2019 AIOM REVIEW: FROM CHICAGO TO VERONA

Rocco De Vivo
Dirigente Medico Oncologia,
ULSS8 Berica, Ospedale San Bortolo,
Vicenza

GENITOURINARY CANCERS

Highlights

Associazione Italiana di Oncologia Medica

OUTLINE

- PROSTATE CANCER
  - ✓ ENZAMET
  - ✓ TITAN
- KIDNEY CANCER
  - ✓ Update KEYNOTE 426
  - ✓ Post hoc analysis CheckMate 214
- BLADDER CANCER
  - ✓ CALGB 90601
  - ✓ EV-201

OVERALL SURVIVAL (OS) RESULTS OF A PHASE III RANDOMIZED TRIAL OF STANDARD OF CARE THERAPY WITH OR WITHOUT ENZALUTAMIDE FOR METASTATIC HORMONE SENSITIVE PROSTATE CANCER (mHSPC)

ENZAMET (ANZUP 1304): AN ANZUP-LED INTERNATIONAL CO-OPERATIVE GROUP TRIAL (NHMRC CTC, CCTG, CTI, DFCI)

Christopher Sweeney, Andrew Martin, Robert Zielinski, Alastair Thomson, Thean Hsiang Tan, Shahneen Sandhu, M. Neil Reaume, David Pook, Francis Parnis, Scott North, Gavin Marx, John McCaffrey, Ray McDermott, Nicola Lawrence, Lisa Horvath, Mark Frydenberg, Simon Chowdhury, Kim Chi, Martin Stockler, Ian Davis

ANZUP Cancer Trials Group Limited

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Christopher Sweeney, MBBS

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Metastatic Hormone Sensitive Prostate Cancer (mHSPC): History and Current State of the Art

- Until 2014 testosterone suppression ± standard nonsteroidal antiandrogen was the only therapy for mHSPC[1]
  - Patients with higher burden of mHSPC have shorter survival[2,3]
- Improvements in mHSPC overall survival (OS) from agents with survival benefits in castration-resistant prostate cancer (CRPC)
  - Docetaxel (a cytotoxic chemotherapy, microtubule spindle inhibitor) [4,5,6,7] (CHAARTED)
  - Abiraterone (a C17,20 lyase inhibitor, decreases extragonadal androgens) [8,9,10,11] (LATITUDE)
- Enzalutamide: potent direct AR inhibitor with OS benefit in CRPC[12,13]
  - Enzalutamide improves rPFS in mHSPC (± prior docetaxel) [ARCHES][14]
  - Apalutamide improves rPFS and OS in mHSPC (± prior docetaxel): [TITAN] [15]

ENZAMET: first mHSPC trial to report OS data of enzalutamide + testosterone suppression and outcomes if patients also received concurrent docetaxel

[1]Huggins and Hodges Cancer Res 1941; [2]Tangen et al J. Urol, 2012; [3]Millikan et al J.Clin Oncol, 2008; [4]Tannock et al NEJM, 2004; [5]Petrylak et al NEJM, 2004; [6]Sweeney et al NEJM 2015; [7]James et al Lancet 2015; [8]Debono et al NEJM 2011, [9]Ryan et al Lancet Oncology 2015; [10]Fizazi et al NEJM 2017, [11]James et al NEJM 2017, [12]Scher et al NEJM 2012, [13]Beer et al NEJM 2014, [14]Armstrong et al GUASCO 2019; [15]Chi et al ASCO 2019

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

ENZAMET Treatment

- Prior to randomization testosterone suppression up to 12 weeks and 2 cycles of docetaxel was allowed.
- Intermittent ADT and cyproterone were not allowed
- NSAA: bicalutamide; nilutamide; flutamide
- *High volume: visceral metastases and/or 4 or more bone metastases (at least 1 beyond pelvis and vertebral column)
- **Adult Co-morbidity Evaluation-27

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Study Endpoints

- **Primary Endpoint**
  - Overall survival
- **Secondary Endpoints**
  - Prostate specific antigen progression free survival (includes clinical progression if occurs first, PCWG2)
  - Clinical progression free survival (imaging, symptoms, signs)
  - Adverse events (CTCAE v4.03)
  - Health related quality of life (EORTC QLQ C-30, PR-25 and EQ-5D-5L)
  - Health outcomes relative to costs
  - Translational biological studies

PCWG2: Prostate Cancer Working Group Criteria version 2
CTCAE: NCI Common Terminology Criteria for Adverse Events

Supplementary Table S2: Participant baseline characteristics

Characteristic		Anti-androgen (N=562)	Enzalutamide (N=563)
N stage*	N0	237 (42.2%)	226 (40.1%)
	N1	194 (34.5%)	205 (36.4%)
	NX	65 (11.6%)	63 (11.2%)
	Unknown	66 (11.7%)	69 (12.3%)
M stage*	M0	157 (27.9%)	155 (27.5%)
	M1	347 (61.7%)	335 (59.5%)
	MX	27 (4.8%)	27 (4.8%)
	Unknown	31 (5.5%)	46 (8.2%)
Months since primary diagnosed	Mean (SD)	23.9 (40.2)	26.9 (45.3)
	Median (IQR)	3.1 (1.7 to 32.7)	2.0 (2.0 to 39.1)
Months since metastases diagnosed	Mean (SD)	3.1 (7.2)	2.9 (6.9)
	Median (IQR)	1.9 (1.0 to 2.8)	1.9 (0.9 to 2.8)
Gleason Score	≤7	163 (29.0%)	152 (27.0%)
	8-10	321 (57.1%)	335 (59.5%)
	Missing	78 (13.9%)	76 (13.5%)

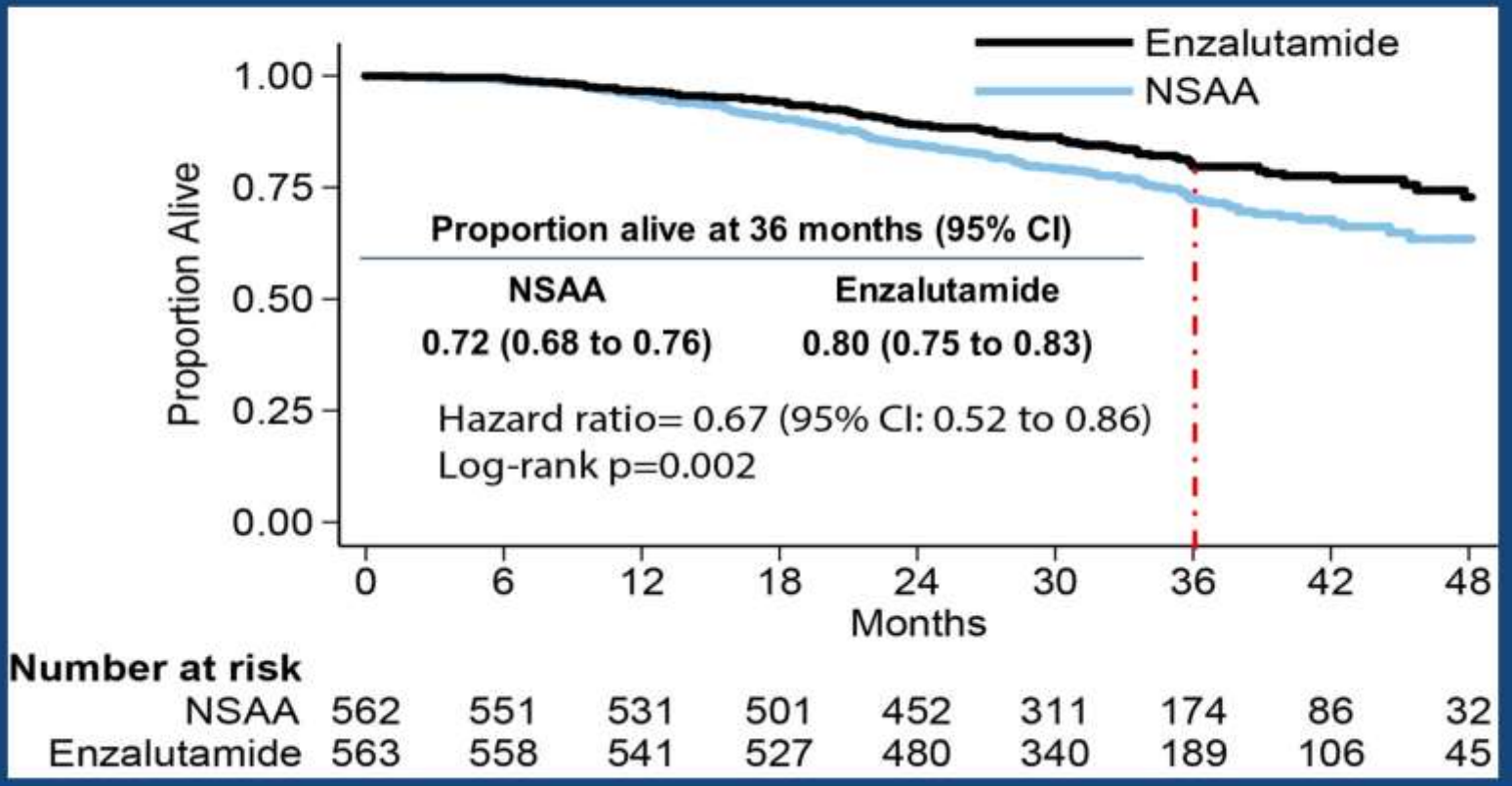
* Stage at first diagnosis.

Patient characteristics

- Early docetaxel
  - 61% high volume; 27% of low volume
- ADT: androgen deprivation therapy
- ACE: Adult Co-morbidity Evaluation-27
- SRE Rx: Skeletal related event antiresorptive bone therapy
- **Prostatectomy or radiation

	TS + NSAA (N=562)		TS + Enzalutamide (N=563)	
	N	%	N	%
Planned Early Docetaxel				
Yes	249	44%	254	45%
No	313	56%	309	55%
Volume of Metastases				
High	297	53%	291	52%
Low	265	47%	272	48%
ACE-27 Stratum				
0-1	419	75%	422	75%
2-3	143	25%	141	25%
Prostate Cancer Related Therapies				
Planned SRE Rx	58	10%	55	10%
Prior Local Rx**	235	42%	238	42%
Prior Adjuvant ADT	40	7%	58	10%

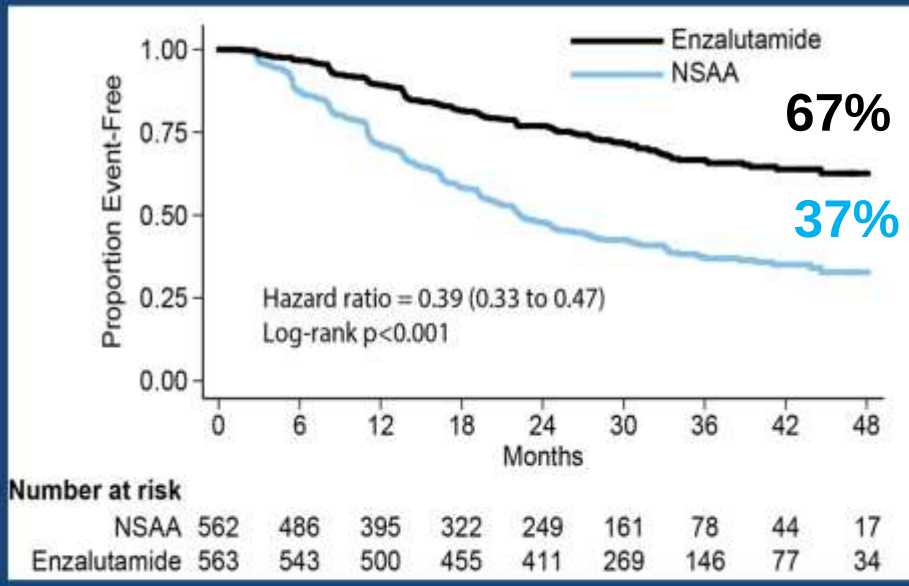
Primary endpoint: Overall survival



Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Secondary Endpoints: Progression-free survival (PCWG2)

Time to PSA rise, clinical progression or death

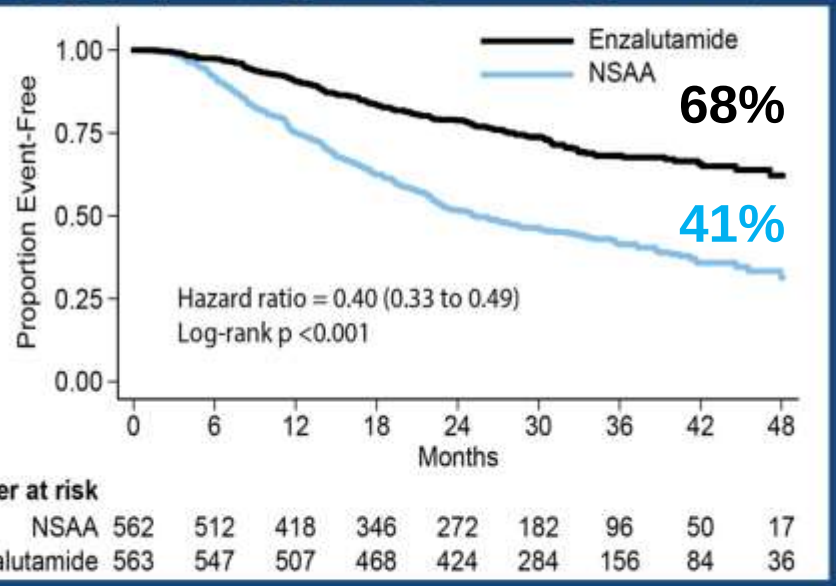


Number at risk

NSAA	562	486	395	322	249	161	78	44	17
Enzalutamide	563	543	500	455	411	269	146	77	34

Time to clinical progression

(imaging, symptoms, signs, change of therapy or death)



Number at risk

NSAA	562	512	418	346	272	182	96	50	17
Enzalutamide	563	547	507	468	424	284	156	84	36

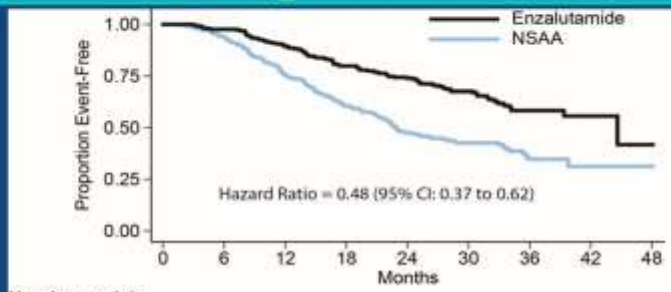
Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Concurrent Docetaxel: Prespecified Subgroup of Interest (Biology and Treatment Implications)

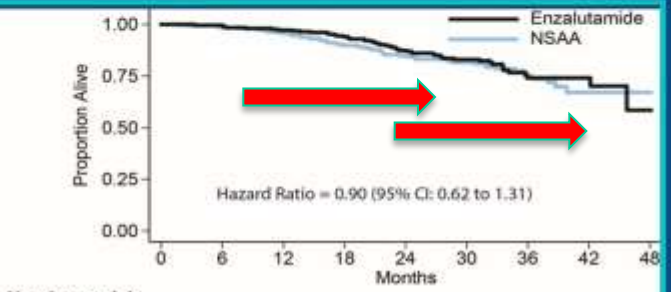
Clinical Progression-Free Survival

Overall Survival

Testosterone Suppression + Docetaxel N=503 (71% High Volume)

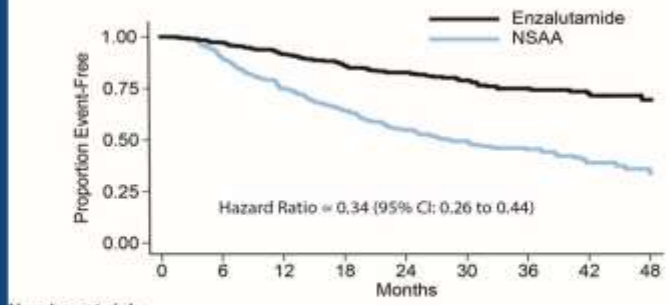


Number at risk									
NSAA	249	230	185	148	112	73	21	6	1
Enzalutamide	254	248	226	202	178	109	35	12	2

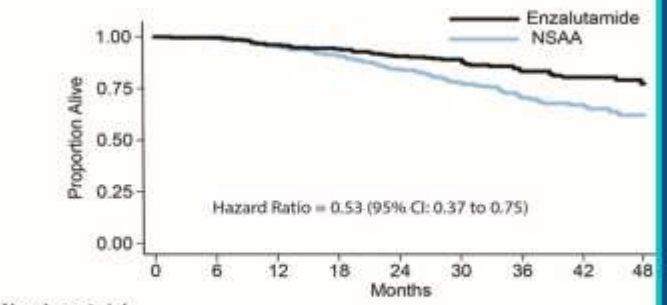


Number at risk									
NSAA	249	241	235	220	203	135	56	13	2
Enzalutamide	254	252	246	238	210	139	54	19	3

Testosterone Suppression + No Docetaxel N=622 (37% High Volume)



Number at risk									
NSAA	313	282	233	198	160	109	75	44	16
Enzalutamide	309	299	281	266	246	175	121	72	34



Number at risk									
NSAA	313	310	296	281	249	176	118	73	30
Enzalutamide	309	306	295	289	270	201	135	87	42

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Christopher Sweeney, MBBS

3 year OS point-estimates in biologically and clinically relevant predefined subgroups

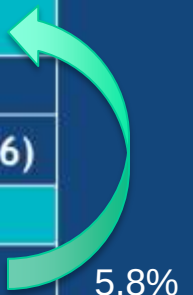
	TS + NSAA (N=562)		TS + Enzalutamide (N=563)	
	3 year OS (%)	95% CI	3 year OS (%)	95% CI
Early Docetaxel				
Yes	75	68 to 81	74	66 to 80
No	70	64 to 76	83	78 to 87
Volume of Metastases				
*High	64	58 to 70	71	64 to 76
Low	82	75 to 87	90	84 to 93

**356 (61%) of 588 high volume patients received early docetaxel - OS is better than testosterone suppression alone in CHAARTED and LATITUDE: ~50% 3 year OS*

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

Duration of study therapy and reasons for discontinuing

	TS + NSAA N=558	TS + ENZA N=563
6 cycles of early docetaxel*	76% of 238	65% of 243
Proportion on Rx at 36 months (95% CI)	0.34 (0.29 to 0.38)	0.62 (0.57 to 0.66)
Reasons for discontinuing	N=356	N=201
Discontinue due to adverse event	14 (4%)	33 (16%)
Imaging	144 (40%)	88 (44%)
Symptoms	55 (15%)	32 (16%)
New anti-cancer Rx	45 (13%)	7 (4%)
Clinician Preference	58 (16%)	13 (6%)
Death	7 (2%)	6 (3%)



*of those who received at least one cycle of docetaxel

Selected adverse events (AE)*:

All patients at anytime

	TS + NSAA N=558		TS + ENZA N=563	
Serious AE rate per yr of Rx exposure	0.33	95% CI: 0.28-0.39	0.34	95% CI: 0.29-0.40
AEs of Interest	N	%	N	%
Hypertension: Gde 3	24	4%	43	8%
Gde 2	30	5%	60	11%
Fatigue: Gde 3	4	1%	31	6%
Gde 2	80	14%	142	25%
Falls: Gde 3	2	<1%	6	1%
Gde 2	8	1%	28	5%
Syncope	7	1%	20	4%
Concentration Impairment: Gde 1/2	6	1%	24	4%
Any Seizure	0	0%	7	1%

*worst grade AE shown

Conclusion

Early enzalutamide improved time to progression and overall survival when added to standard mHSPC therapy (testosterone suppression ± docetaxel).

Clinical interpretation

- Enzalutamide added to testosterone suppression represents an appropriate option for men with metastatic prostate cancer commencing testosterone suppression
- Clear benefit in patients with low and high volume metastatic disease
  - Delays progression and improvement in overall survival
  - More expected toxicity was seen with enzalutamide alone
  - More docetaxel-related toxicity was reported with addition of enzalutamide
- For patients who are candidates for docetaxel when starting testosterone suppression, quality of life analyses and longer follow-up are needed to determine whether the delay in progression with concurrent enzalutamide
  - Results in a meaningful clinical benefit and / or
  - Is compounded by CRPC therapy and augments survival beyond 3 years

Presented By Christopher Sweeney at 2019 ASCO Annual Meeting

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer

I.D. Davis, A.J. Martin, M.R. Stockler, S. Begbie, K.N. Chi, S. Chowdhury, X. Coskinas, M. Frydenberg, W.E. Hague, L.G. Horvath, A.M. Joshua, N.J. Lawrence, G. Marx, J. McCaffrey, R. McDermott, M. McJannett, S.A. North, F. Parnis, W. Parulekar, D.W. Pook, M.N. Reaume, S.K. Sandhu, A. Tan, T.H. Tan, A. Thomson, E. Tu, F. Vera-Badillo, S.G. Williams, S. Yip, A.Y. Zhang, R.R. Zielinski, and C.J. Sweeney, for the ENZAMET Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group*

ANZUP®
Cancer Trials Group Limited

In collaboration with:

cancer trials ireland
Together, we're finding answers to cancer.

Canadian Cancer Trials Group
A national program of the Canadian Cancer Society

DANA-FARBER CANCER INSTITUTE

NHMRC Clinical Trials Centre

All slides can be downloaded at:
www.anzup.org.au/enzamet

PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19

PRESENTED BY: Christopher Sweeney, MBBS

Abstract 5006

First Results From TITAN: a Phase 3 Double-Blind, Randomized Study of Apalutamide Versus Placebo in Patients With Metastatic Castration-Sensitive Prostate Cancer Receiving Androgen Deprivation Therapy

Kim N. Chi,[1] Neeraj Agarwal,[2] Anders Bjartell,[3] Byung Ha Chung,[4] Andrea Juliana Pereira de Santana Gomes,[5] Robert W. Given,[6] Álvaro Juárez Soto,[7] Axel S. Merseburger,[8] Mustafa Özgüroğlu,[9] Hirotsugu Uemura,[10] Dingwei Ye,[11] Kris Deprince,[12] Vahid Naini,[13] Jinhui Li,[13] Shinta Cheng,[14] Margaret K. Yu,[15] Ke Zhang,[13] Julie S. Larsen,[15] Sharon A. McCarthy,[14] Simon Chowdhury[16] on behalf of the TITAN investigators

[1]BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada; [2]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; [3]Skåne University Hospital, Lund University, Malmö, Sweden; [4]Yonsei University College of Medicine and Gangnam Severance Hospital, Seoul, South Korea; [5]Liga Norte Riograndense Contra O Cancer, Natal, Brazil; [6]Urology of Virginia, Eastern Virginia Medical School, Norfolk, VA; [7]Hospital Universitario de Jerez de la Frontera, Cadiz, Spain; [8]University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany; [9]Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; [10]Kindai University Faculty of Medicine, Osaka, Japan; [11]Fudan University Shanghai Cancer Center, Shanghai, China; [12]Janssen Research & Development, Beerse, Belgium; [13]Janssen Research & Development, San Diego, CA; [14]Janssen Research & Development, Raritan, NJ; [15]Janssen Research & Development, Los Angeles, CA; [16]Guy's, King's, and St. Thomas' Hospitals, and Sarah Cannon Research Institute, London, UK

Presented By Kim Chi at 2019 ASCO Annual Meeting

TITAN Study Design

"All-comer" patient population

Key Eligibility Criteria
Castration sensitive
Distant metastatic disease by ≥ 1 lesion on bone scan
ECOG PS 0 or 1

On-Study Requirement
Continuous ADT

Permitted
Prior docetaxel
ADT ≤ 6 mo for mCSPC or ≤ 3 yr for local disease
Local treatment completed ≥ 1 yr prior

Stratifications
Gleason score at diagnosis (≤ 7 vs ≥ 8)
Region (NA and EU vs all other countries)
Prior docetaxel (yes vs no)

N = 1052

Dec 2015 – Jul 2017

1:1 RANDOMIZATION

- Apalutamide 240 mg daily + ADT (n = 525)
- Placebo + ADT (n = 527)

Dual primary end points
- OS
- rPFS

Secondary end points
- Time to cytotoxic chemotherapy
- Time to pain progression
- Time to chronic opioid use
- Time to skeletal-related event

Exploratory end points
- Time to PSA progression
- Second progression-free survival (PFS2)
- Time to symptomatic progression

ECOG PS, Eastern Cooperative Oncology Group performance status; NA, North America; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.

Presented By Kim Chi at 2019 ASCO Annual Meeting

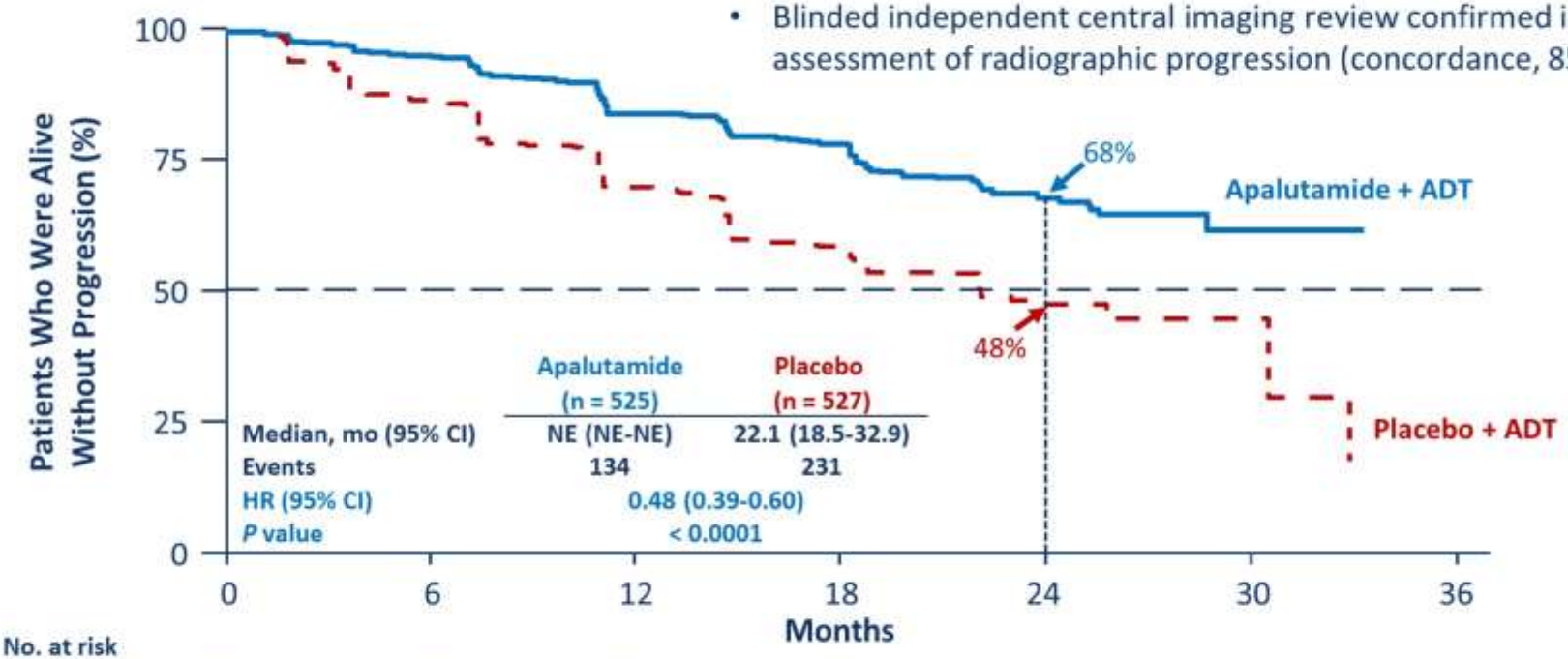
TITAN Demographics and Baseline Characteristics

		Apalutamide + ADT (n = 525)	Placebo + ADT (n = 527)
Median age, yr (range)		69 (45-94)	68 (43-90)
ECOG PS score, n (%)	0 1	328 (63) 197 (38)	348 (66) 178 (34)
Gleason score at initial diagnosis, n (%)	≤ 7 ≥ 8	174 (33) 351 (67)	169 (32) 358 (68)
TNM stage at initial diagnosis, n (%)	M0 or MX M1	114 (22) 411 (78)	86 (16) 441 (84)
Disease volume, n (%)	Low High[a]	200 (38) 325 (62)	192 (36) 335 (64)
Prior docetaxel[b], n (%)		58 (11)	55 (10)
Prior therapy for localized prostate cancer[c], n (%)		94 (18)	79 (15)
Mean baseline BPI-SF pain score[d], n (%)	0 to 3 (none to mild) 4 to 10 (moderate to severe)	393 (75) 110 (21)	407 (77) 106 (20)
Median baseline PSA, µg/L (range)		5.97 (0-2682)	4.02 (0-2229)

BPI-SF, Brief Pain Inventory-Short Form; TNM, tumor, node, metastasis.
[a]High-volume disease included: 1) visceral metastases and ≥ 1 bone lesion, or 2) ≥ 4 bone lesions, with ≥ 1 outside the axial skeleton. [b]27 patients (46.6%) in the apalutamide group and 22 patients (40.0%) in the placebo group were N1 at diagnosis. [c]Prior therapies for localized prostate cancer included prostatectomy and radiotherapy. [d]Scores range from 0 to 10, with lower scores representing lower levels of pain intensity; a change of 2 was the minimally important difference.

TITAN rPFS: Apalutamide Significantly Reduced Risk of Radiographic Progression or Death by 52%

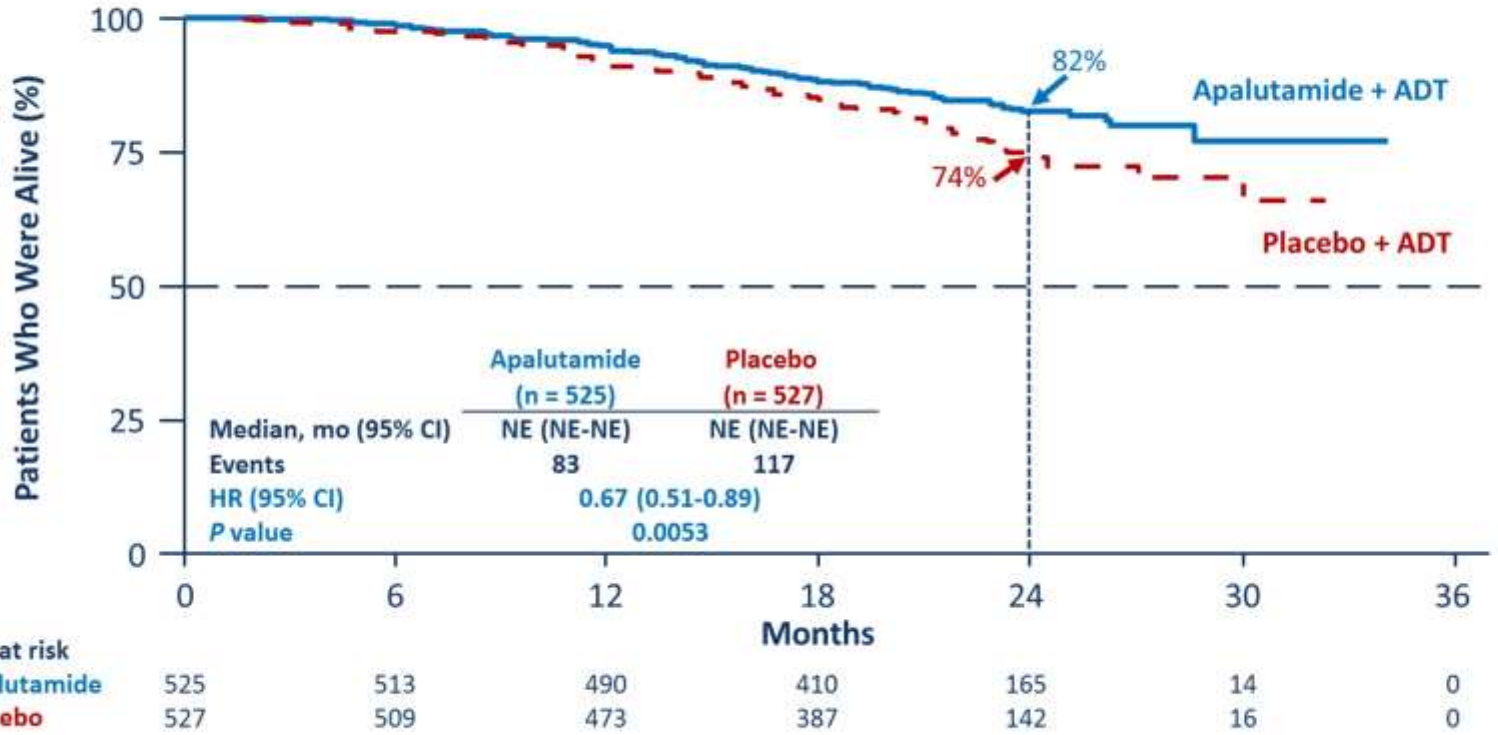
- Blinded independent central imaging review confirmed investigator assessment of radiographic progression (concordance, 85%)



CI, confidence interval; NE, not evaluable.

Presented By Kim Chi at 2019 ASCO Annual Meeting

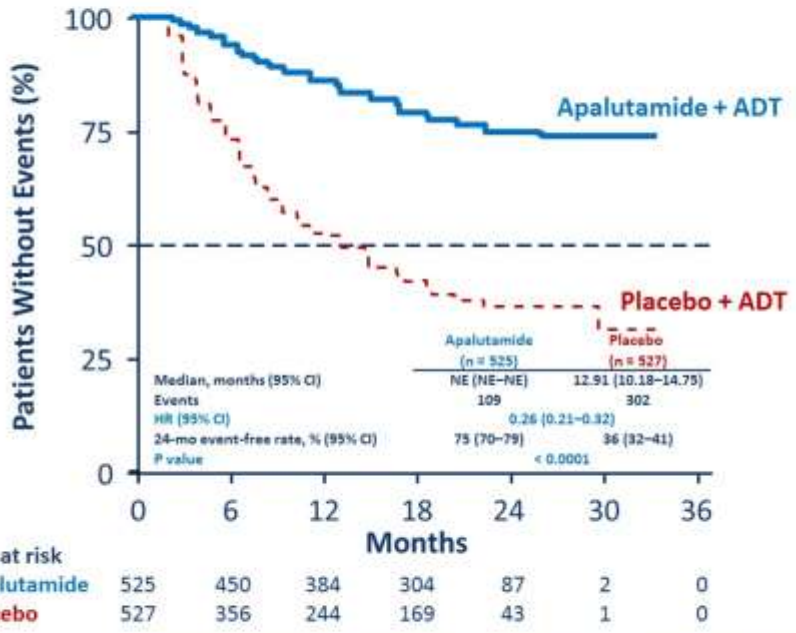
TITAN OS: Apalutamide Significantly Reduced the Risk of Death by 33%



Presented By Kim Chi at 2019 ASCO Annual Meeting

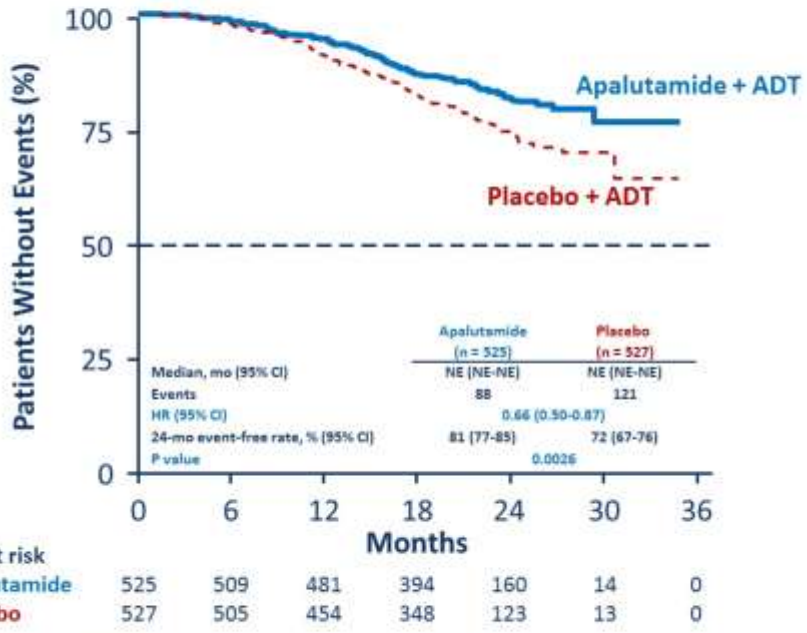
TITAN Exploratory End Points Favored Apalutamide

Time to PSA Progression[a]



No. at risk							
Apalutamide	525	450	384	304	87	2	0
Placebo	527	356	244	169	43	1	0

Second Progression-Free Survival (PFS2)[b]



No. at risk							
Apalutamide	525	509	481	394	160	14	0
Placebo	527	505	454	348	123	13	0

[a]Time to PSA progression was defined as the time from randomization to date of PSA progression based on Prostate Cancer Working Group 2 criteria.
[b]Time to second progression-free survival was defined as the time from randomization to first occurrence of investigator-determined disease progression (PSA progression, progression on imaging, or clinical progression) while patient was receiving first subsequent therapy for prostate cancer, or death due to any cause, whichever occurs first.

Presented By Kim Chi at 2019 ASCO Annual Meeting

TITAN Summary of Treatment-Emergent Adverse Events

Patients, n (%)	Apalutamide + ADT (n = 524)	Placebo + ADT (n = 527)
Any adverse event	507 (96.8)	509 (96.6)
Grade 3 or 4 adverse event	221 (42.2)	215 (40.8)
Any serious adverse event	104 (19.8)	107 (20.3)
Any adverse event leading to treatment discontinuation	42 (8.0)	28 (5.3)
Adverse event leading to death	10 (1.9)	16 (3.0)

- Adverse events were assessed monthly and graded according to NCI CTCAE version 4.0.3
- The most common adverse events leading to treatment discontinuation were rash (2.3% for apalutamide vs 0.2% for placebo) and new neoplasm (1.3% for apalutamide vs 0.9% for placebo)

NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events.

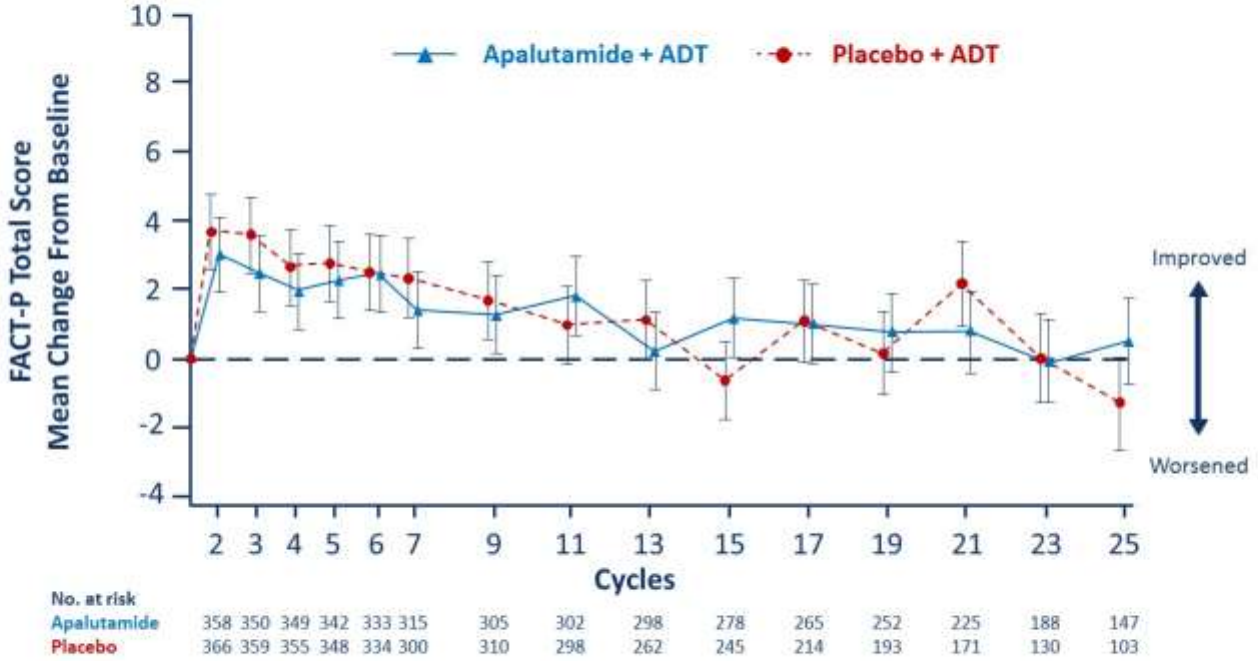
TITAN Adverse Events of Special Interest

	Apalutamide + ADT (n = 524)		Placebo + ADT (n = 527)	
Adverse Event, n (%)	**All Grades**	**Grade ≥ 3**	**All Grades**	**Grade ≥ 3**
Rash[a]	142 (27.1)	33 (6.3)	45 (8.5)	3 (0.6)
Fatigue	103 (19.7)	8 (1.5)	88 (16.7)	6 (1.1)
Fall	39 (7.4)	4 (0.8)	37 (7.0)	4 (0.8)
Hypothyroidism[b]	34 (6.5)	0	6 (1.1)	0
Fracture[c]	33 (6.3)	7 (1.3)	24 (4.6)	4 (0.8)
Seizure[d]	3 (0.6)	1 (0.2)	2 (0.4)	0

[a]Rash was a grouped term including rash, butterfly rash, erythematous rash, exfoliative rash, follicular rash, generalized rash, macular rash, maculo-papular rash, papules, papular rash, pruritic rash, pustular rash, genital rash, blister, skin exfoliation, exfoliative dermatitis, skin reaction, systemic lupus erythematosus rash, toxic skin eruption, mouth ulceration, drug eruption, conjunctivitis, erythema multiforme, stomatitis, and urticaria.
[b]Hypothyroidism was a grouped term including autoimmune thyroiditis, blood thyroid-stimulating hormone increased, and hypothyroidism.
[c]Fracture was a grouped term including acetabulum fracture, ankle fracture, clavicle fracture, femoral neck fracture, femur fracture, fibula fracture, foot fracture, forearm fracture, fracture, fractured ischium, fracture pain, hand fracture, hip fracture, lower limb fracture, patella fracture, radius fracture, rib fracture, skull fracture, spinal compression fracture, spinal fracture, sternal fracture, thoracic vertebral fracture, tibia fracture, traumatic fracture, ulna fracture, upper limb fracture, and wrist fracture.
[d]Seizure was a grouped term including seizure and tongue biting.

Presented By Kim Chi at 2019 ASCO Annual Meeting

TITAN Health-Related Quality of Life Was Preserved With Apalutamide + ADT and Not Different From Placebo + ADT



Error bars are standard errors of the mean. Raw FACT-P scores range from 0 to 156, with higher scores indicating more favorable health-related quality of life; a 6- to 10-point change in FACT-P total score would be the minimally important difference. However, this figure presents mean changes in total scores compared with baseline rather than raw total scores.
FACT-P, Functional Assessment of Cancer Therapy-Prostate.

Presented By Kim Chi at 2019 ASCO Annual Meeting

TITAN Conclusions

- The TITAN study met its dual primary end points, demonstrating significant benefits with apalutamide + ADT in an all-comer mCSPC population
  - Significant improvement in OS, with a 33% reduction in the risk of death
  - Significant improvement in rPFS, with a 52% reduction in the risk of progression or death
- Secondary and exploratory end points also favored apalutamide
  - Prolonged time to cytotoxic chemotherapy (61% risk reduction), PSA progression (74% risk reduction), and second progression-free survival (PFS2; 34% risk reduction)
- Treatment was tolerable and the safety profile was consistent with the known side effects of apalutamide
- Health-related quality of life was maintained and not different from placebo

TITAN Conclusions (cont'd)

- These results support the addition of apalutamide to ADT for a broad range of patients with mCSPC
  - High or low disease volume
  - Prior docetaxel
  - De novo metastatic disease or relapsed metastatic disease after initial diagnosis of localized disease
  - Prior treatment for localized disease

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D., Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D., Axel S. Merseburger, M.D., Mustafa Özgüroğlu, M.D., Hirotsugu Uemura, M.D., Dingwei Ye, M.D., Kris Deprince, M.D., Vahid Naini, Pharm.D., Jinhui Li, Ph.D., Shinta Cheng, M.D., Margaret K. Yu, M.D., Ke Zhang, Ph.D., Julie S. Larsen, Pharm.D., Sharon McCarthy, B.Pharm., and Simon Chowdhury, M.D., for the TITAN Investigators*

Presented By Kim Chi at 2019 ASCO Annual Meeting

OUTLINE

- PROSTATE CANCER
  - ✓ ENZAMET
  - ✓ TITAN

- KIDNEY CANCER
  - ✓ Update KEYNOTE 426
  - ✓ Post hoc analysis CheckMate 214

- BLADDER CANCER
  - ✓ CALGB 90601
  - ✓ EV-201

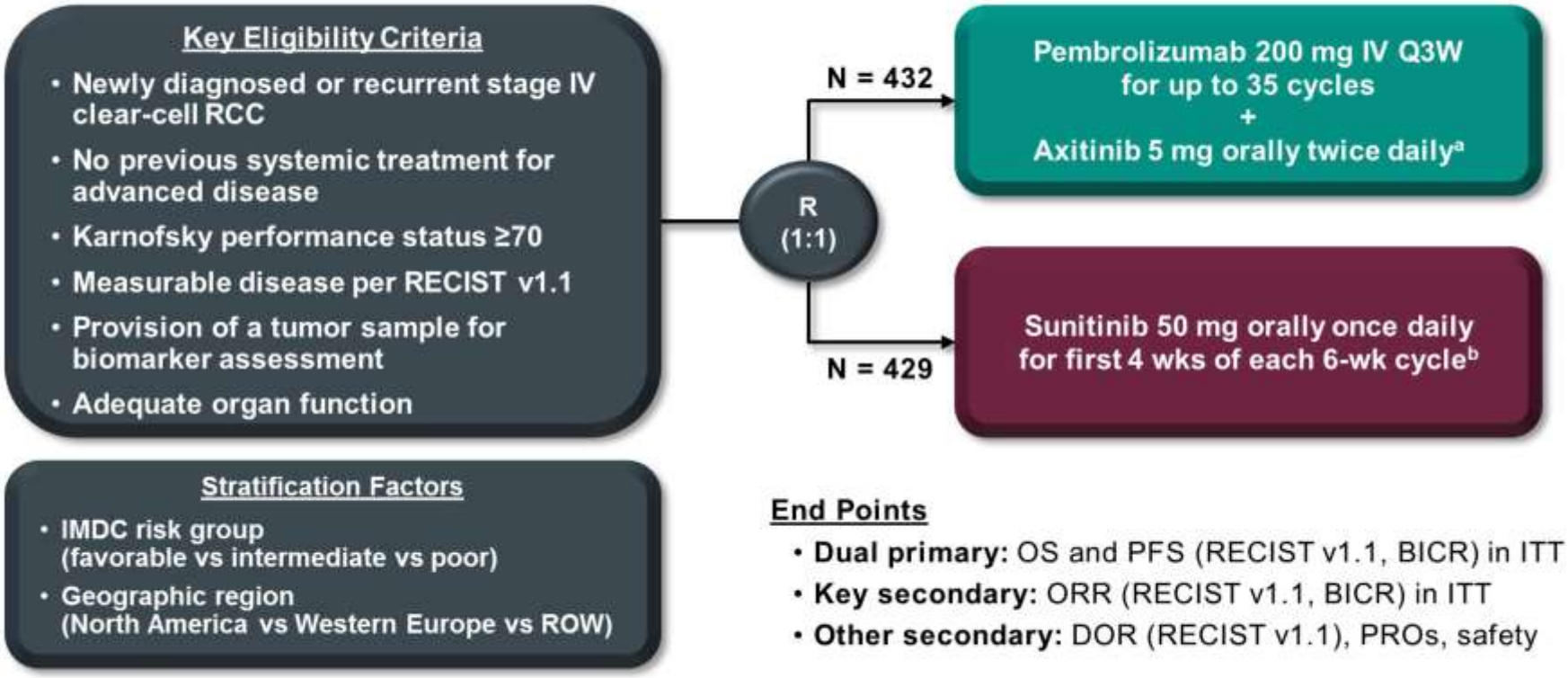
Pembrolizumab plus Axitinib as First-Line Therapy for mRCC: Outcomes in the Combined IMDC Intermediate/Poor Risk and Sarcomatoid Subgroups of KEYNOTE-426

Brian I. Rini,[1] Elizabeth R. Plimack,[2] Viktor Stus,[3] Rustem Gafanov,[4] Robert Hawkins,[5] Dmitry Nosov,[6] Frédéric Pouliot,[7] Denis Soulières,[8] Bohuslav Melichar,[9] Ihor Vynnychenko,[10] Sergio J. Azevedo,[11] Delphine Borchiellini,[12] Raymond S. McDermott,[13] Jens Bedke,[14] Satoshi Tamada,[15] Shuyan Wan,[16] Scot Ebbinghaus,[16] Rodolfo F. Perini,[16] Mei Chen,[16] Michael B. Atkins,[17] Thomas Powles[18]

[1]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Dnipropetrovsk Medical Academy of Ministry of Health of Ukraine, Dnipro, Ukraine; [4]Russian Scientific Center of Roentgenoradiology, Moscow, Russia; [5]The Christie NHS Foundation Trust, Manchester, UK; [6]Central Clinical Hospital with Outpatient Clinic, Moscow, Russia; [7]CHU de Québec and Université Laval, Quebec City, QC, Canada; [8]Centre Hospitalier de l'Universitaire de Montréal, Montréal, QC, Canada; [9]Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; [10]Sumy State University, Sumy Regional Oncology Center, Sumy, Ukraine; [11]Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil; [12]Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; [13]Adelaide and Meath Hospital and University College Dublin, Dublin, Ireland; [14]Department of Urology, Eberhard-Karls University Tübingen, Tübingen, Germany; [15]Osaka City University Hospital, Osaka, Japan; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]Georgetown–Lombardi Comprehensive Cancer Center, Washington, D.C., USA; [18]Barts Health and the Royal Free NHS Trusts, Barts Cancer Institute, and Queen Mary University of London, London, UK

Presented By Brian Rini at 2019 ASCO Annual Meeting

KEYNOTE-426 Study Design



[a]Axitinib dose could be increased to 7 mg, then 10 mg, twice daily if safety criteria were met; dose could be reduced to 3 mg, then 2 mg, twice daily to manage toxicity.
[b]Sunitinib dose could be decreased to 37.5 mg, then 25 mg, once daily for the first 4 wks of each 6-wk cycle to manage toxicity.
BICR, blinded independent central radiologic review; DOR, duration of response; PROs, patient-reported outcomes; ROW, rest of world.
KEYNOTE-426 is a randomized, open-label, phase 3 study (ClinicalTrials.gov identifier NCT02853331).

Baseline Characteristics

	Pembrolizumab + Axitinib N = 432	Sunitinib N = 429
Age, median (range)	62 yrs (30-89)	61 yrs (26-90)
Male	308 (71.3%)	320 (74.6%)
Region of enrollment		
North America	104 (24.1%)	103 (24.0%)
Western Europe	106 (24.5%)	104 (24.2%)
Rest of world	222 (51.4%)	222 (51.7%)
IMDC risk category		
Favorable	138 (31.9%)	131 (30.5%)
Intermediate	238 (55.1%)	246 (57.3%)
Poor	56 (13.0%)	52 (12.1%)
Sarcomatoid features	51/285 (17.9%)	54/293 (18.4%)
PD-L1 CPS ≥1[a]	243/410 (59.3%)	254/412 (61.7%)
≥2 metastatic organs	315 (72.9%)	331 (77.2%)
Previous nephrectomy	357 (82.6%)	358 (83.4%)

[a]Assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay. CPS = combined positive score = number of PD-L1–positive cells (tumor cells, lymphocytes, macrophages) divided by total number of tumor cells × 100.
Data cutoff date: Aug 24, 2018.

KEYNOTE-426: OS in the ITT Population

Pembrolizumab plus Axitinib for mRCC

- Other key findings from KEYNOTE-426[1]
  - PFS: HR 0.69 ($P < 0.001$)
  - ORR: 59.3% vs 35.7% ($P < 0.001$)
  - Benefit observed across subgroups, including the IMDC favorable, intermediate, and poor risk groups and in PD-L1–expressing and non-expressing tumors
  - Manageable safety profile
- Combination of pembrolizumab and axitinib approved by the FDA for first-line treatment of advanced RCC

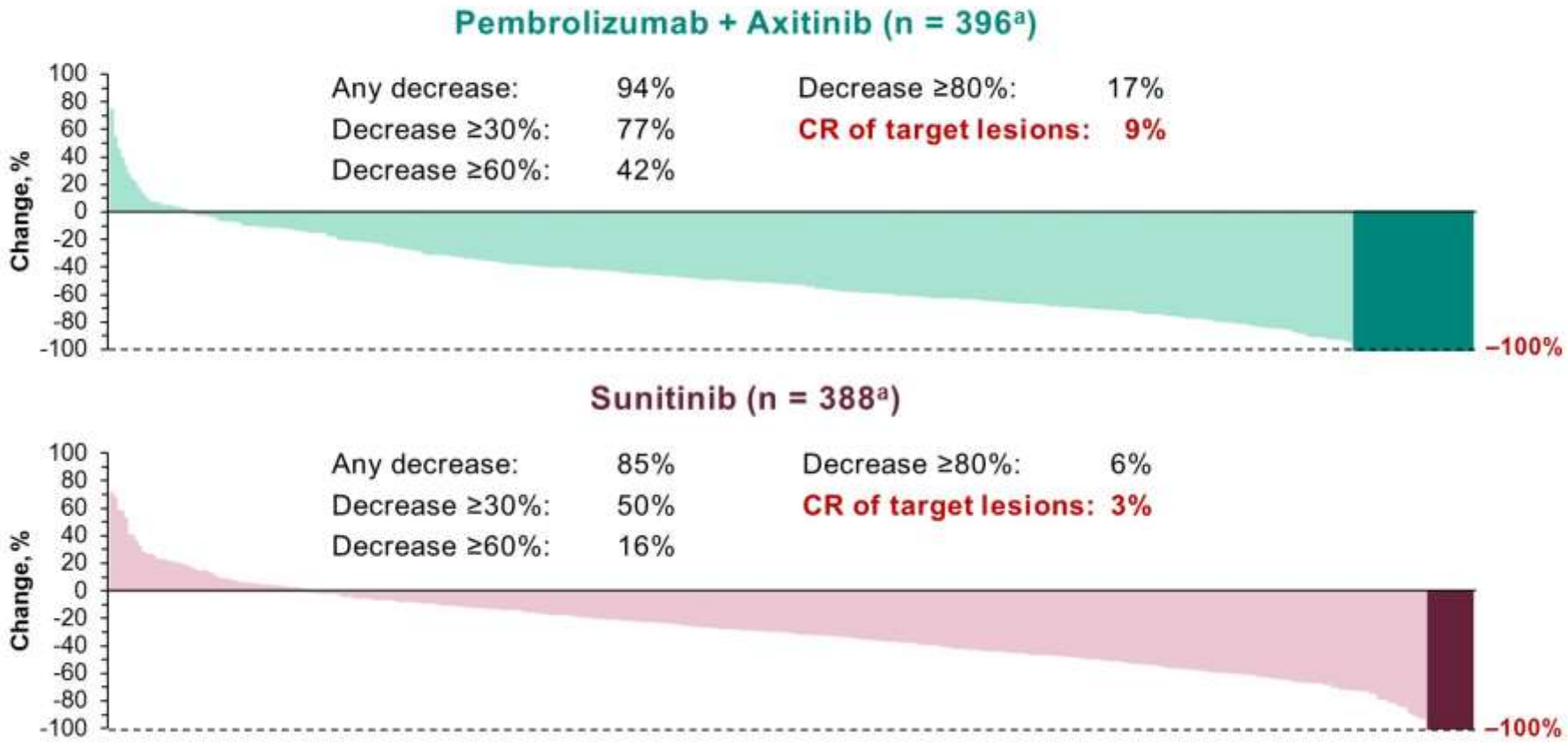
Rini BI et al. *N Engl J Med* 2019;380:1116–27.

Objectives of Current Analysis

- Evaluate different thresholds of percentage of tumor shrinkage[a]
- Assess OS, PFS,[b] and ORR[b] in subgroups of clinical interest:
  - IMDC favorable risk
  - IMDC intermediate/poor risk
  - Sarcomatoid differentiation

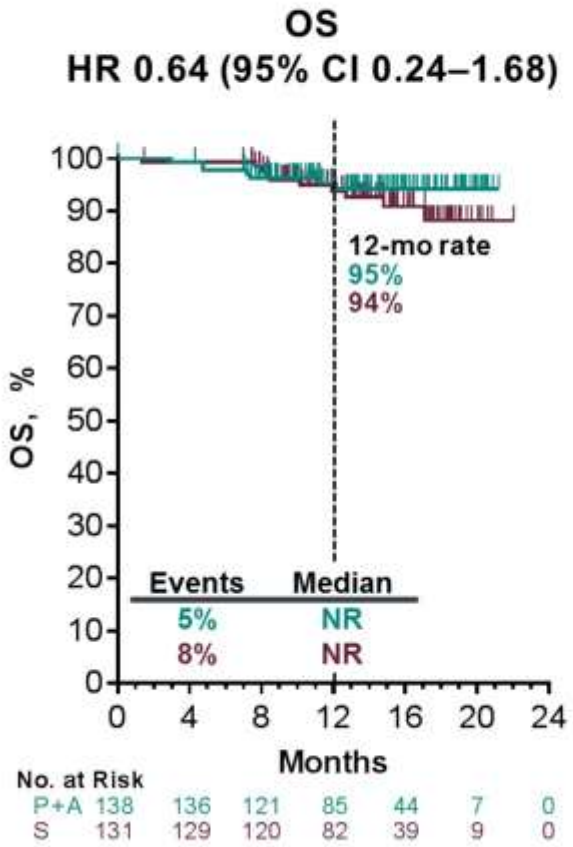
[a]Assessed as best percentage change from baseline per RECIST v1.1 by blinded, independent central radiology review.
[b]Assessed per RECIST v1.1 by blinded, independent central radiology review.
Data cutoff date: Aug 24, 2018.

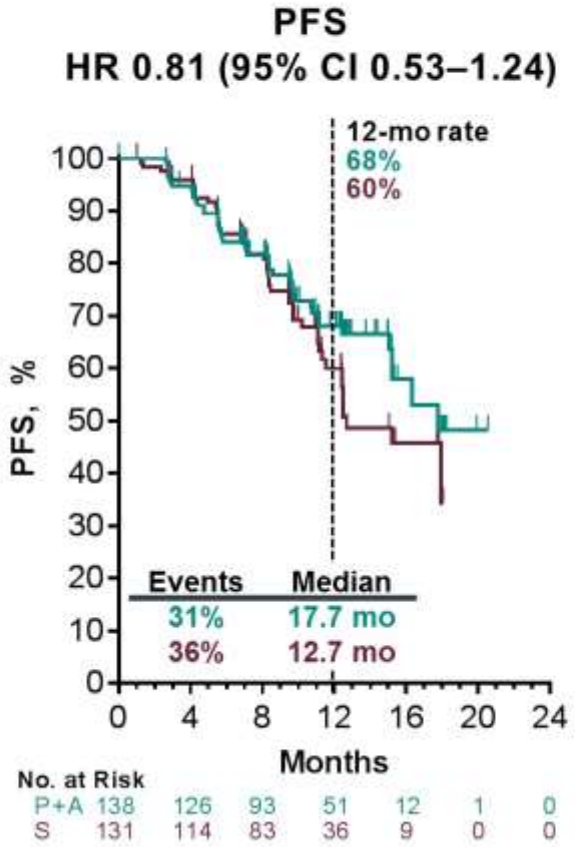
Change From Baseline in Target Lesions (ITT)

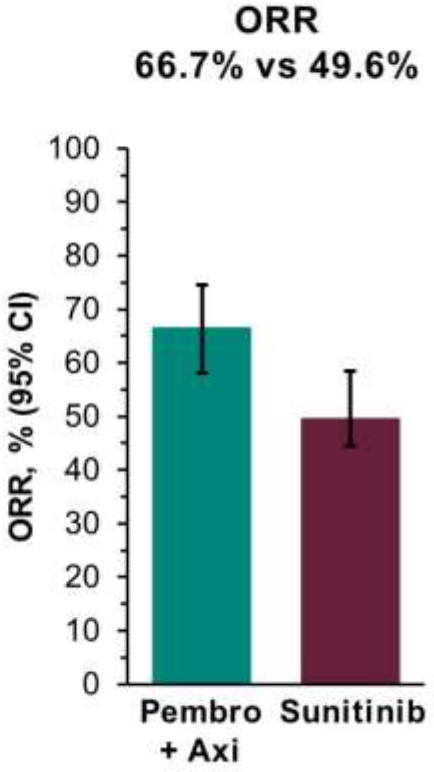


[a]Participants with ≥1 post-baseline imaging assessment evaluable per RECIST v1.1 by blinded, independent central review (BICR). Data cutoff date: Aug 24, 2018.

IMDC Favorable Risk: OS, PFS, and ORR

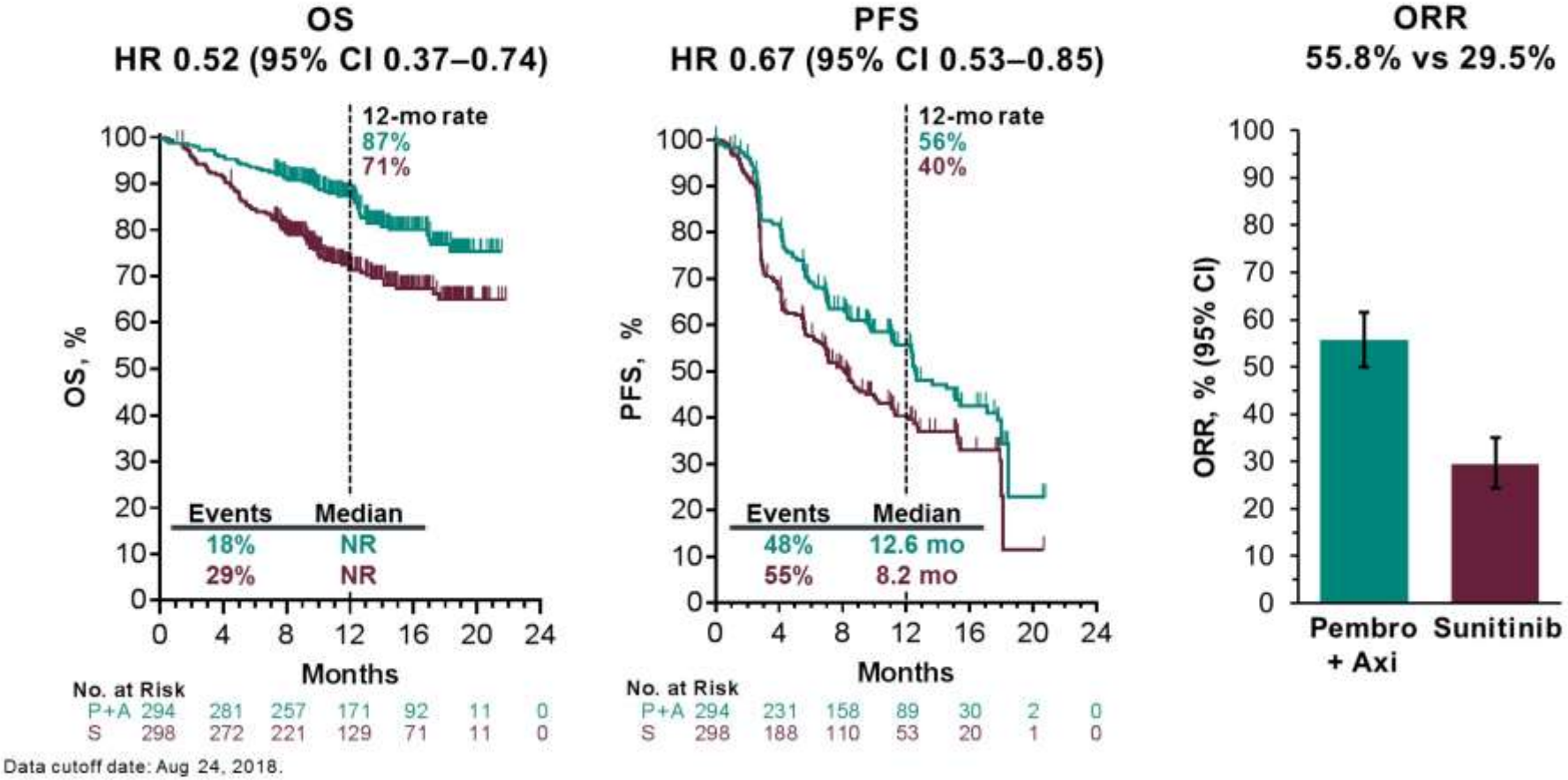




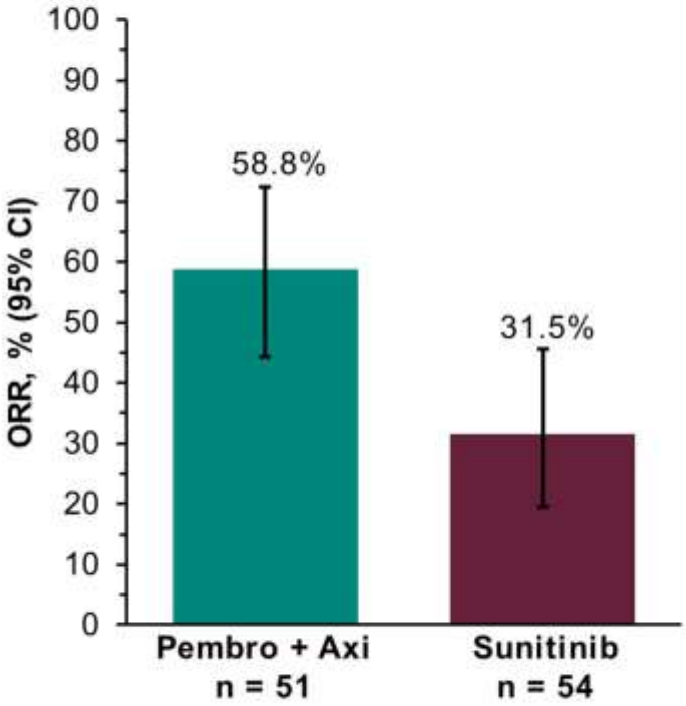


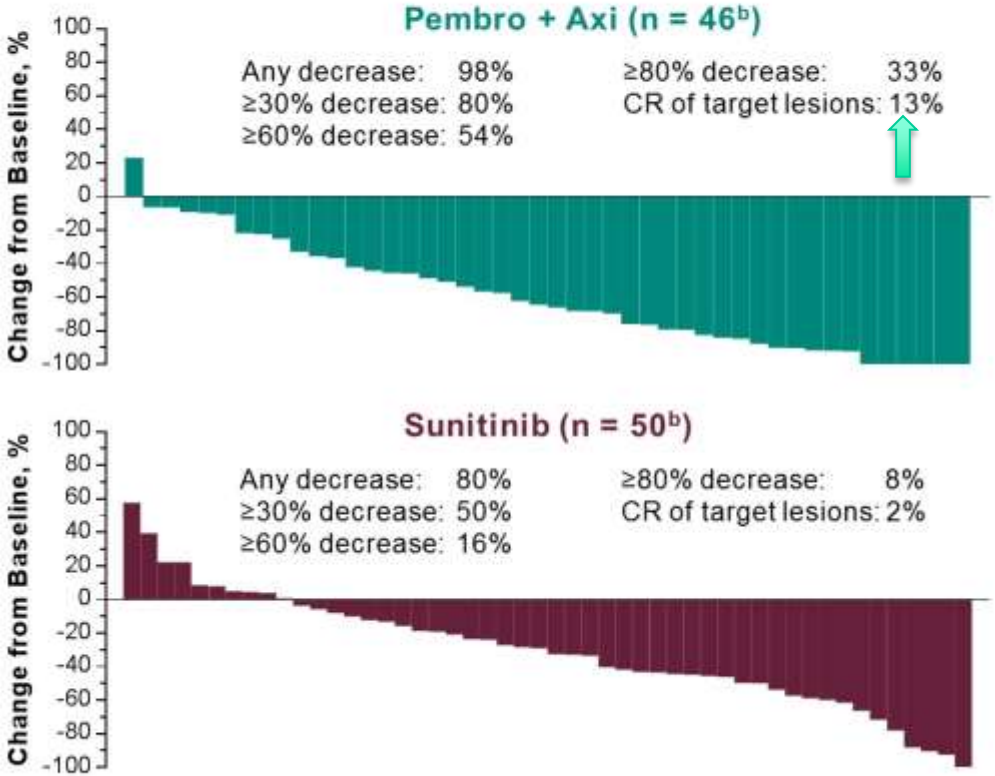
Data cutoff date: Aug 24, 2018.

IMDC Intermediate/Poor Risk: OS, PFS, and ORR



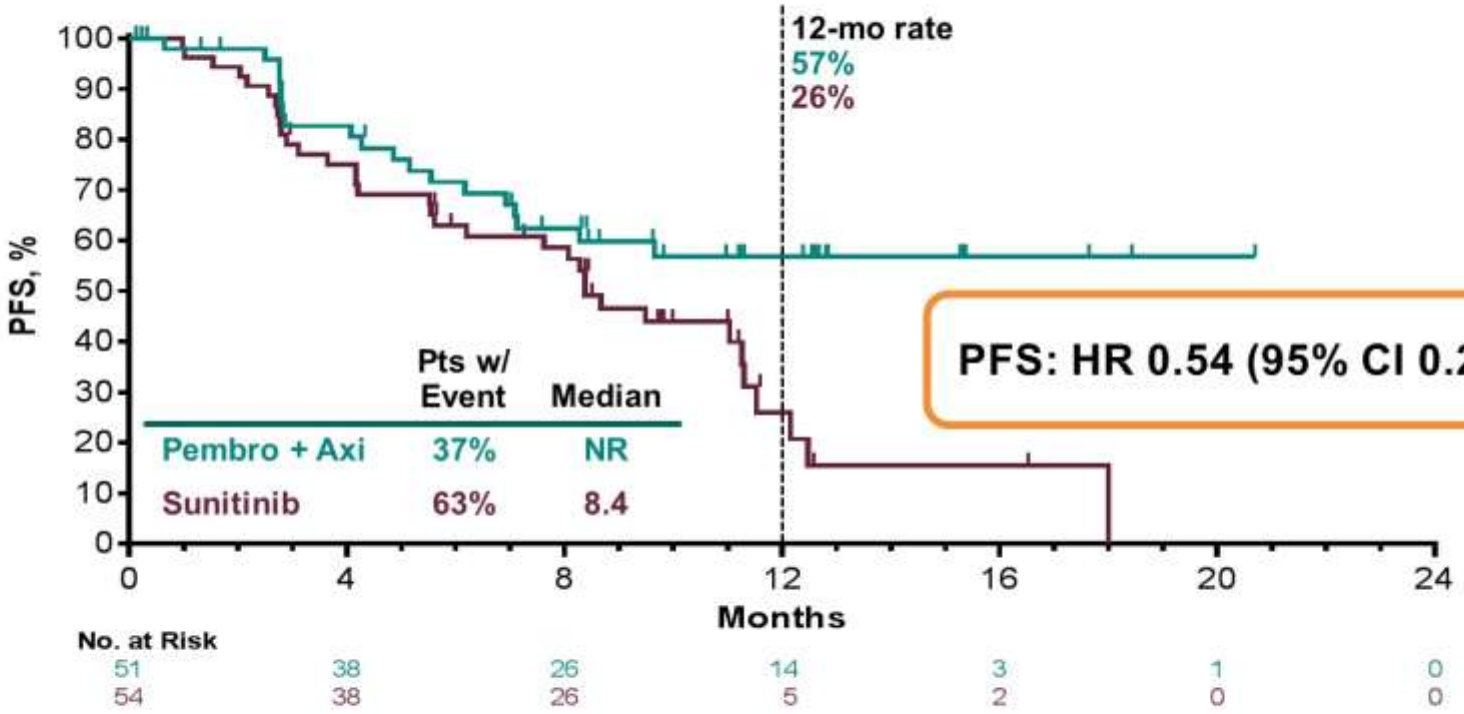
Response: Presence of Sarcomatoid Features[a]





[a]Among the 578 participants with known status assessed by local pathology review and as indicated on the eCRF. [b]Pts with ≥1 measurable lesion per RECIST v1.1 by BICR at baseline and ≥1 post-baseline imaging assessment evaluable per RECIST v1.1 by BICR. Data cutoff date: Aug 24, 2018.

PFS: Presence of Sarcomatoid Features[a]



PFS: HR 0.54 (95% CI 0.29–1.00)

OS: HR 0.58 (95% CI 0.21–1.59); median NR in either arm[b]

[a]Among the 578 participants with known status assessed by local pathology review and as indicated on the eCRF. [b]Pts who died: 16% in the pembro + axi arm, 20% in the sunitinib arm. Data cutoff date: Aug 24, 2018.

Summary and Conclusions

- Percentage of tumor shrinkage was substantially greater with pembrolizumab plus axitinib vs sunitinib
  - 60% reduction in target lesions: 42% vs 16%
  - 80% reduction in target lesions: 17% vs 6%
  - Complete response in all target lesions: 9% vs 3%

- OS, PFS, and ORR benefit of pembrolizumab plus axitinib vs sunitinib observed across key subgroups
  - IMDC favorable risk: OS HR 0.64
  - IMDC intermediate/poor risk: OS HR 0.52
  - Sarcomatoid features: OS HR 0.58

- Pembrolizumab plus axitinib is a new standard of care for first-line treatment of advanced clear-cell RCC, with OS, PFS and ORR benefit in all IMDC risk categories and substantial activity in participants with sarcomatoid RCC

4575

Consistent Efficacy of Nivolumab Plus Ipilimumab Across Number of IMDC Risk Factors in CheckMate 214

Bernard Escudier,[1] Robert J. Motzer,[2] Nizar M. Tannir,[3] Camillo Porta,[4] Yoshihiko Tomita,[5] Sabeen Mekan,*[6] M. Brent McHenry,[6] Brian I. Rini[7]

[1]Gustave Roussy, Villejuif, France; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]University of Texas MD Anderson Cancer Center, Houston TX, USA; [4]University of Pavia, Pavia, Italy; [5]Niigata University, Niigata, Japan; [6]Bristol-Myers Squibb, Princeton, NJ, USA; [7]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA

*Sabeen Mekan was an employee of BMS at the time the analysis was conducted

Presented at the American Society of Clinical Oncology Annual Meeting, May 31–June 4, 2019, Chicago, IL

Methods

- CheckMate 214 was a randomized, open-label, phase 3 trial of NIVO+IPI followed by NIVO monotherapy versus SUN in patients with previously untreated aRCC with a clear cell component[5]
- Patients were randomized 1:1 to receive either NIVO 3 mg/kg plus IPI 1 mg/kg intravenously every 3 weeks for 4 doses followed by NIVO 3 mg/kg every 2 weeks maintenance therapy or SUN 50 mg orally once daily for 4 weeks on and 2 weeks off in each 6-week cycle[5]
- This was a post hoc analysis of efficacy outcomes by number of IMDC risk factors; outcomes included OS, and investigator-assessed ORR and progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors v1.1

Methods

- Patients were categorized into favorable (0), intermediate (1–2), and poor (3–6) IMDC risk groups using an interactive voice response system (IVRS)
- The 6 individual IMDC components were collected on case report forms, which were used to identify the specific number of risk factors present for patients in the intermediate- and poor-risk groups
  - A total of 45 patients were excluded from the analysis due to a discrepancy between the IVRS and the case report form IMDC risk categorization
- Due to small patient numbers, patients with 4–6 risk factors were pooled for efficacy analyses

Results

- Minimum follow-up was 30 months (median, 32.4 months)
- There were 1096 patients in the ITT population. Of these, 23% had 0 risk factors, 61% had 1–2 risk factors, and 16% had 3–6 risk factors
- There were 1051 patients in this analysis, of whom 24% had 0 risk factors, 60% had 1–2 risk factors, and 17% had 3–6 risk factors
- Risk factors were generally balanced between the treatment arms
- In patients with intermediate risk, 58% had 1 risk factor and 42% had 2 risk factors; among poor-risk patients, 58% had 3 factors, 29% had 4 factors, 10% had 5 factors, and 3% had 6 factors (**Table 1**)

Table 1. Incidence of individual IMDC risk factors in CheckMate 214 patients

Patients with 1 risk factor, n (%)	NIVO+IPI n = 189	SUN n = 172
<1 year from diagnosis to randomization	97 (51.3)	89 (51.7)
Hemoglobin <LLN	44 (23.3)	52 (30.2)
KPS ≤70%	24 (12.7)	12 (7.0)
Absolute neutrophil count >ULN	12 (6.3)	11 (6.4)
Corrected calcium >10 mg/dL	12 (6.3)	7 (4.1)
Platelet count >ULN	0	1 (0.6)

KPS, Karnofsky performance status; LLN, lower limit of normal; ULN, upper limit of normal.

Table 1. Incidence of individual IMDC risk factors in CheckMate 214 patients

Patients with 2 risk factors, n (%)		NIVO+IPI n = 125	SUN n = 141
Factor 1	**Factor 2**		
<1 year from diagnosis to randomization	**Hemoglobin <LLN**	67 (53.6)	89 (63.1)
	Corrected calcium >10 mg/dL	18 (14.4)	13 (9.2)
	Absolute neutrophil count >ULN	13 (10.4)	9 (6.4)
	Platelet count >ULN	2 (1.6)	4 (2.8)
KPS ≤70%	**<1 year from diagnosis to randomization**	3 (2.4)	5 (3.5)
	Hemoglobin <LLN	4 (3.2)	5 (3.5)
	Corrected calcium >10 mg/dL	0	1 (0.7)
	Absolute neutrophil count >ULN	0	2 (1.4)
Hemoglobin <LLN	**Corrected calcium >10 mg/dL**	4 (3.2)	0
	Absolute neutrophil count >ULN	6 (4.8)	3 (2.1)
	Platelet count >ULN	3 (2.4)	6 (4.3)
Corrected calcium >10 mg/dL	**Absolute neutrophil count >ULN**	3 (2.4)	2 (1.4)
	Platelet count >ULN	2 (1.6)	1 (0.7)
Absolute neutrophil count >ULN	**Platelet count >ULN**	0	1 (0.7)
Platelet count >ULN	**KPS ≤70%**	0	0

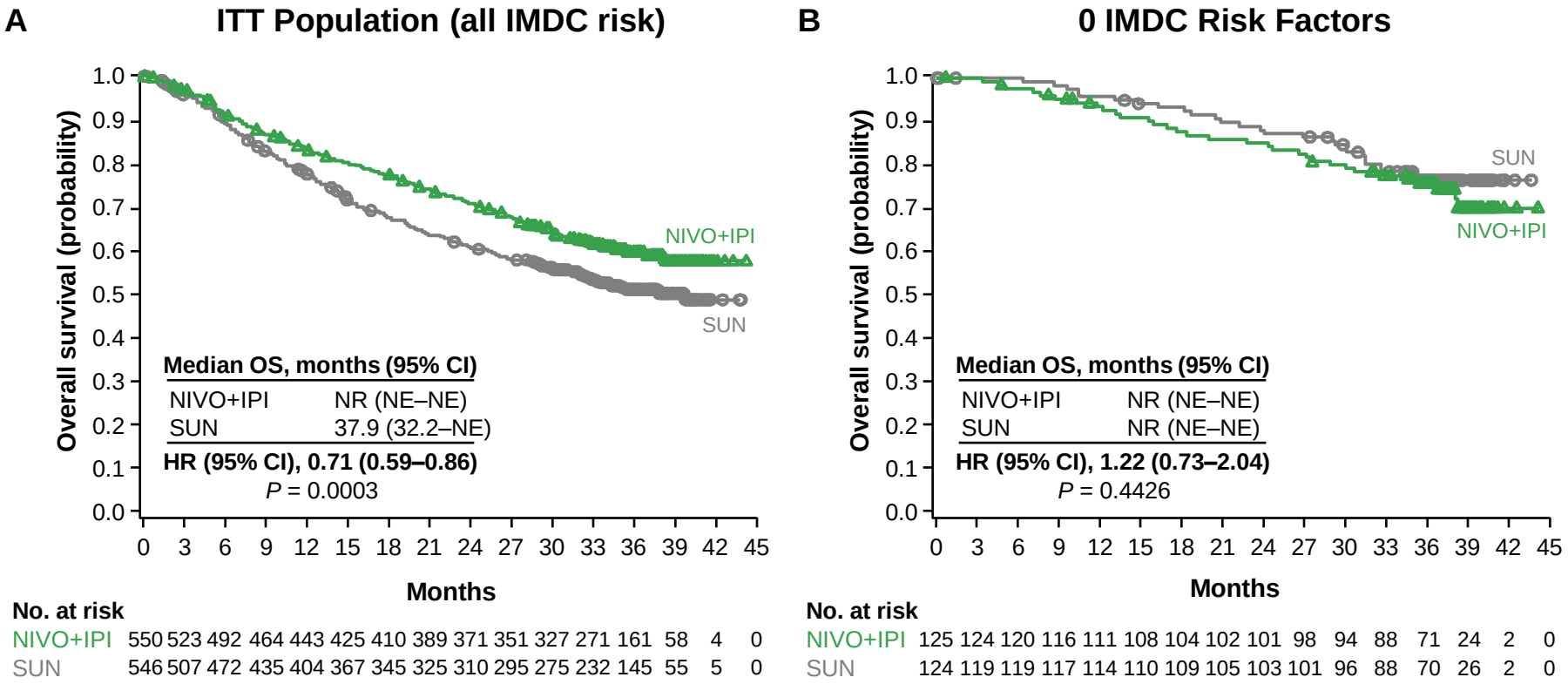
KPS, Karnofsky performance status; LLN, lower limit of normal; ULN, upper limit of normal.

Table 1. Incidence of individual IMDC risk factors in CheckMate 214 patients

Individual risk factors in patients with 3 risk factors, n (%)	NIVO+IPI n = 55	SUN n = 47
<1 year from diagnosis to randomization	50 (90.9)	42 (89.4)
Hemoglobin <LLN	49 (89.1)	38 (80.9)
Absolute neutrophil count >ULN	19 (65.5)	28 (59.6)
Platelet count >ULN	19 (34.5)	18 (38.3)
Corrected calcium >10 mg/dL	14 (25.5)	14 (29.8)
KPS ≤70%	14 (25.4)	10 (21.3)

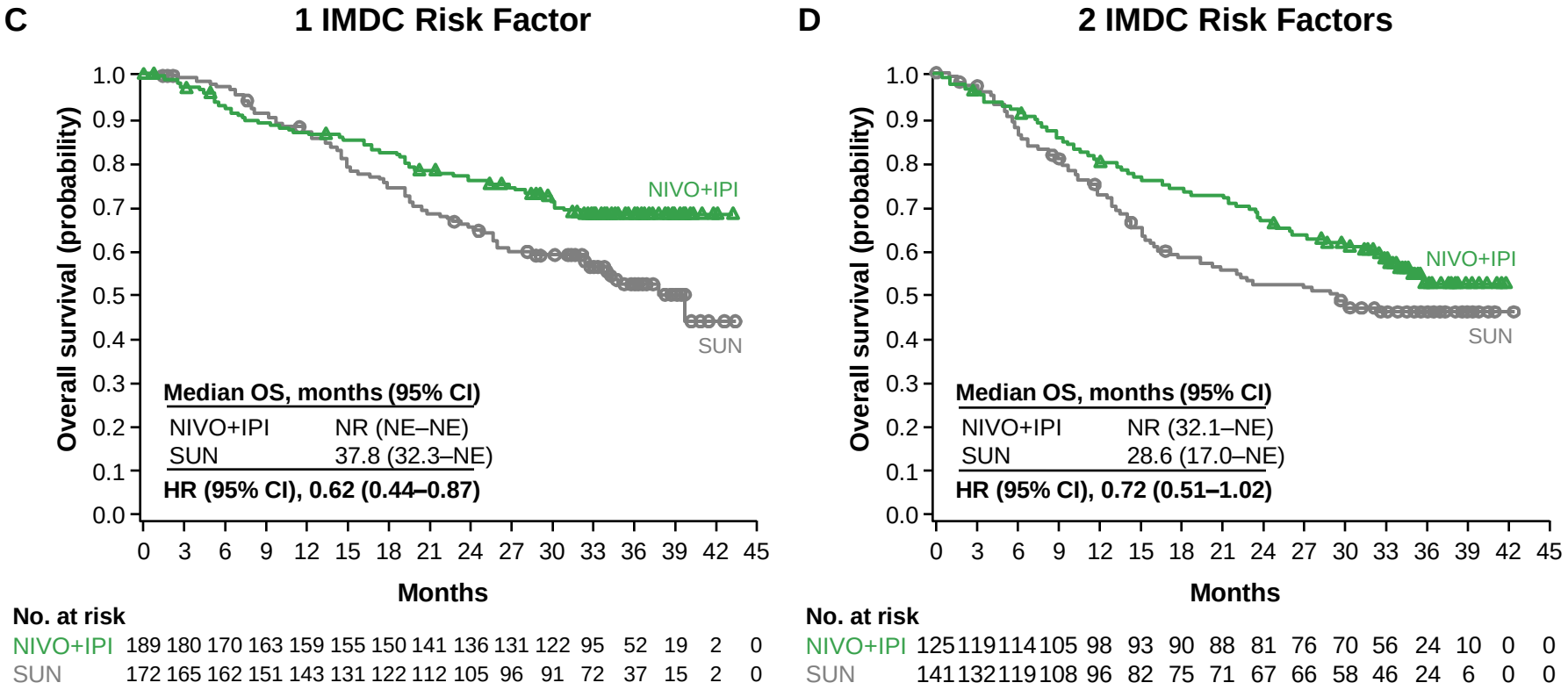
KPS, Karnofsky performance status; LLN, lower limit of normal; ULN, upper limit of normal.

Figure 1. Overall survival by number of IMDC risk factors



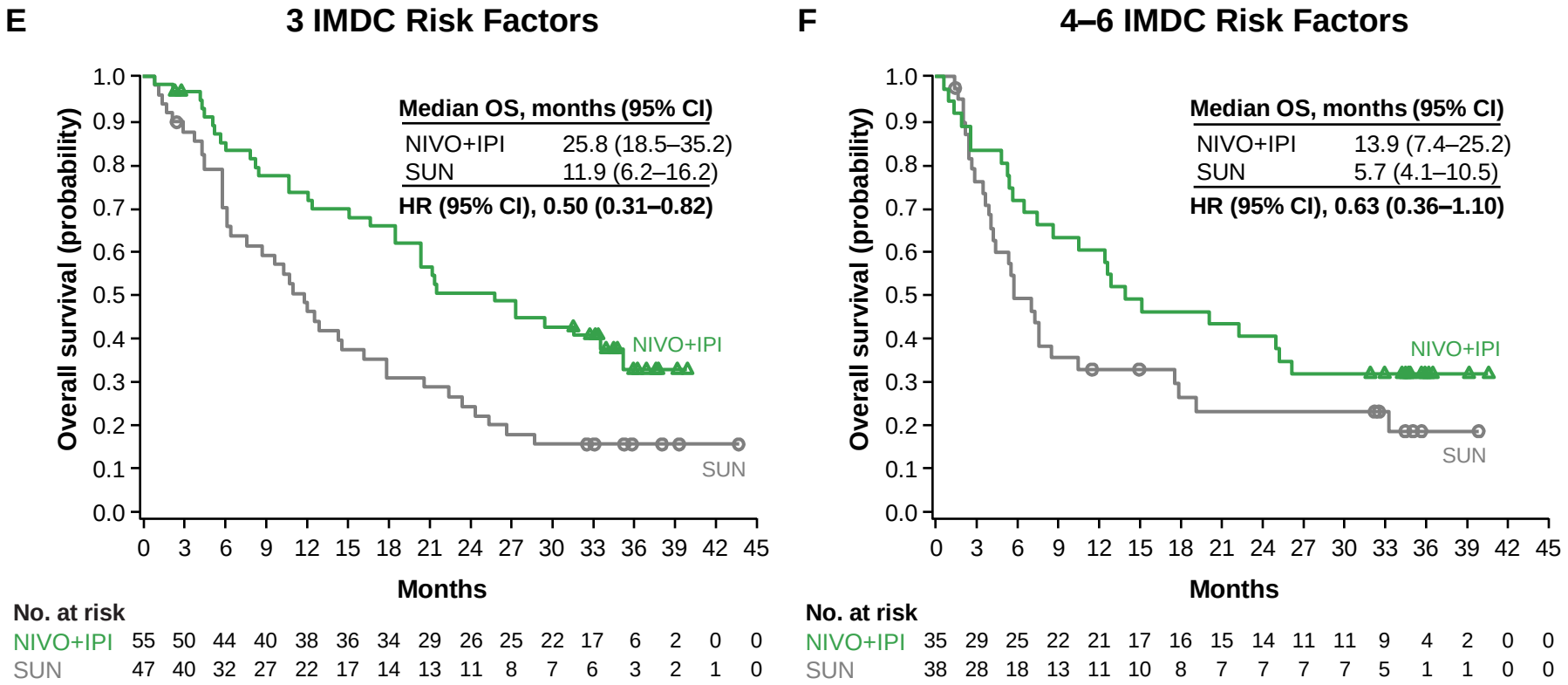
CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached.

Figure 1. Overall survival by number of IMDC risk factors



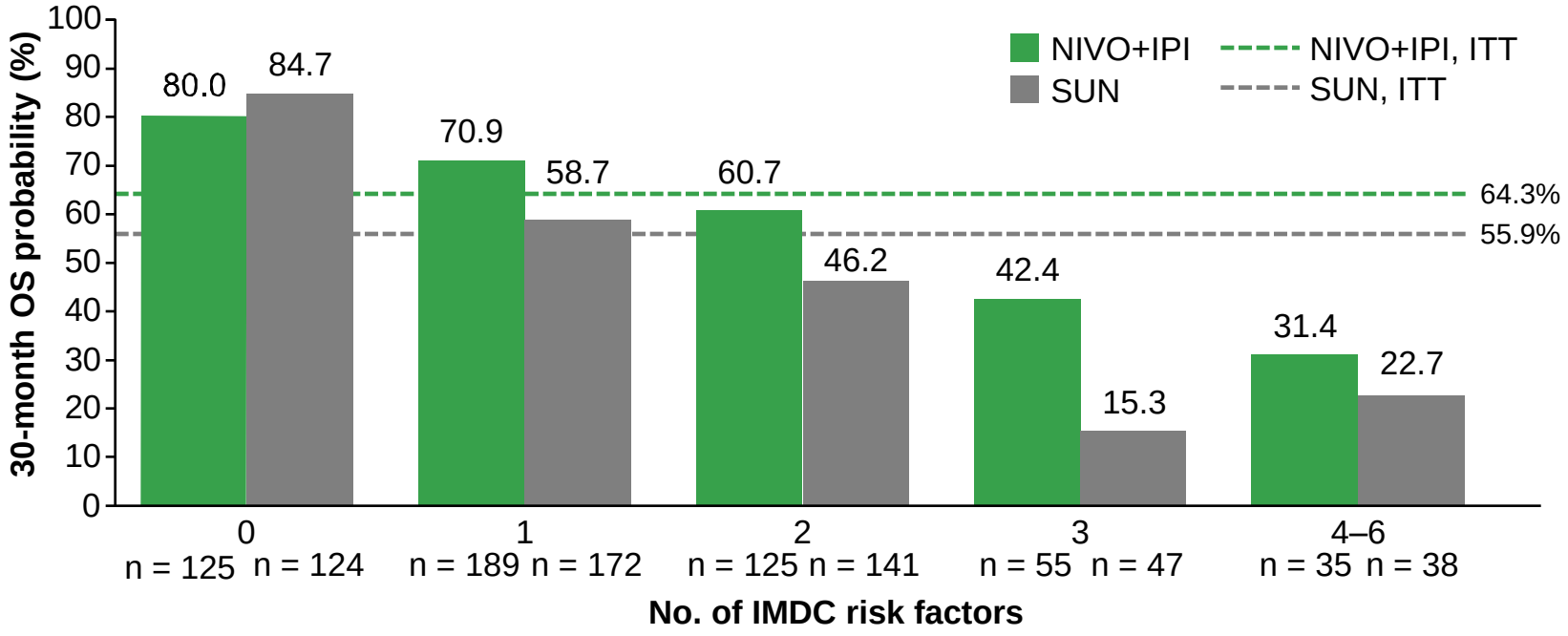
CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached.

Figure 1. Overall survival by number of IMDC risk factors



CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached.

Figure 2. 30-month overall survival probabilities by number of IMDC risk factors



Authors' Conclusions

- With long-term follow-up, consistent differential benefit in OS, PFS, and ORR were observed across all ITT patients and patients with 1–6 IMDC risk factors with NIVO+IPI over SUN
  - ORR with NIVO+IPI was consistent in patients with 0–6 IMDC risk factors, while ORR with SUN decreased with increasing number of risk factors
  - OS, PFS, and ORR benefits were observed with NIVO+IPI over SUN in patients prospectively categorized as having either intermediate- or poor-risk disease, and a majority of this intermediate/poor-risk group had just 1 or 2 IMDC risk factors

OUTLINE

- PROSTATE CANCER
  - ✓ ENZAMET
  - ✓ TITAN
- KIDNEY CANCER
  - ✓ Update KEYNOTE 426
  - ✓ Post hoc analysis CheckMate 214
- BLADDER CANCER
  - ✓ CALGB 90601
  - ✓ EV-201

CALGB 90601 (Alliance): Randomized, double blind, placebo-controlled phase III trial comparing gemcitabine and cisplatin with bevacizumab or placebo in patients with metastatic urothelial carcinoma.

Jonathan E. Rosenberg, Karla V. Ballman, Susan Halabi, Colleen Watt, Olwen M. Hahn, Preston D. Steen, Robert Dreicer, Thomas W. Flaig, Walter M. Stadler, Christopher Sweeney, Amir Mortazavi, Michael J. Morris on behalf of Alliance and NCTN Investigators

Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

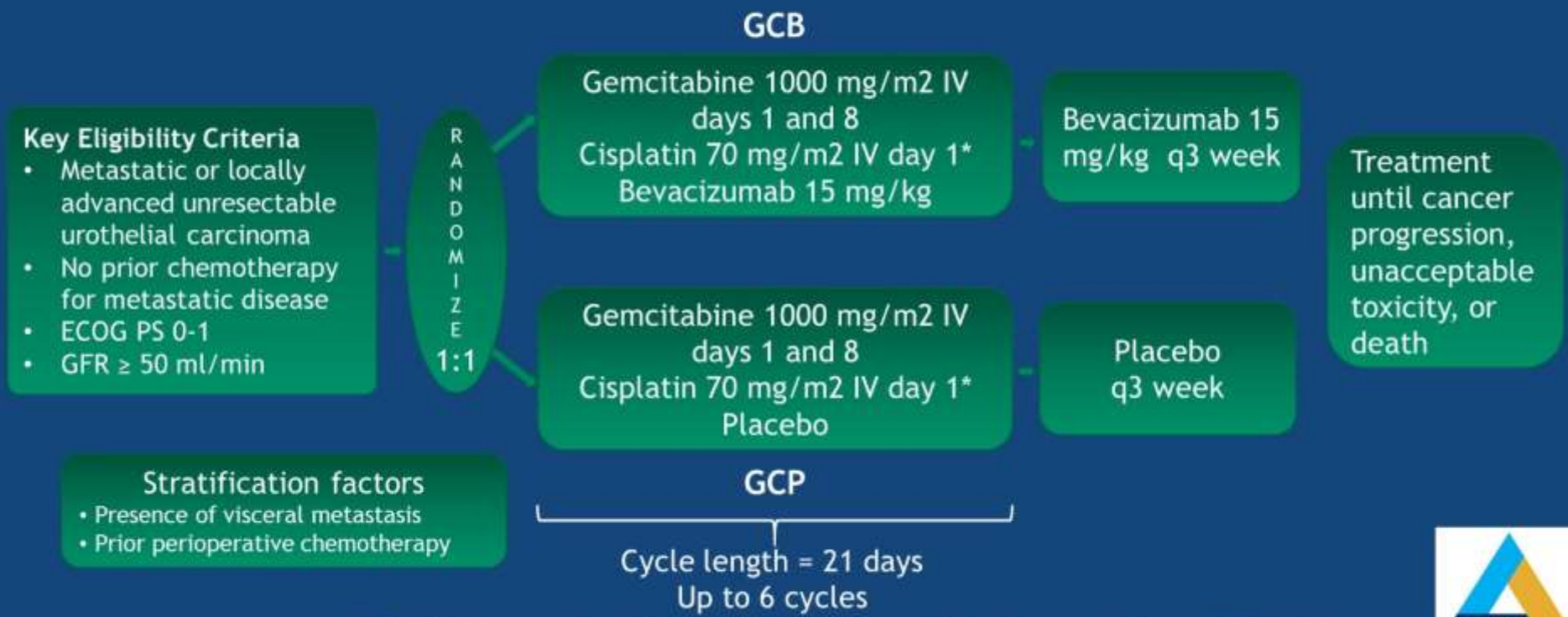
Treatment of locally advanced and metastatic urothelial carcinoma

- Gemcitabine and cisplatin (GC) has become the standard of care based on reduced toxicity and similar outcomes as MVAC[1]
  - Addition of other agents has not improved overall survival in randomized trials
- Upregulation of angiogenesis in urothelial carcinoma (UC) is associated with worse outcomes[2]
- In preclinical models, anti-angiogenic therapies inhibit progression of UC[3]
- VEGF is a primary pro-angiogenic mediator in UC
- Single agent VEGF-targeted TKI's produced low response rates in mUC[4]

1. Von der Maase, et al. *J Clin Oncol* 2000. 2. Inoue K, et al. *Clin Cancer Res* 2000 (a); Canoglu A, et al. *Int Jurol Nephrol* 2004. 3. Inoue K et al. *Clin Cancer Res* 2000 (b); Hu L, et al. *Clin Cancer Res* 2005. 4. Bellmunt et al. *Ann Oncol* 2011. Gallagher, et al. *J Clin Oncol* 2010; Necchi et al. *Lancet Oncol* 2012.

Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

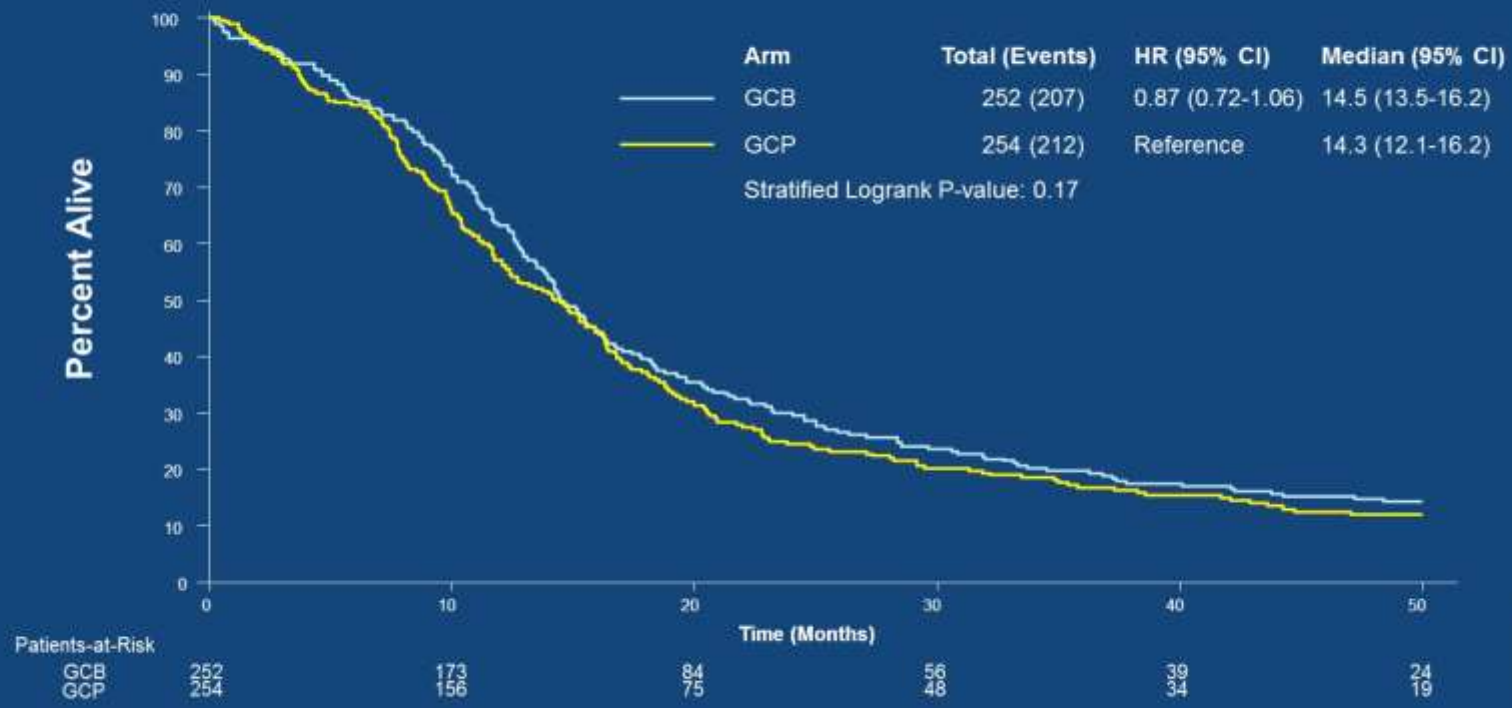
CALGB 90601 Study Design



• Primary Endpoint: Overall survival (OS)

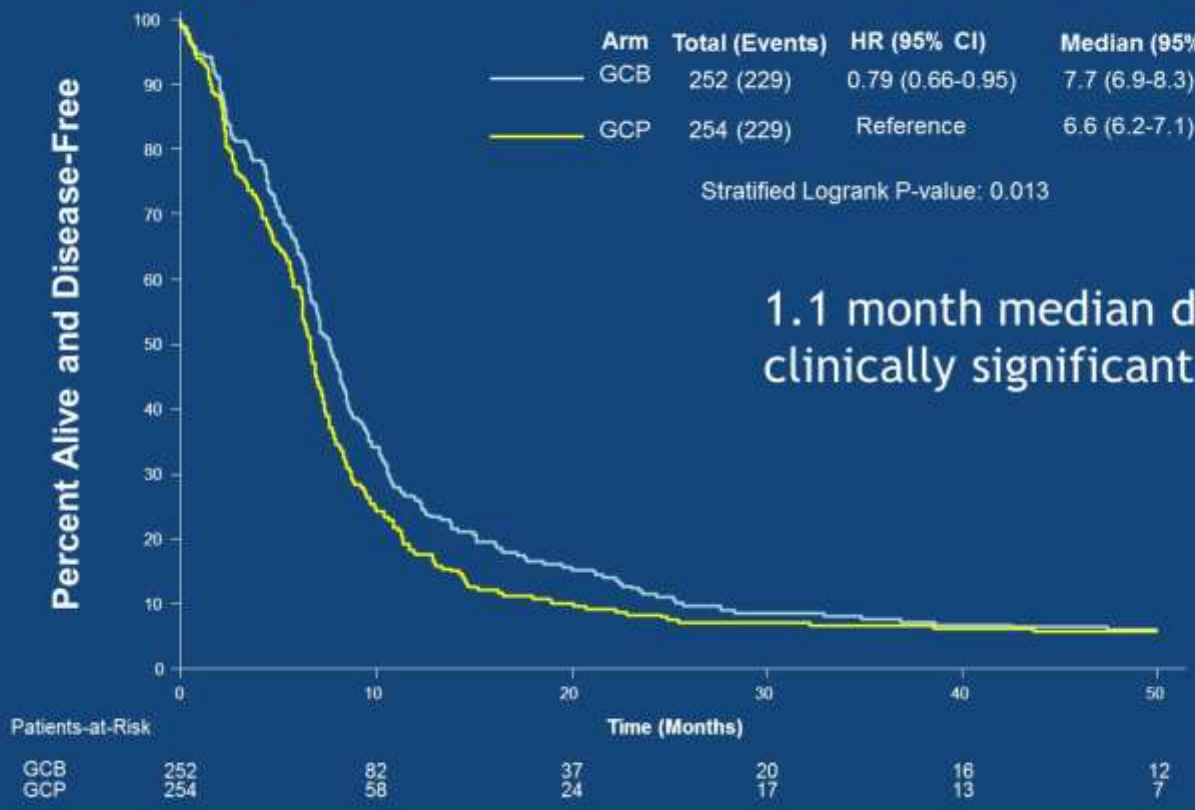
Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

Bevacizumab did not improve overall survival in combination with gemcitabine and cisplatin



Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

PFS was improved with bevacizumab



Arm	Total (Events)	HR (95% CI)	Median (95% CI)
GCB	252 (229)	0.79 (0.66-0.95)	7.7 (6.9-8.3)
GCP	254 (229)	Reference	6.6 (6.2-7.1)

Stratified Logrank P-value: 0.013

1.1 month median difference is not clinically significant

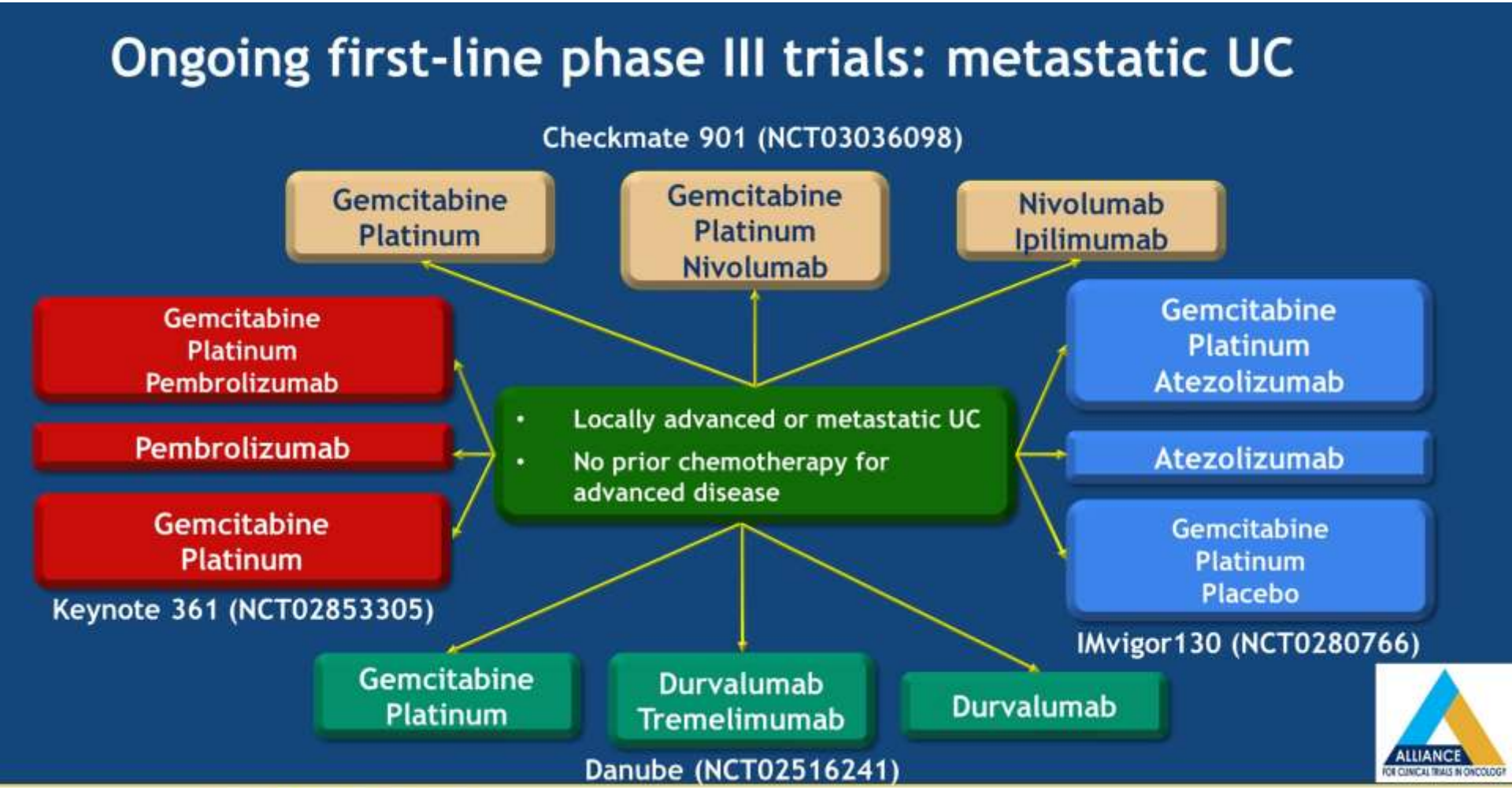
Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

CALGB 90601: Conclusions 1

- Addition of bevacizumab did not improve overall survival when added to gemcitabine and cisplatin chemotherapy as first-line therapy for metastatic urothelial carcinoma
  - Addition of bevacizumab did improve progression-free survival although the improvement was not clinically significant
- Toxicity of GCB was similar to historical data
- Currently, the standard of care remains cisplatin-based chemotherapy without the addition of biologic agents
- Ongoing correlative work may identify subsets of patients who may benefit from anti-angiogenic therapy

Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

Ongoing first-line phase III trials: metastatic UC



Presented By Jonathan Rosenberg at 2019 ASCO Annual Meeting

EV-201: Results of Enfortumab Vedotin Monotherapy for Locally Advanced or Metastatic Urothelial Cancer Previously Treated with Platinum and Immune Checkpoint Inhibitors (NCT03219333)

Daniel P. Petrylak, Arjun V. Balar, Peter H. O'Donnell, Bradley A. McGregor, Elisabeth I. Heath, Evan Y. Yu, Matthew D. Galsky, Noah M. Hahn, Elaina M. Gartner, Juan M. Pinelli, Shang-Ying Liang, Amal Melhem-Bertrandt, and Jonathan E. Rosenberg

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

Advanced and Metastatic Urothelial Carcinoma Has a High Unmet Need

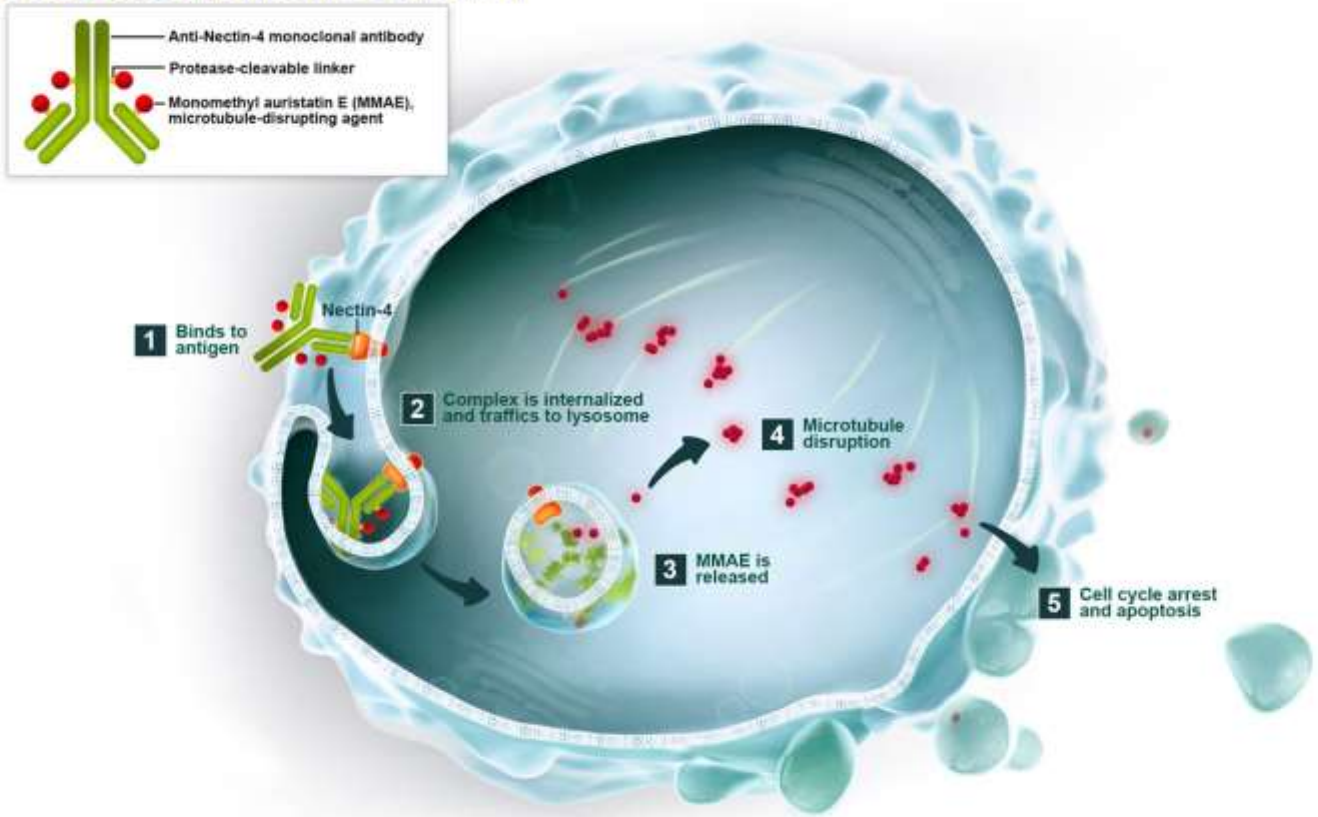
- First-line therapy remains platinum-based combination chemotherapy for most patients
- Response rates to second-line PD-1/L1 inhibitors are 13%–21% with few options once patients progress[1,2]
- Single agent chemotherapy post-platinum and post-PD-1/L1 inhibitors shows limited activity (ORR ~11%)[3]
- Enfortumab vedotin, an antibody-drug conjugate, showed an ORR of 45% in patients with prior PD-1/L1 inhibitors in a phase 1 study[4]
  - FDA granted enfortumab vedotin breakthrough designation based on the phase 1 data

[1] Bellmunt J, et al. N Engl J Med. 2017;376:1015-26; [2] Powles T, et al. Lancet. 2018;391:748-57; [3] Petrylak DP et al. Lancet. 2017;390:2266-77; [4] Rosenberg JE, et al. J Clin Oncol. 2019;37:377.

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

Enfortumab Vedotin: Nectin-4 Targeted Therapy

Proposed Mechanism of Action

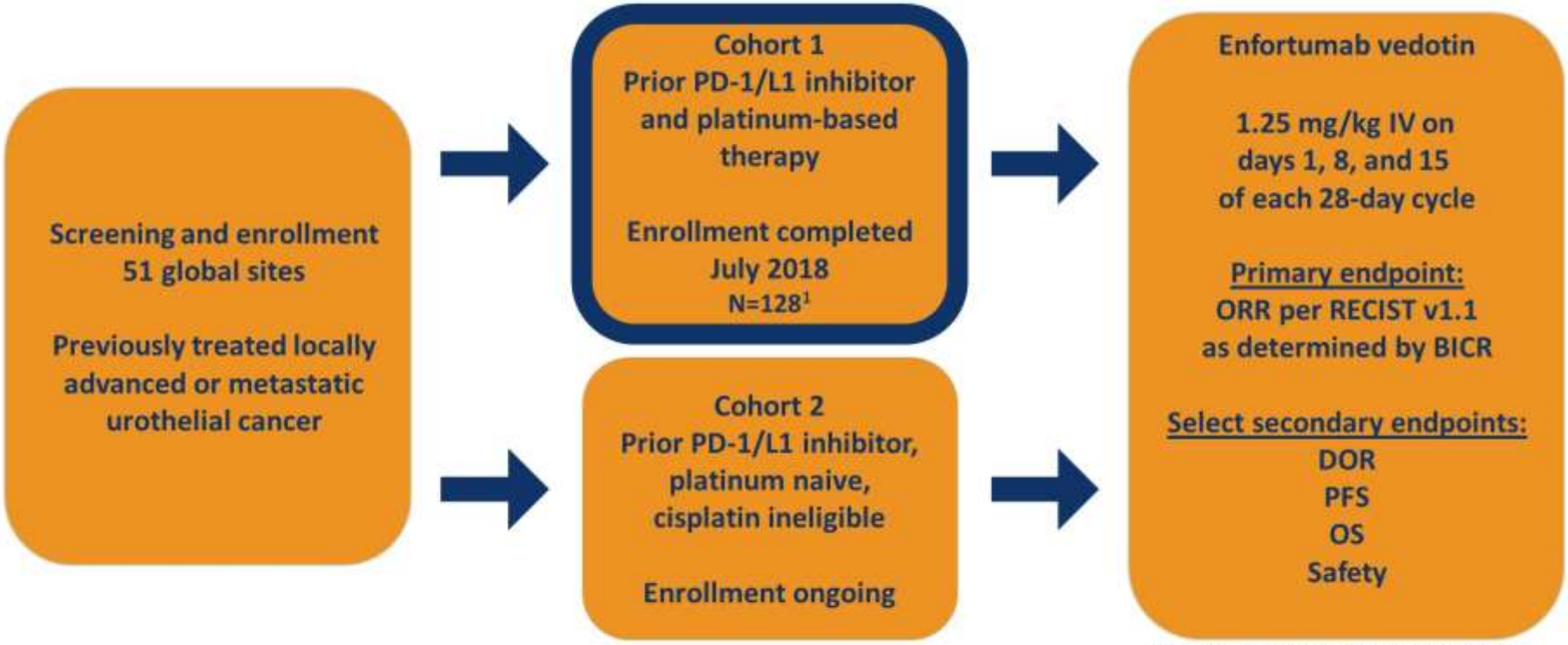


Enfortumab vedotin (ASG-22ME) is an investigational agent, and its safety and efficacy have not been established.

Enfortumab vedotin is being developed in collaboration with Astellas Pharma Inc.

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

EV-201: Single-Arm, Pivotal Phase 2 Trial



[1] 3 patients did not receive enfortumab vedotin treatment: one each due to clinical deterioration, patient decision, and low hemoglobin after enrollment

BICR=blinded independent central review; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

EV-201: Cohort 1 Demographics and Disease Characteristics

	Patients (N=125)
Male sex, n (%)	88 (70)
Age, years	
Median (min, max)	69 (40, 84)
≥75 years, n (%)	34 (27)
ECOG PS of 1, n (%)	85 (68)
Primary tumor location, n (%)	
Bladder/other	81 (65)
Upper tract	44 (35)
Number of prior systemic therapies[1], median (range)	3 (1, 6)
≥2 Bellmunt adverse prognostic factors	52 (42)
Metastasis sites, n (%)	
Lymph nodes only	13 (10)
Visceral disease	112 (90)
Liver	50 (40)
PD-L1 status by combined positive score[2]	
<10	78/120 (65)
≥10	42/120 (35)

[1] Patients with 1 prior therapy had platinum and a PD-1/L1 inhibitor in combination; [2] Five patients were not evaluable for PD-L1

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

EV-201: Cohort 1 Objective Response Rate with Enfortumab Vedotin

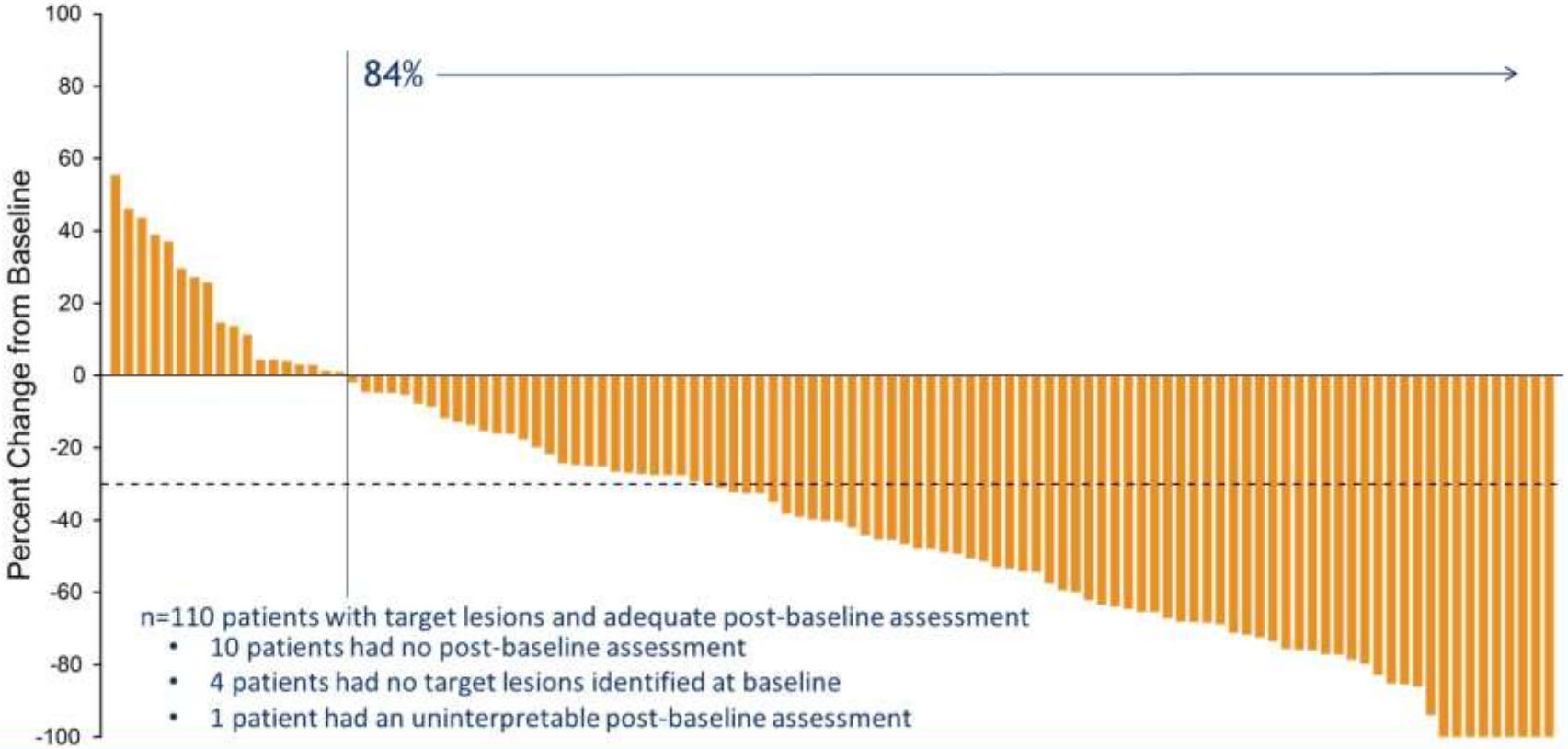
ORR per RECIST v 1.1 assessed by BICR	Patients (N=125) n (%)
Confirmed objective response rate	55 (44)
95% confidence interval[1]	(35.1, 53.2)
Best overall response per RECIST v. 1.1, n (%)	
Complete response	15 (12)
Partial response	40 (32)
Stable disease	35 (28)
Progressive disease	23 (18)
Not evaluable[2]	12 (10)

[1] Computed using the Clopper-Pearson method

[2] Includes 10 patients who discontinued study prior to post-baseline response assessment, 1 patient who had uninterpretable post-baseline assessment, and 1 patient whose post-baseline assessment did not meet the minimum interval requirement for stable disease

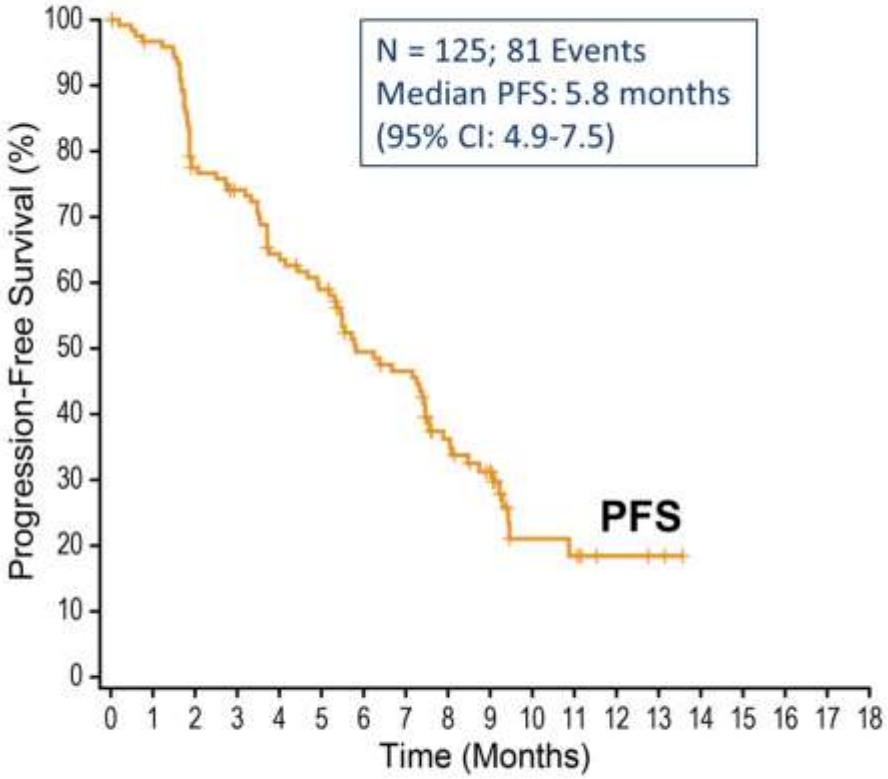
Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

EV-201: Cohort 1 Change in Tumor Measurements per BICR



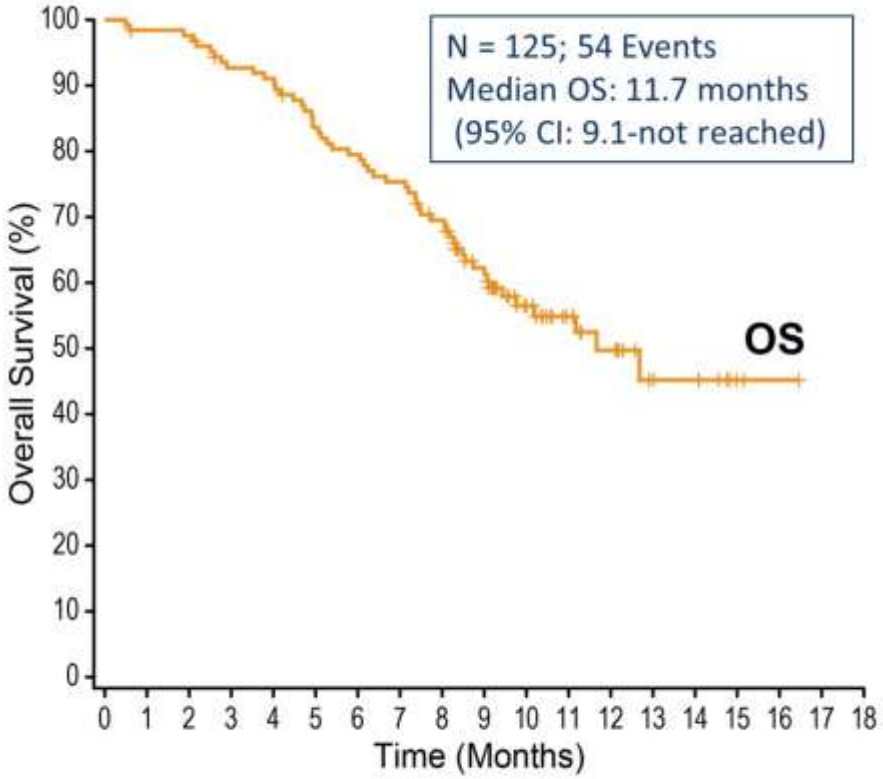
Presented By Daniel Petrylak at 2019 ASCO Annual Meeting

EV-201: Cohort 1 Kaplan-Meier Estimates of Survival



N at Risk (Events)

Cohort 1	125	116	91	84	72	65	51	47	30	22	8	7	3	2



N at Risk (Events)

Cohort 1	125	122	121	113	111	101	96	91	82	61	36	24	18	9	8	2	1

EV-201: Cohort 1 Treatment-Related Adverse Events

Treatment-related AEs by preferred term in ≥20% of patients (any Grade) or ≥5% (≥Grade 3)	Patients (N=125) n (%)	
	Any Grade	≥Grade 3
Fatigue	62 (50)	7 (6)
Alopecia	61 (49)	–
Decreased appetite	55 (44)	1 (1)
Dysgeusia	50 (40)	–
Peripheral sensory neuropathy	50 (40)	2 (2)
Nausea	49 (39)	3 (2)
Diarrhea	40 (32)	3 (2)
Dry skin	28 (22)	0
Weight decreased	28 (22)	1 (1)
Rash maculo-papular	27 (22)	5 (4)
Anemia	22 (18)	9 (7)
Neutropenia	13 (10)	10 (8)

- Treatment-related AEs led to few discontinuations (12%)
  - Peripheral sensory neuropathy was the most common (6%)
- 1 treatment-related death reported by the investigator
  - Interstitial lung disease
  - Confounded by high-dose corticosteroid use and suspected *pneumocystis jiroveci* pneumonia

EV-201: Cohort 1 Summary and Conclusions

- High unmet need for patients with advanced and metastatic urothelial carcinoma
- Enfortumab vedotin: First novel therapeutic to demonstrate substantial clinical activity in patients who progressed after platinum chemotherapy and a PD-1/L1 inhibitor
  - 44% response rate (CR 12%) and 7.6 months median duration of response
  - Responses observed across all subgroups and irrespective of response to prior PD-1/L1 inhibitor or presence of liver metastases
  - Tolerable with a manageable safety profile
  - EV-201 results are highly consistent with the phase 1 EV-101 trial in the same patient population
  - These data support submission to the FDA for accelerated approval
- If approved, enfortumab vedotin may have the potential to become a new standard of care in patients who have progressed after platinum and PD-1/L1 inhibitors

Ongoing enfortumab vedotin trials: **EV-201:** Cohort 2 enrolling cisplatin-ineligible patients without prior platinum (NCT03219333); **EV-301:** Randomized phase 3 trial of EV vs. SOC post-platinum and a PD-1/L1 inhibitor (NCT03474107); **EV-103:** EV in combination with pembrolizumab and/or chemotherapy (NCT03288545)

Presented By Daniel Petrylak at 2019 ASCO Annual Meeting


Thank you !!!