

Medical History



F.L. , 43 years old

- ✓ Premenopausal status, nulliparous
- ✓ Never smoker, no comorbidities
- ✓ No family history for breast/ovarian cancer

November 2012



Acute Dyspnea and tachycardia:

- **Cardiologic evaluation:** negative
- **Thoracic X-ray:** right pleural effusion
 - **Thoracentesis & Cytological evaluation** pleural fluid:
positive for MTC, WT1+ → serous carcinoma
- **c/a CT scan:** limited right pleural effusion with pleural thickening [...] solid masses in both ovaries (diam max 46mm) with pelvic free fluid [...]
- **Ca125** = 144 kU/L (CEA, CA19.9, CA15.3 neg)

Diagnosis & Surgery

- **05.12.2012: PRIMARY DEBULKING SURGERY**
Hysterectomy + bilateral adnexectomy, appendectomy, omentectomy, pelvic and para-aortic lymphadenectomy, peritoneal biopsies (RT=0)
- Final Histological Evaluation:
High grade serous carcinoma of both ovaries, **FIGO IVa** (pleura)
- Germline BRCA test: **wild type**

Treatment

Jan
2013

May
2013

Feb
2014

Aug
2014

1st line

maintenance

2nd line

Follow-up

70% of Stage III/IV patients will **relapse** despite optimal surgery and ChT. Response to second-line ChT is dependent on the progression-free interval following first-line treatment.

ESMO OC Guidelines

CBDCA AUC6 +
Paclitaxel 175 mg/mq +
Bevacizumab 15 mg/kg
q21 x 6

Bevacizumab 15 mg/kg
q21

Surgery:
Right Pleurectomy

PLD 30 mg/mq +
Trabectedine 1,1mg/mq
q21 x 5

Hematologic Toxicity

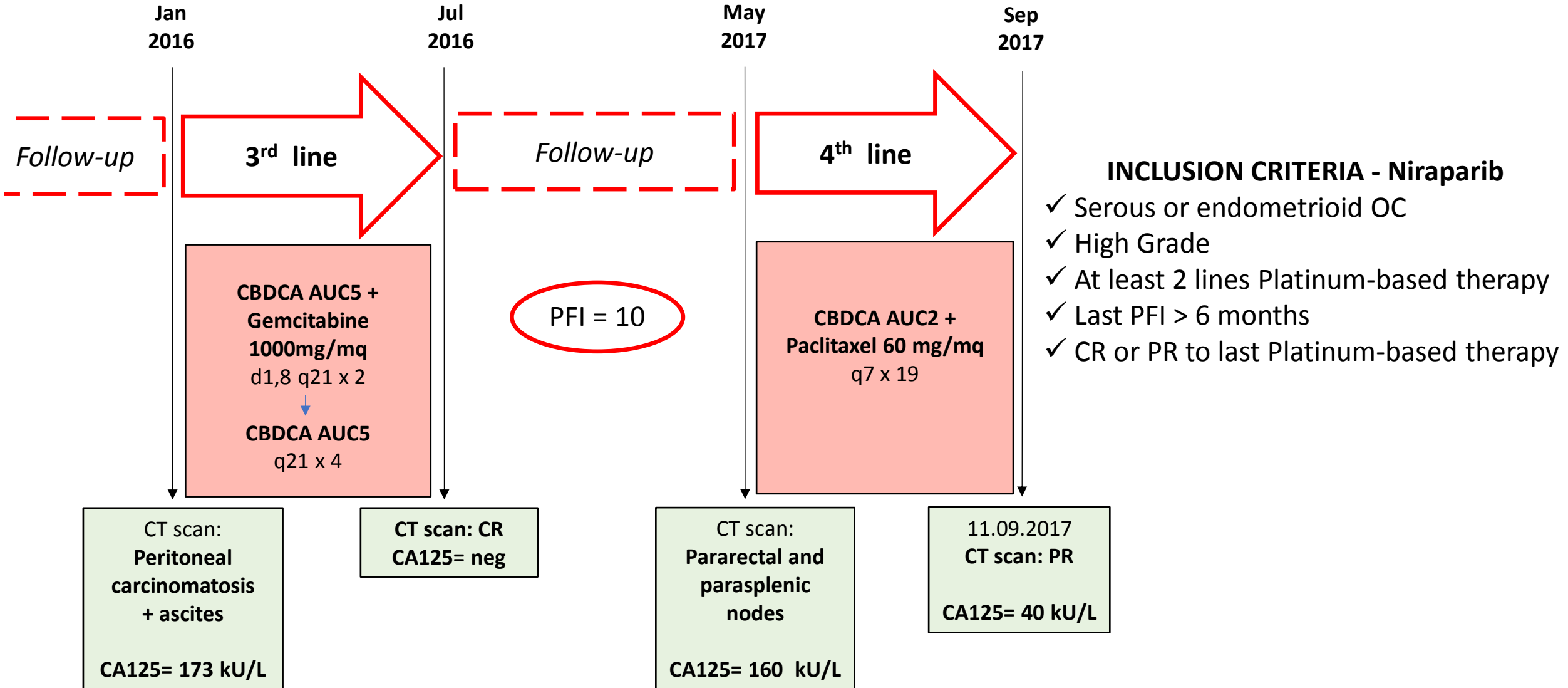
CT scan: NED
CA125= neg

PFI 9 = PPS

CT scan:
Right pleural
effusion

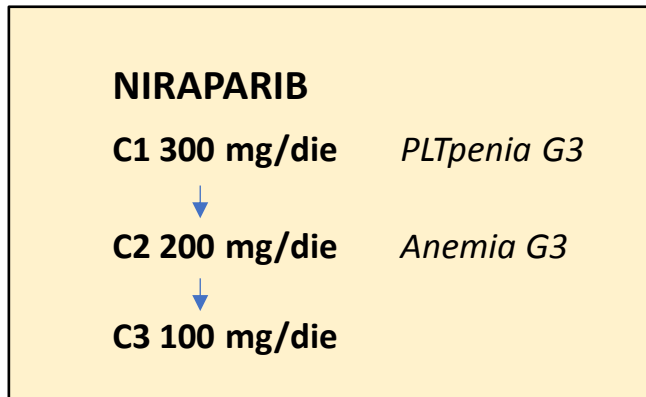
CT scan: NED
CA125= neg

Treatment



Treatment

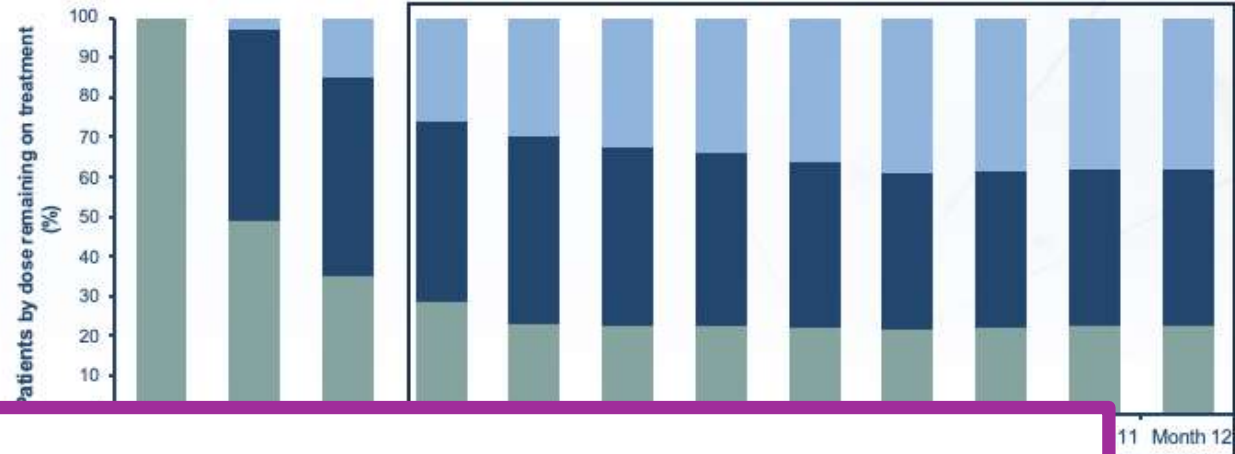
Sep
2017



Niraparib

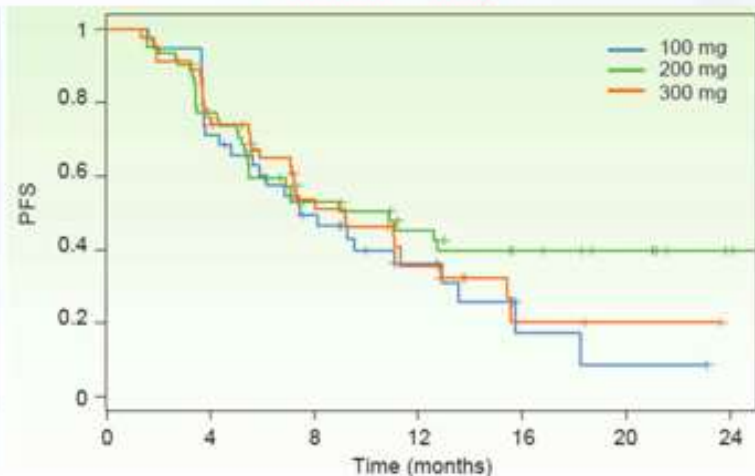
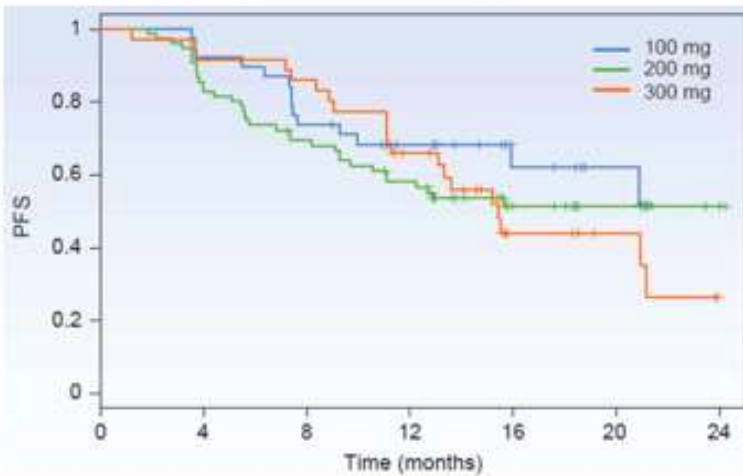
one
size
doesn't
fit
ALL

Niraparib dose level by month on treatment in ENGOT-OV16 / NOVA



- For patients weighing less than 58kg a starting dose of 200mg may be considered

by Dose Level
Patients in the
t



Treatment

Sep
2017

Feb
2019

maintenance

maintenance

ongoing

NIRAPARIB

C1 300 mg/die *PLTpenia G3*

C2 200 mg/die *Anemia G3*

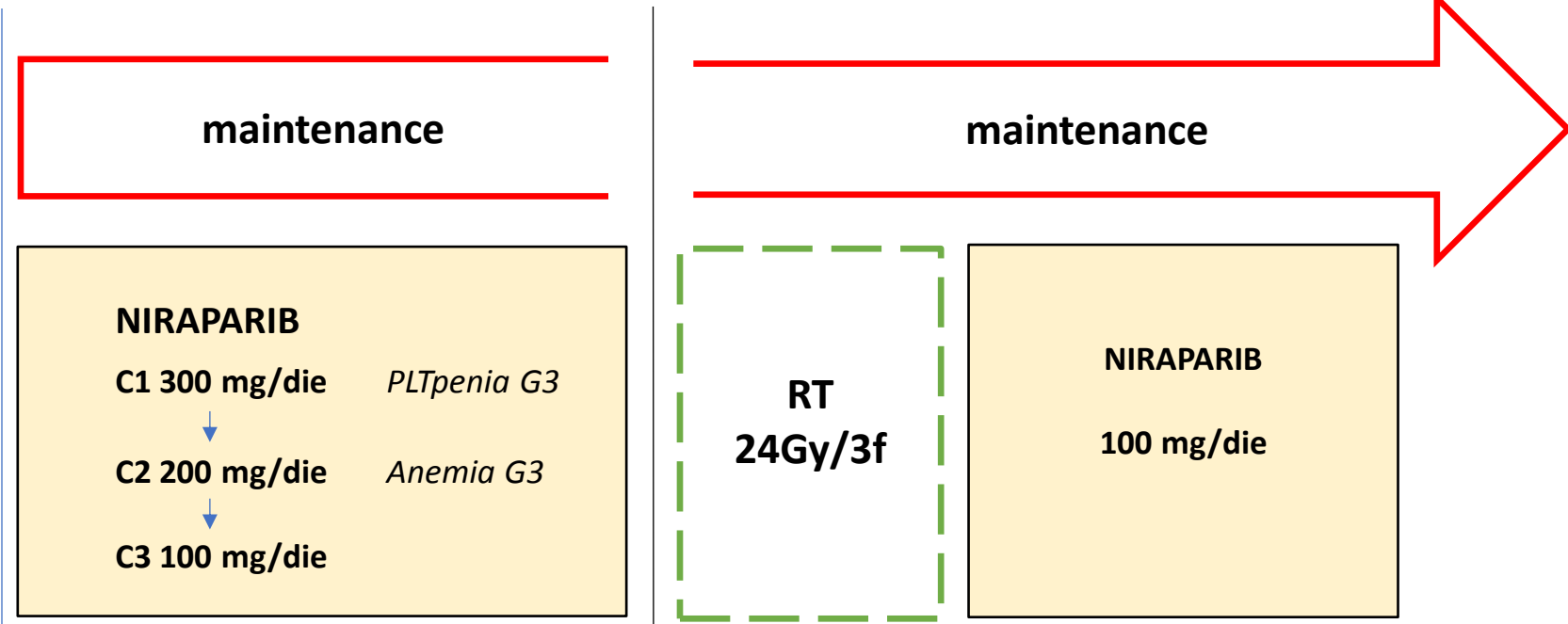
C3 100 mg/die

RT
24Gy/3f

NIRAPARIB

100 mg/die

CT scan:
Increased
single
pararectal node
(29 vs 12mm)





International Journal of
Molecular Sciences



Review

Combining PARP Inhibition, Radiation, and Immunotherapy: A Possible Strategy to Improve the Treatment of Cancer?

Mathieu Césaire^{1,2,3}, Juliette Thariat³, Serge M...
Yannick Saintigny^{1,2} and François Chevalier¹

www.impactjournals.com/oncotarget/

Oncotarget, 2017, Vol. 8, (No. 40), pp: 69105-69124

Review

Poly-(ADP-ribose)-polymerase inhibitors as radiosensitizers: a systematic review of pre-clinical and clinical human studies

...ry¹, Waisse Waissi³, Hélène
...k Saintigny^{1,*} and Florence

... 14000 Caen, France

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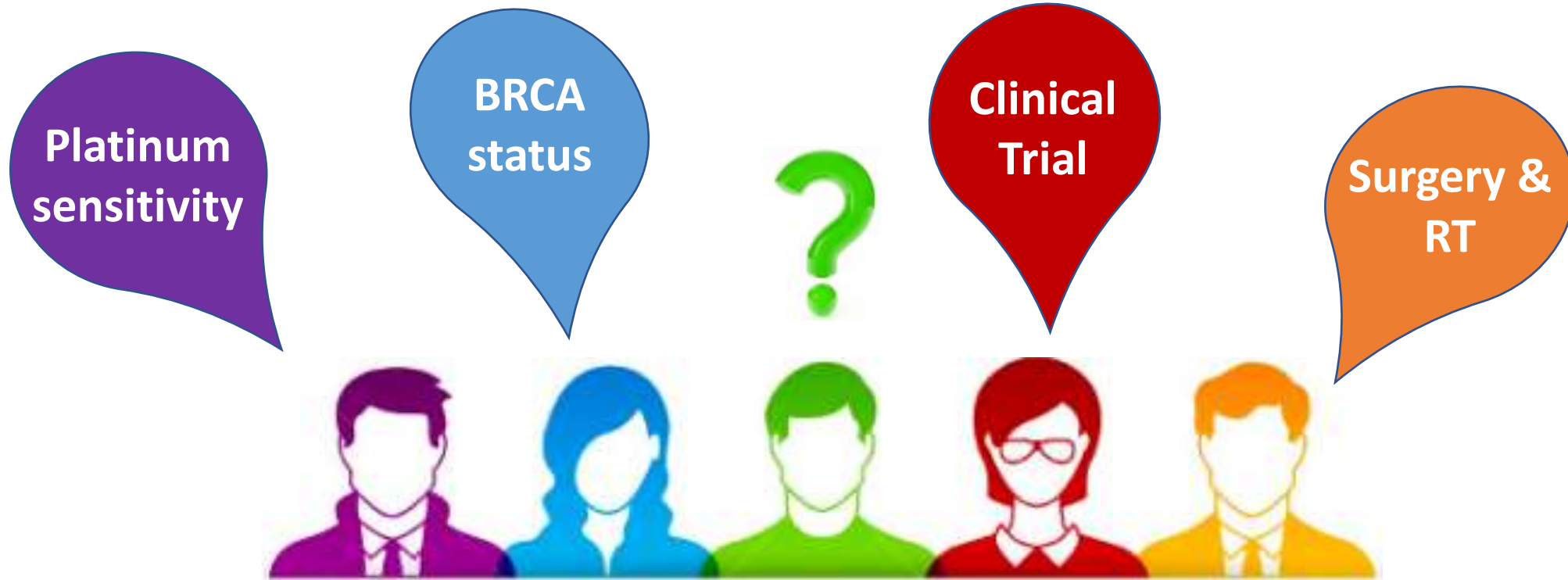
Radiosensitization by the PARP inhibitor olaparib in BRCA1-proficient and deficient high-grade serous ovarian carcinomas☆

Yue Bi^{a,b}, Ioannis I. Verginadis^b, Souvik Dey^b, Lilie Lin^c, Linlang Guo^a,
Yanfang Zheng^{a,*}, Constantinos Koumenis^{b,**}



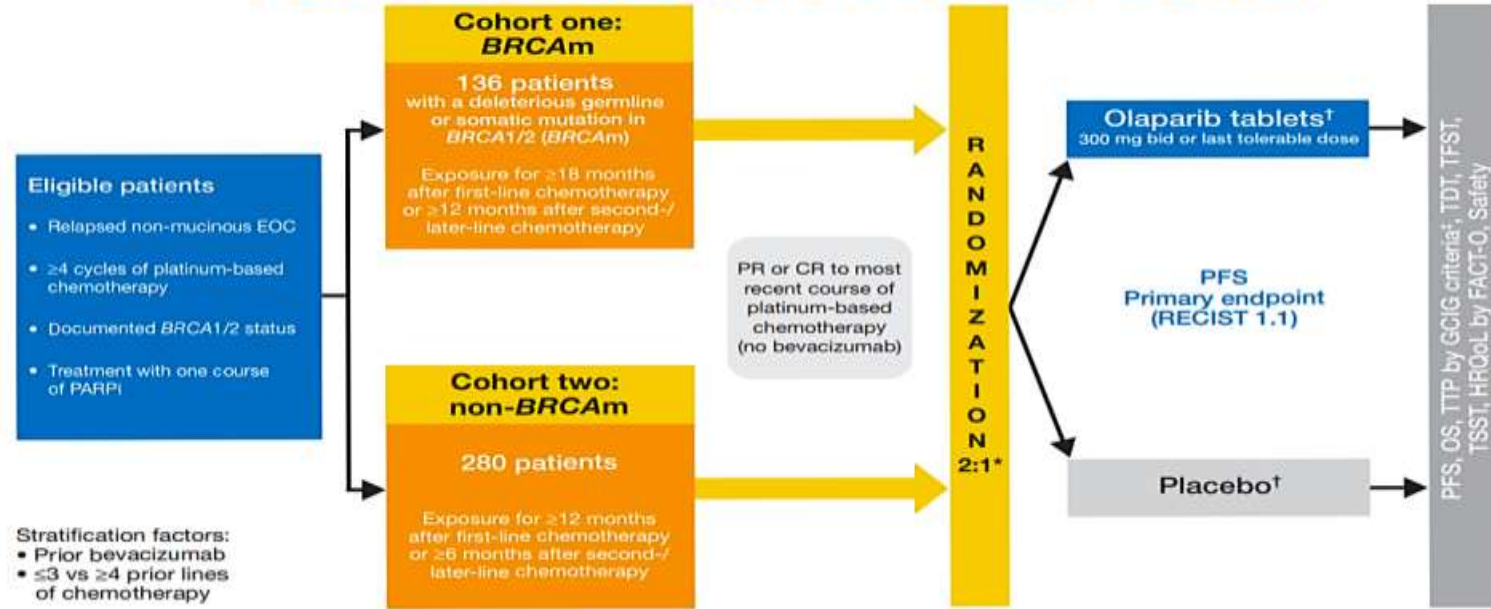
PARPi & RT

...and then?



Clinical Trial: 2 options

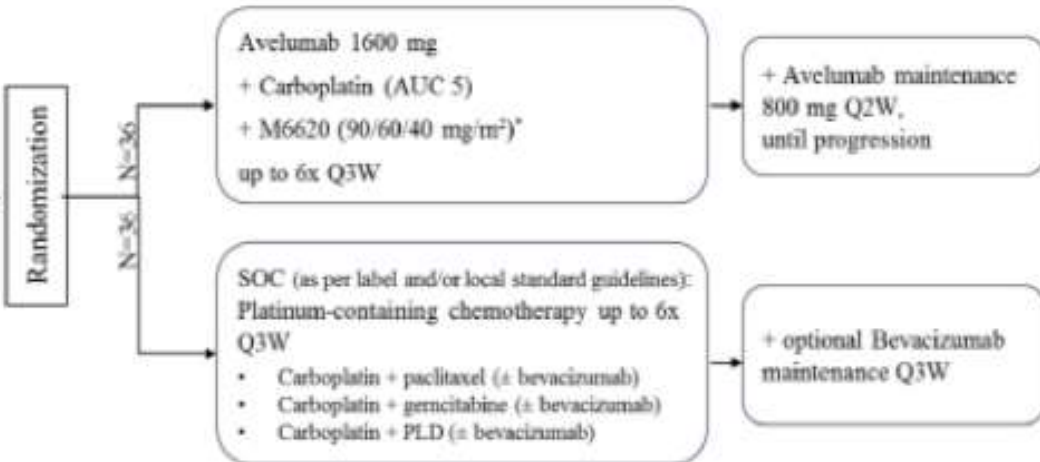
Phase III OReO Study: Olaparib Retreatment in Platinum-Sensitive Ovarian Cancer



National Institutes of Health. <https://clinicaltrials.gov/ct2/show/NCT03106987>. Accessed December 18, 2017

- Patients with recurrent ovarian cancer;**
- ≥2L Platinum-containing Chemotherapy;
 - Responded (PR or CR) to the last platinum-containing therapy
 - Received at least 4 months of maintenance PARPi treatment prior to progression
 - Known BRCA status**

MS201943_0029



Region Name	Number of Studies
World [map]	516
Europe	149
Austria	11 [studies]
Belgium	31 [studies]
Bulgaria	1 [studies]
Denmark	15 [studies]
Finland	8 [studies]
France	55 [studies]
Germany	30 [studies]
Greece	2 [studies]
Hungary	5 [studies]
Ireland	2 [studies]
Italy	33 [studies]
Netherlands	13 [studies]
Norway	4 [studies]
Poland	9 [studies]
Romania	3 [studies]
Slovakia	1 [studies]
Spain	36 [studies]
Sweden	6 [studies]
Switzerland	9 [studies]
United Kingdom	37 [studies]

Clinical Trial

 U.S. National Library of Medicine

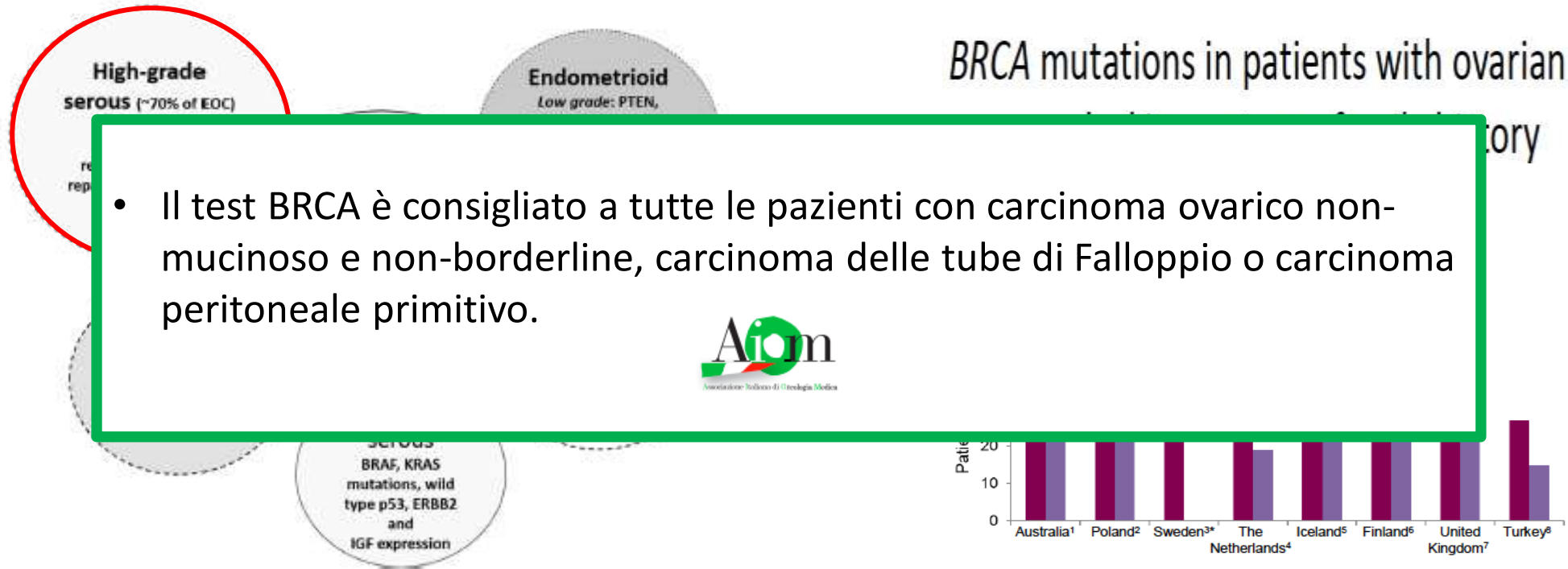
ClinicalTrials.gov

- ✓ *Ovarian cancer*
- ✓ *Recruiting*

Conclusions

- Watch&wait was the prior standard of care for recurrent ovarian cancer after CT.
NOW:
 - maintenance therapy with PARPi changed clinical practice in ovarian cancer
 - pro-active management of side-effects of PARPi maintains quality of life
- Consider local treatment (surgery or RT) for single or oligometastatic relapse, also during PARPi.
- Remember Clinical trials!
- *Open questions:*
 - *Bevacizumab or PARPi, which sequence? (...PRIMA trial?)*
 - *Long-term toxicity of PARPi?*

BRCA test



BRCAMut may be present in 15-44% of individuals with **no family history** of ovarian/breast cancer