baseline ECOG PS was 0 in 36 (48,6%), 1 in 35 (47,3%) and 2 in 3 pts (4,1%). Forty-six pts (62,2%) complained for pain,18 (24,3%) for fatigue and 27 (36,5%) for jaundice. CA19.9 was = upper normal limits (UNL- 37 ng/mL) in 52 (70,3%), LDH (UNL 500 U/L) in 8 (10,8%). NLR = 3 was found in 26 pts (35,1%) and was >3 in 48 (64,9%).Pts were treated with either Gemcitabine (9, 12,2%), FOLFIRINOX (7, 9,5%) or Gemcitabine – Nab-paclitaxel (58, 78,4%). An objective response occurred in 12 pts (16,3%). Median PFS was 5,7 months (95% CI 2,7 – 8,7) and median OS was 7,9 months (95% CI 5,0-10,7). At univariate analysis the impact of the NLR on PFS was marginally significant while achieved the statistical significance for OS. Other factors that had a statistically significant impact on OS were PS, stage of disease, LDH value and the occurrence of fatigue. At multivariate analysis performed using the Cox proportional hazards model PS (0 vs 1-2) LDH (<UNL vs =UNL) and NLR (=3 vs >3) were the only factors retaining statistical significance.

Conclusions: In pts with APC undergoing chemotherapy the NLR could be an adjunctive tool in the prognostic evaluation. Further and wider analyses should be conducted in order to validate the use of this laboratory tool in clinical practice.

	NLR ⩽ 3	NLR>3	p
Median PFS (months)	6,5	3,3	0.085
Median OS (months)	13,8	6,6	0.017

C30

STATINS INHIBIT THE GROWTH OF HEPATOMA CELLS: FINDING THE ANTI-CANCER PATHWAY USING THREE DIFFERENT HUMAN HEPATOMA CELL LINES

Santini S.J.[1], Settepanella I.[2], Balsano C.[1]

[1]MESVA Department, University of L'Aquila; Francesco Balsano Foundation, L'Aquila; [2]Università degli Studi di L'Aquila, L'Aquila

Background: Hepatocellular carcinoma (HCC) is the fifth most common tumor in the world and the third cause of cancer mortality. Systemic chemotherapy is not a suitable option for most patients. Observational studies suggest a modest, but significant, reduction in the risk of liver cancer in patients with chronic liver disease who take statins. Recent studies have shown that statins can have potential protective effects against cancer, but only few and disagree studies have examined the relationship between liver cancer and statins. More research is needed to clarify the mechanism responsible for this effect. The aim of this work is to evaluate both the effect of statins on HCC cell lines, and to highlight the possible pathways involved.

Material and methods: We tested two of the most used statins, atorvastatin and rosuvastatin (Rosu), on three different human hepatoma cell lines: Huh7, Hep3B, and HepG2.

Results: Rosuvastatin was more effective than atorvastatin. Cell viability was reduced by Rosu in all cell lines, but the reduction was significant only in HepG2 and HuH7. Rosu induced cell cycle arrest in the G2/M phase in all the three cell types, and it was more effective on HepG2. A significant increase in apoptotic cells was observed only in Hep3B cells.

Conclusions: In conclusion, Rosu inhibits tumor growth in all the hepatocarcinoma cell lines analyzed, but it is able to induce apoptosis only in Hep3B. The main difference among Huh7, Hep3B and HepG2 is related to different level of p53 expression. HepG2 cells carry wild-type p53, whereas Hep3B and Huh7 cells have null and point mutations at p53, respectively.

The reasons above support the idea that Rosu could cause G2/M cycle arrest in a p53 independent way. In addition, the absence of p53 in Hep3B, seems to make these cells more sensitive to apoptosis after Rosu treatment.

C31

LDH LEVELS AS PROGNOSTIC FACTOR IN SECOND LINE TREATMENT FOR ADVANCED GASTRIC CANCER: THE LINE STUDY

Michelotti A.[1], Ongaro E.[1], De Scordilli M.[1], Gerratana L.[1], Mazzeo R.[1], Di Nardo P.[1], Foltran L.[1], Guardascione M.[1], Basile D.[1], Cortiula F.[1], Miolo G.[1], Fanotto V.[1], Parnofiello A.[1], Lisanti C.[1], Bertoli E.[1], Buriolla S.[1], Buonadonna A.[1], Puglisi F.[1]

[1]Department of Medical Oncology, Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, PN, Italy, Aviano

Background: Serum LDH levels are recognized as indirect marker of tumor hypoxia and angiogenesis for several solid tumors. Ramucirumab is the first target agent approved for second-line therapy in advanced gastric cancer (GC), alone or in association with chemotherapy. To date, no reliable biomarkers can predict the potential benefit from anti-VEGFR2 treatment. This retrospective study aimed to assess the prognostic impact of baseline LDH levels in advanced GC in second-line setting.

Materials and methods: We analyzed a cohort of consecutive patients with advanced GC treated at IRCCS, CRO of Aviano, Italy, from 2010 to 2019. LDH levels prior to second-line treatment were classified as low-normal or high and normalized according to the upper limit of the reference range. To determine the optimal LDH cut-off value, ROC analysis was performed. A multivariate Cox regression analysis assessed the prognostic impact of LDH levels for PFS and OS. Subgroup analyses according to LDH levels were carried out.

Results: Overall, 94 patients were enrolled. Of these, 65 patients (69.15%) received ramucirumab alone or plus paclitaxel as second-line treatment, while 29 (30.85%) had taxanes or fluoropyrimidines combined with irinotecan. Median age was 68 years, 93% had an ECOG PS $\leq$ 1, 62.7% was first diagnosed with metastatic disease and 40.4% underwent primary tumor resection. Median second-line PFS and OS were 3.7 and 7.9 months, respectively. Serum LDH values were reported for 66 patients, exceeding the upper limit in 19.7% of cases. High baseline LDH level was confirmed as a negative prognostic factor by multivariate Cox regression analysis for both PFS (HR 2.35, 95% CI 1.09-5.1, p=0.029) and OS (HR 2.26, 95% CI 1.01-5.07, p=0.04). Notably, ROC analysis identified a normalized LDH value of 0.84 as the optimized cut-off point. Subgroup analyses showed a trend towards worse PFS (HR 2.76, 95% CI 1.09-6.94) and OS (HR 4.29, 95% CI 1.59-11.51) (p of interaction=0.096) in patients treated with ramucirumab-based schemes with high baseline LDH levels.

Conclusions: Elevated serum LDH levels at second-line treatment start is an independent prognostic factor of poor prognosis in advanced gastric cancer. Moreover, this biomarker could have a role in predicting the activity of antiangiogenic agents. Case expansion and prospective validation are needed to assess the efficacy of the optimized LDH cut-off in better defining a poor prognosis subgroup among patients with normal LDH levels.

C32

CLEAR CELL VARIANT OF HEPATOCELLULAR CARCINOMA (HCC-CC): A SINGLE-CENTER OBSERVATIONAL STUDY OF AN UNCOMMON SUBTYPE

Salani F.[1], Pecora I.[1], Vivaldi C.[2], Massa V.[1], Catanese S.[1], Bernardini L.[1], Caccese M.[1], Cesario S.[1], Vasile E.[1], Lencioni M.[1], Fornaro L.[1], Falcone A.[2], Masi G.[2]

[1]Azienda Ospedaliera Universitaria Pisana, Pisa; [2]Università di Pisa, Pisa

Background: HCC-CC is the second most frequent rare pathological variant of HCC subtypes. Despite its epidemiological, clinical, radiological and molecular peculiarities, no dedicated guidelines nor clinical trials are available.

Methods: We retrospectively collected data from HCC-CC patients (pts) followed at our centre from 2015. Our aim was to describe pts' baseline characteristics and outcomes in terms of progression-free survival (PFS) and overall survival (OS), using Kaplan-Meier method.

Results: Among 73 HCC pts with a histologically confirmed diagnosis, 18 (24.7%) had HCC-CC subtype and were therefore included. Of them, 16 (88.9%) were males and 2 females (11.1%), with a mean age at diagnosis of 67 years (range: 53-79). Etiology was dysmetabolic in 9 pts (50.0%), HCV in 1 (5.5%) and 8 cases (44.5%) arose on healthy liver. At baseline, Child-Pugh was A in all pts, while BCLC was A in 12 (66.7%), B in 1 (5.5%) and C in 5 (27.8%). As first treatment, 16 pts (88.9%) underwent surgery, 1 liver transplantation and 1 transarterial chemoembolization (TACE). At first progression, 4 pts received additional locoregional treatments. After a median of 19.0 months (mos) from initial curative-intent treatment, 10 pts (55.5%) progressed, showing extrahepatic spread in 80% of cases (40% peritoneal, 30% lung and 10% skeletal, 20% other). Six metastatic pts received a systemic first-line therapy: 4 sorafenib, 1 durvalumab and 1 lenvatinib plus pembrolizumab/placebo. Best radiological response was disease progression in 66.7% of cases, with a median PFS of 2.76 mos (95% CI 1.38-5.03). Notably, most pts received subsequent systemic therapies (50% second-line, 20% third-line) and 20% were considered for surgery (peritonectomy with hypertermic intraperitoneal chemotherapy), reaching a median OS of 55.23 mos. Surgery was the only treatment in other 2 metastatic pts; of note, 1 of them reached a 50 mos of OS undergoing multiple excisions of extrahepatic localizations.

Conclusion: Our HCC-CC pts showed predominantly non-viral etiology, early-stage at diagnosis, preserved liver function and a relatively favourable outcome, consistently with previously published data. Interestingly, we observed a poor efficacy of systemic treatment, whereas surgery seemed to be effective even in the metastatic setting. Wider multicentric experiences are warranted to shed light on this not-so-rare HCC-subtype.

C33

EFFICACY AND SAFETY OF PERIOPERATIVE CHEMOTHERAPY (FLOT) IN LOCALLY ADVANCED GASTRIC CANCER: REAL-WORLD EXPERIENCE OF A SINGLE CENTRE

Massucci M.[1], Andrini E.[1], Bonucci C.[1], Ricci A.D.[1], Rizzo A.[1], Tober N.[1], Rojas Llimpe F.L.[1], Di Fabio F.[1], Ardizzoni A.[1]

[1]Sant'Orsola-Malpighi Hospital, Bologna

Background: In locally advanced resectable gastric or gastroesophageal junction adenocarcinoma perioperative chemotherapy with 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) improves overall survival compared to perioperative epirubicin, cisplatin and 5-fluorouracil/capecitabine (ECF/ECX).

Material and methods: In this observational-retrospective study we analyzed patients (pts) with locally advanced gastric cancer who received perioperative chemotherapy (FLOT) between December 2017 and January 2020. Our intent was to explore the compliance, safety and effectiveness of FLOT in this setting.

Results: A total of 17 pts were screened to receive perioperative chemotherapy with FLOT. Median age was 68yrs. Performance Status (PS) was 0 in 6 pts (35,3%), 1 in 9 pts (52,9%) and 2 in 1 pt (5,9%). 13 pts (76,5%) were staged by CT scan and FDG-PET, 4 pts (23,5%) with CT scan alone and only 1 pt (5,9%) underwent diagnostic laparoscopy before starting treatment. Clinical stage was I for 1 pt (5,9%), II for 5 pts (29,4%), III for 10 pts (58,8%) and IV for 1 pt (5,9%). After staging, 16 pts were considered eligible to receive FLOT and the final analysis was performed on these pts. 13 pts (81,2%) completed preoperative phase with 4 cycles of FLOT and, among 13 pts (81,2%) who underwent surgery, 6 pts (46%) received postoperative chemotherapy with FLOT. 2 pts (12,5%) died after the first preoperative cycle of FLOT (one of them had poor PS), 3 pts (18,7%) were found to be metastatic during surgery and 1 pt (6,2%) relapsed in a short time. High-grade adverse events occurred in 5 pts. Pathological complete response (pCR) has been obtained only in 1 pt. At a median follow up of 13,6 months (95% C.I. 6,2-21), median OS and RFS were not reached. Only 1 of the pts who completed treatment relapsed.

Conclusions: From this study stands out the importance of a correct clinical selection and thorough staging of pts. Indeed, in our experience, perioperative chemotherapy with FLOT is well tolerated and effective in well selected pts.

CHARACTERISTICS	PTS (n=17)
SEX	
male	13 (76,5%)
female	4 (23,5%)
PS	
0	6 (35,3%)
1	9 (52,9%)
2	1 (5,9%)
STAGING	
I	1 (5,9%)
II	5 (29,4%)

(Continued)

CHARACTERISTICS	PTS (n=17)
III	10 (58,8%)
IV	1 (5,9%)
IMAGING	
ct	4 (23,5%)
ct+ fdg-pet	13 (76,5%)
ct+laparoscopy	1 (5,9%)
COMPLIANCE	
completed preoperative phase	13 (81,2%)
full doses	10 (62,5%)
completed postoperative phase	6 (37,5%)
full doses	2 (12,5%)
PROPHYLAXIS G-CSF	
primary	12 (70,6%)
secondary	1 (6,2%)
PATHOLOGICAL RESPONSE	
pCR	1 (6,2%)
ADVERSE EVENT	
gi G3/G4	1 (6,2%)
hematological G3/G4	2 (12,5%)
stomatitis G3/G4	1 (6,2%)
asthenia G3/G4	1 (6,2%)

C34

FOLFIRINOX VERSUS GEMCITABINE PLUS NAB-PACLITAXEL AS FIRST LINE TREATMENT IN PATIENTS WITH ADVANCED/METASTATIC PANCREATIC CANCER: A RETROSPECTIVE STUDY

Orlandi E.[1], Citterio C.[1], Stroppa E.[1], Vecchia S.[1], Cavanna L.[1]

[1]Ospedale Guglielmo da Saliceto, Piacenza

Background: Advanced pancreatic cancer show a poor prognosis. Fortunately, the treatment of patients with advanced unresectable or metastatic disease is challenging. Current guidelines recommend Nab-Paclitaxel plus Gemcitabine (NabP-GEM) or FOLFIRINOX (FOL) as first-line treatment, thereby leaving the choice up to the treating physician. Data on comparison of efficacy and toxicity of FOL and NabP-GEM in metastatic cancer are fragmentary and poor.

Material (patients) and methods: A total of 123 patients with histologically confirmed diagnosis of advanced or metastatic pancreatic cancer received either first-line therapy (NabP-GEM or FOL) between March 2013 and January 2019 at the Piacenza Hospital. We evaluated retrospectively prognostic factors for PFS and OS; variables which showed potential association in the univariate analyses (p<0.05) were further tested in the multivariate analyses.

Results: 50 (40.65%) patients received first line FOL (86% received a dose reduction) and 73 (59.35%) received first line NabP-GEM, with no significant difference in baseline patient's and disease's characteristics. The median PFS and

OS were comparable between the NabP-GEM and FOL groups: PFS was 15.0 vs 14.3 months; p=0.50. OS was 22.8 vs 22.6 months; p=0.86. There was no difference in the percentage of toxicity G3/G4 event between the two groups (p=0.723). Sex, radiotherapy and treatment duration resulted significant factor related to PFS in the multivariate model (p-value=0.02, <0.001, <0.001 respectively); radiotherapy, treatment duration and subsequent line of therapy resulted related to OS (p-value 0.008, <0.001, <0.001 respectively). 69 (56.10%) patients performed subsequent second-line chemotherapy after progression of first-line, 39 (53.43%) of the NabP-GEM group and 30 (60%) of FOL group, with no significant difference.

Conclusions: The literature suggest first line FOL mainly based on the patient conditions with worse toxicity profile compared to NabP-GEM. Our study demonstrate no difference in the first line in outcome survival between the two treatments; unexpectedly no greater FOL-related toxicity, probably due to safe and effective FOL dose reduction in a variable quote of patients. First treatment choice need to consider the recent result of FOL in neoadjuvant and adjuvant settings, that can shift this regimen before the first line, and the recent data about the PARP inhibitors in a subpopulation first-line platinum-based chemotherapy responders.

C35

MANAGEMENT OF OLDER PATIENTS WITH ADVANCED PANCREATIC CANCER: THE G8 GERIATRIC ASSESSMENT TOOL DOES NOT SEEM TO BE A RELIABLE TOOL TO DETECT FRAILTY

Gebbia V.[1], Mare M.[2], Cordio S.[3], Valerio M.R.[4], Piazza D.[5], Bordonaro R.[6], Firenze A.[7], Giuffrida D.[2]

[1]*Medical Oncology Unit, Casa di Cura La Maddalena, Palermo;* [2]*Medical Oncology Unit, Istituto Oncologico del Mediterraneo, Viagrande (CT);* [3]*Medical Oncology Unit, Ospedale "Paternò Arezzo", Ragusa;* [4]*Medical Oncology Unit, Policlinico "Paolo Giaccone", University of Palermo, Palermo;* [5]*GSTU Foundation for Cancer Research, Palermo;* [6]*Medical Oncology Unit, ARNAS Garibaldi, Catania;* [7]*Risk Management Unit, Policlinico "Paolo Giaccone", University of Palermo, Palermo*

Background: This paper aims to analyze the usefulness of the G8 geriatric oncology questionnaire in patients with advanced/metastatic pancreatic adenocarcinoma (aPAC) and its possible association with different clinical outcomes.

Material and Methods: Patients age > 70 years with aPAC were screened with the G8 tool. Patients were treated at four medical oncology units with a regimen of intravenous nab-paclitaxel 125 mg/m2 and gemcitabine 1000 mg/m2 for 3 consecutive weeks followed by one-week rest as prescribed after clinical evaluation by treating oncologists. Patients charts were evaluated for type and severity of toxicity, 2 cycle rate of completion, discontinuation rate, delays, dose reductions, and other outcomes response rates,

progression-free, and overall survival. Sensitivity, specificity, and possible correlations were analyzed.

Results: Sensitivity and specificity of the G8 score for severe toxicity were respectively 55.9% (95% CI 39,45% to 71,12%) and 50% (95%CI 18,76% to 81,24%). No association between all types of severe grade 3-4 toxicity, delays, or dose reductions, and the G8 score was present (p=0.622, not significant). ORR was 32.5% (95% CI; 20.1-49.3) with no complete responses. Twelve patients achieved stabilization of disease (30%) for a TGCR of 62.5% (95% Cl; 47.7-76.3). Median PFS and OS were 4.5 months and 8.1 months, respectively. Correlation between G8 score and PFS was not statistically significant (r -2944; p=0.0652). Correlation between G8 score and OS was statistically significant (r -0.3539; p=0.0251). Although median survival of G8 fit patients was superior to that of G8 vulnerable patients (6.5 months versus 4 months, respectively) the difference was not statistically different (p=0.1975)

Conclusions: Clinical results in terms of response rate, survival outcomes, and side-effects were in the range reported by others. However, the G8 questionnaire is not a reliable diagnostic tool to predict the risk of severe toxicity, rate of chemotherapy completion, and clinical outcomes in elderly patients with aPAC cancer treated with the nab-paclitaxel and gemcitabine. Future prospective studies should investigate the role of other questionnaires.

D - COVID-19

D01*

COVID-19 ANALYSIS FROM THE MULTICENTER, PROSPECTIVE, OBSERVATIONAL INVIDIA-2 STUDY (INFLUENZA VACCINE INDICATION DURING THERAPY WITH IMMUNE CHECKPOINT INHIBITORS: A TRANSVERSAL CHALLENGE) – A FICOG STUDY

Buti S.[1], Giannarelli D.[2], De Giorgi U.[3], Pignata S.[4], Di Maio M.[5], Clemente A.[6], Verzoni E.[7], Guadalupi V.[7], Giusti R.[8], Garassino M.[7], Taurelli Salimbeni B.[8], Veccia A.[9], Mazzoni F.[10], Aprile G.[11], Baldessari C.[12], Cortellini A.[13], Verderame F.[14], Montesarchio V.[15], Rizzo M.[16], Procopio G.[7], Bersanelli M.[1]

[1]*Azienda Ospedaliero-Universitaria di Parma, Parma;* [2]*Istituto Nazionale Tumori Regina Elena, Roma;* [3]*IRCCS Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola;* [4]*IRCCS Istituto Nazionale Tumori G. Pascale, Napoli;* [5]*Ospedale Mauriziano - Università degli Studi di Torino, Torino;* [6]*IRCCS Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Ravenna;* [7]*IRCCS Istituto Nazionale Tumori di Milano, Milano;* [8]*Azienda Ospedaliero Universitaria Sant'Andrea, Sapienza Università di Roma, Roma;* [9]*Ospedale Santa Chiara, Trento;* [10]*Azienda Ospadaliero Universitaria Careggi, Firenze;* [11]*Ospedale San Bortolo Azienda ULSS8 Berica - Distretto Est, Vicenza;* [12]*Policlinico di Modena, Centro Oncologico Modenese, Modena;* [13]*Ospedale San Salvatore, Università dell'Aquila, L'Aquila;* [14]*Azienda Ospedali Riuniti Villa Sofia Cervello, Palermo;* [15]*Azienda Ospedaliera Specialistica dei Colli - Monaldi, Napoli;* [16]*Istituti Clinici Scientifici Maugeri, Pavia*

Background: The prospective, multicenter, observational INVIDIa-2 study was designed to investigate the clinical efficacy of influenza vaccination in advanced cancer patients receiving immune checkpoint inhibitors (ICIs) from October 2019 to January 2020. The primary end-point was the incidence of influenza-like illness (ILI) until April 30, 2020. All ILI episodes, laboratory tests, complications, hospitalizations and pneumonitis were recorded. Therefore, the INVIDIa-2 study prospectively recorded all the COVID-19 ILI events.

Methods: Patients were included in this non-prespecified COVID-19 preliminary analysis if potentially exposed to Sars-Cov-2 infection, namely alive on January 31, 2020, when the Italian government declared the National emergency. The incidence of confirmed COVID-19 was assessed among patients with ILI symptoms, describing the hospitalization rate and mortality. Cases with clinical-radiological diagnosis of COVID-19 without laboratory confirmation (COVID-like ILIs), were also reported. The COVID-incidence was exploratively compared basing on influenza vaccination.

Results: 1260 patients receiving ICI were enrolled between October 2019 and January 2020; 955 patients were analyzed according to the inclusion criterion. Of them, 66 patients had ILI from January 31, to April 30, 2020. 9 were COVID-19 ILIs with laboratory test confirmation. The COVID-19 ILI incidence was 0.9% (9/955 cases), with hospitalization rate of 100% and mortality rate of 67%. Including 5 COVID-like ILIs, the overall COVID-19 incidence was 1.5% (14/955), with hospitalization in 100% of cases and mortality rate of 64%. COVID-19 incidence was 1.2% for patients vaccinated against influenza (6/482 cases) and 1.7%, among unvaccinated patients (8/473 including 3 confirmed COVID-19 and 5 COVID-like), p = 0.52. The difference was not statistically significant, and the clinical trend in favor of vaccinated patients was lost when considering only confirmed COVID-19 (1.2% in vaccinated vs 0.6% in unvaccinated patients, p = 0.33), probably due to the greater presence of male and elderly patients in the vaccinated group (p = 0.009).

Conclusions: We obtained the first prospective epidemiological data about symptomatic COVID-19 in advanced cancer patients receiving ICIs. The overall symptomatic COVID-incidence is meaningful, requiring hospitalization in all cases and leading to a high mortality rate, likely due advanced cancer more than to ICI therapy [Mengyuan Dai, Cancer Discov 2020].

D02*

THE BEGINNING OF THE COVID-19 ERA. THE PERCEPTION OF ONCOLOGICAL PATIENTS (PTS) IN ACTIVE TREATMENT AT THE BRINDISI AND MAURIZIANO HOSPITAL ONCOLOGY DEPARTMENTS

Loparco D.[1], Di Maio M.[2], Orlando L.[3], Dascanio F.[2], Caliolo C.[3], Ignazzi G.[2], Schiavone P.[3], Lacidogna G.[2], Quaranta A.[3], Marino D.[2], Del Bene G.[3], Vignani F.[2], Fedele P.[3], Sperti E.[2], Caloro M.[3], Terzolo S.[2], Fusco L.[2], Ballaminut D.[2], D'Amico M.[3], Cinieri S.[3]

[1]UOC Oncologia Medica - P.O. Perrino ASL Brindisi, Bindisi; [2]Azienda Ospedaliera Ordine Mauriziano di Torino, Torino; [3]UOC Oncologia Medica - P.O. Perrino - ASL Brindisi, Brindisi

Background: The exceptional circumstances caused by the Covid-19 pandemic have had a strong logistical and psychological impact on the population. A specific attention has been devoted to the organization of activity of Oncology units and to oncological patients' mental health conditions. In fact, together with the anxiety caused by the disease, oncological pts are now experiencing also apprehension because of the pandemic. The aim of this research is to evaluate how the Covid-19 emergency has affected access to treatments, management of disease and the psychological impact on pts in 2 Oncology Units in Brindisi (Apulia) and Turin (Piedmont).

Methods: In a 2 week period between April and May 2020, a structured questionnaire was administered to pts in active treatment at the Day hospital (DH)/ Day Service (DS) of Oncology Dpts at Brindisi and Mauriziano Hospital. The questionnaire was anonymous, self-administered, with 5 closed-ended questions with a "yes/no" answers and 10 questions involving a modified Likert scale of 4 answers (not at all, a little, quite a bit, very much). Percentage data are analyzed for the whole series and the 2 centers separately.

Results: 404 questionnaires were collected (Brindisi 202, Turin 202). The main difference involves the number of pts with relatives tested positive to SARS-CoV2 (Apulia 2% vs Piedmont 11.4%, p=0.002). Overall, 343 pts (84,9%) referred no relevant changes in the treatment of their illness. They indicated no relevant alterations in the access to medical care (n= 362, 90%), in outpatient visits (n= 341, 84.8%), in running diagnostic exams (n= 340, 84.6%) and in drug supply (n= 365, 90.8%). 291 pts (72,4%) did not perceive a significant risk of contagion in accessing their DH/DS. Overall, pts did not believe they have received a significant reduction in assistance (n=372, 92.1%). The communication with the medical staff has been judged effective and clear (n= 374, 93%) and pts claimed it had been easy to reach the staff via phone and/ or e-mail (n=364, 90.1%). There were no relevant differences between the 2 centers.

Conclusions: Despite the changes in the clinical management of cancer pts due to the Covid-19 emergency, our data show that most pts did not perceive any relevant difference in the management, both from an operational and relational point of view. In perspective, we aim to promote a comparative analysis between the 2 regions, to take into account the different morbidity of the Covid-19 infection.

D03*

COVID-19 INFECTION IN CANCER PATIENTS RECEIVING ANTITUMOR TREATMENT AT MEDICAL ONCOLOGY HOSPITAL UNITS IN ITALY. A CIPOMO OBSERVATIONAL STUDY (CIPOMO ONCO COVID-19)

Negru M.E.[1], Pastorino A.[1], Rita C.[2], Oliani C.[3], Repetto L.[4], Canova S.[5], Fasola G.[6], Maestri A.[7], Giordano M.[8], Romaniello I.[9], Nastasi G.[10], Miraglia S.[11], Varese P.[12], Daniele B.[13], Cavanna L.[14], Montesarchio V.[15], Pinotti G.[16], Zamagni C.[17], Blasi L.[18], Aschele C.[1]

[1]*Medical Oncology Department, Ospedale Sant'Andrea, La Spezia;* [2]*Medical Oncology Department, Ospedali Riuniti Padova Sud - AULSS 6 Euganea, Padova;* [3]*Medical Oncology Department, Ospedale S. Maria della Misericordia, Rovigo;* [4]*Medical Oncology Department, Ospedale Giovanni Borea ASL 1, Sanremo;* [5]*Medical Oncology Department, Azienda Ospedaliera San Gerardo ASST Monza, Monza;* [6]*Medical Oncology Department, Presidio Ospedaliero Universitario Santa Maria della Misericordia Azienda Sanitaria Universitaria Integrata Friuli Centrale, Udine;* [7]*Department of Medical Oncology, Ospedale Santa Maria della Scaletta Azienda USL Imola, Imola;* [8]*Medical Oncology Division, ASST-Lariana, Como;* [9]*Medical Oncology Division, Ospedale SS Trinità, Borgomanero;* [10]*Department of Medical Oncology, Azienda Socio Sanitaria Territoriale Bergamo EST, Seriate;* [11]*Medical Oncology Department, Ospedale Martini ASL Città di Torino, Torino;* [12]*Medical Oncology Division, Ospedale Civile ASL AL Piemonte, Ovada;* [13]*Oncology Unit, Ospedale Del Mare, Napoli;* [14]*Oncology-Hematology Department, Hospital of Piacenza, Piacenza;* [15]*Oncology Unit, "Monaldi" Hospital, Napoli;* [16]*Medical Oncology Department, ASST Sette Laghi, Varese;* [17]*Medical Oncology Unit, S.Orsola-Malpighi Hospital, Bologna;* [18]*Medical Oncology Unit, ARNAS Civico, Palermo*

Background: Cancer patients are more susceptible to infections and potentially at higher risk to develop COVID-19. Tumor type and antitumor treatment may also affect both the susceptibility and the severity of SARS COV-2.

Material and methods: To analyze the distribution of patients who developed COVID-19 during active antineoplastic therapy and the related clinical course by tumor type, stage and class of oncologic treatment (chemo, immune, biologic therapy and other) a multicenter, retro-prospective, observational study was proposed to the Hospital Medical Oncologic Units of the National Health Service in Italy (168 centers of the Collegio Italiano dei Primari Oncologi Medici Ospedalieri -CIPOMO). The data were collected on demographics, tumor characteristics, treatment setting, type of ongoing anti-cancer therapy and COVID-19 clinical course (phenotype, hospitalization, therapy, duration and outcome). Eligibility required a positive COVID-19 molecular test before May 4th, 2020 and at least 1 course of antitumor therapy delivered after January 15th .

Results: At present analysis data are available from 116 of 168 centers (7 declined, 28 pending, 17 data awaited). 64 of 116 centers (55%) had COVID-19 positive cases (cases/center: median 3, range 1-40). At these 64 centers, 283 positive cases (males 158, 55.9%, females 125, 44.1%; median age 67 years, range 28-89) were observed among a total population of 40.894 patients receiving active treatment between January 15th and May 4th 2020. 65 of 283 (23%) had cardiovascular comorbidities and 7 (2%) pre-existent pulmonary disease. 239/283 patients (84.4%) were receiving treatment for metastatic disease and 44 (15.6%) were in the adjuvant setting. Breast, lung, colon and prostate cancer were the main tumor types accounting for 61% of cases.

Conclusions: The occurrence of COVID-19 among cancer patients receiving active antitumor treatment appears to reflect tumor epidemiology. Full analysis of the distribution of COVID-19 occurrence and clinical course by tumor type, stage and oncologic treatment will be presented.

D04*

IN-HOSPITAL ACTIVITY FOR CANCER CARE DURING COVID-19 PANDEMIC: A FIRST OVERVIEW IN PIEDMONT REGION

Pagano E.[1], Gilardetti M.[1], Mistrangelo M.[2], Bertetto O.[2], Ciccone G.[1]

[1]*AOU Città della Salute e della Scienza - Epidemiologia clinica e valutativa - CPO Piemonte, Torino;* [2]*Dipartimento Rete Oncologica Piemonte e Valle d'Aosta - AOU Città della Salute e della Scienza, Torino*

Background: Due to COVID-19 pandemic, hospitals had to re-organize their activities and limit care to non-COVID patients. Even oncological care could have registered a partial reduction, both for preventing the risks of infection and to free up resources to be used for the management of COVID-19. To understand the amount of unmet demand in cancer care during the COVID-19 emergency is extremely urgent to foresee appropriate actions of recovering in the coming months.

Material and methods: Hospital discharges records (HDRs) for cancer care to residents in Piedmont Region were analysed during the first quarter of year 2020 and compared with the same data of year 2019. Medical and surgical hospitalizations and day-surgery were included in the analysis. Day-hospitals were excluded as presently highly uncompleted. Differences between the two year were described as percentage difference by month, cancer type, age class and Local Health Unit (LHUs) of residence.

Results: During the first quarter of 2020, in the Piedmont Region, the HDRs for cancer care to residents in Piedmont Region were 9332 for inpatient care and 3689 for day-surgery. Overall (n=13.021) HDRs were lower (-11%) compared with the previous year (n= 14.558). Considering only March, such reduction was 29%.The highest reduction is reported for the day surgery activity (-49.7% in March), with the largest impact for benign tumors and non-melanoma skin-cancers.

In-patient surgical care showed a 17% reduction during March compared with the previous year (corresponding to a reduction of about 400 discharges), with the largest

impact for benign tumors (-53%) and in situ cases (-32%). Among the cancer sites with a high - absolute and relative - reduction are: bladder (-27,4%), breast (-27.5%) and prostate (-13.2%). For all the other cancer sites no difference in HDRs was evidenced compared with 2019.

In-patient medical care during March showed a 24% reduction, involving most of the cancer sites.

Cancer care reduction resulted homogeneous across all the LHUs in the Region and between age classes.

Conclusions: In the Piedmont Region during the first quarter of year 2020 in hospital cancer care was slightly reduced because of the COVID-19 pandemic and limited to few cancer sites, hopefully involving selected cases whose prognosis is not expected to deteriorate due to a delayed surgery. Further analyses are ongoing to include the months of April and May.

D05

ASSESSING THE IMPACT OF COVID-19 OUTBREAK ON THE ATTITUDES AND PRACTICE OF ITALIAN ONCOLOGISTS TOWARDS BREAST CANCER CARE AND RELATED RESEARCH ACTIVITIES

Poggio F.[1], Tagliamento M.[1], Di Maio M.[2], Martelli V.[1], De Maria A.[3], Barisione E.[1], Grosso M.[1], Conte B.[1], Molinelli C.[1], Favero D.[1], Pirrone C.[1], Boccardo F.[3], Pronzato P.[1], Del Mastro L.[3], Lambertini M.[3]

[1]IRCCS Ospedale Policlinico San Martino, Genova; [2]Università di Torino **and** Ospedale Mauriziano, Torino; [3]IRCCS Ospedale Policlinico San Martino **and** Università di Genova, Genova

Background: Coronavirus disease 2019 (COVID-19) outbreak is changing the approach of medical oncologists to cancer management. However, the real impact on cancer care and its potential negative consequences are currently unknown.

Methods: A 29-multiple choice question anonymous online survey was shared with members of the Italian Association of Medical Oncology and the Gruppo Italiano Mammella on April 3, 2020.

The objectives of the survey were to investigate the attitudes and practice of Italian oncologists before and during COVID-19 outbreak on three relevant areas in breast cancer care: 1) (neo)adjuvant setting; 2) metastatic setting; 3) research activities.

Results: The survey was completed by 165 oncologists, of whom 121 (73.3.%) worked in Breast Units. In the (neo) adjuvant setting, compared to before the emergency, a lower rate of oncologists adopted during COVID-19 outbreak weekly paclitaxel (68.5% vs. 93.9%, $P<.001$) and dose-dense schedule for anthracycline-based chemotherapy (43% vs. 58.8%, $P<.001$).

In the metastatic setting, compared to before the emergency, a lower number of oncologists adopted during COVID-19 outbreak first-line weekly paclitaxel for HER2-positive disease (41.8% vs. 53.9%, $P=.002$) or CDK4/6 inhibitors for luminal tumors with less aggressive characteristics (55.8% vs. 80.0%, $P<.001$). A significant change was also observed in terms of delaying the timing for monitoring CDK4/6 inhibitors therapy, assessing treatment response with imaging and flushing central venous devices.

Clinical research and scientific activities were reduced in 80.3% and 80.1% of respondents previously involved in these activities, respectively.

Conclusions: Most of the changes in the attitudes and practice of Italian oncologists were reasonable responses to the current health emergency without expected major negative impact on patients' outcomes, although some potentially alarming signals of undertreatment were observed. These data invite developing cautious recommendations to help oncologists ensuring continuous effective and safe cancer care.

D06

IGG ANTIBODY RESPONSE IN CANCER PATIENTS AND ONCOLOGY HEALTH WORKERS INFECTED WITH SARS-COV-2: AN ITALIAN, MULTICENTER, PROSPECTIVE STUDY

Marra A.[1], Generali D.[2], Zagami P.[3], Gandini S.[4], Cervoni V.[2], Venturini S.[5], Morganti S.[1], Passerini R.[6], Orecchia R.[7], Curigliano G.[1]

[1]Division of Early Drug Development for Innovative Therapies, European Institute of Oncology IRCCS, Department of Oncology and Haematology, University of Milan, Milano; [2]U.O. Multidisciplinare di Patologia Mammaria e Ricerca Traslazionale, Azienda Socio-Sanitaria Territoriale di Cremona, Cremona; [3]Division of Early Drug Development for Innovative Therapies, European Institute of Oncology IRCCS, Department of Oncology and Haematology, University of Milan, Milano; [4]Department of Experimental Oncology, European Institute of Oncology IRCCS, Milano; [5]Department of Management, University of Turin; Centre for Research on Health and Social Care Management (CeRGAS), SDA Bocconi School of Management, Torino; [6]Division of Laboratory Medicine, European Institute of Oncology IRCCS, Milano; [7]Scientific Direction, European Institute of Oncology IRCCS, Milano

Background: Patients with cancer have been reported to experience severe complications and poor outcomes to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related disease (COVID-19). Anti-SARS-CoV-2 immunoglobulin-G (IgG) can be detected within three weeks after infection. However, scant information is available on the seroconversion rates of patients with cancer and COVID-19.

Material: This is a multicenter, observational, prospective study that enrolled patients and oncology health professionals with SARS-CoV-2 infection confirmed by RT-PCR assay, patients and oncology health professionals with clinical or radiological suspicious of infection by SARS-CoV-2, and patients with cancer who are considered at high risk for infection. All subjects were tested with the *2019-nCoV IgG/IgM Rapid Test Cassett*, which is a qualitative membrane-based

immunoassay for the detection of IgG and IgM antibodies to SARS-CoV-2. The aim of the study was to evaluate anti-SARS-CoV-2 seroconversion rate in patients with cancer and healthcare professionals with confirmed or clinically suspected COVID-19.

Results: Between March 30 and May 11, 2020, 166 subjects were enrolled in the study. Cancer patients and health workers were 61 (36.7%) and 105 (63.3%), respectively. Seventy-four subjects (44.6%) had confirmed SARS-CoV-2 diagnosis by RT-PCR testing on nasopharyngeal swab specimen, while 49 (29.5%) had a clinical suspicious of COVID-19 in absence of RT-PCR confirmation. Median time between symptom onset/ RT-PCR confirmation to serum antibody test was 17 days (IQR, 26). Considering the population with confirmation by RT-PCR, 83.8% was IgG positive. Neither differences in terms of IgG positivity rate nor in median time from SARS-CoV-2 diagnosis to IgG detection were observed between cancer patients and health workers (87.9% vs 80.5%; *P*=0.39; 23.0 vs 28.0 days; *P*=0.21).

Conclusions: Our data indicate that SARS-CoV-2-specific IgG antibody detection does not differ between cancer patients and healthy subjects. Fast test for antibody detection can be complementary to RNA RT-PCR testing for the diagnosis of COVID-19 in this vulnerable patient population.

D07

THE EMOTIONAL IMPACT OF COVID-19 OUTBREAK ON CANCER OUT-PATIENTS AND THEIR CAREGIVERS: RESULTS OF A SURVEY IN THE HEART OF THE ITALIAN PANDEMIC

Cona M.S.[1], Dalu D.[1], Rota S.[1], Ferrario S.[1], Gambaro A.R.[1], Tosca N.[1], Filipazzi V.[1], La Verde N.[1]

[1]ASST Fatebenefratelli Sacco - Polo Ospedaliero Luigi Sacco - Department of Oncology, Milan

Background: Cancer patients (pts) during COVID-19 pandemic have to be protected because of higher morbidity and mortality risk. While follow up visits were rescheduled, frequently treatments couldn't be delayed without compromising efficacy. During pandemic, lockdown laws were approved and people were encouraged stay home. The aim of this study is to investigate the emotional discomfort of pts and their caregivers (CG), who need to access to Day Hospital to receive cancer treatment during pandemic.

Materials and methods: This is a single-institutional experience of the Department of Oncology at Luigi Sacco Hospital, one of the most involved Italian hospitals by COVID-19 pandemic. From 5 May to 5 June 2020 we have conducted a survey on out-pts in active cancer therapy and their CG. We have set up 2 different multiple choice questionnaires (15 questions for pts and 17 for CG) enquiring demographic characteristic and changes in emotional status, interpersonal relationships with health professionals

(HCPs) and self-perception of treatments outcomes. The answers could be yes, enough, no and I don't know; yes and enough were put together for data analysis.

Results: 625 pts and 254 CG questionnaires were examined. 65.1% pts and 56.3% CG were female; 69.8% pts were >60 ys while 50.4% CG were 41-60ys old. 40.1% of the pts vs only 25.6% CG think to be at greater risk of contagion because live together or access to the hospital. Both pts and CG consider containment measures (triage at the entrance, social distancing, personal protective equipment) a valid support to avoid the spread of infection (86.3% vs 85.4% respectively) without excessive loss of time (78.2% vs 88.6%). Waiting and performing visits and treatments without CG have no impact on emotional status of pts (64.4%), but generate in CG greater anxiety (58.8%) and fear of a bad home pts management (19.8%). The majority of pts (53.9%) and CG (39.4%) thinks pandemic doesn't influence treatments outcome. Relationships with HCPs was not negatively affected for 73.1% pts and 66.6% CG.

Conclusions: The majority of pts believes to have an higher risk of contagion therefore approves the application of safety standards, that help them feel more protected. Moreover, good relationship with HCPs contributed to face treatments without additional distress. For CG the main trouble is limitations which don't allow to fully share the pts's care route and the perceive an impairment in HCPs relationship.

D08

COVID-19 EMERGENCY: SURVEY BY THE REGIONAL AIOM GROUP FOR HEALTH WORKERS IN ONCOLOGY IN PIEDMONT AND VALLE D'AOSTA

Spadi R.[1], Bironzo P.[2], Vavala' T.[3], Boglione A.[4], Buosi R.[5], Bustreo S.[1], Carnio S.[2], Fanchini L.[1], Pignataro D.[2], Saggia C.[6], Sirotova' Z.[7], Tucci M.[8], Traverso E.[9], Buffoni L.[10]

[1]SC Oncologia 1, AOU Città della Salute e della Scienza di Torino, Torino; [2]Dipartimento di Oncologia, Università degli Studi di Torino, AOU S. Luigi Gonzaga, Orbassano, Torino; [3]SC Oncologia ASL CN1, Ospedale Ss. Annunziata Di Savigliano, Savigliano, Cuneo; [4]SC Oncologia Ospedale San Giovanni Bosco, Torino; [5]SC Oncologia - ASL-AL- Sede Ospedale S. Spirito Casale M.TO, Casale Monferrato, Alessandria; [6]Oncologia AOU "Maggiore della Carità" di Novara, Novara; [7]Oncologia ed Ematologia Oncologica. Azienda USL della Valle d'Aosta, Aosta; [8]Oncologia Ospedale Cardinal Massaia ASL AT, Asti; [9]SC Oncologia Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo Alessandria, Alessandria; [10]SC Oncologia Medica Humanitas Gradenigo, Torino

Background: Dimension and speed of the COVID19 health emergency forced pressing reorganization of the hospital machine with foreseeable repercussions on both cancer patients and healthcare professionals. A survey to the latter had the aim to describe oncology reaction at the time of Coronavirus spread in Piedmont and Valle d'Aosta.

Material and methods: An electronic survey containing questions regarding the organizational, relational and

management aspects of the emergency COVID19 as sent to Piedmont and Valle d'Aosta health workers in oncology on April 7th 2020.

Results: 201 questionnaires were completed: 60% oncologists, 33% nurses, 7% palliativists; 41% <45y; 33% university hospital, 32% non-university hospital 32% ASL. 91% considered the pre-triage model and COVID questionnaire as essential for identifying suspected patients. Structures were converted for assistance of COVID patients in 76% of cases and 26% of the health workers accepted a role change:18% on voluntary basis, while only 24% believe to have received adequate training. On clinical activity, significant reduction (48%) was registered only for first visits (CAS) while interdisciplinary discussions (GIC) have been maintained although with alternative modalities (remotely,77%). 88% of follow-up visits were remotely conducted. Considering relational aspects, discomfort mainly concerned absence of physical contact and forms of non-verbal communication hampered by the PPE, increased communication time. However, healthcare provider-patient relationship has not changed (20%), even allowing a more transparent and empathic interaction despite the use of alternative means of communication. Health professionals suffered the lack of a reference in the management of the pandemic and/or guidelines of behavior and specific skills. Major concern was the lack of PPE and the fear to be a source of infection for one's family (in 67% of cases a physical distancing from one's family nucleus was carried out or would have been desired). 52% operators report they have not yet received the swab test; in case of swab test, this was carried out due to presence of symptoms (8%) or intermediate-high risk due to prolonged contact with a COVID case, with 60% believing times and procedures were inadequate.

Conclusions: This picture is a precious benchmark to face with in order to reorganize the oncological activity in the immediate future, taking great account of the perception and experience of oncology operators. *Submitted on behalf of the AIOM Piemonte & Valle d'Aosta Regional Board*

D09

RESULTS OF A NATIONAL SURVEY EXPLORING THE PERCEPTION AND ATTITUDES OF ITALIAN PHYSICIANS TOWARDS THE MANAGEMENT OF CHECKPOINT INHIBITORS IN ONCOLOGY DURING COVID-19 OUTBREAK

Tagliamento M.[1], Spagnolo F.[1], Poggio F.[1], Soldato D.[2], Conte B.[1], Ruelle T.[1], Barisione E.[3], De Maria A.[4], Del Mastro L.[5], Di Maio M.[6], Lambertini M.[7]

[1]IRCCS Ospedale Policlinico San Martino, Oncologia Medica 2, Genova; [2]IRCCS Ospedale Policlinico San Martino, Clinica di Oncologia Medica, Genova; [3]IRCCS Ospedale Policlinico San Martino, Pneumologia Interventistica, Genova; [4]Università di Genova e IRCCS Ospedale Policlinico San Martino, Malattie Infettive, Genova; [5]Università di Genova e IRCCS Ospedale Policlinico San Martino, Breast Unit, Genova; [6]Università di Torino e Ospedale Ordine Mauriziano, SCDU Oncologia, Torino; [7]Università di Genova e IRCCS Ospedale Policlinico San Martino, Clinica di Oncologia Medica, Genova*

Background: During the COVID-19 outbreak oncological care has been reorganized to face the emergency. Cancer patients have been reported to be at higher risk of severe events related to SARS-CoV-2. Moreover, there are concerns of a possible interference between immune checkpoint inhibitors (ICIs) and the pathogenesis of the infection.

Material and Methods: A 22-item questionnaire was shared with Italian physicians managing ICIs, between May 6 and 16, 2020. This survey aimed at exploring the perception about SARS-CoV-2 related risks in cancer patients receiving ICIs, and whether the management of these patients has been modified during COVID-19 outbreak.

Results: Respondents were 104, with a median age of 35.5 years, mainly females (58.7%), mainly working in Northern Italy (71.2%). 47.1% of respondents were afraid that a synergism could exist between ICIs mechanism of action and SARS-CoV-2 pathogenesis, leading to worse outcomes. 97.1% of respondents would not deny an ICI only for the possible occurrence of COVID-19. Measures for reducing hospital visits have been adopted by choosing the ICIs schedule with fewer administrations, adopting the highest labeled dose of each drug (55.8%) and/or choosing, among different ICIs for the same indication, the one with the longer interval between cycles (30.8%). 53.8% of respondents suggested the need to test for SARS-CoV-2 every cancer patient candidate to ICIs. Regarding the differential diagnosis between immune-related adverse events (irAEs) and COVID-19 manifestations, 71.2% of respondents declared to manage a patient with onset of dyspnea and cough like a COVID-19 patient until otherwise proven (ie, waiting for the result of SARS-CoV-2 test before doing other diagnostic or therapeutic procedures), while the same management has been applied only by the 28.8% of respondents when dealing with a patient with onset of diarrhea; however, 96.2% did not reduce the use of steroids to manage irAEs during the pandemic. No major impact of COVID-19 on physicians' attitudes towards the use of ICIs to manage specific clinical situations in different cancer types (ie, lung, breast, melanoma, urothelial) was observed.

Conclusions: These results highlight the uncertainty of physicians dealing with ICIs in cancer patients during COVID-19 outbreak, supporting the need of dedicated studies on this regard.

D10

"DOMONCOVID PROJECT": AN INNOVATIVE HOMECARE MODEL FOR CANCER PATIENTS DURING THE PANDEMIC ERA

Ratti M.[1], Grizzi G.[1], Bonomi M.[1], Brighenti M.[1], Marchi R.[1], Negri F.[1], Donati G.[1], Gobbi A.[1], Barbin F.[1], Perrucci B.[1], Giganti M.[1], Donini M.[1], Panni S.[1], Curti A.[1], Ferrari B.[1], Foroni C.[1], Gerevini F.[1], Saleri J.[1], Passalacqua R.[1]

[1]ASST Cremona, Cremona

Background: The province of Cremona had one of the highest incidence of COVID-19 (COV-19) infection in Italy. The pandemic determined a significant shrinkage of our healthcare resources with difficulty for many patients (pts) to be assisted in the hospital, especially for the risk of being infected. Therefore, we created a homecare project for cancer pts with the aim of reducing hospitalizations, accesses to the oncology ward and emergency room.

Methods: The team was composed by oncologists and nurses from the Oncology Unit of Cremona Community Hospital, supported by a secretary with a dedicated telephone number. The assistance was provided from Monday to Saturday, 9 AM-5 PM. Cancer pts were eligible if presenting confirmed diagnosis or suggestive symptoms for COV-19. A telephonic triage was performed. Cancer pts and their cohabitants were tested with at least 2 nasopharyngeal swabs (NPS). Blood test, medical examinations and vital parameters were performed. We advised screened individuals to follow the quarantine procedures, providing them with an information leaflet. We administered oral/infusional treatments, including antiviral drugs.

Results: From March 23rd to April 30th 2020, 71 cancer pts were assisted at home, with a total of 191 visits. Of the 71 pts tested with NPS, 26 resulted COV-19 positive (COV-19+). 19 of COV-19+ pts had mild symptoms; 7 pts with stable vital parameters and initial pneumonia were successfully treated at home with hydroxychloroquine, antivirals and NSAIDs. 7 pts with severe symptoms were promptly hospitalized. 4 of them died, 2 due to the infection, 2 to progression disease. 52 cohabitants were screened with NPS, 28 lived with a COV-19+ cancer patient; in this subgroup, 16 resulted COV-19+. 15 of them were completely asymptomatic.

Conclusions: This project demonstrated the feasibility of an innovative model based on homecare assistance for COV-19+ cancer pts with mild symptoms. This strategy, limiting the number of hospital accesses for COV-19+ pts, might be useful to contain the spread of the infection. Further studies are needed to test this strategy in COV-19 negative cancer pts. Moreover, our experience indicates a high probability of identifying asymptomatic positive individuals cohabiting with COVID+ pts. NPS screening for asymptomatic subjects is not routinely performed in Italy. There is a urgent need to extend the screening to this population.

D11

COVID19 PANDEMIC: PATIENTS' PERSPECTIVE DURING CANCER TREATMENT

Merloni F.[1], Ranallo N.[1], Bastianelli L.[1], Vitarelli F.[1], Cantini L.[1], Ballatore Z.[1], Ricci G.[1], Fiordoliva I.[1], Tassone L.[1], Ferretti B.[2], Alessandroni P.[3], Del Prete M.[4], Chiorrini S.[5], Safi M.[6], Ficarelli R.[7], Benedetti G.[8], Faloppi L.[9], Stoico R.[1], Berardi R.[1]

[1]Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona, Ancona, Ancona; [2]U.O. Oncologia, Ospedale B.Eustachio, San Severino, San Severino (MC); [3]U.O. Oncologia, Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro, Pesaro; [4]U.O. Oncologia, Ospedale A. Murri, Fermo, Fermo; [5]U.O Oncologia, Ospedale Profili, Fabriano, Fabriano (AN); [6]U.O. Oncologia, Ospedali C.Urbani, Jesi, Jesi (AN); [7]U.O. Oncologia, Ospedale Civile di Urbino, Urbino, Urbino (PU); [8]U.O. Oncologia, Ospedale di Civitanova, Civitanova Marche, Civitanova Marche (MC); [9]U.O. Oncologia, Ospedale di Macerata, Macerata, Macerata

Background: The coronavirus disease 2019 (COVID-19) outbreak has been declared global pandemic and Italy is one of the first and heavily affected countries. Cancer patients are a population at higher risk from COVID-19 both for intrinsic fragility bound to their underlying disease and oncologic treatment delay. Aim of our survey was to investigate how cancer patients perceived their health condition, their clinical management and information communication by their medical oncologists during the pandemic.

Methods: Between 15th April and 1st May 2020 a survey was submitted to cancer patients under treatment at hospitals of Marche Region which had been invested by the pandemic. It consisted of questions regarding the perception of personal safety, continuity of cancer care and information quality provided by the Oncology Department and individual psychological distress.

Results: A total of 661 patients participated in the survey; 60.2% was female and 40.4% was aged between 46 and 65. Almost all of the attendees (97.7%) stated that the Oncologic Department complied with the appropriate safety standards and 78% was reassured about their concerns during the medical interview, but 41% was worried of being at higher risk of infection upon entry into the Oncology Department and 53.3% felt being at greater risk of infection because of chemotherapy treatment in general. The majority of the participants (62.2%) felt that postponing cancer treatment could reduce its efficacy, however 80% declared they did not feel abandoned at the time of treatment delay. 79.4% of the attendees felt more worried for their underlying disease in this emergency situation, but the mood worsened only for 34.2% of the participants.

Conclusions: Our survey reveals that Oncology Departments have been considered worthy of the emergency in terms of safety standards and care management by cancer patients. However, the majority of attendees perceived the mutual negative influence between their underlying oncologic disease and risk of Sars-CoV-2 infection and manifested concerns about their health condition highlighting the need for special measures to ensure safe continuity of care.

D12

FOLLOW-UP CANCER MANAGEMENT IN COVID-19 ERA: A SINGLE CENTER EXPERIENCE

Doni L.[1], Giorgione R.[1], Palmier V.E.[1], Tomaiuolo M.[1], Dreoni L.[1], Rossi V.[1], Antonuzzo L.[1]

[1]AOUC, Firenze

Background: The COVID-19 global pandemic required a great organizational effort to reduce the n. of patient contacts in Hospital. Based on a recent Italian survey 80% of cancer centers adopted alternative modalities to get in touch with patients. However there are no data on the remote management in follow-up.

Material and methods: In this study we collected data regarding oncological patients in follow-up whose control visit was scheduled between 11/03 and 15/05 at AOUC. Categorical data were analysed by chi square or Fisher exact test; statistical analysis of continuous variables was performed by Mann Whitney U test.

Results: 222 patients were enrolled: 99 man, 123 women (median age 68 yrs). The 43.6% were affected by gastrointestinal tumors, 21.1% genitourinary, 17.5% gynecological/breast, 8.5% thoracic and 7.2% melanoma. 35% were stage I, 30% stage II, 23% stage III and 12% stage IV. The median time from diagnosis was 3 years. 192 out of 222 (86%) did not underwent the planned medical examination; 28% of them postponed (9% managed by call, 1 by email and 89 both). 51% of them were contacted through the caregiver. The % of patients that underwent medical examination was 4.4, 11.7 e 24.25 in March, April and May respectively, suggesting a different compliance with respect to remote management, correlated to a perception of the risk of infection. The median postponement time of was 28 days (5-51). For almost all patients (95.5%) there was no evidence of disease, for 2.7% was registered a relapse and for 1.8% additional examination was ongoing: a correlation was observed between in-person visit and the recurrence (p=0.012) and between elderly patients and caregiver mediated contact (p=0.002).

Conclusions: This experience shows that the remote management of cancer patients in follow-up is feasible. Many aspects need to be clarified: lates outcomes, patient satisfaction, type of patients who can benefit. Almost all patients were managed both by telephonic interview and by e-mail, resulting in longer consultation time. Likely, a preventive and exhaustive patient information and a better technological equipment would improve the quality and the duration of the tele-consultation. The incremental percentage of in-person visits is another aspect to be investigated. Lastly, greater attention and training should be addressed to caregivers. The correlation emerged between in person in-visit and recurrence could be explained by a proper physician screening.

D13

CANCER PATIENTS' PERCEPTIONS, OPINIONS AND FEELINGS DURING THE COVID EPIDEMIC IN THE MOST AFFECTED ITALIAN AREAS: SERIAL CROSS-SECTIONAL STUDY

Bonomi M.[1], Passalacqua R.[1], Maglietta G.[2], Ratti M.[1], Gobbi A.[1], Saleri J.[1], Grizzi G.[1], Barbin F.[1], Buffoni L.[3], Cavanna L.[4], Gallina F.[5], Gervasi E.[6], Giuntini N.[7], Iridile C.[8], Lonati V.[9], Maddalena R.[10], Meriggi F.A.[11], Piloni S.[12], Donati G.[1], Campione F.[13], Caminiti C.[2]

[1]ASST Cremona, Cremona; [2]AOU Parma, Parma; [3]Humanitas Gradenigo, Torino; [4]AUSL Piacenza, Piacenza; [5]ASST Monza, Monza; [6]AUSL IRCCS Reggio Emilia, Reggio Emilia; [7]ASST Bergamo Est, Alzano Lombardo; [8]ASST Mantova, Mantova; [9]ASST Bergamo Ovest, Treviglio; [10]ASST Vimercate, Vimercate; [11]Fondazione Poliambulanza, Brescia; [12]ASST Crema, Crema; [13]Università di Bologna, Bologna

Background: Risks associated with COVID outbreak and consequent restrictive measures taken by the Government, can cause concern and anxiety. The impact on cancer patients (pts) may be even greater. We investigated the influence of COVID pandemic on pts' perceptions, opinions and feelings during the peak of the epidemic and after the loosening of the Government restrictions.

Methods: Multicenter, serial cross-sectional study conducted in 11 cancer centers located in the hardest hit Italian areas. The study is composed by 2 surveys administered to unselected adult pts receiving onsite oncologic treatments: the first during the enforcement of containment measures against COVID spread; the second upon the loosening of Government restrictions. A self-administered questionnaire composed by 11 closed questions (only 1 answer) was used. At least 1000 pts per each survey were deemed necessary. Multivariable logistic regression models will be used to identify factors associated to recorded perceptions and opinions. Main outcomes are: 1) perception of the pandemic effect on feelings 2) perception of changes in the relationship with the medical team 3) opinions on healthcare reorganization and on the information campaign.

Results: The first survey was conducted between March 16th and April 30th. 1027 questionnaires were collected. Mean age was 64 years (SD 11.7), 58% were women, 49% had low educational level. 80% and 20% received i.v. and oral treatment, respectively. As for pts feelings, 45.5% indicated that their fears related to cancer had increased because hope in recovery had diminished (23%). Courage of coping with tumor was increased in 26%, unchanged in 64%; 95% perceived a high availability of healthcare facilities and 97.6% declared confidence in the treating team's handling of the epidemic, while 65.3% stated that the information received from the Government and local bodies was confusing.

Conclusions: Although half of the pts had more fears and concerns about the epidemic, they feel reassured, maintain trust in healthcare facilities and a good communication

with doctors and nurses. Due to the epidemic's course, the second survey could not yet be performed and data will be available by June.

D14

TECHNOLOGY-MEDIATED COMMUNICATION WITH PATIENTS IS A CHALLENGE FOR ONCOLOGISTS IN THE DIGITAL AND PANDEMIC ERA. . . AND THE WINNER IS WHATSAPP!

Torniai M.[1], Marcantognini G.[1], Fiordoliva I.[1], Mentrasti G.[1], Agostinelli V.[1], Pagliacci A.[1], Corsi R.[2], Luzi P.[2], Berardi R.[1], Caporossi M.[3]

[1]*Oncology Clinic, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Ancona;* [2]*TOPS srl a Socio Unico, Roma;* [3]*General Director – AOU Ospedali Riuniti di Ancona, Ancona*

Background: Since December 2019, coronavirus disease 2019 (COVID-19) has spread to every Country taking on pandemic proportions in few months. Physicians were asked to redefine ordinary Hospital organization reprogramming clinically differentiable activities.

Materials and Methods: During COVID pandemia our Institution was supported by a call-center (CC, named TOPS s.r.l.) to make a triage for cancer patients (pts) scheduled for follow up in our outpatient clinics: C1 (dedicated to female tumors), C2 (for gastrointestinal, urogenital and thoracic tumors) and D1 (for tumors in over 5 years follow up). We report preliminary data referred to the period 7th April - 24th May 2020. The activity was divided into two phases (F): April (F1) and May (F2). In F2 pts were interviewed about their preferred visit modality. Physical examination was not postpone in case of clinical needs and first visits. Moreover, CC asked about programmed radiological examinations and collected patient's feedbacks about the service.

Results: A total of 587 pts have been contacted: 341 during F1, and 246 in F2. 317/341 (93%) of the contacts in F1 were successful. A gender-stratified analysis showed a majority of female (72.4%). The CC was able to get in touch with 42.8% C1 pts, 34.6% C2 pts and 22.6% D1 pts. During F2 246 pts (96.5%) of 255 planned were efficiently contacted; female maintained the predominance (74.5%). 170 pts (69.1%) were scheduled in C1, 53 pts (21.5%) in C2 and 23 pts (9.4%) in D1. During F2, among the options provided 97 pts (39.4%) selected the phone call, 142 pts (57.7%) decided for video chat (whatsapp) and 2 (0.8%) for video conference with a dedicated platform (google.meet). Only 5 pts (2.1%) expressed their intention to come to the Hospital for examination. In 69.1% of cases (170 pts) the programmed radiological examinations were confirmed during the pandemic. According to some favorable reports, the service was helpful in preserving continuum of care and preventing cancer pts of being left aside in the emergence.

Conclusions: This study show that cancer patients do appreciate technology-mediated follow up visits mainly including video chat (whatsapp) and therefore we should take this into consideration. Furthermore, a dedicated CC may be helpful to organize follow-up activities during COVID-19 and to strengthen doctor-patient relationship in such a critical moment.

D15

DEVELOPMENT AND VALIDATION OF TELEMATIC FOLLOW-UP FOR CANCER PATIENTS DURING THE COVID-19 OUTBREAK AT THE MEDICAL ONCOLOGY UNIT OF SANT'ANDREA AND SAN BARTOLOMEO HOSPITALS, LA SPEZIA

Pastorino A.[1], Negru M.E.[1], Vigani A.[1], Vaira F.[1], Tognoni A.[1], Ferrari A.[1], Ricci I.[1], Rondini M.[1], Olcese F.[1], Milano A.[1], Latocca M. M.[1], Cozzani F.[1], Aschele C.[1]

[1]*Medical Oncology Unit – Department of Oncology, Ospedale Sant'Andrea, La Spezia, Italy*

Background: The reorganization of patient management was essential to maintain an adequate oncologic care and contain patient exposure during SARS-CoV-2 pandemic. Follow-up in particular was a major area for remodulation with large volume of patients involved, generally at low oncologic risk.

Materials and methods: Pts scheduled for follow-up oncologic visits during the lockdown period (March 9th - May 4th 2020) were included in a program of telematic follow-up (TFU) developed at the Medical Oncology Unit of Sant'Andrea and San Bartolomeo Hospital in La Spezia, Italy. Eligibility for TFU was determined through a pre-screening of medical charts based on tumor type, risk of relapse, geographic accessibility and DFS. Pre-calls were made by skilled nurses to assess pts' availability for next-day phone call and to assess availability of laboratory test and imaging results. A TFU form was conceived to collect pts' clinical history, symptoms, body weight, ongoing medical therapies, DFS, blood tests and imaging results (from Hospital imaging repository or acquired in the pre-call). Pts without signs/symptoms of relapse were scheduled for the next follow-up visit and the filled-in TFU form was attached to the clinical chart. When a suspected disease relapse was found, an ambulatory visit was performed.

Results: There were 547 pts previously scheduled for in-hospital follow-up visit between March 9th and May 4th, 2020. 82 of 547 pts (15%) were considered not eligible for TFU according to the pre-screening assessment. 465 pts out of 547 (85%) were included in the TFU program. All these pts accepted calls with a compliance rate of 100%. The median age was 73 years (34-95); 152 male (33%) and 313 female (67%). The distribution by tumor type was: 179 breast cancer (38%), 86 colorectal (18%), 55 urinary

tract (12%), 39 melanoma and skin (9%), 31 gynecologic (6%), 26 lung cancer (6%), 16 GEP (3%), 15 head and neck (3%), and 18 other tumors (4%). Ten patients with signs/symptoms of tumor recurrence were detected at TFU: 1 had clinical symptoms, 3 abnormal blood tests and 6 suspicious radiological findings. These patients were called for live visit and tumor relapse/progression was confirmed in 10 out of 10 cases. Medical or surgical treatment was started, or planned to start, in all 10 patients.

Conclusions: TFU proved to be feasible with an eligibility rate of 85% and 100% patients' compliance. The detection rate for tumor recurrence was 2.1%.

D16

DEVELOPING A RISK ASSESSMENT SCORE FOR CANCER PATIENTS DURING COVID-19 PANDEMIC

Indini A.[1], Cattaneo M.[2], Rijavec E.[1], Ghidini M.[1], Bareggi C.[1], Galassi B.[1], Gambini D.[1], Grossi F.[1]

[1]*Unità di Oncologia Medica, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Milano; *[2]*Dipartimento di Medicina (DAME), Università di Udine, Udine*

Background: Data on the novel coronavirus (CoV) respiratory disease (COVID19) in cancer patients (pts) are limited. In some individuals, CoV infection triggers an aberrant immune response, leading to lung tissue damage. Cancer pts treated with immunotherapy (IT) may be more at risk for COVID19 and its complication.

Methods: We performed a thorough review of the literature on CoV pathogenesis and cancer. We selected shared features of the two disease entities to develop a risk-assessment score quantifying both the risk of infection and that implied in cancer treatment delay.

Results: The score includes clinical and laboratory variables (Table 1). Pts' characteristics include: age, comorbidities (hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, chronic systemic infections), obesity, sex, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and concomitant steroid treatment (>10 mg/day of prednisone equivalent, lasting for >1-month period). Disease characteristics include: lung cancer diagnosis, history of thoracic radiotherapy (RT) (only for pts with extra-thoracic tumor). Treatment characteristics include: line of treatment, type (IT or combined IT/chemotherapy [CT] considered high-risk, followed by CT, and other anti-cancer drugs), history of immune-related adverse events (irAEs). Laboratory tests include levels of neutrophil-to-lymphocyte ratio (NLR), lactate-dehydrogenase (LDH), and C-reactive protein (CRP). Based on the resulting score, pts are divided in the following risk categories: low (score <4), intermediate (score 4-6), and high risk (score >7).

Conclusions: There is a strong rationale supporting these variables as potential risk factors for COVID19 in cancer pts. The present score is currently undergoing validation on a wide population of cancer pts, to confirm its role and potentially help physicians' treatment decisions.

Table 1. The "Milano Policlinico ONCOVID Score" for risk evaluation during COVID19.

Variables	Score
Sex	F = 0
	M = 1
ECOG PS	0-1 = 0
	2, or higher = 1
Age	<70 = 0
	70, or higher = 1
BMI	<30 = 0
	30, or higher = 1
Comorbidities	NO = 0
	YES = 1
	YES $>$ 1 = 2
Concomitant steroid treatment	NO = 0
	YES = 1
Thoracic tumor	NO = 0
	YES = 1
Previous thoracic RT	NO = 0
	YES = 1
Line of treatment	(neo)adjuvant = 0
	1, or more = 1
Type of treatment	Hormone therapy/targeted therapy/monoclonal antibodies = 0
	CT = 1
	IT/IT + CT = 2
History of irAEs	NO = 0
	YES = 1
	YES, pneumonitis = 2
NLR	<5 = 0
	5, or higher = 1
LDH	$<$ULN = 0
	ULN, or higher = 1
CRP	$<$ULN = 0
	ULN, or higher = 1

D17

HOW COVID-19 PANDEMIC IMPACTED INTEGRATED CARE PATHWAYS FOR LUNG CANCER: THE EXPERIENCE OF TWO ITALIAN CENTERS IN VENETO REGION

Pasello G.[1], Menis J.[1], Pilotto S.[2], Frega S.[1], Pezzuto F.[3], Caliò A.[2], Sepulcri M.[1], Cernusco N.L.V.[2], Schiavon M.[3], Infante M.V.[2], Damin M.[3], Micheletto C.[2], Belluomini L.[2], Bonanno L.[1], Fantoni U.[3], Guarneri V.[3], Calabrese F.[3], Rea F.[3], Milella M.[2], Conte P.[3]

[1]*Istituto Oncologico Veneto IRCCS, Padova; *[2]*University of Verona, Verona; *[3]*University of Padova, Padova*

Background: COVID-19 pandemic has represented a historic challenge to healthcare systems. The management of cancer care has become a crucial issue for clinical services to cancer patients. During the COVID-19 pandemic, raising evidence has been published on lung cancer care but no data have been presented on the integrated care pathways (ICP) impact.

Materials and methods: We retrospectively reviewed the ICPs of consecutive lung cancer patients who accessed two Centres before and after COVID-19 pandemic: the Veneto Institute of Oncology (IOV)/University Hospital of Padua and University Hospital of Verona. Sixteen indicators about oncology, radiaton therapy, thoracic surgery, pathology and pneumology were developed using group-facilitation techniques taking into account their reproducibility, significance, measurability. We report data extracted from electronic medical records and linked softwares, about MDT performance at the two participating Centres, and preliminary data about pathological and oncological indicators in Padua. Additional data about both complete ICPs will be presented at the Conference.

Results: We compared data about ICP performance in two window periods: 1/3/2019–30/4/2019 and 1/3/2020–30/4/2020. MDT meetings were reshaped in order to discuss those cases where more than two specialists were required and whenever possible on a web-basis; therefore, it determined an average reduction of patients discussed of 57.5%. Preliminary data from Padua showed that median time between diagnostic procedure and diagnosis was reduced from 11 days in 2019 to 7.5 days in 2020, mostly due to a prioritization of oncological procedures over any other. Moreover, a 39% reduction of first oncological visits was observed between the two time frames; this was linked to a reduction of out of region second opinion and to optimization of outpatient access. Among patients under oncological treatment, 12(4%) and 8(2%) patients received treatment within 30 days from death in 2019 and 2020, respectively.

Conclusions: Based on the experience the two Centres went through, we identified the key steps in ICP impacted by a pandemic such COVID-19 so to proactively put in place robust service provision in thoracic oncology.

D18

RESILIENCE IN CANCER CARE AT THE TIME OF COVID-19: PRACTICAL APPROACH TO THE MANAGEMENT OF CANCER PATIENTS DURING THE COVID-19 EMERGENCY IN A LARGE ITALIAN COMMUNITY HOSPITAL

Lasagna A.[1], Secondino S.[1], Agustoni F.[1], Monaco T.[1], Imarisio I.[1], Pagani A.[1], Rizzo G.[1], Tancredi R.J.[1], Pozzi E.[1], Ferraris E.[1], Chiellino S.[1], Gandini C.[1], Brugnatelli S.G.[1], Pedrazzoli P.[1]

[1]Fondazione IRCCS Policlinico San Matteo, Pavia

Background: The Fondazione IRCCS Policlinico San Matteo, the largest academic Hospital in the south-west part of Lombardy has been involved in the management of the COVID-19 outbreak since its inception. The Oncology Unit had to face with the challenge of to keep on active oncological treatments without compromising the safety of our pts and healthcare personnel both in the inpatients, as well as in the outpatients.

Patients and methods: From the very beginning of the emergency, the inpatient ward and the outpatient clinic were moved to the main building of the Hospital as their original locations become COVID-19 wards. From Feb. 24th, we reorganized our Unit, with the introduction of a double-step triage strategy for cancer pts under treatment in order to identify pts at risk from COVID-19, and to avoid their admission to Hospital.
- First step: a phone call the day before active therapy or admission (virtual swab); - Second step: a clinical evaluation upon entry the outpatient and inpatient wards.

Results: From February 24 to April 7, 2020, 819 phone calls were performed, leading to the authorization of 788 accesses to the outpatient clinic for active treatments. 26 pts (8.3%) with symptoms were kept at home and managed by repeated telephone calls in collaboration with the family doctor; of these subjects, 3 were hospitalized for suspected COVID, while 23 were managed at home with symptomatic treatments and antibiotics. At the second triage level, 5 pts were hospitalized and proved positive for SARS-CoV-2 by nasal swab. In the same period, 177 pts were admitted to the inpatient ward: none has been found to be COVID-19-suspected or swab-positive. Both outpatient and inpatient areas were still COVID-19 free. No healthcare workers resulted infected by SARS-CoV-2, including 2 physicians who had fever during this period, but resulted SARS-CoV-2 negative by 2 sequential nasal swabs, performed 14 days apart.

Conclusions: During the emergency phase of the COVID-19 outbreak the behavior of health care workers had to be arranged to appropriately manage it, according to risk management strategies particularly to that defined as "resilience". Our screening strategy, which requested neither human nor economic extra resources, put successfully into practice the capacity to adapt the management to a global health emergency as we could maintain the pre-COVID approach to cancer care, while protecting pts and healthcare workers from COVID-19 infection.

D19

PREVALENCE AND CLINICAL IMPACT OF ASYMPTOMATIC OR MILDLY SYMPTOMATIC SARSCOV-2 INFECTION AMONG ACTIVELY TREATED CANCER PATIENTS DURING RECENT COVID-19 PANDEMIC PEAK IN ITALY

Zambelli A.[1], Milesi L.[1], Bonomi L.[1], Tasca C.[1], Rota Caremoli E.[1], Bosetti T.[1], Negrini G.[1], Mandalà M.[1], Fotia V.[1], Di Croce A.[1], Callegaro A.[1], Chiudinelli L.[2], Chirco A.[1], Ghilardi L.[1], Tondini C.[1]

[1]ASST Papa Giovanni XXIII, Bergamo; [2]Università degli Studi di Pavia, Pavia

Background: The European SARS-CoV-2 pandemic had its first epicentre in Italy, particularly in the area of Bergamo. In spite of a significant mortality rate, in the majority of cases the spectrum of Covid-19 ranges from asymptomatic to mildly symptomatic infection. No information is available on the prevalence and clinical impact of asymptomatic or mildly symptomatic SARSCoV-2 infection among actively treated cancer patients during pandemic.

Patients and methods: From April 1st, 2020 to the end of the month, 560 consecutive and unselected patients, scheduled for anticancer treatment at our facility and without clinical suspicious of Covid-19, were evaluated and tested for SARSCoV-2. We implemented a two-step diagnostics, including a rapid serological immunoassay for anti-SARSCoV-2 IgG/IgM and a pharyngeal swab RT-PCR assay in case of IgM seropositivity.

Results: In 560 patients, 172 (31%) resulted positive for SARSCoV-2 IgM/IgG antibodies, regardless of type of cancer, stage and treatment. All IgM-seropositives were then tested with RT-PCR pharyngeal swabs and 55/146 (38%) proved to be SARSCoV-2 carriers, with slightly difference between mildly symptomatic vs. asymptomatic patients (38 vs. 17). Therefore, the two-step procedure allowed the identification of 55 (10%) silent carriers in the whole study population and magnified the number needed to test (NNT) with the pharyngeal swab RT-PCR assay to detect a silent virus carrier (NNT: 2.6 vs. 10, with or without serological selection). At a very early follow up (8 wks), in 114 SARSCoV-2-seropostive/RT-PCR-negative patients, who continued their anticancer therapies, none but one developed a symptomatic Covid-19 illness.

Conclusions: Among cancer patients, the two-step diagnostics strategy with serology followed by pharyngeal swab for asymptomatic or mildly symptomatic SARSCoV-2 infection is feasible and effective and can help selecting cancer patients on treatment who might be silent carriers of the virus. The early safety outcome of patients previously exposed to SARSCoV-2 supports the recommendation to continue active treatment, at least in the case of negative RT-PCR test.

D20

TRIAGE PROCEDURE FOR COVID-19 IN AN ONCOLOGY DEPARTMENT: AN ITALIAN MONOCENTRIC EXPERIENCE

Zara D.[1], Targato G.[1], Fioraso R.[1], Bortot L.[1], Pelizzari G.[1], Corvaja C.[1], Palmero L.[1], Giavarra M.[1], Andreotti V.J.[1], Bin A.[2], Donato R.[2], Garattini S.K.[2], Mansutti M.[2], Minisini A.M.[2], Fasola G.[2]

[1]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale,

Udine, Italy; Dipartimento di Area Medica (DAME) - University of Udine, Udine; [2]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy, Udine

Background: To minimize the risk of COVID-19 infection spreading, we developed a triage procedure, consisting of body temperature measuring and a structured questionnaire that each patient (pt) was asked to fill-in before accessing to our department. This questionnaire explored 4 items: fever, respiratory tract symptoms (flue syndrome, sore throat, cough, dyspnea, loss of taste or smell), previous contacts or personal positivity for COVID-19. From 06 April 2020 we also started to perform nasopharyngeal swabs in all pts who, receiving intravenous therapy, had to stay in the Day hospital (DH) administration area.

Material and methods: We evaluated a consecutive series of outpatients with diagnosis of solid tumor, accessing the DH of Oncology Department at the Udine Academic Cancer Center from 30 March 2020 to 10 April 2020. A multivariate logistic regression model was used to identify factors associated with positive triage ($\geq$1 item).

Results: 1054 triage procedures were performed out of 586 pts, with a median of 2 triage per pt. The median age was 64.9 years. The most common reason for triage submission was programmed access for oncological therapy (82.5%), followed by scheduled procedures, radiological exams or non-oncological consultations (10.7%) and unplanned access for urgencies (1.2%). In 30.7% of cases the neoplasm was in early stage, while was advanced in 69.3%. 58.2% of triage procedures were performed in pts receiving chemotherapy, 10.8% immunotherapy, 18.9% target therapy, 5.2% other therapies and 6.9% in pts without active treatment. In 5.5% of cases the triage resulted positive. 2.9% of all triage were positive for fever, 2.9% for respiratory symptoms and 0.1% for previous contact with a COVID-19 case. Body temperature was $\geq$37°C in 7 pts. Among negative triage, in 6 cases pts were further evaluated and considered as clinically suspect. Overall, in 0.9% of triage procedures the oncologic program was postponed, while a test for COVID-19 was performed for clinical suspect in 0.5%: interestingly no one resulted positive. At multivariate analysis factors associated with positive triage were diagnosis of thoracic cancer (OR 2.06; 95%CI 1.02-4.12; p 0.04) and prior COVID-19 test (OR 2.81; 95%CI 1.46-5.41; p 0.001). As of May 20th, no operator was positive to surveillance swabs.

Conclusions: A well-structured triage procedure for COVID-19 can reduce the risk of further spreading of infection in Oncology facilities with limited impact on scheduled activities.

D21

ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO WITH COVID-19 INFECTION IN CANCER PATIENTS

Cereda V.[1], Formica V.[2], Corona M.[1], Falbo P.T.[1], Iannace A.[1], Semenova D.[1], Menghi A.[1], Manna G.[1], Lanzetta G.[1]

[1]INI-Grottaferrata, Roma; [2]Policlinico Tor Vergata, Roma

In December 2019, coronavirus disease 2019 (COVID-19) emerged in Wuhan and rapidly spread all over the world. Several studies have described the clinical characteristics of patients (pts) with novel coronavirus (SARS-CoV-2) pneumonia, demonstrating that severe pts tend to have higher neutrophil-to-lymphocyte ratio (NLR). A cohort of 61 cancer pts, admitted to the Oncology Unit of INI Grottaferrata (Rome) from March 24th to May 10th and undergoing nasopharyngeal swab and serological tests for COVID-19, was retrospectively analyzed. Age, gender, type of cancer, laboratory tests and electrocardiographic (EKG)/echocardiographic abnormalities were investigated as potential predictors of COVID-19 positivity. Potential linearity in the association with test positivity was assessed by means of logistic regression analysis (LRA) with restricted cubic splines with 3 knots. When not linearly associated with outcome, variables were dichotomized using cut-off values determined by receiver operating curve (ROC) analysis. Multivariate LRA was applied to identify independent predictors of COVID-19 positivity. Wilcoxon rank-sum test was used to estimate differences of continuous variables according to COVID-19 positivity. $P < 0.05$ was defined as statistically significant. The median age was 72 years, and 41 pts (67%) were male. The majority of pts had colorectal cancer (21/61) and lung cancer (18/61). 18 out of 61 cancer pts had a confirmed diagnosis of COVID-19. 13 out of 18 COVID-19 positive pts died within 40 days from nasopharyngeal swab. NLR was found to be significantly associated with COVID-19 positivity (16 out of 24 vs. 2 out of 37 pts for NLR >10 vs. <10, respectively; odds ratio [OR]=35, 95% CI: 6.7-183.8, $P < 0.001$). COVID-19 positive pts had a significantly higher NLR (median 21.2 vs. 4.9, $P < 0.001$) compared with negative cases. Multivariate LRA confirmed that NLR and fibrinogen were significantly and independently associated with COVID-19 infection (OR=17.68, $P < 0.05$ and OR=13.2, $P < 0.05$, respectively). At univariate analysis also incidence of EKG abnormalities, including T-wave inversion and S-T segment elevation, was significantly associated with COVID-19 diagnosis (33% vs. 5%, OR=10.25, $P < 0.05$); however this significance was lost at the multivariate LRA. NLR may be significantly associated with the presence of COVID-19 infection in cancer pts. Whether baseline NLR could be an independent predictor of mortality needs to be investigated.

D22

DOCTORS AND NURSES DURING COVID19 PANDEMIC: A DIFFERENT PERCEPTION OF CANCER CARE

Bastianelli L.[1], Merloni F.[1], Ranallo N.[1], Cantini L.[1], Mariotti L.[1], Lucarelli A.[1], Ballatore Z.[1], Berardi R.[1]

[1]Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona - Ancona, Ancona

Background: The spread of Coronavirus disease brought the need to reorganize clinical activity in oncology. Cancer patients are very vulnerable and it is well known that their treatment has to be strictly planned. The most critical considerations still relate to the entry of the virus into hospitals, the heart of healthcare, where cancer patients are protected. Instead, during COVID19 pandemic the oncologic department had to limit access to care to protect patients from a more dangerous disease for them, witnessing a paradox of health care. This brought with it worries in oncologic healthcare professionals in replanning activities in order to guarantee therapeutic continuity and quality of care. It is well known that physicians and nurses have different role concepts and role expectations. The purpose of our study was to investigate doctors and nurses' perception on cancer patient reorganization during the COVID19 pandemic in a sample of Italian healthcare professionals in oncology.

Methods: We submitted a survey to oncologic healthcare workers (physicians and nurses) of Italian National Health Care System during Pandemic to investigate clinical activity reorganization and cancer patient management through 12 closed questions. The survey promoted by Clinica Oncologica, AOU Riuniti di Ancona-Università Politecnica delle Marche was electronic and anonymous.

Results: A total of 383 oncology health workers completed the survey, 60 nurses (15%) and 323 physicians (85%). 60% of interviewed physicians perceived qualitatively lower than usual the therapeutic path of patients taken in charge in this historical moment, while 45% of nurses declared it was the same ($p < 0.01$). The continuity of the multidisciplinary team was defined as guaranteed for 68% of oncologists, while almost 40% of nurses declared to not know it. Almost all physicians (95%) answered that their clinical activity was reorganized, compared to a lower portion of nurses (80%) that replanned their care role ($p < 0.01$). Deferring treatments caused fear and anxiety in 62% of physicians and 46% of nurses ($p = 0.027$).

Conclusions: The survey underlined the need to integrate skills and involve all professional figures in planning cancer patients' treatment to guarantee optimal therapeutic strategies and a global take in charge in all its details, even during emergencies.

D23

SCIENTIA POTENTIA EST: HOW THE ITALIAN WORLD OF ONCOLOGY CHANGES IN THE COVID19 PANDEMIC

Ballatore Z.[1], Bastianelli L.[1], Merloni F.[1], Ranallo N.[1], Cantini L.[1], Catani C.[1], Mariotti L.[1], Lucarelli A.[1], Burattini M.[1], Berardi R.[1]

[1]Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona - Ancona, Ancona

Background: After COVID-19 was declared a pandemic by the World Health Organization, a response from the Italian Health System to react to an unprecedented condition became necessary and sudden. COVID-19 pandemic required oncologists to redefine clinical organization and management of cancer patients. The aim of our study was to take a picture of the situation of Italian oncologies and to evaluate the difficulties in patients management.

Methods: Between 18th March and 9th April 2020 we conducted an online survey (Google Forms). It consisted of 45 questions ranging from individual perception of pandemic management by oncological centers to physicians and nurses psychological distress and patient care. The survey was anonymous and broadcasted to oncology health workers by mailing contacts, word of mouth and social networks.

Results: A total of 383 oncology health workers participated in the survey. The majority was female (72%) and from central Italy (46%). Impressively, a total of 357 (93%) participants declared the Oncologic Department reorganized routine clinical activity, but only 41% was adequately trained about the required procedures. 20% of the survey attendees think they have not received adequate and timely protective devices with respect to clinical needs and according to 58% the supply of these devices was only partial. 34% of professionals declared they do not have or know a defined common guideline to reschedule patients' treatments. More than 80% of interviewees declared to feel worry about being at greater risk of contagion than the general population, 92% feared to transmit virus to family members. Deferring treatments has caused fear / anxiety in 228 of the interviewed (60%). Symptoms of stressful situations emerged with a deterioration in sleep quality in 62% of professionals, worsening of mood (69%) and lower concentration ability (49%).

Conclusions: Our survey demonstrated the flexibility of oncologic teams. However, the emergency response quality has been heterogeneous, and several drawbacks emerged from this first analyses. Information, protection, testing and training of healthcare professionals are keywords that should be kept in mind to encourage recovery after this tragedy and to be ready to face a similar emergency in the next future.

D24

INCIDENCE OF SARS-COV-2 INFECTION IN PATIENTS WITH ACTIVE CANCER: MONO-INSTITUTIONAL SERIES OF A COMPREHENSIVE CANCER INSTITUTION IN LOMBARDY DURING THE COVID-19 PANDEMIC (NIGUARDA CANCER CENTER, MILANO, ITALY)

Sartore-Bianchi A.[1], Patelli G.[1], Tosi F.[1], Campisi D.[2], Di Ruscio F.[2], Bencardino K.[3], Amatu A.[3], Bonazzina E.[3], Cerea G.[3], Carlo Stella G.[3], Giannetta L.[3], Tartaglione L.[2], Cassingena A.[3], Agostara A.[1], Vaghi C.[1], Pedrani M.[1], Nichelatti M.[3], Alteri C.[2], Perno C.F.[2], Siena S.[1]

[1]Dipartimento di Oncologia ed Emato-Oncologia, Università degli Studi di Milano (La Statale), Milano, Milano; [2]Analisi Chimico Cliniche e Microbiologia, Grande Ospedale Metropolitano Niguarda, Milano, Italy, Milano; [3]Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, Milano, Milano

Background: Lombardy region, Italy, has one of world's largest coronavirus disease 19 (COVID-19) outbreak with over 80,000 cases. Here, we report the incidence of SARS-CoV-2 infection in patients with active cancer at the Division of Oncology, Niguarda Cancer Center, Grande Ospedale Metropolitano Niguarda, a comprehensive cancer institution in the capital of Lombardy, Milano.

Patients and Methods: From April 15th to May 15th, 2020, SARS-CoV-2 testing has been performed in patients with active cancer by paired real time-PCR in nasopharyngeal swab (NPS) (Elitech, Torino, IT) and chemiluminescent immunoassays for detection of antiviral IgG in blood (Abbot, Sligo, IR or Diasorin, Saluggia, IT). Active cancer was defined as a solid tumor requiring anticancer treatment or supportive care. Tested patients were either outpatients with at least one suggestive symptom of COVID-19 assessed by telephone triage per local guidelines, or inpatients routinely tested at hospital admission, irrespective of symptoms. Additionally, patients with COVID-19 requiring hospitalization at Niguarda Hospital during the study period have been tested and results pooled for evaluating concordance of NPS with serology.

Results: 118 patients were tested by NSP, and paired serology is available at the moment for 63 (53.4%). In the outpatient setting, 517 underwent telephone triage and 58 reported at least one symptom (11.2%). Of these, 3/29 and 3/14 (10.3 and 21.4%) tested positive on NSP and serology, respectively. In the cohort of inpatients, tested regardless of symptoms, 2/82 and 4/42 (2.4 and 9.5%) tested positive on NSP and serology, respectively. Finally, among oncology physicians, 2/34 and 2/34 (5.9%) tested positive on NSP and serology, respectively. 7 additional hospitalized patients displaying COVID-19 disease have been tested. Overall, the accuracy between NSP and serology was 82.5% and concordance was 0.415 (Cohen's k). In 5 cases, serology was positive and NSP negative, whereas the opposite was found in 6. Recruitment and testing are still ongoing at the moment of abstract submission and complete results will be presented.

Conclusions: In our series of patients with active cancer during a peak period of the pandemic in Lombardy, 11% of outpatients displayed COVID-19 associated symptoms and 10% had positive NSP. Among inpatients tested regardless of symptoms, 2.4% had positive NSP. The accuracy between NSP and serology was 82.5%.

D25

THE CHALLENGE OF ITALIAN CANCER PATIENT SUPPORT ASSOCIATIONS IN THE ERA OF SOCIAL DISTANCING, QUARANTENEE, AND ISOLATION: SOCIAL MEDIA NETWORKING TO BE. . . FAR BUT NEAR

Franchina V.[1], Franchina T.[2], Ricciardi G.R.R.[1], Longo D.[1], Cacciola F.[1], Aspria P.[1], Adamo V.[3]

[1]*Medical Oncology Unit A.O. Papardo, Messina; [2]Department of Human Pathology, University of Messina, Messina; [3]Medical Oncology Unit A.O. Papardo and Department of Human Pathology, University of Messina, Messina*

Background: Unprecendented emergency measures applied in Italy due to coronavirus pandemic have determined the development of new strategies to support oncological patients. In this context, social networking has represented a privileged tool. The objective of this study is to evaluate how the national cancer patient support associations have used facebook to support oncological patients during lockdown period in Italy.

Material and Methods: Data have been obtained by the analysis of posts inserted on Facebook pages by the Italian cancer patient associations between 31 January 2020 (first cases reported in Italy in Rome) and 4 May 2020 (start up phase II after lockdown).The search of associations was conducted on Facebook and web search engines.

Results: A total of 64 pages of cancer patient associations, primarily residents in the Northern regions (50%), 26% in the center of Italy and 20% in the Southern regions, have been analyzed. A large proportion of the association (42.5%) deal with all tumor pathologies, 20.3% are specially dedicated to breast cancer and 7.4% to melanoma. Ten associations have not updated their pages in the referred period. Published posts in all examined pages are in total 931 and mainly referred to services and initiatives promoted by the associations (psychological support, streaming events, home care: 21,1%); information about the COVID-19 and indications to prevent trasmission (17.4%); update on cancer treatments (17.3%); surveys, vademecum and guidelines for oncological patients (13%); fundraising (6.4%) to donate medical devices for COVID-19 emergency; information about the activation of new clinical trials during the pandemic (5%). The most frequent hashtags have been: #covid19, #coronavirus, #iorestoacasa, #stopcoronavirus. Most liked post, promoting a fundraising to support cancer patients during lockdown period, has obtained 1800 like and 527 emoji heart. A new Care reaction, a virtual HUG launched in late April by Facebook to show support during the COVID-19 crisis has been used 38 times in the different posts. Moreover, several initiatives have been carried out on Facebook such as: home concerts, tutorials, webinar, to share emotions, support and spend time together.

Conclusions: The use of Facebook during COVID-19 lockdown has represented for cancer patient associations a new virtual space of meeting and supporting and a tool to reduce distances and the concerns related not only to cancer, but also to the danger of COVID-19.

D26

IMPACT OF COVID-19 IN GYNECOLOGIC ONCOLOGY: A NATIONWIDE ITALIAN SURVEY

Bogani G.[1], Apolone G.[1], Scambia G.[2], Benedetti Panici P.[3], Angioli R.[4], Pignata S.[5], Greggi S.[5], Scollo P.[6], Franchi M.[7], Ghezzi F.[8], Ferrandina G.[9], Di Donato V.[9], Chiantera V.[9], Trojano V.[10], Salerno G.[11], Malzoni M.[12], Testa A.[9], Lorusso D.[9], Trojano G.[13], Chinatera A.[14], Raspagliesi F.[1]

[1]*Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano; [2]Policlinico Gemelli, Milano; [3]Sapienza, Roma; [4]Campus Biomedico, Roma; [5]Istituto Tumori Napoli, Napoli; [6]Ospedale Cannizzaro, Catania; [7]Università di Verona, Verona; [8]Insubria, Varese; [9]Gemelli, Roma; [10]Università di Bari, Bari; [11]San Camillo, Roma; [12]Malzoni Medical Center, Avellino; [13]University Medical School "A. Moro", Bari, Italy., Bari; [14]President of the Scientific Society SIGO (Italian Society of Gynecology and Obstetrics), Italy, Roma*

Background: The spread of Coronavirus (COVID-19), after involving China, has also begun to interest Europe and the ed States. Several attempts are done in order to control the spread of the virus and promote a fair allocation of resources during COVID-19 outbreak. COVID-19 threatens to curtail patient access to evidence-based treatment. The Italian society of obstetrics and gynecologist (SIGO), and the Multicenter Italian Trials in Ovarian cancer and gynecologic malignancies (MITO) are promoting research activities in the field of gynecologic oncology on a national basis, even in the COVID-19 era.

Methods: The SIGO and MITO group promoted a national survey aiming to evaluate the impact of COVID-19 on clinical activity of gynecologist oncologists and the implementation of containment measures of COVID-19 diffusion.

Results: Overall, 604 participants completed the questionnaire with a response-rate of 70%. The results of this survey suggest that gynecologic oncology units had set a proactive approach to COVID-19 outbreak. Triage methods were adopted in order to minimize the in-hospital diffusion of COVID-19. Overall, only 38% of gynecologic surgeons were concerned about COVID-19 outbreak. Although 73% of the participants stated that COVID-19 has not significantly modified their everyday practice, 21% declared a decrease of the use of laparoscopy in favor of open (19%) and vaginal (2%) surgery. Interestingly, about 5% of the participants stated that the use of laparoscopic surgery has increased during the COVID-19 outbreak. However, less than 50% of surgeons adopted specific protection against COVID-19. Additionally, responders suggested to delay cancer treatment (10-15%), and to perform less radical surgical procedures (20-25%) during COVID-19 pandemic.

Conclusions: National guidelines should be implemented to further promote the safety of patients and health care providers. International cooperation is of paramount importance, as heavily affected nations can serve as an example to find out ways to safely preserve clinical activity during the COVID-19 outbreak.

D27

SUPPORT ONCOLOGIC PATIENT CARE DURING COVID 19: EXPERIENCE WITH TELEMEDICINE

Moraca L.[1], Lombardi M.[1], Ferrara F.M.[2], Cristofaro R.[1], Macchiarola G.[1]

[1]UO Oncologia P.O. San Severo Asl Foggia, San Severo; [2]Altems Alta Scuola di Economia e Management dei Sistemi Sanitari, Università Cattolica Del Sacro Cuore, Roma

Background: After the first weeks in which all efforts were concentrated to prevent contagion and treat Covid-19 patients, it is now increasingly important to secure assistance to ordinary patients suspended from outpatient activity until today and still struggling with the quota policy and precautions required by "phase 2". As established by recent regional resolutions (cf. Tuscany, Veneto, Lombardy), telemedicine is "the strategy" to meet and fulfill the needs. It permits remote assistance to particularly fragile, chronic patients with long term pathologies giving a rapid, practical and economical response through the use of common, free instruments, readily available and already known to patients. These instruments must be structured within a legislative and regulatory organic framework that permits:

a) the integration in existing clinical welfare processes without requesting organizational variations;

b) the use of existing IT systems already in use, without determining additional fragmentation of necessary data for the treatment of the patient, between archives and distinct clouds, owners and those not connected;

c) personal data protection according to that required by GDPR both under a technological profile and an organizational one;

d) the registration and the traceability of carried-out activity, both in the perspective of safety of the patient and in the administrative reports.

Material and methods: From April 2020, our center started a telemedicine project in partnership with ALTEMS. The manual is available for downloading at www.dati-sanita.it . Through this project we were able to continue to assist oncologic patients in follow-up or in therapy with oral drugs.
Results: Between 28th April 2020 and 5th June 2020 thirty patients were enrolled with the median age 59.6 years (range

42-85), 20 women and 10 men with residence throughout the whole province of Foggia. Fifteen of 30 patients used a mobile phone, fifteen pc. The average length of the visit was 17.5 minutes (range 10-30 minutes). A customer satisfaction survey was collected at the end of each visit: 100% of patients expressed maximum value of approval.
Conclusions: A virtual surgery will never be able to substitute a clinical exam of the patient, although in certain circumstances like Covid-19 emergency, difficulty in reaching hospital or in situations that require frequent patient monitoring, technology certainly represents a valid arm in the healthcare setting.

D28

SARS COV2 PANDEMIC: IS CANCER A REAL RISK FACTOR?

Maiolani M.[1], Cubeddu A.[1], Pastorini A.[1], Fusco O.[1], Menatti E.[1], Cantini S.[1], Caponigro G.[1], Deligiannis P.[1], Fregoni V.[2], Crosetto L.[3], Bertolini A.[1]

[1]ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio; [2]ASST della Valtellina e Alto Lario-Breast Unit, Sondrio; [3]ARPA Piemonte Epidemiologia Ambientale, Sondrio

Background: Recent literature suggests that cancer patients are more susceptible to SARS CoV-2 infection and have higher infection-related mortality. These data are certainly influenced by age, stage of the disease, type of antitumour treatment and presence of cardiovascular comorbidity.
Methods: We conducted a retrospective observational study to evaluate the characteristics of patients with a history of oncological/haematological disease who acquired SARS CoV-2 infection during oncologic follow-up or active antineoplastic therapy in our Institution (ASST Valtellina e Alto Lario, Province of Sondrio) from March 1 to April 30, 2020. Eligibility required positive molecular testing on nasopharyngeal swab or bronchoalveolar lavage.
Results: At the present analysis, a total of 1471 subjects resulted positive for SARS COV-2 infection in our Province; among them 43 subjects (2.94%) had a history of oncological or haematological disease. 24/43 (55.8%) were males and 19/43 (44.2%) females; median age was 71.5 (range 53-91). 42/43 patients (97.6%) were hospitalized on a total of 613/1459 positive people who required hospitalization (42/613, 6.8%). 48.8% (21/43) patients died due to viral infection on a total number of deaths of 150 (21/150, 14%); 55% were males and 45% females; 40% had an age range between 70 and 79, 25% between 50 and 59, 20% between 60 and 69 and 15% over 80. 25% of patients had stage IV disease; 80% of patients had cardiovascular comorbidities and preexistent pulmonary diseases. Breast, lung and colon were the tumor types most represented.
Conclusions: In our case study, oncologic/haematologic patients are not significantly represented, constituting only less than 3% of total infected and about 7% of hospitalized

subjects. Although the limited sample, our data reveal, meanwhile, high mortality for SARS CoV-2 in cancer patients. This data suggests the need for new strategies for an earlier detection of positive subjects from SARS Cov-2 within the cancer population.

D29

DEVELOPING A STRUCTURED GUIDANCE AND EDUCATION PROGRAM FOR PATIENTS (PTS) WITH CANCER DURING SARS COVID-2 PANDEMIA IN A NORTH EAST PIEDMONT HOSPITAL

Torazzo R.[1], Fora G.[2], Lattuada S.[2], Manachino D.[2], Posca T.[2], Gasparre T.[2], Virone D.[2], De Marino E.[2]

[1]*ASL VC - PO S. Andrea, Vercelli;* [2]*ASLVC PO S. Andrea, Vercelli*

Background: Rapid outbreak of SARS Covid-2 Pandemia required emergency action by health services. Since March 1st 2020 Vercelli Sant'Andrea Hospital was appointed COVID19 referral center. Infection is associated with worse survival in pts with cancer so we developed a structured guidance and education program for disease prevention and containment. Implemented procedure concerns pts, health care professionals and all those involved in care and management of diagnostic therapeutic pathway.
Methods: Since March 1st pts were divided in 2 groups: 1st off therapy for which access to clinics was postponed; 2nd receiving treatment (chemotherapy, immunotherapy or radiotherapy). To everyone COVID19 WHO hygien standards were recommended. Other directions were: to use leukocyte growth factors also in subjects with risk <10%; to assess opportunity to undertake neo-adjuvant treatment in case of excessive delay of surgery; to transfer as many activities as possible in smart mode (eg.email, phone contacts);to informs pts that the use of internet means does not guarantee privacy; to identify and share path, lifts and spaces (eg. waiting rooms)creating an explanatory and educational brochure with a map of covid free path;to reshape waiting lists for outpatient and day hospital activities both in terms of timing and booking;to recommend attention to subjects undergoing surgical treatment for lung localized tumors, with treatment that has involved a partial or total sacrifice of the pulmonary parenchyma, and in all patients undergoing immunotherapy;to perform pretriage before going into oncology unit;to suspend all activities not strictly necessary for therapeutic purposes such as those managed by Voluntary Associations; to examine information from the General Management (GM), providing for implement them promptly.
Results: Guideline has been laid and immediately applied, then it was formally notified with a flow chart of activity and an explanatory brochure for pts to GM and it was approved on 31th march. Since March 1st to May 4th we performed 520 visits and 760 therapies, and since April 1st

to May 4th explanatory brochure was given to 203/258 (78%) pts; all pts (100%) had pretriage . No pts was affected by COVID-19 and all therapies were administered and were given without delay.
Conclusions: Our experience shows that a structured program of pts information and effective interventions can offer opportunity of safe care in COVID19 referral hospital

D30

PHONE FOLLOW-UP (PFU) FOR BREAST CANCER SURVIVORS (CS) DURING COVID-19 PANDEMIC: A SINGLE BREAST UNIT EXPERIENCE

Messina C.[1], Ferro A.[1], Piras E.[2], Zanutto A.[2], Caffo O.[1], Valeria M.[1]

[1]*Ospedale S. Chiara, Trento;* [2]*Centre for information and communication, Bruno Kessler Foundation, Trento*

Background: The COVID-19 outbreak became a public health emergency, leading to radical changes in care management. Hospitals are considered at risk for viral contamination and telemedicine allows CS to remain out of the hospitals. In our Institution all data concerning cancer patients are available through an Oncologic Web-based Electronic Medical Record (EMR): thus, the clinicians are able to access at any time CS medical history. From the start of COVID-19 pandemic we adopted EMR-assisted PFU instead of usual follow-up visit and this study aims to prospectively assess how breast CS perceived PFU.
Method: We emailed to all breast CS managed by PFU a 15-item survey. Answers were measured with Likert scales. The correlation between CS characteristics and answers were analysed with Pearson test.
Results: From February 2nd to May 20th, 107 out of 261 (41%) women fulfilled the survey. The median age was 61 (range 41-86), median follow up was 43 months (range 1-115). Most of the CS (67.3%) had high school diploma or higher degrees. About half of the CS were previously treated with adjuvant chemotherapy and 80% adjuvant endocrine therapy. 78.5% were able to reach the hospital autonomously. 66.4% suffered from COVID-19 related anxiety for their health and the majority (85%) were waiting for follow up visit to feel relief. 96.3% pts believed to have understood medical advice during PFU and were satisfied for the time and the opportunity to ask clarifications. 92% agreed with the decision to switch the usual follow-up visit in PFU. However, only 41.1% CS would like to have PFU in the future. We found a significant correlation between educational degree and comprehension during the visit (p=0.04) and with expectation for PFU feasibility (p=0.046). Age and educational level were significantly correlated with the ability to reach the hospital (p=0.046). CS treated with endocrine therapy were meaningfully correlated with the PFU satisfaction (p=0.048)

Conclusions: PFU is an important tool to avoid hospital contacts during COVID-19 pandemic and the majority of CS who agree to participate in the survey agreed and felt satisfied from this procedure. The number of CS willing to have PFU in non-emergency situations invites to investigate the possibility to have routine PFU at least for a subset of the CS. Prospective randomized trials are warranted to assess the reliability of PFU compared to standard follow-up visit to implement telemedicine in daily clinical practice.

D31

ON-LINE PSYCHOLOGICAL TREATMENT WITH ONCOLOGY PATIENTS DURING COVID-19 EMERGENCY

Prior M.[1], Bellè M.[1], Burelli M.[1], Favaretto A.[2]

[1]Ulss 2 Marca Trevigiana Servizio di Psicologia Ospedaliera, Treviso; [2]Ulss 2 Marca Trevigiana U.O.C. Oncologia, Treviso

Background: At the start of January 2020, the Coronavirus disease-2019 (COVID-19) originating from China, started to spread throughout Italy. One of the most affected area was the Veneto region which, due to the rapidly increasing numbers of confirmed cases, took necessary restraint measures as social distancing and isolation, in order to avoid the spread of the virus. These limitations led to major consequences in all activities and disciplines that are based on a strict doctor-patient relationship. How can we maintain the therapeutic relationship with oncology patients and their families when both the psychologist and the patient can be a possible source of infection? This is what we tried to understand as psychologists of the Hospital Psychology Service in collaboration with the Medical Oncology Unit of Ca' Foncello Treviso Hospital to continue our clinical activity.

Material (Patients) and Methods: As we has learned from other Chinese realities (Shuai L et al. 2020), our proposal with these patients was to continue our clinical activity using on line services like the internet platform Google Hangouts or mobile phones, according to patient preferences. During 9 weeks, which correspond to 39 working day, we were able to perform 123 on-line clinical conversations, in particular 118 with patients and 5 with a family member; 12% of the psychological interventions took place on Google Hangouts and the 88% were performed by phone.

Results: What we observed is that by this remote modality it was possible to continue the psychological care of oncology patients and their families. This treatment was now more important then ever for the safeguard of patients mental health, patients who already affected by an organic pathology are now forced to deal with a pandemic. As indicated by a Chinese study (Yanping B et al. 2020) the most commonly reported psychological problems were anxiety, depression and fear to go to the hospital, vehicle of a possible infection.

Conclusions: A fundamental achievement in this situation was the ability of the professionals of mental health to find out a strategy to adapt the Hospital Psychology Service to the outside situation, in order to respond to the constant requests made by patients to continue their treatment or to begin a new one.

D32

INCIDENCE OF INFLUENZA-LIKE ILLNESS (ILI) IN CANCER PATIENTS DURING COVID-19: THE ONCOVID PROSPECTIVE OBSERVATIONAL STUDY

Cattaneo M.[1], Indini A.[1], Ghidini M.[1], Rijavec E.[1], Bareggi C.[1], Galassi B.[1], Gambini D.[1], Berti E.F.[1], Grossi F.[1]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano

Background: There are limited data on cancer patients (pts) and the novel coronavirus (SARS-CoV2) respiratory disease (COVID19). Fever and/or respiratory symptoms (influenza-like illness, ILI) is a common finding in cancer pts. We aim to evaluate the frequency of ILI in cancer pts during the pandemic and to identify high-risk subjects to test for COVID19.

Materials and methods: From March 20th to April 17th 2020 we collected data of cancer pts in a prospective clinical trial approved by the local ethics committee. The primary endpoint was to estimate the cumulative incidence of ILI in the study population. The secondary endpoint was to estimate which proportion of pts with ILI had COVID19 diagnosis. A triage procedure with questionnaires was performed in pts accessing the hospital, with laboratory tests (complete blood count, C-reactive protein) in pts on active treatment. Non-urgent visits were converted into telehealth visits and triage: pts with symptoms were addressed to general practitioners. Based on a diagnostic algorithm, pts with ILI symptoms underwent an infectious disease specialist's evaluation and SARS-CoV2 swab. The LepuMedical SARS-CoV2 immunoassay technique was used in pts with suspect symptoms or altered laboratory tests, not falling into the diagnostic algorithm.

Results: Overall, 562 pts were enrolled: 13 (2%) pts had a positive SARS-CoV2 swab, none of which performed on the basis of triage procedures or questionnaires, rather detected through telephone communications and triage; 52 (9%) pts reported suspect symptoms and/or laboratory tests. Forty-five (8%) SARS-CoV2 swab positive, or with suspect symptoms and/or laboratory tests pts underwent SARS-CoV2 antibody tests; 20 (3%) pts were excluded for poor clinical conditions (n=10), death (n=4), or pts' refusal (n=6). Four out of 41 (10%) suspect pts had IgG+ (n=3), or IgM+/IgG+ (n=1); 4 out of 4 COVID-19 positive pts had IgG+ (100%). Antibody tests were negative in the remaining 37 pts.

Conclusions: In our experience, triage procedures and questionnaires were not helpful in detecting COVID19 in cancer pts. The incidence of both COVID19 diagnosis (2%), and SARS-CoV2 antibody positivity in pts tested on the basis of suspect symptoms (<1%), were similar to those observed in the general population.

D33

TRAINING AND INFORMATION DURING COVID19 PANDEMIC: THE MASTERPIECE IN YOUNG ONCOLOGISTS

Ranallo N.[1], Bastianelli L.[1], Merloni F.[1], Cantini L.[1], Ricci G.[1], Ballatore Z.[1], Berardi R.[1]

[1]*Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, Ancona, AOU Ospedali Riuniti-Ancona - Ancona, Ancona*

Background: COVID 19 pandemic was a health emergency that required a rapid response by the Italian National Health System. Healthcare professionals needed to be properly trained and informed about their patients' procedures and proper management. During an emergency, the information must be exhaustive, clear and timely to allow correct diagnostic and therapeutic continuity. It is also important that all health workers are promptly and homogeneously trained to guarantee the best treatment path even during pandemic. Our survey aimed to investigate the level of information and training of health workers in oncology during the pandemic and, in particular, the difference in perception between under and over 35 years operators.
Material and Methods: An on-line multiple choices survey was submitted to oncology health workers during the pandemic to investigate individual perception of resources, information and staff training management by hospital centers. No open questions were included.
Results: A total of 383 health workers replied to the survey (116 under 35 years versus 267 over 35 years). In the under 35s group a total of 65% declared they had been timely and sufficiently informed to understand the extent of the problem compared to 50% of over 35 (p=0.007). About 80% of young professionals were adequately informed and two thirds (63%) was formed about procedures/recommendations to be followed during the pandemic. But in professionals over 35 only 56% declared to have the right information and over 65% did not feel adequately trained (p= <0.01). Furthermore, 44% of over 35 felt not sufficiently prepared for the management of the cancer patient during an epidemic compared to only 28% of the under 35 (p=0.015).
Conclusions: The survey showed a different perception of information and training of healthcare professionals based on the age group. This could be determined by a different degree of task and responsibility but also by the greater and faster readiness of the younger operators to acquire new information and to draw a renewed ability to face an emergency by reorganizing themselves quickly and actively.

D34

THE RELEVANCE OF PRE-TRIAGE AND TRIAGE SEQUENCE FOR CANCER PATIENTS ACCESS TO THE IN-PATIENT AND OUTPATIENT ONCOLOGY UNITS AT THE AOU MATER DOMINI OF CATANZARO TO PREVENT COVID-19 IN HOSPITAL OUTBREAK

D'Apolito M.[1], Siciliano M.A.[1], Staropoli N.[1], Tassone P.[1], Tagliaferri P.[1], Barbieri V.[1]

[1]*Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro*

Background: The progressive diffusion and high mortality rate of the new Coronavirus, SARS-CoV-2, has underlined critical needs for the management of patients with relevant acute and chronic diseases. Cancer patients are often immunocompromised, therefore at higher risk for severe illness from COVID-19 and, at the same time, they experience anxiety and fear due to treatment uncertainty.
Material (patients) and methods: At the aim of protecting the safety of our patients and healthcare workers, a novel sequence of pre-triage and triage has been implemented at our Institution. Despite the importance of protective devices and telemedicine for deferred follow-up outpatient consults, we have also introduced a telephone pre-triage in order to avoid the access of symptomatic patients (asking specific questions relating to the risk and possibly sending a self-certification form by mail) with subsequent confirmation of non-deferrable visits for therapy needs. This predefined approach has proved to be an effective way to generate a stronger sense of patient's responsibility and safety. After the first step, everyone entering our hospital is subject to a careful external triage with an accurate admission assessment and immediate isolation of suspected cases in a surveillance zone separated from other patients, waiting for COVID-19 laboratory testing. All these steps have been performed respecting the safety distancing, temperature monitoring and always wearing at least a surgical mask, whether symptoms exist or not. Moreover, visitors are not allowed at any time during this emergency period.
Results: Between March 9nd and May 15nd 2020, we have registered 1772 triaged accesses compared to 1165 in the same period last year, with a 52% increase for outpatient treatments and without recording any COVID-19 positive case, due to the high pressure on regional Calabrian oncology facilities for the lack of patients referral to out-region institutions. Thanks to the promptly introduction of a containment approach, based on a pre-triage and triage double

algorithm, our daily activities have been guaranteed, without any decrease, preserving the continuum of patients' care and developing a quality approach to reduce distress.

Conclusions: Our institutional procedure of pre-triage and triage sequence has proven to be effective and can serve as model to safely reorganize working activities during the pandemic, without hampering oncologists' desire to assist their patients.

D35

THE APPROPRIATENESS OF INVASIVE VENTILATION IN COVID-19 POSITIVE CANCER PATIENTS: THE HARDEST DECISION FOR ONCOLOGISTS

Ghidini M.[1], Indini A.[2], Rijavec E.[2], Bareggi C.[2], Cattaneo M.[2], Galassi B.[2], Gambini D.[2], Grossi F.[2]

[1]*U.O. di Oncologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano;* [2]*Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano*

Background: Over the last two months we have frequently been contacted to estimate the prognosis of cancer patients (pts) affected by COVID-19 infection. Until now, there have been no clear markers to guide decision making regarding the appropriateness of invasive ventilation (IV) in COVID-19 cancer pts. Therefore, we developed a practical tool which encompasses a prognostic score in order to identify a subgroup of pts likely to have a better outcome and therefore may be potential candidates for IV.

Methods: The Milano Policlinico ONCOVID-ICU score includes three different groups of variables. In the first group we included sex, age, body mass index (BMI) and comorbidities. The second group includes oncological variables, such as the treatment intent (adjuvant or metastatic), life expectancy in months and treatment status (on/off). Furthermore, we included the SOFA score [1] and the d-dimer values, previously reported as risk factors for mortality in the presence of COVID-19 infection.

Results: We identified three different groups. We recommend that pts with a low risk score should be offered IV if necessary, while high-risk pts are best managed with best supportive care. Pts in the intermediate-risk group deserve a case-by-case discussion to derive a decision (Table 1).

Table 1. The Milano Policlinico ONCOVID-ICU score.

Variables	Score
Linked to pts	
Sex	F =0
	M =1
Age	<70 =0
	>=70 =1

(Continued)

Table 1. (Continued)

Variables	Score
BMI	<30 =0
	>=30 =1
Comorbidities	NO =0
	YES =1
	YES>1 =2
Oncological	
Treatment intent	Curative =0
	Palliative =1
Life expectancy	>6 mo =0
	<6 mo =1
Pts on treatment	NO =0
	YES =1
Clinical + lab values	
SOFA score	2-7 =0
	>=8 =1
D-dimer	< 1μg/mL =0
	> 1μg/mL =1

Category of risk for patients
Score <4: low risk –> ICU admission and IV.
Score 4-6: intermediate risk –> Case-by-case evaluation for ICU admission and IV.
Score >=7: High risk –> Palliative care.
SOFA SCORE [1]
- PaO$_2$ / FIO$_2$ (P/F)
- Platelets
- Bilirubin
- Hypotension
- Glasgow coma score scale
- Creatinine
- Ventilatory support

Legend: IV: invasive ventilation; mo: months; pts: patients.

Conclusions: A considerable proportion of oncology pts may experience clinical deterioration due to the worsening course of the infection. These cases require a comprehensive evaluation before considering ICU admission and IV. The division between groups is arbitrary and the score needs further validation. Therefore, we plan to assess the clinical history of all cancer pts admitted to Milano Hospital Maggiore Policlinico's ICU and retrospectively apply the score to this cohort.
[1] Ferreira FL et al. JAMA 2001; 286:1754-8.

D36

A STUDY ABOUT STRESS, DEPRESSION, ANXIETY E INSOMNIA IN HEALTH WORKERS OF ONCOLOGY DURING COVID -19

Marchi A.R.[1], Podda F.[1]

[1]*Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Cagliari*

Background: COVID-19 has shocked the entire planet, leading each State to set ever stricter health regulations,

managing pandemic in very short time. In the oncology department (hospitalization and DH) there have been effects that have changed the working lifestyle of the health workers (director, doctors, nurses, socio-health assistants and administrative staff within the department) therefore an attempt was made to measure their nature and impact. The aspects investigated were stress, anxiety, depression and insomnia.

Methods: The methods used are the naturalistic observation and the self-report questionnaires: the Dass-21 and the index insomnia. The research was very well received by the operators, eager both to make a contribution to the research, and to know their psychological situation, specifically the emotional sphere.

Results: The questionnaires revealed a discomfort distributed on all health workers, in particular: stress 65% (30% severe and extremely severe, 25% moderate, 10% average); anxiety 45% (25% severe and extremely severe, 5% moderate, 15% average); depression 40% (20% severe and extremely severe, 10% moderate, 10% medium); insomnia 30% (15% severe and 15% moderate). We have chosen to report only the clinically significant and deserving percentages of a psychological support intervention. The naturalistic observation confirmed the results obtained in the self-assessment questionnaires: the health staff in the oncology department experienced more stressful situations, anxiety, depression and insomnia especially for those who work in close contact with patients and therefore perceive greater vulnerability to contagion. Nevertheless, the data that emerged disconfirm the expectations, it was in fact thought to record higher scores.

Conclusions: Covid-19 put a strain on the work organization in the oncology department, changing the lifestyle of health workers both in terms of coping and interpersonal interactions. Contrary to expectations, there was a good cognitive and emotional management of the emergency, probably due to precise precautions to be adopted (PPE, reduction of the influx of users and social distancing), pre-existing exposure to death and its processing, good resources personal and social in the management of the covid-19 emergency. Cases of stress, anxiety and depression will be monitored and taken care of for a clinical psychological intervention.

D37

SWAB NEGATIVE NSCLC PATIENTS (PTS) WITH CLINICAL AND RADIOLOGICAL FEATURES SUGGESTIVE FOR COVID-19: A SINGLE CENTER EXPERIENCE

Palesandro E.[1], Bertaglia V.[2], Bironzo P.[2], Reale M.L.[2], Leone G.[2], Tabbò F.[2], Bungaro M.[2], Audisio M.[2], Mariniello A.[2], Rapetti S.[2], Di Stefano R.F.[2], Artusio E.[2], Capelletto E.[2], Sperone P.[2], Caramello V.[3], Calandri M.[4], Perboni A.[5], Passiglia F.[2], Novello S.[2]

[1]Thoracic Oncology Unit. Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Torino; [2]Thoracic Oncology Unit. Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Torino; [3]Emergency Medicine, San Luigi Gonzaga Hospital, Orbassano, Torino; [4]Radiology Unit, Department of Oncology, University of

Turin, San Luigi Gonzaga Hospital, Orbassano, Torino; [5]Pulmonology Unit, S. Luigi Gonzaga Hospital, Orbassano, Torino

Background: During COVID-19 pandemic, timely diagnosis of SARS-CoV-2 infection was crucial, especially in pts with cancer. Real-time polymerase chain reaction (RT-PCR) on nasopharyngeal swab (NPS) is hampered by ≈30% of false negatives. Clinical and radiological features may identify potentially infected cases in presence of negative test.

Materials and methods: We retrospectively retrieved records from 30 pts admitted to our Onco-Covid Unit. Clinical (fever, cough, respiratory failure) and radiological (ground glass opacities – GGO with or without lung consolidation) criteria were assessed. NPS RT-PCR was performed (VIASURE SARS COV-2 RT-PCR Detection Kit) at admission and at 48 hours. Pts underwent laboratory and radiological assessments (chest x-ray, bedside lung ultrasonography, thorax CT scan). Other sources of infection were ruled out (blood cultures, pneumococcal/legionella urinary antigen tests) as well as radiological differential diagnoses (e.g. disease progression).

Results: From March 21st to May 9th 2020, 9 NPS negative pts with both clinical and radiological features suggestive for COVID-19 were identified. Mean age was 65.1 (31-78), 4 were female, all with ECOG PS 1. 4 pts had COPD, 8 were stage IV. All pts were on active antitumor treatment. Most common symptoms were dyspnea (n 8), fever (n 5), dry cough (n 3); radiological features include: GGOs alone (n 6), consolidation (n 1), consolidation + GGOs (n 1). 3 pts had baseline lymphopenia, 7 high lactate dehydrogenase, 8 high C-reactive protein. All pts presented with respiratory failure: PaO2/FiO2 ratio <200 (n 3), 200—300 (n 5), > 300 (n 1). All pts received antibiotics (azithromycin + ceftriaxone 3; piperacillin/tazobactam 6), glucocorticoids, O2-therapy: nasal cannula (n 3), Venturi mask (n 2), non-invasive ventilation (n 4). 4 pts died and 5 were discharged from the hospital, 4 with the indication to active antitumor treatment and 1 to best supportive care.

Conclusions: High suspicion index is necessary in NSCLC pts with respiratory symptoms during COVID-19 pandemic as NPS may not identify all infected pts and the number of "gray cases" is expected to increase in Phase II. Clinical and radiological findings correlation is pivotal in this subgroup.

D38

MANAGEMENT OF NSCLC PATIENTS DURING THE COVID-19 PANDEMIC: RESULTS FROM AN ITALIAN SURVEY

Bertaglia V.[1], Reale M.L.[1], Passiglia F.[1], Palesandro E.[1], Bironzo P.[1], Olmetto E.[1], Leone G.M.[1], Tabbò F.[1], Bungaro M.[1], Audisio M.[1], Mariniello A.[1], Rapetti S.[2], Di Stefano R.F.[3], Napoli V.M.[4], Artusio E.[5], Capelletto E.[5], De Filippis M.[5], Jacobs F.[5], Sperone P.[5], Novello S.[5]

[1]Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy; [2]Pneumologia, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy; [3] Department of Oncology, University of Turin, San

Luigi Gonzaga Hospital, Orbassano, Torino, Italy; [4] Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy; UOC Oncologia Medica B, Università degli Studi di Roma, Sapienza, Policlinico Umberto I; Roma; Italy[5] Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano, Torino, Italy

Background: At the end of 2019, a novel viral pneumonia, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was described in China. Since then, Italy has soon become one of the most affected countries. In this challenging situation, the oncological community was called to protect cancer patients (pts), especially those affected by lung cancer, considered one of the most vulnerable population due to older age, multiple comorbidities and type of infection. This study aimed to investigate the clinical management of NSCLC pts, in order to provide a reliable picture of real-word practice during the COVID-19 outbreak.

Materials and Methods: A 29-questions survey focusing on the clinical management and therapeutic indications for NSCLC pts during COVID-19 pandemic was sent to 95 medical/thoracic oncologists across different Italian regions.

Results: From April 12th to May 2nd, 79 responses were received, with an overall response rate of 83%. The majority (77.3%) of oncologists declared a significant change in the outpatient management of NSCLC pts. The number of consultations in case of suspected NSCLC decreased in about half of cases (46.8%), with a major reduction when considering the number of pts coming from the emergency department for a first oncological evaluation (60% of cases). The total number of pts with any stage, newly diagnosed NSCLC, within the observational period, was reported to be lower than the pre-pandemic era by the 56% of oncologists. For pts candidates to adjuvant chemotherapy and concurrent chemo-radiation, the therapeutic indications followed guidelines in 62% and 72% of cases, respectively. As regards the metastatic disease, the majority of oncologists confirmed their clinical indication to first-line treatment. The collected data revealed major changes in the second line therapeutic options, most related to timing and schedules of administration. Lung cancer pts' accrual in clinical trials dramatically has fallen for 79% of oncologists and follow-up consultations were mostly managed by telemedicine.

Conclusions: This survey showed that Italian oncologists are determined to follow the available guidelines for the clinical management of NSCLC pts during this emergency time, while more complicate is to deal with clinical trials. In this tough landscape, telemedicine provides a valid support to facilitate patient-healthcare interactions.

D39

IMPACT OF COVID-19 OUTBREAK ON CANCER PATIENT CARE IN A LOMBARDY OUTPATIENT CLINIC

Quaquarini E.[1], Saltalamacchia G.[1], Caldana G.[2], Presti D.[1], Mollica L.[1], Balletti E.[1], Teragni C.[1], Biscaldi E.[2], Frascaroli M.[2], Palumbo R.[1], Bernardo A.[1], Sottotetti F.[1]

[1]ICS Maugeri IRCCS, UO Oncologia Medica, Pavia; [2]ICS Maugeri IRCCS, UO Oncologia Traslazionale, Pavia

Background: Coronavirus disease 2019 (COVID-19) is a respiratory tract infection that was first recognized in China at the end of December 2019, later becoming pandemic. Lombardy was among the first areas to have an outbreak of COVID-19 outside China. Oncology societies have been quick to issue guidelines on cancer care during the pandemic, suggesting telemedicine services, reducing clinic visits, switching to subcutaneous or oral therapies, when possible, evaluating the benefit of each treatment. We investigated the management of cancer patients in an outpatient clinic of Pavia, Lombardy, during COVID-19 outbreak.

Patients and methods: Using our electronic databases, we evaluated the number of patients accessing to hospital for anticancer drug infusion from 24th February 2020 to 30th April 2020 taking into account for each patient: diagnosis, line of treatment, reason of a therapy delay, and city of residence. We than compared the data with the same period of the year 2019 and 2018.

Starting from 24th February 2020, caregivers were not admitted to the hospital. Patient were asked to wear mask and gloves; outside the hospital, body temperature was measured and a questionnaire asking for influential symptoms and possible COVID-19 contacts was performed. The day before the visit, a phone call was performed with the discussion of patient clinical conditions and possible symptoms of COVID-19. Patients performed also blood exams. Patients complaining suspected symptoms or having had contact with a COVID-19 positive person were asked to call their doctor of general medicine and not access to hospital for therapy. All healthcare personnel started to wear mask, caps, disposable overall and gloves.

Results: A total of 2552 visits for drug infusion were recorded in 2020 compared to 2728 in 2019 and 2674 in 2018. In 2020, 36% of patients received treatment for an early stage disease and 64% for a metastatic tumour; 66% of patients came from Pavia and province, 3% from Lodi and province, 14% from Milan and province, 5% from other Lombardy provinces and 12% from other regions; 63 patients delayed the visit: 40% for "pandemic fear", 32% for travel restrictions, 16% for toxicity and 12% for worsening of clinical conditions. A total of 7 COVID-19 positive patient occurred.

Conclusions: The prompt adoption of personal protective equipment and controlled access to the hospital may have helped to reduce COVID-19 infections allowing the correct continuation of cancer treatments.

D40

PSYCHOLOGICAL DISTRESS IN OUTPATIENTS WITH LYMPHOMA, LUNG AND BREAST CANCER DURING COVID-19 PANDEMIC

Bafunno D.[1], Romito F.[2], Cormio C.[2], Minoia C.[2], Loseto G.[2], Dellino M.[2], Opinto G.[2], Silvestris E.[2], Guarini A.[2], Giotta F.[2], Catino A.[2], Montrone M.[2], Pizzutilo P.[2], Longo V.[2], Mastrandrea A.[2], Ricci D.[2], Pesola F.[2], Galetta D.[2]

[1]*IRCCS Istituto Tumori "Giovanni Paolo II", Bari;* [2]*IRCCS Istituto Tumori "Giovanni Paolo II", Bari*

Background: The psychological impact of the lockdown experienced during the COVID-19 pandemic has been found detrimental for the general population, but it has still not been evaluated in cancer patients. We have investigated the psychological status of outpatients receiving anti-neoplastic treatmentduring the lockdown in a non-COVID Cancer Center, with the following aims: to measure the levels of post-traumatic stress symptoms, depression and anxiety, to compare patients with different diagnosis. An additional aim was to offer a psychological on-line support to patients who need it.
Material and methods: Outpatients attending the IRCCS "Giovanni Paolo II" in Bari for their therapy were asked to complete these questionnaires: The Hospital Anxiety and Depression Scale (HADs) and the Impact of Event Scale-Revised (IES-r).Worries regarding the COVID-19 on patients' lives, socio-demographic and clinical details were investigated using a brief structured questionnaire.
Results: One-hundred seventy-six outpatients (n.59 with lung cancer, n.40 with breast cancer, n.77 with lymphoma) were enrolled. Mean age was 57.9 y.o. (SD ±14); 48% were male. We found that 54,4% of patients were above the cut-off (score$\geq$16) for HADS general scale. The mean-IES-R score of patients was 25 (SD±17), with 22.8% indicating severe level of PTDS. The HADS-D has been found significantly correlated with IES-R (r= 0.35; p<0.005). The 70% of patients declared that their worries have increased during the pandemic; their bigger concerns were: the risk of getting infected while at hospital (51.4%); the risk of infecting relatives coming back home (38.7%), andthe risk of delaying therapy (35.3%).When comparing the level of anxiety and depression in different diagnosis it has been found that patients with lung cancer have higher distress(HADs-general scale) than patients with lymphoma (F=17.3, p<0.005) and breast cancer (F=8.86, p<0.005).
Conclusions: This study focused on the psychological aspects of cancer patients during the COVID-19 pandemic, finding that one quarter of patients has severe post-traumatic stress symptoms, and has psychological distress. Patients with lung cancer have higher distress compared to the other groups. This condition risks being overlooked by clinical concerns, so weunderline the importance to place even more attention to the psychological needs of patients, especially for those who have symptoms similar to COVID-19 as in lung cancer, in order to offer adequate support.

D41

SHORT-TERM MORTALITY AMONG CANCER PATIENTS WITH SUSPECTED OR ASCERTAINED COVID INFECTION

Fusco V.[1], Alessio M.[2], Rossi M.[1], Zai S.[1], Piovano P.L.[1], Traverso E.[1], Blengio F.[1], Vincenti M.[1], Guglielmini P.F.[1], Bellotti G.[1], Manfredi R.[1], De Martino I.[2], Numico G.[1]

[1]*S.C. Oncologia - Azienda Ospedaliera Ss. Antonio e Biagio e C.Arrigo, Alessandria;* [2]*IRFI - Azienda Ospedaliera Ss. Antonio e Biagio e C.Arrigo, Alessandria*

Background: SARS-2 (COVID-19) infection is recent. Mortality among cancer patients affected by Covid-19 is unknown.
Patients and methods: Since February till to May 2020, we observed cancer patients with ascertained or suspected Covid infection (all symptomatic, or admitted in hospital due to undetermined pneumonia infection). Patients were classified in three subpopulations: a) patients resulted as Covid positive at the first pharyngeal swab; b) patients positive at swab other than first (ie, the second or third one); c) patients with a clinical scenario compatible with Covid infection but with negative swab, or never tested before death We reviewed clinical trajectory and rate of deaths classified as Covid-linked.
Results: We observed 27 possible Covid cases among cancer patients. Sex: 12 M/15 F. Type of cancer: lung in 9, colon in 6, breast in 4, others in 8. The patients were in diagnostic phase (5), under adjuvant treatment (2), on advanced disease therapy (16), in advanced disease not under active treatment (4). Out of 27 patients, 14 resulted as Covid positive at the first pharyngeal swab (group a); 3 were positive at swab other than first (ie, the second or third one)(group b); 10 patients with a clinical scenario compatible with Covid infection but with at least one negative swab (9) or never tested (1) (group c). On 20th May 2020,12 patients are alive, and 15 patients are dead: 9 with ascertained Covid (positive pharyngeal swab) and 6 without Covid confirmation. In the three subpopulations: a) Seven patients died and 4 patients are alive with negativized swab. b) All 3 patients are alive with negativized swab. c) Out of 10 patients with a clinical scenario compatible with Covid infection but not ascertained infection, 7 patients died within the observation time (death attributed to probable Covid infection even in absence of positive swab) and 3 are under observation.
Conclusions: Preliminary data show a high mortality rate (15 out of 27; 55.5%) among cancer patients with ascertained Covid infection but also in cancer patients with suspected infection and severe symptoms.

D42

SARS-COV-2 SCREENING AND MONITORING IN CANCER PATIENTS: AZIENDA USL TOSCANA CENTRO ONCOLOGY DEPARTMENT EXPERIENCE

Martella F.[1], Pozzessere D.[2], Rossi F.[3], Di Lieto M.[4], Milandri C.[5], Santini S.[6], Pazzagli I.[7], Vezzani E.M.[8], Lanini F.[9], Ribecco A.S.[10], Fabbroni V.[11], Moretti S.[12], Giordano C.[13], Manfredi M.[14], Casprini P.[15], Fioretto L.[16]

[1]*SOC Oncologia medica Firenze Ospedale S.M. Annunziata Azienda Usl Toscana Centro, Bagno a Ripoli, Firenze;* [2]*SOC Oncologia medica Prato Azienda Usl Toscana Centro, Prato;* [3]*SOC Radioterapia Firenze Azienda Usl Toscana Centro, Bagno a Ripoli, Firenze;* [4]*SOC Oncologia medica Pistoia Azienda Usl Toscana Centro, Pistoia;* [5]*SOC Oncologia medica Empoli Azienda Usl Toscana Centro, Empoli;* [6]*SOC Oncoematologia Azienda Usl Toscana Centro, Prato;* [7]*SOS Oncologia medica Pescia Azienda Usl Toscana Centro, Pescia;* [8]*SOC Radioterapia Pistoia e Prato Azienda Usl Toscana Centro, Pistoia;* [9]*SOS Oncologia Ospedale S.M. Nuova Firenze Azienda Usl Toscana Centro, Firenze;* [10]*SOS Oncologia Ospedale S. Giovanni di Dio Firenze Azienda Usl Toscana Centro, Firenze;* [11]*SOS Oncologia Ospedale del Mugello Azienda Usl Toscana Centro, Borgo San Lorenzo;* [12]*SOS Oncoematologia Firenze Azienda Usl Toscana Centro, Firenze;* [13]*SOS oncologia media Serristori e S.M. Annunziata Azienda Usl Toscana Centro, Figline Valdarno;* [14]*SOS Laboratorio immunologia allergologia Ospedale San Giovanni di Dio Azienda Usl Toscana Centro, Firenze;* [15]*SOC Patologia Clinica e Immunoallergologia Firenze-Prato Azienda Usl Toscana Centro, Prato;* [16]*Dipartimento Oncologico Azienda Usl Toscana Centro, Firenze*

Background: Inadequate knowledge about extent of coronavirus disease 2019 (COVID19) epidemic challenges health response and planning. COVID19 mortality among cancer patients (pts) is higher than in general population. The identification of asymptomatic COVID19 cancer pts is important from both a personal and a health system point of view as immunosuppression increases COVID19 disease severity. Screening for asymptomatic carriers is being tested in some categories. The best method for screening and monitoring is yet unknown.

Material and methods: Azienda Usl Toscana Centro Oncology department tested pts receiving chemo- or radio- therapy. Aims were checking the prevalence of asymptomatic COVID19 cancer pts and evaluating the need and the best method for subsequent monitoring. Pts were offered both a quantitative serologic IgM and IgG test (Qt-ST) and a RT-PCR test for SARS-CoV-2 in nasopharyngeal and oropharyngeal swabs (NOS). As the Qt-ST is costly and requires hours for response, in S.M. Annunziata Hospital (SMA), pts were also tested with a qualitative serologic IgM and IgG method (Ql-ST) to collect information on different serologic assays.

Results: Between May 11th and 17th, 1148 pts receiving an active antineoplastic treatment signed a written informed consent and were screened with RT-PCR for SARS-CoV-2 in NOS and Qt-ST. 317 pts in SMA were also tested with Ql-ST. 16 pts refused RT-PCR, 3 Qt-ST and none Ql-ST. 89 pts with haematological malignancy didn't receive ST. Only 0.44% (5/1132) of asymptomatic cancer pts had a positive RT-PCR. 1 of them had COVID19 disease and was declared healed 14 days before screening. All pts with a positive RT-PCR in NOS had a positive Qt-ST for IgM. 1/5 had also IgG positivity.

Qt-ST was positive in 26/1145 pts (2.3%): 3 were IgM+/ IgG+, 10 IgM+/IgG- and 13 IgM-/IgG+. 19.2% of pts with a positive Qt-ST (5/26) were asymptomatic carriers of COVID19 disease. In SMA, 6/317 (1.9%) had a positive Qt-ST, 21 (6.6%) a positive Ql-ST and all were negative for RT-PCR in NOS.

Conclusions: With a positivity of 0.44%, RT-PCR for SARS-CoV-2 in NOS may not be cost-effective for screening in asymptomatic cancer pts under antineoplastic treatment from a patient point of view. However, RT-PCR may improve both the compliance and the safety's sense of pts and operators in hospital and is mandatory in case of ST positivity. Qt-ST is more accurate than Ql-ST. Both Qt-ST and Ql-ST were safe and may be a proper option for monitoring cancer pts based on local organization.

D43

SARS-COV-2 INFECTION IN CANCER PATIENTS: A PICTURE OF AN ITALIAN ONCO-COVID UNIT

Reale M.L.[1], Bironzo P.[1], Bertaglia V.[1], Palesandro E.[1], Leone G.[1], Tabbò F.[1], Bungaro M.[1], Audisio M.[1], Mariniello A.[1], Rapetti S.[1], Di Stefano R.F.[1], Artusio E.[1], Capelletto E.[1], Sperone P.[1], Boccuzzi A.[2], Calandri M.[3], Perboni A.[4], Passiglia F.[1], Novello S.[1]

[1]*Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano (TO);* [2]*Emergency Medicine, San Luigi Gonzaga Hospital, Orbassano (TO);* [3]*Radiology Unit, Department of Oncology, University of Turin, San Luigi Gonzaga Hospital, Orbassano (TO);* [4]*Pneumologia, San Luigi Gonzaga Hospital, Orbassano (TO)*

Background: The world, and Italy on the front lines, is experiencing a major medical emergency due to the SARS-CoV-2 outbreak. Cancer patients are one of the potentially most vulnerable cohorts of people, but data about their management are still limited.

Patients and methods: In this monocentric retrospective study we included all SARS-CoV-2 oncological patients accepted at the Onco-COVID Unit at San Luigi Gonzaga Hospital, one of the few oncological departments dedicated to cancer patients with SARS-Cov-2 infection in Italy. Clinical data were obtained from medical records available until April 24th, 2020.

Results: 20 cancer patients were included. The mean (±SD) age of the patients was 66±14 years, 80% were men. Eight (40%) developed infection in their communities and 12 (60%) during the hospitalization. Lung cancer was the most frequent type of cancer (12, 60%), followed by blood/bone marrow cancer (3, 15%). Eight patients (40%) were symptomatic for COVID-19 at the time of diagnosis and symptoms began 2 (±2) days before. The most common were shortness of breath and diarrhea. Fever was present in 7 patients (35%). Among the 12 asymptomatic patients, 8 (67%) became symptomatic

during the hospitalization (mean time of symptoms onset 4 days + 4). C-reactive protein increase was detected in 15 (75%) patients, high lactate dehydrogenase levels in 13 (65%), lymphocytopenia and thrombocytopenia in 6 (30%) and 4 (20%), respectively. Seven patients (35%) were on active anti-tumor treatment, 3 (43%) received anti-tumor therapy within two weeks before SARS-CoV-2 positivity, and 2 (29%) continued oncological treatment (TKIs and chemotherapy) after the infection diagnosis. Nine (45%) patients were prescribed hydroxychloroquine and 5 (25%) antiviral therapy with lopinavir/ritonavir or darunavir/ritonavir. Ten (50%) patients died within a mean of 11 days (+ 8) from the diagnosis of COVID-19 infection. Five patients (25%) have been discharged from the hospital, 4 (20%) of them with the indication to best supportive care and 1(5%) to active antitumor treatment.

Conclusions: Our series confirms the high mortality rate among cancer patients with COVID-19. The presence of asymptomatic cases suggests that typical symptoms and fever may not be the only useful parameters to suspect COVID-19 in oncological patients.

Our Onco-Covid unit suggests the importance of a tailored and holistic approach for cancer patients, even in a challenging situation like SARS-CoV-2 pandemic.

D44

IMPACT OF IMMUNOTHERAPY IN HOSPITALIZATION OF COVID-19 INFECTED CANCER PATIENTS. FIRST RESULTS OF AN ITALIAN STUDY IN THE PROVINCE OF MODENA AND REGGIO EMILIA DURING SARS-COV-2 OUTBREAK

Spallanzani A.[1], Damato A.[2], Rovesti G.[1], Benatti S.[1], Berselli A.[2], Luppi G.[1], Pinto C.[2]

[1]*Division of Oncology, University Hospital of Modena, Modena;* [2]*Medical Oncology Unit, AUSL-IRCCS Reggio Emilia, Reggio Emilia*

Background: Recent reports highlight the higher incidence of severe events in cancer patients (pts) affected by COVID-19, although, insufficient data are available about the association with immunotherapy. Italian scientific society and colleges (AIOM, CIPOMO, COMU) released shared recommendations according to pts risk of infection and tumor characteristics, demanding for telephone consultations and, if suitable, treatments delay.

Material and Methods: In Modena and Reggio Emilia Cancer Centers, medical reports of pts undertaking immunotherapy between January 1st 2020 and April 30th 2020 were collected. For those pts infected with COVID-19, identified by thoracic computerized tomography criteria and RT-PCR of nasopharyngeal specimens according to WHO indications, we estimated the risk of infection and related complications that lead to hospitalization.

Results: A total of 337 pts with solid tumors treated with anti-PD1 and anti-PDL-1 antibody regardless the line of treatment was identified. Cancer diagnosis included 156 (46,3%) lung cancer, 74 (22%) melanoma, 36 (10,7%) kidney, 23 (7%) colorectal, 12 (3,4%) head and neck, and, 36 (10,6%) miscellaneous. Only 3 pts (0.9%), all with metastatic disease and during first line therapy were hospitalized for COVID-19 infection (Table1). The median age was 57 years. 2 pts have been treated with immunotherapy in combination with chemotherapy, and 1 patient with anti-PD1 and anti-CTLA-4. The onset symptom was fever in 2 pts, while 1 patient had subjective dyspnea. Subsequently, they develop respiratory distress and underwent to non-invasive assisted ventilation, receiving treatments with hydroxychloroquine, steroids, low molecular weight heparin. Tocilizumab was administered only in 1 patient according to progressive increase of serum IL-6 values. Nobody was admitted in Intensive Care Unit (ICU). Since the last update, May 15th 2020, 1 patient died while the others have recovered resulting COVID-19 negative to nasopharyngeal swab.

Conclusions: Although not conclusive, in our series, cancer pts infected by COVID-19 receiving immunotherapy do not appear to be exposed to greater risk of recovery.

Table 1. Characteristics of three metastatic cancer pts hospitalized with COVID-19 infection.

Primary tumor	Age (ys)	Gender	Regimens	Hospitalization (days)	Pulmonary infection involvement (%)	Death
Colon	40	F	Atezolizumab FOLFOXIRI Bevacizumab	16	20-40	No
Kidney	76	M	Nivolumab Ipilimumab	14	10	Yes
Pleura	65	M	Pembrolizumab Cisplatin Pemetrexed	65	10	No

D45

RAPID SEROLOGICAL TEST IN THE COVID-19 ERA: OUR EXPERIENCE

Caponigro G.[1], Fusco O.[1], Pastorini A.[1], Deligiannis P.[1], Maiolani M.[1], Cubeddu A.[1], Menatti E.[1], Barbonetti C.[2], Fregoni V.[3], Stiglich F.[2], Cattalini N.[4], Del Barba M.[5], Bertolini A.[1]

[1]ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio; [2]ASST della Valtellina e Alto Lario-Radioterapia, Sondrio; [3]ASST della Valtellina e Alto Lario-Breast Unit, Sondalo; [4]ASST della Valtellina e Alto Lario-Direzione Medica, sondrio; [5]Parlamento Italiano, Sondrio

Background: The COVID-19 was first reported in Wuhan, China, in December 2019 and then spread rapidly around the world also affecting our country.

It caused many deaths, not sparing health workers. The active detection of infection among health professionals is essential to ensure the safety of them and to reduce the spread of the virus.

We evaluated use of the qualitative serological test in asymptomatic healthcare workers in the Sondrio Hospital.

Material (patients) and methods: We analyzed 220 asymptomatic healthcare workers assessed for qualitative serological test from March 2020 to date; trial is actually ongoing.

We chose qualitative NADAL® COVID-19 IgG/IgM Rapid Test (test cassette) REF 243001N-10, by Nal Von Minden GmbH (Germany). This is a lateral flow chromatographic immunoassay for the qualitative detection of anti-SARS-CoV-2 IgG and IgM in human whole blood, serum or plasma specimens. The test procedure is not automated and requires no special training or qualification. It is necessary a finger-prick blood sample and provides a qualitative result within 15 minutes. It has a high sensitivity with 94,1% and 99,2% specificity.

Some of the subjects analyzed were also evaluated with quantitative serological test (Diasorin test).

Results: 25/220 asymptomatic cases tested resulted positive to qualitative serological rapid test (Table 1), 5 of which were conniving with people positive to COVID-19 but not been swabbed.

In 7/25 subject positive we had a quantitative positive IgG response; these people are found to be positive to naso-pharyngeal swab.

We have had 195/220 cases with qualitative negative response, in 43 of which the result of the rapid test has been confirmed by the quantitative serological test; in 152 cases the quantitative test was not carried out.

Conclusions: Rapid qualitative serological test is ready, economic and able to identifies asymptomatic subjects who may have developed immunity.

It could be useful as a rapid screening procedure in the healthcare workers to identify immune or infected people that should be isolated to reduce spread of the COVID-19.

Table 1. Clinical Characteristics of subjects.

Covid 19 unknown	Negative to qualitative	Diagnosis by qualitative	Quantitative detected+ in qualitative + patients	Swab +
n=220	195	25	7	7#

Covid 19 -	Confirmed - quantitative	Quantitative not detected
195	43	152

only 7/25 serological test+ had a swabs detection.

D46

PSYCHOLOGICAL IMPACT OF COVID-19 EMERGENCY ON HEALTH WORKERS IN ITALY: PRELIMINARY RESULTS FROM AN ONLINE SURVEY

Carapezza L.[1], La Rosa V.L[2], Piazza D.[3], Gebbia V.[4], Martines C.[5], Commendatore O.[5], Russo A.E.[5], Bordonaro R.[5]

[1]Oncologia Medica A.R.N.A.S. Garibaldi, Catania, Italy; [2]Dipartimento di Scienze della Formazione, Università degli Studi di Catania, Catania, Italy; [3]GSTU Foundation for Cancer Research, Palermo, Italy; [4]Casa di Cura La Maddalena, Palermo, Italy; [5]Oncologia Medica, A.R.N.A.S. Garibaldi, Catania, Italy

Background: COVID-19 disease quickly spread all over the world starting from Wuhan, China in December 2019.In Italy too, the lockdown was necessary from March to May 2020 to contain the exponential increase in infections. The pandemic outbreak has significantly affected the psychological wellbeing of the general population. However, according to the recent literature, healthcare workers were subject to greater stress and emotional impact due to a number of factors: active role in assisting COVID-19 patients, increased risk of infection, fear of infecting families, social stigma, exhausting working conditions. For this reason, we aimed to evaluate the psychological impact of the emergency in a group of Italian health workers.

Methods: We examined the psychological discomfort, depression, anxiety and stress experienced by health workers in Italy during the outbreak spike through the use of IES, BAI and BDI-II tests and compared them together with the sample's demographic characteristics as well as several measures strictly related to direct and indirect Covid-19 experiences.

Results: From 20th April to 4th May 2020, 96 healthcare workers [60 female, 36 male, median age 46 (28-70)] were invited to participate to the integrated self-administered questionnaire. The results of the IES test were in 42 (44%) cases not clinically significant while in 19 (20%), 9 (9%) and 26 (27%) there was a light, moderate and severe emergency impact respectively. The BAI test indicated a state of anxiety in 76 (79%), 14 (15%) and 6 (6%) respectively as mild, moderate and high. The BDI-II test indicated depression in 71 (74%), 12 (13%), 6 (6%) and 7 (7%) as low, mild, moderate and severe, respectively. The results of the IES and BAI test had a Pearson correlation index of 0.81, while between IES and BDI-II was 0.71. A multiple linear regression analysis between the dependent variable IES and the independent variables BAI and BDI-II showed an adjusted R-square index of 0.66 ($p < 0.000001$).

Conclusions: Applied test results show likely effectiveness in assessing the emotional impact of the COVID-19 emergency. Moreover, having a strong correlation between them and considering the measures of anxiety and depression as independent variables, these seem to be a predictive factor of the event's impact perception in the study population. These results encourage to underline the importance of adequate psychological support for health workers even after the acute phase of the emergency.

D47

SARS-COV2 PANDEMIA AND DELAYED CANCER TREATMENT: A SINGLE CENTRE EXPERIENCE

Pellegrini E.[1], Modesti M.[1], Botteri C.[1], Doni L.[1], Pillozzi S.[1], Antonuzzo L.[1]

[1]*Azienda Ospedaliero-Universitaria Careggi, Firenze*

Background: Pandemic SARS-CoV2 infection was characterized by a severe respiratory syndrome whit a worst course in elderly with comorbidity. Oncology patients (pts) may be at risk for an unfavorable course of infection (1). For this, oncologists had to choose how maintaining therapeutic benefit, minimizing risk of treatments (txs). Oncologist associations had recommended to reduce risk but encouraging continuation of txs. Indeed, one of the risks for oncological pts was inability to receive necessary medical service (2). In this study we reported our experience.

Methods: We analyzed pts with solid tumors which received 1 cycle of therapy from 9 to 30 March 2020 at Medical Oncology Unit of Azienda Ospedaliero Universitaria Careggi. We subsequently followed pts over time to evaluate delays in subsequent cycles, and its cause (COVID19 or not related).

Results: We analyzed 118 pts (27% affected by lung cancer), divided in age groups (172 were over 50, 96 over 70 and 16 over 80), setting (86% metastatic disease, 8%

adjuvant and 7% neoadjuvant/perioperative and type of txs (32% immunotherapy). There were 26 delay in second cycles, 24 in third and only 2 in fourth. In 18 cases delay was scheduled to minimize risk of COVID19 contagion. Expected neutropenia risk did not significantly influenced delay, while age influenced in pts over 60 (13,3% of delay in 80-90 group, 13,3% in 70-79, 17,3% 60-69 and 5,3% in 50-59). Adjuvant txs showed greater delays than metastatic and neoadjuvant /perioperative. 14% of immunotherapies (no difference in lung cancer vs others) was delayed vs 16% of other txs.

Conclusions: The SAR-CoV2 pandemic infection obligated oncologists to establish the risk/benefit ratio of a delay in txs, in absence of data. In our experience, the age> 60 and adjuvant setting have more often delayed txs, while type of therapy and the risk of neutropenia have had less impact. In contrast to cancer society's recommendations, there have been no greater delays in immunotherapy in lung cancer than in other diseases. The delay was more frequent in the first phase of the pandemic, probably due to the progressive reorganization of the cancer department

References

1-Liang W, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020; published online Feb 14

2-Wang H, Zhang L. Risk of COVID-19 for Patients With Cancer. Lancet Oncol 2020 Apr;21(4): e181.

D48

ORAL THERAPY PRESCRIPTION FOR ONCOLOGICAL PATIENTS DURING SARS-COV-2 PANDEMIA

Petrella M.C.[1], Palmieri V.E.[2], Paderi A.[2], Rossi G.[2], Pillozzi S.[2], Doni L.[2], Antonuzzo L.[2]

[1]*Medical Oncology Unit AOU Careggi, Firenze; [2]Medical Oncology Unit, AOU Careggi, Firenze*

Background: The Sars-CoV-2 pandemic led to a reorganization of all hospitals activities and assistance to cancer patients has also undergone changes. Our Medical Oncology Unit-AOU Careggi, in the lockdown phase, has provided guidelines to assist patients who receive oral cancer treatment with "telemedicine". Aim of this work is to analyze the different ways in which the oncological visits scheduled for the prescription of oral therapy were performed.

Material and methods: We consulted the agenda of oncology visits for oral therapies scheduled between 09 March and 26 March 2020: 115 patients were included in the study. We retrospectively compared the agenda with the medical records. Most of the patients (74%) scheduled in March followed a 28-day dosing schedule (q28), 13.04% q21, for the remainder the control was less frequently. Moreover, we also recorded subsequent visits, until May

2020. We divided the visits into 3 groups: the first group includes visits scheduled only in March, the second in April ($>$ 90%) and the third in May ($>$ 90%).

Results At the first scheduled visit during the lockdown, 1 patient did not come, in 2 cases the caregiver came, 3 patients have postponed the visit, 10 were managed by phone, 53 by phone and e-mail, 46 came to visit. In the first and third phase, patients received the drug or prescription mainly directly in the clinic (40.17% and 47.94% respectively), in contrast, in the second phase, shipping by courier was preferred (37.5%). We noticed a correlation between the basal ECOG performance status (PS), assessed before the pandemic spread, and the modality of the visit ($p<$ .001). Most patients (55.75%) with PS ECOG 0 carried out the first visit in the lockdown phase electronically (e-mail and telephone contact). However, no statistically significant correlation emerged between the Charlson comorbidity index and the method of carrying out the visit (p 0.998). Comparing the baseline PS and that recorded at the last visit, a statistically significant deterioration emerged (p $<$ .001). Considering the baseline ECOG PS 0, at the third visit 52.94% of the evaluable patients maintained the PS. In 18 patients the data is missing.

Conclusions: Telemedicine seems to be feasible in some contexts. The challenge is to select the right patient in the right moment. PS could be a screening tool but other factors should be investigated such as availability of appropriate technology for telemedicine.

D49

PRACTICAL APPROACH TO THE MANAGEMENT OF CLINICAL STUDIES DURING THE COVID-19 EMERGENCY IN A LARGE ACADEMIC HOSPITAL

Cicognini D.[1], Zuccarini A.[1], Ciani S.[1], Pasi F.[1], Sovico S.V.[1], Sciancalepore R.[1], Pacciolla P.[1], Arcaini L.[1], Bruno R.[1], Pedrazzoli P.[1], Ferrari A[2].

[1]IRCCS Policlinico San Matteo, Pavia; [2]IRCCS Fondazione Policlinico San Matteo, Pavia

Background: The Fondazione IRCCS Policlinico San Matteo, the largest academic Hospital in the south-west part of Lombardy has been involved in the management of the COVID-19 outbreak since its inception. The emergency required a deep reorganization of our Oncology/Hematology Clinical trial office (CTO-OH) in order to avoid significant disruption to usual practice, while facilitating clinical trials of the Infectous Disease Unit.

Materials and Methods: The activity of the CTO-OH included 141 profit and no profit clinical studies before the COVID outbreak. In addition to conducting already active clinical studies, several clinical trials with active drugs and procedure towards Covid-19 have been activated through

the fast track procedure. For all these studies, Sponsor companies and regulatory agencies requested the insertion of data, as the progress of the patients, was monitored in real time to assess their effectiveness, but also any potential damage through the communication of SAE.

Results: Since February 21st, 2 studies have not been activated at our Institution while 4 were activated through a remote SIV. The screening of new patients was reduced and in 2 studies it was temporarily suspended. Remote monitoring visits were carried out. At the same time the CTO-OH supported the Infectious disease dept. and the whole hospital in conducting clinical studies for COVID-19 pts. Within a month and half about 100 pts were enrolled, monitored; data were collected and entered. A major problem was the management of COVID patients enrolled in the various operative units used for infected patients in which patients were hospitalized or moved following the worsening/improvement of their conditions. We were able to ensure that the staff involved was correctly towed and updated.

Conclusions: The preparation and experience of the CTO-OH team and the motivation of all the hospital staff involved (physicians, nurses and lab personnel) allowed the success of the COVID-19 studies while almost fully preserving the ordinary Oncology-Hematology activity.

D50

SARS-COV-2 INFECTION IN PROSTATE CANCER PATIENTS: DATA FROM A HIGH-INCIDENCE AREA OF NORTH-WESTERN TUSCANY

Bloise F.[1], Sbrana A.[1], Paolieri F.[1], Manacorda S.[1], Bazzurri S.[1], Nuzzo A.[1], Sammarco E.[1], Mercinelli C.[1], Manfredi F.[1], Gadducci G.[1], Giannini N.[1], Paiar F.[1], Pasqualetti F.[2], Antonuzzo A.[2], Falcone A.[1], Galli L.[1]

[1]Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa; [2]Azienda Ospedaliero-Universitaria Pisana, Pisa

Background: Novel SARS-CoV-2 infection has been a severe health problem in Italy since the beginning of March 2020, with around 227,000 confirmed cases on May 18th, 2020. The north-western part of Tuscany has been one of the areas with the highest incidence (342/100,000 inhabitants) and the highest lethality rate (31.2/100,000 inhabitants). People aged 70-79 represented half of this population and the deaths in this subgroup represented 15.9% of all SARS-CoV-2-related deaths. Cancer patients are known to be at higher risk of incidence and complications from SARS-CoV-2. We aimed at analyzing the incidence and the lethality of SARS-CoV-2 in our prostate cancer (PC) patients (pts), in whom hormonal therapy seems to be protective from the first evidences published in the literature.

Material (Patients) and Methods: We reviewed all the clinical files of PC pts' visits performed from March 1st to April 30th, 2020 in the University Hospital of Pisa. We analyzed the demographic characteristics, the comorbidities, the type of hormonal therapy pts received, the incidence of SARS-CoV-2 and the related lethality rate.

Results: 132 pts with PC had face-to-face or telemedicine visits in the considered period. The median age was 76 (range 52-91), the mean age 75.44. The median number of comorbidites was 2 (range 0-6). 115 (87.12%) pts received LHRH analogue, 17 (12.88%) pts received LHRH analogue in combination with an anti-androgen. One pt had a confirmed SARS-CoV-2 infection (0.76%), other 2 pts (1.52%) had a clinical and/or radiological suspicion of SARS-CoV2 infection, but no PCR confirmation. One of these three pts (0.76%) died of ARDS (the considered pt had no PCR confirmation of SARS-CoV-2).

Conclusions: In our population, living in a high-incidence area for SARS-CoV2 infection, though being composed by elderly with a discrete number of comorbidities, the incidence rate was quite low, as well as the lethality rate, corroborating the data published in the literature.

D51

CLINICAL COURSE AND OUTCOMES OF COVID-19 IN CANCER PATIENTS: EARLY RESULT FROM "ONCOVID-19" STUDY

Di Noia V.[1], Squadroni M.[1], Barile R.[1], D'Aveni A.[1], Liguori A.[1], Brena F.[1], Dalto S.[1], Di Cintio D.[1], Sauta M.G.[1], Ceresoli G.L.[1], Salvini P.[1], Beretta G.D.[1]

[1]Oncologia Medica, Humanitas Gavazzeni, Bergamo

Background: Cancer patients (pts) are considered at higher risk of SARS-CoV-2 infection and more serious COVID-19 illness compared to the general population. We present the early results of the "onCOVID-19" study exploring clinical course and outcomes of SARS-CoV-2 infection in cancer pts.

Methods: In this observational study, we collected clinical data of pts referred to our institution with histologically confirmed diagnosis of solid cancer and COVID-19 from Feb 1 to May 20,2020. COVID-19 diagnosis was laboratory or radiologically confirmed or clinically suspected for suggestive symptoms, including fever (>37,5°C) and/or respiratory tract symptoms, without any other causes. Univariate and multivariate analyses were performed to explore the risk factors associated with severe events defined as hospitalization, admission to an intensive care unit, mechanical ventilation or death.

Results: Of the 64 pts enrolled, 35 referring to our Oncology Unit were analysed; the remaining 29, treated for cancer in other institutions, will be included in the analysis after data completion. Pts characteristics: male/female

(63/37%), current or former/never smokers (76/24%); stage IV/III (83/17%); median age 63 (47-86) years. Lung was the most frequent site of primary tumor (43%) or metastases (37%). Out 26 (74%) pts on active anti-tumor treatment, 6 (23%) received immune checkpoint inhibitors (ICI). Most common symptoms were fever (40%), shortness of breath (34%) and cough (23%); lymphopenia (<1000/mm3) was found in 5/15 (33%) tested pts. The diagnosis of COVID-19 was only clinical suspected in 2 (6%) cases and confirmed by RT-PCR or imaging (ground glass opacity and/or patchy consolidation) in 11 (31%) and 31 (88%) pts, respectively. An anti-microbial (antibiotics, antiretroviral drugs, plasma therapy) treatment was administrated in 19 (54%) pts; oxygen supplementation was required in 11 (31%) pts. Eleven (31%) pts had severe events, death occurred in 7 (20%) cases. Higher risk for developing severe events was associated with active treatment (RR 4.03, 95%CI 1.8-8.9,p=0.007) and lymphopenia (RR 4.0, 95%CI 1.1-14, p=0.007).

Conclusions: Early results of our ongoing study confirmed the vulnerability of cancer pts to COVID-19. Although the small sample size, treatment with ICI and lymphopenia seem to be risk factors for death and severe events. Waiting for final results, screening cancer pts for infection should be advisable before starting immunotherapy or in case of lymphopenia.

D52

COVID-19: TRIAGE STRATEGIES FOR PATIENTS MANAGEMENT IN "S. TIMOTEO" HOSPITAL-TERMOLI

Rocchia N.[1], Sciarretta G.[2], Farina P.[3], D'Addario D.[3], Tartaglione P.[1], Santoro T.[1], Corradi R.[1], Olivieri M.[1], Sorella A.[1], Licursi M.[1], D'Uva R.[1], Moio P.[1], Carrozza F.[3]

[1]First AID/ER S. Timoteo Hospital, Termoli; [2]Medicine Internal S. Timoteo Hospital, Termoli; [3]Oncologic D.H. S. Timoteo Hospital, Termoli

Background: On 11 February 2020, the WHO declared the existence of a new viral disease, causing a severe acute respiratory syndrome-Coronavirus-2 (SARS-Cov-2). In Molise, two of the first cases reported were the S. Timoteo hospital of Termoli. On March 5, the hospital closes both routine and emergency/emergency activities until March. At the reopening, a two-tier triage started and from March to May 2020 we collected data to understand the needs of the population for access to the hospital during the pandemic.

Methods: Two triage tents were set up at the entrance for the wards and for access to the emergency room. Oncologists performed an internal triage for their patients. Those who had been in high-risk regions were admitted only after quarantine or a swab. Other measures: pre-triage phone, access to accompanying persons and visitors was

prohibited, non-urgent follow-up visits were cancelled and made by phone. Each case was discussed jointly and assessed the risk/benefit ratio for the continuation of treatments. In suspected cases a PCR test was performed on a nasopharyngeal sample and, if positive, the patient was sent to the infectious disease department.

Results: Dedicated and adequately trained staff, collected access data from 18 March to 31 May 2020. Triage controls were 7856 (F 54%, M 46%): access to the E.R. were 3125 (267 family carers, 150 white codes, 2143 green, 532 yellow, 33 red), among the PTS arrived in PS 139 were suspected of infection and kept in the dedicated area, waiting for their test; of these 6 were positive (1 sent home in quarantine, 5 symptomatic were transferred to the reference centre). Other 3982 accesses have been evaluated to the external triage and 749 to the oncology triage equal to 15,83% of the total accesses entered in hospital (not in PS) to carry out ev therapies, visits and/or not deferable radiological examinations. Of the pts oncology 52.85% was F, 47.15% M with an average age of 66.51 and a median of 67 years (range 35-97).

Conclusions: No pts evaluated at the external triage and in oncology were suspected of COVID infection and, at the moment, no oncological PTS was found positive. The triage procedures put in place can be a first screening for the identification of a potential population at risk.

D53

SARS-COV-2 EMERGENCY: BURNOUT AND ENGAGEMENT IN HEALTHCARE WORKERS OF MEDICAL ONCOLOGY UNIT

Podda F.[1], Marchi A.R.[1]

[1]*Medical Oncology Unit, University Hospital And University Of Cagliari, Cagliari, Cagliari*

Background: The health emergency from Sars-CoV-2 required the implementation of prevention measures that had an important impact on habits and lifestyles. Healthcare workers are among the workers who are most exposed to the risk of contagion, also exposing them to a growing emotional and psychological overload. In this work, Sars-CoV-2 has been examined as a negative factor coming from the external environment that affects negatively on the internal organizational environment. Exposure to the virus, fear of being infected or of infecting your family, prolonged working hours, shortage of personal protective equipment, are just some of the factors that can create situations of stress and burnout. To anticipate and monitor the onset of these conditions in healthcare workers, a psychological analysis and support project has been set up since the beginning of the phase of maximum contagion of Sars-CoV-2.

Methods: The intervention was proposed to all healthcare workers in the Medical Oncology Unit by subjecting them to the Maslach Burnout Inventory (MBI), to investigate the dimensions of emotional exhaustion, depersonalization and personal accomplishment, the Utrecht Work Engagement Scale (UWES), for engagement in the dimensions of vigor, dedication and absorption. From the results obtained, psychological interviews were planned at implementing individual resilience and hardiness, in cases where the subject has reported a high burnout and low value on the engagement scale, and group collaboration and sharing, in the case of burnout of medium level and average engagement, to face the Sars-CoV-2 state of emergency by improving the aspects of group hardiness.

Results: 43% of healthcare workers reported high engagement while 48% are on average 9% report low values. Burnout is present in high value in 39%, average in 35% and not present in 26% of healthcare workers. The dimensions detected in the MBI and UWES are directly opposite, therefore burnout healthcare workers can report high values in engagement and vice versa. Only in 8% of cases did subjects report high burnout values and low engagement values.

Conclusions: Providing cognitive tools through psychological support interviews facilitated greater awareness and understanding of the problem, an understanding of the interactions between health professionals and the emergence of Sars-Cov-2, strengthening positive relationships, the problem solving, compensating for anxiety and reorganizing organizational roles.

D54

MANAGEMENT ORAL CANCER THERAPIES IN ONCOLOGY CLINIC DURING COVID19 PANDEMIA

Pastorini A.[1], Caponigro G.[1], Fusco O.[1], Deligiannis P.[1], Maiolani M.[1], Cubeddu A.[1], Cantini S.[1], Menatti E.[1], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: Since 2017 to optimize the dispensing and administration of the so-called oral cancer therapies, it was decided to set up at our Oncology Unit of the Sondrio Hospital a dedicated clinic. In recent years, since the number of oral therapies available has increased, above all due to the growing indications,consequently the flow of patients to our clinic has increased.

The onset of the pandemic COVID 19 has therefore imposed on us, in order to reduce the gathering of patients and caregivers in the rooms of the clinic, an reorganization to minimizing outpatient visits to mitigate exposure and possible further transmission and, at the same time, to maintain the safety of oncological therapy.

Material and methods: Based on the low haematological toxicity profile, we chose to dispense the therapy bi-monthly

instead of monthly to patients in stabilized therapy: 14 receiving enzalutamide therapy, 5 patients in imatinib (3 GIST and 2 CML), 2 patients in sunitinib, 4 patients on pazopanib, 2 patients on osimertinib, 4 patients on alectinib. However, telephone contact was made in the event of any problem.

Results: All 21 patients showed no relevant toxicity (no G 3 or G 4) and no cases of Covid infection 19 occurred.

Conclusions: In consideration of the absence of significant toxicity, it could be thought to test this outpatient practice on a greater number of patients, perhaps by setting up surveillance by telematic means and not only by telephone, also in anticipation of future epidemic outbreaks.

D55

WHAT ABOUT A MEDICAL ONCOLOGY UNIT DURING THE COVID19 PANDEMIC? ACTIVITY MAINTAINED THANKS TO TIMELY DECISIONS: SONDRIO'S EXPERIENCE

Bertolini A.[1], Doria A.[2], Orsini B.[2]

[1]*ASST della Valtellina e Alto Lario -Oncologia Medica, Sondrio;* [2]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: On February 21, 2020 the first Italian Covid19 patient was diagnosed. From that day the pandemic begins, which spreads with an impressive growth. The Oncology Unit Director has responsibilities, which obliged him to execute orders dropped by the Hospital Management in a top-down manner. Above all, he has direct responsibilities towards his collaborators and patients. It's not allowed to entrench behind the sentence: I've no provisions. For this reason, it is necessary to deal with the emergency with clinical intelligence, notwithstanding specific provisions.

Method: Since March 9, the Sondrio's Medical Oncology team received specific provisions from its Director, more restrictive than that developed by the hospital summarized in:
- obligation to measure body temperature (BT) before leaving home
- light protection during work: surgical mask, gloves, cap.
- complete protection in case of suspect Covid19 patient
- placement of active treatments on at least 2 distinct time slots to avoid gatherings.
- sanitization of the chairs after each patient
- from 3 April 2020 obligation for all staff to use KN95 masks, purchased directly.
- obligation for each patient:
o to stay at home if BT $> 37.5°$ C.
o to monitor BT at home before going out.
o to detect BT before entering in day hospital.
o it's always forbidden to have accompanying persons.
o at least surgical mask
o to disinfect hands using gloves

Results: With the provisions, no one became infected during work in the last 3 months. Only 1 nurse was Covid+, due to her husband. By contrast, 44 patients were Covid+ and 21/44 have died. 3/44 were diagnosed as Covid19 + as hospitalized patients. These data testifies our daily risk. No patient produced written complaints to the hospital management for our new rules.

Discussion: In Sondrio's Province there've been 1,480 infections. Almost 400/1,480 were health employers, a doctor has died. The most serious pandemic of the last 50 years was managed initially with a lack of tampons, delay in the use of serology, ostracism towards the use of personal protective equipment.

The provisions of Oncology Unit Director ensured:

- protection of staff
- guaranteed treatment for all patients

At 31 May 2020, the out-inpatients hospitalization activity was comparable to 2019. We used our knowledge for them without deserting.

On 9 April and 9 May, 2020 all staff underwent rapid qualitative serological tests purchased directly by our decision. All were negative.

D56

VOLUNTEERING AND COMPLEMENTARY SERVICES IN ONCOLOGY DURING THE COVID-19 EMERGENCY

Bazza T.[1], Cantini S.[1], Pastorini A.[1], Maiolani M.[1], Fusco O.[1], Menatti E.[1], Caponigro G.[1], Deligiannis P.[1], Cubeddu A.[1], Doria A.[1], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: Volunteering in oncology has been a well-known and consolidated reality for decades. Alongside this fundamental component, complementary services that deal with providing image consultancy, wigs and onco-aesthetic services to women who undergo oncological surgery and chemotherapy treatments, have been integrated for years

Material (patients) and methods: In the context of the emergency we are going through, within the containment measures of the covid-19 pandemic, volunteering and complementary services have been suspended.

Volunteers are people who for sensitivity devote their time to those who are experiencing a situation of suffering. They follow a specific training path and their activity is supervised by the psychoncologist.

Despite their absence, enhancement of the group and their role, they have been supported through periodic supervisions conducted by the psycho-oncologist online and through the creation of a chat that represents a physical and psychological space for the group.

Technology has made it possible to keep the group united by making each member perceive a sense of continuous belonging overcoming physical distances. The members of the group remained in constant contact with each other and with the operators of the department.

The supervision activity also continued with the onco-aesthetics operators who remained in contact with Medical staff and offered their availability through telephone consultations on body image care. Body image is related to a positive self-image in female patients who undergo surgery or body changes for chemotherapy treatments.

Results: Despite the social distancing measures and the removal of the volunteers from the department the group and its internal dynamics have been preserved. The use of technology in this context ensured the cohesion of the group, the members actively participated in overcoming the limits of physical distance.

Conclusions: Nobody knows how this emergency will evolve and when it will be possible to return to normal. During the upcoming months the group of volunteers can keep their motivation and their investment in oncology services alive and it will be important to keep on working on their involvement and internal cohesion.

Patients who are going through a difficult time and who need moments of "normalcy" along their oncological care pathways know how precious the presence of volunteers is.

D57

A RETROSPECTIVE ANALYSIS DURING SARS COVID-2 PHASE 1 PANDEMIA BETWEEN TWO HOSPITALS: IMPACT OF A STRUCTURED GUIDANCE AND EDUCATION PROGRAM (SGEP) TOWARD A STANDARD OPERATING PROCEDURE (SOP) IN PATIENTS (PTS) WITH CANCER

Manachino D.[1], Lattuada S.[2], Posca T.[2], Torazzo R.[2], Fora G.[2], Gasparre T.[2]

[1]*Oncologia ASLVC Piemonte, Vercelli;* [2]*ASLVC Piemonte, Vercelli*

Background: In Vercelli there is a Spoke Hospital and in Borgosesia there is a little Proximity Hospital: both are in the same district. Since March the 1st 2020, only Vercelli's Hospital has been appointed as COVID19 referral center. Pts with cancer have less chances of survival this infection, so a structured guidance and an educational program has been created and immediately applied in Vercelli, while in Borgosesia, the General Management (GM) standard hygiene procedures were applied to prevent the SARS CoVID19 infection. Our objective is to highlights outcomes and differences between SGEP and SOP on Pts with cancer in these two different cancer wards.

Methods: Since February the 23rd to May the 4th, during COVID-19 Phase 1, we retrospectively conducted an analysis of all patients who entered in Vercelli 's (with SGEP) and Borgosesia's (with SOP) cancer wards and we compared impact on infection between them.

Results: In Vercelli, 433 Pts entered the Oncology unit with SGEP and underwent 796 treatments and 682 nursing services. In Borgosesia, 87 pts entered in Oncology unit with SOP and underwent 220 treatments and 73 nursing services. COVID 19 affected 0/422 (0%) Pts in Vercelli, while 3/87 (3,5.%) Pts in Borgosesia had been infected. These patients have then been hospitalized and 2/3 (66%) of them died (one chemotherapy for colon cancer adjuvant and the other one for advanced lung cancer).

Conclusions: Even if in a limited number of cases, our experience seems to demonstrate that standard measures (SOP) are not enough for cancer patients in course of an epidemic and they need a differentiated approach (SGEP).

D58

PSYCHONCOLOGY IN FRONT OF COVID-19

Cantini S.[1], Caponigro G.[1], Fusco O.[1], Deligiannis P.[1], Pastorini A.[1], Cubeddu A.[1], Maiolani M.[1], Menatti E.[1], Bazza T.[1], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: The emergency state we are living today and the implementation of COVID-19 related restrictions has increased the psychologic distress levels for cancer patients. Measures such as not beingallowed to see other people and forced social distancing, have triggered in in patients negative memories and increased their concerns about the efficacy of their treatment plan. For these patients, lonelinessis linked to a higher likelihood of death and social distancing has a negative impact on their mental health, by increasing their worries. In order to limit these downsides, an important unlock has been to be able to provide continuous psycho-oncology treatments through the remote use of tablets, PCs and smartphones,and thereby reducing the number of visits to hospital.

Material (patients) and methods: The effectiveness of the remote psychologic treatments has been possible by the use of the psychologic distress thermometer and its impact overall. Psychoeducation has helped to normalize the psychologic reactions against COVID-19; patients have experienced daily activities shifts, such as sleep, diet and level of attention, that have reduced security and personal equilibrium in their day to day life. Analysis of individual coping skills and use of mindfulness were key to increase patients personal resilience.

Results: From a 3-month research on cancer patients, from March 3rd to June 3rd, the following results are shown:

Conclusions: Technology has allowed the continuity of this service in such vulnerable times and it has enabled the

implementation of new functional approaches from a personal, relational and social point of view. Now it's time to a new challenge: go back to normality. Without psycho-oncology treatments through the remote use of tablets, PCs and smartphones this would not have been possible, this method will remain a valid alternative over time.

N° Cancer Patients Under treatment or follow up	N° Caregivers	N° Family components with complicated mourning diagnosis
28	9	7

Psychological treatment requests based on most relevant distress cases	Number patients
Anxiety symptoms (sleep and food difficulties, lower level of attention, worry about the future, etc.)	21
Depression symptoms (psychomotor movement, lack of interest, hypersomnia, etc.)	11
Worry to contact COVID-19	6
Worry to no be able to get cancer treatments or follow ups	2
Worry to go to the hospital for cancer treatments	4

D59

IMMUNE CHECHPOINT INHIBITORS (ICIS) IN THE ERA OF COVID-19

Deligiannis P.[1], Pastorini A.[1], Cubeddu A.[1], Maiolani M.[1], Caponigro G.[1], Fusco O.[1], Menatti E.[1], Cantini S.[1], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: The coronavirus pandemic resulted in nearly 400,000 victims. Cancer patients under active treatment with chemotherapy, target therapy, or immunotherapy (ICIs) are considered to be at high risk of SARS-cov-2 infection and of a severe form of Covid 19. In this case (patients on active treatment), it seems appropriate that the possible postponement of access to treatment should be assessed and discussed on a case by case basis, based on the relationship between the risks (for the individual and for the community) related to hospital access and expected benefits from the treatment itself.

Material (patients) Method: Here we assessed the impact that the pandemic had as well as the advice of scientific societies on the administration of immunotherapy in patients who refer to the Day Hospital of Medical Oncology of the Sondrio hospital. Data from the medical records of all patients who were treated with ICIs from the 1st of March until the 06 th of July 2020 were collected. Patients were contacted by telephone the day before the infusion of therapy and on the day of administration they accessed the DH only with a face mask and after measurement of the body temperature.

Results: 29 patients, 15 women, with an age range between 46 and 85 years were identified. There are 14 patients treated with Nivo and 15 patients treated with Pembro (4 of whom have had combination immunotherapy with chemotherapy) The treated tumors were NSCLC, Melanomas, Renal Cancer, Bladder Cancer, Head and Neck cancer. A total of 74 biweekly doses of Nivo and 53 threeweekly doses of Pembro were administered. There was no postponement of therapy. In 3 patients who underwent restaging with TC Chest/Abbdomen there was a suspicious radiological immaging that was not confirmed as SARS-cov 2 infection.

Conclusions: In the current context of the COVID-19 pandemic clinical decisions about cancer patients deserving immunotherapy should be characterized by separated reflections, avoiding generalizations. A careful collection of clinical data in all cancer patients and multicenter retrospective studies will be required to provide more definitive guidance for clinicians.

D60

MANAGEMENT OF A BREAST UNIT AT THE TIME OF COVID 19 (ASST VALTELLINA E ALTO LARIO EXPERIENCE)

Fusco O.[1], Pastorini A.[1], Cantini S.[1], Caponigro G.[1], Deligiannis P.[1], Maiolani M.[1], Cubeddu A.[1], Menatti E.[1], Fregoni V.[2], Grechi A.[3], Poletti P.[3], Prada M.[4], Declich P.[4], Barbonetti C.[5], Stiglich F.[5], Franzini P.[3], Sosio D.[6], Raponi A.[6], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio;* [2]*ASST della Valtellina e Alto Lario-Breast Unit, Sondrio;* [3]*ASST della Valtellina e Alto Lario-Senologia, Sondrio;* [4]*ASST della Valtellina e Alto Lario-Anatomia Patologica, Sondrio;* [5]*ASST della Valtellina e Alto Lario-Radioterapia, Sondrio;* [6]*ASST della Valtellina e Alto Lario-Radiologia, Sondrio*

Background: Revision of the therapeutic diagnostic path of breast cancer during the COVID-19 pandemic.

Material (patients) and methods: The COVID-19 emergency has made appropriate changes in breast cancer treatment in Italy. The Lombardy region organized itself through first level structures connected to several more specialized centers (spoke), this model was sometimes difficult to apply for mileage distances and fear of infection; so the local organization was the best solution.

What we changed in our organization in agreement with recommendations by National and International Oncology Societies (AIOM /ESMO):

- First level screening and surgical activity concerning benign tumor pathology and reconstructive surgery have been suspended.
- Access to the breast surgery visit was guaranteed once a week.
- The surgery was performed according to the priority classes considering the biological characteristics of the tumor.

- Hospital access was planned the day before surgery for preoperative tests provided that nasopharingeal swab for Covid-19 research had to be already done..
- The hospitalization was performed with the utmost respect for preventive hygiene standards and physical distancing; the access to relatives was not allowed.
- Patients were discharged on the evening of the operation if residing nearby the hospital.
- A multidisciplinary discussion was ensured through videoconferencing with subsequent and timely sharing of the treatment program with the patient.
- Access to systemic treatment was a priority for patients with aggressive biological tumor characteristics (triple negative, HER-2 positive, high disease volume).

Results: From the beginning of the pandemic today 56 breast tests and 22 surgical procedures (19 quadrantectomies and 3 mastectomies) have been performed. Multidisciplinary discussions were done every 2 weeks through multimedia support. Hospital access has been maintained only for patients with high priority features who needed to systemic therapy, while the telephone management was performed for those with low priority characteristics.

Conclusions: 5-year survival has been shown to reach 83.9% in high-volume facilities. The efficient work of a multidisciplinary team produces appropriateness, consistency, and better use of human and economic resources. The main purpose of each Breast Unit is trying to keep these results even during the COVID-19 pandemic.

D61

ONCOLOGY CLINICAL TRIALS' MANAGEMENT IN ITALY DURING THE COVID-19 EMERGENCY: CHALLENGES AND IMPROVING OPPORTUNITY

Menatti E.[1], Pastorini A.[1], Fusco O.[1], Cantini S.[1], Caponigro G.[1], Deligiannis P.[1], Maiolani M.[1], Cubeddu A.[1], Doria A.[1], Bertolini A.[1]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio*

Background: The global COVID-19 pandemic has adversely affected all aspects of clinical care and it has not spared even clinical trials on cancer. Indeed the need to adopt precautionary measures for the containment of COVID-19 infection have affected the access of cancer patients in clinical trials. The devastating effects of this global crisis have also negatively impacted the work of our Oncology Unit which has so far conducted more than 120 phase I-III studies.

Method: We faced numerous challenges with conducting clinical trials due to COVID-19. In order to contain infection all the actor involved had to apply several precautions. Pharmaceutical companies, no-profit Sponsors, CROs and either our organization have applied or extended smartworking in order to continue their activities related to clinical trials but monitoring visit on site were suspended. When possible remote monitoring visits have been performed. Start initiation visit for new trial, for which it is essential the presence on site, were strongly postponed. Ethics Committee evaluation of clinical trials or substantial amendments have suffered inevitable strong delays nearly to 3 months because they had to adapt their activities also with organize their meetings by web-conferences. Only access to compassionate use was ever granted.

Results: At site particular attention was needed in the enrollment of new patients in the trials evaluating the risk/benefits ratio. For each patient the possible postponement of access to receive treatment has been assessed on the basis of the relationship between the risks, for the patient and the community related to access to the site, and the expected benefits of the treatment itself. The closure of several Hospital Units due to spread of contagion and limited availability of ancillary services caused the interruption of enrollment in clinical trials.

Conclusions: Our clinical research activity during the pandemic has suffered negative repercussions but we think that what happened could be an useful opportunity to improve and transform clinical trial conduction system for example by simplifying the study design, optimizing the number of on-site monitoring visits and reducing patient's access to the hospital.

E - Breast Cancer

E01*

BLOOD GLUCOSE LEVELS ARE ASSOCIATED WITH THE EFFICACY OF EVEROLIMUS-EXEMESTANE IN PATIENTS WITH ADVANCED HR-POSITIVE/HER2 NEGATIVE BREAST CANCER: THE ITALIAN EVERMET STUDY

Vernieri C.[1], Nichetti F.[1], Guarneri V.[2], Cortesi E.[3], Moscetti L.[4], Del Mastro L.[5], Fabbri A.[6], Curigliano G.[7], Montemurro F.[8], Losurdo A.[9], Generali D.[10], Fabi A.[11], Pedersini R.[12], Ciccarese M.[13], Rocca A.[14], Arpino G.[15], La Verde N.[16], Puglisi F.[17], Mariani L.[1], De Braud F.[1]

[1]*Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [2]Veneto Institute of Oncology IOV, Padova; [3]Policlinico Umberto I, Sapienza, Roma; [4]University Hospital of Modena, Modena; [5]Ospedale Policlinico San Martino, Genova; [6]Belcolle Hospital, Viterbo; [7]IEO, European Institute of Oncology IRCCS, Milano; [8]Candiolo Cancer Institute, FPO-IRCCS, Torino; [9]IRCCS Humanitas Clinical and Research Center, Milano; [10]ASST Cremona, Cremona; [11]IRCCS Regina Elena National Cancer Institute, Roma; [12]University of Brescia at ASST Spedali Civili, Brescia; [13]Vito Fazzi Hospital, Lecce; [14]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [15]University of Naples Federico II, Napoli; [16]ASST Fatebenefratelli Sacco - PO Luigi Sacco, Milano; [17]IRCCS Centro di Riferimento Oncologico di Aviano (CRO), Aviano*

Background: The mTORC1 inhibitor everolimus (EVE) in combination with the aromatase inhibitor exemestane (EXE) is a standard-of-care treatment option for patients (pts) with

hormone receptor-positive (HR+), human epidermal growth factor receptor-negative (HER2-) advanced breast cancer (aBC). However, EVE-induced hyperglycemia and hyperin-sulinemia could reduce EVE-EXE efficacy through the reactivation of the PI3K/AKT/mTORC1 pathway. Material (patients) and methods: We conducted a retrospective, multicenter, Italian study to investigate the association between glycemia, as evaluated at baseline and during the first 3 months (mos) of EVE-EXE therapy, on progression-free survival (PFS) of HR+ HER2- aBC pts. To exclude variables not associated with clinical outcomes, we used a machine-learning approach through a Random Forest method. Then, we fitted a Cox proportional hazard model to investigate the independent impact of the selected variables on PFS.

Results: Out of 848 pts evaluated, 35 and 4 pts were excluded because of the lack of sufficient information about blood glucose levels and clinical outcomes, respectively. Of 809 pts finally included in the study, all pts had previously received letrozole/anastrozole in the adjuvant or advanced disease setting, while 54% of them had been treated with anti-estrogens (i.e. fulvestrant and/or tamoxifen) in the advanced disease setting. With a median follow-up of 37.4 mos, median PFS and OS were 7.13 and 32.1 mos, respectively. During the first three mos of therapy, EVE-EXE induced a significant increase of blood glucose concentration ($p < 0.0001$). At multivariable analysis, baseline and on-treatment glycemia were independently associated with PFS, with a significant interaction of these two variables on clinical outcome ($p < 0.0001$). In particular, pts with low baseline glycemia (<95 mg/dl, 50th quantile) who experienced on-treatment diabetes ($>=126$ mg/dl, 90th quantile) had significantly lower PFS (mPFS: 4.14 mos) when compared to both pts who were hyperglycemic ($>=95$ mg/dl) at baseline but did not develop diabetes (mPFS: 8.15 mos), and to pts who showed stably low or stably high glycemia (mPFS: 7.13 mos) ($p=0.0002$).

Conclusions: EVE-induced diabetes is associated with lower antitumor efficacy of EVE-EXE in HR+ HER2- aBC pts with normal baseline glycemia. While these data need prospective validation, experimental dietary or pharmacological strategies that prevent or reverse EVE-induced diabetes could improve the efficacy of EVE-EXE.

E02*

SURVIVAL ANALYSIS OF THE PROSPECTIVE RANDOMIZED CHER-LOB STUDY EVALUATING THE DUAL ANTI-HER2 TREATMENT WITH TRASTUZUMAB AND LAPATINIB PLUS CHEMOTHERAPY AS NEOADJUVANT THERAPY FOR HER2-POSITIVE BREAST CANCER

Guarneri V.[1], Dieci M.V.[1], Bisagni G.[2], Generali D.G.[3], Cagossi K.[4], Sarti S.[5], Frassoldati A.[6], Gianni L.[7], Cavanna L.[8], Pinotti G.[9], Musolino A.[10], Piacentini F.[11], Michelotti A.[12], Cinieri S.[13], Griguolo G.[1], Miglietta F.[14], De Salvo G.L.[15], Conte P.[1]*

[1]Università di Padova - Istituto Oncologico Veneto IOV-IRCCS, Padova; [2]Azienda USL-IRCCS, Reggio Emilia; [3]University of Trieste - ASST Cremona, Cremona; [4]Ospedale Ramazzini, Carpi; [5]IRST, Meldola; [6]S Anna University Hospital, Ferrara; [7]Azienda USL Romagna, Rimini; [8]G. da Saliceto Hospital, Piacenza; [9]ASST Sette Laghi, Varese; [10]University Hospital, Parma; [11]University Hospital, Modena; [12]Azienda Ospedaliera Universitaria Pisana, Pisa; [13]Antonio Perrino Hospital, Brindisi; [14]Università di Padova, Padova; [15]Istituto Oncologico Veneto IOV-IRCCS, Padova*

Background: The CHER-LOB randomized phase II study showed that the combination of lapatinib and trastuzumab plus chemotherapy increases the pathologic complete response (pCR) rate compared with chemotherapy plus either trastuzumab or lapatinib. Here we report the results of survival analysis according to treatment arm and pCR.

Methods: The CherLOB study randomized 121 HER2-positive, stage II-IIIA breast cancer patients to anthracyclines/taxane-based chemotherapy plus trastuzumab, lapatinib, or both. Patients received adjuvant trastuzumab for up to 1 year. The primary end point of the study was met, with a relative increase of 80% in the pCR rate achieved with chemotherapy plus trastuzumab and lapatinib compared with chemotherapy plus either trastuzumab or lapatinib (Guarneri, J Clin Oncol 2012). Relapse-free survival (RFS) was calculated from randomization to breast cancer recurrence (locoregional or distant) or death from any cause, whichever first. Overall survival (OS) was calculated from randomization to death from any cause.

Results: At a median follow up of 8.8 years, RFS rates at 5 years were: 85.8% in the trastuzumab + lapatinib arm, 77.8% in the trastuzumab arm, 78.1% in the lapatinib arm (log-rank p=0.160). Patients treated with dual HER2 blockade (trastuzumab + lapatinib arm) experienced numerically better RFS as compared to patients treated with single HER2 blockade (trastuzumab arm and lapatinib arm combined): 5-yr RFS 85.8% vs 78.0%, log-rank p=0.087; HR=0.51, 95% CI 0.23-1.12, p=0.093. The achievement of pCR was a strong prognostic factor. 5-yr RFS rate was 97.3% for pCR patients vs 72.9% for non-pCR patients (log-rank $p < 0.001$, HR=0.12, 95% CI 0.03-0.49, p=0.003); similar significant results were observed in both the estrogen receptor-negative and estrogen-receptor positive subgroups. OS was also improved in pCR patients: 8-yr OS rates were 97.2% vs 80.0% (log-rank p=0.028, HR=0.14, 95% CI 0.02-1.08, p=0.060).

Conclusions: In the Cher-LOB study, there was a not statistically significant signal for a better RFS for patients who received dual HER2 blockade with trastuzumab and lapatinib plus neoadjuvant chemotherapy experienced improved RFS as compared to patients treated with single anti-HER2 agent (trastuzumab or lapatinib) plus chemotherapy. Patients achieving a pCR had longer RFS and OS as compared to non-pCR patients.

E03*

RESISTANCE TO CDK4/6 INHIBITORS (CDK4/6I): THE CLINICAL USEFULNESS OF LIQUID BIOPSY IN METASTATIC BREAST CANCER (MBC)

Raimondi L.[1], Gozzi E.[2], Bitca V.[2], Pietranera M.[2], Rossi L.[2], Spinelli G.P.[2]

[1]*Università La Sapienza, Roma;* [2]*Università La Sapienza, Aprilia*

Background: Despite therapeutic improvements, most patients (pts) acquire resistance to CDK4/6i. KRAS tumor mutations have been associated with worse PFS in several tumor types but have not been analysed extensively in breast cancer in the era of Palbociclib and Fulvestrant (P+F). In this study, using liquid biopsy, we evaluated the opportunity to reveal the onset of resistance to P+F, detecting *KRAS*-mutated ctDNA and CDK4/9 expression in HR+/HER2-MBC treated with P+F as first metastatic line.

Methods: We assessed 106 consecutive pts with HR+/HER2-MBC treated with P+F as first-line metastatic therapy, with sensitivity to previous endocrine therapy (Dec17-Mar20). Using Bio-Rad QX200 ddPCR system and exoRNeasy kit we determined *KRAS* ctDNA levels and CDK4/9 expression in plasma, respectively.

Results: A total of 948 blood samples were collected. In 54%(57 pts)we observed *KRAS*-mutated ctDNA before starting P+F: the detection was associated with lower LMr and significantly correlated with the onset of resistance to P+F within 6months from the evidence of *KRAS* mutation and worse PFS ($p<0.001$). At 18-month follow up[1-NA], pts with baseline *KRAS*-mutated ctDNA, low CDK4 levels and overexpression of CDK9 had a median PFS of 3 months [1-6months,95%CI 0.8-3.6]contrary to ones with *KRAS* wild-type whose PFS has not yet been reached (*p<0.001*). Correlating the results of liquid biopsy both to tumoral burden and pts clinical features, we observed a higher *KRAS*-mutated circulating copies-number in those patients with two or more metastatic sites (*p<0.001*) and with lower lymphocyte-monocyte ratio (*p=0.003*).

Conclusions: Despite the study's limitations,our data suggest the appearance of *KRAS* mutations leads to P+F resistance acquisition within 6months and provide critical information for the prediction of therapeutic responses in MBC. Monitoring *KRAS* status with liquid biopsy, we could predict who will take advantage from P+F, decreasing wastes of resources ensuring the best pts' quality of life.

E04*

MOVING FROM THE CLEOPATRA STUDY TO REAL LIFE: FINAL RESULTS FROM THE G.O.N.O. SUPER TRIAL

Garrone O.[1], Giarratano T.[2], D'Onofrio L.[3], Michelotti A.[4], Blondeaux E.[5], Saggia C.[6], Merlini L.[7], Cazzaniga M.E.[8], Donadio M.[9], Farnesi A.[10], Montemurro F.[11], La Verde N.M.[12], Coltelli L.[13], Vandone A.M.[1], Collovà E.[14], Blasi L.[15], Ardito R.[16], De Conciliis E.[17], Airoldi M.[9], Merlano M.C.[1]

[1]*Azienda Ospedaliera S. Croce e Carle Ospedale di Insegnamento, Cuneo;* [2]*Istituto Oncologico Veneto IRCCS, Padova;* [3]*Campus Biomedico, Roma;* [4]*Azienda Ospedaliera Universitaria, Pisa;* [5]*IRCCS Ospedale Policlinco San Martino, Genova;* [6]*Azienda Ospedaliera Universitaria Maggiore della Carità, Novara;* [7]*Ospedale San Bortolo, Vicenza;* [8]*Ospedale San Gerardo, Monza;* [9]*Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Torino;* [10]*Azienda USL Toscana Nordovest, Livorno;* [11]*Candiolo Cancer Center FPO-IRCCS, Candiolo (TO);* [12]*ASST Fatebenefratelli Sacco, Milano;* [13]*Ospedale Lotti, Pontedera;* [14]*ASST Ovest Milanese, Legnano;* [15]*ARNAS Civico, Palermo;* [16]*IRCCS CROB, Rionero in Vulture (PZ);* [17]*Ospedale Cardinal Massaia, Asti*

Background: The association of Trastuzumab (T) and Pertuzumab (P) plus taxane is the standard first line therapy for HER2 positive (HER2+) metastatic breast cancer (MBC) patients (pts). Results from CLEOPATRA have underlined a significant advantage both in PFS and OS in pts treated with T+P and docetaxel (D) over T and D. With the aim to describe the applicability of CLEOPATRA results in real world pts, we performed a multicenter, retrospective-prospective, observational study, in HER-2+ MBC pts.

Material and Methods: We analyzed the outcome of all HER-2+ MBC pts treated with P+T and taxanes as first line therapy since the availability of P in Italy, at 18 general and university hospitals.

Results: Up to March 2019, 347 pts were recorded. 5 were excluded due to incomplete data. Overall data on 342 pts are evaluated. Main pts characteristics were: median (m) age 55 y (19-80), m ECOG PS 0 (0-2). 170 pts (49.7%) had metastatic disease at presentation. HR+ 230 pts (67%); 96/172 pts (56%)received neo/adjuvant chemotherapy (CT) + T and 119/129 HR+ pts (92%) received adjuvant endocrine therapy. Visceral involvement was present in 216 pts (63%). Most common metastatic sites:bone 185 pts (54%), liver 138 pts (40%), lung 108 pts (38%), soft tissues 244 pts (71%); 14 pts (4%) had CNS involvement. 205 pts (60%) and 136 pts (40%) received D and paclitaxel (Pa) respectively. 1 pt received vinorelbine. M number of CT cycles was 6 for both drugs (D range 1-14; Pa range 1-24). 144 pts (42%) are on maintenance, 177 pts (52%) received ET concomitantly with P+T maintenance. ORR is 77% (CR and PR in 79 and 184 pts respectively), PD in 22 pts. With 198 events recorded (58%), M PFS is 26.9 months (95% CI 20 – 33.8). In 96 pts previously exposed to adjuvant T, with 66 events (68%), m PFS is 20.7 months (95% CI 15.6 - 25.8). Any grade leucopenia and neutropenia were recorded in 24% and 26% of pts respectively; febrile neutropenia in 11 pts. 30 pts (8.8%) developed cardiac toxicity leading to discontinuation of P+T maintenance in 14 pts. Any grade non-hematological toxicities: diarrhea 162 pts (47%), asthenia 212 pts (62%), peripheral neuropathy 133 pts (39%).

Conclusions: Our results support the activity and safety of the combination of CT (D or Pa) plus P and T in real world HER2+ MBC pts. The advantage is also evident in pts

previously exposed to adjuvant T. No new concerns about toxicity. Final results on OS will be presented.

E05*

IDENTIFICATION OF PROGNOSTIC AND PREDICTIVE PHARMACOGENOMIC BIOMARKERS BY DMET PLATFORM: A RETROSPECTIVE MULTICENTRIC STUDY IN ADVANCED BREAST CANCER PATIENTS TREATED WITH CDK4/6 INHIBITORS

Cucè M.[1], Staropoli N.[2], Arbitrio M.[3], Labanca C.[4], Scionti F.[4], Ciliberto D.[4], Strangio A.[4], Tafuni M.[4], Romeo C.[4], Barbieri V.[4], Renne M.[5], Correale P.[6], Tassone P.[7], Tagliaferri P.[8]

[1]Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro; [2]Medical Oncology Unit, Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro; [3]CNR-Institute for Biomedical Research and Innovation, 88100 Catanzaro, Italy, Catanzaro; [4]Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy;, Catanzaro; [5]Surgery Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy, Catanzaro; [6]Medical Oncology Unit, "Bianchi-Melacrino-Morelli" Grand Metropolitan Hospital, Reggio di Calabria, Italy, Reggio Calabria; [7]Translational Medical Oncology Unit, Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy, Catanzaro; [8]Medical Oncology Unit, Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy, Catanzaro

Background: The CDK 4/6 inhibitors (CDK4/6i) produced a clear improvement in the hormone receptor positive (HR+) and HER2-negative metastatic breast cancer (MBC) therapeutic scenario, with a significant benefit both in term of progression free survival (PFS) and overall survival (OS). Despite the efficacy results, intrinsic or acquired resistance to CDK4/6i represent a limiting factor for the success of these treatments. Mechanisms underlying resistance are multifactorial and patient's genetic make-up may play a role in interindividual variability. We performed a case-control retrospective study in MBC patients to identify potential predictive and prognostic pharmacogenomics biomarkers related to the CDK4/6i response to treatment by the microarray-based DMET platform which allows genotyping of 1936 single nucleotide polymorphisms (SNPs) in ADME genes (Absorption, Distribution, Metabolism, Excretion).

Patients and Methods: Patients with HR+, HER2-negative MBC, treated with CDK4/6i and with age ≥ 18 years old were eligible with written informed consent. Between December 2017-November 2019, we enrolled 41 matched patients in two groups: responders to therapy (case) and resistant to therapy (control) if disease progression occurred within 6 months. Moreover, we evaluated the correlation among the main clinical-laboratory parameters with (PFS) and response to treatment. Samples from peripheral blood were collected and analyzed by DMET platform. Genotyping profiles of each patient were calculated by the DMET Console® software and genotype frequencies between cases and controls were evaluated by DMET-Analyzer tool by two-tailed Fisher exact test. Power of Genetic Analysis system was used to investigate the association of identified SNPs and PFS.

Results: Two SNPs in CYP2B6 (rs8192709, p=0.0475) and UGT2B4 gene (rs1966151, p=0.0023) showed a statistically significant association with response, despite the small sample size. Moreover, a SNP in ABCB1 (rs2235015, p=0.0261) results associated to treatment-induced neutropenia.

Conclusions: Our results demonstrated association between the SNPs here reported and response to treatment. The pharmacokinetic pathways in which a drug is involved are very complex and the presence of specific polymorphisms in ADME genes can produce changes in drug activity and/or toxicity and can provide valuable biomarkers for clinical practice. Follow up validation studies must be extended to a larger sample.

E06

ASSOCIATION BETWEEN THE NEUTROPHIL-TO-LYMPHOCYTE AND PLATELET-TO-LYMPHOCYTE RATIOS AND EFFICACY OF CDK 4/6 INHIBITORS IN ADVANCED BREAST CANCER: THE OBSERVATIONAL MULTICENTER ITALIAN PALMARES STUDY

Zattarin E.[1], Zattarin E.[1], Fabbroni C.[1], Ligorio F.[1], Marra A.[2], Corti C.[2], Bernocchi O.[3], Sirico M.[4], Generali D.[4], Curigliano G.[2], Bianchi G.[1], Capri G.[1], Rivoltini L.[5], De Braud F.[1], Vernieri C.[1]

[1]Istituto Nazionale dei Tumori, Milano; [2]Istituto Europeo di Oncologia, Milano; [3]Department of Medical, Surgery and Health Sciences, Università di Trieste, Trieste; [4]Azienda Socio Sanitaria Territoriale di Cremona, Cremona; [5]Unit of Immunotherapy of Human Tumors, Fondazione IRCCS Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano

Background: According to preclinical evidence, Cyclin-Dependent Kinase 4/6 inhibitors (CDK 4/6i) stimulate anti-tumor immunity as part of their antineoplastic activity. The neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR) reflect systemic inflammation and immune system functional status. We aimed at investigating their association with CDK 4/6i efficacy in patients (pts) with hormone receptor-positive advanced breast cancer (HR+ aBC).

Patients and Methods: A retrospective, observational, multicenter Italian study was conducted to investigate the association between NLR or PLR, as measured at baseline and after the first 3 treatment cycles, and progression free survival (PFS) in HR+ HER2- aBC pts treated with CDK 4/6i plus endocrine therapies (ETs). The thresholds for

NLR and PLR were defined through the maximally selected rank statistics. The impact of these parameters on PFS was evaluated at univariate and multivariable analysis by using Cox proportional hazard model.

Results: 308 pts were treated with palbociclib (n=256), ribociclib (n=39) or abemaciclib (n=13) plus ETs. Of them, 168 (54.5%) pts received CDK 4/6i as first-line, 88 (28.6%) as second-line, and 52 (16.9%) as third- or subsequent line of treatment for advanced disease between January 2017 and March 2020. With a median follow-up of 16.8 months (95% CI, 15.1-18.2), median PFS in the whole pt population was 17.1 months (95% CI, 14.6-25.0). At multivariable analysis, we found an independent association between high NLR or PLR and lower PFS, both when these parameters were evaluated at baseline (aHR 1.57, 95% CI 1.07-2.29, p=0.02 and aHR 1.97, 95% CI 1.29-3.02, p=0.002, respectively) and after 3 treatment cycles (aHR 2.73, 95% CI 1.37-2.295.46, p=0.005 and aHR 2.13, 95% CI 1.21-3.77, p=0.009, respectively). Previous treatment with taxanes and the presence of liver metastases were independently associated with worse PFS, as well.

Conclusions: High baseline or on-treatment NLR or PLR values were significantly associated with lower PFS in HR+ HER2- aBC pts. Although our results need prospective validation, they suggest that NLR and PLR could be used as precocious biomarkers of treatment efficacy.

E07

MONARCH 3: UPDATED TIME TO CHEMOTHERAPY AND DISEASE PROGRESSION FOLLOWING ABEMACICLIB PLUS AROMATASE INHIBITOR (AI) IN HR+, HER2- ADVANCED BREAST CANCER (ABC)

Martin M.[1], Johnston S.[2], Huober J.[3], Di Leo A.[4], Sohn J.[5], Andre V.A.[6], Martin H.R.[7], Hardebeck M.C.[7], Goetz M.P.[8], Biganzoli L.P.[9]

[1]Instituto De Investigacion Sanitaria Gregorio Marañon, Ciberonc, Geicam; Universidad Complutense, Madrid; [2]Breast Unit, The Royal Marsden NHS Foundation Trust, London; [3]University of Ulm, Ulm; [4]Department of Oncology, Hospital of Prato, Istituto Toscano Tumori, Prato; [5]Yonsei Cancer Center, Seoul; [6]Eli Lilly and Company, Paris; [7]Eli Lilly and Company, Indianapolis; [8]Department of Oncology, Mayo Clinic, Rochester; [9]Dipartimento di Oncologia Medica, Ospedale S. Stefano, Via Suor Niccolina Infermiera, Prato

Background: MONARCH 3, a randomized, double-blind, phase 3 trial of abemaciclib+AI (anastrozole/letrozole) conferred significant clinical benefit in HR+, HER2- ABC. We report data from additional 12-month (mo) follow-up including analysis for clinically prognostic subgroups.

Patients and methods: From 31 Oct 2018 data cutoff, exploratory intermediate efficacy parameters including time to subsequent chemotherapy ([TCT] time from randomization to 1st chemotherapy [CT]) and time to 2nd disease progression ([PFS2] time from randomization to discontinuation date of 1st post-discontinuation treatment [PDT] or start date of 2nd PDT or death) were assessed. TCT and PFS2 were analyzed by Kaplan-Meier method in intent to treat (ITT) and subgroups previously identified as significantly prognostic.

Results: Updated PFS in ITT population: 28.2 vs 14.8 mo (HR[95%CI]: .525[.415, .665]; p<.0001) in abemaciclib vs placebo arms respectively. More patients discontinued study in placebo vs abemaciclib arm thereby starting PDT. Systemic PDT: 178 (54%; abemaciclib) and 123 (74.5%; placebo) arm, of which 93(28.4%) and 82 (49.7%) received CT respectively. Abemaciclib+AI deferred initiation of CT in ITT (HR[95%CI] .513[.380, .691]; p<.0001) and subgroups (Table). PFS2 was prolonged for abemaciclib (HR .637[95%CI] .495, .819; p<.0004). Consistent with ITT population, PFS2 favored abemaciclib in all subgroups of prognostic factors (Table).

Conclusions: Abemaciclib+AI prolonged PFS2 and TCT in ITT and prognostic subgroups. Previously presented at ESMO2019, FPN326P Martin M et al. Reused with permission.

	TCT			PFS2		
	Abemaciclib+AI Events/N	Placebo+AI Events/N	HR (95%CI)	Abemaciclib+AI Events/N	Placebo+AI Events/N	HR (95%CI)
ITT						
	93/328	82/165	.513 (.380, .691)	152/328	106/165	.637 (.495, .819)
ECOG PS						
1	34/136	36/61	.342 (.214, .548)	64/136	45/61	.504 (.344, .74)
0	59/192	46/104	.639 (.435, .940)	88/192	61/104	.762 (.549, 1.059)
Bone-only disease						
Yes	13/69	16/40	.440 (.211, .914)	21/69	23/40	.523 (.289, .945)
No	80/259	66/125	.495 (.357, .686)	131/259	83/125	.66 (.501, .871)

	TCT			PFS2		
	Abemaciclib+AI Events/N	Placebo+AI Events/N	HR (95%CI)	Abemaciclib+AI Events/N	Placebo+AI Events/N	HR (95%CI)
Liver metastases						
Yes	21/47	21/31	.572 (.313, 1.048)	32/47	25/31	.677 (.401, 1.142)
No	72/281	61/134	.504 (.358, .709)	120/281	81/134	.663 (.5, .881)
Progesterone receptor status						
+ve	66/255	57/128	.529 (.371, .753)	115/255	78/128	.694 (.52, .927)
-ve	25/70	24/36	.414 (.236, .725)	35/70	27/36	.537 (.325, .889)
Tumor grade						
High	22/65	21/32	.369 (.203, .672)	27/65	23/32	.418 (.24, .73)
Intermediate/Low	52/179	48/96	.512 (.345, .757)	86/179	63/96	.671 (.484, .931)
Treatment-free interval						
<36 mo	15/44	18/32	.465 (.234, .924)	21/44	24/32	.506 (.281, .91)
≥36 mo	32/95	18/41	.798 (.448, 1.422)	48/95	24/41	.895 (.548, 1.461)

E08

CYCLIN-DEPENDENT KINASES 4/6 INHIBITORS (CDKI) TREATMENT IN GOOD-PROGNOSIS PATIENTS (PTS) WITH METASTATIC HORMONE RECEPTOR (HR)-POSITIVE HER2-NEGATIVE BREAST CANCER

Bertoli E.[1], Debora B.[2], Gerratana L.[3], Pelizzari G.[4], Franceschin G.[5], Corvaja C.[6], Palmero L.[6], Zara D.[6], Alberti M.[2], Mazzeo R.[2], Da Ros L.[3], Cinausero M.[7], Bonotto M.[7], Mansutti M.[7], Spazzapan S.[3], Minisini A.M.[7], Puglisi F.[8], Fasola G.[7]

[1]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy. Department of Oncology, ASUFC University Hospital of Udine, 33100 Udine, Italy, Udine; [2]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy., Aviano; [3]Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, 33081 Aviano, Italy, Aviano; [4]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy, Aviano; [5]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy, Udine; [6]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy. Udine; [7]Department of Oncology, ASUFC University Hospital of Udine, 33100 Udine, Italy, Udine; [8]Department of Medicine (DAME), University of Udine, 33100 Udine, Italy. Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, 33081 Aviano, Italy, Aviano*

Background: Current treatment option in metastatic HR-positive/HER2-negative breast cancer (luminal MBC) is based on endocrine therapy (ET) combined with CDKi. However, few real-world evidence explore whether pts with good prognosis might benefit from ET alone.

Methods: This multicentric, retrospective study investigated 717 consecutive luminal MBC pts treated between Jan 2008 and Jan 2020 at the Cancer Centre of Aviano and the Oncology Department of Udine, Italy. A multivariate model and ROC analysis (variables: previous ET, visceral metastases, Ki-67>14%, ECOG PS>1, >3sites and =5lesions) was used to define a prognostic score and individuate low-risk pts (score<3). A final cohort of good-prognosis luminal MBC pts was analyzed. A Cox regression model was implemented to evaluate the impact of treatment strategies in terms of progression-free survival (PFS1 and PFS2) and overall survival (OS).

Results: A low-risk score was associated with prolonged median OS (53.6 vs. 20.7 months (m), p<0.001). In this group, 85% of pts aged=45, 74% were post-menopausal, 82% had an ECOG PS=0, and 33% were metastatic de novo. Ductal histotype, Ki-67=14%, estrogen receptor (ER)>10% and visceral involvement were recorded in 70%, 55%, 82% and 42% of pts, respectively. Notably, 59% of pts were chemotherapy (CT) naïve, 58% ET pre-treated and 41% ET resistant. The 1°line therapy was ET (48%), ET-CDKi combined (22%) and CT (29%). After a median follow-up of 73 m, median PFS1 was 17 m and median OS was 55 m. Median PFS1 was 15, 17 and 25 m for CT, ET and ET-CDKi, respectively (p=0.0007). Median OS was 41, 48 m and not reached (but numerically higher) for CT, ET and ET-CDKi, respectively (p=0.13). Intriguingly, OS was significantly higher for pts treated with ET-CDKi followed by ET (p<0.001). Noteworthy, the advantage of CDKi addition was consistent among all subgroups analyzed.

Conclusions: Along with subgroup analysis of prospective trial, this real-world study showed that CDKi combined with ET represents the mainstay of 1°line treatment

in all subgroup of low-risk luminal MBC pts. Moreover, ET after ET-CDKi represents a viable option. However, prospective randomized trials are needed to investigate optimal sequence strategy.

Table 1. First-line therapy – PFS1 (p<0.001).

Treatment	HR	p	95%CI
ET vs. ET-CDKi	1.74	0.001	1.28-2.42
CT vs. ET-CDKi	1.89	<0.001	1.35-2.67

Table 2. First-line therapy – OS (p= 0.133).

Treatment	HR	p	95%CI
ET vs. ET-CDKi	1.23	0.486	0.68-2.22
CT vs. ET-CDKi	1.51	0.169	0.83-2.75

E09

SARCOPENIC OBESITY PHENOTYPE IS ASSOCIATED WITH VERTEBRAL FRACTURE PREVALENCE IN WOMEN WITH EARLY BREAST CANCER UNDERGOING ADJUVANT AROMATASE INHIBITOR THERAPY

Monteverdi S.[1], Pedersini R.[1], Gallo F.[2], Maffezzoni F.[3], Dalla Volta A.[1], Di Mauro P.[1], Turla A.[1], Vassalli L.[1], Ardine M.[1], Formenti A.M.[4], Simoncini E.L.[1], Giustina A.[4], Maroldi R.[3], Amoroso V.[1], Berruti A.[1]

[1]Università degli studi di Brescia, ASST-Spedali Civili di Brescia, Oncologia Medica, Brescia; [2]Università di Genova, Section of Biostatistics, Department of Health Sciences, Genova; [3]Università degli studi di Brescia, ASST-Spedali Civili di Brescia, Radiologia, Brescia; [4]Università San Raffaele Vita e Salute, Ospedale San Raffaele, Endocrinologia, Milano

Background Aromatase inhibitors (AIs) are widely used as adjuvant therapy in postmenopausal women with endocrine-sensitive early breast cancer (BC). AIs induce bone mineral density (BMD) loss and increased fracture risk. Our group previously showed that high fat body mass (FBM), as measured by dual-energy X-ray absorptiometry (DXA), is an independent factor associated with a higher proportion of morphometric vertebral fractures (VFs) in BC patients undergoing AI therapy. In the present study, we explored the role of lean body mass (LBM) as well as the interaction of LBM with FBM in predicting the occurrence of VFs in BC patients who were either AI-naïve or AI-treated in the adjuvant setting.

Patients and methods Six hundred eighty-four early BC patients were selected to take part to this cross-sectional study. This initial number was restricted to 480 women, 240 AI-naïve and 240 AI-treated, after propensity score adjustment, applied to control for potential confounders. Each patient underwent a DXA scan at baseline, assessing

BMD, FBM, and LBM. VFs were assessed independently by two of the authors using a quantitative morphometric analysis of DXA images. We used logistic regression analyses to explore the associations between baseline characteristics and the VF prevalence and the interaction between LBM, FBM and AI therapy on the VF prevalence.

Results The proportion of VFs was significantly higher in AI-treated than in AI-naïve patients, 26% and 16% respectively (OR, 1.90; 95% CI, 1.29 to 2.78; p=0.0196). No association was found between BMD and VFs in AI-treated patients. LBM alone was not associated with bone fragility fractures. Conversely, in patients having a sarcopenic obesity phenotype (FBM > and LBM < the median value), we observed 4.8 times increased chance of having a prevalent VF in AI-treated (prevalence, 48%;OR, 4.81; 95% CI, 1.82 to 13.21) as compared with AI-naïve women (prevalence, 16%). The highest proportion of VFs in the AI-naïve population was observed in the subgroup with both LBM and FBM < the median value (prevalence, 27%).

Conclusions: These data favour the notion that bone fragility in women under AI therapy has different pathophysiology than postmenopausal osteoporosis. Our data suggest that the assessment of the body composition parameters LBM and FBM using DXA may add valuable information when analyzing fracture risk in early BC patients undergoing AI therapy. This observation is new and deserves further investigation.

E10

FIRST- AND SECOND-LINE TREATMENT STRATEGIES FOR HORMONE-RECEPTOR (HR)-POSITIVE HER2-NEGATIVE METASTATIC BREAST CANCER: THE PLBC STUDY

Basile D.[1], Gerratana L.[2], Pelizzari G.[2], Franceschin G.[2], Buriolla S.[2], Corvaja C.[2], Bertoli E.[2], Palmero L.[2], Zara D.[2], Alberti M.[2], Da Ros L.[3], Mansutti M.[4], Spazzapan S.[3], Bolzonello S.[3], Bonotto M.[4], Minisini A.M.[4], Cinausero M.[4], Fasola G.[4]

[1]Università degli Studi di Udine, Dipartimento di Area Medica; Dipartimento di Oncologia Medica a Prevenzione Oncologica, CRO, IRCCS, Aviano, Udine; [2]Dipartimento di Area Medica, Università degli Studi di Udine, Udine; [3]Dipartimento di Oncologia Medica e Prevenzione Oncologica, Centro di Riferimento Oncologico, IRCCS, Aviano, Udine; [4]Dipartimento di Oncologia Medica, Azienda Sanitaria Universitaria Friuli Centrale di Udine, Udine

Background: Endocrine therapy (ET) plus cyclin-dependent kinases 4/6 inhibitors (CDK4/6i) represents the standard treatment for HR-positive HER2-negative metastatic breast cancer (MBC). However, prospective head-to-head comparisons are still lacking for many 1° line (L) options, and it is still crucial to define the best treatment strategy for both 1° and 2°L. This study aims to describe real-world treatment outcomes for luminal MBC.

Materials and methods: This study evaluated 717 consecutive luminal MBC pts treated from 2008 to 2020 at the Cancer Centre of Aviano and the Oncology Department of Udine, Italy. Differences in terms of overall survival (OS), progression-free survival (PFS1 and PFS2), and post-progression survival (PPS) were tested by log-rank test and represented by Kaplan-Meier survival curves. The attrition rate (AR) between 1° and 2°L was calculated. A Cox regression model was implemented to identify prognostic factors.

Results: At 1°L, pts were treated with ET (49%), chemotherapy (CT) (32%) and ET-CDKi (19%), while 33% received ET, 33% CT and 9% ET-CDKi at 2°L. AR was 10% for the whole cohort, 7% for CT, 8% for ET and 17% for ET-CDKi. By multivariate analysis, including potential confounders, 1°L ET-CDK4/6i showed a better median PFS1 and OS (Table 1). Moreover, 2°L ET-CDK4/6i improved median PFS2 compared to ET and CT. Notably, 1°L ET-CDKi resulted in higher median PFS than 2°L use (22 months vs 12). Intriguingly, 1°L ET-CDK4/6i is associated with worse median PPS compared to CT and ET. Secondarily, treatment strategies were analysed: 1°L ET-CDK4/6i followed by CT had worse OS compared to 1°L ET-CDK4/6i followed by ET (Table 1). Notably, none of baseline characteristics at 2°L, including fast-progressive disease, influenced 2°L treatment choice (ET vs. CT) after ET-CDKi.

Conclusions: Our real-world data demonstrated that ET-CDKi represents the best option for 1°L luminal MBC compared to ET and CT. Also, the present study pointed out that 2°L ET, potentially combined with other targeted molecules, could be a feasible option after CDK4/6i failure, postponing CT on later lines.

Table 1. Survival Outcomes.

	PFS		OS	
	HR; 95% CI; P	Median (mo)	HR; 95% CI; P	Median (mo)
1°L				
ET-CDKi	1	22	1	Not reached (NR)
ET vs ET-CDKi	1.93; 1.37-2.73; <0.001	14	1.40; 0.86-2.28; 0.17	27
CT vs ET-CDKi	1.93; 1.35-2.74; <0.001	12	1.25; 0.75-2.03; 0.40	49
2°L				
ET-CDKi	1	12		
ET vs ET-CDKi	1.72; 1.17-2.51; 0.005	7		
CT vs ET-CDKi	1.86; 1.28-2.72; 0.001	6		
2°L after CDKi				
ET			1	NR
CT			5.04;1.12-22.7; 0.035	20

E11

POPULATION-BASED TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER IN A COHORT OF 1,346 PATIENTS FROM SOUTHERN ITALY (SICILY): CAN HISTORICAL BACKGROUND AFFECT GENETICS?

Fanale D.[1], Incorvaia L.[2], Bono M.[1], Calò V.[1], Cancelliere D.[1], Fiorino A.[1], Barraco N.[1], Brando C.[1], Perez A.[1], Corsini L.R.[1], Madonia G.[1], Ricciardi M.R.[1], Cucinella A.[1], Lisanti M.C.[1], Filorizzo C.[1], Maria Tomasello L.M.[1], Gristina V.[1], Cusenza S.[1], Bazan V.[2], Russo A.[1]

[1]Department of Surgical, Oncological and Oral Sciences, Section of Medical Oncology, University of Palermo, Palermo; [2]Section of Medical Oncology, Department of Biomedicine, Neuroscience and Advanced Diagnostics (Bi.N.D.), University of Palermo, Palermo

Background: Recent advances in detection of germline pathogenic variants (PVs) in BRCA1/2 genes allowed a deeper understanding of the BRCA-related cancer risk. Several studies showed a significant heterogeneity in the prevalence of PVs across different populations. The development of new population-based genetic approaches may help to detect the 50% more BRCA-carriers than those identified by conventional clinical and familial criteria, as already shown in other studies. Because little is known about this in Sicilian population, our study was aimed at investigating the prevalence and geographic distribution of inherited BRCA1/2 PVs in families from this specific geographical area of Southern Italy.

Patients and methods: We retrospectively collected and analyzed all clinical information of 1,346 hereditary breast and/or ovarian cancer patients genetically tested for germline BRCA1/2 PVs by Next-Generation Sequencing analysis at University Hospital Policlinico "P. Giaccone" of Palermo from January 1999 to October 2019.

Results: 102 BRCA-positive subjects carried a BRCA1 PV, 96 harboured a BRCA2 PV, and 2 showed simultaneous presence of PVs in both genes. The BRCA1-5083del19 founder variant is resulted to be the most widespread PV in the Sicilian population, together with other two PVs named BRCA2-1466delT and BRCA1-633delC. Interestingly, several

founder variants present in several European populations were observed also in some Sicilian families. Globally, thirty PVs were more frequently observed in the Sicilian population, but only some of these showed a specific territorial prevalence, unlike other Italian and European regions. This difference could be attributed to the genetic heterogeneity of the Sicilian people and its historical background due to the crucial geographical location of Sicily in the centre of Mediterranean Sea, crossroads of several cultures. Therefore, hereditary breast and ovarian cancers in Sicily could be predominantly due to BRCA1/2 PVs different from those usually detected in other geographical areas of Italy and Europe.

Conclusions: Our investigation led us to hypothesize that a higher prevalence of some germline BRCA PVs in Sicily could be a population-specific genetic signature. Population-based genetic approaches, in the future, could help to increase the BRCA carrier detection rates and maximize prevention strategies.

E12

VALUE OF GENOMIC TEST (ONCOTYPE DX®) IN ELDERLY PATIENTS: AN ITALIAN SURVEY

Barni S.[1], De Placido S.[2], Masetti R.[3], Naso G.[4], Santini D.[5], Tondini C.A.[6], Cognetti F.[7]

[1]ASST Bergamo Ovest, Treviglio; [2]Policlinico Federico II, Napoli; [3]Policlinico A. Gemelli, Roma; [4]Policlinico Umberto I - Università La Sapienza, Roma; [5]Policlinico S. Orsola-Malpighi, Bologna; [6]ASST-PG23, Bergamo; [7]Istituto Nazionale Tumori Regina Elena, Roma

Background: The PONDx national decision impact study, initiated in 2016, collected data on real-life use of the Oncotype DX® assay in current clinical practice for 1788 Italian patients and results were consistent with other international decision impact studies showing changes in treatment decisions for more than 50% of cases with a significant change of recommendations from adjuvant chemo-endocrine therapy to endocrine therapy only.

Material and methods: Data from 230 patients aged > 70 were collected and analyzed to assess how the genomic test was used in this subset of patients to guide treatment decisions.

Patients characteristics (N=230):

Patients Characteristics	N	%
Nodal status		
N0	172	75%
N+	58	25%
Tumour grade		
G1	28	12%
G2	123	53%
G3	79	34%

(Continued)

Patients Characteristics	N	%
Ki67		
<10%	19	8%
10-20%	87	38%
21-30%	72	30%
> 30%	52	23%
RS group		
0-17	132	57%
18-30	73	32%
>30	25	11%

Results: This subgroup of patients > 70 years of age presented relatively higher clinical risk based on clinical and pathological features yet a significant proportion had lower Recurrence Score results suggesting, based on the landmark TAILORx study, they would not benefit from chemotherapy. A reduction of chemotherapy recommendation based on the RS results was observed for 32 women (14%) who were initially recommended chemotherapy. This represent a relative reduction in chemotherapy use of 38%. This study was conducted prior to the publication of the TAILORx results, a simulation using the TAILORx cut off would estimate a larger reduction in chemotherapy of 62%. Recommendations for chemo-endocrine therapy or endocrine therapy before and after knowledge of RS results:

Treatment	Pre-test	Post-test
Chemo+Endocrine therapy	84	52
Endocrine therapy	140	173
Others	6	5

Conclusions: In this Italian real-life setting, the Oncotype DX test provides critical information that changed and supports final treatment decisions also in elderly breast cancer patients clinically identified as higher clinical risk according to traditional tumor grade and high Ki67 levels. 38% of the women who would have been treated with chemotherapy were able to spare it. This is particularly relevant in this subset of patients for whom chemotherapy is most likely to produce acute and late toxicity.

E13

SAFETY AND EFFICACY OF ABEMACICLIB PLUS ENDOCRINE THERAPY (ET) IN ELDERLY PATIENTS WITH HORMONE RECEPTOR-POSITIVE/HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-NEGATIVE (HR+, HER2-) ADVANCED BREAST CANCER: AN AGE-SPECIFIC SUBGROUP ANALYSIS OF MONARCH 2 AND 3 TRIALS

Goetz M.[1], Okera M.[2], Wildiers H.[3], Campone M.[4], Grischke E.[5], Manso L.[6], Andre V.A.M.[7], Lee Chong A.[8], San Antonio B.[9], Toi M.[10], Sledge Jr G.[11], Biganzoli L.P.[12]

[1]Department of Oncology, Mayo Clinic, Rochester; [2]Adelaide Cancer Center, Adelaide; [3]Department of General Medical Oncology, University Hospitals Leuven, Leuven; [4]Institut de Cancerologie de l'Ouest-René Gauducheau, Saint Herblain; [5]Women's Hospital, University Hospital Tübingen, Tübingen; [6]12 de Octubre University Hospital, Madrid; [7]Eli Lilly and Company, Paris; [8]Eli Lilly Canada Inc, Toronto; [9]Eli Lilly and Company, Madrid; [10]Department of Breast Surgery, Kyoto University Hospital, Kyoto; [11]Stanford University School of Medicine, Stanford; [12]Dipartimento di Oncologia Medica, Ospedale S. Stefano, Via Suor Niccolina Infermiera, Prato

Background: Abemaciclib demonstrated clinically meaningful PFS improvement in combination with endocrine therapy (ET) in HR+, HER2- advanced breast cancer patients (pts) in MONARCH 2 and 3. Here we report exploratory subgroup analyses to provide age-specific outcomes.

Material (patients) and methods: In MONARCH 2, pts progressing while on prior ET received abemaciclib/ placebo+fulvestrant; in MONARCH 3, postmenopausal women (no prior systemic therapy for recurrent/metastatic breast cancer) received abemaciclib/placebo+ letrozole/ anastrozole. Exploratory outcome analyses were performed for <65, 65-74 and ≥75 years age groups. Using pooled safety data, we performed age-specific subgroup analyses of the most common TEAEs associated with either ET or ET+abemaciclib. To assess the impact of age on efficacy, a subgroup analysis of PFS was performed by Cox model for each trial independently.

Results: Pooled safety data were available for 1152 pts, including 59.7% pts <65 years, 28.7% pts between 65-74 years, and 11.5% pts ≥75 years. Of those, 768 women received abemaciclib+ET and 384 received placebo+ET. Most frequent TEAE was diarrhea and most common Grade≥3 TEAE was neutropenia. Clinically relevant diarrhea (Grade2/3) was higher in abemaciclib-treated elderly pts (<65, 39.5%; 65-74, 45.2%; ≥75, 55.4%); however, in the ≥75 group, diarrhea (Grade2/3) incidence was also higher for placebo+ET (<65, 6.8%; 65-74, 4.5%; ≥75, 16%). Nausea and decreased appetite were moderately higher (by 10-20%) in the 2 abemaciclib-treated elderly subgroups. Fatigue (any grade) was higher in the 2 abemaciclib-treated elderly subgroups (<65, 34.8%; 65-74, 48.4%; ≥75, 51.8%); no differences were found across the 3 placebo subgroups. The rates of Grade3/4 neutropenia did not differ as a function of age for either abemaciclib+ET (<65, 25.8%; 65-74, 27.4%; ≥75, 18.1%) or placebo+ET. For efficacy, consistent PFS benefit was observed with abemaciclib+ET vs placebo+ET across all three subgroups in both studies (MONARCH 2 HR [95%CI]: <65, .52 [.40, .68]; 65-74, .63 [.43, .94]; ≥75, .62 [.34, 1.11]; p=.695 and MONARCH 3 HR [95%CI]: <65, .48 [.35, .67]; 65-74, .64 [.40, 1.02]; ≥75, .54 [.26, 1.13]; p=.634).

Conclusions: Abemaciclib+ET demonstrates tolerable safety profile and consistent efficacy benefit across all

age subgroups, supporting use of this combination in elderly pts.

E14

HIGH BODY MASS INDEX (BMI) IS ASSOCIATED WITH WORSE OUTCOME IN PATIENTS WITH HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 (HER2)–POSITIVE EARLY BREAST CANCER TREATED WITH ADJUVANT TRASTUZUMAB

Ligorio F.[1], Zambelli L.[2], Bottiglieri A.[2], Castagnoli L.[2], Zattarin E.[2], Lobefaro R.[2], Belfiore A.[2], Vingiani A.[2], Pruneri G.[2], Bianchi G.[2], Capri G.[2], Pupa S.[2], De Braud F.[2], Vernieri C.[2]

[1]Istituto Nazionale dei Tumori, Milano; [2]Istituto Nazionale dei Tumori di Milano - Fondazione IRCCS, Milano

Background: Besides the established role of Body Mass Index (BMI) as a risk factor for developing different types of tumors, including breast cancer (BC), there is increasing evidence of a positive association between adiposity and worse BC outcomes. However, the impact of excess weight on the prognosis of specific BC subtypes is still undefined.

Material (patients) and methods: We conducted a retrospective analysis to evaluate the impact of BMI on relapse-free survival (RFS) and overall survival (OS) in patients with early-stage HER2-positive (HER2+) BC treated with adjuvant trastuzumab-containing chemotherapy in our Institution between January 2008 and September 2018. We subsequently validated our results in a population of patients with HER2+ BC receiving trastuzumab in the neoadjuvant setting. Maximally selected rank statistics were used to estimate the best BMI and glycemia cut-points dividing our population according to the risk of recurrence.

Results: Among 505 patients included in the study, 390 (77.2%) had a low (<27.77 kg/m2) BMI, while 115 (22.7%) had a high (=27.77 kg/m2) BMI. Both high BMI and hyperglycemia were found to be associated with worse RFS and OS at univariate analysis; however, only high BMI was an independent predictor of worse RFS (HR 2.26; 95% CI: 1.08 - 4.74, p=0.031) and OS (HR 2.25; 95% CI: 1.03-4.94, p=0.043) at multivariable analysis. A subgroup analysis showed that BMI effect on patient prognosis was mainly driven by the HR-negative subtype. Finally, in a validation cohort of 132 BC patients treated with neoadjuvant trastuzumab we observed a trend towards better progression free survival (PFS) in low vs high BMI group (p=0.056, log rank test).

Conclusions: This is the first study to show the negative impact of high BMI on both RFS and OS in HER2+ early BC patients treated with adjuvant trastuzumab in

the real-life setting. Further studies are needed to investigate the biologic mechanisms underlying these findings.

E15

CLINICAL AND BIOCHEMICAL FEATURES OF RAPIDLY PROGRESSIVE DISEASE DURING FIRST-LINE THERAPY IN HORMONE RECEPTOR (HR) POSITIVE HER2 NEGATIVE METASTATIC BREAST CANCER

Corvaja C.[1], Basile D.[2], Bertoli E.[2], Franceschin G.[3], Pelizzari G.[3], Gerratana L.[2], Zara D.[1], Palmero L.[1], Alberti M.[2], Bonotto M.[4], Da Ros L.[5], Cinausero M.[6], Minisini A.M.[6], Spazzapan S.[5], Mansutti M.[6], Fasola G.[6], Puglisi F.[2]

[1]Dipartimento di Area Medica (DAME), Università degli studi di Udine; Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy, Udine; [2]Dipartimento di Area Medica (DAME), Università degli studi di Udine; IRCCS, Centro di Riferimento Oncologico (CRO), Aviano, Italy, Udine; [3]Dipartimento di Area Medica (DAME), Università degli studi di Udine, Udine; [4] Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy, Udine; [5]IRCCS, Centro di Riferimento Oncologico (CRO), Aviano, Italy, Udine; [6]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy, Udine

Background: Recent breakthroughs in anti-cancer therapy have consistently improved prognosis in luminal metastatic breast cancer (LMBC) patients (pts). However, a subset of pts develops more aggressive and rapidly progressive diseases. Aim of this study was to evaluate the impact of clinico-patological features on fast progression during first-line therapy.

Material and methods: We retrospectively analyzed a consecutive cohort of 717 LMBC pts treated from 2008 to 2019 at the Oncology Departments of Udine and Aviano Cancer Centre, Italy. The association between baseline clinico-pathological features and rapidly progressive disease, defined as progression within the first six months of treatment, was assessed by uni- and multivariate logistic regression.

Results: Overall, 41% pts were aged>65 and 78% were post-menopausal. ECOG PS was >1 in 15% pts, and Ki-67=14% was detected in 60%. Almost 29% had de novo LMBC. Visceral involvement was detected in 49% whereas 30% had bone-only disease. Interestingly, 23% pts had ≥3 metastatic sites and >5 metastatic lesions. Only 38% pts were ET naïve whereas 56% were CT naïve. First-line therapy included ET alone or combined with CDK4/6 in 49% and 20% pts, respectively, and CT in 31% pts. By univariate analysis on the overall cohort, age (45-65: OR 2.49, 95%CI 1.29-4.83 p=0.007; >65: OR 2.40, 95%CI 1.23-4.66 p=0.010), ECOG PS>1 (OR 2.36, 95%CI 1.50-3.72, p<0.001), visceral crisis (OR 8.68, 95%CI 1.73-43.53 p=0.009), MLR>0.28 (OR 2.08,

95%CI 1.24-3.49 p=0.006), LDH >480UI (OR 1.88, 95%CI 0.99-3.58, p=0.054), menopause status (OR 2.10, 95%CI 1.21-2.97 p=0.009), prior ET (OR 2.21, 95%CI 1.46-3.33 p<0.001) and visceral involvement (OR 1.89, 95%CI 1.21-2.97 p=0.005) were associated with fast progression. By multivariate analysis, ECOG PS>1 (OR 4.94, 95%CI 1.56-15.69 p=0.007), prior ET (OR 3.39, 95%CI 1.32-8.68 p=0.011) and high baseline LDH levels (OR 2.93, 95%CI 1.28-6.74 p=0.011) were independently associated with fast progression. No differences were observed according to treatment type (ET vs ET-CDKi: OR 0.95, 95%CI 0.54-1.68 p=0.879; CT vs ET-CDKi: OR 0.95, 95%CI 0.52-1.72 p=0.869)

Conclusions: In our analysis, ECOG PS>1, prior ET and high LDH levels represent the baseline features determining rapidly progressive diseases in LMBC. Although the retrospective nature, our results might support further trials specifically designed to evaluate tailored disease monitoring, targeted treatments and new biomarkers as ctDNA.

E16

MUTATION AGNOSTIC CTDNA-BASED WORKFLOW FOR EARLY RESPONSE EVALUATION IN HR POSITIVE, HER2 NEGATIVE METASTATIC BREAST CANCER: A PROOF OF CONCEPT PROSPECTIVE STUDY

Bortot L.[1], Corvaja C.[2], Franzoni A.[3], Allegri L.[4], Basile D.[5], Viotto D.[6], Bertoli E.[5], Buriolla S.[5], Targato G.[2], Da Ros L.[7], Russo S.[8], Di Nardo P.[7], Alberti M.[5], Mazzeo R.[5], Bonotto M.[8], Belletti B.[9], Gerratana L.[10], Baldassarre G.[9], Damante G.[3], Puglisi F.[5]

[1]Dipartimento di Area Medica (DAME) Università degli studi di Udine; Dipartimento di Oncologia Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy, Udine; [2]Dipartimento di Area Medica (DAME), Università degli studi di Udine; Dipartimento di Oncologia Azienda Sanitaria Universitaria Friuli Centrale, Udine (Italia), Udine; [3]Istituto di Genetica Medica, Azienda Sanitaria Universitaria Friuli Centrale, Udine (Italia), Udine; [4]Dipartimento di Area Medica (DAME), Università degli studi di Udine;, Udine; [5]Dipartimento di Area Medica (DAME), Università degli studi di Udine; IRCCS CRO Centro di Riferimento Oncologico Aviano, Udine; [6]Unità di Oncologia Molecolare, IRCCS CRO Centro di Riferimento Oncologico Aviano, Aviano; [7]IRCCS CRO Centro di Riferimento Oncologico Aviano, Aviano; [8]Dipartimento di Oncologia Azienda Sanitaria Universitaria Friuli Centrale, Udine (Italia), Udine; [9]Unità di Oncologia Molecolare, IRCCS CRO Centro di Riferimento Oncologico Aviano, Udine; [10]IRCCS CRO Centro di Riferimento Oncologico Aviano; Udine

Background: Endocrine therapy (ET) is the treatment of choice for HR positive, HER2 negative Metastatic Breast Cancer (Luminal MBC) but there is a paucity of markers apt to characterize early disease dynamics. The aim of the study was to proof the concept of a mutation-agnostic workflow based on circulating tumor DNA (ctDNA) for early response monitoring.

Methods: A multicenter cohort of 49 women with Luminal MBC was prospectively enrolled and characterized for

ctDNA through droplet digital PCR (ddPCR). ctDNA% was defined as the proportion of the different lengths of ACTB DNA fragments: 136 bp (ACTB_short) more likely to be related to ctDNA over 420 bp and 2000 bp (ACTB_medium and ACTB_long) the genomic portion mainly derived from cytolysis. The overall DNA yield was measured through Qubit. Blood samples were collected before treatment start (BL) and after 3 months concomitantly with CT scan restaging (E1). Matched pairs variations were tested through Wilcoxon test, the prognostic impact of ctDNA% and DNA yield was tested in terms of PFS though uni-and multivariate Cox regression analyses.

Results: The main treatment regimen was ET+CDK4/6 inhibitors (92%), only 6% of pts received ET as a single agent. While DNA yield categorized at the 75th percentile failed to show a prognostic impact, pts with a ctDNA% >75th percentile were burdened by a significantly worse outcome (Median PFS: 7.8 months, P=0.0290). When compared with E1, a significant decrease in ACTB_short (71% P=0.0162), ACTB_medium (66% P=0.0011) and ACTB_long (78% P=0.0001) was observed. As expected, a significant drop in neutrophils count was also observed during treatment with CDK4/6 inhibitors (decrease in 94% of cases P<0.0001). The prognostic impact of a drop higher than 10% was then investigated for the different fragments of ACTB in terms of PFS. While a significant impact was observed for ACTB_short (HR: 5.98, 95%CI1.61 - 22.24, P = 0.008), no significance was observed for ACTB_medium and ACTB_long (respectively HR: 3.08, 95%CI 0.8 - 10.79, P=0.079 and HR: 2.27, 95%CI 0.47 - 10.92, P=0.305). The prognostic impact of ACTB_short was also retained after correction for ACTB_medium and ACTB_long in multivariate analysis (HR: 4.88, 95%CI 1.07 -22.17, P=0.040).

Conclusions: The study proofed the concept of a feasible mutation-agnostic workflow for a more granular disease monitoring and prognostication in MBC. Although prospectively generated, these results need to be confirmed on a larger population.

E17

DEVELOPMENT OF A CLINICO-PATHOLOGICAL NOMOGRAM FOR PREDICTING PATHOLOGICAL COMPLETE RESPONSE (PCR) IN LUMINAL BREAST CANCER (LBC) PATIENTS (PTS) UNDERGOING NEOADJUVANT CHEMOTHERAPY (NACT)

Garufi G.[1], Carbognin L.[1], Orlandi A.[1], Paris I.[1], Palazzo A.[1], Fiorio E.[2], Miglietta F.[3], Dieci M.V.[3], Pasqualoni M.[1], Pannunzio S.[1], Cannizzaro M.C.[1], Pontolillo L.[1], Cutigni C.[1], Indellicati G.[1], Sperduti I.[4], Milella M.[2], Scambia G.[1], Tortora G.[1], Bria E.[1]

[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma; [2]Azienda Ospedaliera Universitaria Integrata, Verona; [3]Istituto Oncologico Veneto IRCCS, Padova; [4]Regina Elena National Cancer Institute IRCCS, Roma

Background: Given the low chance of response to NACT in locally advanced LBC pts, the identification of predictive clinico-pathological factors of pCR represents a challenge for daily clinical practice. With this purpose, a multicenter retrospective analysis was performed in order to develop a predictive nomogram for pCR, on the basis of pre-treatment clinico-pathological features.

Methods: Clinical and pathological data of stage I-III LBC pts undergone NACT and surgery at 3 Italian Institutions were collected. Descriptive statistics were adopted. For continuous variables, the Receiver Operating Characteristic (ROC) analysis was applied. A multivariate model was used to identify independent predictors of pCR. The obtained log-Odds Ratios (OR) were adopted to derive weighting factors of the predictive nomogram, aimed to recognize differential risks of pCR. The ROC analysis was also applied to determine the nomogram accuracy.

Results: Data from 446 pts were gathered (median age 49 years [yrs], range 28-79 yrs). Many pts were pre-menopausal (60%) and presented a Luminal-B immunophenotype (74%) and a ductal histology (70%). Overall pCR rate was 12.1%, 95% Confidence Interval (CI) 8.9-14.9% (Luminal-A 5.3%, 95% CI 1.1-13.2% and Luminal-B 14.2%, 95% CI 13.5-23.8%). The optimal Ki67 cut-off obtained from the ROC analysis to predict pCR was 48% (AUC 0.70; SE 0.05). At the multivariate analysis, clinical stage I-II (OR 3.01, 95% CI 1.43-6.33, *p=0.004*), Ki67 >48% (OR 3.59, 95% CI 1.82-7.07, *p<0.0001*) and the progesterone receptor (PgR) <1% (OR 2.97, 95% CI 1.30-6.77, *p=0.01*) independently predicted pCR. According to the resulting nomogram, the probability of pCR ranged from 7.1% for pts with clinical stage III, PgR >1% and Ki67 <48% to 63.8% for pts with a clinical stage I-II, PgR <1% and Ki67 >48%. At the ROC analysis a differential probability of pCR was found among pts with a continuous score >1 and <1 with a predictive accuracy of 77% (AUC 0.77; SE 0.04; *p<0.0001*).

Conclusions: The combination of commonly available clinico-pathological pre-NACT factors allows to develop a nomogram which appears to reliably predict pCR in LBC pts. Given the retrospective nature of the study, an external validation of the nomogram is currently ongoing.

E18

UPDATED SUBGROUP TUMOR RESPONSE OF ABEMACICLIB PLUS AROMATASE INHIBITOR (AI) FOR HORMONE RECEPTOR POSITIVE (HR+), HER2 NEGATIVE ADVANCED BREAST CANCER (MONARCH 3)

O'Shaughnessy J.[1], Johnston S.[2], Martin M.[3], Huober J.[4], Toi M.[5], Andre V.A.M.[6], Martin H.R.[7], Hardebeck M.C.[7], Di Leo A.[8], Goetz M.P.[9], Biganzoli L.P.[10]

[1]Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas; [2]Breast Unit, The Royal Marsden NHS Foundation Trust, London;

[3]Department Servicio de Oncologia Médica, Instituto De Investigacion Sanitaria Gregorio Marañon, Ciberonc, Geicam, Universidad Complutense, Madrid; [4]Comprehensive Cancer Center Ulm, University of Ulm, Ulm; [5]Department of Breast Surgery, Kyoto University Hospital, Kyoto; [6]Eli Lilly and Company, Paris; [7]Eli Lilly and Company, Indianapolis; [8]Sandro Pitigliani Medical Oncology Department, Hospital of Prato, Istituto Toscano Tumori, Prato; [9]Department of Oncology, Mayo Clinic, Rochester; [10]Dipartimento di Oncologia Medica, Ospedale S. Stefano, Via Suor Niccolina Infermiera, Prato

Background: We report data from the additional 12 months of follow-up on tumor response for the intent-to-treat (ITT) MONARCH 3 population and exploratory subgroups previously identified as significantly prognostic.

Patients and methods: In MONARCH 3 (randomized, double-blind, phase III trial), 493 postmenopausal women with HR+, HER2- advanced breast cancer and no prior systemic therapy in advanced setting received an AI (anastrozole/letrozole)+abemaciclib or placebo. From October 31, 2018 cutoff, secondary endpoints including objective response rate ([ORR], complete response [CR]+partial response [PR]), time to response (TTR), and duration of response ([DoR], time from a confirmed CR/PR until disease progression/death) were assessed in ITT population and exploratory subgroups previously reported as significantly prognostic.

Results: In patients with measurable disease, ORR was 62.5% (95%CI: 56.7, 68.2) for abemaciclib+AI and 44.7% (95%CI: 36.2, 53.2) for placebo+AI (p≤.001). Additional follow-up confirmed that all prognostic subgroups benefitted from addition of abemaciclib to AI (consistent with ITT population), as evidenced by change in ORR (abemaciclib+AI minus placebo+AI; largest effects observed in patients with liver metastases [37.45%], progesterone receptor-negative tumors [33.07%], high-grade tumors [29.13%], or treatment-free interval of <36 months [32.11%]). Median TTR was 3.62 and 3.65 months for abemaciclib+AI and placebo+AI, respectively (generally consistent across subgroups). Responses were more durable for abemaciclib+AI (median DoR:32.71 months; 95%CI:25.74,-) versus placebo+AI arm (median DoR:17.49 months; 95%CI:11.61,22.19), including in poor prognostic subgroups.

Conclusions: Extended follow-up in MONARCH 3 confirmed that addition of abemaciclib to AI shows durable tumor responses, including those in patients with clinically poor prognostic characteristics. Reused with permission 2019 SABCS®.

E19

MONARCHE: A PHASE 3 STUDY OF STANDARD ADJUVANT ENDOCRINE THERAPY WITH OR WITHOUT ABEMACICLIB IN PATIENTS WITH HIGH RISK, NODE POSITIVE, HORMONE-RECEPTOR POSITIVE (HR+), HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-NEGATIVE (HER2-) EARLY-STAGE BREAST CANCER

Rastogi P.[1], Toi M.[2], Martin M.[3], O'Shaughnessy J.[4], Headley D.[5], Wei J.[5], Cox J.[6], Harbeck N.[7], Johnston S.[8], Moscetti L.P.[9]

[1]University of Pittsburgh Medical Center, Pittsburgh; [2]Kyoto University, Kyoto; [3]Instituto De Investigacion Sanitaria Gregorio Marañon, Ciberonc, Geicam; Universidad Complutense, Madrid; [4]Texas Oncology, Baylor Charles A. Sammons Cancer Center, Dallas; [5]Eli Lilly and Company, Indianapolis; [6]Eli Lilly and Company, Windlesham; [7]Breast Center, University of Munich (LMU), Munich; [8]The Royal Marsden NHS Foundation Trust, London; [9]Dipartimento di Oncologia Medica, Azienda Ospedaliero-Universitaria, Modena

Background: Abemaciclib improved efficacy in patients with HR+, HER2- advanced breast cancer as monotherapy (MONARCH 1) and in combination with endocrine therapy (ET) in MONARCH 2 and 3. Neoadjuvant abemaciclib+anastrozole (ANZ) (neoMONARCH) given for 2 weeks significantly reduced Ki67 expression relative to ANZ alone. Endocrine monotherapy is the current standard of care (SOC) in adjuvant setting, although there is risk of relapse in patients with high-risk disease, identified by clinicopathological characteristics of disease. Primary objective: evaluate invasive disease-free survival (IDFS) per STEEP System. Secondary objectives include IDFS in patients with central Ki67 index ≥20%, distant relapse-free survival, overall survival (OS), safety, pharmacokinetics and health outcomes.

Patients and methods: monarchE (multicenter, randomized, open-label phase 3 trial) evaluates adjuvant abemaciclib in node-positive, high-risk, HR+, HER2- early advanced breast cancer. Patients are randomized 1:1 to abemaciclib 150mg twice daily+SOC adjuvant ET vs SOC adjuvant ET alone and stratified by prior chemotherapy (neoadjuvant, adjuvant or none), menopausal status (pre/postmenopausal) and region (North America/Europe, Asia or Other). The investigation arm receives abemaciclib for up to 2 years or until discontinuation criteria are met. All patients receive ET for 5 years/as clinically indicated. Patients are followed for 10 years/until study completion, whichever comes first. Final evaluation for OS will mark study completion.

Eligibility criteria: Early stage resected HR+, HER2- invasive advanced breast cancer with either ≥4 pathological positive axillary lymph nodes (pALNs) or 1 to 3 pathological pALNs with at least one of the following high-risk factors: primary invasive tumor size ≥5cm, histological grade 3 tumor or central Ki67 index ≥20%. Patients must have completed definitive locoregional therapy (+/- [neo]adjuvant chemotherapy). Before randomization, patients may receive up to 12 weeks of ET after completing their last non-ET and must be randomized within 16 months of the definitive surgery. Assuming an IDFS hazard ratio of .73, the study is powered to ~85% to test the superiority of abemaciclib+standard ET at 1-sided α=.025 using a stratified log-rank test.

Results and Conclusions: This study is being conducted in ~600 centers in 38 countries to enroll ~4580 patients. Accrual began in July 2017. Recruitment is complete. Reused with permission 2019 SABCS®.

E20

TRIPLE NEGATIVE BREAST CANCER: TIL'S QUALITATIVE STUDY AND PROGNOSTIC IMPLICATIONS

Della Mora A.[1], Santinelli A.[2], Pistelli M.[3], Crocetti S.[3], Tassone L.[3], Bastianelli L.[3], Merloni F.[3], Cantini L.[3], Scortichini L.[3], Agostinelli V.[3], Savini A.[3], Maccaroni E.[3], Berardi R.[3]

[1]*UO Oncologia di Macerata, Area Vasta 3, Macerata;* [2]*AO- Ospedali Riuniti Marche Nord, Pesaro;* [3]*Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, AOU Ospedali Riuniti, Ancona*

Background: Triple negative breast cancers (TNBC) represent 15-20% of all breast cancer, but determine up today a high number of death because of their aggressive behaviour, with a high growth rate and the frequent late diagnosis. Due to the lack of target for specific therapies, in the last years, immune system and its interaction with breast cancer gained importance, in particular the role of tumoral immunitary infiltrate (TIL) and its cellular components, given the advent of immunotherapy.

Material and Methods: In this retrospective study, we enrolled 148 female patients affected by infiltrating triple negative breast cancer treated at Azienda Ospedaliero-Universitaria Ospedali Riuniti of Ancona from 2003 to 2016. We attested the presence of TIL in E&E stained histological pieces with a cut-off of positivity of 5% and we searched the possible correlation between TIL, the clinical-pathological features and prognosis (in terms of disease free survival-DFS- and overall survival -OS). Then in TIL positive pieces we analysed the components of TIL itself, using immuno-histochemical staining for CD8 (cytotoxic T lymphocytes), CD4 (helper T lymphocytes), FOXP3 (regulatory T lymphocytes) and CD56 (Natural Killer cells), in order to assess the possible correlations between the single components and the clinical-pathological features and the prognosis.

Results: At the chi-square analysis, stromal TIL correlates with high histological grade, ductal histology and the presence of peritumoral follicles. The TIL has a positive impact on the prognosis (p=0.0001), in particular when it is more than 50% (p=0.0087) and/or when it is organized in peritumoral follicles (p=0,0071). Moreover, tumor size, age, pausal status and lymphovascular invasion are prognostic in terms of DFS and OS. From the qualitative analysis of TIL emerges that FOXP3 expression in the lymphocytic infiltrate is statistically significant for disease free survival (p=0.0492) and overall survival (p=0.0390), while there are no association with other TIL components.

Conclusions: Our study confirm that the immune system plays a role in regulating tumour growth and can be used as prognostic parameter, in particular evaluating stromal TIL and the presence of FOXP3 in the lymphocytic infiltrate. These data have a not negligible importance given the upcoming insert of immunotherapy in clinical practice in various setting of treatment of TNBC and are worthy of further studies.

E21

PROGNOSIS AND RESPONSE TO NEOADJUVANT CHEMOTHERAPY ACCORDING TO HER2 EXPRESSION IN EARLY BREAST CANCER: A RETROSPECTIVE SINGLE INSTITUTION ANALYSIS

D'Onofrio R.[1], Omarini C.[1], Barbolini M.[1], Nasso C.[1], Isca C.[1], Dominici M.[1], Piacentini F.[1]

[1]*University Hospital of Modena, Modena*

Background: The assessment of HER2 status plays a key role in the treatment decision making process of early breast cancer (BC).HER2 status is routinely assessed by immunohistochemistry and/or in situ hybridization (ISH), according to ASCO/CAP 2018 guidelines. The dichotomous definition of HER2+ versus HER2- disease does not reflect the spectrum of variable levels of HER2 protein expression. We have analyzed the clinical outcomes of a cohort of BC patients treated with neoadjuvant chemotherapy (NACT) according to HER2 score.

Patients and methods: We performed a retrospective analysis of 483 women with early BC treated with NACT from March 2002 to November 2018 at Modena Cancer Center. Clinical and pathological characteristics of patients and disease were collected and compared to HER2 score by Pearson's chi square test. The impact of HER2 status on pathological complete response (pCR) was set according to logistic regression model.

Results: According to HER2 score, patients were divided in 5 groups: 79 (16,3%) of them in HER2 score0 group, 153 (31,7%) in HER2 score1+, 53 (11%) HER2 score2+/ISH-, 43 (9%) score2+/ISH+ and 155 (32%) score3+. Of note, 59% of women had hormone receptor positive BC. Overall, the HER2 status significant correlated to histotype (p=0,003), grading (p=0,026) and pCR (p=0,0001). The pCR was achieved in 132 (27%) patients: 46 (9,5%) in HER2 score0/1+ group, 9 (1,9%) in HER2 score2+/ISH-, 8 (1,7%) in HER2 score2+/ISH+ and 69 (14,3%) in HER2 score3+. The pCR rate was not statistically different when both HER2 score0/1+ and HER2 score2+/ISH- groups were compared to HER2 score2+/ISH+ one. Considering HER2+ BCs, the pCR rate was significantly higher in HER2 score3+ compared to HER2 score2+/ISH+ (p=0,002). No statistically significant differences in terms of RFS and OS inter-subgroups were observed.

Conclusions: The HER2 protein expression levels better correlated to pCR compare to HER2 gene amplification. In particular, the lack of difference in pCR rate between

HER2 score2+/ISH+ and HER2 score2+/ISH– groups may suggests a paradigm shift in the current classification of HER2 status, consistently with emerging data on "HER2 low" BC landscape.

E22

CIRCULATING TUMOR DNA-BASED LONGITUDINAL EVALUATION OF ESR1 EPIGENETIC STATUS IN HORMONE RECEPTOR POSITIVE HER2 NEGATIVE METASTATIC BREAST CANCER

Gerratana L.[1], Basile D.[2], Franzoni A.[3], Allegri L.[4], Viotto D.[5], Corvaja C.[6], Bortot L.[6], Bertoli E.[2], Buriolla S.[2], Targato G.[6], Da Ros L.[1], Russo S.[7], Di Nardo P.[1], Alberti M.[2], Mazzeo R.[2], Bonotto M.[7], Belletti B.[5], Baldassarre G.[5], Damante G.[3], Puglisi F.[8]

[1]Dipartimento di Oncologia Medica, Centro di Riferimento Oncologico di Aviano IRCCS, Aviano; [2]Dipartimento di Area Medica, Università degli Studi di Udine - Dipartimento di Oncologia Medica, Centro di Riferimento Oncologico di Aviano IRCCS, Udine; [3]Istituto di Genetica Medica, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [4]Dipartimento di Area Medica, Università degli Studi di Udine, Udine; [5]SOC Oncologia Molecolare e Modelli Preclinici di Progressione Tumorale, Centro di Riferimento Oncologico di Aviano IRCCS, Aviano; [6]Dipartimento di Area Medica, Università degli Studi di Udine - Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [7]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [8]Dipartimento di Area Medica, Università degli Studi di Udine - Dipartimento di Oncologia Medica, Centro di Riferimento Oncologico di Aviano IRCCS, Aviano

Background: Although endocrine therapy (ET) is the mainstay of treatment for Hormone Receptor positive HER2 negative Metastatic Breast Cancer (Luminal MBC), secondary resistances ultimately emerge mainly due to gene alterations. Epigenetic-mediated events are less known and potentially involved in alternative adaptive mechanisms. The aim of this study was to test the feasibility of *ESR1* epigenetic characterization through circulating tumor DNA (ctDNA) and its potential application for early sensitivity assessment.

Methods: The multicenter pragmatic study prospectively enrolled 49 women with Luminal MBC. Patients (pts) where characterized through ctDNA using Next Generation Sequencing and methylation specific droplet digital PCR (MSddPCR) before treatment start (BL) and after 3 months concomitantly with CT scan restaging (E1). *ESR1* epigenetic status was defined by assessing the methylation of its main promoters (prom A and B). Associations were tested through Mann–Whitney U test, matched pairs variations through Wilcoxon test and survival was analyzed by Cox regression.

Results: The ET backbone was mainly based on aromatase inhibitors (71%) in association with CDK4/6 inhibitors (94%). Bone metastases were the most represented (65%), *ESR1* and *PIK3CA* were mutated (mut) in 7 (14%) and 11 (23%) pts respectively. Notably, both genes were mut in 1 patient. The median methylation for promA was 38.5%

(inter quartile rage, IQR 33 – 43) and 33% (IQR 21.8 – 46) for promB, with no significant differences in the overall population (P = 0.1127). Significantly lower promA at baseline was observed in pts with liver metastases (P=0.0212) and in pts with *ESR1* mut (median 41, IQR 33 – 46; median 25, IQR 18.5 – 34.5 respectively in *ESR1* wild-type and mut; P = 0.0091). No significant impact on PFS was observed for promA and promB dichotomized at the median, while a ≥200% increase in promB or in either promA or B at E1 resulted in a significantly worse prognosis (respectively HR 4.42, P = 0.010 and HR 3.61, P = 0.017). A significant increase at E1 was observed for promB among pts with *PIK3CA* mut (P = 0.0173). A trend was observed for promB in *ESR1* wild-type pts and for promA in the *ESR1* mut subgroup.

Conclusions: The study proofed the concept of an epigenetic characterization based on ctDNA apt to be integrated in the current clinical workflow to give useful insights on early treatment sensitivity. Although exploratory, these results support the emerging new strategy of dynamic epigenetic profiling.

E23

TISSUE IMMUNE PROFILE CAN PREDICT RESPONSE TO NEOADJUVANT THERAPY IN TNBC

Scagnoli S.[1], Cerbelli B.[2], Mezi S.[2], Pisegna S.[2], De Luca A.[2], Amabile M.[2], Roberto M.[3], Strigari L.[4], Fortunato L.[5], Costarelli L.[5], Della Rocca C.[2], Marchetti P.[2], D'Amati G.[2], Botticelli A.[2]

[1]Università di Roma "Sapienza", Roma; [2]Università di Roma "Sapienza" - Policlinico Umberto I, Roma; [3]Università di Roma "Sapienza" - Policlinico Sant'Andrea, Roma; [4]Università di Bologna - Policlinico Sant'Orsola Malpighi di Bologna, Bologna; [5]Azienda Ospedaliera San Giovanni Addolorata, Roma

Background: Pathological complete response (pCR) after neoadjuvant chemotherapy (NACT) can predict better survival outcomes in patients with early triple negative breast cancer (TNBC). However, only about 40% of patients will achieve a pCR. Therefore, the identification of new biomarkers is an urgent need. Tumor infiltrating lymphocyties (TILs), PD-L1 and CD73 are immune-related biomarkers that can be evaluated in cancer cells and tumor microenvironment.. We investigated if the combination of these biomarkers in a Tissue Immune Profile (TIP), can predict pCR better than a single biomarkers.

Methods: TILs, CD73 expression by cancer cells and PD-L1 expression by immune cells have been evaluated on pre-NACT biopsies. TILs ≥ 50% were defined as high-TILs (H-TILs). We defined CD73 low (CD73 ≤40%) and CD73 high (CD73 >40%) using the median value of expression in our population as cut-off. PD-L1 =1% was considered positive. We defined TIP positive (TIP+) as the concomitant presence of TILS≥50%, PD-L1≥1% and

CD73≤40%. A multivariate analysis was performed to consider the effects of variables on the pCR. Akaike information criterion (AIC) and Bayesian information criterion (BIC) were used for model selection. The optimal model is selected based on the minimum AIC and BIC.

Results: We retrospectively analysed 60 biopsies from patients with TNBC who received standard NACT. Pathological complete response was achieved in 23 patients (38%). Seventeen cases (28.3%) had H-TILs and 31 (51.6%) had low-CD73, significantly associated with pCR (p=0.001, p=0.009, respectively). PD-L1= 1% was found in 49 patients (81.7%). No significant difference in pCR has been highlighted between PD-L1 positive and negative patients (p=0.734). Twelve (19.7%) cases could be considered TIP+. The pCR rate was significantly different between TIP+ (91.7%; 11/12 patients) and TIP- (25%; 12/48) patients (p <0.0001). Using a multivariate analysis TIP was confirmed as an independent predictive factor of pCR [OR 49.7 (6.30-392.4)], p<0.0001). Finally, the combined immune-profile is more accurate in predicting pCR (AIC 68.3; BIC 74.5) as compared to single biomarkers.

Conclusions: An association between immune background and response to neoadjuvant chemotherapy has been found and TIP, based on the contemporary expression of PD-L1, TILs and CD73, has been identified as a possible independent predictive biomarker of pCR, highlighting the need to consider an immunological patients' profile rather than single biomarkers.

E24

IMPACT OF BMI ON OUTCOME AND CARDIAC SAFETY IN HER2 POSITIVE BREAST CANCER PATIENTS TREATED WITH ADJUVANT TRASTUZUMAB. RESULTS OF A MONOCENTRIC OBSERVATIONAL STUDY

Molinelli C.[1], Del Mastro L.[2], Giraudi S.[3], Ballestrero A.[4], Carli F.[4], Poggio F.[4], D'Alonzo A.[4], Dellepiane C.[4], Buzzatti G.[4], Blondeaux E.[4], Conte B.[4], Pastorino S.[4], Pirrone C.[4], Favero D.[4], Gallo M.[4], Ruelle T.[4], Lambertini M.[4], Bighin C.[4]

[1]Ospedale Policlinico San Martino, genova; [2]IRCSS Ospedale Policlinico San Martino, Genova; [3]Ospedale San Paolo, Savona; [4]IRCCS Ospedale Policlinico San Martino, Genova

Background: The impact of Body Mass Index (BMI) on receptor positive (HR+) breast cancer (BC) risk of recurrence has been deeply investigated but there are still few data concerning the BMI role in HER2 positive (HER2+) BC patients (pts). The aim of our study is to evaluate the impact of BMI on HER2 positive BC pts treated with adjuvant Trastuzumab in terms of disease-free survival and cardiac toxicity.

Materials and Methods: From 1992 to 2016, 694 consecutive HER2+ BC pts were enrolled in a monocentric observational study. Among these pts we selected 201 pts treated with adjuvant Trastuzumab after surgery of the primary tumor and with available BMI data. Exclusion criteria were neoadjuvant chemotherapy (117 pts), metastatic disease ab initio (26 pts), treatment with adjuvant Pertuzumab or Lapatinib (30 pts), not receiving adjuvant Trastuzumab (92 pts), missing adjuvant therapy data (27 pts) and missing BMI data (201 pts). 5-year disease free survival (5yDFS) rates analyses were performed using Kaplan Meyer method to evaluate differences between the following groups: BMI<25 vs BMI≥25, HR+ BMI<25 vs HR+ BMI≥25, receptor negative (HR-) BMI<25 vs HR- BMI≥25. Moreover, in 151 pts with available cardiac data, we analyzed the number of cardiac events, defined as a left ventricular ejection fraction (LVEF) decline of ≥10% from baseline and/or LVEF<50%, in BMI<25 pts and in BMI≥25 pts, using χ(2) test.

Results: Median age was 56 years (28-85), 72 pts (36%) were premenopausal and 129 pts (64%) were post-menopausal. 123 pts (61%) had BMI<25 and 78 (39%) had BMI≥25. HR were negative in 79 pts (39%) and positive in 122 pts (61%). At a median follow up of 7.2 yrs, there was no difference in 5yDFSbetween BMI<25 pts and BMI≥25 pts (93% vs 94%, p=0.653). 5yDFSwas 95% in HR+ BMI<25 vs 97% HR+ BMI≥25 (p=0.535), 91% in HR- BMI<25 vs 91% HR- BMI≥25 (p=0.730), consistent with overall population result. In 151 pts with available cardiac toxicity data we identified 15 cardiac events (15%) in BMI<25 group and 10 cardiac events in BMI≥25 group (19%) (p=0.522).

Conclusions: Our retrospective analysis did not show a significant impact of BMI on 5yDFS or cardiotoxicity in early HER2+ BC pts treated with adjuvant Trastuzumab.

E25

AN ITALIAN REAL WORD EXPERIENCE ABOUT MODALITY OF DETECTION OF RECURRENT BREAST CANCER

Palmero L.[1], Zara D.[1], Targato G.[1], Giavarra M.[1], Basile D.[2], Vitale M.G.[1], Bertoli E.[2], Bortot L.[1], Noto C.[1], Poletto E.[3], Pascoletti G.[3], Andreetta C.[3], Russo S.[3], Mansutti M.[3], Bonotto M.[3], Fasola G.[3], Puglisi F.[2], Minisini A.M.[3]

[1]Dipartimento di Area Medica (DAME) - University of Udine; Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy, Udine; [2]Dipartimento di Area Medica (DAME) - University of Udine; Dipartimento di Oncologia Medica, IRCCS, Centro di Riferimento Oncologico di Aviano (CRO), Aviano, Italy, Udine; [3]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine, Italy, Udine

Background: There is a lively debate in the oncologic community about the role of follow-up and its impact on the clinical outcome in recurrent breast cancer (rBC). In this study we report the modalities of detection of inoperable rBC. Material (patients) and methods: 169 pts with rBC diagnosis from January 2012 to December 2016 at the

Department of Oncology of Udine, were retrospectively analyzed. Pts with de novo advanced BC were not included. We described baseline features at the diagnosis of early BC (eBC) and modalities of detection of rBC.

Results: At diagnosis of eBC the most common immunophenotype was Luminal HER2-neg subgroup (63%), followed by triple negative (TN) subgroup (17%) and HER2-pos subgroup (15%) and the main disease characteristics were pT1 (46%), N+ (57%), Ki-67≥14% (60%). The median time to recurrence was 66.6 months. At the diagnosis of rBC, 54% of pts presented with visceral metastases and 2% with visceral crisis. 53% of pts had ECOG PS 0. Of note, 25% of pts had a previous loco-regional recurrence treated with radical resection. Overall, almost half of the pts was symptomatic (46%); among this pts, 40% reported pain, 21% thoracic symptoms, 19% had locoregional symptoms/signs of relapse, 12% neurological symptoms and 8% constitutional symptoms. 47%, 34% and 7% of rBCs in asymptomatic pts were detected by radiological exams, serum markers and other changes in blood test, respectively. Of note, the majority of rBC were detected by oncologist (43%), followed by other specialists (33%) and general practitioner (14%). 30% of rBC diagnosis were made during a scheduled oncological follow-up visit. Biochemical alterations were mainly evident in ER-pos (OR 4.61, 95%CI 1.01-21.22, p=0.05), while clinical symptoms were detected mainly in Ki-67≥14% pts (OR 2.75, 95%CI 1.01-7.51, p=0.04). The multivariate logistic regression model did not confirm these results. None of analyzed factors were associated with detection through radiological exams.

Conclusions: We report the modality of detection of rBC in a monocentric real word experience. Albeit purely descriptive, our results could be relevant in drawing prospective randomized studies to explore the prognostic impact of surveillance programmes.

E26

LACTATE DEHYDROGENASE AS A PROGNOSTIC BIOMARKER IN PATIENTS WITH HORMONE RECEPTOR-POSITIVE METASTATIC BREAST CANCER TREATED WITH PALBOCICLIB

Pelizzari G.[1], Bertoli E.[1], Basile D.[1], Giavarra M.[1], Gerratana L.[2], Michelotti A.[1], Avoledo D.[3], Da Ros L.[3], Bonotto M.[4], Bolzonello S.[3], Di Nardo P.[3], Fasola G.[4], Mansutti M.[4], Spazzapan S.[3], Minisini A.M.[4], Puglisi F.[2]

[1]*Dipartimento di Area Medica (DAME), Università degli Studi di Udine, Udine, italy, Udine;* [2]*Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Aviano (PN), Italy; Dipartimento di Area Medica (DAME), Università degli Studi di Udine, Udine, italy, Udine;* [3]*Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Aviano (PN), Italy, Aviano (PN);* [4]*Dipartimento di Oncologia di Udine, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy, Udine*

Background: Cyclin-dependent kinases (CDK) 4/6 inhibitors reshaped the therapeutic scenario for hormone receptor (HR)-positive/HER2-negative metastatic breast cancer (MBC). Serum lactate dehydrogenase (LDH) has been correlated with poor prognosis in various malignancies, including MBC. However, no data are available for patients treated with CDK4/6 inhibitors. Henceforth, this study aimed to explore the prognostic impact of elevated plasmatic LDH levels in patients with luminal MBC treated with endocrine therapy (ET) and palbociclib.

Material and Methods: This retrospective study analyzed data of patients with HR-positive/HER2-negative MBC treated consecutively with palbociclib at two Italian cancer centers from 2017 to 2019. A multivariate Cox regression model evaluated the independent prognostic impact of baseline plasmatic LDH levels for both progression-free survival (PFS) and overall survival (OS). Relevant clinico-pathological factors included in the model were: age, progesterone receptor (PgR) status, tumor grade, performance status, treatment line, bone-only or visceral disease, tumor burden, companion ET.

Results: Overall, 202 patients were deemed eligible. Of these patients, 133 (65.8%) received palbociclib plus fulvestrant, 69 (34.2%) palbociclib plus aromatase inhibitors, and 111 (55.0%) were treated first-line. 37.2% of cases were PgR-negative, and 33.2% were grade 3 tumors. Visceral involvement was detected in 46.5% of patients, whereas 34.1% presented with bone-only disease. Of note, 60.9% of patients received a prior chemotherapy, 25.2% in the metastatic setting. After a median follow-up of 15.2 months, the median PFS was 14.1 months (95%CI: 10.97-18.17), and the median OS was not reached. At baseline, 20% of evaluable patients (24/120) had elevated pre-treatment LDH levels according to the local laboratory cut off. Through multivariate analyses, baseline LDH levels emerged as negative independent prognostic factor in terms of both PFS (HR: 2.18, 95%CI: 1.12-4.25, p=0.02) and OS (HR: 4.65, 95%CI: 1.59-13.55, p=0.004). Consistently, high LDH levels correlated with shorter median PFS (9.5 vs. 17.4 months, p=0.01) and median OS (15.3 months vs. not reached, p=0.0004).

Conclusions: Serum LDH levels independently predict PFS and OS in patients with luminal MBC treated with palbociclib. Despite the small sample size and the limited follow-up, this is the first study to confirm the prognostic role of LDH during treatment with CDK4/6 inhibitors.

E27 − The Abstract has been withdrawn at the request of the Authors

E28

PROGNOSTIC FACTORS ASSOCIATED WITH CLINICAL OUTCOMES IN HR+, HER2- ADVANCED BREAST CANCER (ABC): SYSTEMATIC LITERATURE REVIEW

Cuyún Carter G.[1], Stenger K.[1], Mohanty M.[2], Lee Chong A.[1], Basa P.[2], Singuru S.[2], Singh S.[2], Tongbram V.[2], Kümmel S.[3], Guarneri V.[4], Tolaney S.M.[5]

[1]Eli Lilly and Company, Indianapolis; [2]Global Health Technology Assessment, Health Economics, Reimbursement and Outcomes, Access, Commercialisation & Communications, ICON plc., New York; [3]Interdisciplinary Breast Unit, Kliniken Essen-Mitte (KEM), Essen; [4]Division of Medical Oncology 2, Veneto Oncological Institute, University of Padua, Padova; [5]Dana-Farber Cancer Institute, Brookline

Background: This systematic literature review identified strength and consistency of evidence for prognostic factors in HR+, HER2-, ABC patients.

Patients and methods: A search of major electronic databases (MEDLINE, EMBASE, Cochrane Controlled Register of Trials) was conducted in Nov 2018 for clinical studies published since 2010 in HR+, HER2- ABC patients (pts). Endpoints of interest: tumor response, progression-free survival (PFS), overall survival (OS) and BC specific survival (BCSS).

Results: 79 studies with ABC pts ($\geq$50% HR+, HER2-) were included; 67 assessed OS.

Negative progesterone receptor (PR) status, higher tumor grade, higher CTC count, higher Ki67 level, number of metastatic sites (multiple vs single) and sites of metastases (presence of liver metastases vs absence), relapsed BC vs de novo metastatic BC, shorter time to recurrence/progression to ABC, poor performance status, prior therapy attributes in the early or metastatic setting therapy type and line, response to prior therapy) and race (black vs white) were consistently associated with worse OS; the relationship was inconsistent for tumor size, histological type (lobular vs ductal), lymph node involvement and age. Strength of association with OS was moderate (HR between 1.5-2.9) for PR status, tumor grade, CTC count, and Ki67 level, number and site of metastases, time to recurrence/progression to ABC, performance status, prior therapy attributes, and weak (HR<1.5) for de novo metastatic BC and race. Heterogeneity was observed across studies in the composition of the pt population, definition and categorization for a few prognostic factors (number and sites of metastases, prior therapy, age). Similar results were seen for tumor response, PFS, BCSS.

Conclusions: Based on consistency and strength of the data, PR status, tumor grade, CTC count, number and sites of metastases, time to recurrence/progression to ABC, performance status and prior therapy attributes were identified as the prognostic factors. Reused with permission 2019 SABCS®.

Association between prognostic factors and OS.

Prognostic factor	Total no. of studies assessing association	Total no. of studies reporting significant association	No. studies with significant multivariate analysis
PR status	10	8	5
Tumor grade	21	14	11
CTC count	10	9	7
Ki67	5	4	2
No. of metastatic sites	26	23	13
Site of metastasis	33	21	17
De novo metastatic BC	5	4	3
Tumor size	12	5	5
Lymph node	11	4	1
Histological type	5	1	1
Time to disease recurrence/progression	18	13	8
Performance status	14	11	8
Prior therapy	35	27	20
Age	37	17	13
Race	13	7	6

E29

CORRELATIONS BETWEEN NEUTROPENIA AND CLINICAL BENEFIT (CB) IN WOMEN WITH ESTROGEN-RECEPTOR (HR)–POSITIVE AND (HER2)–NEGATIVE ADVANCED BREAST CANCER TREATED WITH PALBOCICLIB: A "REAL LIFE" SINGLE INSTITUTION EXPERIENCE

Sinjari M.[1], Ceddia S.[1], Cosimati A.[1], Brandi M.[1], Verrico M.[1], Rossi L.[1], Cimino G.[1], Tomao S.[1]

[1]Oncologia Medica Universitaria, Sapienza Università di Roma, Aprilia (LT)

Background: Palbociclib is a selective CDK4/6 inhibitor approved for locally advanced or metastatic (HR)–positive, (HER2)-negative breast cancer treatment.

Most common AEs reported are hematologic, in particular neutropenia, often not complicated and rapidly reversible; dose modification occurs in a limited number of patients (pts). Questions were raised regarding a possible correlation between higher incidence of G3/4 AEs and better clinical outcome. We present our "real life" results.

Material and methods: We retrospectively reviewed records of all pts treated with palbociclib, from 2017-2020, in first or second line of treatment.

We evaluated the CB in terms of Partial Response (PR), Complete Response Rate (CR) and Stability of Disease (SD); compared then G3/4 neutropenia rates with CB and Progression Disease (PD) pts and their relationship with progression free survial (PFS) at 1 year follow-up (FU).

Results: We enrolled 50 female pts: 26 had not performed previous treatments (52%). Palbociclib was associated with aromatase inhibitor and fulvestrant respectively in 54% and 46% of pts.

The only G3-G4 toxicity reported was neutropenia which occurred in 24 pts (48%), with 1 case of febrile neutropenia (2%). At least one therapeutic cycle was delayed in 31 pts (62%) but only 8 (16%) had to reduce the dosage of the CDK-inhibitor.

PD rate at first diagnostic evaluation was 14% (7). PR was 12% (6), CR 2% (1), SD 72% (36) translating into a CB in 86% (43) of the pts. No G3/4 neutropenia differences were observed in these 3 subgroups.

G3/4 neutropenia was reported in 67% (29) of CB pts and 57% (4) of PD pts.

At 12 months of FU, 33 pts were evaluable: 36% (12) had PD while 63,4% (21) had still CB. No difference in G3/4 neutropenia was observed between PD and CB pts at 1 year FU (33% vs 38%).

Conclusions: No significant difference in G3/4 neutropenia incidence was observed in CB pts compared with PD pts; also at 1 year FU no difference in PFS was registered. Yet these results can be reassuring because high rate hematologic toxicities and frequent postponed cycles do not compromise pts clinical outcome.

E30

PRIMARY TREATMENT STRATEGY IN ELDERLY PATIENTS WITH HORMONE RECEPTOR POSITIVE EARLY BREAST CANCER: IS BREAST CANCER SURGERY ALWAYS BETTER?

Nasso C.[1], Barbolini M.[1], Isca C.[1], D'onofrio R.[1], Cortesi G.[1], Dominici M.[1], Piacentini F.[1], Omarini C.[1]

[1]*AOU Policlinico Modena, Modena*

Background: Older age, ECOG performance status, major comorbidities and concomitant medications influence the primary treatment strategy of hormone receptor positive (HR+) early breast cancer (EBC) patients. In case of frail patients, oncologist may choose primary endocrine therapy (ET) instead of breast cancer surgery (BCS) even if its clinical impact is still unknown.

Methods: We performed a retrospective study on women aged 75 years and older with HR+ EBC diagnosed at the Modena Cancer Center from 2010 to 2016. According to primary treatment strategy patients were divided into two groups: patients who underwent BCS (BCS group) versus patients treated with only ET (ET group). Patients' clinical data and tumor characteristics were collected. Disease Free Survival (DFS) and Breast cancer-specific survival (BCSS) were estimated by long rank test and Kaplan-Meier curves.

Results: 143 patients were involved in the study: 105 in BCS group and 38 in ET one. Patients who underwent surgery had significantly better ECOG (p=0.000001), low tumour grade (p=0.04) and early clinical stage (p=0.0001) compared to those in the ET group. In patients with negative lymph-nodes at the diagnosis, tumor stage I-II and low ki67 (<20%), BCS did not improve 5-years DFS in univariate and multivariate analysis (p = 0.099, 95%CI 0.152-1.175). No differences were found in terms of 5-years BCSS between the two groups (p = 0.195).

Conclusions: Stage I-II at the diagnosis, negative axillary lymph nodes and low ki67 identified a subgroup of HR+ EBC patients aged > 75 with low risk of disease progression who may not benefit from primary BCS. In elderly frail patients, primary ET instead of BCS could be a valid treatment strategy that should be considered on a case-by-case basis.

E31

HEMATOLOGICAL TOXICITY IN PATIENTS (PTS) TREATED WITH PALBOCICLIB AND FULVESTRANT (P+F): OLDER AGE AND PRIOR ADJUVANT THERAPIES AS PREDICTIVE FACTORS OF PALBOCICLIB-INDUCED NEUTROPENIA

Bitca V.[1], Raimondi L.[1], Gozzi E.[1], Mannino A.[1], Pietranera M.[2], Spinelli G.P.[3], Rossi L.[3]

[1]*Università La Sapienza Roma, Aprilia;* [2]*Centro Medico Diagnostico-Salus, Civitavecchia;* [3]*Oncologia Territoriale, Aprilia*

Background: Despite P+F is an treatment for hormone receptor-positive (HR+), HER2-negative metastatic breast cancer (MBC), neutropenia continues to remain the major dose limiting toxicity. In this study, we evaluated the role of age and previous therapy for predicting Grade 3 (G3) or Grade4 (G4) or febrile (FN) neutropenia in HR+/HER2-MBC treated with P+F as first-line metastatic therapy.

Methods: We retrospectively analyzed a consecutive cohort of 106 pts diagnosed with HR+/HER2-MBC treated with P+F as first line metastatic therapy between December 2017 and March 2020. Demographics, prior treatments, blood tests and hematological toxicities were recorded.

Results: The pts'median age was 61 (range 33-81). Neutropenia was reported in 78 (73%) pts: slightly less than half (44,3%) of pts experienced G3, 31 pts (29,2%) G4 and 14pts (13,2%) febrile neutropenia. Dose delays were in median a week. Beacause of hematological toxicity reported, 61 pts (57%) had a dose reduction, down to 100 mg in 51 pts (48,1%) and 75 mg in 10 pts (9,4%).

Of the 54 pts whose age was under 65, 28(51.8%) developed neutropenia: 21pts (75%) experienced G3, 5pts (17.8%) G4 and 2pts (7.2%) FN. Otherwise, of the 52 pts whose age was over 65, 50 (96.1%) developed neutropenia: 12pts (24%) experienced G3, 26 pts (52%) G4 and 12pts (24%) FN. In pts who received no chemotherapies but only hormonotherapy, G3 neutropenia occurred in 15 pts (31,25%) and G4 in 5 pts (10,41%); in one patient, FN was observed. In pts who received adjuvant chemotherapy (Anthracyclines and Taxanes), G3 neutropenia occurred in 32 pts (55,1%) and G4 in 26 ones(44,8%); in 13 pts (22,4%) FN was observed. The risk of Palbociclib-induced neutropenia was higher in pts over 65years (p<0.001) and in those undergoing multiple lines of therapy (p<0.001). The univariate and multivariate analysis revealed that both age and the adjuvant chemotherapy were statistically associated with both G4 neutropenia and FN (p<0.001).

Conclusions: Palbociclib has shown significant improvement in survival in pts diagnosed with MBC, at the cost of increased hematological toxicity. Older age and prior adjuvant chemotherapies are associated with increase in Palbociclib-related neutropenia.

E32

PREDICTORS OF HER2 GENE AMPLIFICATION IN IMMUNOHISTOCHEMISTRY SCORE 2+ EARLY BREAST CANCER ACCORDING TO 2018 ASCO/CAP GUIDELINES: A SINGLE INSTITUTION ANALYSIS

Barbolini M.[1], Omarini C.[1], Bettelli S.[1], Manfredini S.[1], Dominici M.[1], Piacentini F.[1]

[1]*Università degli Studi di Modena e Reggio Emilia, Modena*

Background: HER2 overexpression occurs in approximately 15-20% of invasive breast cancers (BC). From a pathological point of view HER2 positivity is defined by intense circumferential membrane complete staining in more than 10% of tumour cells in immunohistochemistry (IHC score 3+). When complete circumferential staining is weak to moderate (IHC score 2+) double probe in situ ibridation (ISH) is mandatory to define HER2 status. In 2018 ASCO/CAP guidelines were updated to provide additional guidance in HER2 equivocal cases to allow a greater discrimination between positive and negative cases. Our aim is to find predictors of HER2 positivity among IHC score 2+ early breast cancer specimens analysed according to 2018 ASCO/CAP guidelines.

Patients and methods: 253 cases of early BC diagnosed at Modena Cancer Center between November 2013 and August 2017 were identified. Stage, ISH result, hormonal receptor status (HR), proliferation index (MIB1), and histological grade were captured; menopausal status was available too. All IHC score 2+ cases were reclassified according to 2018 ASCO/CAP guidelines. The association between pathological tumour features, clinical characteristics and ISH positivity was assessed using Fisher test.

Results: Overall, 25.7% IHC score 2+ BC resulted HER2 amplified in double probe ISH. High tumour grade (G3 vs G1-2) and MIB1 > 20% significantly predict HER2 ISH amplification (p=0,0001). No correlation was found according to HR, stage, or menopausal status. The majority (185; 98.4%) of HER2-ve BC were reclassified as group 5 (HER2/CEP17 ratio <2 and HER2 copy number <4 signals/cell) except for 3 specimens classified as group 4 (HER2/CEP17 RATIO <2 and HER2 copy number ³4 but <6 signals/cell). In HER2+ve group the majority (62; 95.3%) specimens were group 1 (HER2/CEP17 RATIO >2 and HER2 copy number =4 signals/cell), no specimen was group 2, and only 3 cases were classified as group 3 (HER2/CEP17 RATIO <2 and HER2 copy number >6 signals/cell).

Conclusions: In this IHC score 2+ BC series, reclassification according to 2018 ASCO/CAP guidelines identified only 4.6% group 3 and 1.6% group 4 cases. The routinely assessment of grading and proliferation index could help to predict HER2 amplification in IHC score 2+ samples even if it must not substitute ISH assay in determining eligibility for HER2 targeted therapies.

E33

EXTENDED ADJUVANT ENDOCRINE TREATMENT FOR PREMENOPAUSAL PATIENTS: AN ATTEMPT TO REACH CONSENSUS THROUGH DELPHI METHODOLOGY

Buono G.[1], Arpino G.[2], Del Mastro L.[3], Fabi A.[4], Generali D.[5], Puglisi F.[6], Zambelli A.[7], De Laurentiis M.[8]

[1]*Oncology Unit, Ospedale San Rocco, Sessa Aurunca, Azienda Sanitaria Locale Caserta, Caserta;* [2]*Department of Clinical Medicine and Surgery, Oncology Division, Federico II University, Napoli;* [3]*Department of Internal Medicine, University of Genova; Ospedale Policlinico San Martino-IRCCS, Genova;* [4]*Division of Medical Oncology1, IRCCS Regina Elena National Cancer Institute, Roma;* [5]*Breast Cancer Unit, Azienda Socio Sanitaria Territoriale di Cremona; Department of Medical, Surgery and Health Sciences, University of Trieste, Cremona; Trieste;* [6]*Department of Medicine, University of Udine; Department of Medical Oncology, IRCCS Centro di Riferimento Oncologico Aviano - National Cancer Institute, Udine; Aviano;* [7]*Medical Oncology, Ospedale Papa Giovanni XXIII, Bergamo;* [8]*Department of Breast and thoracic oncology, Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale, Napoli*

Background: Endocrine therapy (ET) represents the mainstay of adjuvant treatment for hormone receptor positive (HR+) early breast cancer (EBC). Currently, international guidelines recommend the use of ovarian function suppression (OFS) plus aromatase inhibitors (AIs) as preferred choice in intermediate/high-risk premenopausal patients, according to SOFT and TEXT study results. In

the last years, several studies investigated the role of adjuvant ET (AET) extension beyond the first 5 years, globally demonstrating a reduction in the rate of disease relapse, particularly in high-risk patients. However, the vast majority of trials exploring AIs extension included postmenopausal women only. Therefore, compelling evidence supporting the extension of AET with AIs in premenopausal patients is currently missing. The aim of the present study was to reach an Italian expert consensus on the extended AET in premenopausal patients.

Material and methods: Firstly, a Steering Committee defined relevant statements on the topic. Subsequently, a panel of 8 Italian oncologists with expertise in breast cancer participated in this Delphi consensus study in January 2020. According to the Delphi method, experts voted anonymously each statement, expressing their level of agreement using a five point Likert scale. For each statement, the consensus was reached if either the sum of negative or positive answers exceeded 66%. Currently, the study has been extended to additional 12 Italian oncologists, using a web-based format, due to the COVID-19 pandemic. Altogether, the 20 participants represent oncological institutions distributed over the country.

Results: A total of 44 statements were defined and voted to gain consensus. The statements concerned clinical, pathological and genomic factors that could be used to assess the utility, the type (AIs vs. tamoxifen) and the duration (2-2.5 vs. 5 years) of extended AET in premenopausal patients. The consensus reached on each statement will be presented during the congress.

Conclusions: Intermediate/high-risk premenopausal EBC patients are likely to benefit from extended AET, although studies specifically designed in premenopausal setting are still missing. In the lack of direct evidence, this methodologically sound expert consensus may guide practicing oncologists in the choice of the best treatment and duration based on clinical, pathological and genomic information.

E34

FERTILITY AND PREGNANCIES IN YOUNG WOMEN WITH EARLY BREAST CANCER

Bottari M.[1], Maisano R.[2], Foti G.[3]

[1]U.O. Ginecolgia e Ostetricia, A.O.U. G. Martino Policlinico Messina, Messina; [2]U.O. Oncologia Medica G.O.M., Reggio Calabria; [3]U.O. Ginecologia e Ostetricia A.O.U. G. Martino Policlinico Messina, Messina

Background: Chemotherapy (CT) in younger women (W) with early breast cancer (EBC) has improve outcome with some long-term toxic effects among which premature menopause and infertility. In developed countries the age of first pregnancy (P) is often delaying and median age at first live birth is 30 years. In younger W with EBC eager to have children is needed to preserve fertility without reduce

therapy efficacy. Temporary ovarian suppression with GnRH analogue may preserve ovarian function even if clinical data are conflict.

Patients and methods: From 1/2013 to 12/2017 we have selected young W $\leq$ 35 years with triple negative and HER2 positive hormonal receptors negative EBC, who were anxious about preserving fertility after surgery, to receive leuprolide (L) 3.75 mg every 28 days (D) starting between 7 and 14 D before CT while the last injection was administered between 7 D before and 21 D after the last CT. During trastuzumab (T) monotherapy was not administered leuprolide.

Results: 21 W, median age 33 years, interested to go physiological pregnant after CT accepted to participate at the study, 12 were HER2 positive and 9 triple negative, all received CT and 9 CT+T. Although it is hard to give an exact length of time to wait before P after CT, we recommended at least. End points were recovery of menstruation within 6 months (M) and rate of successful conception within 3/2020. All pts recovered menses within 6 M (4-6 M) after the last dose of L. After the end of CT, 3 pts in trastuzumab refused to continue the study and 1 pt resulted with BRCA mutation was excluded. 17 pts completed the follow-up. At the time analysis 11 pts (65%) have managed to achieve P. 13 P among 11 pts, 11 were natural birth 2 caesarean delivery. All newborns were healthy. Moreover 2 pts used assisted fertility. Median time to achieving P from the EBC diagnosis was 36 M. 1 pt had local relapse after P.

Conclusions: Fertility preservation is an important issue for young W. CT increases the risk of premature menopause and GnRH analogues preserve ovarian function through some ways. To date the options to avoid sterility CT induced include embryo cryopreservation and oocyte or ovarian cryopreservation but these procedures are costly, complex and have a significant failure rate. Our results as well as other experiences support the efficacy of GnRH in the preservation of ovarian function and fertility moreover the treatment is simple, has low cost and does not require delaying the CT.

E35

ESTRADIOL MONITORING IN PREMENOPAUSAL WOMEN TREATED WITH LEUPROLIDE PLUS EXEMESTANE AS ADJUVANT THERAPY

Foti G.[1], MaisanoU R.[2], Bottari M.[3]

[1]U.O. Ginecologia e Ostetricia, A.O.U. G. Martino Messina, Messina; [2]U.O. Oncologia Medica G.O.M., Reggio Calabria; [3]U.O. Ginecologia e Ostetricia A.O.U. G. Martino Policlinico Messina, Messina

Background: For many years, tamoxifen (T) has been the standard adjuvantendocrine treatment option for premenopausal women with hormone receptor–positive tumors. In recent years, evidence on the role of ovarian function

suppression (OFS) added to T or to an aromatase inhibitor (AI) has radically changed the endocrine treatment landscape in this setting. In the joint analysis of TEXT and SOFT, OFS plus exemestane (E) was superior in terms of DFS to OFS plus T without difference in OS. In premenopausal women receiving an AI complete OFS must be obtained usually using a gonadotropin-releasing hormone agonist GnRHa. However, incomplete OFS is expected in approximately 20% of the patients receiving a GnRHa plus AI. Hence when a GnRHa plus an AI is chosen, a continuous monitoring of treatment adherence and the possible signs that suggest potential recovery of ovarian function-are critical. Estradiol and FSH monitoring during treatment can be considered.

Patients and methods: From 6/2017 to 12/2019 twenty-one consecutive premenopausal women with hormone positive HER2 negative early breast cancer participated in the observational study. The treatment was leuprolide (L) 3.75 mg every 4 weeks plus E 25 mg daily. 14 pts received treatment after chemotherapy (CT) and 7 as monotherapy (M). The serum levels of E2, FSH and LH were assayed prior the administration of L plus E and then 1, 3, 6, 9 and 12 months after starting therapy. The laboratory standard values for menopausal levels are 10-40 pg/mL for E2 (limit detection 5 pg/ml), 25.8–134.8 mIU/ml for FSH and 7.7-58.5 mIU/ml for LH.

Results: All pts completed the observational period. The baseline E2 value was menopausal in 8/14 CT pts and normal in all M pts. After 1 month E2 value was menopausal in 12/14 CT pts and normal in all M pts. Three-months E2 values showed menopausal status in 13/14 CT pts and in 5/7 M pts. At six months from the start, the hormonal status remained unchanged therefore after discussion with these pts switched toT. At 12 months all pts in L plus E were in menopausal status. FSH and LH levels showed a marked reduction from the start of treatment.

Conclusions: The majority of the pts (18/21), regardless CT or M, had menopausal E2 value within six months from the start, special attention should be given to chemotherapy-naïve pts.

E36

HIGH PLASMATIC LEVELS OF IL-4 AND IL-13 ARE ASSOCIATED WITH RECURRENCE AND WORSE SURVIVAL IN BREAST CANCER

Onesti C.E.[1], Onesti C.E.[2], Josse C.[3], Boulet D.[3], Bours V.[3], Jerusalem G.[2]

[1]University Hospital of Liège Sart Tilman, Liège, Belgium; [2]Department of Medical Oncology, University Hospital of Liège Sart Tilman, Liège, Belgium; [3]Laboratory of Human Genetics, GIGA Research Institute, Liège, Belgium

Background: The immune system has a role in breast tumor, in particular in triple negative (TNBC) and in hormone receptor-negative/HER2-positive breast cancers. The aim of this study is to analyze the association between baseline cytokines expression with cancer relapse and outcome.

Material and methods: Baseline plasmatic samples of 66 stage I-III breast cancers treated with surgery with or without radiotherapy and systemic treatment between 2011 and 2017 were collected. A panel of 24 cytokines were analyzed by Luminex MAGPIX technology, using multiplex Luminex Magnetic Assay kits (®R&D System).

Results: Sixty-six breast cancer patients were included in the study. The median follow-up was of 78 months (range 18-99). The median age at diagnosis was of 58.5 years (range 32-86). The stage at diagnosis was I in 29 (43.9%) patients, II in 26 (39.4%) and III in 11 (16.7%). The histological type was ductal in 47 cases (71.2%), lobular in 13 (19.7%) and mixed in 6 (9.1%). Fifty-three (80.3%) patients were estrogen-receptor-positive, 11 (16.7%) HER2-positive and 12 (18.2%) TNBC. All the patients received surgery, combined with neo/adjuvant chemotherapy in 35 (53%) cases, anti-HER2 in 9 (13.6%), hormonotherapy in 53 (80.3%) and radiotherapy in 52 (78.8%). During the follow-up we observed 11 relapses and 4 deaths. IL-4 was associated with relapse, that occurs in 30.7% of the cases in the group with IL-4 > 0.07 (IL4-H) mean fluorescence intensity (MFI) vs in 7.5% in the group with IL-4 ≤ 0.07 MFI (IL4-L) (p 0.013), with a ROC curve AUC of 0.745. In multivariate analysis relapse was associated with IL-13 (p 0.048) and T stage (p 0.049). Survival analysis showed a better time to treatment failure (TTF) for the group IL4-L (5y-TTF 87% vs 63% for IL4-L and IL4-H, p 0.022) and for the group with IL-13 ≤ 0.1 MFI (IL13-L) compared IL-13 > 0.1 MFI (IL13-H) (5y-TTF 90% vs 45%, p 0.017). A separation of the curves was also observed for breast cancer specific survival (5y-BCSS: 95% vs 84% for IL4-L vs IL4-H, p 0.118; 91% vs 75% for IL13-L vs IL13-H, p 0.029).

Conclusions: Higher baseline plasmatic level of IL-4 and IL-13 are associated with a worse prognosis in early stage breast cancer. These are two structurally and functionally related cytokines known for regulating the immune system activity, leading to a T helper-2 response and to a macrophage M2 polarization. Data should be confirmed in a larger cohort and a mechanistic study is advisable.

E37

SUPPORT BREASTFEEDING FOLLOWING BREAST CANCER

Testa I.[1], Gallese M.[1], Giuntini N.[1], Nastasi G.[1], Cattaneo E.[1], Ionio C.[2], Andreol A.[2], Smorti M.[3], Peccatori F.A.[4], Pravettoni G.[4], Pisoni C.[5], Cassani C.[5], Fenaroli V.[1], Bonassi L.[1]

[1]ASST Bergamo Est, Seriate; [2]Università Cattolica del Sacro Cuore, Milano; [3]Università degli Studi di Pisa, Pisa; [4]Istituto Europeo d'Oncologia, Milano; [5]IRCCS San Matteo di Pavia, Pavia

Background: Breast Cancer (BC) is the most common oncological disease diagnosed in pre-menopausal women.

With the rising trend in delaying pregnancy later in life, the topics of pregnancy and lactation following BC diagnosis become increasingly more current. Oncological pregnancy is beset with specific worries about recurrence and women may believe that their milk transfers oncologic disease to the baby. BC women might face a unique set of emotional and physical factors during the perinatal period that might also have an impact on their decision and ability to breastfeed. Breastfeeding after BC diagnosis and treatments could also be difficult because of the lack of specific support and guidelines. Our study aimedto explore feeding practices in mothers with a history of BC. Specifically, we explored the relationship between different feeding methods and mood states of BC survivors compared to women without a past cancer diagnosis.

Material and methods: At three months after childbirth, 28 women with a history of BC (clinical sample) and 30 without a past oncological diagnosis (control sample) were asked for socio-demographics and clinical data, information about feeding practices and to complete the Profile of Mood States (POMS) questionnaire.

Results: Feeding practices of both samples are illustrated in *Table 1*. Women with past BC breastfeed significantly less than women of control sample (χ^2=13.39; p<.001) and tend to feel more confused (F=3.01; p=.06). Instead, breastfeeding women without a cancer diagnosis feel more vigorous (F=5.91; p<.05) than BC mothers.

Conclusions: Puerperae with a BC history are faced with unique challenges when they attempt breastfeeding. These findings may have a wide range of clinical implications which could be useful in order to develop tailored treatment, interventions and specific guidelines for this population.

		Breastfeeding	Formula	Mixed method	Total
Clinical sample	Count	4	17	7	28
	% within sample	14,3%	60,7%	25,0%	100,0%
	% within feeding methods	21,1%	77,3%	41,2%	48,3%
	% of Total	6,9%	29,3%	12,1%	48,3%
Control sample	Count	15	5	10	30
	% within sample	50,0%	16,7%	33,3%	100,0%
	% within feeding methods	78,9%	22,7%	58,8%	51,7%
	% of Total	25,9%	8,6%	17,2%	51,7%
Total	Count	19	22	17	58
	% within sample	32,8%	37,9%	29,3%	100,0%
	% within feeding methods	100,0%	100,0%	100,0%	100,0%
	% of Total	32,8%	37,9%	29,3%	100,0%

[1.]Crosstab samples*feeding methods

E38

KI67 EXPRESSION AND CDK4/6I ACTIVITY: AN EMERGING ROLE FOR PIK3CA MUTATIONS IN METASTATIC BREAST CANCER PATIENTS

Del Re M.[1], Lorenzini G.[2], Crucitta S.[2], De Angelis C.[2], Cucchiara F.[2], Diodati L.[2], Cavallero D.[2], Bargagna I.[2], Cinacchi P.[2], Fratini B.[2], Salvadori B.[2], Fontana A.[2], Danesi R.[2]

[1]*Azienda Ospedaliero Universitaria Pisana, Pisa;* [2]*Azienda Ospedaliero Universitaria di Pisa, Pisa*

Background: Preclinical studies indicate that alterations of PIK3/AKT/mTOR pathway may be correlated with resistance to CDK4/6 inhibitors (CDK4/6i) in breast cancer (BC) cells and that PI3K inhibitors could prevent resistance to CDK4/6i [Abreu H MT, et al. Cancer Res 2016;76:2301]. For these compelling evidences the present study evaluated the impact of PI3K mutations on treatment outcome in metastatic BC (mBC) patients (pts) receiving CDK4/6i in association with hormonal therapy as per approved indication.

Methods: Thirty pts treated with palbociclib (n=26) or ribociclib (n=4) plus hormonal therapy were enrolled. Plasma samples were obtained prior to CDK4/6i treatment and circulating free DNA (cfDNA) extraction was performed using the QIAamp Circulating Nucleic Acid Kit (Qiagen). PI3K mutations (C420R, E542K, E545A, E545D, E545G, E545K, Q546E, Q546R, H1047L, H1047R, H1047Y) were analysed on cfDNA using a QX100 ddPCR (Bio-Rad).

Results: In pts with (n=12) vs. without (n=18) PI3K mutations, PFS was significantly shorter (5.9 vs 11.6 months, p=0.01, respectively). The univariate and multivariate analysis comparing PFS and clinically relevant data (i.e., age, metastasis, previous lines of hormonal or chemotherapy), confirmed PI3K as the only biomarker significantly associated to PFS (p=0.01). A significant correlation was observed between Ki67 expression in primary lesions and PI3Kstatus. Higher Ki67 levels were associated with PI3K

mutations vs. none (Ki67%, 25.36±11.02 vs. 13.17±10.14; p=0.006). The significance was maintained when PI3K mutant pts were stratified as low (<14%), intermediate (14–20%) and high (>20%) Ki67 levels (p=0.009). Despite the strong correlation, Ki67 did not appear significantly associated with median PFS to CDK4/6i, and the presence of PI3K mutations remained an independent predictor of clinical outcome to CDK4/6i.

Conclusions: In conclusion, PI3K status should be considered a potential predictive biomarker of CDK4/6i and, based on these data, the sequence of treatments (CDK4/6 vs. PI3Ki) may be reconsidered.

Clinical trial identification Circus study - ID 5694

E39

PLATINUM-BASED NEOADJUVANT CHEMOTHERAPY IN TRIPLE-NEGATIVE BREAST CANCER (TNBC) PATIENTS WITH OR WITHOUT GERMLINE BRCA MUTATION: A RETROSPECTIVE SINGLE INSTITUTION ANALYSIS

Diodati L.[1], De Angelis C.[1], Fontana A.[1], Cavallero D.[1], Lorenzini G.[1], Bargagna I.[1], Cinacchi P.[1], Fratini B.[1], Salvadori B.[1], Ferrari P.[1], Landucci E.[1], Cucchiara F.[1], Ghilli M.[1], Roncella M.[1], Del Re M.[1], Michelotti A.[1], Falcone A.[1]

[1]*Azienda Ospedaliero-Universitaria Pisana, Pisa*

Background: Neoadjuvant chemotherapy (CT) is currently considered the preferred approach for the majority of early-stage TNBC patients (pts) according to the high sensitivity to cytotoxic CT and the strong prognostic value of achieving a pathological complete response (pCR). However, only 30%-40% of TNBC pts achieve a pCR after standard anthracycline-taxane based neoadjuvant CT. The role of platinum agents and BRCA status remain highly controversial in this setting of pts.

Material and methods: We retrospectively collected all consecutive TNBC pts treated at our institution with neoadjuvant CT. We reported pts characteristics, outcomes and adverse events (AEs).

Results: 116 pts were identified between 2002 and 2019. Median age was 47 years (range 24-77); 58 pts (50%) were premenopausal. Clinical stage at diagnosis was: I in 5 pts (4%), II in 78 pts (67%) and III in 33 pts (29%). NST was the most frequent histology (105 pts, 90%), followed by lobular in 4 pts (3%) and other rare histotypes in 7 pts (7%).94pts(81%)receivedastandardanthracycline±taxane CT (P-), and 22 pts (19%) received platinum agents in addition (P+). Outcome data were available for 113 pts out of 116. P+ pts had a significant higher probability to reach pCR compared to P- pts (47% vs 23%; OR 2.95, 95%CI 1.06-8.16; p=0,038). 68% of P+ pts received a conservative surgery. 18 pts out of 116 (15%) reported

BRCA mutations, 14 pts (78%) in BRCA1 and 4 pts (22%) in BRCA2. Among them, 4 pts (22%) were P+ and 14 pts (78%) were P-; pCR rate was similar in both groups (25% in P+ vs 21% in P-). G3/4 haematological AEs were more frequent in P+ pts (68%) compared to P- pts (22%). Neurotoxicity was similar in both groups. Early discontinuation of CT was more frequent in P+ vs P- pts (36% vs 5%). 31 pts out of 113(27%) experienced progression disease (PD), but only 4 of them had pCR after neoadjuvant CT. Interestingly PD rate was lower in P+ pts compared to P- pts (5% vs 31%).

Conclusions: In line with literature data, our real-life experience showed that platinum-based neoadjuvant CT was associated with significant increased pCR rates in TNBC pts, at the cost of worse haematological toxicities. BRCA germline mutation did not represent a sensitivity factor to platinum agents. The addition of a platinum agent to standard anthracycline-taxane-based CT may be considered an option in TNBC pts. Long-term outcome data are required to further clarify the role of platinum as neoadjuvant treatment of TNBC pts.

E40

COULD FIRST-LINE TRIPLET PERTUZUMAB-TRASTUZUMAB-TAXANE NEGATIVELY AFFECT PROGRESSION-FREE SURVIVAL (PFS) OF PATIENTS TREATED WITH SECOND-LINE TRASTUZUMAB-EMTANSINE (TDM-1) IN METASTATIC HER2+ BREAST CANCER? A SINGLE MONOCENTRIC EXPERIENCE

Sanò M.V.[1], Castellana L.[2], Dimarco R.[1], Giuseppa F.[1], Caffarelli S.[1], Alì M.[1], Di Leo V.M.G.[1], Chiarenza M.[1], Aiello R.A.[1], Picone A.[1], Caponnetto D.[1], Caruso M.[1]

[1]*Humanitas Istituto Clinico Catanese, Catania;* [2]*Università Palermo, Palermo*

Background: The antibody-drug conjugate T-emtansine (T-DM1) showed benefit in terms of both progression free survival (PFS) and overall survival (OS) vs lapatinib-capecitabine in HER2+ patients treated at least with a previous T/taxane-based therapy (EMILIA TRIAL). However a paucity of data is available on T-DM1 efficacy after dual blockade with pertuzumab plus trastuzumab, which raprents the current first line standard of care. We conducted a monocentric retrospective analysis on the sequence of anti-Her2 treatments.

Matherial and Methods: Between June 15, 2014 and January 31, 2020 we identified HER2+ (IHC: 3+ or 2+/ FISH amplified) mBC pts treated with T-DM1, either as second-line after progression on dual blockade PT (CohortPT) or after ≤ 3 T-combined (chemo- or endocrine-therapies or both) regimens (Cohort T). We evaluated for each Cohort demographics features, mPFS, best response

rate, and correlation between T-DM1 efficacy and IHC status($3+$ vs $2+$/FISH+).In total, 74 pts received T-DM1: Cohort T n=34 (all females, median age=52,7), Cohort PT n=40 (39 females, 1 male, median age=52,2). Within Cohort T 64,7% of pts (n=22) received T-DM1 after 1 previous T-combined regimen, 20,6% (n=7) and 14,7% (n=5) in third and fourth lines, respectively. Instead, the whole Cohort PT received T-DM1 after a first-line dual blockade PT.

Results: We found 10,2 months as mPFS for the Cohort T. Whereas, the Cohort PT mPFS was equal to 3,7 (range: 1,4 – 26,2 m). As regards the best response rate, 8,8% (n=3/34) and 52,5% (n=21/40) of pts reported a progressive disease (PD) into the Cohorts T and PT, respectively; stable disease (SD) 38,2%(n=13/34) versus 15% (n=6/40); partial response (PR) 23,5% (n=8/34) vs 15% (n=6/40); complete response (CR) 23,5% (n=8/34) vs 12,5% (n=5/40). Almost 2/3 (n=21/34) of Cohort T and half (n=20/40) of Cohort PT pts had a $3+$ IHC status.

Conclusions: Our results show a lower efficacy of T-DM1 after progression on dual HER2-blockade PT. Probably, the dual blockade PT-induced HER2 extracellular-domain downregulation makes cells resistant to T-DM1, which binds to HER2 external portion too. Our analysis does not take over a significant correlation between IHC status and T-DM1 efficacy, especially in the Cohort PT. Obviously, larger prospective studies are necessary in order to optimize the best sequence strategy in the treatment of metastatic HER2+ BC.

E41

TRIPLE NEGATIVE BREAST CANCER (TNBC): CASES ANALYSIS IN OUR MULTIDISCIPLINARY BREAST UNIT WITH MEDIAN FOLLOW-UP OF 58.8 MONTHS

Rodà G.[1], Basilico V.[1], Di Cesare P.[1], Galeassi A.[1], Carnaghi C.[2], Andreoli C.[1], Branchini L.[1], Arlant V.[1], Bossi P.[3], Crespi L.[1], Formenti S.[1], Zuliani W.[1]

[1]*Humanitas Mater Domini, Castellanza;* [2]*Ospedale Provinciale San Maurizio, Bolzano;* [3]*Istituto Clinico Humanitas, Rozzano*

Background: TNBC accounts for approximately 10-15% of breast cancers diagnosed worldwide.TNBCs are biologically aggressive with poor prognosis.This is due to two factors:shortened disease-free interval in the adjuvant and neoadjuvant setting and a more aggressive clinical course in the metastatic setting. Despite this, the schedule for follow-up care for TNBC is the same as it is for other types of BC.

Material and methods: From 01.01.2011 to 31.12.2015 in our Breast Unit 1158 cases of BC were treated, 96 of which were TN (8.3%). Median age of the TN patients (pts) was 56.3 years (range 31 - 87). 41% of pts were in premenopausal status. A total of 66 quadrantectomies and 30 mastectomies were performed. Axillary staging was performed with sentinel lymph node biopsy in 86 cases, resulting positive in 20 (23%) pts who have undergone axillary dissection. Of the 66 conservatively treated pts, 54 (81.8%) completed local treatment with radiotherapy on the residual breast. In 71 pts adj treatment was planned, 5 received neo-adj therapy. The schedule used was in all cases: ACx4 followed by Paclitaxel x 12 weeks. Currently most pts would have received neoadjuvant treatment.

Results: 4 of the 96 pts were subsequently followed elsewhere after surgery and are therefore excluded from the present analysis. All other 92 pts have been regularly followed in our Unit for at least 5 years. The median follow-up is 58.8 months (range 48 - 96). At 31.12.2019 there were a total of adverse events in 29 cases: distant recurrence 22, local recurrence 4, controlateral BC 2, axillary lymph node recurrence 1. Medium interval in months between surgery and disease recurrence was 26.2 (range 3.8-61.5). Ki67 index was high in most cases ($>$20% in 90% of pts) and in particular in pts with disease recurrence($>$ 20% in 28/29 pts). The current status of the pts at 31.12.2019 is: living NED 60; living after local recurrence 4; living after controlateral BC 2; living after distant recurrence 9; died from BC 13; died from another cause 4; lost at follow-up 4.

Conclusions: Data analysis shows that TNBC pts, in addition to often having a high Ki67 index, have a disease recurrence after an average of 2 years. This suggests that a systematically more intensive follow-up in this setting should be implemented even if the relationship between earlier diagnosis of recurrence, more timely and novel treatments, correlation with biomarker (BRCA and others) and improvement of overall survival is to be verified more.

E42

RETROSPECTIVE ANALYSIS ON SURVIVAL IMPACT OF LIVER METASTASECTOMY (LM) IN PATIENTS (PTS) WITH METASTATIC BREAST CANCER (MBC)

Pontolillo L.[1], Orlandi A.[1], Mele C.[2], Pasqualoni M.[1], Pannunzio S.[1], Cutigni C.[1], Garufi G.[1], Indellicati G.[1], Vellone M.[2], Palazzo A.[1], Cassano A.[1], Giuliante F.[2], Bria E.[1], Tortora G.[1]

[1]*Oncologia Medica, Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli-IRCSS, Università Cattolica Del Sacro Cuore, Roma;* [2]*Comprehensive Cancer Center, Fondazione Policlinico Universitario Agostino Gemelli-IRCSS, Università Cattolica Del Sacro Cuore, Roma*

Background: Liver represents the first metastatic site in 5-12% of MBC. While current evidence support LM for advanced colorectal cancer in improving survival, on the basis that hepatic parenchyma filters circulating tumor cells (CTC) from primary to systemic circulation, MBC-LM is considered a possible therapeutic option for selected MBC pts in clinical practice, in absence of reliable evidence.

Material and Methods: A retrospective analysis including MBC pts undergone LM after Tumor Board discussion at hepatobiliary surgery unit of Fondazione Policlinico Universitario Agostino Gemelli-IRCCS between January 1994 and December 2019 was conducted. Theprimary endpoint was overall survival (OS) after MBC-LM; secondary endpoint was diseasefree interval (DFI) after surgery. An exploratory analysis was performed to evaluate the impact of immunophenotype and others clinical factors (age, menopausal status, number of metastatic sites, synchronous or metachronous disease, prior systemic therapy and tumor free resection margin).

Results: Forty-nine MBC pts underwent LM. Clinical data were available for 22 pts. After a median follow-up of 71 months (m), median OS and DFI were 67m (95%CI 45-103) and 15m (95%CI 11-46), respectively. The histotype was ductal carcinoma for 21 pts, only 1 was lobular; 14 pts had a luminal tumor, 5 pts were triple negative (TNBC) and 3 pts were HER2+. At univariate analysis, the presence of a negative resection margin was the only factor which statistically significantly influenced OS (78 vs 16m; HR 0.083,p< 0.0001) and DFI (16 vs 5m; HR 0.17, p=0.0058). None of the other factors were significantly associated with OS and DFI. An interesting trend toward significance was observed in OS analysis for menopausal status (pre- vs post-, 50 vs 78 m, p 0.56), metastatic sites (only liver vs other sites, 103 vs 50m, p=0.14) and prior systemic therapy (none vs >1-line, 50 vs 78m, p=0.89).

Conclusions: Resection of breast cancer liver metastasis might represent a therapeutic option for selected pts. The radical nature of the surgical procedure performed in a high-flow center and after a multidisciplinary discussion appears essential for this therapeutic option.

E43

METASTATIC HER2-POSITIVE BREAST CANCER: DOES THE BENEFIT OF FIRST-LINE PERTUZUMAB EXTEND OVER TIME?

Cantini L.[1], Merloni F.[1], Pistelli M.[1], Crocetti S.[1], Bastianelli L.[1], Della Mora A.[2], Scortichini L.[1], Tassone L.[1], Ranallo N.[1], Agostinelli V.[1], Ballatore Z.[1], Savini A.[1], Berardi R.[1]

[1]Clinica Oncologica - Università Politecnica delle Marche - Ospedali Riuniti Ancona, Ancona; [2]UO Oncologia Macerata, Ancona

Background: In metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC), dual HER2 blockade with pertuzumab and trastuzumab plus taxane (PHT) represents the standard 1st line treatment. In HER2-negative hormone receptor (HR)-positive BC, the cyclin-dependent kinases (CDK) 4/6 inhibitors have proven to extend their benefit over the subsequent therapy lines. Conversely, the potential influence of anti-HER2 treatments on subsequent therapy lines outcome has been scarcely investigated. Aims of our study were to describe our institution experience in the treatment of metastatic HER2-positive breast cancer and to investigate the prognostic influence of pertuzumab on subsequent therapy lines.

Patients and methods: We retrospectively analyzed data of consecutive patients treated for metastatic HER-2 positive BC between 2004 and 2020. Patients receiving pertuzumab as 1st line treatment were compared with those who did not. Median overall survival (mOS) and progression-free survival (mPFS) were estimated using Kaplan-Meier method and strata were taken into account by long-rank test.

Results: A total of 78 patients were enrolled: median age at diagnosis was 53 years, 45 HER2 patients (58%) were also HR-positive, 50% were relapsed patients; 22% patients were previously treated with trastuzumab in the adjuvant setting; 29% of patients were treated beyond 3rd line. mOS from starting of 1st line treatment was 54.3 months. In 1st therapy line (mPFS 19.9 months) 29 patients (37%) patients were treated with PHT and 21 patients (27%) with trastuzumab and vinorelbine; other therapeutic combinations were less represented. In 2nd line (mPFS 8.2 months) the most represented therapeutic agent was TDM-1 (36%) and 24% of patients were treated with capecitabine plus lapatinib. In 3rd line (mPFS 8.3 months) therapeutic decision was balanced between different combinations. Patients treated with pertuzumab had better PFS in 1st line (mPFS 31.5 vs 15.2 months, HR 1,89, 95%CI 1.07-3.20, p=0.02) but this benefit was lost for PFS in 2nd (mPFS 5.6 vs 9.5 months, p=0.31) and 3rd (mPFS 4.2 vs 8.3 months, p= 0.30) lines.

Conclusions: In our experience PHT and TDM-1 were the most represented therapy choices in 1st and 2nd lines, respectively. 3rd line treatment was more heterogeneous. Unlike CDK 4/6 or programmed death-(ligand) 1 (PD-(L)1) inhibitors, the use of pertuzumab in HER2-positive BC seems not capable to extend its benefit over subsequent therapy lines.

E44

COLLABORATION ACTIVITIES OF GENETIC COUNSELLING ONCOLOGY AND BREAST UNIT IN ASST-MANTOVA

Adami F.[1], Panizza E.[1], Carbonardi F.[1], Carra S.[2], Pisanelli M.B.[1], Rinaldi R.[3], Busani M.[4]

[1]ASST "Carlo Poma" S.C. Oncologia, Mantova; [2]ASST "Carlo Poma" Screening Mammografico, Mantova; [3]ASST "Carlo Poma" Anatomia Patologica, Mantova; [4]ASST "Carlo Poma" Chirurgia senologica, Mantova

Background: BRCA-mutation carriers have a lifetime risk of breast cancer that ranges between 36 to 90%. Bilateral prophylactic mastectomy were both associated with a decreased breast cancer risk in BRCA1/2 mutation

carriers (RR, 0.552; 95%CI, 0.448-0.682; RR, 0.114; 95%CI, 0.041-0.317, respectively) (Xiao Li, 2016). The risk of contralateral breast cancer in women with a BRCA mutation is approximately 40% at 10 years (Metcalfe K, 2014). Contralateral prophylactic mastectomy significantly decreased breast cancer incidence in BRCA1/2 mutation carriers (RR, 0.072; 95%CI, 0.035-0.148). The radical surgical option which should be reserved for patients with BRCA1/2 mutation and breast cancer diagnosis, is still debated. However, several aspects should be considered before the radical surgical decision-making: the risk of ipsilateral breast recurrence, the risk of contralateral breast cancer, the potential survival benefit, the quality of life, woman's age, morbidity, type of mutation, individual preferences and expectations and psychological-relational profiles. A multidisciplinary consultancy is advisable. In the last few years the Genetic Counseling Oncology (CGO), the Mammography Screening and the Breast Unit of Mantova, have been sharing a PDTA to propose a tailored management for patients at increased risk of breast-cancer.

Patients and results: Since 2016 in CGO-screening, 760 families have been selected for their risk of hereditary breast and ovarian cancer. We identified 66 mutations (38 pathogenic mutations and 28 VUS, variants of uncertain significance) in 275 index cases. 56 patients, 20% of these index cases, were discussed in the Breast Unit after radiological and histological diagnosis of invasive breast cancer or DCIS. To these patients, genetic counseling was recommended. 6 of these women (10%) were BRCA-mutation carriers and they accepted prophylactic mastectomy. Moreover 12 women, in CGO-screening, BRCA-mutation carriers, after early diagnosis of breast cancer (60% pTis, 40% pT1), decided to get a bilateral prophylactic mastectomy, which was proposed after multidisciplinary discussion of each individual case. 12 of 18 patients accepted prophylactic bilateral oophorectomy and a woman received a diagnosis of stage I ovarian cancer throughout the procedure.

Conclusions: From our experience mutation carriers with unilateral breast cancer need to be discussed by a multidisciplinary team and the counseling should be managed on a case-by-case basis.

E45

LOX-1: A NEW POTENTIAL PROGNOSTIC MARKER FOR BREAST CANCER PATIENTS

Pucci S.[1], Torino F.[2], Polidoro C.[3], Greggi C.[3], Iossa F.[3], Giannetti E.[2], Costantini M.[4], Novelli G.[3]

[1]Dipartimento di Biomedicina and Prevenzione, Università di Roma "Tor Vergata", Roma; [2]Oncologia Medica, Dipartimento Medicina dei Sistemi, Università Roma Tor Vergata, Roma; [3]Dipartimento di Biomedicina e Prevenzione, Università di Roma Tor Vergata, Roma; [4]IRCCS Isituto Nazionale Tumori "Regina Elena", Roma, Roma

Background: LOX-1 is a membrane receptor encoded by the OLR-1 gene, responsible for the recognition, binding and internalization of oxidized low-density lipoproteins. Studies in our laboratory showed that LOX-1 is overexpressed in different cancer types, including breast cancer (BC). Moreover, LOX-1 expression in BC is closely related to the disease molecular phenotype. LOX-1 may confer proliferative advantage once overexpressed through expression vectors in vitro, both in neoplastic cells and in stabilized normal cell lines, modulating proteins involved in cell cycle regulation and apoptosis. These data suggest that LOX-1 may represent a new "metabolic" oncogene. The present work was aimed at retrospectively evaluating in a series of BC patients the prognostic value of LOX-1, by correlating LOX-1 expression with loco-regional and distant disease recurrence.

Patients and methods: Formalin-fixed, paraffin-embedded specimens of 47 BC patients (pts) were assessed for LOX-1by immunohistochemistry and pts' data on clinical-pathological prognostic markers were charted. Twenty-three of those pts were assessable for either loco-regional or distant relapsing disease along their 5 years follow-up and for the potential prognostic value of LOX-1 expression.

Results: In 32 specimens of 47 (~70%) BC pts, a strong upregulationof LOX-1 (tumors versus controls: p<0.01) was observed, positively correlating to tumor stage (T) and histological grade (G). A strong LOX-1 overexpression was observed in invasive BC as compared to normal tissues of the same individuals, aside the neoplasia (p<0.01). Eight out of the 23 pts evaluated for disease recurrence showed a relapsing disease. LOX-1 high expression was found in 75% of pts who showed relapsing disease, while LOX-1 low expression was found in 83% of cases with no evidence of disease along their 5 years follow-up. When the prognostic value of LOX-1 expression was retrospectively evaluated in that cohort of pts, in comparison with T, nodal status and G, LOX-1 expression and T size, N status, and G, were all recognized as independent prognostic markers (further correlations with the level of ER, PR, HER2 and Ki67 of BC specimens will be shown during the meeting).

Conclusions: These preliminary data suggest that LOX-1 is a promising independent prognostic marker in BC pts. However, larger correlative trials are needed to confirm LOX-1 as a new prognostic marker and to define its potential role in the management of BC pts.

E46

SEXUALITY IN CANCER PATIENTS: A STUDY ON FEMALE SEXUAL DYSFUNCTIONS IN WOMEN WITH BREAST CANCER

Aiello M.[1], Moschetto M.[2]

[1]A.O.U. Policlinico Vittorio Emanuele - U.O Oncologia Medica, Catania; [2]AOU Policlinico Vittorio Emanuele - U.O. Oncologia Medica, Catania

Breast cancer (BC) is the most common cancer among women. The diagnosis and treatments of BC negatively affect quality of life (QoL) and sexual functioning (SF). Cancer treatments, including surgery, chemotherapy, radiotherapy and hormone therapy, can directly affect body image, disrupt relationship closeness and sexuality. The beauty of the breast is an important aspect to femininity, self estimate and self confidence in women. Sexuality appear less important than the short and long-term adverse effects of treatment in cancer patients. Sexual Dysfunction is when at least one aspect of sexual response cycle does not function properly. It may be libido, arousal or orgasm that is involved.

Purpose: The purpose of the present study was to assess to determine the QoL levels of patients with BC during chemotherapy (A) and follow-up (B) and to find out the problems that affect their QoL and SF.

Methods: The data were collected using the '36-Item Short Form Health Survey' (SF-36), a set of generic, coherent, and easily administered quality-of-life measures and the 'Female Sexual Function Index' (FSFI) a multidimensional scale for assessment of sexual functioning.

Results: Overall QOL for this sample (N=60) was moderate and treatment procedures caused important problems that had a negative effect on physical, psychological, social aspects of QoL. In addition, the main causes of sexual dysfunctions were in group A lack of arousal (2.33) and lubrification (2.42) while in group B lack of sexual desire (2.62) and arousal (2.35). The real impact of psychological aspects of therapy on female sexual functions should be prospectively studied.

Conclusions: Evaluation of the above variables in BC women is actually the only way to allow them to face a relevant aspect of their QoL, most of the times neglected both by health professionals and themselves too. Importance of data will suggest hospital institutions to consider sexual it as a key point in cancer rehabilitation.

E47

WHAT HIDES BENEATH THE SCAR: SEXUALITY AND BREAST CANCER WHAT WOMEN DON'T SAY

La Manna A.[1], Gozzi E.[2], Rossi L.[2], Angelini F.[3], Raimondi L.[2], Bitca V.[2], Regini D.[4], Cimino G.[5], Tomao S.[6], Calogero A.[1], Fontana A.[1], De Masi C.[1], Busco S.[1], Fara M.A.[1], Dorkin M.[1], Di Filippo S.[1], Ulgiati M.A.[1], Tarallo M.[1], Tozzi R.[1], Ricci F.[1]

[1]Ospedale Santa Maria Goretti, Latina; [2]Università la Sapienza di Roma, Aprilia; [3]Ospedale Regina Apostolorum Albano Iaziale, Albano; [4]Università la Sapienza di Roma, Albano; [5]Università la Sapienza di Roma, Latina; [6]Università la Sapienza di Roma, Roma*

Background: Breast is a symbol of femininity, motherhood and sexuality. Breast cancer (BC) is the most frequent cancer in Italy: in 2019, 53.500 new cases were diagnosed. BC and its treatment (surgery, radiation, chemotherapy and

endocrine therapy), the disturbances of body image, and mental health problems such as anxiety and depression could influence sexuality. Very often the aspect of sexuality in BC is likely not to be fully investigated: cultural barriers may also contribute to lack of attention to these issues. In Italy, there are very few Breast Units that provide the figure of the sexologist. The aim of our study was to evaluate the influence and changes of BC on the bodily image and sexuality.

Patients and methods: We enrolled 54 BC pts, mean age was 54 years. 40 pts (74%) had undergone surgical intervention. Participants were invited to complete a structured questionnaire, which included four close-up questions regarding self-image, sexual activity, sexual satisfaction, analyzing these aspects before and after BC and its treatments. Finally the participants were asked if they needed the sexologist.

Results: Only 3/54 pts (5.5%) refused to participate in our study. Of 51 participants, 44 (86.3%) reported that sexuality was an important or a very important aspect in their lives, while only 7 pts (13.7%) considered it as an unimportant aspect. 22 pts (43.13%) had disturbances of body image, 24 (47%) had sexuality greatly affected, and 36 (70.5%) sexual dissatisfaction after BC. 17 pts (33.3%) would require the help of the sexologist.

Conclusions: Our results suggest that despite the significant changes and negative influence in their sexuality, few pts require the help of the sexologist. Further studies will be needed to understand the reasons for this disparity.

E48

WHAT IS THE BEST THERAPEUTIC SEQUENCE FOR ER-POSITIVE/HER2-NEGATIVE METASTATIC BREAST CANCER IN THE ERA OF CDK4/6 INHIBITORS? A SINGLE CENTER EXPERIENCE

Crocetti S.[1], Pistelli M.[1], Tassone L.[1], Marcantognini G.[1], Bastianelli L.[1], Della Mora A.[2], Merloni F.[1], Cantini L.[1], Scortichini L.[1], Agostinelli V.[1], Ballatore Z.[1], Savini A.[1], Maccaroni E.[1], Berardi R.[1]

[1]Clinica Oncologica e Centro Regionale di Genetica Oncologica, Università Politecnica delle Marche, AOU Ospedali Riuniti, Ancona; [2]UO Oncologia di Macerata, Area Vasta 3, Macerata*

Background: Endocrine therapy has historically formed the basis of treatment for ER+/HER2- metastatic breast cancer (MBC). The development of endocrine resistance has led to the development of newer endocrine drug combinations. Use of CDK4/6 inhibitors (CDK4/6i) has significantly improved progression-free survival in this group of patients. There are many options in the sequencing of therapy for ER+ MBC in post-menopausal women. In this retrospective analysis, we evaluated the sequencing of

therapy since the advent of CDK4/6i combined with endocrine therapy (ET).

Patients and Methods: ER+/HER2- MBC patients referred to our Institution from January 2011 to December 2019 and treated with CDK4/6i in association with ET as 1-2 lines settings were included.

Results: 61 patients were included; median age was 61 years (range 35-78). As first line, 45.9% received CDK4/6i + ET, 31.1% ET and/or Everolimus and 23% chemotherapy. mPFS was respectively not reached vs 16 months(m) vs 20.9m (p=0.0231). There was a relevant but not statistically significant difference of mPFS between patients treated with or without neo/adjuvant chemotherapy (35.83m vs 18.33m) (p=0.5362). Patients hormone-naïve showed a longer mPFS (31.03m) compared to ones treated with adjuvant ET (22.17m) (p=0.9108). Patients with visceral disease (VD) had poor mPFS (17.53m vs 31.03m) (p=0.3088). 67.6% of patients in first line setting had VD progression. 56.7% of patients received a second line: 54% CDK4/6i + ET (mPFS: 5.53m), 22% ET +/- Everolimus (mPFS: 5.1m) and 24% chemotherapy (mPFS: 4.25m) (p=0.0948). VD was correlated to poor prognosis (7.47m vs 4.33m) (p=0.4242). 83.9% of patients in second line had VD progression. Patient treated with CDK4/6i + ET in second line after ET showed a longer mPFS of 9.57m, compared to after chemotherapy (4.47m). About CDK4/6i + ET in first line setting, 8.8% received ET +/- Everolimus in second line, while 5.8% chemotherapy, reporting a longer mPFS (3.015m vs 5.65m respectively) (p=0.1707).

Conclusions: Our study confirms the benefit in PFS using CDK4/6i + ET as first line of treatment in patients with ER+/HER2- advanced breast cancer, according to literature. Our results suggest that this therapeutic strategy is recommended in second line if not used previously. Finally, chemotherapy seems to be the better option after CDK4/6i, although further prospective studies will be necessary to define the best therapeutic strategy.

E49

WHEN CANCER AFFECTS GENDER IDENTITY: LOOKING IN THE MIRROR AND FEELING DIFFERENT. EXPERIENCE OF WOMEN WITH BREAST CANCER

Ricci F.[1], Rossi L.[2], Fontana A.[1], Angelini F.[3], Tomao S.[4], Gozzi E.[2]

[1]Ospedale Santa Maria Goretti, Latina; [2]Università La Sapienza di Roma, Aprilia; [3]Ospedale Regina Apostolorum Albano Laziale, Albano; [4]Università La Sapienza di Roma, Roma

Background: Breast cancer (BC) is the leading cause of cancer death in women worldwide. Breast is a symbol of femininity, motherhood and sexuality: it represents women's gender identity. Within the basic oncological procedures – surgery, chemotherapy, radiotherapy, and hormone therapy– there will be a lot of changes in the body.

The trauma of being diagnosed and treated for breast cancer can impact greatly on women's gender identity and bodily image. The aim of our study was to evaluate the influence and changes of BC on the bodily image and the impact on women's quality of life.

Patients and methods: We enrolled 54 BC pts, mean age was 54 years.

Participants were invited to complete a structured questionnaire which included four close-up questions regarding self-image, before and after BC and its treatments, and the impact of changes to body image on women's quality of life.

Results: 3/54 pts (5.5%) refused to participate in our study. Of 51 participants, 22 (43.13%) had worsened self-image after BC. 15 pts (68.1%) feeling of losing control over one's own body and 7 (31.8%) had low moods, anxiety and feelings of shame. 19 pts (86.3%) had negative impact on their quality of life: they stayed at home and neglected some of their duties. Worsened self-image occurred after BC diagnosis in 15 pts (68.1%) while in 7 pts (31.8%) after BC treatment.

Conclusions: Our results suggest that changes of BC on the bodily image can negative impact on women's quality of life and functioning in society. In our experience most patients have had a worsening of their body image before BC treatment. Focusing on pts's bodily image before starting treatment could prepare pts for the treatment outcomes and the changes that await them.

E50

HER 2 LOW BREAST CANCER: FROM THE STATE OF THE ART TO FUTURE DEVELOPMENTS

Cubeddu A.[1], Fusco O.[1], Pastorini A.[1], Menatti E.[1], Caponigro G.[1], Cantini S.[1], Deligiannis P.[1], Bertolini A.[2], Maiolani M.[2], Declich P.[3], Prada M.[3], Poletti P.[4], Grechi A.[4], Franzini P.[4], Fregoni V.[5]

[1]ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio; [2]ASST della Valtellina e Alto Lario-Cure Palliative, Sondrio; [3]ASST della Valtellina e Alto Lario-Anatomia Patologica, Sondrio; [4]ASST della Valtellina e Alto Lario-Senologia, Sondrio; [5]ASST della Valtellina e Alto Lario-Breast Unit, Sondrio

Background: Breast cancer includes several biological entities with different significance both from a prognostic and clinical point of view. Her 2 low breast cancer represents a new entity whose prognostic characteristics and predictive meaning are still unclear. However, the advent of novel anti HER2 active agents in non amplified tumors suggests the potential predictive role of Her 2 low.

Methods: A retrospective monocentric observational trial has been proposed to define the characteristics of the HER 2 low population within our institution. Inclusion criteria required patients with breast cancer who performed biopsy and/or surgery from 1 January 2018 to 31 December 2019 with HER 2 with immunohistochemistry 1+ or 2+ with negative ISH.

Results: At the present analysis, in a case study of 269 patients within our institution who performed biopsy or surgery, 77 patients were enrolled. The median age was 64.9 (range 34-87). 52 (67.5%) were luminal A, 21% (27.3) luminal B, 4 (5.2%) triple negative. 44 were in Stage I (57.1%), 28 in Stage II (36.4%), 3 in Stage III (3.9%), 2 in Stage IV (2.6%). 6 patients (7.8%) received neoadjuvant treatment, 2 patients (2.6%) received first line treatment for metastatic disease, 7 patients (7.9%) received adjuvant treatment with chemotherapy, 9 patients (11.6%) 12 patients (15.6%) received an adjuvant hormonal therapy with tamoxifene and 43 patients (55.8%) with aromatase inhibitors.

Conclusions: The data suggest the extreme heterogeneity of breast cancer and how therapeutic decisions are conditioned by the main histopathological and clinical factors. New studies on cancer biology HER 2 low and the benefit of new anti HER 2 drugs are needed to implement diagnostic and therapeutic algorithm.

E51

BREAST CANCER : TIME BETWEEN ACCESS TO RECEPTION SERVICE CENTRE (CAS), INTERDISCIPLINAR TEAM (GIC) VISIT IN A SPOKE HOSPITAL OF PIEDMONT ONCOLOGY NETWORK (ROP)

Lattuada S.[1], Fora G.[1], Gasparre T.[1], Torazzo R.[1], Manachino D.[1], Posca T.[1], Zecchin D.[1], De Marino E.[1]

[1]*Sant'Andrea Hospital, Vercelli*

Background: Delay of therapies in oncology is one of prognostic factors determining the outcome. The Piedmont oncological network has proposed a new organisational model by setting the timing between visits cas and gic; these are affected by the mode of onset of neoplasia. Objective of the study is to assess the adherence to the indications of the rop and the interval between cas gic and surgery for breast cancer in the hospital spoke with the purpose to define classes of priorities for intervention.

Materials and Methods: The time between the cas visit and the gic visit was assessed in the light of the reports prepared by the service reception center.

Results: From January to December 2019, 740 patients for suspected cancer were visited. 104/740 (14%) visits were for suspected breast cancer. 99/104 (95%) visits confirmed breast cancer. cas and gic visits were performed for 37/104 (36%) patients. the waiting time of 24 days between the cas visit and the gic visit indicated by the oncological network of piedmont was respected for 21/37 (57%) patients. for 14/37 (38%) patients gic was performed after 24 days. for 2/37 (5%) the gic was discussed before the cas.

Conclusions: In consideration of the times indicated by the Piedmontese regional guidelines, the review of the clinical cases of the Sant'Andrea Hospital of Vercelli shows that for more than 50% of our patients the 24-day time between cas and gic has been respected.

E52

GENETIC SUSCEPTIBILITY OF BREAST AND OVARIAN CANCER IN SARDINIAN POPULATION

Palomba G.[1], Palmieri G.[2], Cossu A.[3], Paliogiannis P.[3], Pisano M.[2], Manca A.[2], Casula M.[1], Colombino M.[1], Rozzo C.[2], Sini M.C.[1]

[1]*ICB-CNR, Sassari;* [2]*IRGB-CNR, Sassari;* [3]*AOU, Sassari*

Patients who carry a high-risk mutation in one or both of the BRCA genes (BRCA1 or BRCA2) have a significantly increased risk of developing breast/ovarian cancer (BOC) and other cancers (eg, prostate cancer in male). Epidemiological data on incidence distribution of breast/ovarian cancer from 2016 at 2019 in North Sardinia are obtained from the local tumor registry and from the cumulative results of 209 genetic testing for BRCA gene mutations performed to all young breast cancer patients and all women (over 50 years) with family history of BOC (total of 164 cases); further 45 genetic testing are performed, on ovarian cancer patients, at any age. The results provide a different distribution of fraction mutations carrying by women and a higher prevalence of the brca2 mutation in the north of Sardinia than the entire population and highlight the presence of specific germline mutation associated with the "founder effect" in distinct genetic subgroups reflecting genetic drift. With advances in genome sequencing technology and reductions in the cost of next-generation sequencing, molecular profiling has become more accessible for clinical investigation and cancer research and allow to characterize those individuals who are potential targets for BRCA molecular-based therapeutics agents.

E53

REAL LIFE INCIDENCE OF ADVERSE EVENTS (AES) IN PATIENTS AFFECTED WITH ER-POSITIVE, HER2-NEGATIVE ADVANCED BREAST CANCER TREATED WITH PALBOCICLIB: A SINGLE INSTITUTION EXPERIENCE

Bolzacchini E.[1], Pugliese P.[1], Marussi D.[1], Epifani R.[1], Luchena G.[1], Bianchi R.[1], Gini G.[1], Gilardoni M.[1], Giordano M.[1]

[1]*ASST-Lariana, Como*

Background: Palbociclib in an oral inhibitor of cycline-dependent kinase 4/6, approved based on results of PALOMA trials for the treatment of ER-positive,HER-2 negative locally advanced or metastatic breast cancer(mBC) in combination with endocrine therapy(ET).

Methods: We retrospectively collected and analyzed clinical data of patients(pts)treated in our institution with Palbociclib plus ET between 2017 and 2019.We reported pts characteristics, adverse events (AEs),dose reduction, discontinuation rates.

Results: We treated 36 pts; median age was 62(range: 34-77);12 pts (33%) had newly diagnosed mBC;14 pts (38,8%) were diagnosed during adjuvant therapy; one pts presented with locally advanced inoperable disease,17/36(47%) had visceral disease and most of the pts 30/36(83%) had less than 3 metastatic sites;16/36(44%) were previously exposed to chemotherapy in neo/adjuvant setting.24/36 pts(66.6%) received adjuvant ET and 14/24(58%) progressed during adjuvant ET. Most all of the pts received palbociclib associated with ET in first line metastatic setting, one pts received palbociclib in 3rd line. Palbociclib was administrd in combination with an aromatase inhibitor in 50% patients and with fulvestrant in 50%. Hematological AEs were the most common toxicities reported: any grade neutropenia was observed in 30/36 pts(85%),G3/G4 neutropenia in 20/36(55.5%). Anemia G3 that required blood transfusion was recorded in one case during the 1st cycle. Thrombocytopenia G3 was observed in two pts (at 1st and 2nd cycle). Two pts experienced skin toxicity (G3 dermatititis at 3rd cycle and a G2 dermatitis at 8 cycle). The dose of palbociclib was reduced to 100 mg in 19 pts (52,7%) mostly for severe neutropenia and one patient for dermatitis. Palbociclib was subsequently reduced to 75 mg in 11 pts (in 10 pts for recurrent neutropenia and 1 patient for headache and nausea). The main reason for permanent discontinuation was progression; permanent discontinuation due to AEs occured in two pts (5.5%) for severe hematological toxicity. Three pts developed distal thrombosis during therapy (8%) and 2 of them (5.5%) were complicated with pulmonary embolism. Only one of them was previously exposed to chemotherapy. None of them had other risk factors.

Conclusions: Incidence of hematological AEs and outcome were similar to clinical trials. Incidence of venous thromboembolism rates seems much higher in clinical practice compared with PALOMA trials.Larger studies are required to confirm our preliminary findings.

F - Gynaecological Tumours

F01

CHARACTERISATION OF PATIENTS (PTS) WITH LONG-TERM RESPONSES TO RUCAPARIB IN RECURRENT OVARIAN CANCER (OC)

Lorusso D.[1], Oza A.M.[2], Tinker A.V.[3], Ray-Coquard I.[4], Oaknin A.[5], Coleman R.L.[6], Burris H.A.[7], Aghajanian C.[8], O'Malley D.M.[9], Leary A.[10], Welch S.[11], Provencher D.[12], Shapiro G.I.[13], Chen L.[14], Shapira-Frommer R.[15], Goble S.[16], Lin K.K.[16], McNeish I.A.[17], Kristeleit R.S.[18], Swisher E.M.[19]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome; [2]Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada; [3]BC Cancer, Vancouver, British Columbia, Canada; [4]Centre Léon Bérard and University Claude Bernard and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Lyon, France; [5]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [6]US Oncology Research, The Woodlands, Texas, USA; [7]Sarah Cannon Research Institute at Tennessee Oncology, Nashville, Tennessee, USA; [8]Memorial Sloan Kettering Cancer Center, New York, New York, USA; [9]The Ohio State University, James Cancer Center, Columbus, Ohio, USA; [10]Gustave Roussy Cancer Center, INSERM U981, and Groupe d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens (GINECO), Villejuif, France; [11]London Regional Cancer Centre, London, Ontario, Canada; [12]Institut du Cancer de Montréal, CHUM Centre hospitalier de l'Université de Montréal, Université de Montréal, Montreal, Quebec, Canada; [13]Dana-Farber Cancer Institute, Boston, Massachusetts, USA; [14]University of California San Francisco, San Francisco, California, USA; [15]Oncology Institute, Sheba Medical Center, Tel Hashomer, Israel; [16]Clovis Oncology, Inc., Boulder, Colorado, USA; [17]Imperial College London, London, United Kingdom; [18]UCL Cancer Institute, University College London and UCL Hospitals, London, United Kingdom; [19]University of Washington, Seattle, Washington, USA

Background: Molecular interrogation of pts who derive durable benefit from PARP inhibitor treatment would allow insight into features associated with improved outcomes. We describe long-term responders from Study 10 (NCT01482715) and ARIEL2 (NCT01891344), studies of the PARP inhibitor rucaparib for the treatment of high-grade recurrent OC.

Methods: This analysis included pts enrolled in Study 10 (*BRCA1* or *BRCA2* [*BRCA*]-mutant OC; Part 2A: platinum sensitive, 2–4 prior chemotherapies; Part 2B: any platinum status, 3–4 prior chemotherapies) and ARIEL2 (*BRCA*-mutant or wild-type OC; Part 1: platinum sensitive; Part 2: any platinum status, 3–4 prior chemotherapies). Final results from Study 10 (n=54) and ARIEL2 (n=491) were pooled. Long-term responders were defined as pts with duration of response (DOR) ≥1 y, and short-term responders as pts with a response followed by a short duration to disease progression, resulting in a DOR ≤20 weeks; responses were evaluated using RECIST v1.1. Targeted next-generation sequencing was used to detect deleterious mutations and loss of heterozygosity (LOH) in tumours.

Results: Overall, 29% (159/545) of enrolled pts were responders; 25% (138/545) had confirmed responses. 28% (38/138) had confirmed long-term responses, including 16/138 (12%) with DOR ≥2 y; 29 pts had a short-term response, including 16 with confirmed responses. Both long- and short-term responders received a median of 2 prior platinum-based therapies. Among pts with *BRCA* mutations, *BRCA* homozygous deletion or rearrangement was detected in 15% (4/27) of long-term responders vs 0% (0/15) of short-term responders. In an expanded analysis of the 95 pts with a *BRCA* mutation and a confirmed response (regardless of DOR), pts with *BRCA* homozygous deletion or rearrangement had significantly longer DOR to rucaparib than pts with other mutation types (median not reached vs 0.6 y; HR=0.22; *P*=0.016). There

was no apparent difference in *BRCA* gene or mutation location for long- vs short-term responders. Nine of the 11 long-term responders with *BRCA* wild-type OC had high genome-wide LOH (≥16% LOH) including OC associated with deleterious *RAD51C/D* mutations (n=2).

Conclusions: Long-term responders to rucaparib include OC with *BRCA* mutation, particularly homozygous deletion or rearrangements, which would not be susceptible to somatic reversion mutations, and *RAD51C/D* mutations.

F02

CORRELATION BETWEEN MIRNA EXPRESSION PATTERN AND PLATINUM SENSITIVITY IN HIGH GRADE SEROUS OVARIAN CANCER: A MONOCENTRIC RETROSPECTIVE EXPERIENCE

Lancia F.[1], Mauro E.[1], Tiberi E.[1], Trimarchi E.[1], Marzola M.[1], Gafà R.[1], Negrini M.[1], Frassoldati A.[1]

[1]*Nuovo Arcispedale Sant'Anna, Ferrara*

Background: Despite the therapeutic innovations of recent years, ovarian cancer remains a leading cause of morbidity and mortality. Therefore, markers for disease prediction and prognosis are highly desirable for early diagnosis as well as for helping optimize and personalize treatment. Recently, miRNAs, short-sequence of non-coding RNAs, have emerged as new biomarkers in the clinical diagnosis and treatment of ovarian cancer. The dysregulation of miRNAs is involved in the initiation and progression of human cancers including ovarian cancer, and strong evidence that miRNAs can act as oncogenes or tumor suppressor genes has emerged. The aim of our study is to evaluate if platinum sensitivity is associated to a specific pattern of miRNA expression.

Matherials and Methods: We retrospectively selected pts with histological diagnosis of HGSOC from 2010 to 2019, stage FIGO IIC-IIIC, treated with a first line platinum-based chemotherapy. PTS were divided in 2 groups: 1) highly platinum-sensitive (PFI>12months); 2) Partially platinum-sensitive/platinum-resistant (PFI<12months). For each pts we evaluated miRNA expression pattern in formalin-fixed paraffin-embedded samples (primary tumor or metastasis) using NGS with the Illumina platform.

Results: We collected 6 pts with HGSOC diagnosis for each group (a total of 12pts). Among the 2500 miRNA detected using NGS we identified 26 miRNA with a different expression pattern between the 2 groups, in particular: 16 miRNA (miR-3928-3p, miR-501-5p, miR-382-3p, miR-432-5p, miR-3403p, miR-885-5p, miR-675-3p, miR-218-2-3p, miR-218-5p, miR-491-5p, miR-181a-3p, miR181a-5p, miR-9-3p, miR-9-5p, miR-6832-3p, miR-3607-3p) were over-expressed in Group 2 and had a low expression in Group 1. Vice versa 10 miRNA (miR-4271,

miR-6125, miR-205-3p, miR-3180-5p, miR-6255p, miR-194-5p, miR-192-5p, miR-215-5p, miR-378j, miR-6860) had a low expression in Group 2 and a over expression in Group 1.

Conclusions: Despite the small sample size, this study showed the correlation between some miRNA and the platinum sensitivity of HGSOC, suggesting that these short-sequences of non-coding RNAs could have a prognostic and predictive value. Probably in the near future we could use miRNA expression pattern as a biomarker to select the most effective treatment for each patient affected by ovarian cancer.

F03

PHENOTYPIC AND FUNCTIONAL PROPERTIES OF NATURAL KILLER CELLS IN PATIENTS WITH OVARIAN CANCER

Provinciali N.[1], Pesce S.[2], Greppi M.[2], Tabellini G.[3], Patrizi O.[3], Rampinelli F.[4], Obino V.[2], Olive D.[5], Sivori S.[2], Buttiron Webber T.[6], Paleari L.[7], Rutigliani M.[6], Di Luca M.[6], Gorlero F.[6], Parolini S.[3], DeCensi A.[6], Marcenaro E.[2]

[1]*Ente Ospedaliero Ospedali Galliera, Genova;* [2]*Department of Experimental Medicine (DI.ME.S.), University of Genoa, Genoa;* [3]*Department of Molecular and Translational Medicine, Brescia, Italy, Brescia;* [4]*Department of Obstetrics and Gynecology, Spedali Civili of Brescia, Brescia;* [5]*Team Immunity and Cancer, CRCM, Aix Marseille Univ, CNRS, INSERM, Institut Paoli-Calmettes, Marseille;* [6]*Ente Ospedaliero Ospedali Galliera, Genoa;* [7]*ALiSa, Liguria Health Authority, Genoa*

Background: Natural Killer cells (NK) can recognize and kill tumor cells; this cytotoxic activity is regulated by activating and inhibitory signals. Different mechanisms of tumor escape have been described for cancer. We recently identified two mechanisms of tumor escape from NK cell immunosurveillance in ovarian cancer patients: the downregulation of the activating receptor NKp30 mediated by a soluble form of its ligand B7-H6 (sB7-H6) in the tumor microenvironment (TME), and the expression on NK cell surface of the immune checkpoint PD-1, originally identified in T cells. However, little is known about the impact of these mechanisms on ovarian cancer survival rate and the application of innovative immunotherapeutic approaches.

Material and methods: We isolated NK from peritoneal/ascitic fluid (PF) and peripheral blood (PB) of 50 patients with papillary serous ovarian cancer and from PB of healthy donors. NK cells have been analyzed for expression of both immune checkpoints, including PD-1, and activating NK receptors and their role in the modulation of NK cytotoxicity towards PD-Ls+ tumor cells.

Results: PD-1 expression on PB-NK was shown in 25% of samples from Human Cytomegalovirus+ otherwise healthy donors. PD-1 was confined to fully mature NK cells with low level of activating NK receptors, including NKp30. PD1+ve NK were also found in PF and PB from

most patients, with a higher proportion in PF than in PB for the same patient. Our preliminary data indicate that PD-1+ve PF-NK cells, different from PD-1-ve PF-NK and PB-NK cells, express a most immature phenotype, a proliferative ability and high levels of activating receptors. This subset has the ability to efficiently kill cancer cells once the PD-1-PD-Ls inhibitory interactions have been overcome.

Conclusions: In the ovarian cancer TME, different mechanisms of tumor escape exist that may impair the NK cell capability to kill the tumor, including the expression of PD-1. However, these NK cells are not anergic, but are able to efficiently kill the tumor in the presence of PD-1/PD-Ls blockade monoclonal antibodies. These data may partially explain why PD-1/PD-L1 inhibitors are being investigated in clinical trials of gynecological cancers. Further studies will be needed to understand how to fully activate these cells, for example by blocking other inhibitory interactions existing between NK/tumor cells.

F04

INFLUENCE OF BRCA1/2 STATUS AND CHEMOTHERAPY RESPONSE SCORE IN PATIENTS WITH ADVANCED OVARIAN CANCER UNDERGOING NEOADJUVANT CHEMOTHERAPY AND SURGERY

Tuninetti V.[1], Tuninetti V.[1], Marocco F.[1], Maldi E.[1], Robella M.[1], Maggiorotto F.[1], Vaira M.[1], Magistris A.[1], Campanella D.[1], Turinetto M.[1], Scotto G.[1], Aimar G.[1], Pisacane A.[1], Sapino A.[1], De Simone M.[1], Valabrega G.[1], Ponzone R.[1]

[1]*Istituto di Candiolo, FPO - IRCCS, Candiolo (Torino)*

Background: In advanced ovarian cancer (AOC), complete cytoreduction (CC0) at primary debulking surgery (PDS) is associated with the best outcome; however, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) may increase CC0 rates and decrease surgical morbidity. BRCA1/2 status and chemotherapy response score (CRS) have been associated with improved chemosensitivity and survival.

Patients and Methods: All patients with BRCA1/2 status available and submitted to NACT-IDS at the Candiolo Cancer Institute between 2010-2019 were included. The CRS was assessed (patients operated before 2015) and reassessed (patients operated afterwards) by two dedicated pathologists. The distribution of main clinical-pathological variables was compared between patients with (BRCA$_{mut}$) vs. without (BRCA$_{wt}$) mutations and in patients with low (CRS1-2) vs. high (CRS3) response to NACT. Furthermore, all variables were correlated with the likelihood of achieving CC0 at surgery vs. not (CC>0)? Progression free survival (PFS) was computed using the Kaplan-Meier method and the log-rank test was used to assess survival differences. A multivariate Cox regression analysis was performed to control for confounders.

Results: Out of 68 patients included, 16 (23.5%) were carriers of germ-line mutations of either *BRCA1* (10, 14.7%) or *BRCA2* (6, 8.8%). Age at diagnosis was higher in patients with BRCA$_{wt}$ vs. BRCA$_{mut}$ (median 66.0 vs. 59.5 years; P=.02), while response to NACT assessed by Ca 125 reduction or CRS was not significantly different. Attainment of CC0 at surgery was correlated with CRS3 vs. CRS1-2 (78.7% vs 21.3%; P=.003), age <60 vs. >60 years (86.4% vs 13.6%; P=.04) and IDS vs. postDS (78.7% vs. 21.3%; P = 0.1). Longer PFS was associated with CRS3 (median PFS 51.3 vs 23.1 months; P=.009) and low (<200 U/mL) preoperative Ca 125 levels (median PFS 42.3 vs 19.1 months; P=.001). Conversely, the attainment of CC0 (median PFS 36.8 months vs 19.1 months P = .06) or BRCA$_{mut}$ status (median PFS 42.9 months vs 28.0 months; P=.14) were not associated with significant survival gains. At multivariate analysis, both CRS3 [Hazard Ratio (HR) 3.75; P=.017] and low post NACT Ca 125 levels (HR: 2.55; P=.009) retained their prognostic significance.

Conclusions: In patients with AOC, chemosensitivity assessed by both CRS and post-NACT Ca 125 levels predicts complete surgical cytoreduction and it is associated with improved survival irrespective of surgical outcome and BRCA1/2 status.

F05

PREDICTIVE FACTORS OF CARBOPLATIN-INDUCED THROMBOCYTOPENIA IN OVARIAN CANCER

De Scordilli M.[1], Bartoletti M.[1], Mazzeo R.[1], Alberti M.[1], Michelotti A.[1], Lisanti C.[1], Parnofiello A.[1], Bertoli E.[1], Buriolla S.[1], Pelizzari G.[1], Cortiula F.[1], Basile D.[1], Gagno S.[2], Scalone S.[1], Nicoloso M.S.[1], Corsetti S.[1], Lombardi D.[1], Gerratana L.[1], Sorio R.[1], Puglisi F.[1]

[1]*Department of Medical Oncology, Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, Italy, Aviano;* [2]*Clinical and Experimental Pharmacology Unit, Centro di Riferimento Oncologico (CRO), IRCCS, Aviano, Italy, Aviano*

Background: Carboplatin-induced thrombocytopenia (CIT), defined by platelets count < 150.000/μL, frequently requires dose reductions and/or delays of therapy, with impaired dose intensity and potentially worse outcome. No predictive factors of CIT have yet been established in clinical practice.

Material (patients) and methods: We retrospectively analyzed a cohort of 227 consecutive ovarian cancer patients treated with carboplatin-based chemotherapy after primary debulking surgery between May 2004 and April 2020 at National Cancer Institute in Aviano (Italy). Clinicopathological characteristics and laboratory values at baseline were tested with uni-/multivariate logistic regression to create a predictive score for CIT. ROC analyses were performed to identify optimal cut-off values for variables significantly associated with CIT. Known prognostic factors were evaluated in overall survival (OS) with Cox regression model.

Results: Overall, 148 (66.1%) patients had a FIGO stage III and 29 (13%) a FIGO stage IV; residual disease was present in 93 (42.1%) patients after radical surgery. A total of 70 (30.8%) patients experienced haematologic toxicity, 51 (24.1%) with carboplatin dose reduction, among which 22 (43.1%) for CIT. Median OS was 74.6 months and known prognostic factors for a lower OS, such as residual tumor after radical surgery (HR 2.15, p = 0.031) and FIGO stage IV (HR 4.82, p = 0.008), were confirmed by uni-/multivariate analysis. Platelets count (PLT) (OR 0.99, CI 95% 0.98-0.99, p = 0.009) and weight (OR 1.04, CI 95% 1.01-1.07, p = 0.016) at baseline were significantly associated with CIT. After ROC-defined cut-off definition, PLT and weight were both statistically significant at multivariate analysis with a cut-off value of 295.000/μL (OR 0.13, p < 0.001) and 79.4 kg (OR 4.86, p = 0.006), respectively. A score combining PLT < 295.000/μL and weight > 79.4 kg was implemented and was able to stratify the study population into low, intermediate and high risk groups according to CIT (OR 5.38, p = 0.005 with one of the two conditions, OR 39.75, p < 0.001 with both conditions).

Conclusions: In patients with ovarian cancer receiving a carboplatin-based adjuvant therapy, platelets count and weight at baseline are two easy-to-assess parameters to predict CIT risk. Prospective validation is planned to prove the clinical efficacy and utility of the present score.

F06

BEVACIZUMAB AND OVARIAN CANCER: A MATTER OF PHARMACOKINETICS

Fiordoliva I.[1], Maccaroni E.[1], Giampieri R.[1], Agostinelli V.[1], Tronconi F.[1], Zepponi L.[1], Bianchi F.[1], Pagliacci A.[1], Pistelli M.[1], Savini A.[1], Belvederesi L.[1], Pagliaretta S.[1], Brugiati C.[1], Murrone A.[1], Berardi R.[1]

[1]Clinica Oncologica-Universita' Politecnica Delle Marche-Ospedali Riuniti di Ancona, Ancona

Background: Bevacizumab is a humanized monoclonal antibody against vascular endothelial growth factor and is used as both first- and second-line treatment in combination with standard chemotherapy and subsequent maintenance for FIGO stage IIIB-IV ovarian cancer (OC). FIGO stage, residual disease after surgery or lack of surgery altogether are prognostic factors in this setting. Aim of the study is to assess whether estimates in Bevacizumab pharmacokinetics might have an impact on patients' survival.

Materials and methods: We retrospectively enrolled OC patients treated between May 2015 and May 2020 at our institution. Clinico-pathological data and blood tests results of OC patients treated with bevacizumab were collected. Volume of distribution (VD, mL) and clearance (CL, mL/h) were calculated using body weight, albumin and alkaline phosphatase at baseline, as previously published. Bevacizumab time to elimination (TTE) was calculated as [VD/CL] and expressed in days. Cut-off values for all tests were set by using median

values of VD, CL and TTE. Kaplan-Meier method was used to calculate Progression-Free Survival (PFS). Level of statistical significance of all tests was set at 0.05.

Results: Thirty-two first-line patients were enrolled; median age was 59.6 years (range 32-80). Most frequent histology was high-grade serous OC (88%). Most patients had stage IIIB-IIIC (81%) disease. Median VD was 2461.35 mL, median CL was 7.88 mL/h and median TTE was 13.14 days. At the time of analysis, 53% (17/32) patients had already progressed to bevacizumab. Low vs high bevacizumab VD was not associated with significantly different PFS (p=0.4118). Low vs high bevacizumab CL was also not associated with statistically significant differences in PFS (p=0.7045). TTE was associated with statistically significant differences in PFS: in patients with greater TTE median PFS was 23.34 vs 12.86 months of patients with shorter TTE (HR:2.92, 95%CI:1.05-8.11, p=0.0391). Residual disease after surgery, histology, age, BRCA status were not associated with differences in PFS also.

Conclusions: Our study suggests that Bevacizumab pharmacokinetics could determine differences in first-line treatment PFS in OC patients treated with this drug. We intend to enlarge our patients' series to better estimate the role of bevacizumab pharmacokinetics in this setting.

G - Neuroendocrine Tumours and Sarcomas

G01

TEMOZOLOMIDE ALONE OR COMBINED WITH CAPECITABINE FOR THE TREATMENT OF METASTATIC NEUROENDOCRINE NEOPLASIA: A "REAL WORLD" DATA ANALYSIS

Bongiovanni A.[1], Liverani C.[1], Foca F.[2], Fausti V.[1], Signoretti M.[3], Pieri F.[4], Tartaglia A.[5], Galassi R.[6], Cavaliere D.[7], Severi S.[8], Di Menna G.[9], Mercatali L.[9], De Vita A.[9], Riva N.[9], Calpona S.[10], Miserocchi G.[10], Spadazzi C.[10], Gurrieri L.[10], De Bonis S.A.[10], Ibrahim T.[10]

[1]Centro di Osteoncologia e Tumori Rari, Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori IRST, IRCCS, Meldola; [2]Unità di Biostatistica, Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori IRST, IRCCS, Meldola; [3]U.O. di Gastroenterologia/Endoscopia digestiva, Ospedale G.B. Morgagni-L.Pierantoni, AUSL Romagna, Forlì; [4]U.O. di Anatomia Patologica Ospedale G.B.Morgagni-L.Pierantoni, AUSL Romagna, Forlì; [5]U.O. di Endocrinologia Ospedale G.B. Morgagni-L. Pierantoni, AUSL Romagna, Forlì; [6]U.O. di Medicina Nucleare Ospedale G.B. Morgagni-L. Pierantoni, AUSL Romagna, Forlì; [7]UO di Chirurgia Generale e Terapie Oncologiche Avanzate, Ospedale G.B. Morgagni-L. Pierantoni, AUSL Romagna, Forlì; [8]UO di Medicina Nucleare, Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori IRST, IRCCS, Meldola; [9]Centro di Osteoncologia e Tumori Rari, Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori IRST, IRCCS, Meldola; [10]Centro di Osteoncologia e Tumori Rari, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST, IRCCS, Meldola

Background: Neuroendocrine Neoplasia (NEN) are rare and groups tumors with different prognosis and response

to therapy. This heterogeneity depends of site of origin, morphology and ki67. Temozolomide (TEM) seems to be active in metastatic NEN but there are limited evidence in gastrointestinal (GI) NENs. In this paper we analyzed the "real-world" data on TEM alone or associated to capecitabine (CAPTEM) in patients (pts) with mNEN.

Patients and methods: One hundred consecutive advanced NEN pts treated with TEM or CAPTEM between 2009 and 2019 were included. A pre-treatment Tumor growth rate (TGR0) was calculated. Overall survival (OS), Progression-free survival (PFS), tolerance, objective response (ORR) and disease control rate (DCR)were analyzed. To balance baseline covariates for pts treated with TEM and CAPTEM treatment a propensity score analysis and Cox regression models were used.

Results: TEM–based therapy was administered to 95 pts (26.3% CAPTEM and 83.7% TEM) with 59 (range:26-85) years median age. ECOG performance status was 0-2. About half of pts (49.5%) has more than 2 sites of metastasis. Twenty (21.1%) G3 neuroendocrine carcinoma and 9(9.4%) patients G3 neuroendocrine tumors (NET) were included. On whole group mPFS was 10.4 (95%CI:6.0-11.5) months (m). In multivariate analysis, an higher risk of progression was observed for NEC G3 pts (HR:2.70,95%CI:1.25-5.84) and for a TGR $\geq$19.55 (HR:2.53, 95%CI:1.45-4.40). Well differentiated morphology had a protective effect, although not statistically significant due to collinearity (HR: 0.62, 95%CI: 0.36-1.07). Median OS was 23.4 m (95%CI: 17.0-29.0) and it was similar comparing TEM and CAPTEM (23.9 vs. 20.5 m, p=0.585). In multivariate analysis, pts with TGR =19.55 had an higher risk of death (HR:2.18, 95%CI:1.16-4.11) than those with TGR<19.55, as well as NEC G3 (HR: 2.42, 95%CI:1.04-5.59) compared with NET pts. No differences in terms of mPFS and mOS were seen according the primitive site. On 86 pts evaluable for response, ORR was 44.1% with a DCR of 70.9%. Mild adverse events (grade I-II) included anemia, neutropenia and headache. Rare cases of grade 3 neutropenia and thrombocytopenia were recorded.

Conclusions: TEM-based regimens are associated with a high DCR and a relatively tolerable toxicity profile in NENs of Pancreatic, GI, Lung and other origins. Also pts with NET G3 tumors have a benefit. This regimen warrants further exploration in a prospective clinical trial not only in pancreatic but also intestinal and lung NETs.

G02

ACTIVITY AND SAFETY OF LANREOTIDE AUTOGEL (LAN) AND TEMOZOLOMIDE (TMZ) COMBINATION IN PATIENTS WITH PROGRESSIVE THORACIC NEUROENDOCRINE TUMOURS (TNETS): THE ITALIAN ATLANT STUDY RESULTS

BRIZZI M.P.[1], Berruti A.[2], Spada F.[3], Ibrahim T.[4], Colao A.[5], Faggiano A.[6], Marconcini R.[7], Vaccaro V.[8], Giuffrida D.[9], Rivaroli A.[10], Houchard A.[11], Fazio N.[12], Ferolla P.[13]

[1]Oncologia Medica, A.O.U. San Luigi Gonzaga, Orbassano; [2]ASST-Spedali Civili di Brescia, Brescia; [3]European Institute of Oncology, IRCCS, IEO, Milan; [4]IRCCS Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola (FC); [5]Università Federico II di Napoli, Naples; [6]Dipartimento di Medicina Sperimentale, Università Sapienza di Roma, Rome; [7]AOU Pisana, Santa Chiara Hospital, Pisa; [8]Regina Elena National Cancer Institute, IRCCS, Rome; [9]Istituto Oncologico del Mediterraneo, Viagrande (CT); [10]Ipsen, Assago, Milan; [11]Ipsen, Boulogne-Billancourt, France; [12]European Institute of Oncology, IRCCS, IEO, Milan; [13]Multidisciplinary NET Center, Umbria Regional Cancer Network, Perugia

Background: LAN and TMZ are among the main therapies recommended for progressive TNETs but prospective data are lacking. We present safety and efficacy outcomes of this combination in progressive TNETs.

Patients and methods: ATLANT was a 12-month, phase 2, multicentre, single-arm, open-label study. Eligible patients had unresectable, locally advanced or metastatic, well-differentiated TNETs (bronchial or thymic, typical or atypical carcinoid) with baseline radiological progression (RECIST v1.1) in the previous 12 months. Patients received subcutaneous LAN 120 mg and oral TMZ 250 mg/day over 5 days, every 28 days. Primary endpoint: disease control rate (DCR) at 9 months (RECIST v1.1 complete response, partial response or stable disease [clinically relevant: $\geq$30%, unacceptable: $\leq$10%]). Data were analysed using exact binomial proportion tests for one-way tables.

Results: Patients (N=40; 60% male) had a mean (SD) age of 64.9 (11.8) years. The primary tumour site was: lung, 90%; thymus, 10% (typical, 20.0%; atypical, 52.5%; carcinoid, 27.5%). Mitotic count (mitoses/2 mm²): <2: 30%; $\geq$2–<10: 42.5%; $\geq$10: 2.5%; not done: 25%. Ki-67 expression (N=20): <4%: 10%; 4–<25%: 80%; $\geq$25%: 10%. TNM staging: primary tumour TX: 5.1%, T0: 46.2%, T1: 7.7%, T2: 12.8%, T3: 10.3%, T4: 17.9%; regional lymph node N0: 56.4%, N1: 2.6%, N2: 23.1%, N3: 17.9%; distant metastasis M0: 5.1%, M1: 94.9%. Locally assessed DCR at 9 months (ITT population; N=40) was 35.0% (95%CI: 20.63; 51.68) (significantly higher than 10% p<0.0001 but not superior to 30% p=0.297). Median progression-free survival was 37.1 (95%CI: 24.1; 52.9) weeks. In total, 97.5% of patients had treatment-emergent adverse events (TEAEs; >90% of TEAEs were Grade 1/2), 9 (22.5%) patients had serious TEAEs (of which 2 were treatment related), 2 TEAEs led to withdrawal of study treatment, and 2 led to death. The observed TEAEs were in line with the known individual drug profiles, and there were no new or unexpected AEs. Most common TEAEs included nausea (52.5%), vomiting (32.5%) and diarrhea (30.0%).

Conclusions: These results suggest that the LAN and TMZ combination was generally well tolerated and could

be an effective regimen for managing progressive TNETs. Trial registration numbers: NCT02698410; EudraCT: 2014-005579-10.

G03

THERAPEUTIC SEQUENCES IN ADVANCED GRADE 1-2 PANCREATIC NEUROENDOCRINE TUMORS (PNET)

Maggio I.[1], Panzuto F.[2], Manuzzi L.[1], Dall'Olio V.[3], Rinzivillo M.[2], Campana D.[4], Lamberti G.[4]

[1]Sant'Orsola Malpighi University Hospital, Alma Mater Studiorum University of Bologna, Bologna; [2]Digestive Disease Unit, Sant'Andrea University Hospital, ENETS Center of Excellence, Rome; [3]Alma Mater Studiorum University of Bologna, Bologna; [4]NET Team Bologna, ENETS Center of Excellence, Sant'Orsola Malpighi University Hospital, Alma Mater Studiorum University of Bologna, Bologna

Background: There are several approved treatments in well-differentiated pancreatic neuroendocrine tumors (pNET) but there is no evidence about the best therapeutic sequence for these patients (pts). The objective of this study was to identify the optimal therapeutic sequence.

Methods: We retrospectively collected data about pts with metastatic or locally advanced well-differentiated grade 1 or 2 pNET treated at 2 neuroendocrine neoplasia (NEN)-dedicated Italian Centers who received at least two lines of treatment for pNET. Radiological progressive disease must have had occurred before switching to the second line of treatment. Factors associated with progression-free survival (PFS) and overall survival (OS), including treatment sequences, were analyzed.

Results: Of the 68 included pts, 34 (50%) were male. Fifteen pts (22.1%) had a G1 pNET and 53 (77.9%) a G2 tumor, with median Ki67 of 6.9% (range 0.6-20). Four (5.9%) pts presented localized disease, 55 (80.9%) hepatic lesions, and 9 (13.2%) extrahepatic disease. Primary tumor had been resected in 40 pts (58.8%). First-line therapy was somatostatin analog (SSA) in 52,9%, SSA + peptide receptor radionuclide therapy (SSA+PRRT) in 30.9%, and everolimus (11.8%), chemotherapy (CHT) in 2,9%, and other in 1.5%. Second-line therapy was SSA in 8.8% of pts, high-dose SSA in 7.4%, SSA+PRRT in 9.1%, sunitinib in 11.8%, everolimus in 30.9%, CHT in 16.2%, and other in 5.9%. Median PFS was 14 mo (95%CI 6.9-21.1) for first line and 14.2 mo (95%CI 11.1-17.3) for second line. To evaluate which was the best therapeutic sequence, we compared outcome of 33 pts who received either first-line SSA+PRRT (concomitant) to first-line SSA followed by SSA+PRRT at progression (sequential). In this cohort, median time to strategy failure (TSF) was 46 mo (95%CI 35-56.9) and OS was 94.6 mo (95%CI 61.8-127.6). Median TSF was longer with the sequential than with the concomitant strategy (74.4 vs 40 months, respectively; p= 0.007). At multivariate analysis, sequential therapy was associated with a reduced risk for progression (HR 0.28, 95%CI 0.11-0.74, p= 0.011).

Conclusions: Sequential SSA-PRRT therapy was associated with improved TSF in patients with pNET.

G04

EFFICACY OF POST-OPERATIVE RADIATION THERAPY IN NON-METASTATIC MERKEL CELL CARCINOMA: A REGISTRY-BASED ANALYSIS

Manuzzi L.[1], Maggio I.[1], Lamberti G.[1], Siepe G.[2], Campana D.[3]

[1]DIMES - Università di Bologna, Bologna; [2]Radioterapia "Morganti" - Policlinico di Sant'Orsola, Bologna; [3]DIMEC - Università di Bologna, Bologna

Background: Merkel cell carcinoma (MCC) is a rare aggressive neuroendocrine tumor of the skin. The optimal management of non-metastatic MCC is still unclear but it is crucial to decrease relapse risk and improve survival. We sought to assess the efficacy of radiation therapy (RT) of MCC without distant metastases (M0 MCC) by analyzing data from the Surveillance, Epidemiology, and End Results (SEER) registry.

Methods: We extracted from the SEER Registry data about M0 MCC patients, identified by the 8247 ICD-03 code, irrespective of the site of origin. We collected data about stage at diagnosis, site and size of primary, extent of surgery, lymph node directed surgery, number of involved lymph nodes, RT, and survival outcome. Primary endpoint was overall survival (OS).

Results: Of 9773 MCC patients in the SEER registry, 2335 were M0 MCC (63% male, median age 77 years). MCC originated from skin of the limbs in 994 (61.6%), head and neck district in 386 (23.9%), and trunk in 234 (14.5%). Lymph nodes were negative in 1577 patients (67.5%), while among the 687 (32.5%) MCC with nodal involvement this was microscopic in 214, macroscopic in 233, not otherwise specified (NOS) in 240; 71 had in-transit metastases. Post-operative RT was performed in 1212 (51.9%) patients. Overall, median OS of M0 MCC patients was 56 months (95%CI: 50.7-61.3) and was affected by age, site, tumor size, nodal involvement, type of surgery of primary and RT (HR for RT: 0.65 [95%: 0.53-0.79]; p<0.001) at multivariate analysis. In the 1577 with negative lymph nodes, after correcting for confounding factors, OS was affected by age, sex, site, size of primary, extent of surgery and RT (HR for RT: 0.63 [95%: 0.47-0.82]; p<0.001). Among 687 patients with positive lymph nodes (67% male, median age 74), at multivariate analysis OS was affected by age, nodal involvement, number of positive lymph nodes and RT (HR for RT: 0.67 [95%CI: 0.49-0.92]; p=0.012).

Conclusions: RT was associated with a decreased risk for death in M0 MCC, irrespective of nodal status.

G05

IMMUNOGENETIC AND IMMUNOPHENOTYPIC CHARACTERIZATION OF MERKEL CELL CARCINOMA

De Summa S.[1], Strippoli S.[2], Fucci L.[1], Mangia A.[1], Armenio A.[1], Figliuolo F.[1], Pinto R.[1], Lorusso C.[1], Quaresimini D.[1], Catacchio I.[1], Saponaro C.[1], Zambetti M.[1], De Risi I.[1], Palermo L.[1], Ruggieri E.[1], Tommasi S.[1], Guida M.[1]

[1]IRCCS Istituto Tumori Giovanni Paolo II, Bari; [2]Barletta Hospital, Barletta

Background: Merkel Cell Carcinoma (MCC) is a rare and aggressive malignancy, commonly occurring in elderly white men mostly over 50 years and in sun-exposed areas. MCC seems to be associated to exposure to ultraviolet radiation and polyomavirus (MCPyV) infection. To date, the major peculiarity in the MCC genomic patterns have been described in relation to the presence or not of the viral infection. Brisk response and high $CD8^+$ lymphocytic infiltration together with tumor PD-L1 expression have been found associated to a better outcome. The approval of immune-checkpoint inhibitors (ICIs) has been a fundamental step forward in the management of MCC, which historically was treated with chemotherapy. ICI treatment displayed improved overall survival and durable response irrespectively of virus infection.

In the present study, we aimed to focus on immune-related genes, both at DNA and expression levels, integrating microenvironment data to better elucidate the immunological setting of MCC.

Material and methods: A cohort of 25 MCC patients, 50% presenting MCPyV infection, underwent mutational analysis through a custom-designed NGS targeted amplicon-based panel related to 41 genes involved in immune checkpoint/response and inflammation. $iCD4^+$, $pCD4^+$, $iCD8^+$ and $pCD8^+$ lymphocytic infiltration and PDL-1 have also been analyzed by IIC.

Results: Unsupervised analysis showed two groups of patients: one characterized by 30% with sun-exposed lesions, 50% of MCPyV-positivity and 80% PD-L1 positive cases; the other was associated to the predominant presence of CD276, immuboglobulin family gene alteration, (73%), is mostly enriched in MCPyV-positive and subject with sun-exposed lesions. Moreover, 53% of MCCs expressed PD-L1 and 60% showed low $iCD4^+$ lymphocytic infiltration. Expression study identified a cluster characterized by 71% of MCPyV-positive subjects, 71% of Ki-67 low expression, 85.71% of PD-L1 expressing cases and $iCD8^+$ lymphocytic infiltration. Integrated analysis highlighted a cluster with the presence of CD276 mutation, low TMB, negative expression of PD-L1, low levels of $iCD4^+$ and $iCD8^+$ lymphocytic expression.

Conclusions: To fully benefit from the survival advantage of ICI treatment, a multilayer approach, including somatic alterations, microenvironment and gene expression could be the best one, also to eventually test combination therapies (e.g., targeted therapy and ICI)

G06

FIRST-LINE FLUOROPYRIMIDINE AND OXALIPLATIN CHEMOTHERAPY IN GASTRO-ENTERO-PANCREATIC GRADE 3 WELL-DIFFERENTIATED NEUROENDOCRINE TUMORS (NET G3)

Lamberti G.[1], Pusceddu S.[2], Ibrahim T.[3], Bongiovanni A.[3], Berardi R.[4], Torniai M.[4], Prinzi N.[2], Manuzzi L.[1], Campana D.[1]

[1]NET Team Bologna Centro di Eccellenza ENETS - Università di Bologna, Bologna; [2]IRCCS Fondazione Istituto Nazionale dei Tumori, Milano; [3]IRCCS Istituto Scientifico Romagnolo Per Lo Studio E La Cura Dei Tumori, Meldola (FC); [4]AOU Ospedali Riuniti, Ancona

Background: The 2019 World Health Organization (WHO) classification of neuroendocrine neoplasia (NEN) introduced the new category of well-differentiated NEN with Ki67 proliferation index $\geqslant 20\%$ (NET G3). Fluoropyrimidine-based regimens with oxaliplatin (FOLFOX/XELOX) were a treatment option in neuroendocrine carcinomas with low Ki67, but their efficacy in the newly defined NET G3 category is unknown. Objective of this study was to describe FOLFOX/XELOX efficacy in NET G3 and identify factors associated with outcome.

Patients and methods: We retrospectively collected consecutive gastro-entero-pancreatic NET G3 patients who received a FOLFOX/XELOX as first-line treatment at 4 NEN-dedicated Italian Centers. Concomitant somatostatin analog (SSA) treatment was allowed. Factors associated with response by RECIST, progression-free survival (PFS), and overall survival (OS) were analyzed.

Results: Thirty-four NET G3 patients (median age 55 years) were identified. Twenty-two patients (65%) had a pancreatic NET, while 12 (35%) had a gastrointestinal primary. Median Ki67 was 30% (range 20-50). Treatment was FOLFOX in 17 (50%) and XELOX in 17 patients (50%), while 16 (47%) received also concomitant SSA. After a median follow-up of 21.9 months, median PFS was 7.9 months (95%CI: 6.8-11.4) and median OS was 30.0 months (95%CI: 13.8-NA). The 13 patients whose tumor responded to FOLFOX/XELOX (38% [95%CI 22-56]) had longer PFS (21.9 vs 7.3 months; p<0.001) and OS (78.9 vs 10.0 months; p=0.01) compared with those who did not respond. After correcting for potential confounding factors with multivariate analysis, objective disease response to FOLFOX/XELOX was associated with a reduced risk for progression (HR: 0.20 [95%CI: 0.07-0.58]; p=0.003) and death (HR: 0.26 [95%CI: 0.07-0.98]; p=0.046) while higher Ki67 was associated with an increased risk for progression (HR: 1.09 [95%CI: 1.02-

1.14]; p=0.013) and for death (HR: 1.09 [95%CI: 1.01-1.17]; p=0.023).

Conclusions: Fluoropyrimidine-based regimens with oxaliplatin (FOLFOX/XELOX) may be active and effective in NET G3 of gastro-entero-pancreatic origin.

G07

DLL3 IS EXPRESSED IN HIGH-GRADE GASTROENTEROPANCREATIC NEUROENDOCRINE NEOPLASMS AND HAS PROGNOSTIC SIGNIFICANCE

Liverani C.[1], Bongiovanni A.[2], Mercatali L.[2], Pieri F.[3], Spadazzi C.[2], Miserocchi G.[2], Di Menna G.[2], Foca F.[4], Ravaioli S.[5], De Vita A.[2], Aprile M.R.[6], Cocchia C.[2], Recine F.[2], Ibrahim T.[2]

[1]PhD, Meldola; [2]Osteoncology and Rare Tumors Center, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [3]Pathology Unit, Morgagni-Pierantoni Hospital, Forlì, Italy, Forlì; [4]Unit of Biostatistics and Clinical Trials, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [5]Biosciences Laboratory, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [6]e AUSL Romagna, Ospedale Santa Maria delle Croci, Ravenna

Background: Gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) are a rare and heterogeneous subgroup of tumors with an extremely variable clinical behaviour and challenging management. A critical need is to identify molecular diagnostic criteria to discriminates grade 3 neuroendocrine tumors (NETs) from neuroendocrine carcinomas (NECs). These two entities have a completely different natural history, but their recognition is based only on the assessment of cell differentiation. The negative Notch regulator DLL3 is a new therapeutic target that was found to be highly expressed in certain tumors with neuroendocrine features.

Methods: A retrospective immunohistochemical analysis of DLL3, RB1 and PD-L1 expression was performed on FFPE samples from 43 patients with GEP-NEN and correlated with clinical characteristics and outcome.

Results: DLL3 was found to be expressed only in high-grade (G3) GEP-NEN. Moreover, it was significantly associated with the presence of poorly differentiated NEC classification: the 77.8% of NEC patients (7 out of 9) had a DLL3 positive neoplasia, while none of the 4 patients with G3 NET showed expression of this marker (p= 0.021). Expression of DLL3 correlated with loss of RB1 (p< 0.001), negative 68Ga-PET/CT scan (p= 0.001) and unfavourable clinical outcome with implication for patient treatment and follow-up. Median progression-free survival (PFS) and overall survival (OS) were, respectively, 41.9 and 72.9 months in patients with a DLL3-negative neoplasia versus 7.9 and 11.7 months in DLL3-positive patients (p= 0.0054 for PFS and p= 0.0036 for OS) .

Conclusions: DLL3 might represent an objective histological marker to be combined with cell morphological

analysis for the diagnosis of poorly differentiated NEC. The high percentage of DLL3 expression in NEC patients also indicates a potential opportunity for a DLL3 targeted therapy in this subset.

G08

PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) IS AN EFFECTIVE FIRST LINE TREATMENT IN AIDS-RELATED KAPOSI'S SARCOMA (AIDS-KS) IN COMBINATION ANTIRETROVIRAL THERAPY (CART) NAIVE PATIENTS

Dalu D.[1], Ammoni L.[1], De Francesco D.[2], Cona M.S.[1], Fasola C.[1], Foschi A.[3], Filipazzi V.[1], Rota S.[1], La Verde N.[1]

[1]ASST Fatebenefratelli Sacco - Polo Ospedaliero Luigi Sacco - Department of Oncology, Milan; [2]UCL - Institute for Global Health - London, London; [3]ASST Fatebenefratelli Sacco - Polo Ospedaliero Luigi Sacco - Department of Infectious Disease, Milan

Background: The widespread introduction of effective cART has had a major influence on the epidemiology of AIDS-associated cancer. Nevertheless AIDS-KS remains the most common malignancy among people living with HIV (12-20%). In advanced stage or progressive forms chemotherapy (CT) in combination with cART is the treatment of choice. The aim of the study is to evaluate efficacy and tolerability of PLD as first line CT in AIDS-KS.

Materials and Methods: This is a single institution retrospective study conducted in ASST Fatebenefratelli Sacco, PO Luigi Sacco (Milan, Italy). We selected HIV+ patients (pts) with KS from March 2009 to March 2019. cART was continued during CT. AIDS-KS pts were staged according to AIDS Clinical Trials Group Oncology Committee. CT was administered in poor risk and some cases of good prognosis/limited cutaneous disease. Treatment plan: PLD 20 mg/m2 IV every 2 weeks for 6 to 12 cycles. Efficacy of CT was evaluated as response rate (RR) = complete response (CR) + partial response (PR) and disease progression (DP) from the beginning of CT. CR was defined as total regression of complications, smoothing of all lesions, only pigmented inactive patches remaining. Adverse events were evaluated according to CTCAE v5.0.

Results: We enrolled 33 pts with AIDS-KS: median age at KS diagnosis 44ys (37, 49), male 90.9%, Caucasian 72.7%, cART-naïve (simultaneous diagnosis of HIV infection and KS) 84.4%, median lymphocyte CD4+ count 134 cells/μL (43, 288), median HIV viral load 4.9 log10 copies/ml (4.5, 5.6). KS stage was classified as Poor Risk in 32 (97%) pts. In 2 (6.1%) pts disease was limited to skin. A median of 6 cycles (range 6-12) of PLD were administered. During CT, grade 3-4 toxicity was observed in 8 (33.3%) pts: neutropenia 3 (12.5%), thrombocytopenia 2 (8.3%), hand-foot skin syndrome 2 (8.3%), infections 2 (8.3%), anemia 1

(4.2%). No cardiovascular events or severe sepsis were detected. In 6 (25%) pts CT was delayed due to toxicity. 26 pts were evaluable for response. KS RR and CR were achieved in 24 (92.3%) and 20 (76.9%) pts respectively. After a median follow-up of 27 (12, 65) months, no disease related deaths were reported. DP incidence rate was 0.78 (0, 2.31) per 1000 PY.

Conclusions: PLD associated with cART is an effective, feasible and well-tolerated first-line therapy in advanced AIDS-KS. We found a RR higher than other previous clinical studies (RR 58.7-84%), probably due to no prior systemic therapy and high percentage of cART-naïve pts.

G09

EVALUATION OF PROGNOSTIC ROLE OF INFLAMMATORY INDEX IN FIRST LINE CHEMOTHERAPY SOFT TISSUE SARCOMA PATIENTS

Fausti V.[1], Foca F.[1], Gurrieri L.[1], Debonis S.A.[1], Bongiovanni A.[1], Riva N.[1], De Vita A.[1], Mercatali L.[1], Ibrahim T.[1]

[1]IRST-Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola, Forlì-Cesena

Background: Soft tissue sarcomas (STS) are rare malignancies with different prognosis and response to therapy. Hematologic markers of inflammation have been shown to be prognostic in several malignancies. Aim of the study is to evaluate retrospectively the prognostic role of these markers in patients (pts) affected by STS receiving a first line chemotherapy for metastatic disease.

Methods: Adult pts with STS receivin first line chemotherapy from 2008 to 2019 were selected for this study. Data on blood counts were carried out the day before starting therapy. Neutrophil and Platelet lymphocyte ratio (NLR and PLR) were computed as the ratio of the absolute neutrophil count and absolute platelet count by the absolute lymphocyte count respectively. Systemic Inflammatory Index (SII) was calculated as platelet count$\times$neutrophil count/lymphocyte count. Overall survival (OS) and Progression-free survival (PFS) using Kaplan-Meier method were stratified considering different cut off for hematologic markers, found using X-tile software version 3.6.1.

Results: Ninety-four pts were enrolled. Pts characteristics are showed in Table 1. Pts with a SII <2693 showed a better OS compared to patients with SII $\geq$2693 (15.3 mo Vs 5 mo p- value 0.005); no statistical significant difference was seen in terms of PFS. Pts with a NLR < 6.7 showed a better OS and PFS compared to patients with NLR $\geq$ 6.7 (OS: 16.1 mo Vs 3 mo p- value <0.001; PFS 5.4 mo VS 2.3 mo p- value 0.010). Pts with a PLR < 85 showed a better OS compared to patients with PLR $\geq$ 85 (33 mo Vs 12.8 mo p- value 0.052); no statistical significant difference was seen in terms of PFS. No statistical significant

difference was seen in PFS or OS among different histology or kind of first line treatment.

Conclusions: This retrospective study confirms the prognostic role of inflammatory indices in STS, suggesting that a systemic inflammatory status is associated with more aggressive and less responsive to standard treatments diseases.

Table 1. Patients characteristics.

	N 94 (%)
Gender	
Male	41 (43.6)
Female	53 (56.4)
Age at diagnosis	
Median (range)	62 (22-84)
Age at treatment	
Median (range)	64 (24-84)
Surgery at diagnosis	
None	31 (33.0)
Not radical	17 (18.1)
Radical	47 (48.9)
Adjuvant therapy	
None	40 (63.5)
CT only	13 (20.6)
RT only	9 (14.3)
RT+CT	1 (1.6)
Histotype	
Leiomiosarcoma	29 (30.8)
Liposarcoma	17 (18.1)
UPS	11 (11.7)
Other	37 (39.4)
First line treatment	
Antracycline based	57 (60.7)
Gemcitabine based	14 (14.9)
Trabectidine	13 (13.8)
Other	10 (10.6)

G10

SAFETY AND HIGH RATES OF RESPONSE WITH AVELUMAB AS FIRST LINE OF TREATMENT IN MERKEL CELL CARCINOMA: A REAL WORD EXPERIENCE

Savastano C.[1], Lombardi F.[1], Rispoli A.I.[1], Fusciello C.[1], De Divitiis C.[1]

[1]AOU San Giovanni di Dio e Ruggi D'Aragona, Salerno

Background: Merkel cell carcinoma (MCC) is a rare and aggressive primary neuroendocrine cutaneous carcinoma of the skin which can be distinguished from other malignancies by the expression of cytokeratin 20 (CK20).The National Comprehensive Cancer Network (NCCN)guidelines recommend multidisciplinary tumor board consultation for patients

with metastatic and locally advanced disease to consider any or a combination of radiation, surgery, and chemotherapy. MCC is associated with poor survival outcomes in patients with metastatic disease. For this setting, results of part A of the JAVELIN Merkel 200 trial (avelumab in patients with Merkel cell carcinoma) showed that avelumab, an anti-programmed cell death ligand 1 (PD-L1) antibody, demonstrated efficacy in second-line or later treatment of patients with metastatic MCC. So, as we know from the results of recent scientific literature, avelumab is indicated as monotherapy for the treatment of adult patients with metastatic MCC.

Methods: In our experience, from march 2019 tojune 2020, we have treated in first line four patients affected by advanced MCC (all women; median age, 75 years [range, 65-83 years]), with avelumab (10 mg/kg, by 1-hour intravenous infusion every 2 weeks until confirmed disease progression, unacceptable toxic effects, or withdrawal occurred), with a median follow-up of 8 months (range, 2-12 months). Neither dose reductions nor G3/G4 toxicities were registered. The most common Grade 2 adverse events observed until today were fatigue and leukopenia; An objective response was obtained in 3 patients [complete response in one, partial response in 2, stable disease in the third, progressive disease in one patient]. The median progression free survival was 12 months. In the case of one patient, we continued with avelumab beyond cerebral instrumental progression, in consideration of the clinical benefit and the partial response on the other abdominal lymph node target lesions, with median follow up of 11 months.

Conclusions: In our experience, first-line avelumab treatment was generally well tolerated, and no treatment-related deaths or grade 4 adverse events occurred, with high rates of response. Maturing progression-free survival data suggest that responses are durable.

G11

RADIOINDUCED SARCOMAS. A MONOINSTITUTIONAL EXPERIENCE

Bochicchio A.M.[1], Omer L.C.[1], Ardito R.[1], Sgambato A.[2], Aieta M.[2], Vita G.[1], Patitucci G.[1], Fabrizio T.[1]

[1]IRCCS-CROB, Rionero in Vulture; [2]IRCCS-CROB, Potenza

Background: The oncologic risk of ionizing radiation is widely known. Sarcomas developing after radiotherapy as a "iatrogenic disease of success" have been reported, and they are a growing problem because rapid advancements in cancer management and screening have increased the number of long-term survivors. Although many patients have undergone radiation treatment, only few data are available on radio induced sarcomas (RIS).

Material (patients) and methods: We examined the records of 131 patients with soft tissue sarcomas, confirmed by immunohistochemistry treated in our Centre from 2009 to 2019. Five patients had a histologic diagnose of secondary RIS, 36 months passed from primary to secondary tumor, consistent with literature data. In our experience, we have observed 3 radio induced sarcoma after breast cancer, 2 after head and neck cancer (H&N), out of 131 total cases, M/F:59/71, mean age 63, (r:15-91). At present, 63 patients are still in a mean follow-up of 22 months (range:1-384). The in/out geographic origin is: Basilicata 18/63, Campania 27/63, Puglia 11/63, others 7/63. The first diagnose was made at CROB for 100/131 patients. Surgical treatment involved a radical excision in 72 patients, in 56 patients metastases were diagnosed at the first CT exam, while 42 cases had the mets. during the follow-up. All patients except one, were treated in our Centre; 22 patients received external radiotherapy, 1 brachytherapy, 6 elettrochemoterapy (ECT). Out of 72 patients who received chemotherapy, 36 had first line, 30 the second and 5 patients had three lines. In 3 cases Olaratumab was comprised in the first line treatment, 1 received Crizotinib for a miofibroblastic inflammatory tumor of a sclero-congiuntive localization with ALK+, 1 with cordoma received Imatinib. Out of the 5 RIS, 1 received radiotherapy, 1 surgery and ECT, 3 had 3 lines of chemotherapy.

Results: The histology of RIS is: 1 desmoid tumor cervical localized, 1 angiosarcoma, 1 condrosarcoma, 2 leiomiosarcoma.

Conclusions: Radioinduced sarcoma is a possible complication of oncologic long patient survival, requiring attention for an early diagnose and possible new life saving therapies. Key words: RIS, Head and neck, ECT

H - Genitourinary Tumours

H01

EFFECTIVENESS OF ABIRATERONE ACETATE PLUS PREDNISONE IN CHEMOTHERAPY-NAÏVE PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER IN A LARGE PROSPECTIVE REAL-WORLD COHORT: THE ABITUDE STUDY

Procopio G.[1], Chiuri V.E.[2], Giordano M.[3], Mantini G.[4], Maisano R.[5], Bordonaro R.[6], Calvani N.[7], Facchini G.[8], De Placido S.[9], Airoldi M.[10], Sbrana A.[11], Gasparro D.[12], Ludovico G.M.[13], Guglielmini P.F.[14], Naglieri E.[15], Fagnani D.[16], Aglietta M.[17], Schips L.[18], Sciarra A.[19], Livi L.[20], Santini D.[21]

[1]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [2]Medical Oncology Department, Ospedale Vito Fazzi, Lecce; [3]Medical Oncology Division, ASST-Lariana, Como; [4]Radiochemotherapy Unit, Department of Diagnostics for Imaging, Oncological Radiotherapy and Hematology, Fondazione Policlinico A. Gemelli IRCCS, Rome - University Department of Radiological and Hematological Sciences, Università Cattolica Sacro Cuore, Rome; [5]Department of Oncology, A.O. Bianchi-

Melacrino-Morelli, Reggio Calabria; [6]MD - ARNAS Garibaldi, Catania; [7]Medical Oncology Unit, Antonio Perrino Hospital, Brindisi; [8]Departmental Unit of Experimental Uro-Andrological Clinical Oncology, Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale, Naples; [9]Department of Clinical Medicine and Surgery University of Naples, Naples; [10]Oncology Unit 2 - Città della Salute e della Scienza di Torino, Torino; [11]Medical Oncology Unit 2, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa; [12]Medical Oncology Unit, Department of General & Specialistic Medicine, University Hospital of Parma, Parma; [13]Department of Urology, Ospedale F. Miulli, Acquaviva delle Fonti, Bari; [14]Oncology Unit, SS Antonio e Biagio e Cesare Arrigo Hospital, Alessandria; [15]Medical Oncology Unit, IRCCS Giovanni Paolo II, Bari; [16]Medical Oncology Division, ASST Vimercate, Vimercate; [17]Department of Oncology, University of Turin; Candiolo Cancer Institute - FPO- IRCCS, Candiolo, Candiolo (TO); [18]Department of Medical, Oral and Biotechnological Sciences, G. d'Annunzio University of Chieti, Urology unit, "SS. Annunziata Hospital", Chieti; [19]Department of Urology, Sapienza Rome University Policlinico Umberto I, Rome; [20]Department of Radiation Oncology, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence; [21]Department of Medical Oncology, University Campus Biomedico, Rome

Background: In pivotal trials, abiraterone significantly improved survival in both chemotherapy-naive and docetaxel pretreated patients with metastatic castration-resistant prostate cancer (mCRPC). Real-world data in the chemotherapy-naïve setting are limited, largely deriving from small retrospective studies.

Methods: ABitude is an observational, prospective study aiming at describing outcomes of mCRPC patients treated with abiraterone in clinical practice. Chemotherapy-naive mCRPC patients were consecutively enrolled in 49 Italian centers at abiraterone start (February 2016-June 2017) and are being followed for 3 years, with evaluation every ~6 months. Several clinical and patients reported outcomes were examined. Kaplan–Meier curves and multivariable Cox regression models were used for the analyses.

Results: This is the second interim analysis of the ABitude study. Among 481 enrolled patients, 453 were evaluable for analyses. At baseline, median age was 77 years and ~69% of patients had comorbidities (mainly cardiovascular diseases). Metastases were located mainly at bones and lymph nodes (42% only bones, 22% only lymph nodes, 23% both sites); 8.4% of patients had visceral metastases. During a median follow-up of 18 months, 1- and 2-years probability of radiographic progression free survival (rPFS) were 73.9% and 56.2%, respectively; the corresponding rates for overall survival (OS) were 87.3% and 70.4%. In multivariable analyses, the number of bone metastases significantly affected rPFS and OS. During abiraterone treatment, 65% of patients had a ≥50% prostate-specific antigen (PSA) decline, and quality of life (QoL) remained appreciably high. Among symptomatic patients according to the Brief Pain Inventory (BPI) (32%), BPI scores significantly declined after 6 months of treatment, and 1-year rPFS and OS were, respectively, 66.4% and 77.2%. Eight patients (1.7%) had serious adverse reactions to abiraterone.

Conclusions: Abiraterone is effective and safe for chemotherapy-naive mCRPC patients in clinical practice; symptomatic patients improve pain and have similar clinical outcomes to the overall patients' population.

H02

TREATMENT WITH SORAFENIB (SOR) VS OBSERVATION (OBS) FOLLOWING RADICAL METASTASECTOMY IN PATIENTS (PTS) WITH METASTATIC RENAL CELL CARCINOMA (mRCC): UPDATED DATA ON THE RANDOMIZED PROSPECTIVE RESORT TRIAL

Mennitto A.[1], Apollonio G.[1], Verzoni E.[1], Cognetti F.[2], Miceli R.[1], Milella M.[3], Mosca A.[4], Chiuri V.E.[5], Bearz A.[6], Morelli F.[7], Ortega C.[8], Atzori F.[9], Donini M.[10], Claps M.[1], Sepe P.[1], Guadalupi V.[1], De Braud F.[1], Montone R.[1], Procopio G.[1]

[1]Fondazione IRCCS Istituto Nazionale Tumori, Milan; [2]Regina Elena National Cancer Institute, Rome; [3]University of Verona - Faculty of Medicine, Verona; [4]Candiolo Cancer Institute, FPO-IRCC, Candiolo; [5]Ospedale Vito Fazzi, Lecce; [6]Centro di Riferimento Oncologico - CRO, Aviano; [7]IRCCS Fondazione Casa Sollievo della Sofferenza, San Giovanni Rotondo; [8]ASL CN 2, Alba e Bra; [9]Azienda Ospedaliero-Universitaria di Cagliari, Cagliari; [10]Istituti Ospitalieri di Cremona, Cremona

Background: In well-selected mRCC pts radical metastasectomy can prolong survival. Previously we reported that SOR following surgery did not increase relapse free survival (RFS) over obs in a randomized prospective trial. Now we present the updated follow up data of the RESORT trial (NCT0144487).

Material and methods: The multicenter, randomized, phase II RESORT trial enrolled pts with clear-cell mRCC undergoing radical surgery of the primary tumor and metastases (≤3 lesions). Within 12 weeks from metastasectomy, pts were randomized (1:1) to obs or SOR 400 mg BID for 52 weeks. Stratification factors were time from nephrectomy to metastases (≤ or >12 months [mos]), site (lung vs others) and number of metastases (single vs multiple). Primary endpoint of the study was RFS, defined as the time from randomization to disease relapse or death. The secondary were overall survival and toxicity. RFS curves were estimated with the Kaplan-Meier method and compared with the log-rank test. We used the Cox model to estimate the hazard ratio (HR) SOR vs obs.

Results: Between November 2012 and November 2017 we enrolled 76 pts, of whom 69 randomized. The analysis was performed on 68 pts (32 in SOR and 36 in obs arm) because one of them never started therapy. 81% in SOR and 80% in obs arm had a single metastasis and lung was the main involved site in 31% and 24%, respectively. At a median follow up time of 42 mos (interquartile range 31-58) the median RFS was 35 mos in obs arm vs 21 mos

in SOR arm. At 24 mos, RFS probability was 57% (95%CI 42-76%) in obs arm and 50% (95%CI 34-71%) in SOR arm; at 48 mos, RFS probability was 44% (95%CI 30-65%) in obs arm and 32% (95%CI 18-57%) in SOR arm (p=0.342; HR 1.35; 95%CI 0.72-2.54). In obs arm, 2 pts died at 4 and 14 mos. 17/36 pts (47%) and 12/32 (37.5%) are relapse-free in obs and SOR arm, respectively. Recurrence was observed mostly in lung,

lymphnodes, brain, bone, liver and pancreas, regardless of the previous metastasectomy site.

Conclusions: Metastasectomy followed by SOR in mRCC pts does not offer clinical benefit in terms of RFS. Anyway, surgery of metastases may be an option in well-selected pts to potentially prolong survival. Actually, in this trial most pts (47% in obs arm) are relapse-free at a median follow-up of 42 mos.

Table 1. Available evidence.

Comparison	RCTs	Cognitive impairment (Investigator-assessed)		Cognitive function (PRO-based)	
		N	Toxicity (any grade)	N	Main results
Abi vs Ctrl	5	1	STAMPEDE: Cog imp. 6.4% vs 3.8%	0	-
Enz vs Ctrl	7	3	PROSPER: Cog / memory imp. 5% vs 2% ARCHES: Cog / memory imp. 4.5% vs 2.1% ENZAMET: Cog dist. 2.8% vs 0.5%; concentration imp. 5.3% vs 1.1%; memory imp. 14.6% vs 3.6%.	1	ENZAMET: mean changes worse for Enz (p<0.0001); deterioration-free survival better for Enz (3-yr 33% vs 21%, p=0.0003)
Apa vs Ctrl	2	1	SPARTAN: mental imp. 5.1% vs 3.0%	0	-
Dar vs Ctrl	1	1	ARAMIS: Cog disorders 0.4% vs 0.2%; memory imp. 0.5% vs 1.3%	0	-
Cabazitaxel vs Abi / Enz	1	0	-	0	-
Abi vs Enz	1	1	NCT02125357: Montreal <26 at week 12: 47% vs 54%	0	-
TOTAL	**17**	**7 (41.2%)**		**1 (5.9%)**	

H03

EVALUATION OF COGNITIVE FUNCTION (COGF) IN RANDOMIZED TRIALS TESTING NEW-GENERATION HORMONAL TREATMENTS (NGHT) IN PATIENTS WITH PROSTATE CANCER (PC): A SYSTEMATIC REVIEW

Vignani F.[1], Marandino L[2], Buttigliero C.[3], Gamba T.[4], Necchi A.[5], Tucci M.[6], Di Maio M.[7]

[1]SCDU Oncologia Medica, AO Ordine Mauriziano, Torino; [2]Dipartimento di Oncologia, Università degli Studi di Torino / Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano; [3]Dipartimento di Oncologia, Università degli Studi di Torino / AOU San Luigi Gonzaga, Orbassano (TO); [4]Dipartimento di Oncologia, Università degli Studi di Torino / AO Ordine Mauriziano, Torino; [5]Istituto Nazionale dei Tumori di Milano - Fondazione IRCCS, Milano; [6]Ospedale C. Massaia, Asti; [7]Dipartimento di Oncologia, Università degli Studi di Torino, AO Ordine Mauriziano, Torino

Background: In recent years, NGHT initially approved for metastatic castration resistant PC (mCRPC) have also shown efficacy in non-metastatic CRPC (nmCRPC) and in hormone sensitive PC (HSPC). An earlier use and a longer duration of NGHT, added up to androgen deprivation therapy, requires evaluation of the impact on patient-reported outcomes (PROs), and particularly on CogF. Aim of this systematic review is to focus on the evidence about CogF

in all randomized trials (RCTs) testing NGHT in patients (pts) with PC.

Methods: RCTs testing abiraterone acetate (Abi), enzalutamide (Enz), apalutamide (Apa), darolutamide (Dar) were searched in Pubmed and major meetings. For each RCT, we assessed (i) availability of investigator-assessed cognitive impairment and disorders; (ii) availability of PRO-based evaluation of CogF.

Results: 17 RCTs (17300 pts, 9793 assigned to NGHT) were included (**Table 1**). Investigator-based evaluation of the incidence of CogF impairment was available in 7 RCTs (41.2%): 1 mCRPC, 3 nmCRPC, 3 HSPC. 17 / 17 RCTs (100%) included PROs collection, but PRO tools adopted allowed evaluation of CogF in 2 RCTs (11.8%). Among them, PRO-based CogF results were presented only in 1 RCT (5.9%): in ENZAMET, mean changes were worse with Enz (p<0.0001), but deterioration-free survival favored Enz vs placebo (p=0.0003).

Conclusions: Clinical development of NGHT has not included a systematic evaluation of CogF. Assessment by investigators is at risk of underreporting, but CogF deterioration could be relevant, at least in a proportion of pts. Commonly used PROs do not allow or allow only partially CogF analysis, and methodology of analysis can jeopardize interpretation of CogF results. Although direct comparisons are scanty, there could be differences between different NGTH.

H04

IMPACT OF PREVIOUS NEPHRECTOMY ON CLINICAL OUTCOME OF METASTATIC RENAL CARCINOMA TREATED WITH IMMUNE-ONCOLOGY (I-O). A REAL-WORLD STUDY ON BEHALF OF MEET-URO GROUP (MEETURO-7B)

Stellato M.[1], Santini D.[2], Verzoni E.[1], De Giorgi U.[3], Casadei C.[3], Zielli T.[4], Maruzzo M.[5], Damassi A.[6], Sbrana A.[7], Di Lorenzo G.[8], Anesi C.[2], Sorarù M.[9], Naglieri E.[10], De Vivo R.[11], Vignani F.[12], Grillone F.[13], Mucciarini C.[14], Roviello G.[15], Pignata S.[16], Procopio G.[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [2]Campus Bio-Medico University of Rome, Roma; [3]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [4]University Hospital of Parma, Parma; [5]Istituto Oncologico Veneto IOV IRCCS, Padova; [6]IRCCS Ospedale Policlinico San Martino, Genova; [7]Azienda Ospedaliera Universitaria Pisana, Pisa; [8]Ospedale di Pagani, Pagani (Salerno); [9]Camposampiero General Hospital, Camposampiero (Padova); [10]Istituto Tumori Bari Giovanni Paolo II - IRCCS, Bari; [11]San Bortolo General Hospital, Vicenza; [12]AO Ordine Mauriziano, Torino; [13]Azienda Ospedaliero-Universitario "Mater Domini", Policlinico of Catanzaro, Catanzaro; [14]Ospedale Ramazzini, Carpi-AUSL Modena, Carpi; [15]University of Florence, Firenze; [16]Istituto Nazionale Tumori IRCCS Fondazione "G. Pascale", Napoli

Background: Immune-oncology (IO) treatment demonstrated to improve Overall Survival (OS) in metastatic renal cell carcinoma (mRCC). The prognostic impact of previous citoreductive nephrectomy (CN) and radical nephrectomy with curative intent in patients (pts) treated with IO is not well defined. Patients and methods 229 eligible pts, with a least one radiological assessment of response according to the RECIST 1:1 criteria, were retrospectively collected from 16 Italian referral centers. Baseline characteristics, outcome data including progression-free survival (PFS) and OS were collected. Kaplan-Meier method and log-rank test were performed to compare PFS and OS between groups.

Results: 153(66.8%) pts received IO as second line, 61(26.6%) as third line and 15(6.6%) pts as further line. 54 pts (23.6%) were good risk, 144(62.9%) were intermediate and 31(13.5%) were poor risk according to IMDC score. 189(82.5%) pts underwent nephrectomy (of them 72(32.4%) pts had synchronous metastatic disease and underwent CN), while 40(17.4%) pts did not. Nephrectomy was performed before IO treatment. ECOG PS, at the beginning of IO, was 0 for 167 pts (72.9%), the other 62 (27.1%) had ECOG PS 1 or 2. At a median follow up time of 17.5 months (mo), 13 (5.7%) pts are still in treatment while 216 (94.3%) experienced progression. 81 (35.3%) pts were treated after IO progression with mTOR and VEGFR inhibitors. 63 (27.5%) pts continued IO beyond progression. G3-G4 iAE were reported in 46 pts (20%). Median IO-PFS was 4.5 months in pts who did not undergo nephrectomy and 2.9 mo in pts who did (HR log rank 0.713, 95%CI 0.4788 to 1.063; p=0.0582). Median IO-OS was 18.4 mo in pts who underwent nephrectomy and 10.3 mo in pts who did not (HR log rank 1.915, 95%CI 1.118 to 3.281; p=0.0024). The difference in OS was irrespective of the IMDC criteria and the line of treatment.

Conclusions: In our real world experience, in mRCC pts treated with IO, previous nephrectomy was associated with a better outcome in terms of OS with all the limitations of a retrospective collection.

H05

ADJUVANT CHEMOTHERAPY IN UPPER TRACT UROTHELIAL CARCINOMAS (UTUCS): IS THE TIME RIPE FOR CHANGE? A META-ANALYSIS OF 16 STUDIES

Ricci A.D.[1], Rizzo A.[1], Mollica V.[1], Maggio I.[1], Ardizzoni A.[1], Massari F.[1]

[1]Division of Oncology, S-Orsola-Malpighi Hospital, Bologna

Background: Upper tract urothelial carcinomas (UTUCs) are a rare malignant disease comprising 5–10% of urothelial carcinomas overall. Radical nephroureterectomy (RNU) represents the treatment mainstay of the early stages of UTUCs, but the high rate of relapse and death means that adjuvant treatments are required. We conducted a meta-analysis aims to evaluate the role of platinum-based adjuvant chemotherapy (AC) for patients with locally advanced UTUCs (staged as either pT2–T4 N0–N3 M0 or pTany N1–3) after RNU.

Material and methods: The PubMed/MEDLINE, EMBASE, Cochrane Library databases and meeting abstracts were searched for relevant studies in English up to March 2020. Eligible studies reported survival and/or disease-free survival (DFS) outcomes expressed as hazard ratio (HR) and 95% confidence intervals (CIs) for patients treated with platinum-based AC compared to observation alone. The endpoints were overall survival (OS), cancer-specific survival (CSS) and DFS.

Results: A total of 16 studies were eligible for analysis: 15 retrospective studies and 1 phase 3 randomized control trial (RCT). Overall, 1740 patients received AC after RNU and 4535 patients underwent RNU alone, with a median follow-up of 37,5 months (range 17,8-53,9 months). A significant benefit in DFS was identified in patients receiving platinum-based AC (pooled HR 0.49; 95%CI: 0.36–0.66), while the benefit in OS (pooled HR 0.80; 95%CI: 0.51–1.26) and CSS (pooled HR 0.87; 95%CI: 0.65–1.17) was not statistically significant. Additionally, platinum-based AC showed a modest OS benefit with a pooled HR 0.75 (95%CI: 0.57–0.99) in a post-hoc analysis combing multivariable HRs with estimated HRs from Kaplan-Meier curves.

Conclusions: The available data suggest that platinum-based AC is associated with improved DFS and a modest OS benefit after RNU in patients with locally advanced UTUCs.

H06

PROGNOSTIC ROLE OF SYSTEMIC INFLAMMATORY INDEXES IN GERM CELL TUMORS TREATED WITH HIGH DOSE CHEMOTHERAPY

Cursano M.C.[1], Kopf B.[2], Scarpi E.[2], Menna C.[2], Casadei C.[2], Schepisi G.[2], Lolli C.[2], Altavilla A.[2], Gallà V.[2], Santini D.[1], Tonini G.[1], Chovanec M.[3], Mego M.[3], De Giorgi U.[4]

[1]Università Campus Biomedico di Roma, Roma; [2]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, 47014, Meldola, Italy; [3]Second Department of Oncology, Faculty of Medicine, Comenius University, Klenova, Bratislava; [4]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy

Background: Conventional dose chemotherapy (CDCT) and high dose chemotherapy (HDCT) with support of peripheral blood progenitor cells (PBPC) are the two salvage curative approaches in relapsed/refractory germ cell tumors (GCT). Since the complexity of this population and the toxicity of HDCT, this study evaluated the association between blood-based systemic inflammatory indexes and outcome of GCT patients undergoing salvage treatment with HDCT in order to define additional prognostic factors able to orient clinical decision.

Methods: Between August 2009 and April 2018 we retrospectively collected baseline characteristics, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and the systemic immune-inflammation index (SII) of 62 patients undergoing HDCT for GCT. The aim is to evaluate the correlation between each inflammatory marker (NLR, PLR and SII) and response to HDCT, overall survival (OS) and progression free survival (PFS).

Results: Patients with GCT with NLR ≥3.3 and SII ≥844000 had shorter PFS and inferior OS. In the multivariable analysis including inflammatory markers, IPFSG risk group, age and previous line of treatment, NLR ≥3.3 and SII ≥844000 were identified to be independently associated with shorter PFS and OS. Moreover, NLR, PLR and SII significantly correlate with overall response to HDCT.

Conclusions: Inflammation markers may improve prediction of oncologic outcome in the heterogeneous population of patients with relapsed/refractory GCT. Associating the International Prognostic Factor Study Group (IPFSG) prognostic score to inflammation markers at baseline of HDCT adds prognostic information and might help physicians to make more personalized treatment decisions.

H07

PRIMARY RESISTANCE (PRR) VERSUS ACQUIRED RESISTANCE (ACR) TO IMMUNE CHECKPOINT INHIBITORS (ICI) IN FIRST-LINE METASTATIC RENAL CELL CARCINOMA (mRCC)

Guida A.[1], Alves Costa Silva C.[2], Colomba E.[2], Flippot R.[2], Salviat F.[2], Bracarda S.[2], Escudier B.[2], Albiges L.[2]

[1]Ospedale Santa Maria Terni, Terni; [2]Institute Gustave Roussy, Villejuif

Background: ICI have revolutionized first-line treatment paradigm of mRCC, achieving durable responses and longer survival. However, a subset of patients (pts) developed resistance immediately (PrR) or after an initial clinical benefit (AcR). The aim of the study is to identify key differences between these two subgroups.

Methods: Retrospective analysis was performed from IGReCC (Institut Gustave Roussy Renal Cell Carcinoma) database on pts treated with first line (1L) ICI. PrR was defined as progression disease (PD) or stable disease (SD) lasting <6 months (mo) as best response; AcR was defined as complete, partial or SD=6 mo. Statistical tests as appropriate were used to describe differences between groups and investigated established prognostic markers (IMDC, metastatic sites). The Kaplan-Meier and Cox regression methods were used to estimate overall survival (OS)

Results: A total of 50 pts received 1L ICI and were evaluated for best response. The majority of pts (86%) received Nivo+Ipi and 8 pts (6%) received ICI monotherapy (6 nivo, 2 atezo). PrR and ArR were 21 (42%) and 29 (58%) respectively. PrR and ArR groups were compared for main clinical features and only significant differences are reported in the table and considered for multiple regression. From multivariate analysis time to treatment start (TTT) (odds ratio [OR] 19.4; 95%CI 1.7-224, p=0.016) and number of metastatic sites =3 (OR 10.2; 95%CI 1.8-56.1, p=0.005) seems associated with PrR. With a median follow-up of 19 mo (range 1-55), 12mo-OS rate was 96% (95%CI 72-99) vs 53% (95%CI 25-75) and 24mo-OS rate was 81% (95%CI 48-94) vs 35% (95%CI 12-62) for AcR and PrR, respectively HR 5.8 (95%CI 1.8-18.9), p 0.0009

Conclusions: Deciphering first-line PrR and AR subsets of pts may become a key challenge for decision-making in mRCC. This is the first report to describe different patterns of resistance potentially related to different clinical outcomes

	PrR N/%	AcR N/%	P
TTT <= 1 year	20/95	19/66	0.016
Metastatic sites >= 3	12/60	4/17	0.005
Haemoglobin < LNL	12/52	7/25	0.049

H08

FINDING THE RIGHT BIOMARKER IN METASTATIC RENAL CELL CARCINOMA (mRCC): SOLUBLE PD-1, PD-L1, PAN-BTN3AS, BTN3A1, BTN2A1 AND PLASMA DYNAMIC CHANGES AS PREDICTIVE BIOMARKERS OF IMMUNOTHERAPY RESPONSE

Incorvaia L.[1], Fanale D.[2], Badalamenti G.[2], Iovanna J.[3], Porta C.[4], Olive D.[5], Corsini L.[6], Brando C.[6], Bono M.[6], Fiorino A.[6], La Mantia M.[6], Barraco N.[6], Rizzo M.[7], Gri N.[4], Gristina V.[6], Di Miceli S.[6], Bazan V.[1], Russo A.[6]

[1]University of Palermo, Department of Biomedicine, Neuroscience and Advanced Diagnostics (Bi.N.D.), Section of Medical Oncology, Palermo; [2]Department of Surgical, Oncological and Oral Sciences, Section of Medical Oncology, University of Palermo,, Palermo; [3]Centre de Recherche en Cancérologie de Marseille (CRCM), Team Pancreatic Cancer,, Mareselle; [4]University of Pavia and Division of Translational Oncology, IRCCS Istituti Clinici Scientifici Maugeri,, Pavia; [5]Centre de Recherche en Cancerologie de Marseille (CRCM), INSERM U1068, Aix-Marseille Universite' and Institut Paoli-Calmettes, Mareselle; [6]University of Palermo, Department of Surgical, Oncological and Oral Sciences, Section of Medical Oncology, Palermo; [7]IRCCS Istituti Clinici Maugeri, Pavia

Background: Despite immunotherapy has revolutionized the treatment of metastatic RCC (mRCC), predicting which patient will benefit from the treatment still remain an issue. Many elements represent a barrier to the assessment of PD-L1 expressions using immunohistochemistry (IHC) as biomarker of immunotherapy activity and more dynamic biomarkers are required for patient selection.
Patients and methods: We performed a prospective study including a cohort of 56 patients with clear cell RCC (ccRCC): 21 metastatic patients (mccRCC), 15 with localized disease and a validation cohort of 20 mccRCC. In the group of mccRCC patients candidate to nivolumab as second line treatment, peripheral blood samples were collected at baseline, before starting nivolumab (T0), and after a 4-weeks period (T1). The plasma sPD-1, sPD-L1 and pan-sBTN3A, sBTN3A1 and sBTN2A1 levels were measured by specific ELISA assays not yet commercially available.
Results: In the sub-population of long-responders patients (PFS>18 months), the mean pre-treatment (T0) levels of sPD1 and sPD-L1 were higher respect to the patients with shorter PFS (<6 months); conversely, the T0 levels of sBTN2A1 were lower than short-responders. Particularly, the median PFS of patients with sPD1<8.05 ng/ml measured before starting nivolumab (T0) was 5.8 months, whereas in patients with sPD1 >8.05 the median PFS was 17.5 months (p=0.0274). We investigate the dynamic change of plasmatic immune-checkpoints after nivolumab treatment (T1). In the patients with PFS>18 months, the Wilcoxon test for paired samples showed a statistically significant difference between T0 and T1 for both sPD1 and sBTN2A1 (sPD1: T0 vs T1 p=0.0078; sBTN2A1 T0 vs T1 p=0.0007). For sPD-L1 probably the small number of samples did not allow us to reach statistical significance (p=0.097). An exploratory analysis in metastatic versus localized ccRCC patients, showed that the concentrations of sPD-1 and sPD-L1 were elevated in the plasma of metastatic in comparison with localized RCC patients (sPD-1 p=0.003; sPD-L1 p=0.164).
Conclusions: Soluble PD-1, PD-L1 and BTN2A1 could help to identify patient's subgroups for immune-checkpoint treatment, driving the therapeutic choice and monitoring the patient's response.

H09

CABOZANTINIB (CABO) PLUS DURVALUMAB (DURVA) IN PATIENTS (PTS) WITH ADVANCED UROTHELIAL CARCINOMA (UC) AFTER PLATINUM CHEMOTHERAPY: SAFETY AND PRELIMINARY ACTIVITY OF THE OPEN-LABEL, SINGLE-ARM, PHASE 2 ARCADIA TRIAL

Marandino L.[1], Raggi D.[1], Giannatempo P.[1], Calareso G.[1], Alessi A.[1], Colecchia M.[1], Madison R.[2], Ross J.S.[3], Necchi A.[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [2]Foundation Medicine, Cambridge, MA, USA; [3]Foundation Medicine Inc., Cambridge, MA, USA; Upstate Medical University, Syracuse, NY, USA

Background: Both DURVA and CABO, an inhibitor of MET, AXL, and VEGFR, have shown single-agent activity in pts with UC. ARCADIA is a phase 2 study evaluating the combination of CABO with DURVA in pts with advanced UC or non-UC histology (NCT03824691). Herein we report the results of the interim safety analysis and the preliminary activity.
Methods: Pts receive CABO 40 mg daily, orally, and are administered DURVA 1500 mg, intravenously, q28 days, until disease progression (PD, by RECIST 1.1) or onset of unacceptable toxicity. Key inclusion criteria are ECOG-PS 0-1, UC and non-UC histology, failure of 1 or 2 platinum-based regimens for metastatic disease. The response is evaluated by RECIST criteria v.1.1 q2 cycles by CT and PET/CT scans. The primary endpoint of the study is OS. Other endpoints include safety (CTCAE v.5.0), objective response rate (ORR), duration of response, progression-free survival. PD-L1 expression is assessed using the Ventana SP142 assay. Next-generation sequencing tests (FoundationOne) on pre-therapy tumor samples are also performed.
Results: As of May 20, 2020, 14 pts were enrolled with a median follow-up of 5 mo (range 1-8). The median age was 66 yrs (range 44, 74), 21% were female, and 60% had an ECOG PS 1. 2 pts had pure neuroendocrine (NE) histology. Four pts (28%) had received 2 prior systemic anticancer therapies. The median tumor mutational burden (TMB) was 6 mut/Mb. Treatment-related AEs (TRAEs) occurred in 9 pts (64.3%), all of Grade 1-2, within the first 2 cycles. One pt (7%) discontinued CABO due to toxicity, none DURVA. The most common TRAEs were asthenia (28.6%), diarrhea, creatinine increase and hypertension (all 21.4%). In 10 response-evaluable pts, partial response (PR) was obtained in 2 (20%), ongoing at 6+ mo in one case harboring a driver RET (F116L) mutation. Clinical benefit (PR + stable disease) was obtained in 28.6%. 0/2 NE tumors responded.
Conclusions: CABO in combination with DURVA demonstrated encouraging clinical activity in pts with advanced UC with an acceptable safety profile. More mature results,

with longer follow-up, according to CABO-related response biomarkers and histology will be presented.

H10

PSYCHOLOGICAL AND SEXUAL IMPACTS OF TESTICULAR CANCER DIAGNOSIS: AN EXPLORATORY STUDY

Ottaviano M.[1], Condello C.[2], Tortora M.[3], Dolce P.[4], De Giorgi U.[5], De Padova S.[6], Facchini G.[7], Tommaselli S.[8], Riccio V.[9], Parola S.[9], Picozzi F.[9], De Placido P.[9], Marretta A.L.[9], Vaia A.[9], Botti G.[8], Daniele B.[1], De Placido S.[10], Giuliano M.[10], Palmieri G.[3]

[1]Oncology Unit, Ospedale del Mare, Naples, Italy, Napoli; [2]Department of Clinical Medicine and Surgery, Oncology Unit, University of Naples Federico II, Naples, Italy, Napoli; [3]CRCTR Rare Tumors Reference Center of Campania region, Naples, Italy, Napoli; [4]Università degli studi di Napoli "Federico II", Department of Public Health, Napoli; [5]Istituto Scientifico Romagnolo per lo studio e la Cura dei Tumori IRST IRCCS, Meldola, Italy, Napoli; [6]Psycho-Oncology Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST), IRCCS, Meldola, Italy, Napoli; [7]Direzione Scientifica, Istituto Nazionale Tumori, IRCCS, "Fondazione G. Pascale", Naples, Italy., Napoli; [8]Istituto Nazionale Tumori, IRCCS "Fondazione G. Pascale", Naples, Italy, Napoli; [9]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy, Napoli; [10]Department of Clinical Medicine and Surgeryand CRCTR Rare Tumors Reference Center of Campania region, University of Naples Federico II, Naples, Italy, Napoli

Background: In Western countries Testicular Cancer (TC) is the most common solid tumor in young men aged between 15 and 40 years. The existential challenge of receiving a life threatening diagnosis at a young age may cause considerable psychological distress. Indeed, the TC diagnosis triggers off long-term consequences, including coping with adverse events, decreased quality of life (QoL), and often a reduced ability to work and a less active social life. The aim of this study was to evaluate the impact of TC diagnosis on the psychological and sexual sphere of patients aged > 18 years.
Methods: This was a multi-center prospective study conducted from January 2014 to June 2019. All data were collected at three time-points (TP): first TP at TC diagnosis, second TP at 3 months from treatment start, third TP at 6 months from treatment end. The following questionnaires were administered to TC patients (TCP) at each TP: International Index of Erectile Function (I.I.E.F.); Hospital Anxiety and Depression Scale (HAD'S); EORTC QLQ-C30 version 3.0 plus the EORTC QLQ-TC26 Sheet; Mini-MAC (Mini Mental Adjustment to Cancer). Statistical analysis using R (R Core Team, 2018) and lme4 tests (Bates et al., 2015) were used to find differences between two groups of TCP (Stage I vs Stage II-III and Surveillance vs Chemotherapy) over time (1TP-2TP-3TP).
Results: 102 TCP were enrolled. Regarding differences between Surveillance vs Chemotherapy: the effect of desperation (DE) on depression (D) was positive and significant (b = 0.145, p <0.001), but constant over time (COT), as well as the effect of anxious concern (AC) on D (b = 0.107, p <0.001). The effect of erectile function (EF)

on anxiety (A), on D and on DE was negative and significant, but COT (b = -0.069, p = 0.002; b = -0.091, p <0.001; b = -0.090, p <0.016, respectively). Regarding differences between Stage I vs Stage II-III: the effect of A on General Health Status (GHS) increased significantly over time (b = 0.627, p = 0.035); the effect of D on GHS was positive and significant (b = 0.761, p = 0.032), but COT. The effect of AC on the GHS was negative and significant (b = -0.687, p <0.001), but COT.
Conclusions: This is the first study to analyse TC diagnosis impact on psychological and sexual sphere, over time. Our data suggest that the experience of TC has an impact on adaptation, psychological distress, sexual functioning and QoL, in relation to the phase of TCP taking charge and to the delivered treatments.

H11

PLASMA TUMOR DNA AS EARLY PREDICTIVE BIOMARKER IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

Casadei C.[1], Conteduca V.[1], Wetterskog D.[2], Scarpi E.[1], Romanel A.[3], Gurioli G.[1], Jayaram A.[2], Lolli C.[1], Gasi Tandefelt D.[4], Schepisi G.[1], Wingate A.[2], Matteucci F.[1], Paganelli G.[1], Gonzalez-Billalabeitia E.[5], Demichelis F.[3], Attard G.[2], De Giorgi U.[1]

[1]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [2]University College London Cancer Institute, London; [3]Department of Cellular, Computational and Integrative Biology, University of Trento, Trento; [4]Department of Urology, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [5]Hospital Universitario Morales Meseguer-IMIB and UCAM, Murcia

Background: Plasma tumour DNA (ptDNA) levels are a promising minimally-invasive biomarker potentially useful to measure treatment efficacy in several types of cancers. However, in prostate cancer there is an urgent need to determine the potential predictive role of ptDNA monitoring. Here we analyzed on-treatment ptDNA variations and investigated its potential association with treatment outcomes for metastatic castration-resistant prostate cancer (mCRPC).
Methods: Between 2011 and 2016, we prospectively included 43 mCRPC abiraterone-treated patients, performing targeted next-generation sequencing on 114 sequential plasma samples, to evaluate ptDNA fraction. The primary endpoint was to determine the role of ptDNA fraction changes and radiographic/biochemical response at 3 month therapy. ptDNA progression was defined as any increase in the fraction compared to the baseline.
Results: A rise in ptDNA levels in the first on-treatment sample (interquartile range (IQR) 2.6-3.7 months) was significantly associated with increased risk of early radiographic progression or prostate-specific antigen (PSA) rise (OR=15.8, 95%CI 3.5-60.2, p=0.0002 and OR=6.0, 95%CI 1.6-20.0, p=0.01, respectively). We also observed exemplar cases that had an increase in PSA or pseudo-progression due

to bone remodeling without rise in ptDNA. In an exploratory analysis, we found that initial ptDNA change correlates with the duration of response to prior androgen deprivation therapy (p<0.0001) but not to prior docetaxel (p=0.32).

Conclusions: PtDNA assessment could be useful and feasible biomarker for therapy monitoring in mCRPC, providing relevant information to the clinical management. Prospective evaluation of these findings is now merited.

H12

CHANGES IN PLASMA AR COPY NUMBER AND OUTCOME TO ABIRATERONE AND ENZALUTAMIDE

Gurioli G.[1], Casadei C.[1], Virga A.[1], Conteduca V.[1], Schepisi G.[1], Gargiulo S.[1], Altavilla A.[1], Lolli C.[1], Scarpi E.[1], Filograna A.[1], De Giorgi U.[1]

[1]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Forlì-Cesena*

Background: Liquid biopsy, such as cell free DNA (cfDNA) has emerged as a minimally invasive and good source of biomarkers deriving from multiple metastases. Androgen receptor (AR) copy number (CN) is considered one of the main mechanisms of hormone-sensitive to hormone-resistant transition. Baseline AR CN status, detected in plasma cfDNA, identifies castration-resistant prostate cancer (CRPC) patients with worse outcome on abiraterone/enzalutamide. However, the impact of AR CN changes during these treatments on CRPC clinical outcome is unknown.

Material and methods: Plasma samples from 73 patients treated with abiraterone or enzalutamide in pre- or post-chemotherapy settings were collected at baseline and at the time of progression disease (PD). Droplet digital polymerase chain reaction was used to assess AR CN status.

Results: We showed that 11 patients (15.1%) changed AR CN status from baseline to PD (9 patients from normal to gain, 2 from gain to normal). Patients changing AR CN status from normal at baseline to gain at PD had intermediate median overall survival (OS) of 20.5 months (95%CI 8.0-44.2) between those who remained AR CN normal from baseline to PD (27.3 months [95%CI 21.9-34.4]) and those who remained AR CN gain from baseline to PD (9.1 months [95%CI 3.8-14.5]) (p < 0.0001). Patients changing AR CN from normal at baseline to gain at PD had a median progression-free survival (PFS) of 9.2 months (95%CI 2.0-14.7), patients who remained AR CN normal had a median PFS of 9.1 months (95%CI 7.2-10.1) and patients who remained AR CN gain had a median PFS of 5.4 (95%CI 3.6-6.5) (p= 0.0005). Both OS and PFS were not significantly different between patients with AR CN that changes from normal to gain and patients with stable AR CN normal, suggesting that the difference on clinical outcome depends on AR CN status at baseline.

Conclusions: We showed that CRPC patients changing AR CN status from baseline to PD time point had intermediate OS and we suggested that AR CN evaluation at baseline could be the most informative for clinical outcome of CRPC patients treated with abiraterone or enzalutamide. Larger prospective studies are warranted.

H13

INTERIM ANALYSIS OF CASSIOPE, A EUROPEAN REAL-WORLD STUDY OF CABOZANTINIB FOR THE TREATMENT OF ADVANCED RENAL CELL CARCINOMA (aRCC) FOLLOWING VEGF-TARGETED THERAPY

Masini C.[1], Hamberg P.[2], Bigot P.[3], Suárez C.[4], Barthelemy P.[5], Eymard J.[6], Gajate P.[7], Dutailly P.[8], Perrot V.[8], Staehler M.[9], Procopio G.[10]

[1]*Oncology Unit, AUSL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [2]Franciscus Gasthuis & Vlietland, Rotterdam, Netherlands; [3]Centre Hospitalier Universitaire d'Angers, Angers, France; [4]Vall d'Hebron University Hospital and Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain; [5]Hôpitaux Universitaires de Strasbourg/ICANS, Strasbourg, France; [6]Institut Jean Godinot, Reims, France; [7]Hospital Universitario Ramón y Cajal, Madrid, Spain; [8]Ipsen, Boulogne-Billancourt, France; [9]Universität München, Klinikum Grosshadern, Munich, Germany; [10]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy*

Background: Cabozantinib is approved in Europe for the treatment of aRCC in treatment-naive patients with intermediate or poor risk, or following VEGF-targeted therapy. We report interim safety data on real-world use of cabozantinib as second- or later-line aRCC therapy.

Materials (patients) and methods: CASSIOPE (NCT03419572) is an ongoing, non-interventional study in patients with aRCC initiating cabozantinib after prior VEGF-targeted therapy. This pre-planned interim analysis was conducted when 50% of patients had completed ≥ 3 months of follow-up. The primary objective was to describe dose modifications due to adverse events (AEs) during the first 3 months of treatment; secondary objectives include AE characterisation and best overall response (BOR) by RECIST 1.1.

Results: The Full Safety Population comprised 337 patients receiving cabozantinib (median age, 66 y; 73.0% male; 83.7% clear-cell histology; 96.4% metastatic disease, 85.7% ECOG 0–1); 265 (78.6%) remained on treatment at 3 months. The Primary Safety Population comprised 217 (64.4%) patients initiating cabozantinib at the recommended 60 mg dose; 109 (32.3%) initiated at 40 mg, and 6 (1.8%) at 20 mg. In the Full Safety Population, 30 (8.9%) patients died during the first 3 months of treatment (disease progression, 19; serious AE, 9; other, 2); of those in whom BOR was evaluable (n = 131), 31.2% had a partial response, 53.4% had stable disease and 15.3% had progressive disease. AE-related dose modifications and AE intensity are shown in the Table.

Conclusions: In this real-world study, 64.4% of patients initiated cabozantinib at the recommended dose; AE-related dose modifications were similar for the Full and Primary Safety populations. No new safety signals were seen in this 3-month interim analysis. Dose modifications may be required to optimize cabozantinib use in routine care.

	Primary Safety Population (initiated at 60 mg)			Full Safety Population (initiated at any dose)		
	2L (n = 106)	≥ 3L (n = 111)	Total (n = 217)	2L (n = 146)	≥ 3L (n = 191)	Total (n = 337)
Dose modification due to AEs, n (%)						
Any	68 (64.2)	74 (66.7)	142 (65.4)	84 (57.5)	122 (63.9)	206 (61.1)
Reduction	42 (39.6)	57 (51.4)	99 (45.6)	51 (34.9)	81 (42.4)	132 (39.2)
Interruption	46 (43.4)	51 (45.9)	97 (44.7)	55 (37.7)	88 (46.1)	143 (42.4)
Discontinuation	8 (7.5)	15 (13.5)	23 (10.6)	11 (7.5)	24 (12.6)	35 (10.4)
AE intensity, n (%)						
Grade 3	37 (34.9)	42 (37.8)	79 (36.4)	54 (37.0)	72 (37.7)	126 (37.4)
Grade 4	7 (6.6)	5 (4.5)	12 (5.5)	8 (5.5)	10 (5.2)	18 (5.3)

H14

A PHASE 2 OPEN LABEL STUDY OF CABOZANTINIB IN PATIENTS WITH ADVANCED OR UNRESECTABLE RENAL CELL CARCINOMA PRE-TREATED WITH ONE IMMUNE-CHECKPOINT INHIBITOR: THE BREAKPOINT TRIAL (MEETURO TRIAL 03 - NCT03463681)

Pircher C.[1], Claps M.[1], Montone R.[1], De Giorgi U.[2], Guadalupi V.[1], Mennitto A.[1], Sepe P.[1], De Braud F.[3], Verzoni E.[4], Procopio G.[4]

[1]*Medical Oncology Unit, Fondazione IRCSS Istituto Nazionale dei Tumori di Milano, Milan, Italy, Milano;* [2]*Department of Medical Oncology, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST IRCCS, Meldola, Italy, Meldola;* [3]*Medical Oncology Unit, Fondazione IRCSS Istituto Nazionale dei Tumori di Milano, Milan, Italy. Department of Medical Oncology & Hematology, University of Milan, via Festa del Perdono 7, 20122 Milan, Italy, Milano;* [4]*Medical Oncology Unit, Fondazione IRCSS Istituto Nazionale dei Tumori di Milano, Milan, Italy., Milano*

Background: Antiangiogenic therapy was the milestone of metastatic renal cell carcinoma (mRCC) treatment for many years. Recently, immunotherapy (IM) showed to improved survival of mRCC patients (pts), thus bringing new light for the frontline standard of care. Prospective data evaluating the efficacy of vascular endothelial growth factor (VEGF)-targeted therapy in pts progressed to immune-checkpoint inhibitors (ICI) are lacking. Among VEGF pathway blockers, the multi-kinase inhibitor cabozantinib (cabo) significantly prolonged survival in pre-treated mRCC pts.

Material and methods: This is an ongoing open label, single arm, multicenter, phase II study to evaluate efficacy and safety of cabo in pts with advanced or unresectable RCC pre-treated in adjuvant or I line with a PD-1/PD-L1 inhibitor in monotherapy or combined with an anti-VEGF or anti-CTLA-4. Cabo 60 mg/daily was given until progressive disease (PD) or unacceptable toxicity. The primary endpoint was progression free survival, secondary endpoints were overall survival, objective response rate and safety.

Results: To date, 15/49 planned pts were enrolled. Pts median age was 56 years (range: 29-74), men in 80% of cases. The average duration of the first line was 5.7 months (range: 1-23). Baseline Karnofsky PS was 100 in 53% of pts, 80-90 in 33% and 70-80 in 13%. 20% of pts had a good Heng score, 33% intermediate and 40% poor. Pts received on average 4 cycles of cabo (range 1-17 months). 8 pts interrupted therapy for PD, 1 did not start cabo yet and 6 are on treatment. Grade (G) 3 adverse events (AEs) occurred in 40% of pts; the most common AEs were diarrhea (G1, 20%; G2, 40%), hypothyroidism (G2, 26%), mucositis (G1, 40%; G2, 6%), and fatigue (G1, 13%; G2, 33%). AEs led to transitory withholding of drug administration in 66% of pts and dose reduction in 20%.

Conclusions: So far, the treatment with cabo after a I line anti-PD-1 based immunotherapy resulted safe and feasible. The Breakpoint is the first prospective trial to provide evidence of efficacy and safety of the ICI-cabo sequence. Moreover, the study includes the analysis of tumor and blood samples in order to recognise biological and immunological signatures to correlate with outcome and tolerability.

H15

PTEN AND ARV-7 STATUS IN CIRCULATING TUMOR CELLS BY FLOW CYTOMETRY IN MEN WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER RECEIVING ENZALUTAMIDE

Ribera D.[1], Buonerba C.[1], Di Lorenzo G.[1], Zappavigna S.[2], Scafuri L.[1], Giuliano M.[1], Bruzzese D.[1], Morra R.[1], Facchini S.[2], Iaccarino S.[1], Costabile F.[1], Onofrio L.[1], Viggiani M.[1], De Placido P.[1], Marretta A.L.[1], Pietroluongo E.[1], Morelli F.[2], Facchini G.[3], Caraglia M.[4], De Placido S.[1]

[1]AOU Federico II, Napoli; [2]S. Giovanni di Dio Hospital, ASL Napoli 2Nord, Oncology Unit, Frattamaggiore, Italy; [3]IRCCS Pascale, Napoli; [4]Department of Pharmaceutical and Biomedical Sciences, University of Salerno, Fisciano, Italy

Background: Since demonstration of enzalutamide efficacy in mCRPC men after failure of docetaxel, enzalutamide has proven to be effective in PCa patients in an increasing number of clinical settings. CTCs count has shown prognostic value in patients with advanced PCa regardless of the systemic treatment administered, the majority of available data in mCRPC populations selected for a certain treatment has been obtained in patients receiving abiraterone, with only limited data available in populations receiving enzalutamide Presence of ARV-7+ CTCs has been associated with resistance to enzalutamide and abiraterone.

Material (patients) and methods: CTCs in the peripheral blood were assessed within 28 days to the start of enzalutamide and after 12 weeks. Radiographic evaluation was performed by whole body CT scan with and without contrast and bone scan every 12 weeks. Continued surgical or medical castration was required during enzalutamide treatment. Anti-cytokeratin 8/18 and anti-CD45 antibodies were used to identify neoplastic cells in peripheral blood. Moreover, we evaluated the levels of PTEN and AR-V7 in prostate cancer cells in order to validate these antibodies.

Results: A total of 53 patients were enrolled since September 2016 to October 2018 at three participating centers. Median (interquartile range) CTCs count at baseline was 5 (3;8). CTCs count, PTEN- CTC count, ARV-7+ CTC count were associated with both PFS and OS at univariate analysis. At baseline, $\geq$5 vs. <5 CTCs were associated with worse PFS (HR = 2.35; 95%CI: 1.14–4.84; p=0.021) and OS (HR = 3.08; 95%CI: 1.45–6.54; p=0.003); $\geq$2 vs. <2 PTEN- CTCs were associated with worse PFS (HR = 3.96; 95%CI: 1.8–8.72; p= 0.001) and OS (HR =2.36; 95%CI: 1.12–5; p =0.025); $\geq$ 1 vs. < 0 ARV7+ CTCs was also associated with worse PFS (HR = 5.05; 95%CI:2.4–10.64; p <0.001) and OS (HR = 2.25; 95%CI:1.1 – 4.58;p=0.026).

Conclusions: ARV-7+ CTC count, which ranged from 0 to 20, was associated with rPFS as a continuous variable also (HR 1.25 (1.13 to 1.37) <0.001), which may suggest that additional information may be provided by counting circulating ARV-7+ cells and not by just assessing presence vs. absence. Furthermore, our results show that flow cytometry has potential to assess PTEN status in CTCs as a prognostic and possibly predictive marker in patients treated with enzalutamide. In conclusion our data add supporte the role of flow cytometry not only in enumeration but also in molecular profiling of CTCs.

H16

IS CABOZANTINIB EFFICIENT IN METASTATIC HLRCC PAPILLARY RENAL CELL CARCINOMA?

Cerbone L.[1], Carril-Ajuria L.[2], Colomba-Blameble E.[3], Crouzet L.[4], Laguerre B.[4], Thibault C.[5], Vicier C.[6], Caron O.[3], Richard S.[7], De Velasco G.[2], Flechon A.[8], Saldana C.[9], Ronan F.[3], Boccardo F.[10], Escudier B.[3], Albiges L.[3]

[1]Department de Medicine Oncologique, Institut Gustave Roussy, FR, Villejuif; [2]Hospital Universitario XII Octubre, Madrid; [3]Institut Gustave Roussy, Villejuif; [4]Centre Eugene Marquis, Rennes; [5]Hopital Europeen Georges Pompidou, Paris; [6]Institut Paoli-Calmette, Marseille; [7]Hopital Kremlin-Bicetre, Kremlin Bicetre; [8]Centre Leon Berard, Lyon; [9]APHP Hopital Henri Modor, Creteil; [10]Università degli Studi di Genova, Genova

Background: Hereditary Leiomyomatosis and RCC (HLRCC) is a rare autosomal dominant inherited disorder confering an increased risk to develop cutaneous and uterine leiomyomas and type 2 pRCC, caused by a germline mutation in FH, a Krebs cycle enzyme. Data on efficacy of systemic therapy in FH mutated pRCC population is limited. Recently the combination of Erlotinib and Bevacizumab proved a great efficacy in this specific subgroup of patients in a phase 2 trial. However, this data is still partial, with limited applicability to routine clinical practice. Cabozantinib (CABO), a potent tyrosine-kinase inhibitor (TKI), has become the standard of care after failure of first line in ccRCC and achieved an Overall Response Rate of 27% in all-comers pRCC patients (pts). The aim of this study is to describe the activity of CABO in HLRCC pts.

Methods: We included all FH mutated pRCC pts treated with CABO for metastatic disease from December 2014 to February 2020 in a multicentric retrospective study. Clinical, laboratory and survival data were retrospectively reviewed. Disease control rate (DCR) was defined as complete response (CR) + partial response (PR) + stable disease (SD) (CR+PR+SD). Objective response rate (ORR) as CR+PR. Time to treatment failure (TTF) was definded as time from CABO initiation to discontinuation of treatment for any reason and Overall Survival (OS) as time from CABO initiation to the date of last follow-up (FUP) or death. OS and TTF were estimated by Kaplan-Meier method. We reported the rates of grade 3-4 toxicities per CTCAE v 5.0.

Results: Overall, 10 patients with metastatic pRCC FH mutated treated with CABO were included in this study. Median age was 38 (28-56) years, 3(30%) were male, and 5(50%) had prior nephrectomy. Performance status was $\geq$ 80% in 50%. IMDC risk group was good, intermediate and poor in respectively 30%, 40%, and 30%. Among them, 40% had a family history of kidney cancer. Fifty% received CABO as second line and 50% received CABO as a third line. ORR and DCR were 50% and 80% respectively. TTF and OS were 13.8 months (95% IC: 9.50-18.12) and 23.2 months (95%IC: 7.08-39.32) respectively. The median follow up was 23.2 months (95%IC: 5.7-34.1). Grade 3-4

TRAE were reported in 50% (diarrhea 30%, HFS and mucitis 10% each). Three patients (30%) received erlotinib + bevacizumab as a further line after CABO.

Conclusions: In a context of lacking definitive evidences supporting clinical practice, CABO seems a powerful option in metastatic HLRCC patients.

H17

PROGNOSTIC FACTORS IN METASTATIC CASTRATION RESISTANT PROSTATE CANCER (MCRPC) PATIENTS (PTS) TREATED WITH RADIUM 223 (RA-223): A RETROSPECTIVE STUDY

Di Stefano R.F.[1], Angusti T.[1], Parente A.[1], Turco F.[1], Pisano C.[1], Leone G.[1], Samuelly A.[1], Vignani F.[2], Ortega C.[3], Scagliotti G.V.[1], Di Maio M.[2], Tucci M.[4], Buttigliero C.[1]

[1]A.O.U. San Luigi Gonzaga, Orbassano; [2]A.O. Ordine Mauriziano, Torino; [3]Ospedale San Lazzaro ASL CN2 Alba-Bra, Cuneo; [4]Ospedale Cardinal Massaia, Asti

Background: Ra-223 (Ra-223) improved overall survival (OS) in mCRPC pts. Our study aims to identify baseline prognostic factors that affect OS in mCRPC pts treated with Ra-223.

Methods: All CRPC pts treated with Ra-223 at Orbassano Hospital were included in this retrospective study. Data about demographics, ECOG PS, number and site of bone metastasis (mets), lymph node (LN) involvement, local treatment for prostate cancer (PC), previous treatments, number of Ra-223 doses, cell blood count, PSA, ALP, albumin, LDH, bone protecting agents use (BPA), analgesic use and survival were collected. OS was estimated by Kaplan Meier (log-rank) analysis.

Results: Seventy-five men received Ra-223 between September 2013 and December 2019, median age was 73 years (range 48-87). Thirty-four (45.3%) had ECOG PS 0, 41 (54.7%) PS 1-2. Median radium doses was 5 (range 1-8). 47 (62.7%) have received previous chemotherapy and 55 (73.3%) new hormonal agents. 34 (45.43%) had ≤20 bone mets and 41 (54.7%) >20. LN involvement (<3 cm) was detected in 23 pts (30.7%). 62 (82.7%) received BPA. 20 pts (26.7) had not received local treatment for PC. Median baseline laboratory results were: PSA 78.55 ng/ml (range: 1.33-3489), hemoglobin 12.2 g/dl (9.4-15.8), albumin 3428 g/L (2516-5400), ALP 174 U/L (38-3769), LDH 262 U/L (147-1062). 24 pts (32%) stopped treatment due to toxicity, 13 (17.3%) to progression and 33 (44%) completed treatment. In the whole series, median OS was 11.15 months (95%CI 9.54 – 12.76), with different prognosis according to number of previous lines for CRPC: median OS was 15.99, 14.61, 11.45 and 9.61 months in pts receiving radium as 1st, 2nd, 3nd and 4th /further line, respectively. On univariate analysis LN involvement (yes vs no,

HR 1.68, 95%CI 1.01-2.80, p=0.047), absence of local treatment on primary tumor (HR 1.93, 95%CI 1.13-3.29, p=0.016), baseline analgesic use (HR 1.82 95%CI 1.08-3.06, p=0.024), platelets to lymphocyte ratio (PLR) (high vs low, HR 1.91, 95%CI 1.06-3.45, p=0.03), baseline ALP (high vs low, HR1.81, 95%CI 1.10-2.99, p=0.019) and baseline LDH (high vs low, HR 3.86 (95%CI 2.01-7.41), p<0.001) were significantly associated with worst OS.

Conclusions: Baseline ALP, LDH, analgesic use, PLR, LN involvement and treatment on primary site are associated with different OS. Pending validation also in external series, these factors could be used to identify patients most likely to benefit from Ra-223.

H18

PREDICTORS OF OUTCOME IN METASTATIC RENAL CELL CARCINOMA PATIENTS TREATED WITH NIVOLUMAB PLUS IPILIMUMAB: FOCUS ON INFLAMMATORY LABORATORY MARKERS

Paolieri F.[1], Sbrana A.[1], Bloise F.[1], Sammarco E.[1], Nuzzo A.[1], Manacorda S.[1], Bazzurri S.[1], Manfredi F.[1], Mercinelli C.[1], Antonuzzo A.[2], Cianci C.[2], Falcone A.[1], Galli L.[1]

[1]Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa; [2]Azienda Ospedaliero-Universitaria Pisana, Pisa

Background: Nivolumab plus Ipilimumab (N+I) is a new standard of care for patients (pts) with not-pretreated intermediate- (IR) and poor-risk (PR) metastatic renal cell carcinoma (mRCC). So far there are no validated predictive biomarkers in this population.

Material (Patients) and Methods: We have prospectively collected blood samples of pts starting a treatment with N+I for mRCC since May 2019. For each patient we collected efficacy and tolerability data and evaluated several baseline laboratory Parameters, that included: complete blood count, reticulocyte count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lactate dehydrogenase, alkaline phosphatase, albumin, corrected calcemia, transferrin, ferritin, fibrinogen, TSH, fT3, and fT4. We analysed median progression-free survival (mPFS) and overall survival (mOS) in the general population and in the IR and PR subgroups with Kaplan-Meier method. We then performed regression analysis in order to highlight correlation between baseline laboratory parameters and clinical outcome.

Results: 14 pts were included in the analysis (7 IR, 7 PR). At the time of the analysis 7 pts progressed and 4 died. mPFS was 3.43 months (mos) (95%CI 2.23-7.93) in the general population: mPFS was not reached in the IR group, whereas it was 2.37 mos (95%CI 2.07-7.93) in the PR

group. mOS was not reached in the general population and in the IR group, whilst it was 7.93 mos (95%CI 2.23-7.93) in the PR group. At the regression analysis we observed a statistically significant correlation between baseline CRP levels (r^2 = 0.4028, p = 0.0148), neutrophil-to-lymphocyte ratio (NLR) (r^2 = 0.2979, p = 0.0435), platelet-to-lymphocyte ratio (PLR) (r^2 = 0.3143, p = 0.037) and OS. We also found a correlation between baseline ESR and OS, though not statistically significant (r_2 = 0.2334, p = 0.0801). No further correlation between other laboratory parameters and OS was found.

Conclusions: NIVO plus IPI is highly effective in IR and PR mRCC pts, but there are still some pts who do not benefit from this treatment. The research of new baseline predictive biomarkers is then a main goal for medical oncologists. In our little experience, lower values of baseline CRP, NLR, and PLR seem to be correlated with a better clinical outcome. However, further investigations in a wider number of patients are needed in order to prospectively validate our findings.

H19

INVASIVE UROTHELIAL CARCINOMA AND NEURAL PHENOTYPE: ALTERNATIVE SCORE DETECTION (PIESCORE) AND PROGNOSTIC IMPLICATIONS

Zucali P.A.[1], Colombo P.[2], De Carlo C.[2], Giordano L.[3], Ciceri M.[2], Hurle R.[4], Lazzeri M.[4], Elefante G.M.[4], D'antonio F.[5], Perrino M.[5], De Vincenzo F.[5], Guazzoni G.[4], Roncalli M.[2], Santoro A.[3]

[1]Department of Oncology, Humanitas Clinical and Research Center, IRCCS, Rozzano (Milano); [2]Unit of Pathology, Humanitas Clinical and Research Center, IRCCS, Rozzano, Milano; [3]Departement of Oncology, Humanitas Clinical and Research Center, IRCCS, Rozzano, Milano; [4]Deprtement of Urology, Humanitas Clinical and Research Center, IRCCS, Rozzano, Milano; [5]Deprtement of Oncology, Humanitas Clinical and Research Center, IRCCS, Rozzano, Milano

Background: Several molecular subtyping studies (NGS) identified a subset (5-15%) of muscle invasive urothelial carcinoma (MIBC) with transcriptomic patterns consistent with neuroendocrine (NE) differentiation in the absence of NE histology (NE-like). It represents a potentially high risk subgroup of carcinoma which may require a different treatment strategy. In order to discriminate Luminal from Basal from Neural carcinoma, we set an alternative immuno-phenotypical score (Piescore). Aim of this study is to test the ability of Piescore in identifying NE-like cases in a mono-institutional cohort of patients (pts) treated with trans-urethral resection and radical cystectomy (RC) and to correlate them with clinical outcomes.

Methods: Transurethral resection specimens harbored foci of high grade pT2 (MIBC) urothelial carcinoma from 173 pts who subsequently underwent RC have been submitted

for IHC analysis, using relevant gene-expression-based markers for Luminal type (CK20 and pPARg) and Basal type (CD44, CK5/6). The Piescore divided Basal and Luminal types when at least 3 of the 4 markers were consistent with a specific phenotype; Mixed if two luminal and two basal markers were present simultaneously; NE-like when all four markers were negative.

Results: Overall, the Piescore identified Basal phenotypes in 77 pts (45%), Luminal in 52 (30%), Mixed in 13 (8%), and NE-like in 31 (18%). Among NE-like phenotypes, 6 cases presented morphological NE differentiation and 25 urothelial differentiation. With a median FU of 97.1 months, pathological stage of disease (pT2 versus ≥pT3 and/or N+) and vascular invasion (absent vs present) resulted prognostic (Stage: 5-years DFS rate 50.7% vs 26.8%, p=0.008; 5-years OS rate 64.8% vs 38.2%, p=0.04) (vascular invasion: 5-years DFS rate 42.5% vs 16.6%, p<0.0001; 5-years OS rate 56.3% vs 25.2%, p<0.001) in all population. No statistically significant differences in terms of pathological stage of disease, vascular invasion, DFS, and OS were observed in NE-like cases compared with non-NE-like cases.

Conclusions: The NE-like urothelial carcinoma identified by Piescore immunophenotyping NE-like did not show any statistically significant association with prognosis.

H20

CLINICAL AND PATHOLOGICAL FEATURES OF ELDERLY PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (mRCC): A MONOCENTRIC EXPERIENCE

Bardasi C.[1], Caputo F.[1], Baldessari C.[1], Vitale M.P.[1], Fanelli M.[1], Cerma K.[1], Riggi M.L.[1], Pipitone S.[1], Dominici M.[1], Sabbatini R.[1]

[1]Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena

Background: Although more than 60% of metastatic renal cell carcinoma (mRCC) occurs in patients (pts) older than 60 years (y) and 20% in those older than 75y, elderly pts are often excluded or under-represented in clinical trials. The management of this mRCC subpopulation is not standardized, although age should not be considered a barrier to effective treatment, especially after the introduction of novel therapies. In this retrospective and monocentric study, we evaluated the disease characteristics of elderly pts (≥ 75y) comparing with youngers (< 75y).

Material and Methods: 133 pts with mRCC treated at University Hospital of Modena between 2006 and 2019 were analyzed. Statistical analysis was performed using χ^2 test, Kaplan-Meier method and log-rank test. Overall survival (OS) was calculated from the date of metastatic disease.

Results: Median age at diagnosis was 65 y. 28 pts (21%) were ≥ 75y while 105 pts (79%) were < 75y. No difference was revealed in terms of gender (male vs female, p=0,760), T stage (T1-2 vs T3-4, p=0,381), metastasis at

diagnosis (yes vs no, p=0,158), Heng and MSKCC prognostic scores (good vs other, p=0,945 and p=0,444, respectively) and number of lines of therapies received (⩾3 vs <3, p=0,110). The occurrence of lung, bone, lymph-nodes and central nervous system (CNS) metastases was similar among the two groups (p=ns), while liver metastases were higher in elderly pts (p=0,006). Elderly pts received more pazopanib as I line tyrosine-kinase therapy than youngers (p=0,0026). Median progression-free survival (mPFS) for first-line therapy was similar (8,6 and 8,5 months in youngers and elderly respectively, p=0,117). Globally, median OS (mOS) was 27 months (CI 95% 20,9-38,2), with no significant difference among youngers and elderly: 27,4 (CI 95% 16,3-40,4) and 24,1 months (CI 95%, 12,5-61,3), p=0,418. Interestingly, among youngers mOS was significantly different between pts with metastatic disease at diagnosis and pts relapsed (11,3 vs 44 months, p=0,0004), but not among elderly pts (23,9 vs 24,2 months).

Conclusions: Despite elderly being more fragile pts because of their greater comorbidities, age seems not to impact on survival outcomes in our small series. Therefore, considering the overall increase in life expectancy, studies aimed at the specific evaluation of elderly population are eagerly awaited in order to define the best therapeutic strategy and the biological characteristics of their disease.

H21

PROSTATE CANCER ASSOCIATED NK CELLS ARE ENDOWED WITH PRO-ANGIOGENIC PHENOTYPE/FUNCTIONS AND INDUCE M2-LIKE MACROPHAGE POLARIZATION

Albini A.[1], Gallazzi M.[2], Baci D.[2], Naselli A.[1], Guarnieri A.[1], Mortara L.[2], Deho F.[3], Noonan D.[4], Bruno A.[4]

[1]*IRCCS MultiMedica, Milano;* [2]*Department Biotechnologies and Biosciences, University of Insubria, Varese;* [3]*S.C. of Urology, ASST Settelaghi, Ospedale di Circolo e Fondazione Macchi, Varese;* [4]*Science and Technology Park (PST), IRCCS MultiMedica, Milano*

Background: Prostate cancer (PCa) remains the second most common cancer worldwide in men. Natural killer (NK) cells, effector lymphocytes of the innate immunity, have been found to be compromised in solid cancers, including PCa. We demonstrated that NK cells in lung and colorectal cancer, acquire a pro-angiogenic phenotype, similar to NK cell within the decidua (dNK), and functionally support angiogenesis, via TGFb and Stat3/Stat-5 activation. Here, we phenotypically and functionally characterized circulating NK cells from PCa patients (PTANKs) and investigated their interaction with endothelial cells and macrophages.

Material (patients) and methods: NK cell subset distribution was investigated by multicolor flow cytometry

(FC) for surface antigens on peripheral blood samples PCa patients. Conditioned media (CM) from FACS-sorted PTANKs were used for functional studies of angiogenesis, on human umbilical-vein endothelial cells (HUVEC), studies for macrophage recruitment (migration assay on Boyden chambers) and polarization. Molecular studies were performed by real time PCR (qPCR) on HUCECs and macrophages exposed to CM of PTANKs. Protein arrays were performed to characterize the secretome on FACS-sorted PTANKs.

Results: We found that PTANKs acquire the pro-angiogenic/decidual-like CD56^{bright}CD9$^+$CD49a$^+$CXCR4$^+$ phenotype. The same phenotype was observed on cytolytic NK cells, from healthy donors, exposed to CMs of three different PCa cell lines. These results were confirmed also exposing heathy-donor derived NKs to CMs of 3 different prostate cancer cell lines (PC-3, DU-145, LNCaP), together with increased production of CXCL8, Angiogenin, Angiopoietin1 and reduced production of TNFa, IFNg and GranzymeA. CMs from PTANKs support the formation on capillary-like structures on HUVEC, together with increased expression of VEGF, VEGR-2, CXCL8, ICAM-1 and VCAM-1. Secretome analysis revealed the ability of PTANKs release pro-angiogenic factors (CLXL8, MMP-1, MMP-9; uPAR) and cytokines/chemokines involved in macrophage recruitment (CCL1, CCL2, CCL5, CCL7, CCL13, CXCL1, CXCL11) and M2-like polarization (IL-10). Finally, CMs from PTANKs can recruit THP-1 monocyte and polarize THP-1 macrophage towards CD206, Arginase1, CXCL8-expressing M2-like/TAM phenotype.

Conclusions: Our results place PTANKS as effector cells able in supporting angiogenesis in PCa by directly interaction with endothelial cells and via macrophage polarization.

H22

LONG-TERM SURVIVAL OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (mRCC): A RETROSPECTIVE ANALYSIS OF DISEASE CHARACTERISTICS

Fanelli M.[1], Vitale M.G.[1], Caputo F.[1], Cerma K.[1], Bardasi C.[1], Riggi M.L.[1], Baldessari C.[1], Dominici M.[1], Sabbatini R.[1]

[1]*University Hospital of Modena, Division of Oncology, Modena, Modena*

Background: Targeted therapy and immunotherapy have improved clinical outcomes of patients (pts) with metastatic renal cell carcinoma (mRCC) recently, resulting in median overall survival (mOS) around 25 months (mos). However, a subgroup of pts draws scarce benefit from these therapies. In this retrospective study, we evaluated the disease characteristics potentially related to long- and short-term survival.

Material and methods: Data from 133 pts with mRCC treated at Modena Oncologic Center between 2006 and 2019 were collected. We defined as long-term survivors (LTS) the pts with mOS ≥36 mos, and as short-term survivors (STS) those with mOS ≤12 mos from the date of mRCC diagnosis. All pts received a 1st line therapy. A Chi-square test was used to compare variables between both groups. OS and progression-free survival (PFS) were evaluated by the Kaplan-Meier method and log-rank test.

Results: The mOS of the whole population was 27 mos (CI 95% 19.57-34.42). 42 pts (31.5%) were LTS, and 44 (33%) were STS. No significant differences in terms of median age at mRCC diagnosis (around 64 years) and gender (mainly males) were found between the two groups. Among the LTS, 43% and 16.6% were classified according to Heng score as good/poor risk pts, as compared to 13.6% and 34% among the STS. 27 LTS pts (64.3%) had metachronous metastases, while 31 STS (70.5%) had synchronous metastases. The most common metastatic sites at diagnosis were lung, lymph nodes, and bone in both groups, whereas liver metastases were observed in 7% of LTS and 34% of STS pts. mOS was 61 (CI 95% 31.14-90.86) and 7 mos (CI 95% 5.56-8.44), in the two groups. Median PFS (mPFS) for 1st line therapy was 24.5 and 3 mos, respectively, with a remarkably higher disease-control rate (DCR) for LTS (88% vs 34%). Furthermore, 83.3% of LTS pts received 2nd line therapy with a mPFS of 8 mos, while only 41% of STS pts underwent a 2nd line therapy with a mPFS of 1.5 mos. Comparing the two groups, metachronous disease (p=0.001), absence of liver metastases at the diagnosis of metastatic disease (p=0.002), and Heng good risk (p=0.003) emerged as associated with long survival.

Conclusions: According to literature, our series shows a favorable prognostic role for metachronous disease, absence of liver metastases, and good risk score in pts with mRCC. However, further investigations are needed to better understand the biological and molecular mechanisms underlying the observed differences between the two populations.

H23

EFFECT OF OBESITY ON OVERALL SURVIVAL IN PATIENTS WITH METASTATIC PROSTATE CANCER: A RETROSPECTIVE INSTITUTIONAL STUDY

Vitale M.G.[1], Cerma K.[1], Baldessari C.[1], Fanelli M.[1], Caputo F.[1], Riggi L.[1], Bardasi C.[1], Pipitone S.[1], Dominici M.[1], Sabbatini R.[1]

[1]*University Hospital of Modena, Division of Oncology, Modena, Modena*

Background: Prostate cancer is the second most frequent tumour among males in Western countries. Recent evidences suggest that elevated Body Mass index (BMI) is associated with aggressive disease and a higher risk of recurrence in prostate cancer patients (pts). We aimed to evaluate the association between BMI and overall survival (OS) in patients with metastatic prostate cancer (mPC).

Material and Methods: This retrospective study included 189 mPC pts diagnosed between 2003 and 2019 in Modena Cancer Centre and categorised according to BMI (normal/low BMI <25 kg/m2 and high BMI ≥25 kg/m2) calculated from height and weight extracted from medical records at the time of mPC diagnosis. Overall survival (OS) curves were drawn using the Kaplan-Meier method and long rank test was used to compare OS within BMI groups.

Results: The median OS of the whole group was 47,7 months (mo) (95%CI, 42,8-190,9). 121 (64%) pts had a high BMI. The median age of pts in high and normal/low BMI group at baseline was 72 and 74 years, respectively. At diagnosis there were no significant differences between the two groups regarding stage, T classification, age (<75 vs ≥75 years), bone, lymph-node and liver metastasis. Among pts with high BMI, a higher Gleason Score (≥8: 64,7% vs 49,2%, p=0,043) and less lung metastasis (presence: 3,1% vs 15,4%, p=0,006) were evidenced. No significant differences were noted between the two groups regarding response to I line of treatment (progressive disease vs complete response, partial response or stable disease), toxicities of I line treatment and number of lines of therapy received (<3 vs ≥3). Pts with higher BMI had better OS (median OS 58,4 mo, 95%CI, 43,0-78,6) than patients with normal/low BMI (39,8 mo, 95%CI, 32,1-190,9), but difference did not reach statistical significance (p=0,102).

Conclusions: BMI is not associated with statistically significant differences in overall survival in patients with mPC treated with new drugs. Larger studies are needed to confirm these findings.

H24

EFFICACY AND SAFETY OF NIVOLUMAB AFTER SUNITINIB OR PAZOPANIB: RETROSPECTIVE ANALYSIS OF A CASE SERIES FROM ONCOLOGY CENTERS OF NORTH-WESTERN TUSCANY

Sbrana A.[1], Paolieri F.[1], Bloise F.[1], Sammarco E.[1], Nuzzo A.[1], Manacorda S.[1], Bazzurri S.[1], Manfredi F.[1], Mercinelli C.[1], Biasco E.[2], Farnesi A.[3], Caparello C.[4], Pacetti P.[5], Antonuzzo A.[6], Dargenio F.[4], Falcone A.[1], Galli L.[1]

[1]*Dipartimento di Ricerca Traslazionale e delle Nuove Tecnologie in Medicina e Chirurgia, Università di Pisa, Pisa; [2]Dipartimento Oncologico, Azienda USL Toscana Nord Ovest, Portoferraio (LI); [3]Dipartimento Oncologico, Azienda USL Toscana Nord Ovest, Livorno; [4]Dipartimento Oncologico, Azienda USL Toscana Nord Ovest, Piombino (LI); [5]Dipartimento Oncologico, Azienda USL Toscana Nord Ovest, Massa-Carrara; [6]Azienda Ospedaliero-Universitaria Pisana, Pisa*

Background: A subgroup analysis of the CheckMate 025 trial, a phase III trial of nivolumab (NIVO) versus everolimus in second-line metastatic renal cell carcinoma (mRCC),

hypothesized that patients (pts) that had received pazopanib (PAZO) as a first-line treatment had a better outcome than those treated with sunitinib (SUN) when receiving a second line therapy with NIVO.

Material (Patients) and Methods: In a collaboration between the Oncological Department of the University Hospital of Pisa and three Oncology Units in the North-Western Area of Tuscany (Azienda USL Toscana Nord Ovest) we retrospectively analyzed a series of pts who received at least three lines of therapy and in whom a second line therapy with NIVO was administered. We performed Kaplan-Meier analysis for median progression-free survival (mPFS) and median overall survival (mOS) of second-line treatment with NIVO in the two subgroups PAZO>NIVO and SUN>NIVO. We also registered immune-related adverse events (IRAEs) in the two subgroups.

Results: 37 pts were included in the analysis: 20 received the sequence SUN>NIVO and 17 PAZO>NIVO. mOS for the second line treatment with NIVO was similar in the two subgroups (44.77 months for PAZO>NIVO vs 42.1 months for SUN>NIVO, p = 0.36). mPFS of second-line treatment with NIVO was slightly higher in the PAZO>NIVO group, even if such difference was not statistically significant (14.03 months vs 8.73 months, p = 0.72). The immune-related toxicities were slightly more frequent in the SUN>NIVO subgroup: 15 pts out of 20 had any kind of IRAEs, whereas only 8 pts out 17 had any kind of IRAEs in the PAZO>NIVO group, though this difference was not statistically significant (Fisher's exact test: p = 0.0536). As far as severe events are concerned, we observed 2 grade-3 IRAEs in the SUN>NIVO group (a hypothyroidism and a pneumonia) and 1 grade-3 colitis in the PAZO>NIVO group (Fisher's exact test: p = 1).

Conclusions: In our series NIVO seems to be equally effective when administered after either SUN or PAZO. The toxicity rate of NIVO in the sequence SUN>NIVO seems to be slightly higher than in the PAZO>NIVO subgroup, even if such difference is not statistically significant.

H25

THE "BURNED OUT" OR "BURNT OUT" TESTICULAR CANCER (BTC): AN ANALYSIS OF A RARE PHENOMENON IN A VIRTUAL COHORT OF PATIENTS

Iannantuono G.M.[1], Torino F.[1], Capotondi B.[1], Dell'Aria F.[1], Filomeno L.[1], Guerriero S.[1], Martinelli F.[1], Roselli M.[1]

[1]Oncologia Medica, Dipartimento Medicina dei Sistemi, Università Roma Tor Vergata, Roma

Background: The BTC indicates the spontaneous and complete regression of a testicular germ cell tumor (TGCT) in the presence of distant metastases (mts) at the diagnosis. Features describing BTC are sparse, as only case reports and case series are available in the literature. Moreover, it has never been reviewed systematically. Therefore, we reviewed the literature to thoroughly describe the clinical and histological characteristics of patients (pts) diagnosed with BTC.

Patients and methods: Medline was appropriately searched from inception to 19 April 2020. Eligible publications had to be at least case reports or case series in English or European languages, reporting clinical and histological relevant details. Out of 451 papers resulting from the search, 57 were included in the study and provided the pts' data of interest.

Results: A virtual cohort of 69 pts diagnosed with BTC was created. The median age was 34 (17-64) years. At the diagnosis, prevalent symptoms were abdominal pain (31%) and back pain (28%); only 4% of pts reported testicular swelling or palpable mass. The most common mts site was retroperitoneum (75%), and the mts histology was compatible with seminoma (SEM) and non-seminoma (nSEM) in 45% and 25% of pts, respectively. In orchiectomy specimens, a testicular scar/fibrosis was found in 86% of pts, germ cell neoplasia in situ in 26%, reduced spermatogenesis in 11%, calcification in 11%, and microlithiasis in 8%. Our findings highlighted some inconsistencies. Firstly, the BTC diagnosis was attributed to 6% of pts not having mts. Secondly, BTC was diagnosed in 5% of cases only based on testicular imaging, in the absence of a histological assessment on orchiectomy specimens. Lastly, a partial regression was detected in 23% of pts' testes, as demonstrated by the presence of residual tumor, attributed to SEM and nSEM in 40% and 27% of cases, respectively.

Conclusions: Our large virtual cohort of pts offers a detailed and updated picture of BTC's clinical and histological features. SEM is the most common histotype associated with BTC. The high occurrence of retroperitoneal mts in BTC pts indicates that it must be considered in the diagnostic workup for retroperitoneal extragonadal germ cell tumors. The inconsistencies that emerged in the study highlight the need for a clearer definition of this phenomenon. Larger, multi-institutional registries are needed better to understand the phenomenon of BTC and its clinical implications.

H26

PROGNOSTIC IMPACT OF AGE ON METASTATIC PROSTATE CANCER TREATED WITH NEW DRUGS

Cerma K.[1], Vitale M.G.[1], Baldessari C.[1], Fanelli M.[1], Caputo F.[1], Bardasi C.[1], Riggi L.[1], Pipitone S.[1], Dominici M.[1], Sabbatini R.[1]

[1]University Hospital of Modena, Division of Oncology, Modena, Modena

Background: New treatments (abiraterone acetate, enzalutamide, cabazitaxel, Radium-223) have changed the natural history of metastatic prostate cancer (mPC). The objective of this study is to evaluate the impact of age on clinical outcomes of mPC patients (pts).

Patients Aand Methods: We conducted a retrospective analysis of 200 pts with mPC treated at Modena Cancer Center between 2003 and 2019. Pts were divided into two groups according to median age of the whole group (young <72 years and elderly ≥72 years). Differences between groups were investigated with χ2 test. Overall survival (OS) and progression free survival (PFS) curves were drawn using the Kaplan-Meier method and log-rank test was used to compare OS and PFS within age groups.

Results: Among all pts, 58,1% had Gleason Score≥ 8 and 46,4% were stage IV at initial diagnosis. Among pts without evidence of metastasis at diagnosis median time for mPC was 69,3 months (mo). 59.3% of pts received prostatectomy. Median OS (mOS) of all pts was 47 mo (95%CI, 41,7-190,9). Median follow up was 37,7 mo. Young group included 92 pts (46%). These pts had higher initial stage (IV: 57,1% vs 36,8%, p=0,007), similar BMI (=25: 66% vs 62%, p=ns), Gleason score (=8: 57,8% vs 58,4%, p=ns) and T stage distribution (p=ns) compared to elderly pts. There was a trend of less bone metastasis at mPC diagnosis (57,1% vs 71,6%, p=0,059) and more lymph-node involvement (51,2% vs 39,7%, p=ns) in this group. They received more docetaxel as I line treatment (52,2% vs 31,5%, p=0,003) and more lines of therapy than others (=3 lines: 44,6% vs 29,6%, p=0,029). There was a statistically significant difference in OS between the two groups: mOS was 59 mo (95%CI, 43,0-190,9) in young group and 41,7 mo (95%CI, 33,2-50,4) in elderly group, p=0,0019. No significant difference in term of PFS in I, II, II and IV lines of therapy (PFS1, PFS2, PSF3 and PFS4) was evidenced between the two groups, but higher PFS5 was seen in young group (8,2 vs 2,1 mo, p=0,0418). It was underlined that only few pts both young and elderly received IV and V lines of therapy (23-18 and 10-5, respectively).

Conclusions: To our best knowledge, this is the first analysis that takes into consideration the impact of age on the clinical outcome of patients treated with new drugs in a real word setting. Younger patients with mPC seem to have a better OS statistically significant compared with old patients but our data are limited for the retrospective nature of the study.

H27

A SINGLE CENTER EXPERIENCE OF MULTIDISCIPLINARY TEAM (MDT): IMPROVING CARE OF PATIENTS WITH PROSTATE CANCER

Ermacora P.[1], Zattoni F.[2], Girometti R.[3], Povolato M.[4], Toso F.[3], Pizzolitto S.[5], Delneri C.[6], Vescini F.[7], Barban F.[8], Moretti E.[9], Romanin M.[10], Garattini S.K.[11], Trovò M.[10], Dal Moro F.[2], Fasola G.[11], Magli A.[10]

[1]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [2]Clinica Urologica, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [3]Dipartimento di Radiodiagnostica, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [4]Medicina Nucleare, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [5]Anatomia Patologica, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [6]Istituto di Medicina Fisica e Riabilitazione Gervasutta, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [7]Endocrinologia e Malattie del Metabolismo, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [8]Associazione Cure Palliative Mirko Špacapan - Amore per sempre Onlus; ASUFC – Day Hospital Oncologico, Dipartimento di Oncologia di Udine, Udine; [9]Fisica Sanitaria, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [10]Radioterapia, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine; [11]Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero di Udine, Udine

Background: The heterogeneity of treatment of prostate cancer often results in controversies. Therefore, coordination of care is needed to assure best clinical practice and high quality performances. For all these reasons, a MDT approach to prostate cancer has been implemented at ASU-FC since June 2019 This report describes the methodology and the initial experience of our external ISO9001 certifier approved MDT.

Material and methods: Each member of MDT drafted its own reference treatment guidelines on a matrix. The most used were from Italian Association of Medical Oncology (AIOM) and European Association of Urology (EAU). Agreement on standards, as for protocol of service, were developed for each professional area (e.g. radiological diagnosis within 15 days for mpRM and 30 days for abdomen CT and total body bone scan, final histological diagnosis within 20 days, start of either surgery or radiotherapy in less than 45 days for high risk patients as well as less than 120 days for low risk cancers). The process indicators (managerial, diagnostic and quality of life-related) individuated in the light of local health care system availability were: reduction of time to reach diagnosis, improvement of adherence to guidelines for optimization of resources, improvement of biopsy sampling to facilitate histological reports, increase of the number of patients under active surveillance and research improvement. Finally, a specific evaluation system related to the general, operational and specific ISO9001-2015 accreditation requirements was developed to assess the starting level and elaborate an "action plan for improvement".

Results: Methodology phase was started on March 2019 defining the structures involved in the core team (oncology radiotherapy, urology, medical oncology, radiology and nuclear medicine) along with the non-core ones (pathology, bone health endocrinology, physiatry, psychology and medical physics). Bi-weekly meetings produced a specific flow diagram for each disease stage and a histology reporting system shared with physicians. From September, MDTs were initiated leading to medical reviews shared on the Hospital computer system. Finally, an external audit resulted into ISO9001-2015 certification.

Conclusions: Implementation of MDT and continous verification of outcomes through objective indicators results into optimization of prostate cancer care.

H28

A PHASE 3 STUDY (COSMIC-313) OF CABOZANTINIB IN COMBINATION WITH NIVOLUMAB AND IPILIMUMAB IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED RENAL CELL CARCINOMA OF INTERMEDIATE OR POOR RISK

De Giorgi U.[1], Choueiri T.K.[2], Albiges L.[3], Powles T.[4], Scheffold C.[5], Wang F.[5], Motzer R.J.[6]

[1]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola FC;* [2]*Dana-Farber Cancer Institute/Brigham and Women's Hospital and Harvard University School of Medicine, Boston;* [3]*Institute Gustave Roussy, Villejuif;* [4]*Barts Cancer Institute, Queen Mary University of London, London;* [5]*Exelixis, Inc., Alameda;* [6]*Memorial Sloan Kettering Cancer Center, New York*

Background: Cabozantinib (C) inhibits tyrosine kinases involved in tumor growth, angiogenesis, and immune regulation, including MET, VEGFR, and TAM kinases (Tyro3, AXL, MER), and may promote an immune-permissive tumor environment, resulting in enhanced response to immune checkpoint inhibitors. C has shown preliminary clinical activity and tolerability in combination with the PD-1 inhibitor nivolumab (N) and as part of a triplet combination with N and the CTLA-4 inhibitor ipilimumab (I) in patients (pts) with advanced renal cell carcinoma (aRCC) (Nadal et al. ASCO 2018). C is approved for pts with aRCC, and N+I is approved as a combination therapy in pts with previously untreated aRCC of intermediate or poor risk. We present the study design of a phase 3 trial of C+N+I vs N+I in previously untreated pts with aRCC of IMDC intermediate or poor risk (NCT03937219).

Methods: This randomized, double-blind, controlled phase 3 study evaluates the efficacy and safety of C+N+I vs N+I in previously untreated pts with IMDC intermediate or poor risk aRCC. Eligible pts are randomized 1:1 to receive C+N+I or N+I in combination with placebo, stratified by IMDC prognostic score and geographic region. Pts receive C (40 mg oral QD) + N (3 mg/kg IV Q3W) x 4 doses + I (1 mg/kg IV Q3W) x 4 doses, followed by C (40 mg oral QD) + N (480 mg IV flat dose Q4W). Control pts receive C-matched placebo and the same treatment regimen for N+I as the experimental arm. N will be administered for a maximum of 2 years. Eligibility criteria include histologically confirmed metastatic or aRCC with a clear cell component, intermediate or poor risk RCC per IMDC criteria, measurable disease per RECIST 1.1, KPS ≥70%, adequate organ and marrow function and age ≥18 years. Exclusion criteria include prior systemic therapy for aRCC and uncontrolled significant illnesses. The primary endpoint is PFS per RECIST 1.1 by BICR; the secondary endpoint is OS. Additional endpoints include ORR, safety, correlation of biomarkers with outcomes, and pharmacokinetics of C in combination with N+I. The first patient was enrolled in June 2019 and enrollment is ongoing.

H29

RARE CASES OF METASTASIS TO THE THYROID GLAND FROM RENAL CLEAR CARCINOMA SOME YEARS AFTER NEPHRECTOMY, AS THE FIRST AND ONLY SITE OF METASTASIS

Ricci I.[1], Intersimone D.[1], Dessanti P.[1], Vaira F.[1], Tognoni A.[1], Ferrari A.[1], Milano A.[1], Negru M.E.[1], Pastorino A.[1], Rondini M.[1], Vigani A.[1], Olcese F.[1], Barillaro F.[2], Camilli M.[2], Conti E.[2], Aschele C.[3]

[1]*ASL5 Spezzino-Ospedale Sant'Andrea, La Spezia;* [2]*ASL5 Spezzino-Ospedale San Bartolomeo, Sarzana;* [3]*ASL5 Spezzino-Ospedale Sant' Andrea, La Spezia*

Background: Renal cell carcinoma (RCC) is known to cause metastasis to unusual sites, which can be both synchronous or metachronous. Thyroid gland is a rare site for metastasis but, when it occurs, RCC is the most common primary neoplasm and can develop many years after initial diagnosis.

Patients and methods: We retrospectively reviewed our database of RCC patients with thyroid metastases. Our aim was to investigate the incidence of thyroid metastasis from RCC and describe patients' characteristics, initial presenting symptoms at the diagnosis of the thyroid metastasis, status and size of the metastatic lesions, diagnostic and therapeutic modalities used, the average latency time before the detection of metastasis after nephrectomy, presence of metastatic sites other than the thyroid gland, follow-up time after detection of thyroid metastasis with the final status of the patients.

Results: The total number of RCC patients observed from 2004 to 2019 in our institution was of about 208 cases. Out of these, only 3 patients developed thyroid metastasis from RCC, 1 male (a 79-year-old) and 2 females (respectively 71 and 78-year-old). The average lag time to diagnosis of thyroid metastases was ten years for two females and three years for male. Only one patient had symptoms. Regarding the tests performed for the diagnosis of RCC metastases to the thyroid gland, ultrasound of the neck was the most frequently used radiological imaging modality followed by computed tomography and positron emission tomography. The patients subsequently underwent fine needle aspiration cytology. Immunohistochemistry is helpful in differential diagnosis. All patients underwent radical thyroid surgery. The histopathological examination showed metastatic RCC of clear cell type in all three cases. The subsequent follow up was negative.

Conclusions: A thyroid nodule in a patient with a history of RCC should be considered as potentially metastatic. It's impossible distinguish between primary and secondary thyroid neoplasms on imaging, in fact clinical manifestation and radiographic findings are nonspecific. FNA cytology and immunohistochemistry are helpful in establishing diagnosis and should be obtained in suspected cases. Definitive diagnosis of metastatic RCC is usually made by histopathological examination after thyroidectomy. Our cases demonstrate the importance of considering RCC metastasis to the thyroid even years after nephrectomy to decrease potential delays in diagnosis.

M - Melanoma and Skin Cancers

M01

CONCORDANCE OF MUTATION PATTERNS BETWEEN PRIMARY AND METASTATIC MELANOMA THROUGH A NEXT-GENERATION SEQUENCING ASSAY

Manca A.[1], Paliogiannis P.[2], Lissia A.[2], Cossu A.[2], Casula M.[3], Colombino M.[3], Sini M.C.[3], Palomba G.[3], Rozzo C.[1], Pisano M.[1], Team M.U.S.[2], Palmieri G.[1]

[1]IRGB-CNR, Sassari; [2]AOU, Sassari; [3]ICB-CNR, Sassari

Background: Cutaneous malignant melanoma (CMM) is one of the most common skin cancers worldwide. Limited information is available in the current scientific literature on the concordance of genetic alterations between primary and metastatic CMM. In the present study, we performed next-generation sequencing (NGS) analysis of the main genes participating in melanoma pathogenesis and progression, among paired primary and metastatic lesions of CMM patients, with the aim to evaluate levels of discrepancies in mutational patterns.

Methods: Paraffin-embedded tumor tissues of the paired lesions were retrieved from the archives of the institutions participating in the study. NGS was performed using a specific multiple-gene panel constructed by the Italian Melanoma Intergroup (IMI) to explore the mutational status of selected regions (343 amplicons; amplicon range: 125-175 bp; coverage 100%) within the main 25 genes involved in CMM pathogenesis; sequencing was performed with the Ion Torrent PGM System.

Results: A discovery cohort encompassing 30 cases, and a validation cohort including eleven Sardinian patients with tissue availability from both the primary and metachronous metastatic lesions were identified; the global number of analyzed tissue specimens was 90. A total of 829 genetic non-synonymous variants were detected: 101 (12.2%) were pathogenic/likely pathogenic, 131 (15.8%) were benign/likely benign, and the remaining 597 (72%) were uncertain/unknown significance variants. Considering the global cohort, the consistency in pathogenic/pathogenic like mutations was 76%. Consistency for BRAF and NRAS mutations was 95.2% and 85.7% respectively, without statistically significant differences between the discovery and validation cohort.

Conclusions: Our study showed a high level of concordance in mutational patterns between primary and metastatic CMM, especially when pathogenic mutations in driver genes were considered.

M02

ROLE OF EOSINOPHILIA AS PROGNOSTIC BIOMARKER IN METASTATIC MELANOMA (MM) PATIENTS RECEIVING ANTI-PD1 INHIBITORS: A RETROSPECTIVE SINGLE INSTITUTION ANALYSIS

Conca R.[1], Zoppoli P.[2], Laurino S.[2], Aieta M.[1], Passarelli A.[1]

[1]Unit of Medical Oncology, Department of Onco-Hematology. IRCCS-CROB Referral Cancer Center of Basilicata. Rionero in Vulture (PZ), Italy, Rionero in Vulture (PZ); [2]Laboratory of Preclinical and Translational Research. IRCCS-CROB Referral Cancer Center of Basilicata. Rionero in Vulture (PZ), Italy, Rionero in Vulture (PZ)

Background: Eosinophilia has been identified as a prognostic marker in immunotherapy of MM and suggested to contribute to anti-tumor host defense. Nevertheless, the influence of anti-PD1 monoclonal antibodies (mAbs) on eosinophils (Eos) is poorly studied. Recently, it has been reported that early increase of Eos in peripheral blood could be associated with immunotherapy efficacy in MM.

Patients and methods: We retrospectively evaluated clinical data and Eos count of 28 cutaneous MM patients (pts) receiving anti-PD1 mAbs from January 2018 to April 2020. Eos peripheral count was evaluated at different time-points: baseline (T0), at second infusion (T1) and at first tumor assessment (T2). Baseline Eos count and its variation during treatment were analyzed for the association with efficacy (responders group versus non-responders group), and survival (overall survival [OS]). Log-rank test and Cox proportional hazards identified the eosinophilia role on OS. Data were analyzed using R software.

Results: In our cohort 14 patients were male (50%) and median age was 68 years. Stage classification was III, M1a, M1b, M1c, and M1d in 2 (7.1%), 7 (25%), 6 (21.3%), 10 (35.8%) and 3 (10.8%) pts, respectively. BRAF was mutated in 4 (15%) pts. 9 patients (32%) received prior therapy for MM. A clinical response occurred in 21 patients (75%; responders group) and included 2 with complete response, 10 with partial response and 9 with stable disease, whereas progressive disease was observed in 7 patients (25%; non-responders group). The difference of Eos count (defined as DEos) between T1-T0 and T2-T0

was correlated to the clinical response and survival. In specific, exploratory univariate logistic regression revealed that both higher DEos at T2-T0 and DEos at T1-T0 were significantly associated with better disease control rate (p <0.05 and p =0.078, respectively). In addition, log-rank test performed on both DEos at T2-T0 and DEos at T1-T0 revealed that higher variation during treatment was correlated with improvement in terms of OS (p-value <0.01), identifying only DEos at T1-T0 as a positive prognostic factor of survival.

Conclusions: Our data suggest that anti-PD1 mAbs can influence Eos count and its increase appears to be a potential biomarker associated with immunotherapy benefit and better OS, thus offering eosinophilia as a peripheral, readily available biomarker of response to immunotherapy. Anyway, further large studies are needed.

M03

CEMIPLIMAB IN ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA: PRELIMINARY DATA FROM A SINGLE INSTITUTION

Greco S.[1], Rimini M.[1], Riggi M.L.[1], Pipitone S.[1], Pugliese G.[1], Dominici M.[1], Depenni R.[1]

[1]*Azienda Ospedaliero Universitaria Policlinico di Modena, Modena*

Background: Advanced cutaneous squamous cell carcinoma (aCSCC), which include both metastatic disease (mCSCC) and locally advanced (laCSCC) disease not suitable to curative RT or surgery, have an unfavorable prognosis with scarce therapeutic options. Cemiplimab is an anti-PD1 human antibody with positive results in Phase I/II studies in aCSCC that lead to EMA approval on June 2019. Here wepresent our preliminary data.

Matherial and Methods: Prospective analysis of medical records of patients (pts) with aCSCC treated with Cemiplimab from July 2019 to May 2020 at Modena Cancer Center were conducted. Clinical parameters deemed of interest were collected. Disease Control Rate (DCR) at 2 and 3 months of treatment were evaluated by logistic regression analysis.

Results: During the study period, 13 pts aged 50 to 95 years (Median age 86 years) and with aCSCC were treated with Cemiplimab. ECOG Performance Status (PS) was 0-1 in 9 pts (69.2%) and 2 in 4 pts (30.8%). Median OS and PFS has not yet been reached at the cut off time of analysis (May 19, 2020). Up to now 8 pts are still on treatment; in these pts Median Duration of response was 3.45 months (0.7-12.1 months). An objective response was observed in 8 (61.5%) of 13 pts. The best overall response was: 4 (30.8%) pts with a complete response and 4 (30.8%) with a partial response. DCR was obtained in 10 pts (76.9%). By performinglogistic regression analysis,we

found that both ECOG (0-1 vs 2) and previous RT (No vs Yes) statistically impacted on DCR after 2 months (p=0.0180 and 0.0471, respectively) and 3 months (p= 0.0145, p= 0.0067, respectively) of treatment. Concerning the safety profile, 8 pts (61.5%) experienced adverse events (AEs). Grade 3-4 AEs occurred in 1 (7.7%) pt (Myasthenia), which leads to therapy suspension. The most common AEs were pruritus (38.5%), asthenia (30.8%), constipation (23.1%), diarrhea (15.4%).

Conclusions: In our experience Cemiplimab confirmed an high antitumoral activity with a good safety profile in advanced cSCCs. We highlighted that pts with ECOG PS 0-1 and without previous RT treatment seem to benefit most from Cemiplimab. A larger sample of pts and a longer follow up will provide us more detailed data about efficacy and safety of this new drug.

M04

IMMUNOTHERAPY IN METASTATIC UVEAL MELANOMA: A ITALIAN SINGLE-CENTER EXPERIENCE

Defferrari C.[1], Clavarezza M.[2], D'Amico M.[2], Gozza A.[2], Provinciali N.[2], Rutigliani M.[2], Corradengo D.[3], Rossi U.[3], Bacigalupo L.[2], Banderali S.[2], Mosci C.[2]

[1]*ospedale Galliera, Genova; [2]E.O. Ospedale Galliera, Genova; [3]Ospedale San Martino, Genova*

Background: Metastatic Uveal Melanoma (MUM) is an aggressive neoplasm with limited treatment options and poor prognosis. Despite the excellent immunotherapy response in cutaneous melanoma, anedoctal studies have shown very low response rates were shown in Uveal Melanoma. However, current guidelines on Cutaneous Melanoma and Uveal Melanoma are the same. We collected data from 10 MUM patients treated with pembrolizumab in our Hospital.

Material and Methods: A total of ten patients with MUM were treated with Pembrolizumab 200 mg (flat dose) as first line therapy from February 2018 to March 2020 for metastatic disease. All the patients had hepatic disease localizations, one patient had lung lesions also. At baseline all patients underwent liver biopsy, BRAF and PDL1 analysis, abdomen resonance (RM), total body CT scan (CT scan) which were repeated every 3 cycles.

Results: The mean age was 66 +SD years. The median time lapse from the first diagnosis of Uveal Melanoma to the onset of metastasis was 5 years (range 0.5-17 years). The median largest baseline metastatic hepatic lesion was 59 mm (range 22 to 100 mm).

All patients were BRAF and PDL1 negative and performed Pembrolizumab as first line therapy. Only one patient, with lowest tumoral burden, had stable disease after 3 cycles and low progression disease subsequently. The other nine

patients had rapid disease progression after 3 cycles with increased LDH and dimensional median disease increase by 42% (range 15-69%). Median os was 6.4 months (range2-15). Five patients had a PS deterioration (from 0 to 1). Median progression-free survival was 4.5 months (range 2-14). We have not recorded grade 3-4 toxicities.

Conclusions: These data suggest that MUM rarely respond to immunotherapy with pembrolizumab. Only a very small group of patients could benefit with durable stability. MUM and cutaneous melanoma are two different disease with different response to immunotherapy. Given the high cost, current guidelines should be amended to reflect this poor response of immunotherapy.

M05

COST-EFFECTIVENESS AND COST-UTILITY ANALYSIS OF CEMIPLIMAB IN PATIENTS WITH ADVANCED CUTANEOUS SQUAMOUS CELL CARCINOMA IN ITALY

Ghetti G.[1], D'Avella M.C.[2], Ascierto P.[3], Pradelli L.[1]

[1]*AdRes, Torino;* [2]*Sanofi, Milano;* [3]*Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Napoli*

Background: In Italy, cutaneous squamous cell carcinoma (CSCC) represents about 20-25% of non-melanoma skin cancers. About 3-5% of patients with localized CSCC develops advanced CSCC (aCSCC), which include metastatic (mCSCC) and locally advanced (laCSCC) disease, and are no longer responsive to surgery or radiation. aCSCC is associated with high morbidity and mortality, including severe disfigurement which can significantly increase the burden to the patient. Cemiplimab, a human monoclonal antibody, is the first systemic therapy approved for aCSCC patients. This study aims to assess the cost-effectiveness and cost-utility of cemiplimab vs chemotherapy from the Italian National Health Service (SSN) perspective.

Material and methods: A three-state partitioned survival model was developed to estimate, over a 30-year horizon, costs and outcomes for patients with aCSCC. A one-month model cycle was chosen and half-cycle correction was applied. Clinical efficacy, safety and quality of life (QoL) data for cemiplimab were collected from the EMPOWER-CSCC 1 study, whereas data for chemotherapy were taken from publications identified via a systematic literature review. In the absence of head-to-head randomized clinical trials, a simulated treatment comparison using a Cox model was performed to predict cemiplimab progression-free survival and overall survival given target population as observed in the Jarkowski et al. study. Costs of drug acquisition/administration and management of adverse events were included. Annual discount rate was 3%. Incremental cost-effectiveness ratio (ICER) and incremental cost-utility

ratio (ICUR) were calculated as cost/Life Years (LY) gained and cost/Quality-Adjusted Life Years (QALY) gained. Sensitivity and scenario analyses were performed to assess the robustness of results.

Results: Treatment with cemiplimab led to an increase of life expectancy of 4.89 LYs and 3.99 QALYs and an incremental cost of € 136,047, resulting in an estimated ICER and ICUR of 27,821 €/LY gained and 34,110 €/QALY gained, respectively. The probabilistic sensitivity analysis showed that both the ICER and the ICUR are below the Italian SSN willingness to pay thresholds (60,000 €/LY gained and 25,000-40,000 €/QALY gained, respectively).

Conclusions: Compared with chemotherapy, cemiplimab improved both survival, in pre- and post-progression health states, and patients' QoL. Cemiplimab can also be considered a cost-effective option for treatment of aCSCC patients in Italy.

M06

CELLULAR ANALYSIS OF BRONCHOALVEOLAR LAVAGE FLUID TO NARROW DIFFERENTIAL DIAGNOSIS OF CHECKPOINT INHIBITOR-RELATED PNEUMONITIS IN METASTATIC MELANOMA

Strippoli S.[1], Fucci L.[2], Negri A.[2], Putignano D.[2], Cisternino M.L.[2], Napoli G.[2], Filannino R.[2], De Risi I.[2], Sciacovelli A.M.[2], Guida M.[2]

[1]*IRCCS Istituto Tumori Giovanni Paolo II Bari, Bari;* [2]*IRCCS Istituto Tumori Bari Giovanni Paolo II, Bari*

Background: The diagnosis of check-point inhibitor-related pneumonitis (CIP) relies on radiological and clinical patterns which are not specific and can mimic other conditions (cancer progression, infectious diseases or interstitial pneumonitis). Cell pattern analysis of bronchoalveolar lavage (BAL) is well-known to support the diagnosis of interstitial lung disease; nevertheless, this analysis is not suggested by immune-toxicity management guidelines for CIP.

Methods: We conducted a single-center study by recruiting patients with stage IV melanoma treated with anti PD-1 alone or with anti-CTLA4 who underwent BAL after developing respiratory symptoms associated with computed tomography (CT) scan imaging suspected for CIP. We also correlated the BAL features with the CT scan patterns and with various peripheral blood parameters to better define the profile of this patient population.

Results: Among 112 patients treated with check-point inhibitors in 2018–2019 we identified 5 (4%) cases of CIP. There were 3 men, median age 58 years (43-77), in four cases the ongoing therapy was anti-PD1. Median time of onset was 44 weeks (6-88), according to CTCAE 5.0 we observed grade 3 toxicity in 4 cases and grade 2 in 1 case. One patient also had grade 3 colitis and two patients developed vitiligo as skin

toxicity. BAL cellular analysis showed typical and homogeneous features with predominantly macrophage elements, an increased lymphoid population with prevalent CD8+ T cells, and inversion of the CD4/CD8 ratio. These BAL features were associated with blood leukocytosis, hypoxemia, normal values for procalcitonin and lactate dehydrogenase, a cryptogenic organizing pneumonia-like (COP) radiologic pattern. All patients recovered from pulmonary toxicity after corticosteroid treatment for a median time of 2 months (range 2-12). PD1 inhibitors were permanently discontinued in 4 patients, whereas one patient was re-started on treatment until disease progression. Interestingly, in all our patients CIP was associated with previous or subsequent partial or complete response.

Conclusions: Identification of a specific BAL cellular pattern allows clinicians to place this investigation in the appropriate position of CIP diagnosis and management to avoid considering the condition as progressive disease and delaying proper treatment.

M07

IMMUNE-RELATED BELL'S PALSY IN MELANOMA PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS

Cimminiello C.[1], Fucà G.[1], Di Guardo L.[1], Beninato T.[1], Patuzzo R.[2], Maurichi A.[2], Gallino G.[2], Mattavelli I.[2], De Braud F.[3], Santinami M.[2], Del Vecchio M.[2]

[1]Unit of Melanoma Medical Oncology, Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [2]Unit of Melanoma Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; [3]Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

Background: The advent of immune checkpoint inhibitors (ICIs) was a revolution in cancer therapy, leading to remarkable long-lasting responses in the metastatic setting in some histotypes, especially melanoma. Together with unprecedented clinical benefit, immunotherapy has exposed the cancer healthcare community to novel immune-related adverse events (irAEs), usually unpredictable and capable of involving virtually any organ or system. Here we report a retrospective analysis of patients (pts) with melanoma who developed an immune-related, unilateral, acute, peripheral facial nerve paralysis (Bell's palsy) following treatment with ICIs.

Patients and methods: All consecutive pts with melanoma treated with ICIs at the Unit of Melanoma Medical Oncology of the Fondazione IRCCS Istituto Nazionale dei Tumori from January 2015 to January 2020 were retrospectively reviewed. Pts with a clinical diagnosis of ICI-related Bell's palsy were identified and clinicopathological characteristics, treatment specifics and Bell's palsy outcomes were retrieved. Descriptive statistics were used to summarize study data.

Results: During the study period, a total of 5 pts developed Bell's palsy as an irAE. Notably, all the pts were treated within the phase III clinical trial Checkmate 238 of nivolumab compared to ipilimumab after complete resection of stage IIIb/c or Stage IV melanoma (NCT02388906). At time of the present report, information about study treatment was available only for one pt (ipilimumab). Median age at the time of Bell's palsy diagnosis was 63 years (range, 48-69). 4 pts were male and one pt was female. Median time-to-onset of Bell's palsy from ICIs initiation was 15 weeks (range, 4-39). In 3 pts the acute onset of hemifacial weakness required ER consultation. 4 pts were treated with prednisone alone whereas one pt was treated with prednisone plus valaciclovir. The maximum daily dose of prednisone administered was 50 mg in 4 pts and 75 mg in one pt, whereas the median treatment duration was 36 days (range, 10-99). All the pts had a favorable outcome with a complete regression of signs and symptoms of the facial nerve paralysis. Median time-to-recovery was 41 days (range, 10-99).

Conclusions: In melanoma patients treated with ICIs, Bell's palsy is a rare, acute neurologic irAE with a favorable outcome following administration of oral corticosteroids.

N - Head and Neck Tumours

N01

SELPERCATINIB (LOXO-292) IN PATIENTS WITH RET-MUTANT MEDULLARY THYROID CANCER

Shah M.H.[1], Sherman E.J.[2], Robinson B.[3], Solomon B.[4], Kang H.[5], Lorch J.H.[6], Worden F.[7], Brose M.S.[8], Leboulleux S.[9], Godbert Y.[10], Meurer M.[11], Morris J.[12], Owonikoko T.K.[13], Tan D.S.[14], Weiler D.[15], Patel J.[16], Yang L[17], Kherani J.[17], Cabanillas M.E.[18], Wirth L.J.[19], Locati L.O.[20]

[1]The Ohio State University Comprehensive Cancer Center, Columbus; [2]Memorial Sloan Kettering Cancer Center, New York; [3]Royal North Shore Hospital, St. Leonards; [4]Peter MacCallum Cancer Center, Melbourne; [5]University of California, San Francisco; [6]Dana-Farber Cancer Institute, Boston; [7]University of Michigan, Ann Arbor; [8]Abramson Cancer Center at the University of Pennsylvania, Philadelphia; [9]Gustave Roussy, Villejuif; [10]Institut Bergonie, Bordeaux Cedex; [11]Hospital La Timone, Marseille; [12]Mayo Clinic, Rochester; [13]Emory University School of Medicine, Atlanta; [14]National Cancer Centre, Singapore; [15]Medical Oncology, Cantonal Hospital Lucerne, Lucerne; [16]Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago; [17]Loxo Oncology Inc., a wholly owned subsidiary of Eli Lilly and Company, Stamford; [18]The University of Texas MD Anderson Cancer Center, Houston; [19]Massachusetts General Hospital, Harvard Medical School, Boston; [20]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan

Background: Selpercatinib (LOXO-292) is a highly selective and potent small molecule RET kinase inhibitor. Here we report an update on the efficacy and safety of selpercatinib in *RET*-mutant medullary thyroid cancer (MTC).

Patients and methods: Patients with *RET*-mutant MTC were enrolled to the Phase 1/2 LIBRETTO-001 trial (NCT03157128), a global, multicenter trial (16 countries,

89 sites). Following the Phase 1 dose escalation portion of the trial, patients received the recommended dose of 160 mg orally twice daily. Each cycle was 28 days. The primary endpoint was objective response rate (ORR) per RECIST 1.1. Secondary endpoints included duration of response (DoR) and safety. Per health authority agreement, the primary analysis set was defined as the first 55 consecutively enrolled patients previously treated with multikinase inhibitors cabozantinib and/or vandetanib. Patients naïve to cabozantinib and vandetanib treatment were analyzed separately. All analyses were based on a 16-Dec-2019 data cutoff date.

Results: In the primary analysis set of prior cabozantinib and/or vandetanib-treated patients with MTC (n=55), the ORR by investigator assessment was 62% (95%CI 47.7–74.6, n=34/55) and the median DoR was not reached (95%CI 18.4 months–not estimable) despite a median follow-up of 14.8 months. In cabozantinib/vandetanib treatment-naïve patients (n=88), the ORR by investigator assessment was 69% (95%CI 58.6–78.7, n=61/88, including 2 responses pending confirmation). Of the 59 confirmed responding patients, with a median follow-up of 8 months, responses were ongoing for 57 responders at the time of the analysis. In the safety analysis set consisting of all selpercatinib dosed patients (N=702), the most common treatment-related adverse events (TRAEs) that occurred in ≥15% of patients were dry mouth (33.3%), increased AST (24.5%), increased ALT (23.8%), hypertension (23.2%), diarrhea (19.7%), and fatigue (16.8%). Only 2% (14 of 702) of patients discontinued selpercatinib for TRAEs.

Conclusions: Selpercatinib use was associated with marked and durable antitumor activity in prior cabozantinib and/or vandetanib-treated patients and in cabozantinib/vandetanib-naïve patients with *RET*-mutant MTC, with the majority of responses ongoing in both cohorts. Selpercatinib was well tolerated. Efficacy data assessed by independent review committee based on the 16-Dec-2019 data cutoff date will be presented. ©2020 ASCO, Inc. Reused with permission.

N02

RADIOMICS OF PRE-TREATMENT MAGNETIC RESONANCE IMAGING (MRI) CAN PREDICT RECURRENCE IN EFFECTIVELY CURED HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) PATIENTS

Alfieri S.[1], Romanò R.[1], Bologna M.[2], Corino V.[2], Calareso G.[3], Mirabile A.[4], Ferri A.[5], Marcantoni A.[6], Grosso E.[7], Tarsitano A.[8], Valerini S.[9], Vecchio S.[10], Deantonio L.[11], Blengio F.[12], Ibrahim T.[13], Locati L.D.[14], Bergamini C.[14], Bossi P.[15], Mainardi L.[2], Licitra L.[16]

[1]S.C. Oncologia Medica 3 Tumori della Testa e del Collo, Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Milano; [2]Dipartimento di Elettronica, Informatica and Bioingegneria (DEIB), Politecnico di Milano, Milano; [3]Dipartimento di Radiologia, Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Milano; [4]Dipartimento di Oncologia, Divisione di Medicina Sperimentale, Fondazione IRCCS Ospedale San Raffaele, Milano; [5]Divisione di Chirurgia Maxillo-Facciale, Dipartimento di Chirurgia, Azienda Ospedaliera Universitaria di Parma, Parma; [6]Dipartimento di Otorinolaringoiatria, Ospedale Santa Chiara di Trento, Trento; [7]Istituto Europeo di Oncologia (IEO), Milano; [8]Unità di Chirurgia Maxillo-facciale, Dipartimento di Scienze Biomediche e Neuromotorie, Ospedale S. Orsola-Malpighi, Alma Mater Studiorum Università di Bologna, Bologna; [9]Unità di Otorinolaringoiatria, Dipartimento di Neuroscienze, Azienda Ospedaliero Universitaria di Modena, Modena; [10]Fondazione IRCCS Istituto Nazionale dei Tumori (IST) di Genova e Università di Genova, Ospedale San Martino, Genova; [11]Radiation Oncology Clinic Oncology, Institute of Southern Switzerland (IOSI), Bellinzona-Lugano, Switzerland, Bellinzona-Lugano (Switzerland); [12]Dipartimento di Oncologia Medica, A.O. SS Antonio e Biagio e Cesare Arrigo, Alessandria, Alessandria; [13]Centro di Osteoncologia and Tumori Rari, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Meldola; [14]Fondazione IRCCS Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Milano; [15]Università di Brescia e Ospedale Civili di Brescia, Brescia; [16]S.C. Oncologia Medica 3 Tumori della Testa e del Collo, Fondazione IRCCS Istituto Nazionale dei Tumori (INT) di Milano, Università di Milano, Milano

Background: Emerging data suggest that radiomics can be used to predict outcomes in HNSCC. At present, only few data are available for baseline MRI (b-MRI)

Methods: The training set (TS) was retrieved from an ongoing multicenter, randomized, prospective trial (HETeCo) and consisted of effectively cured stage III-IV (VIII TNM ed.) HNSCC. Patients (pts) with both pre- and post-contrast enhancement T1 and T2-weighted b-MRI and at least 2 years (2y)-FUP were selected. The validation set (VS) was based on a multicenter H2020-funded project (BD2Decide) and selected by same inclusion criteria of TS. In total, 1608 radiomic features (RF) were extracted by b-MRI. The best RF combination was used to classify risk of disease recurrence: high risk (HR) and low risk (LR). In HR vs. LR, Overall Survival (OS) and 3y-disease free survival (DFS) Kaplan-Meier (KM) curves were compared. The radiomic model was evaluated using 10-fold cross-validation in the TS and external validation in the VS. Sensitivity, specificity and area under the curve (AUC) were evaluated. The radiomic-based risk class was used in a multivariate Cox model with well established prognostic factors in HNSCC (TNM, subsite, HPV).

Results: In total, 57 pts of TS and 72 of VS met the eligibility criteria. Baseline TS and VS were also well balanced (Table).

Sensitivity, specificity and AUC of the classifier were 82%, 70%, and 79% on TS, and 70%, 68% and 69% on VS, respectively.

The radiomic risk class (HR/LR) was found to be an independent prognostic factor for 3y-DFS (TS, p=0.02; VS, p=0.02) and OS (TS, p=0.042; VS, p=0.004).

The KM curves for HR and LR groups differed for both 3y-DFS (TS, p=0.019; VS, p=0.024) and OS (TS, p=0.045; VS, p=0.002). In the TS, within HR vs LR comparison, 3y-DFS was 63% [47-85%] vs 95% [87-100%] and OS was 88% [75-100%] vs 96% [88-100%], respectively. In

the VS, 3y-DFS was 66% [52-85%] vs 91% [82-100%] and OS was 88% [75-100%] vs 96% [88-100%], respectively.
Conclusions: In HNSCC, radiomics of b-MRI can help to predict recurrence and survival outcomes.

	TS (N=57)	VS (N=72)
Median (m) age (IQR)	67 (38-86)	63 (32-87)
Sex (%)		
M	47 (82%)	55 (76%)
F	10 (18%)	17 (24%)
m-Smoking history, packs/y (IQR)	30 (1-100)	33 (3-125)
Subsite (%)		
Oral cavity	26 (46%)	36 (50%)
Oropharynx	23 (39%)	25 (35%)
HPV+	15 (65%)	15 (60%)
Larynx	6 (11%)	5 (7%)
Hypopharynx	2 (4%)	6 (8%)
m-FUP, months (IQR)	40,5(7-76)	40(8-62)
Status (%)		
Alive	51 (90%)	58 (81%)
Dead	6 (10%)	14 (19%)
Recurrence (%)	11 (19%)	17 (24%)
Locoregional	9 (82%)	10 (59%)
Distant	2 (18%)	7 (41%)

N03

SOLUBLE IMMUNE CHECKPOINTS IN HEAD AND NECK CANCER PATIENTS TREATED WITH NIVOLUMAB: A PILOT STUDY

Botticelli A.[1], Mezi S.[2], Pomati G.[2], Zizzari I.G.[3], Cerbelli B.[2], Cirillo A.[2], Mammone G.[2], Di Filippo A.[3], Scirocchi F.[3], Pellegrino D.[2], Della Rocca C.[4], Polimeni A.[5], Nuti M.[3], Marchetti P.[6]

[1]*Sapienza Università di Roma, Dipartimento di Medicina Clinica e Molecolare, Roma;* [2]*Sapienza Università di Roma, Dipartimento di Scienze Radiologiche, Oncologiche ed Anatomo Patologiche, Roma;* [3]*Sapienza Università di Roma, Dipartimento di Medicina Sperimentale, Roma;* [4]*Sapienza Università di Roma, Dipartimento di Scienze e Biotecnologie Medico-Chirurgiche, Roma;* [5]*Sapienza Università di Roma, Dipartimento di Scienze Odontostomatologiche e Maxillo-Facciali, Roma;* [6]*Sapienza Università di Roma, Dipartimento di Medicina Clinica e Molecolare, Roma*

Background: The anti-programmed death-1 (PD-1) agent nivolumab is the standard of care in platinum refractory recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC). However, only a small subset of patients really benefit from immunoherapy, suggesting the need of novel predictive biomarkers of response or resistance. Soluble immune checkpoints (sIC) represent a novel and intriguing field of research. The aim of this study was to investigate a novel circulating immune profile of

HNSCC patients in order to better select prone to respond to immunotherapy.
Methods: Patients (pts) treated with Nivolumab were enrollerd. The patients blood samples were collected at the baseline (T0). The immune profile was studied by multiplex assay, evaluating sIC: CD137, CTLA4, PD1, PDL1, PDL2, CD27, Tim3, Lag3, GITR, HVEM and BTLA. The association between baseline circulating levels of sIC and early progression (within 3 months from the start of nivolumab) was investigated.
Results: Thirteen pts with platinum refractory R/M HNSCC were enrolled. Median age was 65 (46-81), 8 pts were men. Early progression occurred in 7 pts (53.8%); 5 pts (38.4%) were alive at 6 months. Median progression free survival and median overall survival were 3 months (1-11) and 5 months (2-11), respectively. CD137, CTLA4, PD1, PDL1, PDL2, Tim3, Lag3, GITR, HVEM, and BTLA were evaluated at T0 and the median value for each sIC was defined. In 7 pts (53.8%), 5 or more sIC were higher than the median value, while in 6 pts (46.2%) less than 5 sIC were higher; the detection of lower baseline levels of sIC were significantly associated with early progression (*p=0.04*).
Conclusions: High baseline circulating levels of soluble checkpoints may indicate an effective immune system activation. Conversely, lower levels of sIC could suggest an "immune dormancy profile" in HNSCC patients. A larger sample size is needed to confirm these preliminary results.

N04

CYTOKINES AND INTERLEUKINS PERFORMANCE DURING NIVOLUMAB TREATMENT. A SUBGROUP ANALYSIS OF NIVACTOR STUDY

Falletta A.[1], Paccagnella M.[1], Denaro N.[2], Abbona A.[1], Galizia D.[3], Fiorino E.[3], Gammaitoni L.[3], Sangiolo D.[3], De Zarlo L.[3], Merlano M.[2]

[1]*Department of Traslational Oncology, Ospedale S.Croce e Carle Cuneo, Cuneo;* [2]*Ospedale S.Croce e Carle Cuneo, Cuneo;* [3]*IRCCS Candiolo Institute, Turin, Torino*

Background: Recurrent or Metastatic Platinum-refractory Squamous Cell Carcinoma of the Head and Neck (R-M SCCHN) is a major clinical issue with 1 year survival rate of 20-30% and a median OS of 10 months. Nivolumab, anti-PD1 mAb, is approved for 2nd line R-M HNC, but only 15-20% of patients will benefit.
Patients and methods: Aim of the study was to analyze the changes of a panel of 17 circulating cytokines and interleukins during nivolumab treatment at baseline (T0), at day 1 cycle 3 (T1), at day 1 cycle 7 (T2) and at disease progression (PD), (T3). Cytokines' concentrations were assessed in plasma samples using the Simple Plexsystem (ProteinSimple, San Jose, CA, USA). Basal values and

longitudinal changes were correlated with outcome. P<0.05 was considered for statistical significance.

Results: 16 patients were analyzed. Longitudinal analysis showed that CXCL-10, TNF-α and IFN-γ increased from T0 to T3 (P=0.0233; P=0.049 and P=0.035, respectively). IL-15 increased from T0 to T2 (P=0.024), but decreased at PD (P=0.024). No other significant longitudinal changes were observed. Considering the basal values, we used ROC analysis to cluster all patients in two groups, observing a better PFS in those whose T0 values of IL-5, IL-6 and IL-10 were below than the respective cut-off points (HR 0.12, P=0.01; HR 0.056, P=0.008; HR 0.055, P=0.009) but only IL-5 below the cut-off positively correlated with OS (HR 0.05, P=0.007). We could not perform multivariate analysis due to the limited number of events. Therefore we use PCA analysis to group patients with good or poor PFS using T0 levels of IL-5, IL-6, IL-10, CCL-22 (KMO 0.574, P=0.025); the same analysis allowed to clusterize patients with OS above or below median value using T0 levels of IL-5, IL-6, IL-10, IL-15 (KMO 0.636, P<0.001).

Conclusions: Our results show that nivolumab therapy could increase the levels of IL-15. CXCL-10, TNF-α and IFN-γ increased at PD. Moreover our data suggest that IL-5, IL-6 and IL-10 might predict the benefit from the treatment.

N05

MYB-REARRANGED AND NON-REARRANGED ADENOID CYSTIC CARCINOMA: ARE THERE ANY CLINICAL DIFFERENCES?

Filippini D.M.[1], Cavalieri S.[2], Quattrone P.[2], Bergamini C.[2], Resteghini C.[2], Colombo E.[2], Platini F.[2], Alfieri S.[2], Locati L.[2], Licitra L.[2]

[1]IRCCS Istituto Nazionale dei Tumori, Policlinico Sant' Orsola Malpighi, Milano, Bologna; [2]IRCCS Istituto Nazionale dei Tumori, Milano

Background: Adenoid cystic carcinoma (ACC) is the second most common salivary gland carcinoma (SGC) subtype. MYB/MYBL1 rearrangements have been detected in more than 60% of cases. The impact of these rearrangements on clinical behaviors is still unclear.

Material (Patients) and Methods: This is a retrospective monocentric observational study. Both salivary gland and extra salivary ACC patients (pts) tested for MYB rearrangement have been included. Demographic characteristics, histological pattern and disease stage at diagnosis were analyzed. Differences in clinical and pathological characteristics were compared between MYB rearranged (MYB+) and non-rearranged (MYB-) ACC pts. MYB rearrangements were tested by FISH.

Results: From 2006 to 2019 48 ACC pts have been identified. Median follow-up was 7.8 years (y) (95%CI 5.4-9.8). Thirty-three pts (13 males) were MYB+ and 15 (9 males)

MYB-. Median age in the MYB+ group was 48 y (27-73) while in MYB- it was 51 (21-77). Histologically, the solid pattern was mainly associated with MYB+ (N 13, 40%) while the tubular- cribriform pattern was mainly represented in MYB- (N10, 66%), p=0.097. Data about clinical history were available in 44 out 48 pts. At initial diagnosis, 36 pts (26 MYB+ vs 10 MYB-) had local or loco-regional disease, and 8 pts (4 MYB+ vs 4 MYB -) had metastatic disease (lung metastases only). Four pts (2 MYB+, 2 MYB-) were alive and disease-free at last follow-up, 12 pts relapsed locally/locoregionally (in MYB + only, p-value 0.018), and 28 pts (16 MYB+ and 12 MYB-) relapsed at distant sites. The most common metastatic site was lung. Time to progression requiring active treatment was 55 and 12 months in MYB+ and MYB-, respectively. In 16 pts (33%), genome sequencing data were available: single mutations of *KIT (7%), TP53 (7%)*, and *MET (15%)* genes were found in MYB+, a *PIK3CA* mutation in 1 MYB- was discovered. In 1/6 MYB+ pts microsatellite instability (MSI) was found.

Conclusions: In this small cohort of ACC pts (MYB+ vs MYB-), clinical, pathological and genomic characteristics seem to identify different ACC subtypes. In particular loco-regional recurrence has been associated only to MYB+. A trend to a higher number of genetic alterations has been observed in MYB+. Further studies are warranted to deepen the knowledge about the clinical significance of the MYB/MYBL1 rearrangements to better stratify patients' prognosis.

N06

PROGNOSIS AND MANAGEMENT PRINCIPLES OF HEAD AND NECK CANCERS DURING PREGNANCY: A CASE SERIES

Bergamini C.[1], Cavalieri S.[1], Locati L.[1], Alfieri S.[1], Resteghini C.[1], Platini F.[1], Colombo E.[1], Licitra L.[1]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano

Background: Pregnancy-associated cancer is a cancer occurring during pregnancy or within 12 months after it. Head and neck cancer (HNC) during pregnancy is a rare phenomenon. The diagnosis of HNC in the gestational period poses many difficult decisions as multiple clinical, personal, and ethical factors need to be considered. Therapeutic approaches need to be tailored to each pregnant woman with HNC.

Methods: This is a retrospective study on women whose HNC was diagnosed during pregnancy to investigate both pregnancy and oncological outcomes.

Results: During the period 2005-2019, 15 pregnant women with HNC were treated at the Istituto Nazionale Tumori of Milan. Five patients (pts) suffered from salivary

glands cancers, 4 from nasopharyngeal cancer, 3 from thyroid, 2 from oral cavity and 1 from oropharyngeal cancer. Median age of pts was 37 years (y), with range 27-43 y. In 10 pts (67%), HNC diagnosis occurred at a median gestational age of 28 weeks (range: 16-40 weeks). In other 5 pts (33%), diagnosis was done post-partum with a median of 5 months (range: 1 week – 6 months). Stage distribution was as follows: stage I (14% of pts), II (20%), III (26%), IV (40%). Radiological staging was completed after childbirth in 80% of pts. Pregnancy outcome was an elective childbirth in 3 pts and a therapeutic abortion in 1 case. In the majority of pts (73%) delivery at term occurred. In pregnant subjects, surgery of the primary tumor was performed in 3 pts, 2 pts with salivary glands cancer and one with oral cavity cancer. Preterm delivery, congenital anomalies of foetus and major maternal morbidities were not observed. After childbirth, other 5 pts received surgery (3 pts with thyroid cancer - of which 2 with metastatic disease - 2 pts with salivary gland cancer and one with oral cancer), 8 pts received chemoradiation with curative (33%) or postoperative intent, and 4 pts with metastatic disease "ab initio" were treated with chemotherapy. The median survival was 5.8 y (range: 15 months to 12 y). Seven pts are still in complete remission at 6.5 y after diagnosis and 2 metastatic pts (salivary gland and thyroid carcinoma) are alive at 10 y after diagnosis. Six pts died of disease; half of them had salivary cancer.

Conclusions: All pts received state-of-the-art therapy according to their clinical condition with encouraging long term results suggesting that optimal treatment can be safely delivered in women with HNC during pregnancy.

N07

CLINICAL AND HISTOLOGICAL PROGNOSTIC FACTORS OF RECURRENT AND/OR METASTATIC SALIVARY GLAND ADENOID CYSTIC CARCINOMA

Lorini L.[1], Gurizzan C.[1], Tomasoni M.[1], Lombardi D.[1], Mattavelli D.[1], Paderni A.[1], Deganello A.[1], Ardighieri L.[1], Battocchio S.[1], Bozzola A.[1], Ravanelli M.[1], Maddalo M.[1], Zamparini M.[1], Magrini S.M.[1], Maroldi R.[1], Nicolai P.[2], Berruti A.[1], Bossi P.[1]

[1]Azienda Ospedaliera Spedali Civili di Brescia, Brescia; [2]Azienda Ospedaliera di Padova, Padova

Background: About 40% of radically treated adenoid cystic carcinoma (AdCC) patients (pts) will recur locoregionally and up to 60% will develop distant metastasis. Factors influencing the risk of recurrence have been studied, but very few data exist about prognostic factors in recurrent/metastatic (RM) disease that could guide clinicians in the selection and tailoring of further treatments. Main aim of the study is to evaluate patient, treatment and disease characteristics impacting on survival for RM pts.

Material and Methods: We retrospectively evaluated a series of 135 head and neck AdCC treated with curative surgery at the Otolaryngology Head and Neck Surgery Department of the University of Brescia, Italy, from 1997 to 2016 and we retrieved data from 41 pts who relapsed. The following clinical and histological characteristics, both at first treatment and at diagnosis of relapse, were analysed and linked to overall survival (OS): gender, age, pain, cranial nerve deficit, stage, grading (according to Perzin), subsite of origin, biochemical analysis (neutrophil/lymphocytes, albumin), disease free interval (DFI), site of relapse and site of metastasis.

Results: Relapsing patients were mainly female (59%), with median age 55 years (21-83) and with primary disease in major (27%) or minor (73%) salivary gland. Grading was scored as low, intermediate, high in 27%, 39%, and 34% of cases, respectively. 71% of patients had undergone adjuvant radiotherapy after primary surgery. Site of recurrence was local in 73%, regional in 12% and distant in 39%; lung represented the most frequent site of distant failure. Median disease free-interval (DFI) was 25 months (4-142). Only high grade (HR 5,1; 1,2-20,7; p= 0,021) was associated with worse 2-year OS since the diagnosis of RM disease; on the contrary, patients with DFI longer than 25 months had higher 2-year OS (HR 0,351; 0,157-0,786; p= 0,01)

Conclusions: Grading of disease at the time of first diagnosis and DFI are the main factors guiding prognosis after relapse of AdCC. Given the paucity of clinical prognostic data, we support extensive molecular analysis as next step of research.

N08

GENE EXPRESSION PROFILING TO IMPROVE PROGNOSTIC CHARACTERIZATION OF OLFACTORY NEUROBLASTOMA AND TO DEFINE NEW TARGETABLE PATHWAYS

Romani C.[1], Lorini L.[1], Ravaggi A.[1], Bignotti E.[1], Paderno A.[1], Mattavelli D.[1], Rampinelli V.[1], Schreiber A.[1], Ferrari M.[1], Nicolai P.[2], Deganello A.[1], Ravanelli M.[1], Ardighieri L.[1], Bozzola A.[1], Battocchio S.[1], Castelnuovo P.[3], Calza S.[4], Magrini S.M.[1], Turri Zanoni M.[5], Bossi P.[1]

[1]Azienda Ospedaliera Spedali Civili di Brescia, Brescia; [2]Azienda Ospedaliera di Padova, Padova; [3]Università dell'Insubria, Brescia; [4]Università degli Studi di Brescia, Brescia; [5]Università dell'Insubria, Varese

Background: Olfactory neuroblastoma (ONB) is a rare neoplasm of sinonasal tract with a peculiar behaviour. Limited prognostic factors are available, consisting in stage, grading (according to Hyams' criteria) and Ki67 value. The project aims at studying the pathways of ONB through gene expression analysis and correlating them with clinical outcome.

Material and Methods: We collected a series of ONB treated with curative intent at the ENT of Spedali Civili, Brescia and Ospedale di Circolo Varese, Italy. Clinical data of the patients were retrieved, as well as histological specimens, whose diagnosis was re-evaluated by two expert pathologists. We performed gene expression profiling on FFPE samples using Affymetrix Clariom S microarray, and carried out functional enrichment analysis to investigate key pathways associated with progression-free survival (PFS).

Results: A series of 42 patients treated between 2001 and 2019 was considered. One patient was excluded due to poor quality of FFPE sample. Main characteristics of the patients: mainly male (52%); median age 53 year; stage I-II 17%, III-IV 83%; Hyams grade I 7%, II 45%, III 48%. Patients were treated by surgery and 79% received postoperative radiation, while only 1 patient received also neoadjuvant chemotherapy. After a median follow up of 51 months, we identified disease progression in 12 cases. Median PFS was 38,8 months (5 - 99). Clinical characteristics (gender, global stage, Hyams grade, T stage and N stage) were not associated with outcome. Patients experiencing recurrence had a disease characterized by enrichment mainly in pathways related to TGF-beta binding, regulation of cytokine biosynthesis, toll-like receptor 4, PIP3, p-53 mediated apoptosis signalling in response to DNA damage, TNF and IFN alfa; on the contrary, patients without any recurrence after surgery showed increased expression of genes related to DNA methylation, ubiquitin ligase complex and retinoid acid binding.

Conclusions: ONB is characterized by heterogeneous gene expression pathways, related to patient's outcome. Definition of characterizing transcriptomic pathways may pave the way to tailored treatment approaches.

N09

NIVOLUMAB FOR TREATMENT OF RECURRENT/METASTATIC SQUAMOUS-CELL CARCINOMA OF THE HEAD AND NECK (R/M HNSCC): REAL-WORLD DATA AND POSSIBLE PROGNOSTIC FACTORS

Trudu L.[1], Shoval Y.[2], Napolitano M.[1], Schipilliti F.M.[1], Depenni R.[1], Dominici M.[1], Milella M.[2], Bertolini F.[1], Tondulli L.[2]

[1]*Azienda Ospedaliero - Universitaria di Modena, Modena;* [2]*Azienda Ospedaliera Universitaria Integrata di Verona, Verona*

Background: Immune checkpoint inhibitors (ICIs) represent a new active class of agents recently approved for platinum-refractory R/M HNSCC. Despite the increase of overall survival (OS), no prognostic factors have been established to predict outcome, yet.

Methods: We retrospectively reviewed 37 patients (pts) with platinum-refractory R/M HNSCC who received at least 2 doses of nivolumab 240 mg every 2 weeks from 2016 to 2020 at University Hospitals of Modena and Verona. We investigated nivolumab efficacy in real-world patients and prognostic factors associated with the response to treatment.

Results: The overall cohort include 37 pts: 27(73%) males, 27(73%) smokers, median age 62 (43-77), median BMI 22.5 (17.22-34.6). Most of the pts had a primary cancer in oral cavity (11, 30%) or oropharynx (11, 30%). 34 pts (92%) received previous locoregional treatments (surgery + radio + chemotherapy), while nivolumab was administered as > second line therapy in 33 pts (89%). Median follow-up was 7 (1-18) months (mos); median progression-free survival (PFS) and OS were 5 (0.5-17) and 8 mos (2-17), respectively. Best overall response (BOR) was complete response in 3 pts (8%), partial response in 5(14%), stable disease in 9(24%), progression disease (PD) in 20 pts (54%). We divided patients in 2 prognostic groups: long survival (LS) group, 23 pts (62%) with OS ⩾ 6 mos and early progressors (EP), 14 pts (38%) with OS<6 mos. Among clinical variables, performance status (PS) confirmed its prognostic role: in LS group 9 pts (39%) had PS 0 vs 1(7%) and 13(57%) with PS 1 vs 12(86%) in EP group. Among bio-humoral variables (haemoglobin, eosinophil count, neutrophil/lymphocyte ratio, LDH), only eosinophil count significantly differed among LS vs EP (median value of 0.17 vs 0.06 x 10^3/mmc). Among molecular variables: PD-L1 TPS expression was evaluated in 20 pts: 7 pts had PD-L1 < 1%, 10 PD-L1 1-49%, 3 PD-L1 ⩾ 50%; no correlation with OS was detected, but all responsive pts had detectable PD-L1. Finally, immune-related adverse events (irAEs) were investigated: 15 pts (40%) experienced toxicity (10 pts G1-G2, 2 pts G3); among them 10 (67%) were in LS group.

Conclusions: Nivolumab is the standard of care in platinum refractory R/M HNSCC, not pre-treated with ICIs. However, not all pts would benefit from this treatment. In order to improve survival, biomarkers and prognostic factors for patient's selection are needed.

N10

CANCER OF THE ORAL CAVITY: A SINGLE INSTITUTION EXPERIENCE

Gusmaroli E.[1], Violati M.[2], Careri C.[2], Provenzano L.[2], Luciani A.[2], Codecà C.[2], Rabbiosi D.[3], Franzese C.[4], Moneghini L.[5], Biglioli F.[3], Ferrari D.[2]

[1]*Università degli Studi di Milano, Milano;* [2]*Medical Oncology Unit, ASST Santi Paolo e Carlo, University of Milan, Italy., Milano;* [3]*Maxillo-Facial Surgery Unit, ASST Santi Paolo e Carlo, University of Milan, Italy., Milano;* [4]*Department of Radiotherapy and Radiosurgery Istituto Clinico Humanitas, Milano;* [5]*Pathology Unit, ASST Santi Paolo e Carlo, University of Milan, Italy, Milano*

Background: About 6,000 oral cavity squamous cell carcinoma (OCSCC) are diagnosed in Italy each year, which cause about 3,000 deaths. Oral cavity tumors can present as

limited disease or with local invasion, tissue destruction, and lymph node metastases. Distant metastases are rarely found at presentation. In the western world tobacco smoking and alcohol use are the main risk factors for OCSCC. Poor oral hygiene, periodontal disease, radiation, sun exposure, betel nut quid chewing and immune deficiency have also a significant role. While infection with oncogenic human papillomavirus (HPV), is associated with the rising incidence of tonsil and base of tongue cancer, the association between OCSCC and HPV infection is less evident. Males are affected about twice as much as females.

Material (patients) and methods: we retrospectively reviewed the record of the patients undergoing surgery for early or locally advanced OCSCC from January 2012 to December 2019. Excluding those patients coming from distant regions, we identified 186 patients operated, treated with adjuvant radiotherapy or chemoradiotherapy (CRT) as needed, and followed at our center.

Results: Of 186 patients, 96 (52%) were males. We found 67 smokers and 119 never-smokers (64%). Median age was 68 years (28-88) with only 8 patients (3.8%) < 40 years old. The main sites involved were the tongue (37%), the floor of the mouth (36%) and buccal mucosa (24%). Ninety-three patients (50%) had pathological stage I-II, 25 (13%) stage III and 68 (37%) stage IVa-b disease. Sixty-nine patients were pT3-4 (38%; pT3 8% and pT4 30%), nodal involvement was present in 60 cases (32%). HPV+ 8%. Positive or "close" margins were present in 23 cases (12%) and extranodal extension (ENE) in 31 (17%). Radiotherapy or CRT were offered to 25 and 23 patients, respectively. With a median follow-up of 42 months, at the end of December 2019 the 5-y disease-free survival and overall survival rate was 88% and 96%, respectively. Two treatment-related deaths were observed in the group (17 patients) undergoing adjuvant CRT.

Conclusions: With the limits of a retrospective and monocentric study, we believe a multimodality approach supporting the patients in all their needs can lead to optimal results. Our series is characterized by an unusual high prevalence of females and non-smokers. Together with high-quality surgery and accurate management of adjuvant therapies, this can represent an explanation for the long survivals we observed.

P - Brain Tumours

P01

PEMBROLIZUMAB ACTIVITY IN RECURRENT HIGH-GRADE GLIOMAS WITH IMMUNOHISTOCHEMICAL LOSS OF MISMATCH REPAIR PROTEINS: A MONOCENTRIC, OBSERVATIONAL AND PROSPECTIVE PILOT STUDY

Lombardi G.[1], Barresi V.[2], Indraccolo S.[3], Simbolo M.[2], Fassan M.[4], Mandruzzato S.[5], Simonelli M.[6], Caccese M.[1], Pizzi M.[4], Fassina A.[3], Padovan M.[1], Masetto E.[3], Gardiman M.P.[4], Bonavina M.G.[7], Caffo M.[8], Chioffi F.[9], D'Avella D.[10], Dei Tos A.P.[4], Scarpa A.[2], Zagonel V.[1]

[1]Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV - IRCCS, Padova; [2]Department of Diagnostics and Public Health, Section of Pathology, University of Verona, Verona; [3]Immunology and Molecular Oncology Unit, Veneto Institute of Oncology – IRCCS, Padova; [4]Department of Medicine (DIMED), Surgical Pathology and Cytopathology Unit, Padova; [5]Department of Surgery, Oncology and Gastroenterology, University of Padova and IOV - IRCCS, Padova; [6]Humanitas University, Department of Biomedical Sciences, Milano; [7]Medical Direction Unit, Veneto Institute of Oncology, IOV - IRCCS, Padova; [8]Department of Biomedical and Dental Sciences and Morphofunctional Imaging, Unit of Neurosurgery, University of Messina, Messina; [9]Neurosurgery Unit, Azienda Ospedaliera di Padova, Padova; [10]Academic Neurosurgery, Department of Neurosciences, University of Padua, Padova

Backgroung: Pembrolizumab demonstrated promising results in DNA mismatch repair (MMR) deficient tumors of diverse origin, but its activity in HGG patients with MMR deficiency is unknown.

Material and methods: This was a monocentric, observational and prospective study. The objective is to evaluate the efficacy and safety of pembrolizumab in previously treated HGGs with immunohistochemical loss of at least 1 MMR protein. Post hoc exploratory analyses were undertaken to describe the genetic and molecular tumor features. Data were collected from May 2017 to May 2019. The median follow up was 20.6 months. Consecutive eligible patients with recurrent HGG and loss of MMR proteins at immunohistochemistry received pembrolizumab 200 mg once every 3 weeks until disease progression or unacceptable toxic effects. The primary end point was disease control rate (DCR). Secondary end points included progression-free survival (PFS), overall survival (OS), and safety. In 12 of the 13 cases, post hoc exploratory analyses were performed. These included next-generation sequencing to assess tumor mutational burden (TMB) and the mutational and copy number status of 409 cancer genes, and immunostaining for CD8+ cytotoxic T-cells and CD68+ immunosuppressive macrophages.

Results: Among 310 HGG patients screened, 13 cases with MMR loss were enrolled: 8 with glioblastoma, 4 anaplastic astrocytoma, and 1 anaplastic oligodendroglioma. Median age was 43 years and median prior chemotherapy lines was 2. Six HGGs had concurrent loss of MSH2 and MSH6, 2 had concurrent loss of MLH1 and PMS2, 3 of MSH2 alone, and 2 of MSH6 alone. The DCR was 31%: 4 patients had stable disease and no patient had complete or partial response. Median PFS and OS were 2.2 (95%CI 1.6-2.8) and 5.6 (95%CI 0.1-11.9) months, respectively. TMB was obtained in 12 cases and ranged between 6.8 and 23.4 mutations/megabase, and 8 cases were hypermutated (>9 muts/Mb.). Neither TMB nor gene mutations, nor CD8+ T-cell and CD68+ macrophage content were associated with pembrolizumab activity.

Conclusions: Our study demonstrated poor benefit of pembrolizumab in recurrent HGG patients with immunohistochemical loss of MMR proteins. No molecular biomarker was found to be associated to pembrolizumab activity.

P02

DEFINING THE PROGNOSTIC ROLE OF MGMT METHYLATION VALUE BY PYROSEQUENCING ASSAY IN GLIOBLASTOMA PATIENTS: A LARGE ITALIAN MULTICENTER STUDY

Caccese M.[1], Simonelli M.[2], Bellu L.[3], Villani V.[4], Rizzato S.[5], Ius T.[6], Pasqualetti F.[7], Russo M.[8], Franchino F.[9], Amoroso R.[10], Bertorelle R.[11], Cavallin F.[12], Dipasquale A.[2], Carosi M.[13], Pizzolitto S.[14], Cesselli D.[15], Gardiman M.P.[16], Padovan M.[17], Zagonel V.[17], Lombardi G.[17]

[1]Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV - IRCCS - Padova, Padova; [2]Humanitas Cancer Center; Humanitas University, Department of Biomedical Sciences, Milano; [3]Radiotherapy Unit, Veneto Institute of Oncology IOV-IRCCS, Padova; [4]Neuro-Oncology Unit, Regina Elena National Cancer Institute, Roma; [5]Department of Oncology, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [6]Department of Neurosurgery, University Hospital of Udine, Udine; [7]Radiation Oncology, Pisa University Hospital, Pisa; [8]Neurology Unit, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia; [9]Department of Neuro-Oncology, University of Turin and City of Health and Science Hospital, Torino; [10]Divisione di Neurochirurgia, Azienda Sanitaria Alto Adige-Comprensorio Sanitario di Bolzano, Bolzano; [11]Immunology and Molecular Oncology, Veneto Institute of Oncology-IRCCS, Padova; [12]Independent Statistician, Solagna; [13]Pathology Unit, Regina Elena National Cancer Institute, Roma; [14]Department of Surgical Pathology, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [15]Department of Medicine, University of Udine; Institute of Pathology, Azienda Sanitaria Universitaria Friuli Centrale, Udine; [16]Department of Medicine and Surgical Pathology and Cytopahology Unit; University Hospital of Padua, Padova; [17]Department of Oncology, Oncology 1, Veneto Institute of Oncology IOV-IRCCS, Padova*

Background: MGMT methylation (MGMTmet) status represents an important prognostic factor for glioblastoma (GBM) patients (PTS). Quantitative pyrosequencing approach has proven to be feasible for MGMTmet testing but its value is still unclear. We performed a large, multicentre, retrospective study to identify the association between MGMTmet values and clinical outcome.

Material and methods: From 9 Italian neuro-oncology centres, we collected consecutive GBM PTS with assessment of MGMTmet by pyrosequencing approach evaluating CpG islands from 75 to 84. Other inclusion criteria were: histological diagnosis of GBM, ECOG PS =2, therapy with RT+TMZ. Kaplan-Meier method was used to estimate the survival curves, time-dependent ROC curve for defining the optimal cut-off value of mean percentage of MGMTmet in terms of 2y-OS, Cox regression for multivariable analysis, and restricted cubic spline to investigate the non-linear association between methylation values and OS.

Results: 681 PTS were enrolled; median age was 60 ys; ECOG PS was 0 in 292 PTS, 1 in 306 PTS, 2 in 83 PTS; 391 PTS (58%) had a complete resection. 8% of PTS received a second surgery. IDH was mutated in 6%. 2y-OS was 31.6%, median OS was 17.4 ms. Median MGMTmet was 3.5% (IQR 0-22%). ROC curve identified a cutoff of 15% of MGMTmet in terms of 2y-OS (sens 78%, spec 57%, AUC = 0.67). 2y-OS was 19.7% and 53.7% for PTS with MGMTmet < and =15%, respectively (p < 0.0001). At multivariable analysis, MGMTmet < 15% was associated with impaired survival (HR 2.7, 95%CI 2.1-3.4; p < 0.00001), adjusting for age, KPS, type of surgery and second surgery. A non-linear association between MGMT methylation and survival was identified (non-linear term: p < 0.0001), with lower values of MGMT methylation associated with lower survival; indeed, estimated median OS was lowest (14 months, 2ys-OS: 17.4%) with MGMTmet of 4%, 21ms (2yr-OS: 40.9%) with MGMTmet of 20%, 27ms (2yr-OS: 40.9%) when MGMTmet was 40%, then leveled around 30ms (2yr-OS: 54.5-59.8%) when MGMTmet was > 40%.

Conclusions: This study represents one of the largest trials analyzing MGMTmet by pyrosequencing approach. Lower values of MGMTmet were associated with impaired survival and the relationship was non-linear. Noteworthy, we identified a strong prognostic value of MGMTmet which could be used as stratification factor in prospective clinical trials.

P03

MGMT STATUS INFLUENCES PROGNOSIS OF PATIENTS WITH IDH WILD TYPE GRADE III GLIOMAS

Di Nunno V.[1], Franceschi E.[2], Tosoni A.[2], Gatto L.[2], Mura A.[2], Minichillo S.[2], Di Battista M.[2], Lamperini C.[2], Nuvola G.[3], Sisi M.[3], Mosca M.[3], Bartolini S.[2], Brandes A.A.[2]

[1]Department of Medical Oncology, Azienda USL-IRCCS Institute of Neurological Sciences,, Bologna; [2]Department of Medical Oncology, Azienda USL-IRCCS Institute of Neurological Sciences, Bologna, Italy., Bologna; [3]Department of Oncology Sant'Orsola Malpghi Hospital - University of Bologna, Bologna*

Background: WHO grade III gliomas are classified according to the presence of IDHmutation. IDH wild type (IDH wt) is associated with poor prognosis and limited effectiveness of treatments. The aim of this study was to find out if MGMT methylation represents a prognostic factor in this setting.

Methods: We analyzed our Institutional data warehouse for all consecutive patients (pts) with newly diagnosed, histologically proven grade III, IDH wt gliomas. The IDH 1/2 assessment was performed by Next Generation Sequencing (NGS). MGMT methylation was assessed by methylation specific PCR (MSP). Tissue samples were also centrally reviewed for histology.

Results: The analysis included 73 pts with grade III, IDH wt (19.3%) gliomas. The median follow-up time was 69.9

months. Median age was 50 (Range: 18-75), M/F ratio was 40(54.8%)/33(45.2%),. MGMT promoter was methylated in 34 pts (46.6%) and unmethylated in 39 pts (53.4%). After surgery, 9 pts (12.3%) received RT alone, 57 pts (78.1%) received both RT and CT (sequential, concomitant or both). Median survival was 26.2 months. In multivariate analysis age (HR=1.064, 95%CI: 1.030-1.099; P<0.001) and MGMT methylation (HR=0.422, 95%CI: 0.210-0.848; P=0.015) were independently associated with risk for death.
Conclusions: IDH wild type confers a dismal prognosis in patients with grade III glioma. MGMT methylation, as was demonstrated in glioblastoma, represents a prognostic factor that correlated with a reduced risk of death. Further studies will investigate potential correlations with treatments.

P04

GLUCOCORTICOID RECEPTORS (GR) UPREGULATION IN CIRCULATING TUMOUR CELLS (CTCS) AND GLIOMA STEM CELL-LIKE PHENOTYPE (GSCS): ROLE OF DEXAMETHASONE IN PATIENTS DIAGNOSED WITH GLIOBLASTOMA MULTIFORME (GBM)

Spinelli G.P.[1], Di Benedetto L.[2], Tumminello A.[3], Pietranera M.[4], Bitca V.[1], Gozzi E.[1], Sinjari M.[1], Raimondi L.[1]

[1]*UOC Territorial Oncology, Aprilia;* [2]*BIOS SpA, Roma;* [3]*Unità Funzionale Emergenza Sanitaria (UFES), Policlinico Militare Cellio, Roma;* [4]*Centro Medico Diagnostico Salus, Civitavecchia, Roma*

Background: Despite therapeutic improvements,prognosis in GBM remains extremely poor,for CD133+GSCs too, responsible for resistant to therapy. Increasing evidence indicates Dexamethasone(Dex), used to treat peritumoral GBM-associated oedema, could be linked to cell growth and poor prognosis in different tumours but its role in GBM has remained controversial. In our study, we investigated the expression of GR in CTCs from cerebrospinal fluid (CSF) of pts with GBM and we analyzed the potential correlation between Dex treatment and the higher CD133+CTCs levels.
Methods: Serial matched blood and lumbar puncture samples were collected from 20 pts with GBM at day 0(before surgery) and every 2/4 months until progression or death. CTCs from CSF were evaluated by CellSearch system and correlated with citology: Low and High density neutrophils (LDNs and HDNs, respectively) levels and their ratio were determined. GR was assessed on CTCs; flow cytometry and uni-multivariate analysis were performed to detect CD133+ and to correlate cellular subpopulations with OS.
Results: In all pts, MGMT methylation and IDH1/2 status were detected. All samples contained CTCs; at baseline mean CTCs was 112 per 3ml (range 4-350) and 9/20 pts had GR negative CTCs. All samples had CD133+CTCs

(median 17.9%±10.1; range: 2- 31%). For symptom control, all patients received Dex at diagnosis; different doses of Dex were administered. Change in GR CTCs count occurred with higher Dex doses: 5/9 pts changed their GR status from negative to positive and pts with pre-Dex positive GR CTCs, upregulated their GR levels (*p<0.001*). A significantly correlation between CD133+CTCs and GR upregulation was observed (*p<0.001*). After having taken Dex, median CTCs number was 301 (range: 87-521) and CD133+ cells were 72.6% (range: 10-97%, *p<0.001*). Analyzing LDNs/HDNs, we demonstrated an increased ratio in pts with upregulated GR and elevated CD133+CTCs (0.581 ± 0.102 vs. 0.041 ± 0.018, *p=0.001*). All these data were associated with pts' outcome: median PFS and OS in the subgroup with GR-positive CTCs were significantly shorter (5months and 12months, respectively) than in the subgroup with GR-negative (18months and 51months, respectively), regardless of MGMT and IDH1/2 status (*p = 0.002* and *p<0.001*).
Conclusions: GBM remains a crucial public health issue. Survival analyses are consistent with the hypothesis that treatment of GBM with the highest dose of Dex could promote changes in GR CTCs enumeration, contributing to development of GSC-like population and poor prognosis.

P05

MET-EXPRESSION IN GLIOBLASTOMA, A NEW PROGNOSTIC FACTOR?

Caserta C.[1], Mosillo C.[1], Guida A.[1], Macrini S.[1], Peciarolo A.[2], Calandrella M.L.[1], Mannino A.[1], Ascani S.[2], Bracarda S.[2]

[1]*Medical and Translational Oncology Unit, Azienda Ospedaliera S. Maria, Terni, Italy;* [2]*Pathology Unit, Azienda Ospedaliera Santa Maria di Terni, University of Perugia, Terni, Italy*

Background: Glioblastoma (GBM) is the most common malignant primary brain tumor. Despite the use of intensive treatment, GBM still has a poor prognosis (15–18 months). MET overexpression was described in GBM and often relates with worse survival. The aim of our study is to investigate MET expression rate, its prognostic role, and potential correlations with other biomarkers.
Material and methods: Retrospective study on patients (pts) affected by GBM treated at S. Maria Hospital of Terni from Jan 2015 to Dec 2019. Pts were managed according to established diagnostic and therapeutic protocols. Clinical informations were collected from pts' files. MET expression was evaluated by immunohistochemistry using CONFIRM anti-total MET (SP44) rabbit monoclonal antibody. The proportions of positively stained tumor cells were scored as follows: 0) no positive tumor cells; 1) <10%; 2) 10–30%; 3) >30%. Spearman's and Chi's square tests were used to define the correlation and the difference in expression of different tumor markers, respectively. The

Kaplan-Meier was applied to estimate overall survival (OS) and the difference between the groups were compared with log-rank test.

Results: A total of 40 pts have been analysed, median age was 66 years (range 25-84), 50% of pts had MGMT methylation and 7.5% had IDH1/2 mutations. Approximately half of pts (56%) had EGFR mutation and the majority (90%) had TERT mutation. MET expression (score =1) was expressed in 57.5% of pts. In particular, scores 0, 1, 2 and 3 were found in 42.5%, 30%, 17.5% and 10% of the cases, respectively. Median OS for the entire population was 12.1 months (mo) (95%CI 7.8-15), with a median OS of 14 mo (95%CI 5.6-21.6) for MET-negative pts (score 0) and only 7 mo (95%CI 1.9–NR) for pts with high-MET-expression (score 3), HR 3.9; 95%CI 1.2-13; p 0.024. In a multivariable cox-regression analysis high-MET-expression remains as an independent negative prognostic factor also considering MGMT and IDH1/2 status (HR 3.2; 95%CI 0.95-11; p = 0.060). Interestingly, EGFR WT seems to be associated to a MET positive staining (score =1) in 75% of cases (p 0.049).

Conclusions: Our findings confirmed the negative prognostic role of an high-expression of MET in GBM (10% of the cases in our study). Further studies are awaited to assess the role of eventual MET inhibitors in GBM cases expressing this target.

P06

FINANCIAL STATUS IMPACTS OVERALL SURVIVAL IN GLIOBLASTOMA: A PROSPECTIVE CLINICAL TRIAL

Gatto L.[1], Tosoni A.[1], Franceschi E.[1], Di Nunno V.[1], Minichillo S.[1], Mura A.[1], Di Battista M.[1], Lamperini C.[1], Mosca M.[1], Nuvola G.[1], Sisi M.[1], Bartolini S.[1], Brandes A.A.[1]

[1]Department of Medical Oncology, Azienda USL/IRCCS Institute of Neurological Sciences, Bologna

Background: There is some evidence that the socioeconomic status (SES) is associated with survival in glioblastoma (GBM), but the findings are limited.

We conducted a single centre prospective observational study investigating the association between SES and GBM survival in Italy, where exists a national health service that provides universal coverage.

Materials and methods: This study was a prospective analysis of newly diagnosed GBM patients who underwent chemoradiation between 2018 and 2020 in a hub center for brain cancer research. The SES was measured using the income-brackets, extracted from regional health administrative system.

The income-brackets refer to annual gross family income: up to 36,152 euros in income is classified as R1 bracket; between 36,153 and 70,000 euros as R2; between 70,0001 and 100,000 euros as R3; over 100,000 euros as R4.

Results: One hundred six patients were included in the study. In multivariable cox proportional hazard model of survival, a high available income was associated with improved survival HR= 0.623 (95%CI 0.467-0.832; p = 0.001). When adjusted for age, survival remained improved for high-income patients.

Conclusions: We confirm that SES is an important determinant of prognosis in GBM even in the Italian National Health Service which provide universal, largely free and relatively comprehensive healthcare. Despite aspirations to achieve equality in healthcare, socioeconomic differences exist and may impact on clinical outcome.

P07

SHOULD BE USED BEVACIZUMAB IN RECURRENT GBM? A METANALYSIS

Tiberi E.[1], Urbini B.[1], Mauro E.[1], Fasano A.[1], Cecchetto C.[1], Toma I.[1], Lancia F.[1], Martella L.R.[1], Frassoldati A.[1]

[1]Azienda Ospedaliero-Universitaria Sant'Anna Ferrara, Ferrara

Background: GBM is the most common and most aggressive primary brain tumor in adults. The 1 year-OS is almost 35%. The recurrences often are in the nearby of the primary tumor (2/3 of all cases): if the surgery is not indicated, which one is the best second-line treatment? Nitrosourea chemotherapy is the common choice without a significant increasing in OS and PFS versus placebo. FDA approved the use of Bevacizumab in this setting but the clinical trials show different results in terms of OS and PFS. The aim of this metanalysis is to evaluate the efficacy of bevacizumab alone or in combination with standard chemotherapy in the treatment of recurrence GBM.

Material (patients) and methods: It was take into consideration only randomized trails comparing the use of bevacizumab alone or in combination with CHT versus standard chemotherapy in recurrent GBM. A systematic rewiew of this trials using Pubmed was performed. Cochrane Risk of Bias Tool was used to quantify the between-study eterogeneity risk of bias and a random effect model was used to evaluate OS and PFS.

Results: Four randomized phase II-III trials have been selected among 106 Pubmed citations: -two trials : bevacizumab alone in the experimental arm - two trials : combo bevacizumab-chemotherapy in the experimental arm Nitrosourea chemotherapy (lomustine or fotemustine) was used in the control arm and in association with bevacizumab. A total of 668 patients were analized. The metaanalyses showed a statistically significant benefit of bevacizumab in terms of PFS (cumulative HR=0,52,IC 95% 0,39-0,60,p<0.0001, Q= 2,21, df= 3,I2= 0%, for the combination chemotherapy-bevacizumab HR =0.48, IC 95% 0.39-0.60, p <0.0001, Q=0,3 DF=1, I2=0%) but not in term of OS (HR=0,95, 95% IC 0,77-1,17, P=0,63, Q=1,53,df=3, I2=0%).

Conclusions: The improving of PFS but not of OS is probably due to: -lack of biomarkers to select patients to treat with anti -VEGF; -"imaging bias" due to a pseudo-response of bevacizumab versus a pseudo-progression of radio-chemotherapy treatment; -"phenotypic switching" to more aggressive forms after anti-VEGF therapy. The results of this metanalysis are in line with literature: the addition of bevacizumab to chemotherapy in the recurrent GBM shows an increasing of PFS more than bevacizumab alone, without any benefit on OS.

R - Lymphomas and Myeloma

R01

BENDAMUSTINE-BORTEZOMIB-DEXAMETHASONE (BVD) IN HEAVILY PRETREATED MULTIPLE MYELOMA: OLD/NEW IN NOVEL AGENTS' ERA

Cerchione C.[1], Catalano L.[2], Nappi D.[2], Rocco S.[3], Palmieri S.[3], Pareto A.E.[2], Musuraca G.[4], Pane F.[2], Ferrara F.[3], Martinelli G.[4]

[1]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) - IRCCS, Meldola (FC);* [2]*Hematology - AOU Federico II, Napoli;* [3]*Hematology - AORN Cardarelli, Napoli;* [4]*Hematology - Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) - IRCCS, Napoli*

Background: Bendamustine is an old bi-functional alkylating agent which has proved to be effective in relapsed, refractory and in new diagnosed Multiple Myeloma (MM). Thus, aiming to provide further insights in this field, also in novel agents'era, we present here a retrospective, real-life analysis of patients with relapsed/refractory MM (rrMM), who had received salvage therapy with bendamustine in combination with bortezomib and dexamethasone (BVD).
Matherial and methods: 81 patients (44 M/37 F), with rrMM, median age at diagnosis 59.4 years (r. 36-82), median age at start of treatment 63.6 years (r.37-86) treated with several lines of treatments (median 6, r. 2-11), every refractory to all the drugs previously received (also Bortezomib), received BVD (B 90 mg/sqm days 1,2; V 1.3 mg/sqm days 1,4,8,11, D 20 mg days 1,2,4,5,8,9,11,12, Pegfilgrastim day +4) every 28 days, until progression. All patients had previously received bortezomib-based and IMIDs-based treatments, and 32% (26/81) had also received radiotherapy. 69% (56/81) had undergone single or double autologous and three (2%) allogeneic stem cell transplant. All patients were relapsed and refractory to last therapies.
Results: Bendamustine was well tolerated, with grade 3-4 transfusion-dependent anemia in 56% (46/81) of patients, and 43% (35/81) grade 3-4 neutropenia (no ospedalization was required, no septic shocks were observed). No severe extrahematologic toxicity was observed, only grade 1 gastrointestinal side effect (nausea), treated by common antiemetic drugs. According to IMWG, ORR was 63% (51/81: 7 CR, 18 VGPR, 15 PR, 11 MR) with 11 PD and 19 patients in SD, which can be considered as an impressive result in this

subset of patients. In particular, for 11 patients, BVD was, after having achieved at least a PR, a bridge to second auSCT, and for two patients a bridge to alloSCT. Eight patients have surprisingly achieved a notable PR after failure of novel agents (i.e. Carfilzomib, Daratumumab and Pomalidomide). Median time to response was 1.3 months (r.1-3), median OS from diagnosis was 67.3 months (r.6-151), median OS from start of Bendamustine was 9.6 months (r.2-36).
Conclusions: The triplet BVD has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, and, in particular cases, it could be considered as a bridge to a second autologous or allogenic SCT, also after failure of novel agents.

R02

CARFILZOMIB-LENALIDOMIDE-DEXAMETHASONE IN THE MANAGEMENT OF LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA

Nappi D.[1], Catalano L.[2], Pareto A.E.[2], Musuraca G.[3], Pane F.[2], Martinelli G.[3], Cerchione C.[3]

[1]*Department of Hematology & CBMT, Ospedale di Bolzano, Bolzano;* [2]*AOU Federico II, Napoli;* [3]*Hematology - Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) - IRCCS, Meldola (FC)*

Background: In this retrospective observational trial, it has been evaluated efficacy and safety of carfilzomib, epoxyketone proteasome inhibitor of second generation, in combination with lenalidomide-dexamethasone (KRD) as salvage regimen in patients with rrMM, refractory to lenalidomide, where lenalidomide-based regimens have no proven efficacy.
Material and methods: 41 patients (23 M/18 F), with rrMM, median age at diagnosis 63.7 years (r. 43-82), median age at start of treatment 67 years (r. 48-84) previously treated with several lines of treatments (median 3, r. 2-11), underwent to KRD regimen (ASPIRE trial schedule) for a median treatment cycles of 8 (r 2-18). ISS was equally distributed, and all patients had previously been treated with bortezomib and IMIDs, and were refractory to this agents. 61% (19/31) of them had undergone at least to a single ASCT.
Results: According to IMWG criteria, after a median follow-up of 9 months (r. 2-18), ORR was 68,2% (28/41: 9 CR, 12 VGPR, 7 PR) with 5 progressive diseases (PD) and 8 patients in stable disease (SD): this can be considered as an impressive result in this subset of rrMM patients, refractory to lenalidomide. In particular, for 11 patients, KRD was, after having achieved at least a PR, a bridge to second/third autologous SCT. Median time to response was 1.3 months (r.1-4), median OS from diagnosis was 62 months (r. 9-170), median OS from start of Carfilzomib was 11 months (r. 2-18). Carfilzomib was well tolerated, with grade 2 anemia in 39%(16/41) of patients, successfully managed by ESAs,

without necessity of blood transfusions; 29% (12/41) grade 3-4 neutropenia (pegfilgrastim in primary prophylaxis was given, no ospedalization was required, no septic shocks were observed); 34% (14/41) grade 2, 21% (9/41) grade 3 and 12% (5/41) grade 4 thrombocytopenia, without hemorrhagic events and transfusion-dependency. Moreover, it was observed pneumonia in 39% (16/41) of patients, treated by common antibiotic drugs and always solved. A cardiac monitoring was performed for all patients: hypertension (grade 2-3) in 34% (14/41) of patients; fatigue in 39% (16/31) of patients. Carfilzomib-Lenalidomide-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, also lenalidomide, and it could be considered as a bridge to a second autologous or allogenic SCT.

S - Management of Cancer Pain

S01

IMPACT OF ADOPTION OF PATIENT-REPORTED OUTCOMES IN CLINICAL PRACTICE ON THE ACCURACY OF PAIN REPORTING IN MEDICAL RECORDS OF CANCER PATIENTS

Baratelli C.[1], Marino D.[2], Guida G.[2], Turco C.G.C.[2], Lacidogna G.[2], Sperti E.[2], Vignani F.[2], Ballaminut D.[2], Bellezza A.[2], Chiotto P.[2], Ciriolo G.[2], Comite R.[2], Codegone F.[2], Florio S.[2], Fusco L.[2], Polimeno L.[2], Pozzi D.[2], Zillio E.[2], Terzolo S.[2], Di Maio M.[2]

[1]Oncologia Medica - AOU San Luigi Gonzaga/Oncologia Medica, Ospedale Mauriziano Umberto I, Orbassano/Torino; [2]Oncologia Medica, Ospedale Mauriziano Umberto I, Torino

Background: In 2018, we introduced patient-reported outcomes (PROs) questionnaires in clinical practice, demonstrating a significant improvement in quality of life (QoL), compared to usual visit [Baratelli, Support Care Cancer 2019;27:4697-4704]. In this secondary analysis, we describe agreement between patients' (pts) reports and physicians' records of pain. Our hypothesis was that adoption of PROs questionnaire could improve the agreement between what is reported by pts and what is recorded in pts' health files.

Methods: Eligible pts were receiving active anti-cancer treatment as outpatients. All pts filled in QoL questionnaire EORTC QLQ-C30, including 1 question about pain. Pts in the control group (treated in 2017) underwent usual visits (group A), while pts of group B (treated in 2018), before each visit, filled also a paper questionnaire on symptoms and toxicities. No specific instructions were provided to physicians to integrate such information in the medical record. Pain agreement between PRO (EORTC QLQ-C30) and physician records in health files was assessed by Cohen's k. Under-reporting was calculated as proportion of visits when pain was reported by pts but was not recorded by physicians.

Results: 211 patients (412 visits) have been analyzed. Pain (any severity) was reported by pts in 219 (53.2%) visits, while physicians recorded pain in 133 (32.3%). Cohen's k was 0.30 (95%CI 0.21-0.39), better for group B (0.42, 95%CI 0.28-0.56) vs group A (0.22, 95%CI 0.11-0.34). Although pain under-reporting was relevant in both groups, it was lower for group B: 59.6% group A vs. 42.3% group B, p=0.01. Limiting the analysis to visits when pts referred pain as "quite a bit" or "very much", pain under-reporting improved from 41.2% group A to 29.4% group B.

Conclusions: Adoption of paper PROs allowed a significant reduction in pain under-reporting, but agreement remained suboptimal. Direct integration of electronic PROs could minimize the issue of under-reporting of pain in medical records, increasing their accuracy. Table. Agreement between patient reporting and physician recording of pain

				All visits	Group A (receiving usual visit)	Group B (receiving paper PROs questionnaire)
Pain reported by	Patient: NO	Physician:	NO	162 (39.3%)	78 (33.5%)	84 (46.9%)
	Patient: NO	Physician:	YES	31 (7.5%)	14 (6.0%)	17 (9.5%)
	Patient: YES	Physician:	NO	117 (28.4%)	84 (36.1%)	33 (18.4%)
	Patient: YES	Physician:	YES	102 (24.8%)	57 (24.5%)	45 (25.1%)
	Cohen's k* (95%CI)			0.30 (0.21-0.39)	0.22 (0.11-0.34)	0.42 (0.28-0.56)

S02

DEVELOPMENT AND VALIDATION OF THE PATIENT REPORTED OUTCOME FOR FIGHTING FINANCIAL TOXICITY (PROFFIT) INSTRUMENT IN CANCER CARE IN ITALY

Riva S.[1], Efficace F.[2], Di Maio M.[3], Bryce J.[4], Del Campo L.[5], De Lorenzo F.[6], Frontini L.[7], Giannarelli D.[8], Gitto L.[9], Iannelli E.[5], Jommi C.[10], Montesarchio V.[11], Traclò F.[5], Vaccaro C.M.[12], Arenare L.[13], Gimigliano A.[13], Sparavigna L.[13], Piccirillo M.C.[13], Gallo C.[14], Perrone F.[13]

[1]St Mary's University, Twickenham, London, UK, London, UK; [2]Fondazione GIMEMA, Roma; [3]Università di Torino, AO Ordine

Mauriziano, Torino; ⁴Istituto Nazionale per lo Studio e la Cura dei Tumori, Napoli; ⁵FAVO, Roma; ⁶ECPC, AIMAC, Roma; ⁷FICOG, Milano; ⁸Istituto Nazionale per lo Studio e la Cura dei Tumori Regina Elena, Roma; ⁹Dipartimento di Economia, Università degli Studi di Messina, Messina; ¹⁰SDA Bocconi School of Management, Milano; ¹¹Azienda dei Colli, Napoli; ¹²CENSIS, Roma; ¹³Istituto Nazionale per lo Studio e la Cura dei Tumori, IRCCS Fondazione Pascale, Napoli; ¹⁴Università degli Studi della Campania, Caserta

Background: Despite the worldwide growing interest in evaluating the impact of costs in cancer care, and in the development of measures that can capture the so called financial toxicity (FT), no large scale initiative has yet taken place in Italy. We aim to develop the first FT measure fully developed in Italy, a country characterised by a public healthcare system.

Methods: To develop the new Patient Reported Outcome for Fighting Financial Toxicity (PROFFIT) questionnaire, potential items were developed by using gold-standard methods (literature search, patient involvement with focus groups and expert involvement with ad-hoc survey). Subsequently, item reduction was performed by using a combined approach, applying importance analysis and cognitive interviews. The resulting PROFFIT pre-final questionnaire was then tested for its reliability (explanatory factor analysis- EFA), internal consistency (Cronbach's α test) and validity (Test-retest analysis). Initial phases were supported by 3 oncological centres (Napoli, Roma, Torino) and the final step included further 7 centres (Brindisi, Catania, Genova, Napoli2, Padova, Pavia, Sassari).

Results: Guided by literature review analysis, 156 concepts were generated from focus groups and interviews. After controlling for redundancy, 55 items were tested through the importance analysis identifying 29 items that scored at or above the median importance score plus one more item added for clarity purpose. After cognitive debriefing, 9 items (30%) were slightly changed due to ambiguities or lack of specificity leaving a pre-final 30-items instrument. Such instrument entered reliability, consistency and validity analyses. Factor analisys suggested a single factor structure of 7 items (Crombach's α 0.70) measuring the financial toxicity score (outcomes) and an additional set of 9 items measuring the specific determinants (causes) of such toxicity. Test-retest analysis revealed a good validity of the instrument (ICC range= .53-.79; k=.52-.79).

Conclusions: The PROFFIT instrument consists of 16 items and is the first patient-reported measure fully developed in Italy for assessing FT in Italian cancer patients. It is a short, valid and reliable questionnaire that can be used in future clinical studies as well as in routine practice settings. clinicaltrials.gov NCT03473379

S03

IS THE DEXAMETHASONE (DEX)-SPARING STRATEGY READY FOR CISPLATIN? RESULTS OF A PHASE III, CONTROLLED, NON-INFERIORITY TRIAL OF TWO SIMPLIFIED DEX-SPARING REGIMENS INCLUDING NEPA FOR THE PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV)

Celio L.¹, Cortinovis D.², Cogoni A.A.³, Cavanna L.⁴, Martelli O.⁵, Carnio S.⁶, Collovà E.⁷, Bertolini F.⁸, Petrelli F.⁹, Cassano A.¹⁰, Chiari R.¹¹, Zanelli F.¹², Vittimberga I.¹³, Letizia A.¹⁴, Misino A.¹⁵, Gernone A.¹⁶, Bonizzoni E.¹⁷, Pilotto S.¹⁸, De Placido S.¹⁹, Bria E.¹⁰

¹Fondazione IRCCS "Istituto Nazionale dei Tumori", Milano; ²ASST Monza - Ospedale San Gerardo, Monza; ³Azienda Ospedaliero-Universitaria di Sassari, Sassari; ⁴Azienda Ospedaliera di Piacenza, Piacenza; ⁵A.O. San Giovanni-Addolorata, Roma; ⁶A.O.U. San Luigi Gonzaga - Università di Torino, Orbassano (TO); ⁷ASST Ovest Milanese - Ospedale di Legnano, Legnano (MI); ⁸A.O.U. Policlinico di Modena, Modena; ⁹ASST Bergamo Ovest - Ospedale di Treviglio, Treviglio (BG); ¹⁰Università Cattolica del Sacro Cuore - Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Roma; ¹¹AULSS 6 Euganea, Padova; ¹²AUSL Reggio di Emilia - IRCCS Santa Maria Nuova, Reggio Emilia; ¹³ASST Lecco, Lecco; ¹⁴A.O.R.N. dei Colli - Ospedale Monaldi, Napoli; ¹⁵Istituto Tumori "Giovanni Paolo II" - IRCCS, Bari; ¹⁶A.O.U. Consorziale Policlinico di Bari, Bari; ¹⁷Università di Milano, Facoltà di Medicina e Chirurgia, Milano; ¹⁸Azienda Ospedaliera Universitaria Integrata di Verona, Verona; ¹⁹Università degli Studi di Napoli "Federico II", Napoli

Background: To reduce the overall exposure to DEX in cisplatin-based chemotherapy, we evaluated the non-inferiority of DEX on day 1, with or without low-dose DEX on days 2 and 3, combined with NEPA, a fixed combination of the NK-1 receptor antagonist (RA), netupitant and the pharmacologically distinct 5-HT3RA, palonosetron, compared with the guideline-recommended 4-day use of DEX.

Methods: In this open-label, multicenter study, chemo-naïve lung cancer patients receiving cisplatin (≥70 mg/m2), were given a single oral dose of NEPA and DEX (12 mg i.v.) prior to chemotherapy and randomized (1:1:1) to receive no further DEX (DEX1), oral DEX (4 mg once daily) on days 2 and 3 (DEX3), or oral DEX (4 mg twice daily) on days 2 to 4 (DEX4; reference arm). The primary efficacy endpoint was complete response (CR: no emesis and no use of rescue medication) during the overall (days 1-5) phase. Non-inferiority was defined as a lower 95%CI greater than the non-inferiority margin threshold of -15% difference (Arms DEX1 or DEX3 minus Arm DEX4). Impact of CINV on daily life as assessed by the Functional Living Index-Emesis (FLIE) questionnaire was also evaluated.

Results: A total of 222 patients (76% male), 74 in each arm, were evaluated. CR rates during the overall and delayed phases were 77.0% in Arms DEX1 and DEX3 and

74.3% in Arm DEX4 (95%CI, -11.1% to 16.5%). No significant differences were observed between groups in proportions of patients who reported no impact on daily life due to nausea, vomiting, or both during the 5-day observation period after cisplatin administration.

Conclusions: Since efficacy results were comparable between the two DEX-sparing regimens in this study, we conclude that the simplified three-drug regimen with NEPA plus single-dose DEX is an option that is not associated with significant reduction in anti-emetic control during the 5-day period or an impact on patient functioning in the setting of cisplatin.

S04

ANOTHER HOSPITAL ADMISSION THROUGH THE EMERGENCY ROOM? LOOKING FOR A FRAGILITY PATTERN IN ADVANCED CANCER PATIENTS: AN UPDATE

Velutti L.[1], Saetta A.[2], Giordano L.[2], Marinello A.[2], Cammarota A.[2], Grimaudo M.S.[2], Digiacomo N.[2], Cullia L.[3], Villa E.[2], Lopane D.[4], Provasoli C.[2], Poggio C.[5], Giuffrè S.[2], Pavesi C.[2], Rimassa L.[6], Santoro A.[6]

[1]*Unità di Oncologia Medica e Unità di Cure Palliative Domiciliari, Humanitas Clinical and Research Center IRCCS, Rozzano, Milano;* [2]*Humanitas Clinical and Research Center IRCCS, Rozzano, Milano;* [3]*Cooperativa Servizi alla Persona CSAP, Bergamo;* [4]*Cooperativa Sociale 9Coop, Romano di Lombardia, Bergamo;* [5]*Fondazione Insieme con Humanitas, Rozzano, Milano;* [6]*Humanitas Clinical and Research Center IRCCS and Humanitas University, Rozzano, Milano*

Background: Cancer patients (pts) are often treated with specific therapies even in the last period of clinical history. It is common to observe an intensification of care, hospitalization, diagnostic procedures in the last months of life. These pts are more likely to experience hospitalization due to toxicity, worsening, clinical conditions, concomitant non-oncologic diseases, disease progression. They often access palliative care program (PCP) at a very advanced stage of the disease, or never access it at all. It is common to observe that these pts are hospitalized after an admission from emergency room (ER). This is frequently the moment when a PCP is proposed and activated, or when the pts die.

Methods: We made a retrospective analysis of pts admitted from ER in our oncologic ward. We evaluated: pts' characteristics, histology, diagnosis' date, metastases' sites, comorbidities, previous anticancer therapies (CT) and radiotherapy (RT) for advanced disease, invasive and or higt-cost procedures, previous ER access, admissions for supportive care (SC), transfusions, artificial nutrition, use of high-cost antibiotics, in last 90 days. Pts were divided into two fragility groups: less-fragile (LF), candidate to CT or follow-up, and more-fragile (MF), candidate to a PCP or who died.

Results: From August 2017 to July 2018 we recorded 908 admissions, 535 from ER (58.9%) in 450 pts, 85 pts had more than 1 admission. Pts were: women/men 223/227, the median age was 65.4 years. The pts in 2 fragility groups were: LF/MF 248/202. The differences found were: age ≥ 65 years in 45.9% of pts in LF group, 55.4% in MF group, p=0.046; visceral metastases' sites in 70.3% of pts in LF, 84.8% in MF, p<0.001; ≥1 lines of CT in 62.5% of pts in LF, 80.7% in MF, p<0.001; ≥1 RT treatments in 22% of pts in LF, 32% in MF, p=0.023; previous admissions for SC in 45.5% of pts in LF, 61.8% in MF, p<0.001; previous admissions for SC in last 90 days in 21.2% of pts in LF, 38.1% in MF, p=0.004; ER accesses in last 90 days in 38.3% of pts in LF, 63.8% in MF, p<0.001. We find no other differences.

Conclusions: We identified a MF profile: pts with ≥65 years, with visceral metastases' sites, who did ≥1 lines of CT, ≥1 RT treatments, with ≥1 prior admission for SC, =1 admission for supportive care and =1 ER access in the last 90 days. This fragility profile may help oncologists timely offer a PCP to advanced stage pts. This could prevent some ER access and admissions close to the end-of-life.

S05

HOME-BASED MANAGEMENT OF CANCER PATIENTS EXPERIENCING TOXICITIES: HOW A NURSE-LED TELEPHONE TRIAGE (NTT) MAY IMPACT ON LUNG CANCER PATIENTS (LCPS) HOSPITALIZATIONS

Calvetti L.[1], Marta T.[2], Cimenton R.[2], Gentile A.[2], Pretto R.[2], Pavan M.[2], Toniolo A.[2], Valente C.[2], Fusa C.[2], Gasparin B.[2], Pagiusco G.[2], Simionato F.[2], De Vivo R.[2], Merlini L.[2], Aprile G.[2]

[1]*Oncologia Ospedale San Bortolo, AULSS8 Berica, Vicenza, Padova;* [2]*Oncologia Ospedale San Bortolo, AULSS8 Berica, Vicenza*

Background: Novel organization models are needed to ensure early management of new treatment-related toxicity of anticancer treatments, especially in LCPs. Aim of this prospective observational study was to evaluate the impact of the introduction of NTT in reducing hospitalizations of cancer patients on treatment.

Methods: Cancer patients on active medical treatment at the Department of Oncology of San Bortolo Hospital (Vicenza, Italy) were given instructions to refer to NTT in case of treatment-related adverse events (TRAEs). The service was opened Mon to Fri from 8am to 8pm. Assessment of TRAEs was performed by trained oncology nurses according to the CTCAE scale and subsequent actions were taken according to the severity of the events. The assessment was performed made under the supervision of a medical oncologist in charge of the service while on duty. Co-Primary endpoints were to compare

the rate of hospitalization of overall cancer patients and LCPs on anticancer treatment before and after the introduction of NTT.

Results: From September 2018 to September 2019 1,075 patients received systemic anticancer treatment (versus 936 patients in the corresponding 2017 – 2018 period). Total consultations at NTT were 429; 581 TRAEs were reported. 117 patients reported more than one TRAE. CTCAE graded as G1 were 237 (40.8%), G2 231 (39.8%) or G3-G4 113 (19.4%). LCPS were the most frequent callers (96, 22.4%) with 30 (31.3%) patients reporting G3-G4 events. The most common grade ⩾ 3 TRAE among LCPs was fever [11 events (36.7%) that resulted a febrile neutropenia in 1 case] followed by cancer pain [7 (23.3%)] and fatigue [5 (16.7%)]. In the observation period, 109 overall cancer patients on treatment were hospitalized versus 138 in the 2017-2018 period with a normalized hospitalization rate of 10.1% versus 14.7% (p=0.002, chi-square) with a reduction of normalized number of hospitalization of 44 (estimated cost savings of 380.160 Euros). This reduction was mainly due to numerical reduction of hospitalizations of lung cancer patients on treatment (16 vs 36 patients, p=0.105 chi-square).

Conclusions: Our results provided evidence of successful implementation of the NTT system in reducing rates of hospitalization through emergency room in cancer patients receiving modern medical treatments. The benefit was particularly noteworthy for LCPs.

S06

ACCESS TO EMERGENCY DEPARTMENT AMONG ONCOLOGICAL PATIENTS IN TWO DIFFERENT PERIOD: UNDERLYING CAUSES, PATIENTS' CHARACTERISTICS AND OUTCOME

Raitano M.[1], Ferrari V.[2], Bossi P.[2], Terragnoli P.[3], Libertini M.[4], Paolillo C.[5], Zaniboni A.[4], Concoreggi C.[5], Zamparini M.[6], Gritti S.[7], Berruti A.[2]

[1]*Università degli Studi di Brescia, Brescia;* [2]*UO Oncologia Medica Spedali Civili, Brescia;* [3]*Pronto Soccorso Fondazione Poliambulanza, Brescia;* [4]*UO Oncologia Medica Fondazione Poliambulanza, Brescia;* [5]*Pronto Soccorso Spedali Civili, Brescia;* [6]*Spedali Civili, Brescia;* [7]*Università degli Studi di Brescia, Brescia*

Background: Rates of Emergency Department (ED) use among oncological patients is higher than in general population. Reasons for access have been poorly characterized in literature and need to be carefully studied to evaluate their appropriateness.

Methods: We retrospectively analysed two series of oncological patients who accessed the ED in two different period of time: the first one from January 2013 to February 2014 at Spedali Civili and Poliambulanza hospitals in Brescia; the second one only at the ED of Spedali Civili during all 2019.

The following data were gathered: demographic data, oncologic disease, main signs/symptoms causing the access to the ED, the way of accessing ED, the triage results, and the outcome of the visit.

Results: In the first series we evaluated 1654 patients: 979 from Spedali Civili (average of 75 accesses per month) and 675 from Poliambulanza (average of 52 accesses per month); while in the second one 887 patients (average of 74 accesses per month). No significant difference between the 2 Hospitals was identified in the first series.

In the 2013/2014 series, median age was 70.4 (range 15-113), mainly male (58.7%). Main reason of ED access was pain (21.3%), followed by dyspnea (13.2%) and hemorrhages (10.2%); lung cancer was the most frequent primary (18%). Most of the oncologic patients accessed ED by self-presentation (65%) and the visit's outcome was patient's hospitalization in most of the cases (62.8%).

In the 2019 study, median age was 71 (range 15-96), mainly male (61.9%). The main cause of ED access in the 2019 study was pain (22.9%), followed by dyspnea (13.5%), hemorrhages (9.8%) and confusion (9.2%). The most represented tumors were those concerning the urogenital system (22%, mostly prostatic cancer), followed by the lungs (19.4%). Self-presentation happened in 62.4% of cases; outcome of the visit was patient's hospitalization in 42.2% of the cases.

Conclusions: Pain is the main cause of access to ED among oncological patients. In the treatment period analyzed there was a reduction in the rate of patient hospitalization after ED access. Systematic implementation of simultaneous care in cancer patients could reduce ED access by better treating emerging symptoms and by creating a network of care.

S07

END-OF-LIFE CARE IN ONCOLOGY: DO PATIENTS REALLY NEED HOSPITALIZATION?

Marcantognini G.[1], Fiordoliva I.[1], Luminati C.[1], Meletani T.[1], Baleani M.G.[1], Di Pietro Paolo M.[1], Pierantoni C.[1], Antognoli S.[1], Berardi R.[1]

[1]*Clinica Oncologica, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Ancona*

Background: Hospital admission of patients with advanced cancer is often due to increasingly severe symptoms, although it is indeed associated with higher patients' suffering and health care costs. The aim of this study is to analyse consecutive patients died at our institution in order to describe end-of-life needs and define adequate palliative cares.

Material and Methods: We retrospectively enrolled consecutive patients hospitalized at our Oncology Department and died between January 2017 and April 2019. Overall

Survival (OS) was estimated using Kaplan-Meier method. A Cox regression model was carried out for statistical analyses.

Results: One hundred eighty-four patients were enrolled, 96 males and 88 females. Median age was 67 years (19-90). The median duration of hospitalization was 12 days (1-64). The most frequent cancer diagnosis was non-small cell lung cancer (28%) and the majority of patients had a metastatic disease (86%). 44% of patients were admitted from the emergency department requesting treatments for cancer symptoms, such as pain (71%), dyspnoea (39%) and neurological impairment (38%). A quarter of patients received active cancer treatment before dying, of which chemotherapy (54%), radiotherapy (17%) or a combination of both (24%). Clinical parameters that predicted lower survival were: emergency admission (8 vs 15 days, $p=0.0064$, HR 0.64, CI95% 0.47-0.88), reported pain at admission (9 vs 13 days, $p=0.0056$, HR 0.59, CI95% 0.41-0.86), creatinine $=1.2$ mg/dl (7 vs 14 days, $p=0.0002$, HR 0.45, CI95% 0.29-0.69), pleural effusion (9 vs 13 days, $p=0.0206$, HR 0.65, CI95% 0.46-0.94). Procedures that correlated with improved survival were radiotherapy (25 vs 11 days, $p=0.0011$, HR 0.53, CI95% 0.36-0.77), blood transfusions (18 vs 10 days, $p<0.0001$, HR 0.50, CI95% 0.37-0.68) and antibiotics (7 vs 15 days, $p<0.0001$, HR 0.34, CI95% 0.23-0.51). Age, gender, disease stage, chemotherapy, use of terminal sedation, haemoglobin, neutrophil-to-lymphocyte ratio, hyperbilirubinemia, dyspnoea, neurological impairment, fever, haemorrhage did not significantly affect survival.

Conclusions: Our study identified factors which may be useful to predict high risk for death during hospitalization in medical oncology department. It is remarkable that palliative treatments that correlated with better prognosis may be offered in day hospital/home care setting. Further studies are needed to evaluate if territorial end-of life care could prevent inappropriate hospital access.

S08

A PROSPECTIVE, OBSERVATIONAL STUDY ASSESSING SIADH (SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION) MANAGEMENT AND OUTCOME AMONG LUNG CANCER PATIENTS IN ITALY (ASSERT TRIAL)

Berardi R.[1], Garassino M.C.[2], Tiseo M.[3], Palazzo S.[4], Montesarchio V.[5], Tonini G.[6], Cavanna L.[7], Ferrari D.[8], Morabito A.[9], Pinotti G.[10], Buosi R.[11], Scartozzi M.[12], Torniai M.[13], De Marino V.[5]

[1]Oncology Clinic, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Via Conca 71, 60126 Ancona, Italy, Ancona; [2]Fondazione IRCCS Istituto Nazionale Tumori Via Giacomo Venezian, Milan, Italy, Milan; [3]Azienda Ospedaliero-Universitaria di Parma, Parma, Italy, Parma; [4]Ospedale Annunziata, Cosenza, Italy, Cosenza; [5]Azienda Ospedaliera Specialistica dei Colli "Monaldi – Cotugno – CTO", Naples, Italy, Naples; [6]Policlinico Universitario Campus Bio-Medico di Roma, Rome, Italy, Rome; [7]AUSL di Piacenza, Piacenza, Italy, Piacenza; [8]Azienda Ospedaliera San Paolo, Milan, Italy, Milan; [9]Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Naples, Italy, Naples; [10]Ospedale di Circolo e Fondazione Macchi, Varese, Italy, Varese; [11]ASL Alessandria Santo Spirito Hospital, Casale Monferrato AL, Italy, Alessandria; [12]Policlinico Universitario Duilio Casula, Monserrato, Italy, Monserrato; [13]Oncology Clinic, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Ancona

Background: SIADH represents the most common cause of hyponatremia (serum sodium concentration $<$ 135 mEq/l) in cancer patients, particularly in lung cancer.

Methods: ASSERT trial was a prospective, observational, non-interventional study conducted 18 Italian oncology Centers. Cancer patients requiring treatment for hyponatremia secondary to SIADH were enrolled from October 2015 to June 2017. The key objective of the study was to evaluate pharmacological versus non-pharmacological treatments for the management of hyponatraemia in accordance with the local standard of care and guideline recommendations. The primary endpoint was change in sodium level from baseline visit to the end of first month or sixth month of the observational period, or until earlier discontinuation.

Results: The full analysis set (FAS) included 68 adult cancer patients and lung cancer was the most common neoplasm (N = 48, 71%). Regarding lung cancer cohort, the linear regression analysis showed that tolvaptan dose intensity significantly correlated with clinical response (intended as increase of sodium level) after 1 month (p = 0.012) and after 6 months (p = 0.005). Furthermore, the percentage of patients with serum sodium $\geqslant$ 130 mEq/l (target event) resulted significantly higher in the group of patients treated with tolvaptan (Group 1, N = 32) than in other patients not received this drug (Group 2, N = 16) during 6 months of follow-up (87.5% vs 62.5% respectively, p = 0.033). Furthermore, in the whole population, overall survival was significantly higher in patients in Group 1 vs. Group 2, with a median overall survival (OS) of 123 vs 56 days and a mean OS of 299 vs 75 days; both p=0.001. Regarding patient-reported outcomes, no significant between-group differences in in EORTC QLQ-C30 mean scores were observed at follow-up (Visit 2: Month 1), except for the nausea and vomiting item [mean score: 1.17 (Group 1) versus 1.80 (Group 2); p=0.013]. For the EQ-5D, no significant differences in any of the five items were observed for patients in Group 1 versus Group 2 at baseline visit and Visit 2 (Month 1). Similarly, no significant between-group differences in MMSE scores were noted at baseline and at any time point during follow-up.

Conclusions: Hyponatremia secondary to SIADH represents a potentially modifiable risk factor influencing the outcome of cancer patients. Acting effective and timely on the normalization of sodium levels might have a positive effect on outcome in this setting of patients.

S09

LOCAL TREATMENT WITH DEEP PERCUTANEOUS ELECTROCHEMOTHERAPY OF VARIOUS TUMOR LESIONS: CANCER PAIN RELIEF AND OBJECTIVE RESPONSE RESULTS FROM AN OBSERVATIONAL STUDY

Laface C.[1], Gadaleta C.D.[1], Fazio V.[1], De Ceglia D.[1], Macina F.[1], Gisone V.[1], Porcelli M.[1], Vinciarelli G.[1], Carella C.[1], Molinari P.[1], Laricchia G.[1], Laforgia M.[2], Ranieri G.[1]

[1]*Interventional and Medical Oncology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy;* [2]*Pharmacology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy*

Background: Electrochemotherapy (ECT) is a non-thermal technique that has proved to be safe and effective against many types of solid tumors. ECT effectiveness and safety in the treatment of various cutaneous tumors have been extended in the treatment of deep-seated tumors. The aim of this investigation focuses on the evaluation of the efficacy of deep percutaneous ECT in terms of cancer pain relief and local objective response, in pre-treated patients with neither further available pharmacological treatments nor eligible for surgery.

Materials and Methods: Deep Percutaneous ECT has been performed in 20 patients subjected to systemic anaesthesia. Bleomycin was administrated intravenously before the application of the electrical pulses on the target area, employing multiple single needles depending on the size and location of the target tumor.

Results: Pain assessment based on Visual Analogue Scale showed significant pain relief one month after treatment in all patients, reducing from 7,5 to 3 as a median value (*p*-value at Wilcoxon test <0.001). Local symptom-free survival median value was 5.5 months. At the first follow-up (1-2 months), a local disease control rate (LDCR) was observed in 19/20 (95%) patients: complete responses in 2 (10%), partial responses in 8 (40%) and stable disease in 9 (45%). Local progression-free survival median value was 5.7 months. Overall, no major adverse effects were observed.

Conclusions: Our study confirms that deep percutaneous ECT can produce a significant cancer pain reduction and a high LDCR in different tumor lesions, for anatomical site or histotype. In particular, ECT has demonstrated to be effective in various histotypes and deep-seated tumor lesions never treated before by this approach and giving a new chance to physicians to manage cancer pain in patients not eligible to other therapeutic routes. In addition, our study was the first successful application of deep percutaneous ECT on adrenal metastasis, malignant pleural mesothelioma, uterine leiomyosarcoma and the exceptional case of a male müllerian tumor.

S10

PENALTY FOR SIMULTANEOUS CARE DURING THE EMERGENCY COVID-19

Antoniazzi F.[1], Pastorini A.[2], Fusco O.[2], Cubeddu A.[2], Maiolani M.[2], Caponigro G.[2], Deligiannis P.[2], Cantini S.[2], Menatti E.[2], Fregoni V.[3], Geronimi C.[4], De Carlo A.[4], Pedrotti C.[1], Bagassi A.[4], Bertolini A.[5]

[1]*ASST della Valtellina e Alto Lario-Cure Palliative, Sondalo;* [2]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio;* [3]*ASST della Valtellina e Alto Lario-Medicina Generale, Sondalo;* [4]*ASST della Valtellina e Alto Lario-Cure Palliative, Morbegno;* [5]*ASST della Valtellina e Alto Lario-Cure Palliative, Sondrio*

Background: Simultaneous care represents an organizational model based on the global care of the cancer patient through continuous assistance and a progressive integration between cancer therapies and palliative care. The model responds to global needs (physical, psychological, social) of the patient and his family managed by a multidisciplinary team made up of oncologists, palliativists, radiotherapists, psychologists. As compared with cancer patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life and longer survival. In the province of Sondrio ASST Valtellina and Alto Lario has activated simultaneous care for cancer patients for about a year.

Material (patients) and methods: The simultaneous care clinics are structured on defined days and times, managed by a multidisciplinary team which always involve family members. During the emergency period the surgeries underwent changes in terms of organization and frequency. The reduction in the number of doctors available and the limitations of patient access to hospital clinics for their protection have led to a significant reduction in the numbers of cancer patients treated early in simultaneous treatment. The analysis of the data defines a number of 12 cancer patients followed simultaneously in a pre-covid period from 1 November 2019 to 31 January 2020. During the covid-19 emergency, in the period from 1 March 2020 to 31 May 2020, they were followed 5 patients. On average 3 patients versus 1 in the emergency period.

Results: During the covid-19 emergency, the results show a significant reduction in simultaneous care paths. In this phase, the simultaneous care clinic was managed as needed by a single professional with telephone consultations and few home visits without the direct involvement of family members.

Conclusions: The reduction in simultaneous care during the emergency period penalized cancer patients who, in a moment of clinical fragility, experienced a lived experience of abandonment that affected their quality of life.

In memory of dr. Fabio Rubino, Responsible for the Palliative Care Service.

S11

NSAIDS EFFICACY AND PHYSICAL COMPATIBILITY OF KETOPROFEN IN DRUG MIXTURES USED INTRAVENOUSLY IN AN INPATIENT HOSPICE WARD

Ricci M.[1], Maltoni M.[2], Galetti A.[3], Vaca G.[3], Fabbri L.[2], Sansoni E.[2], Bedini A.[3]

[1]IRCCS IRST Meldola, Meldola; [2]Hospice Valerio Grassi, Forlimpopoli; [3]Dipartimento di Farmacia e Biotecnologia Università di Bologna, Bologna

Background: The NSAIDs use in our hospice was retrospectively evaluated in terms of prevalence, modality of administration and clinical outcomes; furthermore, the nonsteroidal anti-inflammatory drug most frequently used in our hospice (ketoprofen) was tested in combination with other drugs to assess its physical compatibility.

Material and Methods: We analyzed the medical records of 185 patients with hematologic malignancies or solid tumors consecutively admitted to our hospice from January 1st to September 30th, collecting data on patient characteristics, type of tumor, ongoing and administered therapies, including analgesics and NSAIDs. We also evaluated the physical compatibility of a binary mixture of ketoprofen and morphine and of eight ternary mixtures of ketoprofen, morphine and a third drug (midazolam, haloperidol, metoclopramide, chlorpromazine, furosemide, diazepam, hyoscine butyl-bromide or dexamethasone) at baseline (0) and 1, 5, 24, 48, 96 and 168 hours after preparation. Single-drug preparations of morphine and ketoprofen, diluted in 0.9% NaCl aqueous solution, were set up as controls. The physical compatibility of the mixtures was tested by visual inspection of the mixtures against black and white backgrounds. The pH of the solutions was determined by a calibrated digital pH meter and spectrophotometric absorbance between 400 and 700 nm was measured by a Jasco V-530 spectrophotometer.

Results: The binary mixture containing ketoprofen and morphine did not show important alterations in pH or spectrophotometric absorbance between 400 and 700 nm at any of the considered time points. The most problematic ternary mixture was that comprising ketoprofen, morphine and chlorpromazine, in which significant changes in color, turbidity and spectrometric absorbance occurred immediately after preparation. From the retrospective analysis we found that the ketoprofen- morphine binary mixture given on demand resolved 94% of 362 episodes of breakthrough pain, without side-effects.

Conclusions: The binary mixture of ketoprofen and morphine was compatible and no alterations assessable with physical methods were observed. Moreover, it proved safe and highly effective in managing episodes of breakthrough pain in cancer patients.

S12

SIMULTANEOUS HOME CANCER TREATMENT IN THE PROVINCIAL HEALTH AUTHORITY OF VIBO VALENTIA

Gabrielli G.[1], Spinoso A.[1], Grillone F.[1], DeCarlo M.[1], Arena M.[1]

[1]Azienda Sanitaria Provinciale di Vibo Valentia, Tropea (VV)

Background: Oral, intramuscular, subcutaneous and topical applications, thanks to their manageability, can be administered easily at home. The oncologist specialist must always collaborate with various socio-health realities which have had or are in charge of the home patient.

Material (patients) and methods: From January 2011 to December 2019: 412 patients with advanced (locally and metastatic) neoplastic diseases. The median age was 68 years; the males was 54%. The oncological pathologies were: Lung cancer (NSCl and SCL) 18.4% Colon-rectum cancer 15.9% Liver, pancreas and biliary tract cancer 12.1% Prostate, bladder and kidney cancer 11.5% Breast cancer 9.6% Hematological malignancies (myelomas, leukemia ...) 6.2% Gastric cancer 5.0% Head-neck cancer 4.4% Gynecological cancers 3.7% Brain tumor 3.4% Skin cancers 3.4% Malignancies undeterminable 3,4% Other malignancies 2.2%.

The patients considered fit to receive specific home cancer treatment were 81 (22% of the total). The drugs used are classifiable from the point of view of the mechanism of action as drugs: - chemotherapy; - organic; - hormonal; - immunological.

The list of drugs used is listed in alphabetical order: 1Abiraterone 2Anastrazole 3Bicalutamide 4Capecitabine 5Cyclophosphamide 6Chlorambucil 7Denosumab 8Enzalutamide 9Erlotinib 10Estramustine 11Exemestane 12Fulvestrant 13Idealsidib 14Hydroxyurea 15Imiquimod 16Lenalidomide 17Letrozole 18Lapatinib 19Leuprorelin 20Medroxiprogesterone acetate 21Megestrol acetate 22Prednisone 23Regorafenib 24Sorafenib 25Tamoxifen 26Temozolomide 27Trifluridine tipiracil 28Triptorelin 29Vinorelbine 30Vismodegib.

Results: The treatment carried out, in the majority of cases, has shown its efficacy from a symptomatic or laboratory point of view.

Conclusions: Home-specific medical cancer treatment has proven practicable in many patients with adequate PS.

S13

DENIAL AND EARLY SIMULTANEOUS PALLIATIVE CARE IN THE ERA OF PREVENTION

Rondini M.[1], Olivieri E.[2], Bormolini G.[3], Aschele C.[4], Ceglie R.[2], Bregnocchi M.[5]

[1]*ASL 5 Spezzino S.C. Oncologia, La Spezia; [2]Asl 5 Spezzino S.P.D.C., La Spezia; [3]Tutto è vita onlus, Firenze; [4]ASL 5 Spezzino SC Oncologia, La Spezia; [5]Asl 5 Spezzino S.S.D. Cure Palliative, La Spezia*

Backgroud: Mammographic screening is a periodic secondary prevention for asymptomatic women. Several studies highlight the reduction of breast cancer mortality, both for mammographic screening and for more innovative cancer treatments. Only 5% of breast cancers are metastatic *de novo*. The communication of tumor disease changes the way of "being in the world"of the person: how the patient handles this emotional crisis determines his entire adaptive structure and the same prognosis. We have developed an integrated multidisciplinary simultaneous approach in patients with *de novo* metastatic breast cancer, with denial of the disease.

Material (patients) and methods: We have analyzed using a HAM-D/HAM-A scale and PPI, 9 patients (median age 50 years, range 46-73 years) admitted to the Oncology Unit of ASL 5 Spezzino, from July 2016 to October 2018, after the access to the Emergency Room for an internistic complication and a simultaneous diagnosis of metastatic breast cancer (Tab.1). In all patients a personalized management has been developed by performing periodic check-ups, in the presence of the oncologist, palliativist, psychologist and psychiatrist in simultaneous care. A pharmacological and psychotherapeutic approach was performed in order to control the deepest anxieties of separation, abandonment, death with a systemic chemotherapy.

Results: The assessment of the patients' mental state revealed some common traits, in particular "anosognosia", sometimes "anosodiaforia", up to indifference. The psychopathological evaluation of the patients highlights a dynamic adaptations such as the euphoric negation or a strong regressive negation. In some patients a more regressive defense mechanisms have been established such as *denial*. All 9 patients have followed active care pathways, despite late diagnosis, sometimes with a surprising median overall survival .

Conclusions: Despite the broad affirmation of mammographic screening, *denial* prevents the adherence to diagnostic-therapeutic procedures. In the metastatic breast cancer, which is less managed in *simultaneous care*, our study shows that an integrated approach allows a greater elaboration of the disease optimizing the adherence to the pathways of care.

Nb pt	Clinical and socio-cultural characteristics
9/9	De novo metastatic breast cancer
3/9	CNS metastasis
2/9	Pulmonary thromboembolism
1/9	Dorsal medullary compression
9/9	No mammography screening
9/9	Upper-secondary education
9/9	Integration in an appropriate socio-family context

S14

PROVIDING NUTRITIONAL CARE TO CANCER PATIENTS DURING THE COVID-19 PANDEMIC: AN ITALIAN PERSPECTIVE

Caccialanza R.[1], Lobascio F.[1], Cereda E.[1], Crotti S.[1], Masi S.[1], Brugnatelli S.[1], Secondino S.[1], Monaco T.[1], Inglardi M.[1], Pozzi E.[1], Pedrazzoli P.[1]

[1]*Fondazione IRCCS Policlinico San Matteo Pavia, Pavia*

Background: The emergence of 2019 novel coronavirus disease (COVID-19) has caused a global public health emergency. Italy was the first European country where the disease widespread and Lombardy is the principal cluster. In the most affected areas, a rapid and thorough reorganization of hospital clinical procedures has taken place: all non-essential clinical activity has been suspended, while the ordinary activity continues for whom diagnostic procedures and treatments cannot be delayed. It is the case of cancer patients undergoing treatments with curative intent; in this situation of deep distress for the health care system, the inability to satisfy cancer patients' needs is an additional concern.

In the light of the above, during the current COVID-19 pandemic it is likely to see a dramatic worsening of cancer patients' nutritional status, due to possible delayed clinical assistance and difficulties in procuring nutritionally adequate quality food as lock-down's repercussion. The consequences are reasonably foreseeable and will have a severe negative impact after the emergency. Hence, it is essential to carry on, as far as possible, the activity of clinical nutrition in oncology, which can be safely provided only by a thorough setting and approach to patients rearrangement.

Methods: For this purpose, the Clinical Nutrition and Dietetics Unit and the Medical Oncology Unit of our hospital have reorganized the clinical routine activity in strict collaboration, to better face up to the challenge, while preserving cancer patients' needs.

Results: Several general actions have been taken to protect both patients and healthcare professionals; remote capabilities have been implemented to minimize interactions, efforts are being done to secure medical resources and supplies. This allowed the regular provision of nutritional counseling and nutritional support in both inpatients and outpatients, in line with the recommended hygienic measures to protect both patients and healthcare professionals. Nutritional follow-up has been planned by regular telephone counseling and laboratory exams have been checked by email.

Conclusions: Implementing appropriate nutritional care in oncology during this unprecedented emergency is a hard challenge. However, any effort should be done to guarantee, along with active treatment, adequate nutritional support to cancer patients, in order to prevent the deleterious consequences of malnutrition on clinical outcomes and quality of life.

S15

HIGH UTILITY OF EARLY SUPPORTIVE CARE: PREVENTION OF COMPLICATIONS AND IMPROVEMENT OF THE QUALITY OF LIFE IN CANCER PATIENTS IN COVID 19 ERA

Parascandolo I.[1], Russo P.[2], Simioli R.[3], Franzese E.[3], Nuzzolillo L.[4], Facciuti P.[5]

[1]Asl Napoli, Napoli; [2]Asl Napoli 2 Nord IOC Oncologia, Napoli; [3]Asl Napoli 2 Nord, Napoli; [4]Asl Caserta, Napoli; [5]Asl Napoli 3 Sud, Napoli

Background: Early palliative care management in advanced cancer patients have been evaluated in numerous studies worldwide. We have monitored 127 cancer patients followed at home and we have collected information on the importance of the early management of supportive / palliative care together with anticancer therapy to prevent complications such as cachexia, hyperalgesia, constipation, insomnia.

Methods: On their first visit, patients were subjected to evaluation with ESAS Pall Score for a quantification of QOL and KarnofskyPS. At the end of January 2020, due to the Pandemic disease from Sars Cov 2, patients were monitored in a protected path in order to avoid hospitalizations from Covid19 (interstitial pneumonia and multiorgan syndrome).

Results: 127 patients we followed in 6 months with fortnightly visits, 19 of whom died from disease progression. The 108 patients on therapy were divided into two groups in relation to the Karnofsky PS: the first group with patients with a KPS> 50 and the second group with patients with a KPS <50. Early supportive therapies were activated in both groups: nutritional support has been applied with ONS in 43 patients. 11 patients used the gastric nasal tube for feeding. 32 had no nutritional support needs. The others received parenteral nutrition through a central venous catheter, with lipid bags. We measured oncological pain with NRS in all visits, in order to manage it, and we administered analgesic therapy to patients, using different therapeutic strategies. Dysphagic patients used transdermal fentanyl patch and nasal fentanyl spray to relief BTCP. Non-dysphagic patients used oxycodone / naloxone or tapentadol titrated in oral morphine, to control neuropathic / nociceptive / mixed pain in basic therapy and ROOs to relief the BTCP, measured with the algorithm. In a subset of 21 patients, pregabalin was added in the evening with a single dose, in order to improve sleep quality. Control of opioid constipation was achieved by using oral tablet naloxegol.

Conclusions: The parameters measured through validated assessments (ESAS) to evaluate QOL and KPS have shown that early management of supportive / palliative care improves pain, nutrition, depression, sleep / wake rhythm and QOL independently of the basic Karnofsky Performance Status.

S16

HAVE WE CHANGED OUR WORK DURING COVID19 PANDEMIC?

Bagassi A.[1], Antoniazzi F.[2], Ghelfi S.[1], Geronimi C.[1], De Carlo A.[1], Pedrotti C.[2], Maiolani M.[3], Cubeddu A.[3], Caponigro G.[3], Deligiannis P.[3], Fusco O.[3], Pastorini A.[3], Fregoni V.[4], Cantini S.[3], Menatti E.[3], Bertolini A.[3]

[1]ASST della Valtellina e Alto Lario-Cure Palliative, Morbegno; [2]ASST della Valtellina e Alto Lario-Cure Palliative, Sondalo; [3]ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio; [4]ASST della Valtellina e Alto Lario-Breast Unit, Sondalo

Background: Pain is one of the most debilitating symptoms in oncological diagnosis, and is present in most cancer patient (in the literature range 20 to 95%).

Cancer pain is a chronic pain with multifactorial pathogenesis with which intense episodic transient acute pain can coexist (Btcp).

Hence the need to assess / correctly measure pain to set an appropriate drug therapy (treatment based on the "three steps of pain" -OMS 1986-) and it is possible to have a more objective evaluation of the results of the established analgesic therapy.

During the emergency period, outpatient visits were reduced both in terms of organization and frequency and the reduction in the number of doctors available and the limitations of patient access to hospital clinics for their protection led to a new approach to taking load.

Material (patients) and methods: Experience of our center, from 1 March 2020 to 31 May 2020, during the covid 19 emergency compared with the pre-covid period from 1 November 2019 to 31 January 2020 regarding the evaluation of pain, the need to set specific analgesic therapy, the need to modify this therapy in the course of time (switching between opioids or association between opioids of two different classes) and the need to add adjuvant drugs.

Results: During this time we followed 15 patients versus 17 patients in pre-covid period. Pain was measured in all the first evaluation (using one-dimensional measurement scales - numerical scale -), in 90% of cases this was done by telephone (versus 0% pre covid). Furthermore, the cargiver's telephone involvement was necessary, especially in monitoring over time to evaluate pain control, Btcp episodes and side effects (in the pre-covid period it was the patient who exposed these data during the visit). On the other hand, as regards the specific analgesic therapy set, the need to rotate the opioids or to associate two opioids of different classes, the prescription of the rescue dose and the adjuvant drugs, there were no differences compared to the pre-emergency period.

Conclusions: During the emergency period, in consideration of the high frequency of pain and the impact on the patient's quality of life, it was necessary to modify our approach to manage the patient with cancer, make a correct assessment (repeated over time) and set up an effective analgesic therapy.

T - Miscellanea

T01

PRELIMINARY RESULTS FROM THE RATIONAL STUDY, THE ITALIAN REGISTRY OF ACTIONABLE MUTATIONS

Esposito Abate R.[1], De Luca A.[1], Novello S.[2], Curigliano G.[3], Marchetti P.[4], Fasola G.[5], Conte P.[6], Milella M.[7], Pruneri G.[8], Frassineti G.L.[9], Cremolini C.[10], Gridelli C.[11], Feroce F.[1], Morabito A.[1], Pinto C.[12], Normanno N.[1]

[1]Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale, Napoli; [2]Università degli Studi di Torino, Torino; [3]Istituto Europeo di Oncologia, Milano; [4]Ospedale Sant'Andrea, Roma; [5]Ospedale Universitario di Udine, Udine; [6]Istituto Oncologico Veneto, Padova; [7]Azienda Ospedaliera Universitaria Integrata di Verona, Verona; [8]Istituto Nazionale dei Tumori di Milano, Milano; [9]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola; [10]Azienda Ospedaliero-Universitaria Pisana, Pisa; [11]Ospedale S.G. Moscati, Avellino; [12]Azienda Unità Sanitaria Locale – IRCCS, Reggio Emilia

Background: Registers of next-generation sequencing (NGS)-based tumor profiling data might facilitate the identification of subgroups of patients carrying actionable genomic alterations who may benefit of molecularly targeted treatments. This approach might be particularly relevant in specific subgroups such as patients with cancers of unknown primary (CUP).

Material (patients) and Methods: The RATIONAL study is a multicenter, observational and prospective clinical trial that involves 41 centers in Italy. The primary objective is the description of the frequency of actionable mutations in patients with advanced disease. The study enrolls either patients who already received a NGS-based profiling of the tumor (*Pathway A*) or patients without NGS-based tumor profiling (*Pathway B*). In the latter case, tissue testing is performed with the FoundationOne CDx assay that identifies genetic alterations in 324 genes, as well as the tumor mutational burden (TMB).

Results: To date, thirty-two centers are active and 337 patients have been enrolled. Sequencing data are available for 240 patients. The most frequent tumor type is lung cancer (n. 130; 54% of cases), followed by tumors of the biliary tract (n.49; 20%), CUP (n.26; 11%), colorectal cancer (n.24; 10%), and other tumor types (5%, n. 2 pancreatic cancers, n.2 thyroid cancers, n. 2 sarcomas, n.1 breast cancer n.1 bladder cancer, n.1 adrenal gland cancer, n.1 ovary cancer and n.1 melanoma). In 228 successfully sequenced patients, 867 genetic alterations in 194 genes were identified. The most frequently altered gene was *TP53* (47% of cases), followed by *KRAS* (31%), *EGFR* (16%), *PIK3CA* (10%), STK11 (9%) and *APC* (8%). In 22 patients with CUP, 84 genetic alterations in 56 genes were observed. The most frequent actionable mutations that might influence treatment decisions, including potential enrollment into clinical trials, were observed in *STK11, KRAS, PI3KCA, ERBB2, PTEN, ATM,* and *BRAF* genes. For

18/22 patients with CUP, TMB analysis was available, with values ranging from 0 to 24 mut/Mb (mean of 6.27 mut/Mb; median 5.0 mut/Mb).

Conclusions: The creation of a national registry of genomic data of cancer patients will help the clustering of patients based on their molecular profile, regardless of the relatively low frequency of many genetic alterations, and will favor the progress of tumor-agnostic therapeutic approaches.

T02

LIFESTYLE CHANGES IN BREAST AND COLORECTAL CANCER SURVIVORS: RESULTS FROM FUCSAM PROJECT

Mistrangelo M.[1], Bertetto O.[1], Barè C.[1], Barone C.[1], Beano A.[1], Bonomi A.[1], Camussi E.[2], Ciccone G.[2], Gambaro G.[1], Miraglia S.[1], Pacquola M.G.[1], Piccinelli C.[2], Romaniello I.[1], Sarli F.[1], Senore C.[2], Zunino S.[1], Giordano L.[2]

[1]Dipartimento Rete Oncologica Piemonte e Valle d'Aosta - AOU Città della Salute e della Scienza, Torino; [2]AOU Città della Salute e della Scienza - CRPT Piemonte, Torino

Background: Lifestyles can improve quality of life and survival in cancer survivors. FUCSAM project assess the impact of preventive interventions (diet, physical activity or both) after treatment for colorectal (CRC) or breast cancer (BC).

Methods: Patients with diagnosis of BC or CRC, at first follow-up after surgery and medical therapy, free of disease, were enrolled. Information leaflets and advices of lifestyle programs were delivered. Each follow-up (for 3 years) the following data were collected: co-morbidities, weight, waist circumference, biological parameters,adherence toprograms, and lifestyles. A lifestyle score was built, assigning 1 point for improvement, -1 for worsening and 0 for stability. Pre-/post- analyses were conducted with McNemar test and, for continuous variables, with a Wilcoxon test. Crude and adjusted ORs were computed, accounting for age, sex and cancer diagnosis.

Results: Participants were 1,847 (311 CRC, 1536 BC), 90.7% female, mean age: 60.2 ± 11.2, and 39% were screen-detected cancers. Most cancers were in stage 1 (49.9%) or 2 (34.1%) at diagnosis, with a majority of early lesions for screen-detected cancers (p<0.001). 99.2% of participants received informative materials and 79.0% suggestions of lifestyle interventions. At 6 months, overweight-obese participants decreased (52.8% to 50%; p<0.001). This outcome was maintained at second FU (1 year) (p<0.001). At 6-month, an improvement was seen in waist circumference (overweight from 74.8% to 72.2; p<0.006), and metabolic syndrome (from 45.8% to 41.1%; p<0.001). Favorable anthropometric outcomes were especially evident in women and participants adherent to the program. An improvement was seen at 6 months for

glycaemia (p<0.001) and triglycerides (p<0.001), both maintained at second FU (p=0.016 and p<0.001). At 6-month,46.2% of participants declared an increase in physical activity, over 80.0% reduced the use of processed and red, while 60.5% increased the intake of legumes and 43.7% of whole cereals. Higher diet scoring associated to improvements in BMI (OR 1.20; 1.02-1.41) and waist circumference (OR 1.32; 1.11-1.56).

Conclusions: At follow-ups, results show improvements in diet, physical activity and anthropometric parameters. These results are encouraging, but need further assessment for long-term maintenance. The Oncology Network of Piemonte and Valle d'Aosta will plan to provide a practical guidance to be included in oncology treatment paths.

T03

CONTRASTING FAKE NEWS IN ONCOLOGY: THE FIRST DECLARATION OF GOOD COMMUNICATION

Caporossi M.[1], Papa R.[2], Scandali V.M.[2], Torniai M.[3], Blasi M.[4], Brusa A.[5], Elisei F.[6], Gregori G.L.[7], Laurenzi G.[8], Marinelli L.[7], Marinelli M.[9], Mazzoli G.[10], Volpini F.[11], Berardi R.[12]

[1]General Director – AOU Ospedali Riuniti di Ancona, Via Conca 71, 60126 Ancona, Italy, Ancona; [2]Healthcare Medical Direction, AOU Ospedali Riuniti di Ancona, Ancona; [3]Oncology Clinic, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Ancona; [4]Chief Editor RAI TGR Marche, Ancona; [5]Il Resto del Carlino, Ancona; [6]President of Order of Journalists – Regione Marche, Ancona; [7]Department of management, Università Politecnica delle Marche, Ancona; [8]Deputy Director of "Il Messaggero" and Director of "Corriere Adriatico", Ancona; [9]Primary Care Physician, Bioethicist and Professor of Narrative Medicine, Ancona; [10]Università degli studi di Urbino Carlo Bo, Urbino; [11]President of IV Commissione Salute Regione Marche and Primary Care Physician, Ancona; [12]Oncology Clinic, Università Politecnica delle Marche, AOU Ospedali Riuniti di Ancona, Via Conca 71, 60126 Ancona, Italy, Ancona

Background: In the ongoing fight against diseases, healthcare professionals ought to make use of any weapon, together with the fundamental role of scientific research. Nowadays, websites, online journals and social media give access to an extraordinary amount of medical information; moreover, many patients and their families employ media searching for additional clarifications about their own malignancies and the prescribed treatments. Even on officially supported websites, misleading news might be disseminated generating false expectations, exaggerated anxiety and confusion. In oncology setting, disinformation is perhaps more deleterious than in other fields, with a considerable impact on single patients and, more in general, on Public Health.

Materials and Methods: In order to promote the best interaction between the world of health and the world of communication, a table of experts was established with the aim to draft a shared document identifying strategies to overcome barriers between communication and healthcare as well as to propose common criteria for an effective dissemination of medical information. On the basis of the "consensus conference" method in the RAND/UCLA variant (a modified version of Delphi methodology), a literature research has been conducted with the aim to select studies related to the best practices applied to health journalism regarding oncology setting.

Results: Sixteen articles met the inclusion criteria, from which 72 recommendations were extracted and submitted to experts in communication and healthcare professionals included in the technical table. After panel evaluation, 57 recommendations scored more than 7 representing the selected statements shared together by communication experts and healthcare professionals.

Conclusions: This consensus and the drawn up shared document represent a concrete attempt to found a renewed and strategic alliance between healthcare and communication operators in order to produce useful and reproducible indications for an effective dissemination of medical information. As the "American Declaration of Independence", our "Declaration of Good Communication" has identified high-impact recommendations for the best management of patients, providing simple but fundamental concepts and recommendations about effective communication, especially in oncology setting.

T04

FUNCTIONAL INACTIVATION OF E-CADHERIN BY TROP-2 DRIVES CANCER METASTASIS

Alberti S.[1], Guerra E.[2], Lattanzio R.[2], Ceci M.[2], Boujnah K.[1], Briguori S.[1], Garbo V.[1], Moschella A.[1], Altomare D.[3], Depalo R.[3], Rotelli M.T.[3], Picciariello A.[3], Trerotola M.[2]

[1]Università di Messina, Messina; [2]Università di Chieti, Chieti; [3]Università di Bari, Bari

Background: Tumor metastasis is the main cause of death of cancer patients and the biggest hurdle for cancer cure. The identification of decisive drivers of metastasis and that of pivotal therapy targets is thus an urgent need.

Material (patients) and methods: Immunofluorescence confocal microscopy and flow cytometry analysis were utilized to quantify expression of target proteins, IHC analysis quantified the expression of target molecules in primary tumors and metastases. Cell-cell adhesion capacity was explored in vitro and in cancer cell spheroid models. Pre-clinical models of orthotopic growth of colon cancer and metastatic diffusion to the liver were utilized. Xenotransplant transcriptome analysis assessed EMT determinant transcription. Patients: 24 distinct case series of breast, colon, uterus, ovary, stomach, lung, and pancreatic cancers, for a total number of 13,042 primary tumors were analyzed. Kaplan–Meier plots were used to illustrate survival and metastatic relapse in investigated cohorts.

Results: We identify functional inactivation E-cadherin, as directed by Trop-2, as a pivotal driver of metastatic diffusion in human cancer. Binding to Trop-2 causes release of E-cadherin from the cytoskeleton, loss of cell-cell adhesion and activation of β-catenin. This leads to increased cell migration and enhanced cancer cell survival. This global, Trop-2/E-cadherin/β-catenin-driven pro-metastatic program was recapitulated in human cancer, and was shown to profoundly impact on breast, colon, uterus, ovary, stomach, lung, pancreas cancer metastatic diffusion.

Conclusions: We identify Trop-2-driven functional inactivation of E-cadherin as a shared driver of metastatic diffusion in human cancer. A Trop-2/E-cadherin/b-catenin–led pro-metastatic program was shown to profoundly impact on the survival of patients bearing breast, colon, uterus, ovary, stomach, lung, pancreas tumours, opening novel avenues for personalized diagnostic procedures and anti-cancer therapies.

T05

THROMBOEMBOLIC EVENTS IN CANCER PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS: DATA FROM RETROSPECTIVE AND PROSPECTIVE STUDIES

Solinas C.[1], Saba L.[2], Sganzerla P.[3], Petrelli F.[4]

[1]Oncology Department, ATS Sardegna, Ozieri; [2]Department of Radiology, University of Cagliari, Monserrato; [3]Cardiology Unit, ASST Bergamo Ovest, Treviglio (BG); [4]Oncology Unit, ASST Bergamo Ovest, Treviglio (BG)

Background: The overall risk of thromboembolism (either venous and arterial) has not yet been estimated in cancer patients treated with immune checkpoint inhibitors (ICIs). We conduced a systematic review to evaluate the incidence of venous and arterial thromboembolic events (VTEs and ATEs) in patients treated with ICIs, as single agents or in combination with other treatments.

Patients and Methods: Retrospective and prospective studies (identified from Pubmed, EMBASE, SCOPUS and The Cochrane Library) reporting on the frequence of VTEs or ATEs were eligible for this study, if they provided the number (or rate) of events and the size of the population included. Efficacy results had to be published in English in peer-reviewed journals or presented in proffered paper sessions of major annual meetings. PRISMA guidelines were followed. Data extraction was performed by two independent investigators (CS and FP), and discordant evaluations were discussed with a third independent observer (LS). The outcome data extracted for each arm were analyzed using random-effects models and were reported as weighted measures.

Results: 20,273 patients from 68 studies were included in the present analysis. VTEs equaled to N=390, whereas ATEs to N=59, with incidence rates (representing the pre-planned primary study outcome) of 2.7% (95%CI 1.8-4%)

and 1.1% (95%CI 0.5-2.1%), respectively. Most ot these events were associated with treatment with anti-PD-1 or anti-PD-L1 agents. When ICIs were used as single agents the incidence of VTEs was 2.3% (95%CI 1.3-4%). The rate of pulmonary embolism was 1.6% (95%CI 0.7-3.2%) whereas that of deep venous thrombosis was 2.7% (95%CI 1.4-5.4%). Rates of stroke and myocardial infarction were 1.1% and 0.7%, respectively, whereas fatalities due to VTEs and ATEs equaled to 0.02% and 0.1%, respectively.

Conclusions: ICIs-associated VTEs and ATEs were detected and not-negligible, particularly in patients with advanced solid tumors. Future research should address their prospective assessment, the evaluation of risk factors and their prevention.

T06

HPV INFECTION AS THE INTERPRETATION KEY TO UNDERSTAND THE PROGNOSTIC ROLE OF EOSINOPHILS IN ANAL SQUAMOUS CELL CANCER AND HEAD AND NECK CANCER

Rimini M.[1], Franco P.[2], De Bari B.[3], Andrikou K.[4], Napolitano M.[1], Zampino M.G.[5], Vagge S.[6], Laffi A.[5], Bacigalupo A.[6], Gervaso L.[5], Tramontano D.[7], Bertolini F.[1], Cascinu S.[8], Casadei A.[1]

[1]Dipartimento di Oncologia - Ospedale Policlinico di Modena, Modena; [2]Dipartimento di Radioterapia - Università di Torino, Torino; [3]Dipartimenti di Radioterapia - CHRU Besancon, Besancon; [4]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCSS, Meldola; [5]Oncologia Medica Gastrointestinale e Tumori Neuroendocrini - Istituto Europeo di Oncologia, Milano; [6]Radioterapia Oncologica - Ospedale San Martino, Genova; [7]Health Science Department (DISSAL), Genova; [8]IRCSS Ospedale San Raffaele, Milano

Background: Anal SCC is a rare tumor associated with the HPV infection. The gold standard is represented by the CT-RT according to the Nigro scheme, but adequate bioumoral predictors of response are lacking. In order to find new biomarkers, and to deepen the significance of the HPV infection, we investigated the role of peripheral eosinophil count in both anal SCCs and HNCs.

Methods: We retrieved clinical and laboratory data regarding patients affected by anal SCCs treated with concomitant CT-RT according the Nigro scheme from 5 oncologic institutions. In parallel, we retrieved clinical and laboratory data regarding patients affected by HNCs with a confirmed diagnosis of SCC and treated with concomitant CT-RT from 2 oncologic institutions. We examined the association between baseline eosinophil count and DFS in both the group of patients. We performed ROC-curve analysis to define the best eosinophil cut-off for our analysis (100 10^9/L). Unadjusted and adjusted hazard ratios by baseline characteristics were calculated using the Cox proportional hazards model.

Results: 304 consecutive patients with anal SCCs and 168 patients with HNCs, 122 (72.6%) HPV-positive and 46

(27.4%) HPV-negative, were analyzed. In the anal SCC setting, patients with low eosinophil count (<100 10^9/L) had a better DFS; at the multivariate analysis eosinophils showed to be independent prognostic factors for DFS (HR=0.59; 95%CI: 0.36-0.97; p= 0.0392). In HPV-positive HNC patients low eosinophil count showed to be related to a better DFS at univariate analysis, with no confirmation at multivariate. HPV-negative HNC patients with low eosinophil count had a worse DFS respect patients with high eosinophil count (> 100 10^9), ad after adjustment for age and sex, eosinophils have been confirmed as independent prognostic factors for DFS (HR=4.55; 95%CI: 1.36-15.22; p= 0.0139).

Conclusions: Peripheral eosinophil count could be used as predictor of response to CT-RT in HPV-positive anal SCCs. The worse prognosis showed in HPV-positive patients with high eosinophil count is likely to derive from the immunomodulation induced by both HPV and eosinophils, which frustrate the RT benefic effects.

T07

RELEVANCE OF PHARMACOGENETIC VARIANT IN DPYD AND MTHFR GENES FOR FLUOROPYRIMIDINE BASED-CHEMOTHERAPY

Cafiero C.[1], Cito P.[2], Friscini A.[3], Luccarelli G.[3], Brunetti C.[4], Modoni G.[3], Russo F.[3], Fanelli F.[3], Nenna C.[3], D'Alessandro A.R.[3], Pastore C.[3], Galeano T.[3], Broussard C.[3], Nisi C.[3], Bruno M.[3], Brunetti A.E.[5], Lazzari G.[6], Silvano G.[6], Vinci M.V.[7], Pisconti S.[3]

[1]*Struttura Complessa di Oncoematologia ASL TA, Ospedale S.G. Moscati, Taranto;* [2]*Struttura Semplice Terapie Oncologiche ASL TA, Ospedale San Pio, Castellaneta (TA);* [3]*Struttura Complessa di Oncologia ASL TA, Ospedale S.G. Moscati, Taranto;* [4]*Struttura Complessa di Oncologia ASL TA, Ospedale Polo Orientale, Manduria;* [5]*Struttura Semplice di Terapie Oncologiche ASL TA, Ospedale San Pio, Castellaneta (TA);* [6]*Struttura Complessa di Radioterapia Oncologica ASL TA, Ospedale S.G. Moscati, Taranto;* [7]*Direzione Medica ASL TA, Ospedale S.G. Moscati, Taranto*

Background: Fluoropyrimidine (5-FU) drugs are extensively used for the treatment of solid cancers. The major targets of 5-FU are folate-metabolizing enzymes and methylenetetrahydrofolate reductase genes, one of more commonly known MTHFR (methylenetetrahydrofolate reductase). Deleterious polymorphisms in some genes may result in that causes life-threatening toxicities when the standard dose of fluorouracil is used. Adverse drug reactions are a major clinical problem, often necessitating dose reduction and treatment discontinuation. Diarrhoea, mucositis, myelosuppression and hand–foot syndrome are the most frequent and troublesome side effects. Currently available pharmacogenetic guidelines suggests in the pre-treatment of Fluoropyrimidine drugs the diagnostic test of five DPYD genetic polymorphisms c.1905+1 G>A rs3918290, c.1679 T>G (rs55886062), c.2846 A>T (rs67376798), c.1236 G>A (rs56038477), c.2194 G>A (rs1801160). Current evidences of pharmacogenomics report the association of

Fluoropyrimidine drugs with toxicity (P<0.0001) of MTHFR c.1298GG homozygous genotype.

Methods: A cohort of 50 patients (30M/20F; age range 50-70) admitted to the " S.G. Moscati Hospital" (January - April 2020) candidates for Fluoropyrimidine treatment are tested by molecular analysis for five DPYD genetic polymorphisms and for MTHFR C677T (rs1801133) and MTHFR A1298C (rs1801131) polymorphisms.

Results: Genotyping analysis of DPYD and MTHFR genes polymorphism revealed the presence of one heterozygous mutation in DPYD gene in 35% of our patient and MTHFR c.1298CC homozygous genotype in 60% of our patients. The presence of a variant in both genes occurred in 20% of patients.

Conclusions: To date the oncologists have new means based on the individual genetic composition, to make treatment decisions maximizing benefits and minimizing toxicity. Based on these purpose, clinician and lab manager may join to evaluate advantages and limitations (costs and applicability) of the most appropriate methods to set up the best molecular diagnostic pharmacogenetic tests for 5-FU drugs. The finding of our study confirms that MTHFR c.C1298T polymorphisms should be incorporated Into clinical practice to enable a better individualization of optimized therapy.

T08

THERAPEUTIC STRATEGIES IN PATIENTS WITH BREAST OR OVARIAN BRCA1/2 MUTATED CANCERS: ROLE OF PARP-INHIBITORS AND INDIRECT COMPARISON WITH PLATINUM. A SYSTEMATIC REVIEW AND META-ANALYSIS

Staropoli N.[1], Ciliberto D.[1], Labanca C.[1], Siciliano M.A.[1], Cucè M.[1], Arbitrio M.[2], Luciano F.[1], Federico S.[1], Salvino A.[1], Barbieri V.[1], Tassone P.[3], Tagliaferri P.[4]

[1]*Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro, Italy, Catanzaro;* [2]*CNR-Institute for Biomedical Research and Innovation, 88100 Catanzaro, Italy, Catanzaro;* [3]*Translational Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro;* [4]*Medical Oncology Unit Department of Experimental and Clinical Medicine, Magna Græcia University and Cancer Center, Campus Salvatore Venuta, Catanzaro*

Background: Poly (ADP-ribose) polymerase inhibitors (PARPis) take advantage from defects in Homologous Recombination (HR) pathways induced by germline BRCA mutations through synthetic lethality. Several trials showed anticancer activity in this selected population. About 25% of hereditary breast cancers and 10% of ovarian cancers are related to BRCA-1/2 mutations. Olaparib and Talazoparib have been recently approved as monotherapy in HER-2 negative metastatic breast cancer (MBC). About 40% of

platinum-sensitive Epithelial Ovarian Cancer (EOC) patients carry a germline/somatic BRCA1/2 mutation and PARPis produced a significant improvement in long-term disease control. Olaparib, Rucaparib and Niraparib represent a choice for these patients. The aim of this study is to ievaluate the role of these agents in BRCA1/2-mutated breast cancer and BRCA1/2-mutated EOC, determining the improvement in Survival (PFS).

Patients and Methods: A systematic literature review of Pubmed and abstracts from major oncological meetings was carried out including all published prospective and randomized controlled trials (RCTs) using pairwise comparisons designed on BRCA-mutated respectively in MBC and EOC in all lines of treatment. Meta-analyses were conducted by random effect model. For HER-2 negative MBC the primary endpoint was PFS. For EOC we updated a previous meta-analysis published on 2018 which was empowered by a Bayesian approach.

Results: Regarding MBC, 10 RCTs for a total of 3127 patients were selected and included in the final analysis. We reported a trend of benefit for PARPis in terms of Overall Survival (OS) (HR 0.86; IC 0.73-1.01) and a significant PFS benefit (HR 0.64; IC 0.55-0.75). About EOC, 10 RCTs for a total of 4342 patients were selected and included in the final analysis. In terms of PFS, we performed an indirect comparison. On these bases it is possible to infer that the concomitant and sequential combination of CT with PARPis was the best therapeutic strategy. Toxicity analysis showed significant differences among different PARPis, confirming that the class effect only regarded the efficacy endpoints.

Conclusions: We highlighted a trend of benefit in survival endpoints in MBC. A longer follow-up and a better selection of patients are clearly required. Concerning the EOC-analysis section we confirmed the role of PARPis in this scenario, hypothesizing that the better performance remains as sequence to chemotherapy. By the Bayesian analysis we confirmed the "class-effect" of these agents, too.

T09

SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) TO PREDICT TAXANES TOXICITIES AND EFFECTIVENESS IN CANCER PATIENTS

Demurtas S.[1], Cheli S.[2], Cona M.S.[1], Dalu D.[1], Filipazzi V.[1], Fasola C.[1], Rota S.[1], Ferrario S.[1], Montrasio C.[2], Gambaro A.[1], Tosca N.[1], La Verde N.[1], Clementi E.[3]

[1]Department of Oncology, Luigi Sacco Hospital, ASST - Fatebenefratelli - Sacco, Milano; [2]Unit of Clinical Pharmacology Luigi Sacco Hospital, ASST Fatebenefratelli Sacco, Milano; [3]Unit of Clinical Pharmacology, Department of Biomedical and Clinical Sciences, National Research Council-Institute of Neuroscience, University Hospital L. Sacco, University of Milano, Milan, Italy, Milano

Background: Taxanes are used in the treatment of several solid tumors. Adverse events (AEs) might be influenced by SNPs in genes encoding proteins responsible for pharmacokinetic and pharmacodynamic. This prospective, monocentric, observational study aims to explore the effect of known SNPs in the main genes involved in taxanes metabolism and transport, on toxicity and efficacy.

Material and methods: Patients (pts) treated with paclitaxel, docetaxel or nab-paclitaxel were enrolled at the Department of Oncology of Luigi Sacco Hospital in Milan. For each patient a blood sample was collected for DNA extraction. DNA were genotyped by RT-PCR to detect c.1236C>T, c.2677G>T/A, c.3435C>T SNPs in *ABCB1* and CYP3A4*22, CYP3A5*3, CYP2C8*3, CYP2C8*4 SNPs in corresponding genes. AEs were evaluated according to CTCAE v5.0 and efficacy according to RECIST.

Results: 125 pts were enrolled. Grade 2-4 AEs: 47.2% hematological, 24% neurological, 24.2% gastrointestinal, 10% mucositis, 7.5% nail changes, 3.3% skin reactions, 3.3% hepatic, 10.5% infusion related reaction.

For CYP SNPs: 12% of pts were heterozygous (het) for CYP3A4*22; 8.8% het for CYP3A5*3; 23.2% het and 1.6% homozygous (hom) for CYP2C8*3; 5.6% het for CYP2C8*4. For the *ABCB1* SNPs, c.1236C>T het in 53.6% and hom in 18.4% of pts; c.2677G>T/A het in 56% and hom in 19.2%. c.3435C>T het in 48.8% and hom in 24%. There was no statistically significant association between the investigated SNPs and AEs.

The het genotype of CYP3A4*22 showed an association with skin reactions in pts treated with paclitaxel and nab-paclitaxel, although without statistical significance (RR=6.92;95%CI0.47,99.8; *p*=0.076). CYP2C8*3/*4 variant carriers showed an association, though not statistically significant, with overall AEs in pts treated with paclitaxel and nab-paclitaxel (RR=1.28;95%CI0.96,1.67; *p*=0.089). There wasn't any statistically significant relationship with treatment efficacy but there was a trend for *ABCB1* 3435TT genotype and a higher treatment response (*p*=0.153).

Conclusions: The study suggested that CYP3A4*22 and CYP2C8 SNPs may influence paclitaxel and nab-paclitaxel toxicity, even if it didn't find any statistically significant association between SNPs and taxanes-induced AEs or efficacy. The increase of sample size could help to achieve statistical significance; the population was heterogeneous, but this reflects clinical practice and the aim of pharmacogenetic studies is to translate laboratory findings into clinical care.

T10

THE IMPACT OF DRUGS MODULATING MICROBIOTA ON THE OUTCOME OF ADVANCED CANCER PATIENTS TREATED WITH IMMUNE CHECKPOINT INHIBITORS. A NEW PROGNOSTIC "DRUG SCORE"

Perrone F.[1], Bersanelli M.[1], Cortellini A.[2], Casartelli C.[1], Bordi P.[1], Tiseo M.[1], Buti S.[1]

¹University Hospital of Parma, Parma; ²St. Salvatore Hospital, L'Aquila

Background: Immune checkpoints inhibitors (ICIs) alone or in combination with chemotherapy are the new standard of treatment in several solid tumors. The different impact of single concomitant drugs administration on the outcome of patients to immunotherapy is already known.

The aim of our study was to evaluate the prognostic value of a "drug score" (DS), including three class of drugs able to modulate the microbiota, in metastatic cancer patients treated with ICIs.

Material and methods: We retrospectively enrolled advanced cancer patients consecutively treated with ICI at our center between October 2013 and October 2018, correlating the DS with overall survival (OS, primary endpoint) and progression-free-survival (PFS, secondary endpoint).

Results: 219 patients were enrolled. Median age was 69 years (32-89). Primary tumors were: non-small cell lung cancer (NSCLC, 69.9%), melanoma (15.1%), renal cell carcinoma (9.1%), other cancers (5.9%). Median follow-up was 21.3 months. 12.3% and 33.8% of patients received antibiotic and corticosteroid therapy within 30 days before first ICI administration, respectively; 47.9% of patients underwent treatment with pump protonic inhibitors (PPIs). The use of PPIs, corticosteroids or antibiotics was individually associated to decreased OS and PFS at the univariate analysis. Therefore, we developed a "drug score" including these three drugs. 37.9% of patients did not receive any drug (DS 0), 35.2% received only one drug (DS 1) and 26.9% received two/three drugs (DS 2). Both OS and PFS were significantly impacted by the DS: median OS was 19.4 months in DS 0 *vs*9.5 months in DS 1 *vs*2.7 months in DS 2 ($p < 0.001$), median PFS was 6.8 months in DS 0 *vs*3.7 months in DS 1 vs 1.6 in DS 2 ($p < 0.001$). The multivariate analysis, including known prognostic factors as ECOG performance status, comorbidities and sites of disease, confirmed the independent prognostic role of the DS both for OS [HR 1.48 (95%CI 1.17-1.88), *p*= 0.001] and PFS [HR 1.44 (95%CI 1.15-1.81), *p*= 0.001].

Conclusions: Our results confirmed the negative prognostic role of PPIs, corticosteroids and antibiotics either as single agents and included in the DS, probably due to the impact of these drugs on gut and lung microbiota [Chalabi, *Ann Oncol* 2020; Arbour, *J Clin Oncol* 2018]. DS will be validated in an extended multicenter retrospective cohort including patients with metastatic NSCLC treated with ICI.

T11

THE ROYAL MARSDEN HOSPITAL (RMH) SCORE AND PRINCESS MARGARET HOSPITAL INDEX (PMHI) AS PROGNOSTIC FACTOR FOR PATIENTS (PTS) WITH ADVANCED SOLID TUMORS ENROLLED IN PHASE I TRIALS (PIT): THE MODENA CANCER CENTER (MCC) EXPERIENCE

Schipilliti F.¹, Fontana A.¹, Pettorelli E.², Migali P.¹, De Pierri Rizzello F.¹, Folloni S.¹, Canino F.¹, Isca C.¹, Omarini C.¹, Dominici M.³, Maur M.¹

¹Oncology Unit, Oncology and Haematology Department, University Hospital of Modena, Italy, Modena; ²Department of Medical and Surgical Sciences for Children and Adults, Division of Oncology, University Hospital of Modena, Modena; ³Department of Medical and Surgical Sciences for Children and Adults, Division of Oncology, University Hospital of Modena, Italy, Modena

Background: The patient selection in PIT represent a significant challenge. The RMH and PMH were developed for the purpose of a better selection for PIT. RMH is calculated by serum albumin (ALB), lactate dehydrogenase (LDH), and number of metastatic site at diagnosis. PMH instead regard ALB, n° of metastatic site and PS ECOG. The OS and PFS of good RMH / PMH score (0-1) group were significantly longer than those of poor score group (2-3).

Patients and methods: We conducted a retrospective analysis of 104 pts enrolled in PIT at MCC, divided into good and poor score groups according to RMH and PMHI. Comparison of overall survival (OS) and progression free survival (PFS) was performed by Kaplan-Meier curves and log-rank tests.

Results: 104 pts enrolled: 68 with good and 36 with poor RMH score; 71 with good and 33 with poor PMHI. Overall, 68 were female, 73 with ECOG 0, 60 with more than 2 metastatic sites, more than 96% with visceral disease. The primary cancer was: lung 24%, breast 23%, ovarian 12%, 41% had de novo metastatic disease at diagnosis, 41% of pts received more than 2 prior therapies. Phase I treatment was: target and immunotherapy alone or in combination with chemotherapy, cytokine-immunoconjugated mAb. Median time of therapy duration was 20,8 weeks. All but 3 pts discontinued treatment: two-thirds for PD, only 17 for toxicity. Analysis for RMH score: at 90-days from the beginning of PIT-therapy 23 pts died: 39% in Good score group and 61% in Poor score one. Good RMH score group had statistically significant PFS and OS benefit compared to poor score one (mPFS 3 vs 1 month, p = 0,0004, HR 2,68 95%CI 1.55-4.63, and mOS 17 vs 5 months, p= 0,0002, HR 2.72 95%CI 1.60-4.62 respectively). Analysis for PMHI score: among 23 pts died at 90-days from the beginning of PIT-therapy: 35% in Good score group and 65% in Poor score one. Good RMH score group had statistically significant PFS and OS benefit compared to poor score one (mPFS 3 vs 1 month, p = 0,0310, HR 1,77 95%CI 1.05-2.98 and mOS 16 vs 3 months, p= 0,0001, HR 3.05 95%CI 1.72-5,4 respectively).

Conclusions: RMH and PMH Scores clearly select a subgroup of patients who could not benefit from enrollment in phase I clinical trials. Our data confirm those previous published in literature.

T12

DO IRINOTECAN (IRI) DOSE REDUCTIONS DRIVEN BY UGT1A1*28 GENOTYPING PREVENT IRI-RELATED SEVERE NEUTROPENIA? A REAL WORLD STUDY

Personeni N.[1], Mineri R.[2], D'Alessio A.[1], Cammarota A.[1], Michelini A.[3], Bozzarelli S.[1], Smiroldo V.[1], Pressiani T.[1], Giordano L.[4], Sandri M.T.[2], Santoro A.[1], Rimassa L.[1]

[1]*Medical Oncology and Hematology Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center - IRCCS, Rozzano;* [2]*Molecular Biology Section, Clinical Investigation Laboratory, Humanitas Clinical and Research Center - IRCCS, Rozzano;* [3]*Department of Biomedical Sciences, Humanitas University, Pieve Emanuele;* [4]*Biostatistics Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center - IRCCS, Rozzano*

Background: IRI is widely used in the treatment of advanced gastrointestinal cancers. Consistent with current guidelines, UGT1A1 genotyping may drive IRI dose reductions, but the usefulness of this approach, performed in a prospective manner, is still unclear. We assessed the incidence of grade ≥3 neutropenia in patients who undergo IRI-based chemotherapies after upfront genotyping of UGT1A1 polymorphisms.

Methods: We genotyped UGT1A1*28 polymorphisms in 247 patients receiving second or third line IRI-based chemotherapy in clinical practice at a single academic center. Concomitant DPYD sequencing was performed in 179 patients receiving also fluoropyrimidines. Based on the results of the UGT1A1 genotyping, in UGT1A1 6/6 and 6/7 carriers full-dose IRI was delivered, whereas in UGT1A1 7/7 carriers initial IRI dose reductions by at least 30% were done. We compared the incidence of grade ≥3 neutropenia occurring in UGT1A1 6/6 and 6/7 carriers, and in UGT1A1 7/7 carriers.

Results: The incidence of UGT1A1 7/7, 6/7, 6/6 genotypes was 11.3%, 51.4%, and 37.2%, respectively. IRI dose reductions were significantly more frequent with UGT1A 7/7 and 6/7 genotypes (odds ratio [OR] = 9.5; 95% confidence interval [CI]: 4.3-21.7), and combination chemotherapy (OR = 3.8; 95%CI: 1.3 – 11.1). Other clinical parameters, including sex, cancer type, baseline neutrophils levels, baseline bilirubin levels, performance status were not significantly associated with dose reductions. Despite initial IRI reductions, UGT1A1 7/7 genotype was associated to an increased, albeit non-significant, risk of grade ≥3 neutropenia, compared to patients with UGT1A1 6/6 and 6/7 genotypes who received full-dose IRI (incidence: 39% versus 21%; OR = 2.4; 95%CI: 0.85 – 7.03).

Conclusions: UGT1A1 testing is a determinant of IRI dose reductions, however this strategy does not reduce the burden of grade ≥3 neutropenia in UGT1A1 7/7 carriers. Further studies beyond the UGT1A1*28 genotype are needed to fully understand the determinants of severe neutropenia in these patients.

T13

NUTRITIONAL COUNSELING IN ONCOLOGY: WHAT IMPACT? A SINGLE INSTITUTION EXPERIENCE

Carnio S.[1], Capizzi I.[1], Mariniello A.[1], Paratore C.[1], Reale M.L.[1], Rapetti S.G.[1], Artusio E.[1], Olmetto E.[1], Capelletto E.[1], Bertaglia V.[1], Pignataro D.[1], Bironzo P.[1], Passiglia F.[1], Bitossi R.[1], Sperone P.[1], Buttigliero C.[1], Palesandro E.[1], Brizzi M.P.[1], Napoli V.[1], Novello S.[1]

[1]*Department of Oncology,University of Turin, AOU San Luigi, Orbassano (TO), Italy*

Background: Cancer patients (pts) often experience weight loss or even cachexia, in severe cases. Malnutrition can affect quality of life and response to treatment, ultimately leading to poor prognosis.

Methods: A nutrition clinic has been set up in our Department. The intervention included: a malnutrition screening through two validated tests (NRS 2002 and MST), a nutritional counselling for malnourished pts and nutritional care for malnourished or at high-risk pts. Also, a quality of life assessment (through ESAS questionnaire) was administered at each visit.

Results: From February 1th to December 31th 2019, 240 pts (57.9% men) were evaluated. Mean age was 67 years (range: 39-85). Two hundred twenty-six pts (94%) had an ECOG performance status of 0-1 and 156 pts (65%) were stage IV. The most common malignancies were lung (n=137), breast (n=18), esophagus-gastric-pancreatic and biliary tract cancers (n=18). Two hundred and nine pts were on active treatment. At baseline, 81 pts reported nausea (moderate-severe grade in 63 pts) and 123 experienced loss of appetite (severe-moderate in 94 cases). At the first screening, an average weight loss of 3.5% and 5.2% was observed for the previous 3 and 6 months, respectively. Across the two screening tests, the scores diverge when considering patients not at risk, where, in the NRS test, 1 point is given for cancer diagnosis and 1 additional point for pts aged 70 and over. On the other hand, the 2 screening tests seem to be consistent in the identification of pts at high nutritional risk, in both cases about 24%. Oral supplements (ONS) were prescribed in 81 pts (34%). An important reduction in the percentage of pts at high nutritional risk was observed 7 months after the first visit. MST detected no pts at high nutritional risk, while NRS 2002 detected only one case. 83.3% of the study population had an NRS screening score of 1 or 2, suggestive for a low nutritional risk. The mean weight loss after 7 months was 1.7% (a small, non significant loss of weight).

Conclusions: Nutritional counselling should be well-planned starting from the first oncological visit to identify and follow cancer pts at risk of malnutritionand and ultimately improving treatment adherence.

T14

PROGNOSTIC IMPACT OF STEROID USE IN IMMUNOTHERAPY TREATMENT IN A REAL WORLD SETTING

Pugliese G.[1], Baldessari C.[1], Guaitoli G.[1], Greco S.[1], Vitale M.G.[1], Depenni R.[1], Barbieri F.[1], Sabbatini R.[1], Dominici M.[1]

[1]*University Hospital of Modena, Modena*

Background: The landscape of non-small cell lung cancer (NSCLC), melanoma (M), renal cell carcinoma (RCC) and urothelial cancer (UC) has changed with the advent of immunotherapy (IT). IT is generally well tolerated, but adverse events may occur requiring use of steroids.

Patients and Methods: We conducted a retrospective analysis of 391 patients (pts) who received at least 1 dose of IT at AOU Policlinico di Modena. Overall survival (OS) curves were built using the Kaplan-Meier method. Log-rank test was made to compare OS within groups according to steroid use (no or yes for toxicities (tox)/yes for other reasons), high doses of steroid use ($<$15 mg prednisone or equivalent/$>=$ for tox/$>=$ for other reasons) and duration of steroids use (no or $<$1 month/$>=$1 month/continuous).

Results: Our series included 56,8% NSCLC, 29,7% M, 8,7% RCC and 4,8% UC. 29,9% of pts received IT in 1st line. At cut off time (reappraisal time), 325 pts (83,1%) showed disease progression and 247 (63,2%) were dead. Most pts had a good performance status (ECOG 0-1 88,7%) and were male (67,5%). 51,9% of pts had tox of any grade and types. 10% had Grade 3-4 tox. 77 pts used steroids for IT tox, 146 for other reasons, 151 made no use and for 17 data were unavailable. OS according to steroid use in the whole population was significantly longer for pts who never had steroids or used for tox vs others (p$<$0,0001) and this was noted also among cancer types: NSCLC (mOS 15 vs 6,1 months (mo), p$<$0,0001), melanoma (mOS 19,4 vs 3,5 mo, p$<$0,0001) and RCC (mOS 31,1 vs 7,4, p=0,0393). In UC mOS was 13,4 vs 3,3 mo, p=ns, due to small number of pts. OS according to high doses of steroids were 9,6 without high doses vs 23,9 mo for high doses for tox vs 5,7 mo for high doses for other reasons (p$<$0,0018) for NSCLC and 14,7 vs 22,2 vs 3,5 mo, respectively (p$<$0,0001) in melanoma. Regarding OS according to steroid therapy duration: in NSCLC mOS without or with short use was 15,8 vs 10,7 for prolonged use vs 5,6 mo for continuous use, p$<$0,0001 and in melanoma mOS was 14,7 vs 19,3 vs 3 mo, respectively, p=0,001.

Conclusions: Our data confirmed that steroid use, especially for toxicities management and for short cycles, doesn't impact on outcome of pts treated with IT in any lines of therapy. The treatment of toxicities is important for quality of life and must be done without fearing detrimental effect on IT.

T15

PROGNOSTIC VALUE AND SAFETY OF LYMPHOCYTE-TO-MONOCYTE RATIO (LMR) IN IMMUNOTHERAPY IN SOLID TUMOURS

Angelini F.[1], Rossi L.[2], Tomao S.[3], Cimino G.[4], Mannino A.[2], Conte D.[1], Lo Russo V.[1], Gozzi E.[2]

[1]*Ospedale Regina Apostolorum Albano Iaziale, Albano;* [2]*Università la Sapienza di Roma, Aprilia;* [3]*Università la Sapienza di Roma, Roma;* [4]*Università la Sapienza di Roma, Latina*

Background: Lymphocyte-monocyte ratio (LMR) represents a new marker of chronic systemic inflammatory response. Several studies examin the prognostic role of LMR in patients undergoing chemotherapy, while in immunotherapy there is minor evidence. In our study, we aimed to investigate the prognostic value of LMR and its correlation with immunotherapy toxicity in solid tumours.

Patients and methods: We enrolled 93 patients (pts) with advanced solid tumours treated with immunotherapy.
80 pts (86%) had non-small-cell lung carcinoma (NSCLC), 4 (4.3%) had renal cell carcinoma (RCC) and 9 (9.6%) bladder cancer. Mean age was 70 years (range 48-82). Pretreatment LMR was calculated by division of lymphocyte to monocyte measured in peripheral blood. Pts were divided into two groups based on the average LMR value found (LMR$<$ 3.6 and LMR $>$ 3.6). We evaluated response and safety of the treatment in relation to LMR value.

Results: 61/93 pts (65.5%) had low LMR, 32/93 (34.4%) had high LMR. At the fist instrumental evaluation, 37 pts with low LMR had disease progression (PD) (60.8%), while 16 pts stable disease (SD) (26.2%), 7 showed partial response (RP) (11.4%), 1 had complete response (RC) (1.6%), with a clinical benefit (CB) (RC+RP+SD) of 39.3%. Pts with high LMR, 12 had PD (37.5%), 9 SD (28.2%), 11 RP (34.3%), with CB of 62.5%. We examined several immune-related toxicities and for some of these we found differences between the groups examined: low LMR versus (VS) high LMR: Diarrhea/Colitis (21.3% VS 9.3%), Hematological toxicity (24.5% VS 3.1%), Endocrine toxicity (42.6% VS 15.6%), hepatic toxicity (37.7% VS 0), Itching (27.8% VS 9.3%), Nausea and vomiting (21.3% VS 6.2%).

Conclusions: Our results suggest that low pre-treatment LMR is associated with lower response rate and greater incidence of toxicity in patients with advanced solid tumours treated with immunotherapy LMR could be considered prognostic and safety markers.

T16

ONCOLOGY CLINICAL TRIALS MANAGEMENT DURING THE PANDEMIC - THE ITALIAN EXPERIENCE

Cresta S.[1], Franchina V.[2], Maggiora P.[1], Stabile S.[3], Taverniti C.[4], Federici I.[5], Monti M.[6], Guarrera A.[7], Testoni S.[6], Cagnazzo C.[4]

[1]*Ospedale Maggiore della Carità, Novara;* [2]*AOU Papardo, Messina;* [3]*Ospedale Niguarda, Milano;* [4]*AOU Città della Salute e della Scienza, Torino;* [5]*Spedale Riuniti, Ancona;* [6]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola;* [7]*AOU Careggi, Firenze*

Background: COVID-19 pandemic, caused by the new SARS-COV-2 virus, has impacted all Italian healthcare areas, including clinical research. This forced a profound reorganization of experimental sites, including the activities of Clinical Trials Units (CTU). Moreover, in March 2020 the Italian Medicines Agency (AIFA) provided guidance on the management of clinical trials in light of the restrictive measures adopted by the Government against the pandemic.

Methods: We decided to investigate how the Italian CTUs have reorganized and how smart working is considered truly effective during the emergency. In April 2020 all members of Italian Group of Clinical Research Coordinators were invited to complete a web survey, consisted of 21 questions about the reorganization of CTUs and the managements of trials since the start of pandemic.

Results: 142 research professionals completed the survey: 120 Clinical research Coordinators, 21 data managers and 1 biostatistician. Women was 86% (n=122) and the age group 26-35ys was the mainly represented (n=72, 50.7%). A total of 15 on 21 Italian regions were represented with a good national coverage. The majority of respondents (n=121, 85.2%) said that, due to the emergency, their activities were reorganized, mainly through the alternation of smart working and shifts on site (n= 78, 64.5%) or the activation of a totally smart working method (n=33; 27.3%). Within the cohort that had the opportunity to work, partially or totally, from home (n=116, 81.7%), most respondents (n=81, 69.8%) stated they benefited from a high level of accessibility to hospital records, in many cases (n= 41, 50.6%) both patient records and shared document areas. In very few cases, the employer has provided additional tools for staff, such as PCs (n=18, 15.5%) or phones (n=1, 0.9%) company while many respondents (n=57, 49.1%) said they had not even received assistance from their IT service. With regard to the opinion on the effectiveness of the smart working activity, the average score was 6.3 on a scale of about 1 – 10.

Conclusion: Most of the Clinical Trials Units have been reorganized so that deferred activities can be carried out away from the hospital, guaranteeing, on average, wide remote access to the necessary documentation. Certainly, it would be necessary to improve the IT and electronic equipment that employees benefit from so as to optimize all activities and ensure rapid and high quality (performances), even in non-emergency situations.

T17

ESTIMATING A SINGLE-PATIENT REAL WORLD ONCOLOGY WORKLOAD FOR FUTURE SUSTAINABILITY OF CANCER CARE

Garattini S.K.[1], Minisini A.M.[1], Valent F.[2], Riosa C.[1], Andreotti V.J.[3], Bortot L.[3], Targato G.[3], Fioraso R.[3], Ermacora P.[1], Fasola G.[1]

[1]*Dipartimento di Oncologia Medica, Azienda Sanitaria Universitaria Integrata di Udine - Ospedale Santa Maria della Misericordia, Udine;* [2]*Istituto di Igiene ed Epidemiologia Clinica, Azienda Sanitaria Universitaria Integrata di Udine - Ospedale Santa Maria della Misericordia, Udine;* [3]*DAME-Dipartimento di Area Medica; Università degli Studi di Udine, Udine*

Background: Over the last years, improved treatments led to a growth in cancer prevalence thus requiring an increase in activities related to Oncology. In this study, we estimated the 2-year oncology workload generated by each new cancer patient referred to the Oncology Department of the Academic Cancer Center of Udine, Italy.

Methods: We investigated the mean number (and standard deviation) of Oncology activities, as defined by the 2017 AIOM-CIPOMO document on Oncology Unit organization, generated in the following 2 years by each new patient referred to our department between 01.01.2012 and 31.12.2017. Patients without a second clinical episode within 12 months from first consultation were censored. We analyzed through our electronic "Data Warehouse" accountability system all the treatment sessions, unplanned presentations, hospitalizations, re-assessments, follow-up visits and inpatient oncology advices. Anonymous aggregate data were retrieved with last follow up to 31.12.2019 (8 years of data).

Results: We analyzed a total number of 98,890 oncology activities deriving from 8,748 new cancer patients referred over a 6-year period. After the first consultation 24.0% of people needed only follow-up, 41.5% were referred for adjuvant treatment and 34.5% started therapy for advanced disease. In the two years following the first consultation each patient generated, on average : 5.99 pre-treatment evaluations (SD 8.75), 1.93 follow-up visits (SD 1.86), 0.42 hospitalizations (SD 1.20), 0.36 inpatient oncology advices (SD 0.83), 1.60 re-assessments (SD 2.27) and 1.01 unplanned presentations (SD 2.15). Further subgroup analyses are ongoing.

Conclusions: Advances in cancer care provided longer "on-treatment" and "on-follow up" overall survival translating into a growing oncology workload. Estimating the amount of clinical activities generated by each new patient will become crucial to plan the resources that will be needed and promote sustainability of Oncology in the near future.

T18

WORKLOAD IMPACT OF 12 MONTHS OF IMMUNOTHERAPY IN METASTATIC CANCER PATIENTS

Cinausero M.[1], Garattini S.K.[1], Minisini A.[1], Valent F.[2], Riosa C.[1], Iacono D.[1], Macerelli M.[1], Rihawi K.[1], Giavarra M.[3], Andreotti V.J.[3], Bortot L.[3], Corvaja C.[3], Palmero L.[3], Targato G.[3], Zara D.[3], Fioraso R.[3], Noto C.[3], Fasola G.[4]

[1]*Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine;* [2]*Istituto di Igiene ed Epidemiologia Clinica Udine, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine;* [3]*Dipartimento di*

Area Medica, Università degli studi di Udine; Dipartimento di Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine; ⁴Dipartimento Oncologia, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine

Background: In the last years, the development of immune checkpoint inhibitors (ICI) is leading to major changes in oncology workload. As very few data are available on this topic, we conducted a study to estimate the shift in workload generated, within 1 year of first consultation, by any new metastatic cancer patient receiving ICI at the Oncology Department of the Academic Hospital of Udine, Italy.

Patients and methods: We collected from our electronic accountability system all new first consultations for metastatic cancer between 01.01.2017 and 31.12.2018, leading to at least a second clinical episode (treatment sessions, unplanned presentations, hospitalizations, re-evaluations, follow-up, and inpatient oncology advices) during the following year. Patients (pts) were divided into those receiving ICI (anti-CTLA4/PD1/PDL1) *versus* pts receiving other treatments. Mean number per patient and standard deviation were calculated for clinical episodes, and the mean numbers in each group were compared using Student's t-test (significance $p<0.05$). Follow-up continued until 31.12.2019.

Results: 969 pts were included (115 ICI; 854 other treatments). Pts treated with ICI generated a statistically significant greater workload in terms of treatment sessions, re-evaluations, and unplanned presentations. On the other hand, follow-up visits workload was greater for other treatments group. In detail, data are reported in Table 1.

Conclusions: ICI have transformed the oncology landscape, leading to increasing survivals and longer lasting treatment periods. The estimate of workload generated by new diagnosis of metastatic cancer requiring ICI is crucial for implementing more sustainable systems and for planning clinical activities.

Table1. Mean number of clinical episodes in the first year of treatment with ICI for metastatic disease.

Metastatic disease	Treatment sessions	Follow-up visits	Hospitalizations	Inpatient oncology advices	Re-evaluations	Unplanned presentations	Total n° of patients
Other cancer treatments	**6.83 (SD 6.48)**	**0.83 (SD 1.24)**	0.73 (SD 1.58)	0.58 (SD 1.09)	**1.88 (SD 1.77)**	**1.51 (SD 2.63)**	**854**
total episodes (N=10548)	N=5829	N=711	N=623	N=493	N=1605	N=1287	
Immunotherapy	**9.59 (SD 5.99)**	**0.63 (SD 0.99)**	0.61 (SD 1.04)	0.60 (SD 1.36)	**2.55 (SD 1.87)**	**2.19 (SD 2.42)**	**115**
total episodes (N=1859)	N=1103	N=72	N=70	N=69	N=293	N=252	
P value	**<0.0001**	**0.0432**	0.2784	0.8641	**0.0002**	**0.008**	

Mean number per patient is represented by mean value and standard deviation (SD). Total number of clinical episodes is shown (N=). Data are reported for ICI *versus* other treatments group.

T19

PRELIMINARY IMPACT ANALYSIS OF RECYCLING DISCARDED ORAL ANTICANCER DRUGS: A SINGLE CENTRE EVALUATION

Chini C.[1], Ciotti O.[1], Conti S.[1], Simonetti L.[1], Boni E.[1], Gabri P.[1], Galli D.[1], Vallini I.[1], Pinotti G.[1]

[1]ASST Settelaghi Varese, Varese

Background: targeted oral agents represent one third of treatment for many cancers. The high cost of the new oral anticancer drugs is well known. In particular, the financial toxicity of new molecules to health institutions and indeed to society is increasingly recognized. Often oral treatments are discontinued because of toxicities, disease progression or death in almost all patients (pts). On the other side pts adherence represents an essential component in evaluating effectiveness of oral medications. As a result, many of them have unused amount of tablets when their treatments are discontinued. We believe that it's time to directly empower physicians who are motivated to be able to recycle drugs, thus increasing access and minimizing waste. The aim of our survey was to explore patients' compliance with oral drugs and to identify the amount of waste drugs.

Material and methods: From August 2019 to January 2020 we dispensed 590 cycles of different oral anticancer drugs to pts referred to our Institution. During the delivery we asked pts to fill in a questionnaire in order to evaluate drug's compliance, adherence and persistence. Wasted tablets were calculated after any cycle. The amount associated with the wastage was determined using the average wholesale price.

Results: The questionnaire was completed by 280 male and 310 female pts (70.3%). Median age was 66 years (range 28-86). Discontinuation occurred for medical indication or toxicity in the majority of pts; forgetfulness in 9,8% of cases. A significant difference in compliance was observed in male/female. Waste occurred in 247 cycles. A total of 6004 tablets were discarded for all causes, with a total priced of € 53.284.

Conclusions: with an estimated waste of € 151.588 per year, oral chemotherapy represents a significant financial burden to society. A system that will allow safe and efficient recycling of drugs from pts who no longer need them to those who do, should be a desirable medically sound solution. Health care practitioners sensibility and support of establishing pharmacies is mandatory to prevent wastage and to recycle discarded drugs.

T20

PERCEPTION OF SEXUALITY DISORDERS IN CANCER PATIENTS AMONG HEALTH PROVIDERS: A SURVEY FROM RETE ONCOLOGICA DEL PIEMONTE E DELLA VALLE D'AOSTA

Sperti E.[1], Caristo T.[2], Terzolo S.[1], Varese P.[3], Di Maio M.[1], Bertetto O.[2], Numico G.[4]

[1]*AOU Mauriziano Umberto I, Torino;* [2]*Dipartimento Rete Oncologica del Piemonte e della Valle d'Aosta, Torino;* [3]*Ospedale Civile Ovada, Ovada;* [4]*AO SS Antonio e Biagio e Cesare Arrigo, Alessandria*

Background: Disorders of the sexual sphere in cancer patients are very frequent (40-100%), but they are underestimated in clinical practice. ASCO guidelines recommend that the health care team introduce a discussion with the patient, regarding sexual health.

Material and methods: The study group "Supportive Care" of the Rete Oncologica del Piemonte e della Valle d'Aosta sent a survey to physicians and nurses of the oncology, hematology and radiotherapy departments of the network. There were 11 questions to understand perception of the problem, degree of preparation of the operators, and presence of structural, cultural, or emotional obstacles for the management of the disorders. Subgroup analysis was performed by profession, gender and age.

Results: Between June and September 2019, 315 people replied: 77% women, 53% nurses, 70% >39y. In a range from 1 to 10, median score of how much sexual disorders have an impact on quality of life was 7, and median score of how much they are taken into consideration was 5. Physicians and nurses believe that attention to sexual disorders are their own duty in 89% and 81% respectively, without significant differences in subgroup analysis. To the question "how often do you talk with patients about sexual disorders" 12,7% answered "never" and 45.5% answered

"rarely", with a significant difference between physicians and nurses (never or rarely 60% vs 74% respectively, p = 0.0001). In 45.5% of cases is the issue is introduced by the patient. Main obstacles to deal with this topic (not mutually exclusive) were insufficient preparation (59.05%), embarrassment (51.4%), and lack of time (28.5%). Subgroup analysis revealed a greater concern for the lack of time by physicians than nurses (p = 0.0001) and by > 39 years than younger respondents (p = 0.0015); and a greater concern for embarrassment by women than men (p = 0.04). The self-evaluation of preparation for the management of female and male sexual disorders was "nothing" / "a little" in 18.7% / 65.7% and 29.1% / 56.5% respectively. 67.6% of respondents declared the absence of availability of a counselling about sexual disorders.

Conclusions: This survey highlighted a high perception and interest for sexual disfunction in cancer patients. Lack of preparation and time, or embarrassment, prevent an adequate management of the problem. There is a clear need for training, both in terms of knowledge of the problems and treatments, and in terms of communication.

T21

CORRELATION BETWEEN HAEMATOLOGICAL, IMMUNOLOGICAL AND ODONTOSTOMATOLOGIC PARAMETERS AND CLINICAL OUTCOME IN CANCER PATIENTS WITH BONE METASTASIS: A SINGLE CENTER EXPERIENCE

Deiana M.[1], Lai E.[2], Ziranu P.[2], Pretta A.[3], Impera V.[3], Liscia N.[3], Mariani S.[2], Tolu S.[3], Camera S.[3], Persano M.[2], Donisi C.[2], Spanu D.[2], Saba G.[2], Dubois M.[2], Migliari M.[2], Massa E.[2], Demurtas L.[2], Madeddu C.[2], Dettori C.[4], Astara G.[2], Scartozzi M.[2]

[1]*Department of Medical Sciences and Public Health, Occupational Health Section, University of Cagliari, Monserrato, Italy; Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari;* [2]*Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari;* [3]*Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari, Italy, Cagliari;* [4]*Department of Conservative Dentistry and Endodontics, University of Cagliari, Cagliari, Italy, Cagliari*

Background: Monocytes (M)/lymphocytes (L) ratio (MLR), neutrophils (N)/L ratio (NLR) and platelets (P)/L ratio (PLR), interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF-α) are cancer inflammation biomarkers. Bone metastasis (BM) are common in advanced cancer patients (pts) and might induce skeletal-related events (SREs), compromising survival and quality of life. Bone target therapy (BTT) delays SREs occurrence but it may lead to odontostomatologic toxicity, thus requiring preliminary oral examination.

Material (Patients) and Methods: We retrospectively collected baseline MLR, NLR, PLR, pro-inflammatory

cytokines, clinical and dental parameters of pts with BM from solid tumours receiving BTT at the Medical Oncology Unit of Cagliari University Hospital (April 2009-April 2018). Pts underwent baseline orthopanoramic radiography and odontostomatological visit at the Department of Conservative Dentistry and Endodontics of Cagliari University. Dental elements were evaluated according to community periodontal index (CPI) and periapical index. The aim of our study was to assess the correlation between haematological, immunological and odontostomatologic parameters and clinical outcome in the study population. MedCalc was used for statistical analysis of survival distribution (Kaplan-Meier method), survival curves comparison (log-rank test) and to assess the independent role of significant variables at univariate analysis (logistic regression). The other variables were evaluated with SPSS program (T Student, Anova and Mann Whitney, Pearson and Spearman correlation coefficient, Chi-square - $p < 0.05$).

Results: Globally, 192 pts (92 males,100 females) were included in the study. Mean age was 60 years. Primary tumours were mainly breast (44,3%), prostate (16,1%), lung (14%) and colorectal (6,5%). Overall survival (OS) was 61 months (m) (95%CI:47-81) in pts with MLR>0,4667 versus (vs) 27 m in pts with MLR≤0,4667 (95%CI:20-35), $p < 0,001$. OS was significantly longer also for NLR=11,25: 56 m (95%CI:42-69) vs 8 m (NLR>11,25, 95%CI:42-69), $p < 0,0001$. Increased IL-6 levels were associated with earlier SREs and shorter survival. Odontostomatologic data were available for statistical analysis for 25% of pts and showed a statistically significant correlation between CPI and NLR in males (0,0337).

Conclusions: An integrated approach evaluating pro-inflammatory cytokines, MLR, NLR and paradontopathy can be a useful tool to predict outcome of cancer pts with BM receiving BTT.

T22

EVALUATION OF CHEMOBRAIN IN CHEMOTHERAPY AND IMMUNOTHERAPY TREATED ONCOGERIATRIC PATIENTS: COULD THE OLFACTORY IMPAIRMENT BE A BIOMARKER?

Leo S.[1], Nestola C.[2], Accogli G.[3], Leucci M.[3], Calogiuri M.[2], Cairo G.[1], Romano G.D.[1], Accettura C.[1], Saracino V.[1], Invitto S.[3]

[1]Ospedale Vito Fazzi - U.O. Oncologia Medica, Lecce; [2]Associazione La Chiave d'Argento Onlus, Lecce; [3]Inspire Lab Università del Salento, Lecce

Background: Aging is a risk factor for cognitive impairment as well as cancer. The cognitive decline due to therapy is usually called "chemobrain" and is associated with deficits in memory, concentration, executive functions, and multitasking and a general feeling of cognitive fogginess. Chemotherapy can also affect chemosensory perception, such as olfaction. Moreover, it is known that olfactory perception can be related to cognitive ability. Aim of this study was to evaluate the correlation between chemobrain and olfactory impairment in elderly cancer patients treated with chemotherapy (CHT) and immunotherapy (IO).

Material and Methods: The research, conducted from July to December 2019, involved 147 patients (pts) (age>70 years) (mean age 78±8 years) with advanced solid tumors at Oncology Unit of Vito Fazzi Hospital in Lecce: 65 pts already in treatment with CHT, 41 with IO and 41 geriatric people without cancer [that represent Control Group (CoG)]. The study was conducted in cooperation with Laboratory of Cognitive and Psychophysiological Olfactory Processes (INSPIRE LAB) of University of Salento. The cognitive function was assessed trough the Mini Mental State Examination (MMSE). The olfactory evaluation was carried out by The Sniffin' Sticks – Screening 12, with score 0-12 (MediSense - http://www.medi-sense.eu). The test uses 12 odour pens and allows to distinguish anosmics and hyposmics from normosmics people. The purpose of the test is to identify the 12 smells presented and the patients have to choose between 4 options for response. The total score is compared to the age-related normal values.

Results: Patients treated with both CHT and IO scored lower in the various tests (MMSE, Sniffin' Sticks) than the CoG. There is, also, a gender effect with lower scores in MMSE for women. About the Sniffin' Sticks test, analysis highlighted lower scores in CHT and IO than in the CoG and shows an olfactory impairment in CHT (score 5) rather than in IO (score 7) and CoG (score 7). In addition, Pearson Coefficient showed a significant correlation between MMSE and Sniffin' Sticks test.

Conclusions: Olfactory impairment can be strictly linked to chemobrain and that more high with CHT, moreover the olfactory perception can be a biomarker of cognitive impairment in oncogeriatric patients. The study is ongoing for evaluation of IO effect on cognitive status and test needs to be repeated after regular and standardized intervals of time.

T23

PRELIMINARY STUDY ON FINANCIAL TOXICITY PERCEPTION AMONG CANCER PATIENTS: THE FINANCIAL TOXICITY QUESTIONNAIRE 16

Bordonaro R.[1], Castagna F.[2], Piazza D.[3], Cordio S.S.[2], Sergi C.[2], Fassari G.E.[2], Martines C.[2], Commendatore O.[2], Sambataro D.[2], Carapezza L.[2], Mattina M.[2], Russo A.E.[2], Gebbia V.[4]

[1]Medical Oncology, National Specialist Hospital Garibaldi, Catania; [2]ARNAS Garibaldi, Catania; [3]GSTU Foundation for Cancer Research, Palermo; [4]Casa di Cura La Maddalena, Palermo

Background: Financial toxicity (FT) among cancer patients (CP) is multifactorial, arising from both related

and non- disease related factors, including socio-cultural, environmental, and psychological attributes. It derives both from costs related to assistance and borne on the patients and its caregivers, and reduction of income capacity also in this case borne on the patients and on the caregivers. Stress levels may escalate to significant proportions in some patient, to present with symptoms of anxiety especially during therapy administration periods.

Materials and Methods: In order to highlight financial toxicity related to the diagnosis of metastatic pancreatic and lung cancer and to measure its evolution over time and any correlation with the prognosis, we developed a questionnaire called FT16 and we conducted a validation study on a sample of 31 patients. The design of the study involved the development and the psychometric assessment of a scale to measure the perceived sources of FT among CP. Following extensive literature review, a table of specification with the initial items was created to guide item construction for developing the scale. The items related to these FT were converted into a 16-item, multipoint questionnaire. We also monitored quality of life of the patients, using the QlQ C-30 questionnaire to capture correlation between FT onset and quality of life deterioration; clinical characteristics of the patients, response to therapy and outcome parameters also have been recorded to evaluate eventual correlation with FT.

Results: The questionnaire was administered to 31 CP, both men and women, who were newly diagnosed and will undergo cancer treatment. Each of them has been informed about the research and written informed consent has been obtained. FT16 internal consistency reliability (Cronbach's alpha) was 0.77. To assess the tool's ability to detect FT, a multiple linear regression model was applied, demonstrating how much the dependent variable of the individual's perception of economic difficulty (item n.16) could be predicted by the remaining independent variables (items n.1-15). The result showed a r-square index of 0.78 (p=0.018).

Conclusions: FT16 questionnaire seems to be a useful tool to capture FT onset in this poor-prognosis subset of patients; the analysis of the data recorded will continue to assess the capability of the FT16 to capture correlations with clinical characteristics at diagnosis and correlations with the prognosis.

T24

C-KIT RECEPTOR AND TRYPTASE POSITIVE MAST CELLS CORRELATE WITH NORMAL TO CANCEROUS TISSUE SHIFTING AND ANGIOGENESIS IN PANCREATIC CANCER

Ranieri G.[1], Laface C.[1], Zuccalà V.[2], Luposella F.[3], Zizzo N.[4], Patruno R.[4], Porcelli M.[5], Gadaleta C.D.[5], Ammendola M.[6]

[1]*Interventional and Medical Oncology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari; [2]Pathology Unit, "Pugliese-Ciaccio" Hospital, Catanzaro, Italy;* [3]*Direction Départementale de la Cohésion Sociale et de la Protection des Populations des VOSGES (DDCSPP88), Vittel, France; [4]Chair of Pathology, Veterinary Medical School, University "Aldo Moro" of Bari, Bari, Italy; [5]Interventional and Medical Oncology Unit, IRCCS Istituto Tumori "G. Paolo II", Bari, Italy; [6]Department of Health Science, Digestive Surgery Unit, University "Magna Graecia" Medical School, Catanzaro, Italy*

Background: Mast cells (MCs) contain pro-angiogenic factors, in particular tryptase, associated with tumoral angiogenesis. Up to now few data have been published on the role of MCs in angiogenesis in both pancreatic ductal adenocarcinoma tissue (PDAT) and adjacent normal tissue (ANT).

Methods: In this study MCs density positive to C-Kit receptor (MCDP-C-KitR), MCs density positive to tryptase (MCDPT), MCs area positive to tryptase (MCAPT), angiogenesis in terms of microvascular density (MVD) and endothelial area (EA) were evaluated by immunohistochemistry and image analysis in both PDAT and ANT. Tissue samples were obtained from 45 patients with stage T2-3N0-1M0 (by AJCC for Pancreas Cancer Staging 7th Edition) who had undergone surgery. For each analyzed tissue parameter mean ± standard deviation was evaluated in both PDAT and ANT and differences were calculated by Student t-test (p ranged from 0.001 to 0.004). Each analysed tissue parameter was correlated each other by Pearson t-test analysis (p ranged from 0.01 to 0.03). Any other correlation among MCDP-C-KitR, MCDPT, MCAPT, MVD, EA and the main clinical pathological characteristic was found.

Results: The mean value ± standard deviation (SD) regarding MCDP-C-KitR, MCDPT, MCAPT, MVD and EA in TT was 14.69 ± 4.57, $13.31 \pm 4,23$, $171.41 \pm 62,39$ µ2, 29.11 ± 7.93, 201.82 ± 70.05 µ2 respectively and the mean value ? SD in ANT was 5.61 ± 2.39, 5.13 ± 2.03, 54.43 ± 16.73 µ2, 11.45 ± 4.96, 67.60 ± 21.96 µ2, respectively. Differences in terms of mean value ? SD between PDAT and ANT were significant for each analyzed tissue biomarker. Data demonstrated that MCDP-C-KitR MCDPT, MCAPT, MVD and EA significantly increased from ANT to PDAT. In PDAT, it was showed a correlation between MCDP-C-KitR and MCDPT (r= 0.87, p= 0.01), MCDP-C-KitR and MVD (r= 0.74, p= 0.02), MCDP-C-KitR and MCAPT (r=0.81, p= 0.01), MCDPT and MVD (r= 0.72, p= 0.02), MCD-C-KitR and EA (r= 0.73, p= 0.02), MCDPT and MCAPT (r=0.85, p= 0.01), MCAPT and MVD (r=0.76, p= 0.02), MCAPT and EA (r=0.66, p= 0.03), MCDPT and EA (r= 0.69, p= 0.03), MVD and EA (r= 0.82, p= 0.01).

Conclusions: Our data suggest that assessed tissue parameters increased from ANT to PDAT and that MCs are strongly associated with angiogenesis in PDAT. On this basis, inhibition of MCs by tyrosine kinase inhibitors, such as masitinib, or inhibition of tryptase by gabexate mesylate may be a novel antiangiogenetic approach in pancreatic cancer therapy.

T25

SURVIVAL OF PATIENTS WITH OBESITY AND CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

Petrelli F.[1], Ghidini A.[2], Cortellini A.[3], Indini A.[4], Tomasello G.[5], Ghidini M.[4], Nigro O.[6], Salati M.[7], Dottorini L.[8], Iaculli A.[8], Varricchio A.[1], Costanzo A.[1], Rampulla V.[1], Bossi A.[1], Barni S.[1], Zaniboni A.[9]

[1]ASST Bergamo Ovest, Treviglio; [2]Casa di Cura Igea, Milano; [3]San Salvatore Hospital, L'Aquila, Italy; Department of Biotechnology and Applied Clinical Sciences, L'Aquila; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano; [5]ASST Grande Ospedale Metropolitano Niguarda, Milano; [6]ASST Sette Laghi, Ospedale di Circolo, Varese; [7]University Hospital of Modena, Modena Cancer Centre, Modena; [8]ASST Bergamo Est, Seriate; [9]Fondazione Poliambulanza, Brescia

Background: Obesity is associated with an increased risk of many cancers and of overall mortality for non-cancer causes. In last years, various studies suggested an obesity paradox that represents the better prognosis of obese cancer patients compared to non-obese patients. We performed a systematic review and meta-analysis to assess the association between obesity and outcome after a diagnosis of cancer and to found eventual setting of obesity paradox in the published literature

Material and Methods: PubMed, the Cochrane Library, and EMBASE were searched from inception to January 2020, for studies reporting survival of patients with obesity and cancer. The primary outcome of the study refers to overall survival (OS). Secondary endpoints were cancer-specific survival (CSS) and progression- or disease-free survival (PFS or RFS).

Results: Overall survival and relapse associated with obesity in patients with cancer were evaluated among n=6,320,365 participants (n=203 studies). Overall, association of obesity and cancer was associated with an increased mortality (hazard ratio [HR] =1.14, 95% confidence interval [CI]: 1.09–1.19; P<.01) and CSS (HR=1.17, 95%CI 1.12-1.23; P<.01). Patients were also at increased risk for relapse (HR=1.13, 95%CI 1.07-1.19; P<.01). Obese with lung cancer, renal cell carcinoma and melanoma had instead a better prognosis than non-obese and satisfied the criteria of obesity paradox.

Conclusions: Most of obese patients with cancer have a reduced survival and an increased risk of relapse. In lung cancer, renal cell carcinoma and melanoma obesity was paradoxically protective in terms of outcome. More intensive follow up, adequate dosing of oncological treatments, calories intake restrictions, physical activity and monitoring of obesity-related complications are effective measures for reducing mortality in these subjects. The mechanism underlying obesity paradox is probably linked to an enhanced performance of immune cells confined in adipose tissue.

T26

INTEGRATION BETWEEN GERIATRIC ONCOLOGY AND PALLIATIVE CARE: A SINGLE CENTER EXPERIENCE FOR ELDERLY CANCER PATIENTS (pts)

Liguigli W.[1], Cengarle R.[1], Rimanti A.[1], Catania G.[1], Faglioni L.[1], Zanardi Di Pietro I.[1], Iridile C.[1], Ravelli A.[1], Rigotti L.[1], Cantore M.[1]

[1]Ospedale Carlo Poma, Mantova

Background: Comprehensive Geriatric Assessment (CGA) is utilized to plan the social and health care of elderly and to complete the diagnostic-therapeutic choice of oncologist also considering early integration with palliative care.

Material (patients) and methods: Cancer pts hospitalized aged ≥ 70 years were screened by G8 questionnaire to define if necessary CGA. CGA identified: fit, unfit and frail pts. Unfit and frail pts were discussed in multidisciplinary meetings to decide the most appropriate strategy.

Results: From Febraury 2019 to April 2020, we evaluated 95 pts (60% male, 40% female; median age: 78). All pts were screened by G8: 2% were not at risk and 98% were at risk. Pts at risk, evaluated by CGA resulted: 3 fit, 45 unfit and 45 frail. 3 fit pts received standard medical or surgical therapy. 41 unfit pts (91%) received personalized care and 4 pts got worse quickly and died. Median age was 76, median score IADL/ADL (Instrumental/Activities Daily Living) was 5, median daily drugs taken was 6 and the median number of geriatric syndromes was 1.3. Malnutrition was present in 31% and MMSE (Mini Mental State Examination) was normal in 62%. Among these 45 pts 32 died with a median survival of 120 days (pts alive had a median follow-up of 145 days) 14 at home, 13 in hospice and 5 during hospitalization.

Among 45 frail pts, 3 received personalized care and 42 received Best Supportive Care. Median age was 81, median score IADL/ADL was 2, median daily drugs taken was 7 and the median number of geriatric syndromes was 2. Malnutrition was present in 55%, MMSE was normal in 22% but was not possible to evaluate 13 ones for poor general medical condition. Among these 45 pts 40 died with a median survival of 36 days: 12 at home, 24 in hospice, and 4 during hospitalization.

In both subgroups main comorbidities were: cardiac (55%), renal (21%), pulmonary (16%), dementia and depression (13%) and comorbidity index of CIRS (Cumulative Illness Rating Scale) was similar.

Conclusions: Unfit pts have a better functional, cognitive and nutritional status than frail pts. Early integration between geriatric oncology and palliative care represents the possibility to create a personalized care pathway and to avoid unnecessary diagnostic pathway especially for frail pts.

T27

MULTIDISCIPLINARY ORAL THERAPY OUTPATIENT CLINIC: AN ITALIAN SINGLE CENTER EXPERIENCE

Marino D.[1], Terzolo S.[1], Bellero M.[2], Sperti E.[1], Ciriolo G.[1], Fazzina G.[2], Zichi C.[1], Paratore C.[1], Codegone F.[1], Pozzi D.[1], De Luca E.[1], Reale M.[1], Audisio M.[1], Gasco A.[2], Di Maio M.[1]

[1]*Dipartimento di Oncologia, Università di Torino, AO Ordine Mauriziano, Torino;* [2]*SC Farmacia Ospedaliera, AO Ordine Mauriziano, Torino*

Background: The increasing use of oral anticancer drugs (OAD) led to new challenges for clinicians. Traditional therapeutic horizon has changed, but data about new cancer care model are still scanty. A multidisciplinary management involving 3 distinct figures (medical oncologist, hospital pharmacist, and nurse) could improve compliance and treatment (trt) safety.

Methods: Aim of this analysis is to describe the Oral therapy Outpatient Clinic (OOC), a multidisciplinary project performed at our Oncology Unit starting from March 2019. In this starting phase, OOC was limited to patients with gastrointestinal (GI) tumors. Three professional figures (medical oncologist, hospital pharmacist, and nurse) performed joint visit (each with specific tasks), with a schedule based on patients (pts) and trt characteristics. Multidisciplinary approach was focused on prescription, therapeutic education, drug interaction, monitoring and follow-up, to improve pts awareness addressing medication safety, trt adherence and adverse events (AEs) management.

Results: Between March 2019 and April 2020, 359 visits were performed in 49 pts: 23 (46.9%) were males, 100% ECOG PS 0-1 and median age was 66y (range 34-80). Overall, 22 pts (44.9%) received adjuvant trt and 27 pts (55.1%) trt for advanced disease. 8 pts (16.2%) had received $\geq$2 previous trt lines. 32 pts (65.3%) had colorectal cancer, 5 pts (10.2%) had hepatocarcinoma, 7 pts (14.3%) had biliary tract carcinoma, and 5 pts (10.2%) had other types of GI tumor. Capecitabine was the most frequent CT, employed as a single agent in 34 pts (69.4%) and in combination with temozolomide in 2 pts (4.1%). 6 pts (12.2%) received trifluridine/tipiracil, 5 pts (10.2%) sorafenib and 2 pts (4.1%) regorafenib. Only 19 pts (38.8%) started a full dose trt, (33.3% among pts >70y vs. 41.9% among pts $\leq$70y). 29 pts (59.2%) had to delay $\geq$1 trt cycle (61.1% >70y vs. 58.1% $\leq$70y). 27 pts (55.1%) required $\geq$1 dose modification due to toxicity, including hematological, cutaneous and GI AEs (50.0% >70y vs. 58.1% $\leq$70y). 35 pts (71.4%) took $\geq$4 concomitant drugs: $\geq$1 drug interaction was found in 32 pts, requiring trt adjustment in 29 pts.

Conclusions: OAD require comprehensive and integrated pts management. Multidisciplinary simultaneous visit involving oncologist, pharmacist and nurse could optimize trt management, safety and outcomes. This innovative cancer care model could improve drug assumption awareness and pts education to promptly recognize and manage AEs.

T28

SPREADING KNOWLEDGE IN THE FIELD OF CARDIO-ONCOLOGY: INTERSOCIETY COLLABORATION AND ONLINE MEDICAL RESOURCES IN ITALY

Inno A.[1], Tarantini L.[2], Barni S.[3], Spallarossa P.[4], Bisceglia I.[5], Coletti Moia E.[6], Parrini I.[7], Canale M.L.[8], Maurea N.[9], Gori S.[10], Russo A.[11]

[1]*IRCSS Ospedale Sacro Cuore don Calabria, Negrar di Valpolicella (VR);* [2]*U.O.C. Cardiologia, ASL 1 Dolomiti, Belluno;* [3]*U.O. Oncologia, ASST Bergamo Ovest, Treviglio, Bergamo;* [4]*Clinica di Malattie dell'Apparato Cardiovascolare, Ospedale Policlinico San Martino, Genova;* [5]*Servizi Cardiologici Integrati, A.O. S. Camillo – Forlanini, Roma;* [6]*Cardiologia, Fondazione Piemontese per l'oncologia – IRCCS, Candiolo; Cardiologia, Humanitas Gradenigo, Torino;* [7]*Cardiologia, Ospedale Mauriziano, Torino;* [8]*Cardiologia, Ospedale della Versilia, Camaiore, Lucca;* [9]*S.C. di Cardiologia, Istituto Nazionale Tumori. IRCCS Fondazione G. Pascale, Napoli;* [10]*Oncologia Medica, IRCSS Ospedale Sacro Cuore Don Calabria, Negrar di Valpolicella (VR);* [11]*Sezione di Oncologia Medica, Dipartimento di Discipline Chirurgiche, Oncologiche e Stomatologiche, Università degli Studi di Palermo, Palermo*

Background: Cardio-Oncology is an emerging discipline focused on prevention, diagnosis and management of cardiovascular adverse events in cancer patients. Due to its intrinsic interdisciplinarity, Cardio-Oncology has prompted collaboration between different scientific societies. In 2011, the Italian Association of Medical Oncology (AIOM) in collaboration with the Italian Association of Hospital Cardiologists (ANMCO,) the Association Outpatient Cardiologists (ARCA), the Italian Society of Cardiology (SIC), the Association of Italian Cardioncology (AICO), the International Cardio-Oncology Society (ICOS), the Italian Society of Hematology (SIE) and the Italian Society of Clinical Biochemistry and Clinical Molecular Biology (SIBioC), set up an intersociety working group with the aim to promote best clinical practice in Cardio-Oncology. Since then, several documents have been published on behalf of the Cardio-Oncology working group: 4 educational books (Cardio-Oncologia 2011-2013, Cardio-Oncologia 2015, Cardio-Oncologia 2017, Cardio-Oncologia 2018), 1 consensus document (Tarantini et al, G Ital Cardiol 2017; Eur Heart Suppl 2017) and clinical practice recommendations (Cardio-Oncologia 2019). Educational books and clinical practice recommendations are available on the AIOM website (www. aiom.it), whereas the consensus document is available on the ANMCO website (www.anmco.it). The authors made all these documents also available on Researchgate (www. researchgate.net). Here we report the number of downloads/reads/views reached by the Cardio-Oncology documents.

Methods: We collected data about number of downloads/reads/views of Cardio-Oncology documents through AIOM, ANMCO and Researchgate websites.

Results: Cardio-Oncology documents reached 6160 downloads through the AIOM website (from 2016 to April 2020), with a trend to increase over time (550, 923, 2136 and 2046 downloads in 2016, 2017, 2018 and 2019, respectively). On Researchgate, Cardio-Oncology documents have obtained 5146 reads up to April 2020. On the ANMCO website, the consensus document has reached 1280 views from June 2017 to May 2020.

Conclusions: In less than 5 years, Cardio-Oncology documents published on behalf of the intersociety Working Group have exceeded 12.000 downloads/reads/views. These data suggest there is a need for continuing education in Cardio-Oncology, and online medical resources created through intersociety collaboration could help to spread knowledge in the field.

T29

INFLAMMATION, CANCER AND PROGNOSIS: A SINGLE CENTER RETROSPECTIVE STUDY IN BREAST CANCER AND LUNG CANCER PATIENTS

Manca F.M.[1], Lai E.[1], Ziranu P.[1], Impera V.[2], Pretta A.[2], Musio F.[1], Donisi C.[1], Persano M.[1], Balconi F.[1], Mariani S.[1], Liscia N.[2], Pinna G.[1], Pireddu A.[2], Madeddu C.[1], Dessì M.[1], Massa E.[1], Atzori F.[1], Ferrari P.A.[3], Cherchi R.[3], Astara G.[1], Scartozzi M.[1]

[1]*Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari;* [2]*Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari, Italy, Cagliari;* [3]*Division of Thoracic Surgery, Oncological Hospital "A. Businco" - Azienda Ospedaliera Brotzu -Cagliari, Cagliari, Italy, Cagliari*

Background: The correlation between inflammation and cancer has been extensively demonstrated in several tumour types. Neutrophils (N)/lymphocytes (L) ratio (NLR), platelets/L ratio (PLR), N/(L+monocytes) ratio (NLMR), albumin, body mass index (BMI), and advanced lung cancer inflammation index (ALI) were reported as cancer inflammation factors. We assessed their prognostic role in breast cancer (BC) and lung cancer (LC) patients (pts).

Material (Patients) and Methods: We retrospectively collected NLR, PLR, NLMR, albumin levels, BMI, ALI and clinical data of LC and triple-negative (TN) and hormone positive (HR+) BC pts attending the Medical Oncology Unit of Cagliari University Hospital and the Division of Thoracic Surgery of Oncological Hospital "A. Businco" - Azienda Ospedaliera Brotzu of Cagliari from 2017 to 2019. We aimed to assess the prognostic role of these inflammation biomarkers in the study population. Statistical analysis was performed with MedCalc package (survival distribution: Kaplan-Meier method; survival curves comparison: log-rank test).

Results: Globally, 92 pts were included in our analysis, 52 with BC and 40 (29 males, 11 females) with LC. In BC pts, mean age at diagnosis was 51,8 years, 28 had TN BC (16

early stage, 12 stage IV) and 24 had HR+ disease (10 early stage, 14 stage IV). In LC pts, mean age at diagnosis was 66,6 years, 20 had early stage disease amenable to surgery and 20 had stage IV cancer. Overall survival (OS) was 85,66 months (m) (95%CI:35,9-98) in pts with NLR≤4.64 versus (vs) 10,33 m (95%CI:2,8-13,26) in pts with NLR>4.64 (p<0,0001). OS was longer also with NLMR≤3,82 (85,66 m vs 10,33 m; 95%CI:35,9-98 and 95%CI:2,8-13,26, respectively; p<0,0001), albumin levels >3,68 g/dl (85,66 m vs 23,96 m; 95%CI:35,9-98 and 95%CI:10,33-23,96, respectively; p=0,0197), and ALI>9,93 (85,66 m vs 10,33 m; 95%CI:35,9-98 and 95%CI:2,8-13,26, respectively; p<0,0001). Biomarkers correlating with better prognosis were observed more frequently in BC than in LC: NLR≤4,6 (p=0,018), NLMR≤3,8 (p=0,0066), albumin levels>3,68 g/dl (p=0,0014) and ALI>9,93 (p=0,045). No differences were observed between TN and HR+ BC pts. PLR (p=0,0495), albumin (p<0,0001) and ALI (p=0,0183) showed significant differences between early stage and stage IV LC.

Conclusions: In our study, inflammation biomarkers showed a negative prognostic role and were more frequent in LC than in BC. Further studies are needed to prospectively validate their role in this population.

T30

RESEARCHERS' PYRAMID - TRICK OR TREAT?

Cagnazzo C.[1], Testoni S.[2], Cenna R.[1], Guarrera A.[3], Monti M.[2], Stabile S.[4], Federici I.[5], Taverniti C.[1], Pirondi S.[6], Ferrari A.[7]

[1]*AOU Città della Salute e della Scienza, Torino;* [2]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola;* [3]*AOU Careggi, Firenze;* [4]*Ospedale Niguarda, Milano;* [5]*AOU ospedali Riuniti Umberto I, Ancona;* [6]*Ospedale di Sassuolo, Sassuolo;* [7]*Fondazione IRCCS Policlinico San Matteo, Pavia*

Background: During the COVID-19 Coronavirus pandemic, public opinion has returned to a great deal of interest in clinical research and the key role of researchers in periods of health emergency. If on the one hand the emergency has reawakened confidence in the work of researchers in the population, on the other it has revealed leaks in the system that insiders have known for a long time. Italian research has always been characterized by great contradictions. While Italy boasts the most prestigious researchers worldwide, it is highly penalized by low investments and the inability to provide a stable career path to researchers and support staff. A first important step to at least partially solve the problem was the ministerial reform known as " Researchers' pyramid", an initiative that has been the subject of strong contradictions.

Methods: In September 2019, the Italian Group of Data Manager shared an online survey, meant for the italian biomedical research personnel, to investigate opinions about the reform.

Results: The questionnaire was completed by 147 respondents, the majority being employed at public IRCCS/IZP (n=78, 53.1%) or public Hospitals/University/Local Health Company (n=50, 34.0%).The respondent's profession was not included in those listed in the Pyramid in the minority of cases (n=28, 19%), while for the greater part it corresponded to a profession included in the "Clinical Research Assistant" (n=21, 55.1%) and "Clinical Researcher" categories (n=38, 25.9%). Over half of respondents declared to be optimistic regarding the actual benefit of the reform for employment stability. Over half (63.4%) of the "not optimistic respondents" considers the Pyramid a false path towards stabilization. Concerns were also expressed in relation to the evaluation criteria during the ten-year period, considered by a third of the interviewed to be too exclusive and often not very suitable. Many individuals (41.5%) report the poor valorization of personnel and much apprehension was recorded relating to the possibility of extending the reform to other institutes.

Conclusions: The reform overall seems like an important opportunity for entry level or inexperienced personnel, a watered-down compromise for expert professionals. But above all: only IRCCS are worthy of doing research? The fear conveyed from the great majority of the interviewed is that the pyramid is only a trick. When the emergency is over, will institutions finally begin to consider research a real job?

T31

WHEN RESEARCH BECOMES "SOCIAL": NOT ONLY FAKE NEWS

Testoni S.[1], Federici I.[2], Guarrera A.[3], Monti M.[4], Stabile S.[5], Taverniti C.[6], Cagnazzo C.[7]

[1]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola (FC);* [2]*Clinica di Ematologia, AOU Ospedali Riuniti Umberto I, G.M. Lancisi, G. Salesi, Ancona;* [3]*Terapie Cellulari e Medicina Trasfusionale, AOU Careggi, Firenze;* [4]*Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola;* [5]*SC Oncologia Falk, Niguarda Cancer Center, ASST Grande Ospedale Metropolitano Niguarda, Milano;* [6]*Oncologia Medica, AOU Città della Salute e della Scienza, Torino;* [7]*Unità di Ricerca e Sviluppo Clinico S.C. Oncoematologia Pediatrica, AOU Città della Salute e della Scienza - Presidio Ospedaliero Infantile Regina Margherita, Torino*

Background: Social Network have become immensely popular in recent years and provides new opportunities for health care professionals and institutions to interact with patients and other professionals, transforming communication, training and healthcare assistance. This transformation relates primarily to doctors and health professionals who, to update and train themselves increasingly use public pages and profiles opened on social networks.

Methods: The Italian Group of Data Managers (GIDMcrc) explored the use of Social Network among professionals involved in clinical research in Italy with an online anonymous survey. The survey consists of 13 questions and was available from mid-February to mid-April.

Results: At 15 April 2020, 100 research professionals completed the survey: 52 clinical research coordinators, 23 physicians, 20 nurses and 5 others, mainly aged between 30 and 49 (n=79). The majority of respondents reported using Social Network rarely or sometimes, mainly to receive information (n=30, 54%), to find and share information in equal measure (n=13, 24%) or to share information only (n=10, 18,5%). 33% of respondents said to use them often. Among frequent users: 73% (n=24) log into Social Networks mostly to find and share information in equal measure (n=23, 70%). Only 13% do not use it. The most used Social Networks are Facebook (65%) and LinkedIn (61%), followed by ResearchGate (26%), Instagram (21%), Twitter (20%) and YouTube (15%). Almost half of the respondents (n=43) say they have been contacted by patients through social networks, mainly via Facebook (60%), e-mail (42%) and WhatsApp (37%). 48% of respondents uses e-mails or other messaging systems to communicate with the patient or manage appointments, but only 15% have been trained on the use of Social Network.

Conclusions: This survey provides insight into the use of Social Network among research professionals, highlights that most of professionals use them to search for information. Half of the interviewees were contacted by patients looking for information or for managing their appointments. However, all this is done without specific training. If patients, healthcare professionals and researchers were informed and instructed about the correct use of Social Network, there could be benefits for research, like faster recruitment in clinical trials, involvement of patients in the study design, sharing of trial results.

T32

THE IMPACT OF ALOPECIA IN PEOPLE UNDERGOING CHEMOTHERAPY: OBSERVATIONAL STUDY BY USING THE ITALIAN VERSION OF THE CHEMOTHERAPY-INDUCED ALOPECIA DISTRESS SCALE

Bernardinis I.[1], Mansutti I.[1], Venturini M.[1], Bin A.[1]

[1]*Università degli Studi di Udine, Udine*

Background: Many chemotherapy agents can be toxic to scalp cells because they can cause a temporary and reversible hair loss, for which a proven and effective preventive intervention is not yet available. Alopecia is considered to be one of the most feared side effects of chemotherapy because potentially leading patients into severe psychological and social implications. Hair is, in fact, thought to be a symbol of life and identity and plays a huge role in social communication. The first aim of this study was to

investigate the psychological and social impact of chemotherapy-induced alopecia by using the Italian Chemotherapy-induced Alopecia Distress Scale (I-CADS), a questionnaire consisted in 16 item and 3 dimensions: self-perception, emotional work and social engagement. Moreover demographical, clinical data and strategies used to face this problem were collected. The secondary aim was to detect any correlations between I-CADS responses and other variables.

Material and methods: A descriptive observational study was conducted at the Day Hospital of Oncology in Udine, between January and February 2020. Using a consecutive sampling method, patients over the age of 18, affected by chemotherapy-induced alopecia, without cognitive problems, able to speech and understand Italian and giving informed consent, were included.

Results: The study sample consisted of 228 patients, predominantly female (78.5%). The results of the study showed that alopecia causes higher distress in "self-perception" dimension than in "emotional work" or "social engagement" dimensions. Moreover, the analysis showed: higher levels of chemotherapy-induced alopecia distress in female (p<0.001); significant negative correlation between age and "self-perception" and "social engagement" dimensions of I-CADS (respectively: r -0,227, p=0.001; r -0,197, p=0.003); higher levels of distress in workers, specifically regarding the "self-perception" dimension of the I-CADS (p=0.012). The majority of the sample likes to use wigs or other headgears to hide their bald scalps.

Conclusions: Chemotherapy-induced alopecia causes considerable distress in "self-perception" (body image), while it seems to have a lower impact on social relationships. Being a woman, young and a worker are factors that could increase this discomfort. This problem is not sufficiently considered by clinicians, but it is important to be aware of this in order to provide adequate information, support and care.

T33

THE COMPLEXITY OF CHEMO DECISIONS AT THE END OF LIFE. WHAT DOES ONCOLOGIST CHOOSE?

Iridile C.[1], Liguigli W.[1], Catania G.[1], Rimanti A.[1], Faglioni L.[1], Rabbi C.[1], Barbieri R.[1], Cantore M.[1], Morselli P.[1]

[1]ASST Mantova, Mantova

Background: A balance between residual Quality of Life and chemotoxicity is not easy, especially in the end of life. The decisional pathway depends not only on clinical characteristics and biology of cancer and its treatment but also on oncologist own human and medical experience.

Materials: In the time before immune therapy, at Oncology Unit of ASST Mantova, we evaluated, the "grey zone" of oncologist world. How do they take the final decision in patients died within 30 days after last chemotherapy? Medical records about 47 patients died within 30 days from chemotherapy, were analyzed by the same oncologists through a questionary, made by a psychologist, with 13 questions about 3 topic areas:

- Individual or group decision
- Relationship with patient and family
- Result of this decision

Results: Decision of going on with therapy, was individual for 33 out of 47 patients (70%) and from an equipe decision for 14 out of 47 (30%). The reasons to go on, were: patient therapeutic expectation, increase number of treatment options available, the small possibility of benefit, emotional difficulty to say stop . For oncologists chemo stop, would have meant less survival possibility, personal discomfort, patient abandonment . With chemo the quality of life was unchanged in 64%, got worse in 32%, improved in 4%.

Conclusions: Individual decision-making can to ease the construction of relationship with patient and communication of therapeutic stop; however it makes oncologists less critical and increases the difficulty of stopping earlier. Group discussion decreases the loneliness of oncologist and assesses the patient's real needs and makes best quality of residual life possible.

T34

PSYCHOLOGICAL APPROACH IN SUPPORTIVE CARE CONTEXT: LILT PROJECT "NEW LIFE"

Farina P.F.[1], D'Addario D.[2], Franchella C.[3], D'Aulerio M.[3], Spina C.[3], Iorio E.[3], Scipioni M.[3], Antonecchia P.[3], Bellomo M.[3], Carfagno G.[3], Fabrizio G.[3], Trivisonne R.[4], Sbrolla B.[4], Giorgi F.[5], Cicconi A.[6], Di Battista S.[6], Carrozza F.[1]

[1]D.H. Oncology S. Timoteo Hospital - ASReM, Termoli; [2]D.H. Oncology S. Timoteo Hospital - ASReM, Termoli (CB); [3]LILT Campobasso Provincial Association, Termoli (CB); [4]LILT Ascoli Piceno Provincial Association, Ascoli Piceno (AP); [5]D.H. Oncology "Madonna del Soccorso" Civil Hospital ASUR Marche - S.Benedetto del Tronto (AP), S. Benedetto del Tronto (AP); [6]LILT Ascoli Piceno Provincial Association, Ascoli Piceno

Background: Numerous cancer and treatment-related factors can contribute to increase the patient's distress, raising the complexity of treatment management and influencing the patients' quality of life. The goal of this study was to understand patients' perceptions and needs in integrated care in cancer.

Material and Methods: Provided data of the LILT project in collaboration with oncologists of Termoli and San Benedetto Hospitals were analyzed. Psychological assistance was offered to the involved patients. A self-administered questionnaire was dispensed to pts undergoing cancer

treatment and/or during follow up. We analyzed data of the questionnaire Psycological Distress Inventory (PDI) and Need Evaluation Questionary (NEQ) in order to investigate: *fatigue*, anxiety, depression and relational disturbances within pts during and after oncology treatments. All pts have also completed a questionnaire of satisfaction of their overall experience.

Results: We enrolled in the study 225 pts (115 pts from Termoli and 110 pts from San Benedetto; 78 males, 147 females, average age: 63- range 31-89) with diagnosis of solid or hematological cancer from November 2018 to December 2019. At the baseline administration of questionnaire, 93 pts (41,3%) were undergoing chemotherapy treatment. The most urgent needs detected through NEQ concerned communication and information on the disease status. Among the 193 pts completing the PDI, 57 pts reported severe distress (>35). Higher levels of distress have been found in female pts and in pts in active treatment for metastatic disease, of these 45 pts (79,3%) with high levels of distress received psychological support. We analyzed data of 121 pts that had followed the PDI questionnaire. The PDI data showed: fatigue in 62.8% of pts at baseline and 52.1% in follow-up; anxiety in 57.9% at baseline and in 48,3% for follow up, depression in 39,7% of pts at baseline and 30,6% for follow up and relational disturbances in 22.3% pts at baseline and in 24.3% for follow-up. After supportive care and psycological counseling, almost all the disorders (*fatigue*, anxiety, depression) decreased.

Conclusions: Our results showed that a large number of pts reported significant levels of distress during treatment for advanced disease. After psychological support prevalence of almost all disorders decreased. These data confirm the need for constant psychological support during cancer treatment to improve their general quality of life.

T35

THE HOSPITAL CARE OF CANCER PATIENTS: A RETROSPECTIVE ANALYSIS OF THE CHARACTERISTICS OF THEIR HOSPITAL STAY IN COMPARISON WITH OTHER MEDICAL CONDITIONS

Numico G.[1], Zanelli C.[1], Ippoliti R.[2], Piovano P.[1], Traverso E.[1], Blengio F.[1], Guglielmini P.[1], Zai S.[1], Vincenti M.[1], Fusco V.[1], Bellotti G.[1], Manfredi R.[1], Bellini R.[1]

[1]AO SS Antonio e Biagio e Cesare Arrigo, Alessandria; [2]University of Bielefeld, Department of Business Administration and Economics, Bielefeld

Background: Hospital admission is a frequent occurrence among patients with cancer, and a significant proportion of patients admitted to medical Units have cancer. Their hospital stay has features that may be different compared with non-cancer patients. We performed a retrospective analysis of the characteristics of cancer patients admitted for medical conditions.

Patients and Methods: We studied the administrative data of patients with solid cancer admitted to the medical Department of a large referral hospital over a 12-month period and compared them with those of patients without cancer.

Results: 7,802 consecutive admissions were analyzed, of which 1,099 (14.1%) had a principal or associated diagnosis of cancer. Admissions were distributed across 12 Units, with 44% concentrated in Medical Oncology and 56% in other Units. Cancer patients were more frequently males and were younger than patients without cancer. Admission less frequently involved the Emergency Department (ED), while discharge was more frequently assisted. The in-hospital death rate was higher, as was the readmission rate. Length-of-stay was longer (11.3 days vs. 9.8 days - p< 0.0001). Cancer patients admitted to the Medical Oncology Unit (489, 44.5%) used the ED even less and their length-of-stay was even shorter.

Conclusions: The in-hospital pathway of cancer patients displays specific issues and adds complexity to hospital stay of patients with medical conditions. The Medical Oncology Unit plays a role in reducing ED use and in providing efficient care. The evidence gathered should help in shaping new models of care and in improving adequate clinical competencies

T36

SHOULD CANCER PATIENTS ALWAYS REQUIRE A NUTRITIONAL ASSESSMENT? THE LILT STUDY "NEW LIFE"

D'Addario D.[1], Carrozza F.[2], Franchella C.[3], Iorio E.[3], Spina C.[3], D'Aulerio M.[3], Scipioni M.[3], Bellomo M.[3], Antonecchia P.[3], Carfagno G.[3], Fabrizio G.[3], Trivisonne R.[4], Di Battista S.[4], Cicconi A.[4], Giorgi F.[5], Sbrolla B.[6], Farina P.[7]

[1]D. H. Oncology S. Timoteo Hospital ASReM, Termoli; [2]D.H. Oncology S. Timoteo Hospital, Termoli; [3]LILT Campobasso Provincial Association, Termoli; [4]LILT Ascoli Piceno Provincial Association, Ascoli Piceno; [5]D.H. Oncology "Madonna del Soccorso" Civil Hospital ASUR Marche - S.Benedetto del Tronto (AP), S. Benedetto del Tronto (AP); [6]LILT Ascoli Piceno Provincial Association, Ascoli Piceno (AP); [7]D.H. Oncology S. Timoteo Hospital - ASReM, Termoli (CB)

Background: The assessment of the nutritional status is currently one of the most important aspects in overall treatment of cancer patients (pts). The goals of this study were to provide nutritional assessment and support in cancer pts during and after treatment and to investigate the effects of nutritional impairments and impacts on outcomes.

Material and Methods: Two oncology center were involved: Termoli and San Benedetto hospitals. Pts were addressed to nutritional assessment by the oncologist during treatment or during follow up. At first evaluation, *Mini Nutritional Assessment questionnaire* (MNA) was filled up by pts and counseling or personalized nutritional program was provided. Parameters such as body mass index

(BMI), phase angle (PA) and bioelectrical impedance analysis (BIA) was recorded at the first evaluation and after 1, 3 and 6 months.

Results: Eighty-three patients pts (37 males, 46 females) from the 120 pts recruited, satisfied the requirements for comparisons and their data were analyzed. In detail: colon (19 pts), breast (18 pts), gastric (13 pts), lung (6 pts), pancreas (3 pts), hematological (3 pts) and head and neck (1 pts), other cancer (20 pts). A personalized nutritional program was required for 61 pts (74,4%). Besides, 42 pts (54%) had a mts disease, malnutrition was reported in 29 of them and sarcopenia in 13 of them. In our sample, 44 pts (53,7%) were overweigh or obeses, and 5 of them had sarcopenia. A very low BMI ($<$21) was reported in pts with gastric, œsophageal, pancreas, head and neck cancer at first evaluation. A low PA (age and sex adjusted) was reported in 25 pts with mts and 10 pts with n-mts. Of 25 pts with mts and low PA, 12 pts passed away. At first evaluation, from the 29 pts with mts that were at risk of malnutrition or malnourished, 11 pts completed the nutritional assessment at 6 months. Of these 11 patients, 6 pts were not malnourished or at risk of malnutrition after 6 months.

Conclusions: The nutritional assessment seems to be required in cancer pts and it should be performed early for pts with gastric, œsophage, head and neck cancer for the high risk of malnutrition as reported in the literature. Our data confirm an improvement of the nutritional status, after a personalized nutritional program in patients that were at risk of malnutrition. PA can be considered a non-invasive indicator of the severity of disease.

T37

DISCOVERED EMOTIONS: A COLLECTION OF AUTOBIOGRAPHICAL TEXTS BY ONCOLOGIC PATIENTS

Bellè M.[1], Pinzi L.[2], Felicetti C.[3], Prior M.[1], Marcon S.[1], Burelli M.[1], Favaretto A.[4]

[1]*Ulss 2 Marca Trevigiana Servizio di Psicologia Ospedaliera, Treviso;* [2]*Ulss 2 Marca Trevigiana Ufficio Stampa, Treviso;* [3]*Ulss 2 Marca Trevigiana Ufficio Relazioni con il Pubblico, Treviso;* [4]*Ulss 2 Marca Trevigiana U.O.C. Oncologia, Treviso*

Background: The Hospital Psychology Service with Medical Oncology Unit promote a program for autobiographical writing to oncologic patients. We think the act of writing offers opportunities for patients to organize and process their thoughts and emotions, finding a new equilibrium as a result of personal growth. Writing is a psychosocial intervention with the aim of reducing psychological distress and a way of processing the experience of an illness in cognitive and emotional terms. The act of writing forces patients to recognize their thoughts and emotions and to express them.

Material (Patients) and Methods: From 2017 to 2019, we organized five groups of patients, 11 participants each, for a total of 56 patients. The median age was 55 years, 32% women and 68% men. During the laboratory, we proposed various types of exercises to help patients express their thoughts and emotions and to share them within the group. We wanted to publish a collection of their works so we asked each component of the group to send us one of their works. Half of the participants (28 subjects) answered our request.

Results: The name we gave to the collection was "Discovered Emotions" and the essays were grouped into six paragraph: "emotions-feels" (which group fear, hope, anxiety, anger), "if I were" (if I were a food or a game), "autobiography" (introspective texts), "the circle with the dot in the middle" (they had to describe what they sensed by a visual stimulus as a circle with a dot in the middle), "letters" (addressed to a celebrity or to someone they care of), "writing" (patient testimonies of the exercise of writing and its significance). Patient texts were integrated with graphic illustrations made by a visual designer who projected and composed the perfect layout for the book, creating original drawings in order to improve the visual end the emotional impact of the work.

Conclusions: Writing has cognitive, emotional and elaborative functions for oncology patients. It is an activity proposed during a particular period of people's lives, a period of illness, during which one can become more susceptible to personal changes but also more creative, more predisposed to new insights. "Discovered Emotions" is a collection of elaboration we want to use to help the process of adaptation of oncologic patients who can identify themselves in the tales and draw inspiration from these.

T38

EVALUATION OF THE ECONOMIC IMPACT OF BODY WEIGHT (BW)-BASED DOSE (3MG/KG) VERSUS FLAT DOSE OF NIVOLUMAB: A SINGLE CENTER EXPERIENCE

Caglio A.[1], Gamba T.[1], Tagini V.[2], Bellero M.[2], Lacidogna G.[3], Vignani F.[3], Sacchi F.[3], Gasco A.L[2], Di Maio M.[4], Fazzina G.[2]

[1]*Dipartimento di Oncologia, Università degli Studi di Torino / AO Ordine Mauriziano, Torino;* [2]*SC Farmacia Ospedaliera, AO Ordine Mauriziano, Torino;* [3]*SCDU Oncologia Medica, AO Ordine Mauriziano, Torino;* [4]*Dipartimento di Oncologia, Università degli Studi di Torino, AO Ordine Mauriziano, Torino*

Background: Nivolumab (N) is approved and reimbursed by Italian Drug Agency (AIFA) in several tumors, including non-small cell lung cancer (NSCLC), head & neck cancer (HNSCC) and renal cell cancer (RCC). Since May 2018, the original schedule (3mg/kg every 2 weeks) - corresponding to the schedule used in pivotal clinical trials

demonstrating treatment efficacy - has been replaced by a flat dose (240 mg every 2 weeks), based on population pharmacokinetic analyses and clinical safety.

In order to optimize our pharmaceutical spending, we conducted an economic assessment to compare the costs of the 2 different schedules, and to estimate the potential economic savings in clinical practice associated with the adoption of a "re-shift" from N 240 mg flat dose to BW-based dose.

Methods: An analysis has been conducted on all N administrations of pts treated between January 2019 and April 2020 in Medical Oncology at Mauriziano Hospital, Turin. For each administration, we calculated the economic gap between the actually administered flat-dose and an hypothetical BW-based dose, keeping 240 mg as the maximum dose for pts > 80 kg. For each administration, we also evaluated the vial residue, assuming no residue for *flat dosage*: a sensitivity analysis has been conducted taking into account the economic value of drug residues.

Results: The analysis included 32 pts, affected by NSCLC (N= 19), RCC (N=6) and HNSCC (N=7), for a total of 237 administrations. Median BW was 67 kg [range 46-115]. From the analysis of all the administrations along the examined period, we calculated that the transition from flat dose to 3mg/kg schedule "with cap" would have allowed a cost reduction equal to 13,16% of the total spending. Sensitivity analysis showed that, even accounting for the drug waste in the calculation, cost savings could be 11,99% of the total spending.

Conclusions: To our knowledge, N 3 mg/kg is the first schedule to be considered off label in oncology despite its use in pivotal trials. Of course, drug price has experienced reductions over the years. However, in a condition of comparable safety and efficacy profile between the 2 different schedules, the "re-shift" from flat dose to BW-based dose could allow a significant cost saving, making the novel therapeutic options more sustainable. In a perspective of prescriptive appropriateness and economic sustainability, the possible waste of drug connected to the use of BW-based schedule could be reduced by a "drug-day" strategy.

T39

ENDOCRINE TOXICITY OF IMMUNE CHECKPOINT INHIBITORS (ANTI-PD-1/PD-L1) IN ADVANCED CANCERS

Dottore A.[1], Ruggeri R.M.[2], Massafra M.[3], Pettineo G.[3], Garipoli C.[3], Giuffrida G.[2], Maisano C.[3], D'Aquino A.[3], Santarpia M.[3], Altavilla G.[3]

[1]Medical Oncology Unit, Department of Human Pathology "G.Barresi", University of Messina, Messina; [2]Endocrine Unit, Department of Clinical and Experimental Medicine, University of Messina, Messina; [3]Medical Oncology Unit, Department of Human Pathology "G.Barresi", University of Messina, Messina

Background: Immune checkpoint inhibitors (ICIs) have changed the therapeutic scenario in cancer treatment, but their use is often associated with immune-related adverse events (IRAEs) involving different organs, i.e. skin, liver, lung, colon and endocrine glands.

We aimed to assess the frequency and management of endocrine IRAEs in clinical practice, in cancer patients (pts) treated with anti-PD1/PD-L1 monoclonal antibodies (mAbs) in a single institution.

Material and Methods: We evaluated a series of pts with advanced cancers, including NSCLC, melanoma, head and neck cancer, renal cell and urothelial cancers, treated with anti-PD1/PD-L1 mAbs in our centre from January 2018 to April 2020.

No pts had received systemic steroid or immunosuppressive therapy prior to the first dose of treatment. We monitored thyroid function (TSH, free T3 and free T4) and thyroid antibodies, blood glucose levels, serum creatinine, liver function, sodium and potassium, cortisol and ACTH, at baseline and during the course of treatment, every 2 cycles. Toxicity was evaluated according to the CTCAE version 5.0. Response to immunotherapy was assessed according to RECIST 1.1 criteria.

Results: We included 61 pts: male/female (84%/16%), median age 65 years (range, 32-81 y), ECOG 0/1 (44%/56%), affected by NSCLC (n=45), melanoma (n=6), head and neck cancer (n=4), renal cell carcinoma (n=5) and urothelial cancer (n=1). They were treated with anti PD-1 mAbs, Nivolumab (35 pts) or Pembrolizumab (22 pts), and the anti-PD-L1 mAb Atezolizumab (4 pts). Immunotherapy was administered as first- (24%), second- (56%) or third-line (20%) treatment.

Within 12-16 weeks from the first dose, we observed grade 1-2 hypothyroidism in 8 pts, of which 5 grade 2 pts required thyroid hormone replacement; 4 pts presented with acute thyrotoxicosis secondary to destructive thyroiditis (immunotherapy was discontinued in 1 for grade 3 toxicity). No one developed autoimmune hyperthyroidism with increased TSH receptor antibodies (TRAb).

There were no cases of hypophysitis and adrenalitis, while 1 pts developed type 2 diabetes mellitus promptly treated with oral hypoglycaemic agents. No correlation was observed between the onset of thyroid side effects and response to treatment.

Conclusions: Thyroid dysfunction is a common AE in pts receiving anti-PD1/antiPD-L1 therapy. Its early recognition, appropriate treatment and monitoring allow continuing ICIs therapy with improved clinical outcomes.

T40

SEX IMBALANCE IN PHASE I CLINICAL TRIALS. FOCUS ON GASTROINTESTINAL CANCER STUDIES

Crivelli F.[1], Montagnani F.[2], Paris M.[2], Perfetti E.[2], Bertolin A.[2], Brioschi D.[3], Tempia P.[3], Leone F.[3]

[1]ASL BI S.C. Oncologia - Fondazione Tempia, Biella; [2]ASL BI S.C. Oncologia, Biella; [3]ASL BI S.S. Psicologia Clinica, Biella

Background: Women continue to be underrepresented in clinical trials, in spite of WHO recommendation.

A poor representativeness of women in clinical trials does not allow to measure differences between men and women in the mechanism of action, metabolism, drug efficacy and potential adverse events of anticancer treatments. Women experience higher rates of adverse drug reactions than do men, due, at least in part, to the fact that women are generally treated with doses extrapolated from studies conducted mainly on men.

We conducted a meta-analysis to address differences in the enrollment in phase I/II clinical trials of gastrointestinal (GI) cancer.

Material and methods: We reviewed all the studies presented at the ASCO GI Cancers Symposium 2020 (n= 923), and analyzed those of Phase I, I/II and pilot studies. Percentage of males and females, mono or multicenter studies, kind of cancer and toxicities divided by gender were retrieved from the abstract . OR for men and women were calculated and pooled using random effect models both for mono and multicenter studies. Sensitivities analyses were also performed.

Results: 38 studies met the desired characteristics and none of these reported gender-specific toxicities. 22 enrolled more males than females, 6 more females, 3 the same number of males and females and for 7 there were no gender data. 23 studies were multicentric and 15 monocentric; 12 treated colorectal cancer, 9 pancreas and biliary tract cancer, 7 all gastro-intestinal cancer, 5 gastric and esophageal cancer, 4 liver cancer and 1 neuroendocrine tumor. On the 1191 patients enrolled, 585 were males and 360 females. In 246 cases sex was not reported. Of the 945 patients, males were 62% and females 38%.

Analysis of all the studies showed a trend towards a greater enrollment of men, but no significant differences were observed, with OR = 1.78 (0.86 – 3.64, p=0.122) in favor of enrolling men. No significant heterogeneity was observed (I^2=0%). Results did not change significantly for mono or multicenter studies. Sensitivities analyses excluding one study at the time and using fixed effects also did not change the results.

Conclusions: Our data suggest that a possible gender-based bias towards men may exists also in phase I/II studies, as the absence of a formal significance is likely due to the small size of studies included. All efforts should be done to minimize it, in order to better assess the efficacy and the safety profile of novel drugs in both sexes.

T41

PROMISING THERAPIES FOR BRAF MUTATED SOLID TUMORS

Sirico M.[1], Bernocchi O.[2], Corona S.P.[2], Strina C.[3], Milani M.[3], Cervoni V.[3], Generali D.[2]

[1]Università Cattolica del Sacro Cuore, Roma; [2]Department of Medical, Surgery and Health Sciences, University of Trieste, Trieste; [3]Breast Cancer Unit and Translational Research Unit, Azienda Socio-Sanitaria Territoriale Cremona, Cremona

Background: Precision medicine, based on molecular and genotyping patients' characterization, is focused on the define specific target treatment for any single solid tumor. BRAF mutation is an oncogenic driver in different cancer types as indicated in the Cancer Genoma Atlas (TCGA). Tumor type agnostic therapy is based on targeting genomic alteration regardless of tumor origin. Within the MOzART Program, we reported two cases related to the use of agnostic target treatment driven by results of NGS using the OncofocusTm Platform (Cambridge, UK).

Clinical results: Case 1 is a chemotherapy refractory BRAF V600E mutated Intrahepatic cholangiocarcinoma (ICC) treated with Vemurafenib and Cobimetinib as third line therapy. The dual BRAF and MEK inhibition resulted in a partial response of 14 months. Moreover, there was an improvement in quality of life (QoL) reducing cancer pain from severe to moderate. Therefore, our patient had partially suspended opioid therapy. **Case 2** is a metastatic chemotherapy refractory Collecting duct of Bellini (mCDC) carrying a BRAF G466A mutation. The patient was treated with Dabrafenib and Trametinib in combination in second line therapy obtaining a stable disease lasting 11 months.

Discussion: Strong evidences on melanoma, colorectal cancer (CRC), non small cell lung cancer (NSLC) and anaplastic thyroid cancer with BRAF mutations responsive to selective BRAF/MEK pathway inhibitors is well known nowadays. VE-BASKET and ROAR basket trial are exploring the efficacy of Vemurafenib and the combination of Dabrafenib/Trametinib respectively in BRAF V600 mutation-positive other solid tumors. Studying the relationship between target therapy and molecular aberration in tumors, the NGS findings supported our decision to treat, in a clinical trial, BRAF mutated cancers with a very poor prognosis with BRAF and MEK inhibitors.

Conclusions: Our results confirm the emerging evidences of molecular tumor profiling for the successful management of solid tumors. Moreover, they highlight the role of the BRAF mutation as a targetable driver in cancers especially in whose with poor prognosis and/or no available systematic therapies with a clear clinical benefit.

T42

MEDICAL RECORDS AND SOURCE DOCUMENTS FOR CLINICAL TRIALS IN ITALY

Stabile S.[1], Taverniti C.[2], Testoni S.[3], Federici I.[4], Guarrera A.[5], Monti M.[3], Cagnazzo C.[6]

[1]SC Oncologia Falck, Ospedale Niguarda, Milano, Italy, Milano; [2]Oncologia Medica 1, AOU Città della Salute e della Scienza, Torino, Italy, Torino; [3]Unità di Biostatistica e Sperimentazioni Cliniche, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy, Meldola; [4]Clinica di Ematologia, AOU Ospedali Riuniti Umberto I, G.M. Lancisi, G. Salesi, Ancona, Italy, Ancona; [5]Terapie Cellulari e Medicina Trasfusionale, AOU Careggi, Firenze, Italy, Firenze; [6]Unità di Ricerca e Sviluppo Clinico S.C. Oncoematologia Pediatrica, AOU Città della Salute e della Scienza - Presidio Ospedaliero Infantile Regina Margherita, Torino

Background: In the last decade, patient's medical records have undergone significant changes: progressively moving from the traditional paper version to the digital one. The consequently increasing importance of digital information technology brought to the implementation of Electronic Medical Record (EMR). The digitalization process proceeds and will lead in the next future to the complete replacement of paper-based documents with full-digital medical records. In this context, ICH-GCP R2 and EU GMP Annex 11 have established the basic requirements for validated EMR systems to preserve integrity and security of data, as well as to define the prerequisites of source documents for clinical trials.

Methods: The Italian Group of Data Managers (GIDMcrc) has spread among the professionals involved in Italian clinical research an online survey aimed to review the characteristic of medical records and source documents used at the experimental sites.

Results: The survey has been filled by 118 professionals (112 study coordinators, 2 quality assurance, 4 others), mainly coming from public hospitals (42,7%) followed by university hospitals (22,3%), public IRCCS (20,39%) and private IRCCS (12.6%). The majority of sites have a mixed digital-paper source documents system (66,0%), while a totally paper system is present in 27,2%, and only the 6,8% have a full digital source documents system. Only 59,2% of the centres has an organized EMR, but just in the 32,8% of these EMR is validated according to ICH-GCP R2 and GMP annex11.

Despite the presence of digital source documents and EMR, the Source Documents Verification (SDV) is carried out on paper certified copies in 60,8% of these sites, in 11,8% on electronic record by the CRA together with the study coordinator and only in 10,7% the CRA has a direct access to electronic source documents/EMR.

Conclusions: This survey highlights the great heterogeneity between experimental sites on their actual level of digitalization. Most of the Italian sites has an organized EMR, although often does not achieve the validation according to GCP and GMPannex11. This situation leads to a prevalence of mixed electronic/paper source documents system against full paper and full electronic system. Furthermore, in most of the cases the SDV is carried out on paper certified copies. This data suggests how digitalization is a currently ongoing process, which still needs more investments and time to achieve the completion, conforming to quality requirements.

T43

"NEW LIFE" LILT PROJECT: RECOVERING THE PSYCHOSOCIAL WELL-BEING OF CANCER PATIENTS

Carrozza F.[1], Farina P.[2], D'Addario D.[2], D'Aulerio M.[3], Spina C.[3], Iorio E.[3], Scipioni M.[3], Antonecchia P.[3], Bellomo M.[3], Carfagno G.[3], Fabrizio G.[3], Trivisonne R.[4], Sbrolla B.[4], Giorgi F.[5], Cicconi A.[4], Di Battista S.[4], Franchella C.[3]

[1]D.H. Oncology S. Timoteo Hospital-ASReM, Termoli (CB); [2]D.H. Oncology S. Timoteo Hospital-ASReM, Termoli; [3]LILT Campobasso Provincial Association, Termoli; [4]LILT Ascoli Piceno Provincial Association, Ascoli Piceno; [5]D.H. Oncology "Madonna del Soccorso" Civil Hospital - ASUR Marche S. Benedetto del Tronto (AP), S. Benedetto del Tronto (AP)

Background: The following study aimed to improve the quality of life of cancer patients undergoing cancer treatment or cancer follow-up through the integration of a psychosocial rehabilitation pathway, and students of high school of Larino (CB) and Ascoli Piceno (AP) involved for the project's didactic part on the relationship between nutrition, physical activity and tumours, and encourage voluteering initiatives.

Patients and Methods: The study involved 225 pts with cancer disease of the Termoli and San Benedetto oncological D.H., 115 and 110 pts, respectively. Pts were included in this longitudinal observational study on a voluntary basis, upon signing an informed consent. A *"Newlife"* IT database was created for collecting data through a dedicated oncology desk. Psychological and nutritional assistance was offered to the involved patients. Psychological assessment of the pts was performed through Psychological Distress Inventory (PDI), Need Evaluation Questionary (NEQ) questionnaires, clinical interviews. Nutritional assessment was performed through Mini Nutritional Assessment (MNA) screening questionnaire and subsequent evaluations. Parameters such as body mass index (BMI), phase angle (PA) and bioelectrical impedance analysis (BIA) were recorded. A satisfaction questionnaire was administered to all 225 pts.

Results: All the pts (147 women, 78 men, average age: 63, range 31-89) were involved from November 2018 to December 2019. The most frequently reported pathologies affected breast (75 pts) and colorectal cancer (41 pts). At the time of recruiting, 123 pts were in active treatment for metastatic disease, 50 pts in adjuvant cancer treatment, and 52 pts in follow up. Among all the pts involved, 193 pts completed a PDI and NEQ questionnaires. Among the pts completing the PDI, 57 pts reported severe distress (>35). The most urgent needs the NEQ detected concerned communication and information on the disease status. A very low BMI (<21) was reported in pts with head-neck, gastric, pancreatic and oesophageal cancer. Experiential and laboratory activities were realised for pts and their families and creative activities were also carried out at schools.

Conclusions: The study has allowed to identify the needs of pts and to activate the psychological and nutritional service in the target hospitals. All the pts involved appreciated the service. Currently follow-ups are done using smart-working or by phone and mail for the COVID-19 emergency.

T44

TRANSLATE: ACTIVATION OF IMMUNE RESPONSE IN REFRACTORY PATIENTS TO STANDARD TREATMENT

Abbona A.[1], Garrone O.[2], Falletta A.[1], Fea E.[2], Paccagnella M.[2], Lo Nigro C.[3], Gammaitoni L.[4], Vanella P.[2], Monteverde M.[2], Granetto C.[2], Occelli M.[2], Denaro N.[2], Merlotti A.[2], Reali A.[2], Sangiolo D.[4], Merlano M.[2]

[1]Department of Traslational Oncology, Ospedale S.Croce e Carle Cuneo, Cuneo; [2]Ospedale S.Croce e Carle Cuneo, Cuneo; [3]E.O. Ospedali Galliera, Genova, Genova; [4]IRCCS Candiolo Institute, Turin, Torino

Background: The TRANSLATE exploratory study tests changes of cytokines over treatment with metronomic cyclophosphamide, daily low dose of IL-2 every other week, and 8 Gy single fraction RT (self vaccination) in end-stage solid tumors.

Patients and methods: Patients with end stage tumors with no further standard treatment available were eligible. A panel of 17 cytokines was analysed. Plasma concentrations were assessed at baseline (T0), day 8 (after RT) (T1), day 28 (T2), and at disease progression (PD) (T3), using Simple Plexsystem (ProteinSimple, USA). Patients were divided in two groups depending on the time of PFS (group A$<$3 months, group B$>$3 months). Values at each time points were compared and correlated to outcome. P$<$0.05 was considered for statistical significance.

Results: 23 patients with breast, colon, kidney and prostate cancer were enrolled. IL-2 progressively increased from T0 to T2 (T0-2 P$<$0.001; T1-2 P=0.002) and decreased at T3. IL-5 progressively increased from T0 to T2 (T0-2 P=0.005; T1-2 P=0.049) and decreased at T3 (T2-3 P=0.048). IL-8 remained stable along the treatment but increased at T3 (T0-3 P=0.057; T1-3 P=0.022; T2-3 P=0.018). CCL-4 decreased from T1 to T2 (P=0.040) but increased at T3 (P=0.008). IFN-γ progressively decreased from T1 to T3 (T1-3 P=0.026; T2-3 P=0.034). VEGF performance differed between group A and B: while it remained stable in group B, increased from T0 to T1 in group A. However, considering all together, VEGF increased at T3 compared to T0 (T0-3 P=0.022). Using ROC analysis at T0 we identified cut-off values for IL-2, IL-12, and CCL-2. Using them, we observed a significant improvement in PFS in patients with values of IL-2 and IL-12 higher than their respective cut-offs and with CCL-2 lower than its cut-off (HR 0.33, P=0.03; HR 0.32, P=0.029; HR 0.37, P=0.049; respectively). We performed a multivariate analysis coupling these three cytokines two by two. Only IL-2 and CCL-2 remained associated with PFS.

Conclusions: The small number of patients limits the interpretation of our results. However, our data suggest that IL-2 and CCL-2 might predict good and poor PFS respectively.

T45

WHEN A DOCTOR BECOMES A PATIENT: AN OVERVIEW OF AN ATYPICAL POINT OF VIEW

Donisi C.[1], Massa E.[1], Liscia N.[2], Lai E.[1], Tolu S.[2], Pireddu A.[2], Balconi F.[1], Persano M.[1], Mariani S.[1], Pinna G.[1], Impera V.[2], Musio F.[1], Dubois M.[1], Migliari M.[1], Spanu D.[1], Saba G.[1], Pretta A.[2], Sancassiani F.[1], Carta M.G.[1], Madeddu C.[1], Scartozzi M.[1]

[1]Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy, Cagliari; [2]Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari, Italy, Cagliari

Background: In 2018, were reported 18,078,957 new cancer cases worldwide. Cancer does not spare doctors but there is a lack of data in the literature on this topic. Thus, an open prospective study was conducted. Its primary endpoint was to evaluate in a sample of doctors becoming cancer patients how their medical background influences some aspects of their life. The secondary endpoint was to validate a questionnaire based on the collected answers.

Material and Methods: An open interview was administered to them by an interviewer (table 1). Table 1. Topics explored in the open interview: How being a doctor influenced the cancer diagnosis? What was your reaction to the diagnosis? Had you looked into the staging, the prognosis, and the therapies of your cancer? How did you choose the oncologic team? Did you receive support from your family, friends, and colleagues? Were you concerned about the loss of your privacy? Had you lost interest in your job? Did you realize that you're not able to do the same job as before? How did you react? Had you been demoted? Were you forced to do it? Did you become more sympathetic with your patients? Did you become more sensitive to unfair behavior towards the patients? Were you a victim of discrimination as a patient? Did your work planning change? Did your consideration of your private life change?

Results: From April to May 2020, ten doctors becoming cancer patients were enrolled, mean age 57,2 years (range 39-79), M/F 4/6 with the following tumors: lung cancer 1, prostate cancer 2, breast cancer 4, melanoma 1, thyroid cancer 1, ovarian cancer 1, colon-rectal cancer 1. One patient had two primary cancers. Their medical specialty was: orthopedic surgeon, general practitioner, endocrinologist, physiatrist, oncologist, anesthetist, geriatrist, gastroenterologist, and doctor of public and environmental health. All patients at the time of diagnosis were actively employed and working. From the collected answers, it turned out that all patients were sure about the choice of the oncologic team and none of them asked for a second opinion; 70% of patients were aware of their inability to work as before cancer. Consequently, the

work planning is lacking, whereas the consideration of the private life changes for the best for all patients.

Conclusions: These preliminary data, although relative to a very small sample, provides promising prerequisites to attain a questionnaire to validate for the use in clinical practice. The study is ongoing.

T46

INDIVIDUAL NUTRIZIONAL COUNSELING IN CANCER PATIENTS DURING FOLLOW-UP PERIOD: FIRST OPPORTUNITY FOR THE PRACTIOTIONER TO REDUCE RISK FACTORS

Cervo G.L.[1], Alberti B.[1], Salerno L.O.[2], Di Pinto G.[1]

[1]Oncologia Medica - Spoke Castrovillari - ASP Cosenza, Castrovillari; [2]Oncologia Medica - Spoke Paola - ASP Cosenza, Paola

Background: Nutritional counseling during follow-up visits can represent a valid opportunity to investigate lifestyle and dietary habits of cancer patients in order to propose nutritional indications for a reduction of the potential risks of relapse. The main objective is to modify the lifestyle of colo-rectal and breast cancer patients in follow-up through a weight management. The aim of this study was to investigate the effect of individual dietary counseling of colo-rectal and breast cancer patients during a 2 year follow-up period.

Materials and Methods: The study has been conducted on 135 colorectal and breast cancer patients of both sexes consecutively recruited from the oncology unit during their first follow-up visit in the period between november 2017 and november 2019. An anamnestic questionnaire about dietary habits and lifestyle were administred and the main anthropometric measurements (weight, height, waist and hip circumferences, bmi) were assessed. All patients received two type of interventions: standard reccomendations about healthy lifestyle and nutritional counseling based on mediterranean diet. Patients were stratified in 4 groups according to the WHO BMI classification.

Results: Among 76 colorectal cancer patients, 9% had underweight, 33% had normal weight, whereas an overweight and obesity was detected in 19% and 39%. Among 56 subject in the breast cancer group bmi was respectively 0%, 21%, 14% and 65%. At the second follow-up visit, patient with colorectal cancer showed a reduction of overweight and obese (14% e 5%) group and a median reduction of waist measurements di 9 cm (3-29 cm). For breast cancer patients, the reduction of overweight and obese groupe was 3% and 15% and the waist circumferences showed a median decrease of 10 cm (3-25cm). Furhter analysis of other antropometric parameters are underway.

Conclusions: There is a strong body of evidence regarding the relation between dietary behaviors, body mass index (BMI), tumors and risk of relapse. An individual nutritionalcouseling, targeted to weight management and to risk factors control, may represent an important moment for cancer patients at the follow-up visit focusing the relationship between dietary habits and risk of relapse.

T47

SAFETY AND EFFICACY ASSESSMENT OF IMMUNOTHERAPY IN ELDERLY CANCER PATIENTS WITH TUMOURS AT DIFFERENT SITES: A SINGLE-CENTER RETROSPECTIVE, OBSERVATIONAL STUDY

Liscia N.[1], Donisi C.[2], Lai E.[2], Tolu S.[3], Mariani S.[2], Balconi F.[2], Pireddu A.[3], Camera S.[3], Persano M.[2], Musio F.[2], Impera V.[1], Pretta A.[1], Pinna G.[2], Spanu D.[2], Dubois M.[2], Saba G.[2], Astara G.[2], Atzori F.[2], Madeddu C.[2], Massa E.[2], Scartozzi M.[2]

[1]Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari, Italy, Cagliari; [2]Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari Italy, Cagliari; [3]Medical Oncology Unit, Sapienza University of Rome-University Hospital and University of Cagliari, Cagliari Italy, Cagliari

Background: Immunotherapy (IT) is nowadays a validated treatment option for several tumours. As for elderly patients (pts), there is a lack of data in the literature about the use of immune checkpoint inhibitors. Elderly pts are characterized by immunosenescence that may lead to immunodepression, so IT should be assessed also in this population. We conducted a retrospective observational study in pts over 65 receiving IT.

Material (patients) and Methods: We retrospectively collected clinical data of pts over 65 with different tumour types treated with IT at the Medical Oncology Unit of Cagliari University Hospital (March 2016-February 2020). Our study aimed to assess the safety and efficacy of IT in the study population. Statistical analysis was performed with MedCalc (survival distribution: Kaplan-Meier method; survival curves comparison: log-rank test).

Results: Globally, 33 pts were included in our analysis, 24 males and 9 females; the mean age was 77,4 (range 66 – 88). 82% of pts had multiple comorbidities. 19 pts had lung cancer, 8 melanoma, 5 kidney cancer, and 1 urothelial cancer. 15 pts received pembrolizumab, 2 atezolizumab and 16 nivolumab. 12,1% of pts showed grade 3 (G3) immunotherapy related adverse events (IrAEs) leading only to temporary IT interruption (1 cutaneous toxicity, 1 arthritis, 1 pneumonia, 1 xerostomia). 42,4% of pts had G1 and G2 IrAEs (14,3% concomitant G1-G2). 1 of pts presented arthritis, 5/14 rash, 2/14 hepatitis, and 6/14 thyroiditis. Complete response was observed in 3,03% of cases, stable disease in 42,4%, partial response in 27,3%, and progression disease in 27,3% of cases. Within the 31st

of May 2020, median progression-free survival (mPFS) was 18,1 months (m) (range 4 – 43) and the median overall survival (mOS) was 41,2m (range 4 – 184). 23 pts are still receiving IT whereas 7 died. IrAEs were correlated both with longer OS (mOS not reached -NR versus -vs 49 m in pts without IrAEs - 95%CI:27-60; p=0,0014) and longer PFS (mPFS NR vs 26 m -95%CI: 9-35 m; p=0,0462). Pts with melanoma and kidney cancer had longer PFS (mPFS: NR) than lung and urothelial cancer (mPFS: 25 m and 3 m, respectively).

Conclusions: Even if retrospective and with small sample size, our study suggests that IT is effective, safe, and well-tolerated by elderly pts in the same way as in adult pts, as confirmed by available literature data. The immunosenescence didn't affect the efficacy and the onset of IrAEs.

T48

PERSONALITY FACTORS, FAMILY DYNAMICS AND RISK OF PSYCHOLOGICAL DISTRESS IN ONCOLOGICAL GENETIC COUNSELING BRCA 1-2

Moschetto M.[1]

[1]A.O.U. Policlinico Vittorio Emanuele - U.O Oncologia Medica, Catania

Backgroud: Oncological genetic counseling (CGC, NSGC, Resta et al., 2006), in Italy since 2013 called CGO (Oncological Genetic Counseling, AIOM, SIGU, 2013), identifies genetic mutations for hereditary neoplastic disease. To date, literature is scarce in relation to the psychosocial factors that characterize patients who follow this path. A deeper understanding would take on clinical relevance in order to identify patients at risk of negative effects subsequent (or previous) to the test and implement consultancy protocols that minimize these effects by also providing tailored psychological support interventions (Lerman, 2008). The present observational study is part of this context with the aim of describing a psychological profile that distinguishes the patient with breast and / or ovarian cancer with previous individual and / or family history of disease accessing the CGO. SAMPLE: In the CGO outpatient clinic of the A.O.P.V.E. of Catania 87 SS were recruited (average age = 48.2; interval 22-64;) with a diagnosis of breast K (N = 35) and / or ovary (N = 10). The present study was conducted during the first preliminary interview of the CGO course.

Material and Method: Each patient underwent a preliminary interview followed by a semi-structured interview during the pre-test consultation and subsequently, in the form of a self-report, he completed the SCL-90-R (Derogatis, 1994); the BFQ (Caprara et al. 1993), the FACES IV (Olson, 2007).

Results: Research is still ongoing. Preliminary data show a tendency towards psychosocial vulnerability correlated with age, family cohesion, cognitive flexibility, experiences of anxiety and depression.

Conclusions: From the comparison with the general population (T-Test for homogeneity), a greater tendency emerges to develop a condition of distress that could interfere with the entire path of the CGO, especially in the process of understanding information; in sharing the outcome to the family context; in choosing between a clinical surveillance pathway vs surgical prophylaxis. Personalized and integrated psychological pathways could therefore represent a protective factor for the well-being of patients who access CGO.

T49

SCALP-COOLING DEVICE TO PREVENT ALOPECIA IN WOMEN RECEIVING CHEMOTHERAPY FOR BREAST OR GYNECOLOGIC CANCERS

Ghidini A.[1], Ferrari D.[1], Cerioli C.[1], Savorana R.[1], Vas L.[1], Viadana S.[1], Bukovec R.[1], Crepaldi C.[1], Roncari L.[1], Pancera G.[1]

[1]Casa di Cura Igea, Milano

Background: Alopecia is a very important side effect for women treated with chemotherapy. Scalp-cooling may reduce hair loss during treatment for cancer.

Patient and methods: Paxman scalp-cooler is a device available in our Institution from 2017. We prospectively collected data of patients receiving chemotherapy for breast and gynecologic cancers. Scalp-cooling was performed with temperature of -4°C from 30 minutes before chemotherapy until 100 minutes afterwards. Efficacy and safety of the device were reported in medical records; alopecia was graded according to CTCAE v.5.0.

Results: From September 2017 to April 2020 we collected data of 50 patients; median age was 55. 94% were breast cancer: 8 women were treated in neoadjuvant and 38 in adjuvant setting with 4 cycles of doxorubicin and cyclophosphamide (1 patient also paclitaxel, another patient carboplatin and paclitaxel, another one paclitaxel plus trastuzumab). Median scalp-cooling cycle were 3,5 (range 1-4). 7 patients stopped use of the cap because of intolerance like headache, cold sensation and neck pain. 9 patients had to use a hair wig. Rate of success was 62% (4 patients without alopecia and 27 patients with alopecia G1).

Conclusions: Our data suggest that use of device scalp-cooler like Paxman reduce alopecia in more than half of women treated for breast or gynecologic cancers, with good tolerability.

T50

CHECK POINT INHIBITORS' TREATMENT IN REAL WORLD SETTING

Filipazzi V.[1], Gambaro A.[1], Ferrario S.[1], Cona S.[1], Rota S.[1], Tosca N.[1], Dalu D.[1], Fasola C.[1], Somma L.[1], La Verde N.[1]

[1]ASST-FBF-SACCO, Milano

Background: Immune ceck-point inhibitors (CKi) are playing a central role in the management of many cancers. The experiences of patients and physicians in routine clinical practice is often different from those in trial setting. This study presents data from a group of consecutive patients in real world setting.

Material and Methods: From 2018 to 2020 all consecutive patients with indication of CKi therapy were enrolled. We record age, PS, PDL-1 expression, smoking status, site of cancer, treatment planning, response, toxicity and survival.

Results: Fifty-two patients were enrolled, 43 NSCLC (32 ADK + 12 SQM) 5 Kidney, 2 bladder and 2 breast cancers, Median Age was 68 y. (range 41-83), 38 Male and 14 Female, no smokers were only 10%, PDL-1 score was 1-49% in 20 pts and negative or unknown in other 32, ECOG score was 0-1 in 44 pts and 2 in 8 pts. Four pts present second synchronous tumors (2 Colon, 1 HCC, 1 Pancreas), and 2 pts suffered by HIV infection. N/L ratio > 3 is present in 13 pts and LDH over normal values in 14 pts. Nivolumab was administered in 27 pts, Pembrolizumab in17 pts and Atezolizumab in 8 pts, while 20 pts, 8 with brain lesions, underwent palliative RT. Duration of treatment was < 6 m in 18 pts, 6-12 m in 24 pts, 12-24 m in 5 pts and > 24 min 5 pts. Recist' evaluation after 3 months of therapy revealed 13 PR+ 20 SD+ 19 PD with a DCR of 63%. In the NSCLC the DCR is 27/43; 80% in 20 PDL-1 positive pts and 49% in 23 negative ones. Overall Survival at 12 m. is 41%; OS at 24 m. is 23%. Treatment continued beyond progression in 4 pts because clinical benefit. Adverse Effects of any grade were reported in 20 pts (39%), while in six pts (12%) G3/4 AE as pneumonia, mucositis, muscle pain, adrenal failure and iper PD were responsible to stop therapy, 5/6 AE occoured in Nivolumab pts.

Conclusions: Our data confirm the efficacy of CKi in the management of advanced cancers, specially in NSCLC when PDL-1 score is present (DCR 80%), but we record a worse toxicity (12%) than expected from clinical trial.

T51

PRELIMINARY DATA ON THE USE OF PAXMAN SCALP COOLING DEVICE TO PREVENT ALOPECIA FROM CHEMOTHERAPY IN ASREM ONCOLOGY CENTERS

Calista F.[1], Musacchio M.[1], Specchia M.[1], Traficante D.[2], Carrozza F.[3], Assalone P.[2], Tomei F.[2], Domenica D.[3], Piscopo A.[1], Cefalogli C.[2], Farina P.[3], Giglio G.[1]

[1]Azienda Sanitaria Regionale del Molise - UOC Oncologia Campobasso, Campobasso; [2]Azienda Sanitaria Regionale del Molise - UOS Oncologia Isernia, Isernia; [3]Azienda Sanitaria Regionale del Molise - UOS Oncologia Termoli, Termoli

Background: Alopecia is one of the most common side effects caused by chemotherapy. It has a strongly negative impact on the quality of life of cancer patients, regardless of gender and age, but women are most affected; it is experienced as a decrease in beauty and sensuality and induces a change in one's body image. It is also experienced as a continuous demonstration of one's illness, altering social relationships; this physical and emotional problem can also lead to less adherence to chemotherapy treatments. Scalp cooling with the use of the Paxman scalp cooling device system has proven to be effective in preventing or reducing this problem, reporting success rates of around 60%. We present the preliminary data of the first 4 months of use of this device at the 3 ASReM Oncology Centers in our region.

Patients and methods: Between January and April 35 women were treated (30 with breast cancer, 5 with gynecological cancer), with an average age of 57 years. CTCA version 5.0 was used to evaluate the results in terms of hair loss. All patients are treated with polychemotherapy regimens containing anthracyclines and / or taxanes.

Results: 7 patients (20%) stopped treatment for intolerance (5) or headache (2). Of the 28 evaluable patients, all still on treatment, 4 (11%) are not yet evaluable because they have just started treatment, 1 had G2 toxicity (3%), 23 (66%) an alopecia G0 or G1. At the moment, all patients treated with Paxman scalp cooling device are satisfied with the presence in terms of tolerability. The most frequently reported side effects were the feeling of cold and migraine. The results we obtained are in line with the studies published so far and patient satisfaction supports the usefulness of the Paxman device to prevent hair loss during chemotherapy. Maintaining the low temperature before and after chemotherapy forces patients to stay longer in the ward (about 2 hours, depending on the scheme used), representing a limit to the use of the device.

Conclusions: The use of Paxman equipment represents in any case an added value offered by our departments in order to improve the quality of life of our patients thus promoting the maintenance of normal social relationships

T52

DENOSUMAB (DMAB) AND OSTEONECROSIS OF THE JAW (ONJ)

Belloni P.[1], Pelliccioni M.[1], Toniolo D.[1], Candido P.[1], Cozzi C.[1], Bollina R.[1]

[1]ASST-Rhodense- UO di Oncologia Medica, Rho, Milano

Osteonecrosis of the jaw (ONJ) is characterized by unexpected appearance of necrotic bone in the jaw (70%), the maxilla (30%) or other bone (10%). This condition occurs in cancer patients receveing biphosphonates (BP) or Denosumab (DMAB) for bone metastatic lesions. Predisposing factors for this adverse event include cancer condition and cancer comedications (chemotherapy, steroids, hand and neck irradiation). An interdisciplinary team

was organized and measures of screening and prevention were adopted: informative letter to family doctor, panoramic radiography and dental examination.

Objectives: This analysis evaluate an unselected cancer patients frequency and risk factor or comorbidities that could lead DMAB associated ONJ.

Results: Since November 2017 to march 2020 we evaluated 78 patients: 29 M and 49 F; median age 66 (range 31-81). Most oncologic diagnoses included breast cancer (20%), NSCLC (30%), SCLC (10%), prostatic cancer (20%) and others (20%). Patients were analyzed according to demographic, oncotypes, concurrent medications and duration of DMAB therapy.

Conclusions: We have found 2 (1.5%) new cases of ONJ: 2 NSCLC and 1 breast cancer and in all patients the lesion was found in the mandible. Presentation symptom was pain and the most common found risk factors were prolonged duration of DMAB therapy and concurrent corticosteroid use. ONJ is rare in patients treated with DNSB but in any case is a serius complication for oncological patients and requires an accurate diagnosis and an appropriate therapy. Prevention measures and patients education seem to decrease ONJ risk.

T53

CORRELATION BETWEEN FATIGUE, PAIN SYMPTOMS AND BMI IN IMMUNOTHERAPY IN SOLID TUMOURS

Fontana A.[1], Rossi L.[2], D'Assisi Cardillo F.[3], Angelini F.[4], Tomao S.[5], Gozzi E.[2]

[1]*Ospedale Santa Maria Goretti, Latina;* [2]*Università la Sapienza di Roma, Aprilia;* [3]*Ospedale Dono Svizzero, Formia;* [4]*Ospedale Regina Apostolorum Albano laziale, Albano;* [5]*Università la Sapienza di Roma, Roma*

Background: Fatigue is one of the main symptoms in cancer patients. In most cases its etiopathogenesis is multifactorial or treatment-related with unknown pathophysiologic abnormalities. However, several factors can contribute to cancer-related fatigue (CRF) such as: anemia, pain, insomnia, depressive symptoms, and elevated BMI.

The aim of our study was to evaluate CRF and its correlation with pain symptoms and BMI in immunotherapy in solid tumours.

Patients and methods: We enrolled 93 patients (pts) with advanced solid tumours treated with immunotherapy. 80 pts (86%) had non-small-cell lung carcinoma (NSCLC), 4 (4.3%) had renal cell carcinoma (RCC) and 9 (9.6%) bladder cancer. Mean age was 70 years (range 48-82). We used a simple visual analog scale (VAS) with anchors of 0 and 10 (with 0 as no fatigue and 10 as the worst imaginable fatigue) to evaluate CRF. Pts were divided into groups based on CRF value: mild (0-3), moderate (4-6) severe(7-10). Then we correlated CRF with pain symptoms (presence or absence) and BMI (< 25 or >25).

Results: 27/93 pts (29%) had mild CRF, 54/93 (58%) moderate and 12/93 (12.9%) severe. Regarding mild CRF, 9 pts (33.3%) had pain symtoms, 15 (55.5%) BMI >25. Regarding moderate CRF, 48 pts (88.8%) had pain symptoms, 46 (85.1%) BMI> 25. Pts with severe CRF, 9 (75%) had pain symptoms and 10 (83.3%) BMI>25.

Conclusions: Our results suggest that in pts with advanced solid tumours treated with immunotherapy, moderate and severe fatigue is associated with greater pain symptoms and elevated BMI.

T54

A SOURCE OF MORTALITY DATA TO BROADEN THE TERRITORIAL KNOWLEDGE OF THE ASL NAPOLI I CENTRO. EPIDEMIOLOGICAL STUDY ON THE PALLIATIVE HOMECARE IN CANCER TO CREATE RISK MAPS OF THE TERRITORY AND DEVELOP PREVENTION PLANS

Rossiello R.[1], Sorrentino I.[2], Maddalena A.[2], Gallo P.[2], De Sangro C.[2]

[1]*Ospedale S.P.S. San Gennaro di Napoli, Napoli;* [2]*Ospedale S.P.S. San Gennaro di Napoli, Napoli*

Bckground: Over the past decade there has been a profound epidemiological and clinical change in patients, especially in areas considered "polluted"; the appearance of tumors, aggressive and at an earlier age and the increase in the possibility of treating oncological pathologies has brought with it the growth of patients in "partial remission" which often become more complicated over time, leading to cases of "incurability" which open space to the typical issues of palliative medicine.

Matherial and Methods: A database of 485 cancer patients being treated at the UOSD Palliative Home Care, who died in 2018, was taken into consideration. The variables used are the following: 1) General data regarding patients, workload and its distribution; 2) Specific data concerning the setting of palliative therapy; 3) Pain and its evaluation (pain evalutated according to NRS scale); 4)"Risk Areas" (geographical areas limited to roads or neighborhoods for tumor mapping).

Results: An analysis of the Mortality data revealed:

– The prevalence of lung and colon cancer in the area adjacent to the Pianura landfill is relevant, for example we have found cases of cancer in different patients coming from the same ways of residence. Given the highest prevalence of advanced tumors in the non-elderly age = 64 years.

– We also found an increase in so-called "emerging" tumors, with a higher prevalence than in previous years, and for this reason we compared the cases of liver cancer with Glioblastoma. On the one hand we

can say that the cure for hepatitis C has certainly reduced the numbers of liver tumors (at least primitive tumors). On the other hand, we have found that cases of Glioblastoma, perhaps related to electromagnetic pollution, are more frequent in areas characterized by a rich presence of antennas and repeaters, see for example the area around the San Stadium Paul.

– The tumor associated with a higher level of pain and difficult to control by therapies is lung cancer. Better results for pain control are generally obtained, especially for this type of tumor, with the association of drugs for cancer pain with drugs for neuropathic pain (anticonvulsant).

Conclusions: Knowing in which area the highest prevalence of a tumor is concentrated, it is possible to act preventively on risk factors, monitor the trend in the following years to see if the preventive actions have been effective.

T55

ONCOLOGY ORIENTATION CANCER CENTER (CORO): THE FUNCTIONAL STRUCTURE TO REDUCE SANITARY MIGRATION - AN APULIAN EXPERIENCE

Ciccarese M.[1], Leo S.[2], Surico G.[3], Attolini E.[4], Benvenuto M.[5], Carbone A.[4], Maiello E.[6], Moschetta A.[7], Pisconti S.[8], Cinieri S.[9], Gorgoni G.[4]

[1]Ospedale Vito Fazzi-Lecce, Lecce; [2]Ospedale V. Fazzi, Lecce; [3]Ospedale "Miulli", Acquaviva delle Fonti; [4]ARESS Puglia, Bari; [5]Università del Salento, Lecce; [6]Ospedale P. Pio da Pietralcina, S. Giovanni Rotondo; [7]Università "A. Moro" di Bari, Bari; [8]Ospedale "S. G. Moscati", Taranto; [9]Ospedale "A. Perrino", Brindisi

Background: In 2019 on behalf of ROP (Rete Oncologica Pugliese), a new functional structure was created, named COrO (Centro Orientamento Oncologico), the Orientation Cancer Center, aimed at reducing the movement of patients outside the Region due to disinformation about the available skills in cancer care inside the Region.

Materials and methods: The COrO structure in Apulia has been defined by a sanitary resolution of The Regional Agency for Social and Health development (ARESS), assessing functions and mission of 18 COrO's. They are monitored through two kinds of indicators: *logistic-organizative,* including 20 items, covering from the location of COrO to dedicated booking slots, to speed up the reach of diagnosis; *activity* ones, such as fraction of patients entering COrO structures and elapsed time before for reaching the multidisciplinary board.

Every three months activity indicators are verified for each COrO through global calls. The transmission of data from Coro structure and the incremental value during time from October 2019 until April 2020 was available for about 17 COrO's out 18 and will represented during meeting.

Results: Indicators are available from 12 COrO's out of 18. We represent the percentage of adherence to Criteria at a data cut off of 12-2019, Tab 1. Tab 1: Adherence of COrO to Criteria-data cut off 12-2019

12 COrO's are fully operating; differences in indicators are due to temporary staff problems or to underreport of data related to treated patients coming directly from surgery.

Conclusions: The COrO structure is the main functional structure on behalf of Apulian Cancer networks. This organization insured a strong collaboration among all Regional cancer centers, which shared the motivations behind the proposal, even in absence of a dedicated funding. The safety and centrality of patients is evident by the fact that they are addressed from the very beginning to the most appropriate Regional cancer center for their specific pathology. This brings along the reduction of the risk of sanitary errors and dumps the wandering across hospitals, inside and outside the Region.

COrO	Logistic-organizative	Activity
"Moscati" – Taranto "Miulli" - Acquaviva delle Fonti Lucera (San Severo) IRCCS-Bari "V. Fazzi" – Lecce	100%	100%
Card. Panico –Tricase (LE) San Giovanni Rotondo (FG) Riuniti di Foggia Policlinico Bari	100%	66%
Castellaneta (TA)	33%	66%
"A. Perrino" – Brindisi Francavilla Fontana (BR)	66%	66%

U - Oncology Nursing

U01*

BOVINE COLOSTRUM IN ORAL MUCOSITIS

Guberti M.[1], Botti S.[1], Caffarri C.[1], Piredda M.[2], De Marinis M.G.[2]

[1]Azienda USL-IRCCS, Reggio Emilia; [2]Università Campus Bio-Medico, Roma

Background: Oral mucositis (OM) is the worst complication for adult hematological patients undergoing pre-transplant ablative chemotherapy, in which it has an incidence between 40 and 80%, which in addition to causing an increase in infectious risk, nutritional deficiencies and intense pain, affects the quality of life of patients, who report states of anxiety, depression and mood disorders in relation to their experience, delays recovery times due to the difficulty in maintaining dose-intensity and finally increases costs.The guidelines for the prevention and treatment of OM in this population contain specific recommendations, but supported by weak evidence or not applicable

in all contexts or finally by studies with methodological bias. The use of bovine colostrum seems to represent an important opportunity to prevent and / or limit the appearance of OM. Colostrum is the "milk" secreted during the first few days after childbirth important for the health of newborns. It contains nutrients and bioactive components, with an immune stimulating function, growth factors and with antimicrobial activities. The bovine one contains even more of these elements.

Material and Methods: In the Hematology of the AUSL-IRCCS of Reggio Emilia, a monocentric study was conducted with a standard design for phase II studies according to Simon (Optimal Design), a two-step design with a cut off after the first for ensure patient safety. The overall sample is 59 evaluable cases (step1_ 19 cases; step2_ 40 cases).

Objective: To evaluate whether the addition of 100% colostrum products to the standard of care oral hygiene protocol can be more active than oral hygiene alone in protecting mucous membranes from the onset of mucositis in patients undergoing myeloablative regimen for bone marrow transplantation. We hypothesized that with the addition of colostrum to standard practice, a reduction in the incidence of severe mucositis of 50% (from 30 to 15%) could be obtained.

Results: The study is over. The first results show that: Severe mucositis decreased from 23.8% to 10.2%, mild intensity mucositis are around 64%, recording a slight increase, while the number of patients who have not developed mucositis has increased.

Conclusions: The data are very encouraging, a RCT is now developing to confirm these results.

YEAR/STEP	2016	2017	STUDY Step 1	STUDY Final
HSCT	42	39	19	59
NO MUCOSITIS	8 (19,0%)	8 (20,5%)	4 (21,0%)	15 (25,4%)
MILD (1-2 WHO)	24 (57,2%)	19 (48,7%)	14 (73,7%)	38 (64,4%)
SEVERE (3-4 WHO)	10 (23,8%)	12 (30,8%)	1 (5,3%)	6 (10,2%)

U02*

HOME SE-CURE: MANAGEMENT OF ORAL, INTRAMUSCULAR AND SUBCUTANEOUS ONCOLOGICAL THERAPIES AT HOME. DAY HOSPITAL EXPERIENCE - MEDICAL ONCOLOGY, E.O. GALLIERA OF GENOA

Franconeri M.[1], Marceca F.[1], Buttiron Webber T.[1], Magnani M.[1], Paciolla F.[1], Patrone C.[1], Cevasco I.[1], Franconeri R.[1], Provinciali N.[1], Defferrari C.[1], Clavarezza M.[1], D'Amico M.[1], De Censi A.[1]

[1]*E.O. Galliera, Genova*

Background: Recent studies show that patients with cancer are more exposed to a greater risk of Covid-19 infection, developing more severe symptoms and higher risk of death. The fear and risks include a source of stress for patients who have to go to the hospital for treatment. To meet their needs, we designed the Home Se-Cure project which aims to guarantee patients the continuity of oral, intramuscular and subcutaneous cancer therapies, delivering treatment at home.

Materials and methods: The project will include patients aged > 65 years, fragile patients with ECOG 2-3-4, living in the neighboring areas of the hospital. We hypothesized to perform about 8 intervention per day. The interventions will include blood sampling, oral, intramuscular and subcutaneous therapies. The activity will be carried out during working hours, from 7.30 to 11 for two days a week. Nurses and oncologists will select the patients who will be contacted by phone to schedule the appointment. The oncologist prescribes and documents the blood tests and / or home cancer therapy to be delivered to the patient. The nurse picks

up the drugs at the hospital pharmacy and goes to the patient's home equipped with the required PPE. Therapy can only be taken after confirmation by telephone from the nurse and doctor based on the result of the blood tests.

A customer satisfaction questionnaire will be administered to patients and will be compared with those who refuse this service or cannot access it because of geographical reasons.

Results: We expect our results to bring: reduce patient travel, ensure continuity of therapy, avoid gatherings at the day hospital. Guarantee the safety of fragile patients by respecting the ministerial recommendations. Avoid the stress related to the dilemma to perform the therapies Vs risk of contagion. Reduce access to the Emergency Room through early recognition of toxicity and non-compliant blood values.

Conclusions: By accomplishing these results we would should achieve a better organization of the work, a reduction of the clinical risk, an improvement of the quality of care and a greater working well-being of the staff.

U03*

NURSING PHONE CALL MONITORING MAY REDUCE THE INCIDENCE OF SERIOUS ADVERSE EVENTS DURING NEW INNOVATIVE TREATMENTS IN MELANOMA PATIENTS

Esposito M.R.[1], Sabatelli P.[2], D'Ausilio T.[2], Esposito F.[2], Barbieri C.[2], Simeone E.[2]

[1]*Istituto Tumori di Napoli, Napoli;* [2]*Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli*

Background: Immunotherapies and molecular targeted treatments have improved the prognosis of melanoma patients (pts) both in adjuvant and metastatic setting. Due to their peculiar mechanism of action, these drugs may cause typical adverse events (AEs) and many of these may be severe and life-threatening. In particular, the therapy with check points inhibitors like anti-PD-1 and anti-CTL-A4 agents require a careful monitoring of patients during the treatment and also after the end due to possible delayed or permanent adverse events. The aim of our study is to evaluate whether nursing monitoring of pts through periodical phone calls may be useful to reduce the incidence of serious adverse events (SAEs) and hospitalizations in melanoma pts treated with immunotherapy.

Methods: We started to collect data from 50 melanoma pts treated with immunotherapy from March 2020 to May 2020 during COVID- 19 pandemia. Thirty-five (70%) pts were treated for metastatic disease and fifteen (30%) for adjuvant aim. Forty-five patients (90%) received an anti-PD-1 treatment (pembrolizumab or nivolumab) and five (10%) an anti-CTL-A4, ipilimumab. Phone calls to patients or to their care-givers were performed by the nurse once weekly and toxicity was evaluated through CTCAE v5.0 (Common Terminology Criteria for Adverse Events). Medical intervention was required according the grade or the type of AE.

Results: The incidence of AEs detected on phone calls were the following in metastatic pts : Grade 1-2 diarrhea (15/35, 43%), grade 1pruritus (10/35, 28%), grade 2 rash (5/35,14%), grade 1fatigue (12/35, 34%). Among adjuvant pts : grade 3 diarrhea (3/15, 20%), grade 2 rash (2/15,13%), grade 2 arthralgia (1/15, 6%), grade 2 peripheral neuropathy (1/15,6%). No SAEs were detected. All AEs resolved with an early treatment with corticosteroids taken at home after medical contact. No hospitalization were necessary.

Conclusions: Our preliminary results show that using a periodical nursing phone calls during the treatment with immunotherapy may help to detect earlier AEs and to avoid SAEs and complications that bring to hospitalization.

U04*

RETROSPECTIVE OBSERVATIONAL STUDY OF SIDE EFFECTS IN PATIENTS RECEIVING HIGH-DOSE CHEMOTHERAPY DURING AUTOLOGOUS AND ALLOGENEIC TRANSPLANTATION AT THE PIACENZA HAEMATOLOGY UNIT

Cappucciati L.[1], Rosselli M.[1], Contini A.[1], Muroni L.[1], Imbriani P.[1], Pattini G.[1], Scopelliti R.[1]

[1]*Ospedale Guglielmo da Saliceto, Piacenza*

Background: In haematopoietic stem cell transplantation, patients are subjected to regimens with high-dose chemotherapy. High-dose chemotherapy often causes side effects

and complications in these patients that negatively interfere with the function of the patient's organs,ausing multiple disorders.he primary endpoint of this study is to detect the most frequent side effects in such patients depending on the regimen of conditioning or mobilization to which they are subjected. Other objectives are to assess whether there is an incidence of side effects associated with procedures and/or therapies (transfusions, infections) Another significant goal is to detect whether patients who first had CSE mobilisation followed by an autologous transplant show the same symptoms.

Method: The retrospective observational type of study analyzed a sample of records about 73 patients,30 of whom having undergone allogeneic transplant while the other 43 the autologous one,who were admitted to the CTMO haematology in the lass of time between January 2017 - December 2018.

Results: Results showed that the most frequent symptoms were fever (96%), mucositis (95%), nausea (84%), diarrhoea (73%), vomiting (71%), asthenia (68%) and pain (55%). Each sympotom has occurred in a more or less significant way depending on the type of conditioning or mobilization regimen. Moreover, as may be seen by the resulting data of this study, it is possible to confirm an important incidence between the appaerance of side effects and the concomitant performance of some therapies and procedures. In particular, transfusions have been shown to have a high statistical significance in relation to fever, mucositis,nausea, while infections have a significant effect on fever and mucositis, not on nausea. I can be concluded that the same patients who had undergone CSE mobilisation and autologous transplantation never had the same symptoms altogether: 15% of the patients did not show matching symptoms, while the remainder of them did. In particular 23% of all patients presented one equal symptom, 32% developed two symptoms in common,18% three symptoms, 9% had 4 symptoms and only 3% 5 symptoms.

Conclusions: The analysis of the data obtained allows to take into consideration the possibility of preventing the occurrence of the most frequent side effects through a preventive chemotherapeutic- based treatment administered during the conditioning or mobilisation regimen, in order to improve the quality of life, the patient'care.

U05*

PAIN EVALUATION AND TREATMENT IN HOSPITALIZED PATIENTS WITH METASTATIC CANCER. A PROSPECTIVE STUDY ON IMPACT OF NURSING EVALUATION FOR PAIN MANAGEMENT IMPROVEMENT

Giordani P.[1], Profili S.[1], Rinaldi D.[1], Bianchi R.[1], Dionigi F.[1], Della Chiara J.[1], Aporta G.[1], Montanari G.[1], Nardi C.[1], Matsko I.[1],

Catalano V.[1], Graziano F.[1], Baldelli A.M.[1], Alessandroni P.[1], Sarti D.[1], Rossi D.[1], Luzi Fedeli S.[1]

[1]Azienda Ospedaliera Ospedali Riuniti Marche Nord, UO Oncologia, Pesaro

Background: This prospective study monitored the impact of regular pain assessment by nurses, as concerning pain management in hospitalized cancer patients. The results of this study were compared with those obtained in a similar investigation that was performed ten years ago, to investigate the attitude changes in pain management.

Material and Methods: A monocentric qualitative and quantitative investigation on cancer-related pain was carried out on patients that were hospitalized in oncology, with pain at admission and hospitalization for at least three days. Pain intensity was asked twice a day to patients and reported by nurses and with a NRS scale (no pain=0, mild=1, moderate=2, strong=3). Pain management evaluation was performed with the Index of pain-management (IPM). IPM measured the health care provided in response to patient's pain. Such response was considered adequate when there was a congruence between patient's reported pain intensity and the type of prescribed drug. IPM was assessed subtracting the pain level from no pain=0 to severe=3) from the analgesic level (four different scores from no analgesic=0 to strong opioid=3).

Results: From march to September 2019, 106 hospitalized patients were enrolled in the study. Their median age was 71 years (34-69), M/F was 65/67 and their median inpatients recovery was 12 days (3-48). Most frequent tumour sites were Lung 25%, Colorectal 15%, Gastric 10%. Single/multiple metastases (liver 24%, bone 21%, nodes 15%, peritoneal 13%, brain 12%, lung 6%) were present in 61/71 patients. 33 pts reported mild PPI, 32 pts moderate PPI and 41 pts strong PPI. No analgesic was administered to 9 pts, Non Opioid drugs were administered to 23 pts, weak opioid to 13 pts and strong opioid to 61 pts. IPM negative levels were observed in 24 pts (-2 in 10 pts, -1 in 14 pts), IPM 0 level in 49 pts, IPM positive level in 33 pts (1 in 20 pts, 2 in 13 pts) and IPM from 0 to 2 level in 82 pts (77%). Pain was reported correctly 99% by nurses and 76% by physicians.

Conclusions: Despite several guidelines there is still a subset of pts whose comfort and pain control is suboptimal. The regular daily reporting by nurses improves the correct evaluation of pain intensity and pain aspects as shown an historical comparison with previously evaluation IPM positive score from 57% to 77%. Adequate training for health care providers in pain management lead to an improvement in cancer pain management.

U06

THA CASE MANAGER AT THE TIME OF THE COVID19

Muroni L.[1], Cremona G.[1], Di Nunzio C.[1], Muroni M.[1], Gubbelini M.[2], Cavanna L.[1]

[1]Dipartimento Oncoematologico AUSL Piacenza, Piacenza; [2]Direzione delle Professioni Sanitarie AUSL Piacenza, Piacenza

Background: In Piacenza it all started on 21 February 2020.The local hospital that the gravity of the situation was perceived more clearly, and the actions that were needed to reorganise happened quickly. Among the various interventions that were rapidly approved, was the creation of a team capable of bringing care home to home. Case managers work to meet patient needs through assessment, coordination, and planning, and by evaluating the available. The nursing directors wanted the presence of a case manager within the team made up of the nursing coordinator and the medical manager.

Materials and methods: The need to give quick answers to a tragic situation has highlighted how telephone contact can be used to integrate take-up interventions aimed at preventing hospitalizations and early treatment. The telephone is an important communication tool and can be used to provide information to the patient, to control it remotely, to prevent it from going to the clinic. In the period between 12 March and 30 April, 240 phone calls were made by the case manager in patients suffering from symptoms attributable to the covid who requested, leaving a message to a dedicated number, a service. Each visit was preceded by a phone call in which the case manager monitored with the aid of a specially designed card the comorbid symptoms, the presence of symptoms, the therapy taken. The telephone interview lasted an average 5 minutes. The completed forms were evaluated by the team that established the priority of access to the home based on the data collected. The evaluation was carried out by the team daily and determined the choice of patients to visit on the following day Home visits were 220 while 20 patients were managed with only telephone contact. It was 20 people who reported a temperature not exceeding 37.5 degrees and no other symptoms. These 20 patients were indicated the drug therapy to be taken by the team's medical contact and given as an indication if there was a worsening recall. For these 20 patients it was decided to make a follow-up call after 10 days.

Results: 20 patients followed by telephone, 15 reported an improvement in symptoms, 5 had the need to be visited. Everyone reported feeling taken care of and reducing anxiety.

Conclusions: The choice of the presence of the case manager allowed, through the intervention of the phone call, to reduce access to the emergency room and the visits n charge. No less important is the reduction of anxiety.

U07

"I ALREADY TAKE TOO MANY DRUGS": A RESEARCH ON THE REASONS OF NON – ADHERENCE TO PAINKILLERS PRESCRIPTIONS IN ONCOLOGICAL PATIENTS IN ACTIVE CARE

Forgelli F.[1], Occhipinti A.[1], Gonella M.[1], Ernandez E.[1], Zatta L.[1], Muri F.[1], De Filippo A.M.[1], Irenze G.[1], Zingaro M.[1], Agnesone M.[1], Comandone A.[1]

[1]ASL Città di Torino Ospedale San Giovanni Bosco Oncologia, Torino

Background: Cancer pain is usually called "total pain". However, it is common for patients to be reluctant to take analgesic drugs and to have negative beliefs about them. Among the most common obstacles, age, education, concomitant pathologies, but also the fear of addiction, of side effects. The consequence is an inadequate therapeutic adherence to treatments.

Outcome: The purpose of this study is to investigate the reasons that lead oncological patients to have inappropriate pain management during active chemotherapy treatments and to not take analgesics.

Materials and methods: For the analysis two questionnaires were administered to patients: the *Morisky Medication Adherence Scale* (MMAS), and the *Barriers Questionnaire II* (BQ II). These questionnaires were administered to 130 patients belonging to the Oncological Day Hospital in the San Giovanni Bosco Hospital and Maria Vittoria Hospital, in the period between March 2019 and August 2019. The analysis of the data was subsequently conducted through the logistic regression model. The statistical analysis was performed with the software IBM SPSS version 25.

Results: Number of patients: 118 (M 59.3%; F 40.7%) with ages between 66 - 75 years. 19.4% had 3 to 5 concomitant pathologies, and 73.1% less than 3. Considering the MMAS, 83.7% said they regularly take painkillers, 60.9% said that not having difficulty adhering to the treatment. As for the BQ, the numbers of those who have negative beliefs towards painkillers remain around 30 - 40% of the total and decreases when it's related to resistance and side effects. More than 40% of the participants say they prefer pain than having adverse effects. For the fifth item of the Morisky Scale, the model estimates 51.3% with the intercept alone, 73.7% with the independent ones, with significant item 7 of the BQ as predictor (odd ratio of 0.507).

Discussion: Considering MMAS, overall adherence to drugs seems good, while we would have expected higher percentages regarding BQ beliefs. The only real result regard the relationship between beliefs and behaviors is the fear of constipation, which seems connected to a greater probability of non – compliant behavior in taking painkillers.

Conclusions: There are numerous tools that research pain experience, but few tools that investigate the beliefs related to it. From the results of the present study, the fear of a side effect such as constipation seems to determine patients' behavior towards painkillers.

U08

THE FIGURE OF THE CAREGIVER OF ONCOLOGICAL PATIENTS IN THE YEARS OF THE TRANSFORMATION OF MEDICAL ONCOLOGY (2017-2020)

Clementi S.[1], Rizzolio C.[1], Zatta L.[1], Comandone A.[1]

[1]ASL Città di Torino Ospedale San Giovanni Bosco Oncologia, Torino

Background: The years following 2015 in Oncology are characterized by profound changes: an increasingly accentuated chronicity of the disease with prolonged survival, the introduction and consolidation of biological target therapies and immunotherapy. The Rete Oncoligica Piedmont and Valle d'Aosta (RO) has over 20 years of experience. One of the founding elements of the assistance introduced by the RO is the CAS (Centro Accoglienza e Servizi) which welcomes the patient and informs him about the services provided, the methods of access and the reservations. Upon admission to the CAS, a patient with a certain or very suspect tumour diagnosis is undergoes a brief epidemiological and family investigation. Through this important amount of data, we want to describe how the figure of the Caregiver has changed in recent years.

Patients and methods: The patients taken into consideration belong to the SC of Oncology of the San Giovanni Bosco Hospital in Turin . From January 2017 to May 2020.

Result: Number of patients: 1820 (M 65.6%; F 34.4%) Median age 72.6 years (20-95) Standard deviation 11.6 years. Pathologies: 549 colorectal, 525 lung, 274 urological, 134 pancreas, 122 gastric, 85 HCC. The first therapy undertaken after the CAS visit was therapy in 31.8% of cases, surgery (18.8%), radiotherapy 3.6%, immediate palliative care. The Caregiver of these patients in 55.8% of the cases is the spouse or partner (46% in women and 61% in men), in 29.2% the children (38.7% in women and 24.3% in men); in 3.4% the brothers; in 1.5% the mother (maximum peak when the patient is 40 years old). Unfortunately, in 6.8% there is no Caregiver. In the temporal analysis, the spouse is the predominant Caregiver figure for cohorts from 40 to 65 years of age. In the older population, children predominate due to the absence or incapacity of the spouse The two cohorts 30-35 years and > 80 show the highest percentage of cases without Caregiver. The role of neighbours or carers such as Caregiver is marginal but not null. (2.4%).

Conclusions: This research detects that, despite the epidemiological changes, of therapy and the changes in social terms that have taken place in Italy, the dominant figures in the caregiving of an oncological patient remain the close circle of first-level family members (spouse or children). The absence of Caregiver in 6.8% of cases is worrying,

which risks configuring a state of abandonment of the patient especially in the terminal stages.

U09

MORAL DISTRESS IN HEALTHCARE PERSONNEL DURING COVID-19 PANDEMIC: EXPERIENCE FROM PIACENZA ONCOLOGY DEPARTMENT

Maserati M.[1], Pisani S.[1], Faverzani C.[1], Stroppa E.[1], Muroni M.[1], Cremona G.[1], Riscazzi V.[1], Cavanna L.[1]

[1]*Dipartimento Onco-ematologico AUSL Piacenza, Piacenza*

Background: Italy has been one of the countries most affected by Covid-19 emergency, in particular Piacenza has reached the record for the number of victims caused by the virus and is still facing a copious number of infections. The healthcare staff of Piacenza Hospital faced this emergency demonstrating a strong spirit of adaptation, alleviating suffering, loneliness and leading many patients infected with the virus towards healing. Moral distress is a common reaction in morally difficult situations, and includes feelings of frustration and lack of power when healthcare professionals are prevented from acting in accordance with their values and ideals (Gustavsson et al, 2019). Morally demanding choices add a greater burden to working in an already stressful environment. The Covid-19 emergency as a pandemic can be considered a real catastrophe, characterized by health needs that exceed existing capacities and so often health professionals have had to make difficult decisions, quickly choose who to treat and how to use optimal limited resources available. The study aims to investigate the Moral Distress of oncologic operators of Piacenza Oncology during Covid-19 emergency period.

Material and methods: We conducted an observational qualitative study, the data collection tool is a semi-structured interview, consisting of sequential and standardized questions. 26 operators were interviewed (8 doctors, 13 nurses and 5 OSS) who worked in the Medical Oncology Unit of Piacenza hospital during the emergency period. The data analysis took place with analysis of the thematic content. Qualitative analysis involves the fragmentation of data into simpler units and the subsequent recomposition in new ways.

Results: The results of the interviews were divided into four macrocodes: Sensations associated with Moral Distress, Negative episodes, Changes, Positive episodes, in turn divided into several microcodes. The Moral Distress therefore emerges that this pandemic has evoked in operators despite their professionalism and preparation for end of life.

Conclusions: Moral Distress is a usual condition for Oncology operators who are used to being in contact with suffering and death, caused by the high psychological and physical contact that is established with the sick person, but the results of our work highlighted how the pandemic has changed the care and perception of operators, intensifying this feeling of psychological imbalance.

U10

NURSING-BASED SCREENING AND PREVENTION STRATEGIES FOR CANCER PATIENTS DURING THE COVID-19 PANDEMICS

Rossi V.[1], Acunzo G.[1], Capuozzo V.[1], Germoglio A.[1], Del Prato F.[1], Ferrillo L.[1], Grizzuti G.[1], Innamorati M.[1], Landolfi C.[1], Micallo G.[1], Palazzo I.[1], Portinaio F.[1], Santucci P.[1], Olivetta R.[1], Mirabella R.[1], D'Auria S.[1], Esposito M.R.[1]

[1]*Istituto Nazionale Tumori - IRCCS - Fondazione G. Pascale, Napoli, Italia, Napoli*

Background: Ensuring treatment continuity during the COVID-19 pandemics was a major commitment of our Institution. To this end a specific response plan, integrating recommendations from relevant networks (AIOM, NCCN, ISS, ANIPIO, FNOPI), was implemented to minimize exposure risks and fatality rates for patients (pts.) and personnel.

Methods: From March 10, triage checkpoints at hospital main entrances were activated to regulate access to wards, outpts. chemotherapy facility and diagnostics units (A). From April, additional stations were established at further building allocating outpts. clinics and surgical day care (B). Nursing staff was involved in several intervention domains: 1. development and updating of triage forms for pts. and caregivers (10 updates). 2. Education and guidance on personal protective equipment (PPE). 3. regulation of inflow at triage stations. This was achieved through a specific protocol including support for access forms compilation, collection of travel/contact history, thermoscan survey, monitoring of peripheral oxygen saturation for unfit patients, direct interaction with referral physicians through point-of-care (POC) audits to secure access for symptomatic patients and 'suspect COVID-19 cases' in need of non-deferrable treatments. These POC audits were mainly aimed at separating cancer and treatment-symptoms from indicators of possible SARS-CoV-2 infection. 4. Nasopharyngeal swabbing for personnel and 'suspect cases' at POC and within a precautionary program for all immunocompromised petients accessing the hematology-oncology Unit. 5. From May 15, setup and administration of rapid testing for SARS-CoV-2 IgG/IgM with POC nasopharyngeal swabbing for those displaying positive antibody results. 6. Health education for pts., caregivers, personnel and outsourcing operators, including hand hygiene, selection and use of PPE.

Results: Overall results (March-May 2020), are shown below.

Conclusions: Efforts made by nursing team significantly contributed to warrant oncology care continuity and operators safety. Nursing triage effectively identified potential SARS-CoV-2 carriers.

Activities	March	April	May
Triage A*	5976	8862	12517
Triage B*	=	3902	9616
N° of suspicious case	41	125	71
N° of suspicious cases not admitted	24	55	9
N° nasopharyngeal swabs performed	461	986	917
N° surgical procedures performed	195	339	359
N° outpatient chemotherapies	2676	2702	2502
N° pts. transferred due to Covid-19	1	1	=
N° triage hours	1318	1581	1912

*N° of checked individuals

U11

ACTIVITY OF A PHASE I CLINICAL UNIT DURING THE COVID-19 PANDEMIC

Sabatelli P.[1], D'Ausilio T.[1], Marsele P.[1], De Pasquale F.[1], Bevilacqua S.[1], Florio M.[1], Di Napoli A.[2], Palazzo I.[2], Morrone L.[1], Perrone F.[1], Schettino C.[1], Gravina A.[1]

[1]*S.C. Sperimentazioni Cliniche - Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli;* [2]*S.C. Farmacia Ospedaliera - Istituto Nazionale Tumori IRCCS Fondazione G. Pascale, Napoli*

Background: Enrolment of patients in phase 1 trials is a difficult task everywhere and at every time. It is reported that on average less than one patient per month is enrolled worldwide in phase 1 trials. COVID-19 pandemic has been a further problem during 2020, with many trials closed by the sponsors for logistic reasons and for the fear of causing a fatal infection in cancer patients.

Materials and methods: We reviewed the activity of our phase 1 unit in terms of enrolment of new patients during six months, three before and three during COVID-19 pandemia, and of treatment of patients enrolled before the pandemic.

Results: Out of 8 trials active at our unit, only one did not close the possibility of enrolling new patients during the pandemic. No treatment was stopped because of the pandemic. During the pandemic we enrolled three new patients in the only one open trial. The same number of new patients had been enrolled during the previous three months. In addition, three further patients were pre-screened during the pandemic resulting not eligible. Operatively, an intensive strategy of testing healthcare workers (nurses, doctors, study coordinators, biologists) with blood testing for anti-COVID19 IgM and IgG, and pharyngeal and nasal swabs was applied. In addition, patients were managed with a triage protocol that similarly included blood testing at each access and swab testing in case of IgM/IgG presence. Overall, no one of the health coworkers resulted positive to blood or swap testing and only one patients was positive to IgM testing, with negative swap and subsequently negative blood testing, possibly representing a false positive case. Sanitization of phase 1 rooms was also performed regularly, once per week or more frequently at need in case of patients or health workers resulting positive to blood testing.

Conclusions: Our phase 1 unit was able to maintain the same level of activity during the pandemic, thanks to one trial that was not suspended by the sponsor and this goal was reached thanks to organization and preventive measures set up by the Institutional dedicated professionals. Overall, a good result was achieved in terms of safety of both patients and healthcare workers.

U12

STAYING AT HOME IN THE COVID-19 PANDEMIC: THE PERSPECTIVE OF PEOPLE LIVING WITH CANCER PARTICIPATING AT THE AIIAO SURVEY

Biagioli V.[1], Belloni S.[2], Albanesi B.[1], Piredda A.[3], Caruso R.[4]

[1]*Sapienza University, Rome;* [2]*Tor Vergata University, Rome;* [3]*European Institute of Oncology, Milan;* [4]*IRCCS Policlinico San Donato, Milan*

Background: During phase 1 of the COVID-19 emergency, all Italian citizens had to quarantine at home to reduce the transmission of the virus. People living with cancer were considered at higher risk for infection and severe events. Moreover, they had to face several challenges in accessing healthcare services, especially those travelling to receive cancer care. Therefore, it is important to get a complete picture of the cancer experience during the lockdown from the patient perspective.

Material and Methods: An online survey was conducted from March 29th to May 3rd, 2020. Italian cancer patients were invited to participate while they were staying at home because of the COVID-19 pandemic. Data about their socio-demographic and clinical characteristics, the perception of self-isolation (ISOLA scale), the measures they adopted to reduce their infectious risk, and beliefs about the impact of the pandemic on their disease were collected. The study was approved by the scientific committee of the Italian Association of Cancer Nurses (AIIAO).

Results: Overall, 195 adult people living with cancer completed the survey. They were mainly women (76%), with a mean age of 50.3 years (SD=11.2), diagnosed with haematological malignancy (51.3%), and at home in self-isolation for more than 6 weeks (39.5%). Most of them never/rarely (80.4%) left their house, except for their health (49.7%) and going to the supermarket (50.3%). About 54% believed to be at higher risk for COVID-19 infection and 51% for complications. To prevent COVID-19 infection, 29% of them used some remedies to boost their immune system. Those who experienced most social problems in quarantine were the older ones, with lower education, and living without children. About 29% of participants reported that their cancer was not under control, as 24% reported that their frequency of going to the hospital had diminished and 38% were not going to the hospital at all during the pandemic.

Conclusions: The COVID-19 pandemic and the lockdown had a significant impact on cancer patients' lives. Living

with cancer in quarantine was sometimes perceived as a scaring and isolating condition of neglect, which added uncertainty to the cancer experience.

U13

THE SAFETY OF ONCOLOGY CARE AT THE TIME OF COVID19

Cremona G.[1], Muroni M.[1], Bacchetta N.[1], Proietto M.[1], Signaroldi A.[1], Paradiso C.[1], Groppi L.[1], Palladino M.[1], Politi S.[1], Fedyniak B.[1], Mele R.[1], Lis A.[1], Gazzola S.[1], Forelli E.[1], Marenghi M.[1], Marchionni M.[1], Biasini C.[1], Madaro S.[1], Piacentini G.[1], Ambroggi M.[1], Cavanna L.[1]

[1]*Dipartimento Oncoematologico AUSL Piacenza, Piacenza*

Background: The U.O. of Oncology DH / DSA of the Piacenza Hospital provides life-saving and indifferent services that could not be postponed or suspended even during the maximum spread of Coronavirus infection in the city of Piacenza. In order to ensure continuity of care and containment of the transmission of infected cases between patients, visitors and health professionals, the organization of the service was planned and changed.

Materials and methods: All patients were invited to wash their hands with hydroalcoholic gel, to wear the surgical mask and their temperature was detected. All patients were accepted after triage performed by a nurse who, through the use of a questionnaire, ascertained the health conditions, the geographical origin and epidemiological criteria at risk. Patients who tested positive for screening were isolated and managed in a specific area identified within the service and assisted by dedicated staff. Access was allowed only to the person who was to receive the service; the presence of Caregiver was allowed for people who are not independent, if linguistic-cultural mediation was required or in specific cases agreed with the staff and the oncologist. The patient paths inside the structure ware redesigned in order to guarantee the safety distance required by current legislation and the ventilation of the locations. Patient appointments were spaced apart to avoid gatherings in common areas. The patients were instructed to contact their oncologist on the day before the appointment if they had symptoms such as dyspnea temperature, gastrointestinal symptoms, dysgeusia. The use of telephone conversation as a tool for active patient surveillance was implemented. All the processes for sanitizing environments, disinfecting surfaces, equipment and care devices ware revised. Specific procedures ware written for the wearing of operators and the use of DPI based on the risk of exposure to Covid19.

Results: In the period from 21/02/2020 to 30/04/2020 there were 2935 DSA accesses with an average value of 60 daily accesses in five daily opening days of the service. During this period, 2 patients, during the first cancer visit were found positive post-nasopharyngeal swab, while no new infections were found in the patients already in charge.

Conclusions: The reorganization of the service has made it possible to provide safe and secure care to cancer patients.

U14

BEING A NURSE IN MEDICAL ONCOLOGY DURING THE COVID19 EPIDEMIC

Doria A.[1], Orsini B.[1], Cometti B.[2], Barbonetti M.B.[1], Gnaccolini R.[1], Panella A.[1], Lenatti C.[1], Speziali V.[1], Brunalli R.[1], Nonini B.[3], Matteri A.[3], Del Re R.[3], Rocca E.[2], Giumelli I.[2], Bonetta S.[2], Pini C.[2], Sosio S.[2], Iancona L.M.[2], Gottarello F.[1], Pruneri R.[2]

[1]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondrio;* [2]*ASST della Valtellina e Alto Lario-Oncologia Medica, Sondalo;* [3]*ASST della Valtellina e Alto Lario-Oncologia Medica, Chiavenna*

Background: Until February 21, 2020, Covid 19 was a disease known exclusively in China. Since that date, our working life has changed considerably. The number of cancer patients has not changed and their needs have always been fulfilled without interruption. Our department has not stopped its activity and the staff have been exposed to the risk of contagion because patients were not able to access the preventive tampon.

Method: Our department has followed the regional and internal directives issued by the Health Department in conjunction with those issued by the Istituto Superiore di Sanità. The staff have protected themselves with PPE such as masks of different types, gloves, sanitization and body temperature monitoring. The same protection methods have been used for patients. In order to avoid our patients' unchecked access to the department, a doorbell has been installed to signal their arrival. We have granted the correct social distancing in the waiting rooms and the shifting in the therapy rooms. Because of the absence of a secretary in our department the staff has had to deal also with the several telephone calls, that in tis period have increased further. Our patients in oral treatment have received medications to continue their treatment for a longer period (two months), all the chemotherapy cycles with a second day (e.g. Folfox-4) have been converted into a single day (Folfox-6 and so on). Periodic checks have been postponed after medical evaluation.

Results: During the months of March to May, 1589 chemotherapy cycles were performed. In the same period 49 patients were discharged from the hospital ward. Just first or emergency visits were granted.

Conclusions: Our workload has not been reduced. Patients were welcomed with new rules. No one has complained about our organizational changes. In a high turnout department like ours, this has been a stressful period for our staff, because in addition to the infectious risk from Covid the nursing and administrative workload have both increased. The volunteer staff to whom the reception is usually delegated remained at home and so did the psychological and nutritional support. From a psychological point of view, this period was not without emotional consequences. None of the staff fell ill, while some of 44 cancer patients tested positive were discovered during our work. 21 of them died.

Late Breaking Abstracts

DLBA02*

EPIDEMIOLOGY AND CLINICAL COURSE OF SARS-COV-2 INFECTION IN CANCER PATIENTS IN THE VENETO ONCOLOGY NETWORK: THE ROVID STUDY

Conte P.[1], Zagonel V.[2], Chiari R.[3], Cattelan A.M.[4], Vianello A.[5], Chiarion Sileni V.[6], Bassan F.[7], Bernardi D.[8], Gori S.[9], Zustovich F.[10], Milella M.[11], Azzarello G.[12], Mandarà M.[13], Morandi P.[14], Oliani C.[15], Pastorelli D.[16], Zaninelli M.[17], Aprile G.[18], Piacentini P.[19], Guarneri V.[20]

[1]*Università di Padova, Oncologia Medica 2, Istituto Oncologico Veneto IOV IRCCS, Padova;* [2]*Oncologia Medica 1 Istituto Oncologico Veneto IOV IRCCS, Padova;* [3]*Oncologia, Ospedali Riuniti Padova Sud, Padova;* [4]*Malattie Infettive e Tropicali, Azienda Ospedale Università di Padova, Padova;* [5]*Fisiopatologia Respiratoria, Azienda Ospedale Università di Padova, Padova;* [6]*Oncologia del Melanoma e dell'Esofago, Istituto Oncologico Veneto IOV IRCCS, Padova;* [7]*Oncologia Medica, AULSS7 Pedemontana, Bassano;* [8]*Oncologia Medica, AULSS4 Veneto Orientale, San Donà di Piave;* [9]*Oncologia Medica, IRCCS Ospedale Sacro Cuore Don Calabria, Negrar (VR);* [10]*Oncologia Medica, AULSS1 Dolomiti, Belluno;* [11]*Università di Verona, Oncologia Medica, Azienda Ospedaliero-Universitaria , Verona;* [12]*Oncologia Medica, AULSS3 Serenissima, Mirano;* [13]*Oncologia, Ospedale Fracastoro, AULSS9 Scaligera, San Bonifacio;* [14]*Oncologia Medica, AULSS3 Serenissima, Venezia;* [15]*Oncologia Medica, AULSS5 Polesana, Rovigo;* [16]*Oncologia Medica, AULSS1 Dolomiti, Feltre;* [17]*Oncologia Medica, AULSS9 Scaligera, Villafranca;* [18]*Oncologia Medica, AULSS8 Berica, Vicenza;* [19]*Oncologia Medica, AULSS9 Scaligera, Legnago;* [20]*Università di Padova, Oncologia Medica 2 Istituto Oncologico Veneto IOV IRCCS, Padova*

Background: COVID-19 pandemic started in Italy with clusters identified in Northern Italy. Since the beginning, the Veneto region started a proactive approach, including testing for SARS-CoV-2 part of the asymptomatic population and healthcare providers. The Veneto Oncology Network ROV licensed a dedicated PDTA to ensure proper care minimizing the risk of infection in cancer patient (pts). At the same time, a regional registry (ROVID) has been set up, to describe epidemiology and clinical course of SARS-CoV-2 infection in cancer pts.

Materials and methods: All pts with cancer diagnosis and documented SARS-CoV-2 infection are eligible. The following information are recorded: age, cancer diagnosis, stage, tumor biology, comorbidities, presence of COVID-19 symptoms, anticancer treatment at the time infection (type, aim, line of therapy, discontinuation, recovery), other medical treatments, hospitalization, treatments for SARS-CoV-2 infection, fate of the infection.

Results: 144 pts from 18 centers have been enrolled. Mean age at the time infection: 69 yrs (25 to 95 yrs). The 5 most common cancer types were breast cancer (n=26), colorectal, prostate, lung cancer (n=16 each), melanoma (n=10). Distribution by stage was as follows: I 19%, II 9%, III 13%, IV 59%. Lung metastases were documented in 15% of the cases. 77% of the pts had at least one comorbidity. COVID-19 symptoms were reported in 78% of the pts.

Active anticancer therapy at the time of the infection was reported for 71 pts (chemotherapy n=37, targeted therapy n=14, hormonal therapy n=13, immunotherapy n=6). Treatment was discontinued because of infection in 44 case. 101 pts were hospitalized; 45 received low flow oxygen support and 26 received non-invasive mechanical ventilation, high flow nasal cannula or endotracheal intubation. The fate of infection is available for 95 cases so far: 44 infection resolution with confirmed negative swab, 16 with clinical resolution discharged with positive swab, and 35 deaths. Among cases with fatal exitus, 22 were attributable to COVID-19.

Conclusions: Data collection is still ongoing, including further follow up and results of serological tests, where available. The mortality rate reported in this study is in line with other registry of cancer patients, confirming the frailty of this population. These data reinforce the need to protect cancer patients from SARS-CoV2 infection.
Supported by research grant from Fondazione Cariparo

ELBA03

HEALTH-RELATED QUALITY OF LIFE, HEART RATE VARIABILITY AND PHYSICAL FITNESS IN BREAST CANCER PATIENTS DURING THE COVID-19 LOCKDOWN: THE IMPACT OF A LIFESTYLE PROGRAM ('MOVIS PROJECT, MOVEMENT AND HEALTH BEYOND THE CARE' (CESU APPROVAL N. 21/10.07.2019)

Emili R.[1], Natalucci V.[2], Ferri Marini C.[2], Lucertini F.[2], Vallorani L.[2], Sisti D.[2], Monaldi S.[1], Somaini M.[3], Annibalini G.[2], De Santi M.[2], Panico A.[2], Barocci S.[4], Flori M.[5], Biancalana V.[2], Rocchi M.B.[2], Stocchi V.[2], Brandi G.[2], Villarini A.[6], Catalano V.[7], Barbieri E.[2]

[1]*U.O.C. Oncologia Medica Ospedale Santa Maria della Misericordia Area Vasta n. 1, Urbino;* [2]*Department of Biomolecular Sciences, University of Urbino Carlo Bo, Urbino;* [3]*Fondazione IRCCS Ca' Granda - Ospedale Maggiore, Policlinico di Milano, Milano;* [4]*U.O.C. Patologia Clinica Ospedale Santa Maria della Misericordia, Area Vasta n. 1, Urbino;* [5]*U.O.C. Cardiologia Ospedale Santa Maria della Misericordia, Area Vasta n. 1, Urbino;* [6]*Department of Research, Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, Urbino;* [7]*U.O.C. Oncologia Medica Ospedale Santa Maria della Misericordia, Area Vasta n. 1, Urbino*

Background: Breast cancer (BC) is the most common invasive cancer in women and evidence has shown that exercise can significantly improve the outcomes of BC survivors. MoviS: 'Movement and Health Beyond Care' is a randomized controlled trial, which aims to educate cancer patients after adjuvant therapy on the benefits of exercise and proper nutritional plan.

Material (patients) and methods: Thirty women with stage 0-III non-metastatic BC recruited 12-month post-surgery (age: 53.5±7.6; BMI: 25.3±4.9) were randomized in two groups: intervention arm received 3-month aerobic

training (40-70% of the heart rate reserve; 20 to 60 min 3-day/week); control arm with usual care recommendations. Patients enrolled in January 2020 were monitored for diet habits by DianaWeb platform, they carried out the exercise training across the COVID-19 pandemic shifting from the gym to a home-based exercise program. The objective was to investigate the effects of lifestyle program on quality of life by EORTC QLQ-C30 and health-related QoL parameters such as cardiac function indexes; heart rate variability (HRV) (by repeated Holter 24h) and cardiorespiratory fitness by estimated maximal oxygen uptake (VO_{2max}).

Results: There were no adverse events and a high attendance was registered considering the challenges to be overcome in shifting to a home-based exercise program. Statistical analysis revealed a significant improvement in both arms in QLQ scale score: in global health status (from 64.7±17 to 15.9±13; coefficient of variation (CV) 15.9%; p=0.0015); physical functioning (from 54.4±12.3 to 6±6.6; CV 13.9%; p=0.0005); fatigue (from 26.3±23.4 to 11.9±14.3; CV -54.9%; p=0.0008) and showed a general improvement over time even on the social functioning (from 47.2 ± 22.8 to 66.7±00; CV 41.2%; p=0.0001). Both groups had a significant improvement in HRV parameters in both time and frequency domain: average SDNN/5min and VLF increased (from 50.6±14.4 to 55.2±16.7msec, p=0.033 and form 1597±967 to 1881±963 msec, p=0.04, respectively); mean heart rate decreased (from 76.6 ±7.8 to 73.7±8.3 bpm after training, p=0.009) and both arms improved the cardiorespiratory fitness level (VO_{2max} from 30.7±5.7 to 33.9±6.64 mL/kg/min; CV 10.3%; p<0.001).

Conclusions: Despite the challenges faced during the pandemic, a change in lifestyle integrating exercises, nutrition and educational counseling provides benefit to BC patients when delivered in a clinic-based setting group including the exercise specialists.

ELBA04

ADVANCED BREAST CANCER AT PRESENTATION (ABC-P) IN OCTOGENARIANS WOMEN(OW):SPECIFIC ELDERLY-DEVOTED RISK TESTS(SEDRT) (CARG+CRASH) AS NEW TOOLS TO PREVENT SERIOUS/IRREVERSIBLE ADVERSE REACTIONS(AR) IN FRAIL PATIENTS

Carreca I.[1], Bazan V.[2], Galvano A.[3], Carreca A.P.[3], Cusenza S.[3], Russo A.[3]

[1]Cattedra di Oncologia Medica -UniPa-International School of Medical Sciences Genève CH, Palermo; [2]BIND, Palermo; [3]Department of Surgical, Oncological, and Oral Sciences- ^Section of Medical Oncology,- *Medical Oncology Unit, Palermo

Due to current lengthening of average lifespan and progressive increase of malignant tumors in mankind, more new strategies must be constantly sought especially for third-age neoplasms. Nevertheless because severe toxicity developed in the majority of frail patients ,administration of therapy may cause high risk of life-threatening

AIM: We have considered in this paper ABC in frail patients like OW. Purpose of the study is preliminary detection of the overall toxicity (OTox) through the possible use of specifics tests adopted specially in frail patients such as OW, to ensure greater control in drugs administration with good effectiveness.

Material (patients) and methods: 62 patients with ABC-p were enrolled between jan2018 dec 2019. **Eligibility Criteria** women aging eighty or older; acquired written consensus; confirmed diagnosis of ABC; one or two measurable lesions (bone or visceral or both); no brain secondarisms; Charlson's Comorbidity Scale 1-3 score points; CGA Evaluation permissive for treatment. CARG-TS (**C**ancer and **A**ging **R**esearch **G**roup-**T**est **S**core) and CRASH-TS(**C**hemotherapy **R**isk **A**ssessment **S**cale for **H**igh-Age Patients **T**est **S**) are rated for predictive assessment of the risk of severe chemotox in all patients. Further Evaluations tools: Clinical Benefit according to ESMO CB scale v.2a;Tox Profile CTCAE v3.0 Criteria; QoL by EORTC QLQ-C30.

Results: CARG-TS predicts severe OTox; CRASH-TS predicts hematologic non-hematologic toxicity. Using a combination of CGA-ES+CARG-TS+CRASH-TS, we were able to divide patients into three categories: **LR** Low risk (score0-5); **MR**: Medium risk (score 5-10); **HR** High risk (score over 10).On this basis HR people was directed to receive endocrine therapy(if ER+PGR+)or RTalone. The MR group experienced a reduced schedule of eribulin (0.90mg/sqm d1,d28 until P-progression or INT-intolerable toxicity. Finally LR group received a schedule with eribulin alone(E 0.96-1.1 mg/sqm IV on d1,d21 dosage depending on Creatinine clearance value according to the Kintzel-Dorr's method and until P or INT-toxicity).

Conclusions: With contemporary use of CGA-ES ,CARG-TS,CRASH-TS we obtained two diagrams, the first "predicted risk" the second "observed risk" for each patient: the first curve was almost perfectly in line (p<0.001)with that of the "observed risk". This allowed to have extremely personalized treatments, negligible OTox, and very good values for both CB and QoL

NLBA05

MAY SARCOPENIA BE A PREDICTIVE FACTOR OF RESPONSE TO NIVOLUMAB IN RECURRENT-METASTATIC HEAD AND NECK (RM-SCCHN) CANCER PATIENTS?

Schipilliti F.M.[1], Trudu L.[1], Napolitano M.[1], Martelli F.[1], Prampolini F.[1], Pecchi A.R.[1], Valoriani F.[1], Reverberi L.[1], Spallanzani A.[1], Depenni R.[1], Massimo D.[1], Bertolini F.[1]

[1]*Azienda Ospedaliera Universitaria di Modena e Reggio Emilia, Modena*

Background: Sarcopenia is an emerging problem in cancer patients (pts), significantly important in SCCHN pts. Aim of this study is to analyze the impact of sarcopenia on efficacy of Nivolumab in RM-SCCHN cancer pts after platinum failure.

Methods: Clinical and radiological data of 24 RM-SCCHN pts undergoing Nivolumab at Modena University Hospital from 2016 to 2019 were retrospectively reviewed. Sarcopenia was assessed using abdominal computed tomography scan (CT) before Nivolumab starting and after 8-12 weeks of therapy. Skeletal Muscle Mass (SMI cm^2/m^2) at L3 levels, Subcutaneous Fat Index (SFI cm^2/m^2), Visceral Fat Index (VFI cm^2/m^2) were considered for the analysis; variables were correlated with survival (short vs long survivors, SS vs LS, considering mOS <6month vs $\geq$ 6mo) and disease control (responders, R, considered as OR + SD vs non-responders, nR). In a subgroup of pts, the variation of SMI between the first and the second CT was described and correlated with survival and response.

Results: 20 pts were evaluable for analysis: 15 (75%) were male; median age: 61 y-o (52-77), most of them had oropharynx (7, 35%) or oral cavity cancers (5, 25%) as primary sites; 13 pts (65%) had a normal BMI before starting Nivolumab. Median OS was 3 mo (0-11): 13 pts (65%) were SS, 7 (35%) LS; R vs nR were 13 (65%) and 7 (35%), respectively. At univariate analysis, no correlation between baseline SMI, SFI, VFI and survival was observed. On the contrary, we found a correlation between mean baseline values of SMI, SFI, VFI and response, in particular for SMI 55,4 in R vs 42,82 in nR, p=0,0008; SFI 61,79 in R vs 38,59 in nR, p=0,0009; for VFI 65,33 in R vs 44,77 in nR, p=0,0431. If we consider 15 pts evaluable for both CTs, 11 pts (73%) had a reduction of SMI at the second CT: mOS was 4 mo (2-9), 7 pts (64%) were SS and 7 pts (64%) were nR. Oppositely, 4 pts (27%) had an increase of SMI: mOS was 10 mo (0-11), 3 pts (75%) were LS and 2 (50%) were R.

Conclusions: Sarcopenia is a widespread, but underestimated problem of SCCHN; it may be simply assessed using CT, employed in clinical practice for disease evaluation. Detection of body composition and identification of sarcopenia may be a simple and suitable tool to predict response to immunotherapy of SCCHN.

ULBA06

PROSPECTIVE VALIDATION STUDY ON THE DEGREE OF DIFFICULTY OF HUBER NEEDLE INSERTION IN TOTALLY IMPLANTED CVADS.

Civetta G.[1], Lombardi L.[1], Lanotte A.[1], Delvecchio A.M.[1], Colonnata M.[1], Todisco A.[1], Cristallo R.[1], Marcone A.[1], Somma M.[1], Vitale E.[2], Gadaleta Caldarola G.[1]

[1]*Dipartimento di Oncoematologia-U.O.C. Oncologia Medica, P.O."Dimiccoli" di Barletta –ASL BT- , Barletta (BT);* [2]*Dipartimento di Scienze Mediche di Base, Neuroscienze e Organi di Senso. Università degli Studi di Bari "A.Moro", Bari*

Background: The safeguarding of venous assessment in cancer patients involves the placement of vascular devices. In those totally implantable, such as, thoracic and brachial port-a-cath, it requires the introduction of the Huber needle to infuse liquids or take blood samples. The purpose of the study is to validate a prognostic index that weighs the difficulty of inserting the needle by NIDS (Needle Inserting Difficulty Scale) implementation, using SPIA (Subcutaneous Port-a-cath Investigator Assessment), to improve the quality of the nursing procedure offered to the patient.

Materials (Patients) and Methods: SPIA defines brachial and thoracic implants into three different groups: Type 1: port visible to the naked eye, well palpable and immobile; Type 2: port not visible to the naked eye, palpable and not very mobile; Type 3: port not visible to the naked eye, hardly palpable, mobile or elusive. Subsequently a questionnaire containing 5 questions was administered to each patient to define the NIDS, specifically: in number of years of use of the CVAD, if over time there have been events of unsuccessful needle insertion, if it has been contacted a specialist/expert nurse, if you have experienced an increase or decrease in your body weight since implantation. The answers to each question were associated with the type of CVAD implantation (SPIA), defined by investigator nurse.

Results: 175 patients were included in the study and identified a low degree of difficulty for thoracic types 1 and 2 and brachial type 1. A high degree of difficulty for thoracic

Table 1. The SPIA different types and NIDS Algorithm

Port-a-cath	Puncture		NIDS	
	Single	Multiple	Generalist nurse	Specialist nurse
Brachial	Type 1	Type 2 / 3	Type 1	Type 2 / 3
Thoracic	Type 1 / 2	Type 3	Type 1 / 2	Type 3

type 3 and brachial type 2 and 3, which required multiple punctures and the intervention of an expert/specialist vascular access nurse (Table 1). The reasons recorded: insertion of the needle outside the perforable membrane, its partial or total inversion, the small size of the device, the presence of scar tissue. Failed attempts were eliminated by NIDS Algorithm using SPIA in subsequent procedures, and appropriate care tools, such as best positioning for exposure of the port, expert nurse and, ultrasound tecnique.

Conclusions: The implementation of NIDS Algorithm using SPIA represents a proactive tool for a more adequate and safe nursing approach to the patient, according to principle of best clinical practice.

AUTHOR INDEX

See you at the

23rd National Congress of Medical Oncology
Rome (Italy), 23-25 October 2021

President of the Congress
Giordano Beretta

Scientific Secretariat
Aiom

Via Enrico Nöe, 23
20133 Milan, Italy
Phone: +39.02.70630279
Fax: +39.02.2360018
aiom.segretario@aiom.it
www.aiom.it

Organizing Secretariat
Aiom Servizi s.r.l.

Milan Office
Via Enrico Nöe, 23
20133 Milan, Italy
Phone: +39.02.26683129
Fax: +39.02.59610555
info@aiomservizi.it

Rome Office
Viale Maresciallo Pilsudski 118
00197 Rome, Italy
Phone: +39.06.8553259
Fax : +39.06.8553221
info@aiomservizi.it

Aims & Scope

Tumori Journal covers all aspects of cancer science and clinical practice with a strong focus on prevention, translational medicine and clinically relevant reports. We invite the publication of randomized trials and reports on large, consecutive patient series that investigate the real impact of new techniques, drugs and devices inday-to-day clinical practice.

State-of-the-art reviews that summarize and critically analyze the clinical, economic, and social consequences of cancer are also welcome.

Affiliated with:

Organisation of European Cancer Institutes (OECI)
Italian Association of Medical Oncology (AIOM)
Italian Association of Radiation Oncology (AIRO)
Italian Cancer Society (SIC)
Italian Society of Surgical Oncology (SICO)

Manuscript Submissions Guidelines

To view the manuscript submission guidelines, please click on the Submit Paper tab at journals.sagepub.com/home/tmj

Tumori Journal

Con il contributo non condizionante di: