SCOS 2021 Annual Conference Featuring ASCO Direct Highlights: GU Cancers

Petros Grivas, MD PhD

Associate Professor

Dept. of Medicine, Division of Medical Oncology

Clinical Director, Genitourinary Cancers Program

University of Washington

Associate Member, Clinical Research Division

Fred Hutchinson Cancer Research Center

Bladder Cancer Advocacy Network BCAN Leading the way to awareness and a cure

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Disclosures (in the last 3 years)

- Consulting to AstraZeneca, Bayer, Bristol Myers Squibb, Clovis Oncology, Dyania Health, Driver, EMD Serono, Exelixis, Foundation Medicine, Genentech/Roche, Genzyme, GlaxoSmithKline, Guardant Health, Heron Therapeutics, Immunomedics/Gilead, Infinity Pharmaceuticals, Janssen, Merck & Co., Mirati Therapeutics, Pfizer, Regeneron Pharmaceuticals, QED Therapeutics, Seattle Genetics, 4D Pharma PLC
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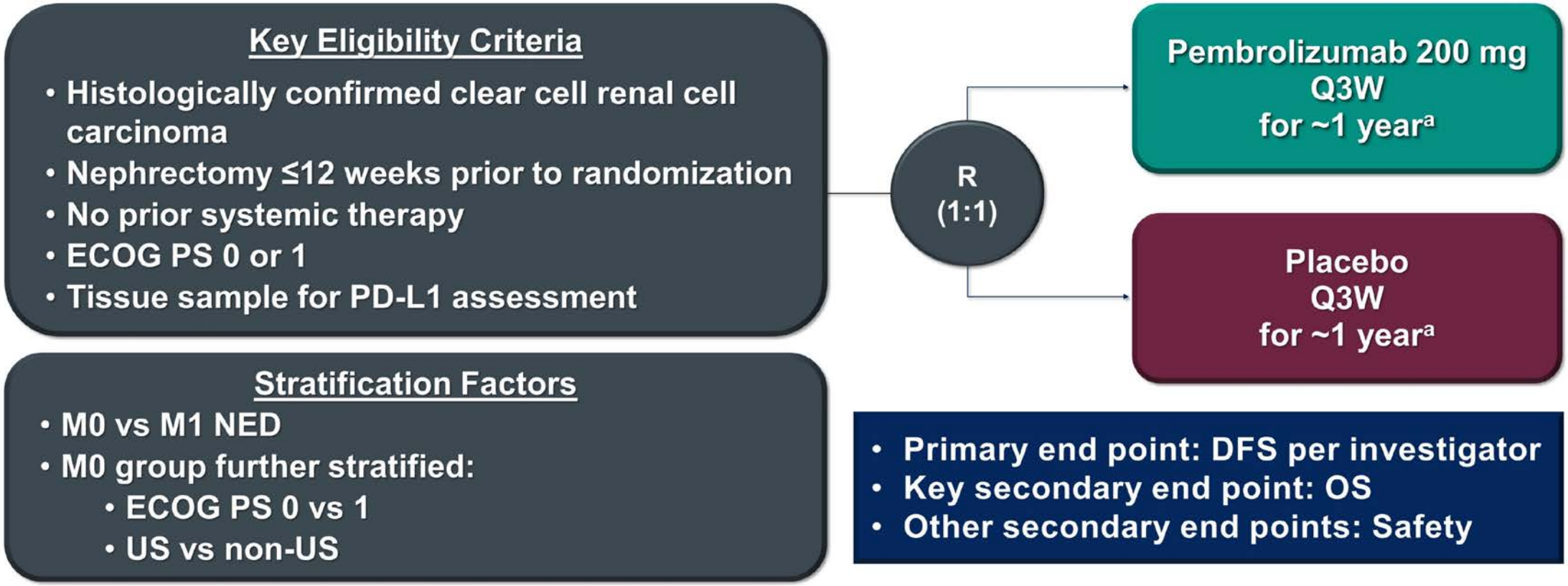
Pembrolizumab vs Placebo as Post Nephrectomy Adjuvant Therapy for Patients with Renal Cell Carcinoma: Randomized, Double-Blind, Phase 3 KEYNOTE-564 Study

Toni K. Choueiri[1]; Piotr Tomczak[2]; Se Hoon Park[3]; Balaji Venugopal[4]; Thomas Ferguson[5]; Yen-Hwa Chang[6]; Jaroslav Hajek[7]; Stefan Symeonides[8]; Jae Lyun Lee[9]; Naveed Sarwar[10]; Antoine Thiery-Vuillemin[11]; Marine Gross-Goupil[12]; Mauricio Mahave[13]; Naomi Haas[14]; Piotr Sawrycki[15]; Rodolfo F. Perini[16]; Pingye Zhang[16]; Jaqueline Willemann-Rogerio[16]; Kentaro Imai[16]; David Quinn[17]; Thomas Powles[18]; on behalf of the KEYNOTE-564 investigators.

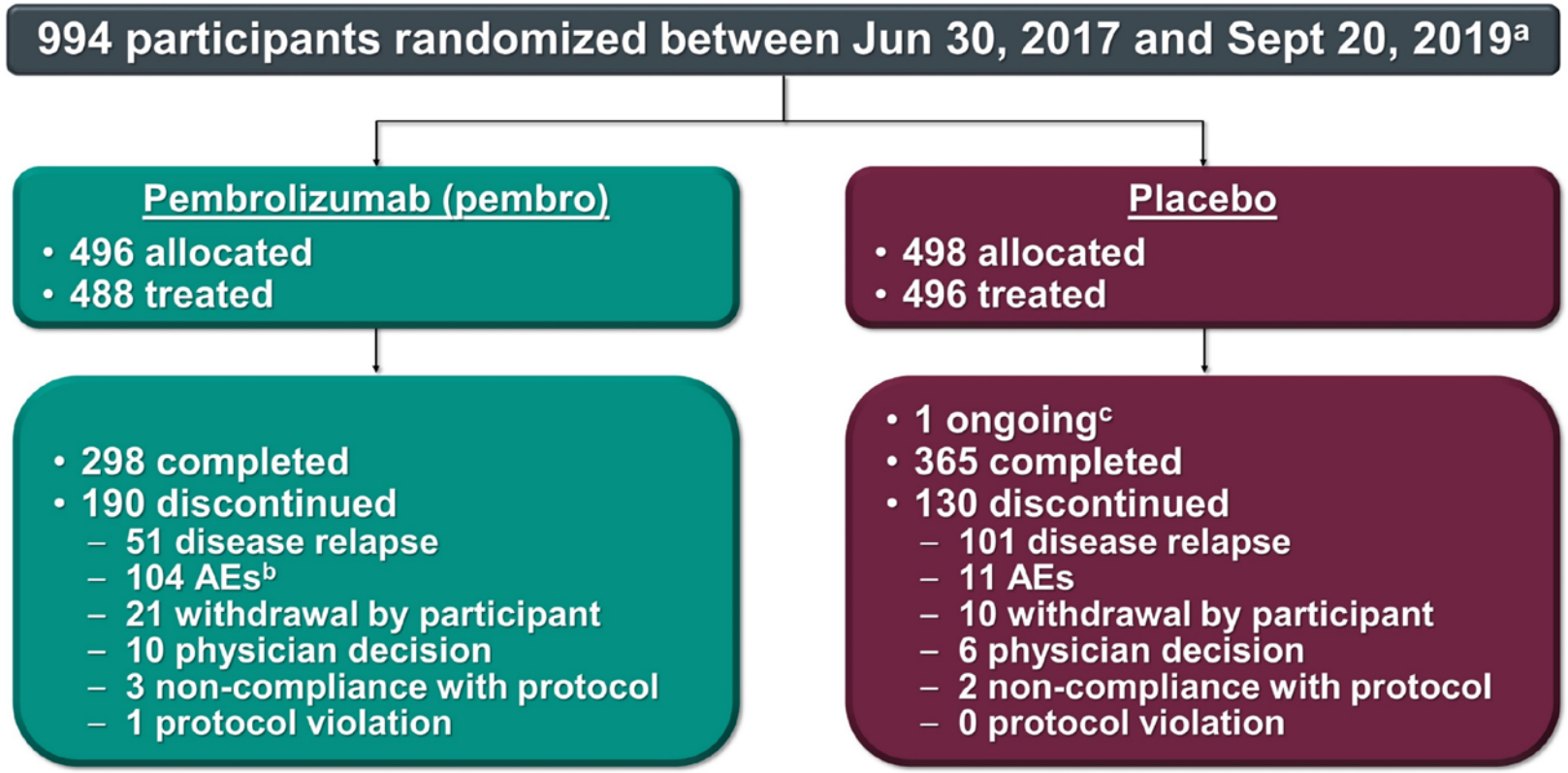
[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Poznań University of Medical Sciences, Poznań, Poland; [3]Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; [4]Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, UK; [5]Fiona Stanley Hospital, Perth, Australia; [6]Taipei Veterans General Hospital, Taipei, Taiwan; [7]Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; [8]Edinburgh Cancer Center and University of Edinburgh, Edinburgh, UK; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [10]Imperial College Healthcare NHS Trust, London, UK; [11]University Hospital Jean Minjoz, Besançon, France; [12]University Hospital Bordeaux-Hôpital Saint-André, Bordeaux, France; [13]Fundacion Arturo Lopez Perez FALP, Santiago, Chile; [14]Abramson Cancer Center, Philadelphia, PA, USA; [15]Wojewodzki Szpital Zespolony im. L. Rydygiera w Toruniu, Torun, Poland; [16]Merck & Co., Inc., Kenilworth, NJ, USA; [17]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [18]Royal Free Hospital NHS Trust, University College London, London, UK.

KEYNOTE-564 Study Design



DFS, disease-free survival; Q3W, every 3 weeks.
[a]≤17 cycles of treatment were equivalent to ~1 year.

Participant Disposition



Median (range) time from randomization to cutoff: 24.1 (14.9–41.5) months

[a]1406 participants were screened. [b]86 treatment-related AEs, 15 other AEs, and 3 AEs that occurred outside of the reporting period. [c]Participant went off placebo prior to December 14, 2020, but data was not entered into database until after database lock. No participants remain on study treatment. Data cutoff date: December 14, 2020.

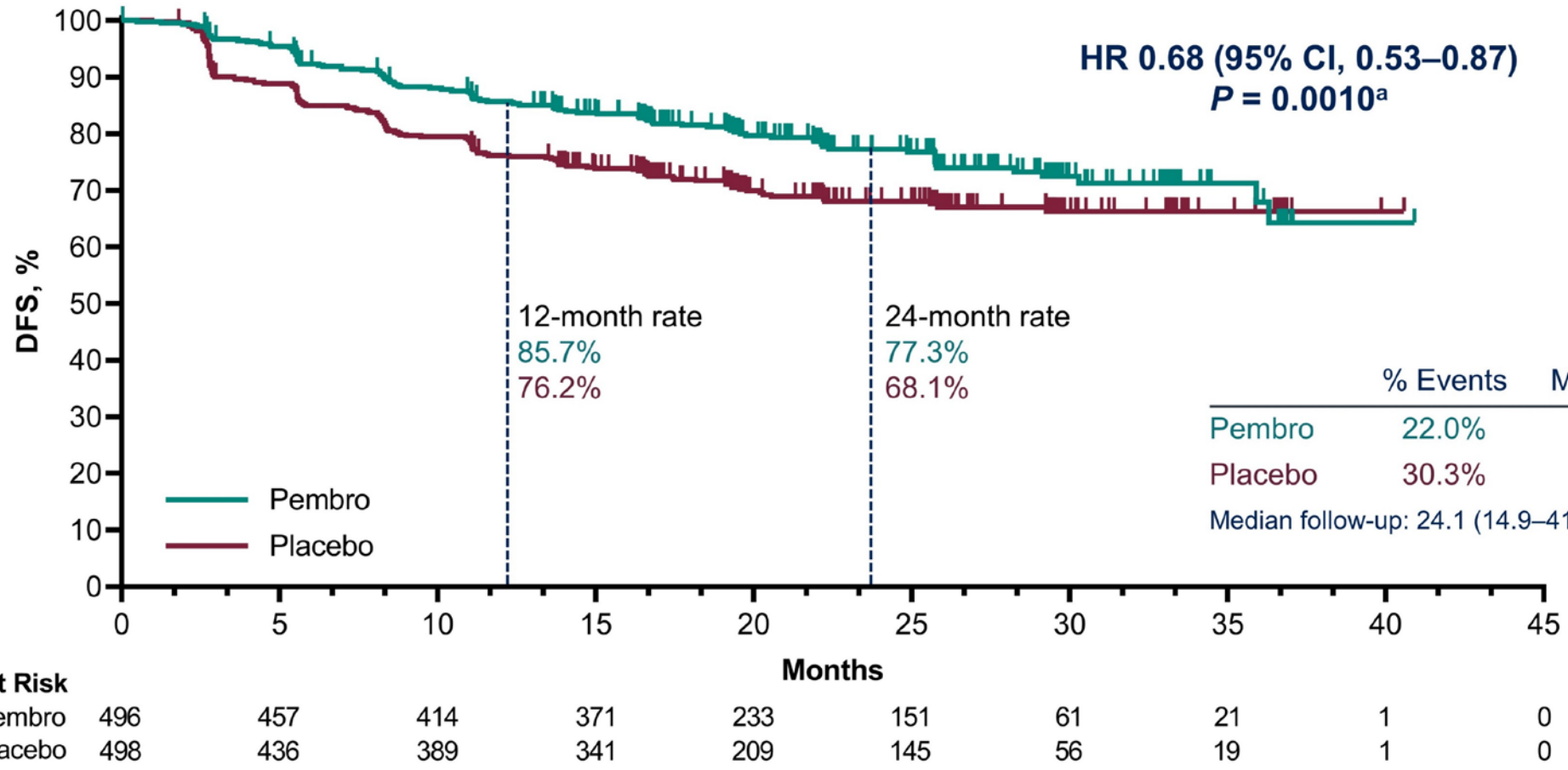
Baseline Characteristics

Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Age, median (range), yrs	60 (27–81)	60 (25–84)
Male	347 (70.0)	359 (72.1)
ECOG PS		
0	421 (84.9)	426 (85.5)
1	75 (15.1)	72 (14.5)
Disease risk category		
M0 intermediate-high risk	427 (86.1)[a]	433 (86.9)
M0 high risk	40 (8.1)	36 (7.2)
M1 NED	29 (5.8)	29 (5.8)

Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Geographic location		
North America	113 (26.8)	125 (25.1)
European Union	188 (37.9)	187 (37.6)
Rest of the world	175 (35.3)	186 (37.3)
PD-L1 status[b]		
CPS <1	124 (25.0)	113 (22.7)
CPS ≥1	365 (73.6)	383 (76.9)
Missing	7 (1.4)	2 (0.4)
Sarcomatoid features		
Present	52 (10.5)	59 (11.8)
Absent	417 (84.1)	415 (83.3)
Unknown	27 (5.4)	24 (4.8)

Intermediate-high risk: pT2, grade 4 or sarcomatoid, N0 M0; or pT3, any grade, N0 M0
High risk: pT4, any grade, N0 M0; or pT any stage, any grade, N+ M0
M1 NED: No evidence of disease after primary tumor + soft tissue metastases completely resected ≤1 year from nephrectomy
[a]Included 5 participants with T2, grade ≤3, N0 M0 or T1 N0 M0. [b]Assessed using the PD-L1 IHC 22C3 pharmDx assay. CPS (combined positive score) is the number of PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) divided by the total number of viable tumor cells, multiplied by 100. Data cutoff date: December 14, 2020.

DFS by Investigator, ITT Population



	% Events	Median (95% CI)
Pembro	22.0%	NR (NR–NR)
Placebo	30.3%	NR (NR–NR)

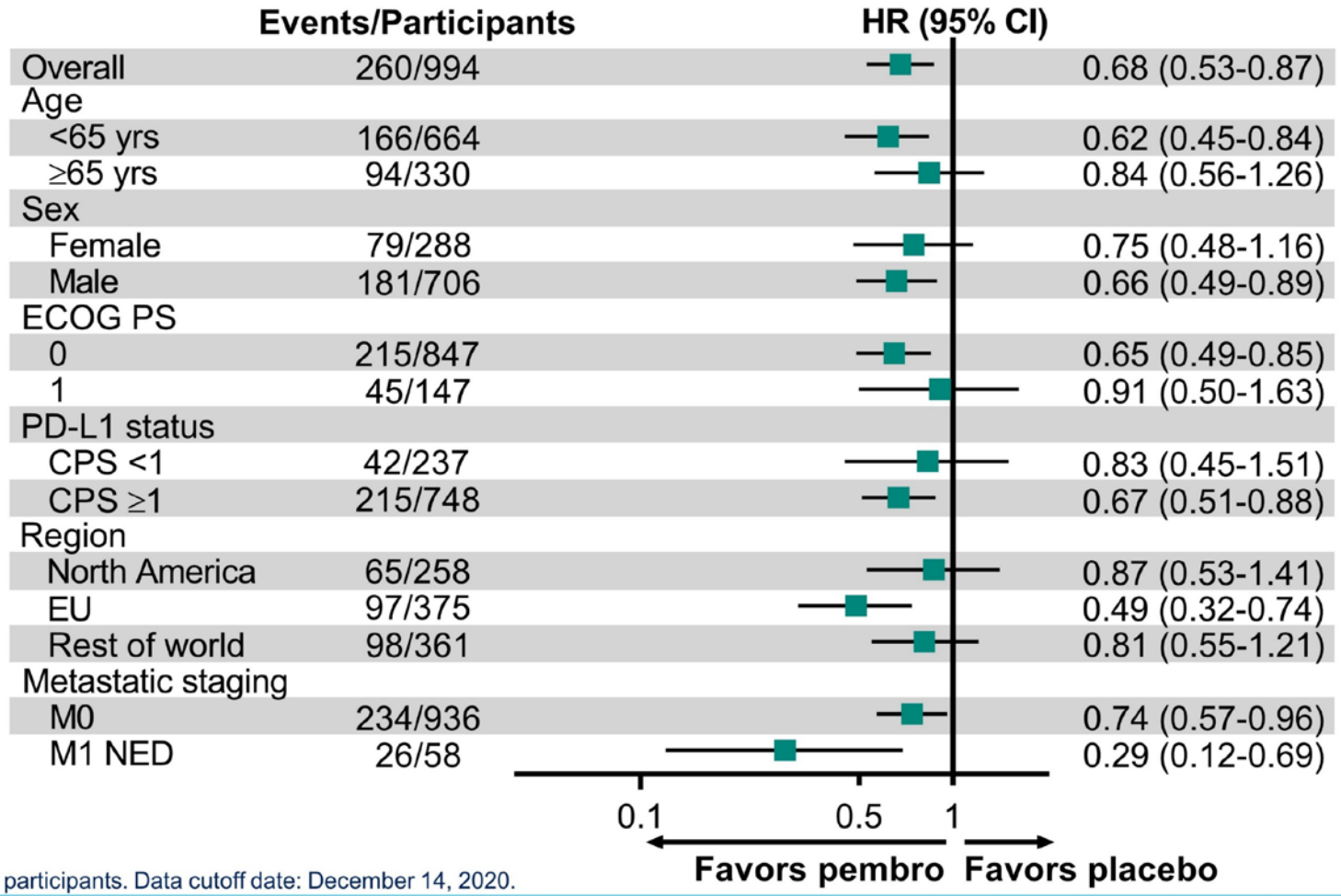
Median follow-up: 24.1 (14.9–41.5) months.

No. at Risk

Pembro	496	457	414	371	233	151	61	21	1	0
Placebo	498	436	389	341	209	145	56	19	1	0

[a]Crossed prespecified p-value boundary for statistical significance of 0.0114.
ITT population included all randomized participants. NR, not reached. Data cutoff date: December 14, 2020.

DFS by Investigator in Subgroups, ITT Population



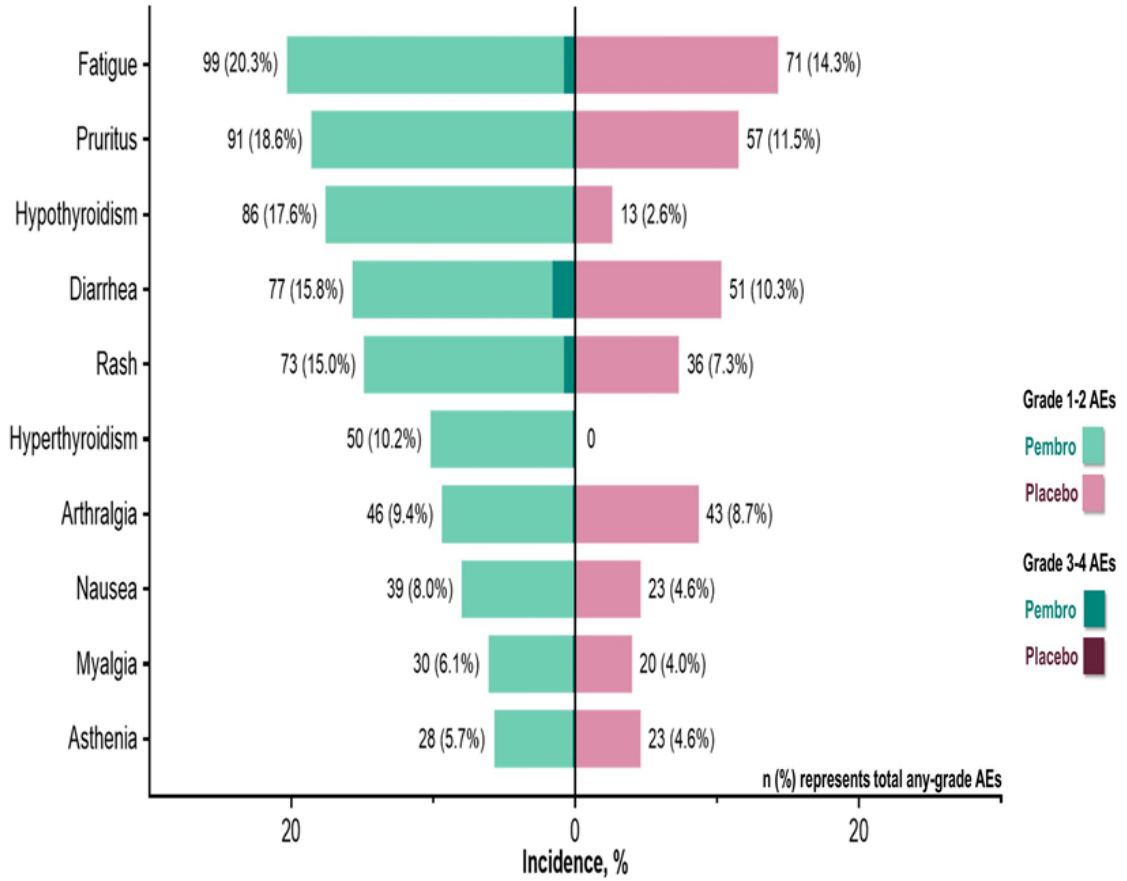
ITT population included all randomized participants. Data cutoff date: December 14, 2020.

Summary of Safety Results, As-Treated Population

Participants with ≥1 AE, n (%)	Pembro N = 488	Placebo N = 496
All-cause AEs	470 (96.3)	452 (91.1)
Grade 3–5	158 (32.4)	88 (17.7)
Led to treatment discontinuation	101 (20.7)	10 (2.0)
Led to death	2 (0.4)	1 (0.2)
Serious all-cause AEs[a]	100 (20.5)	56 (11.3)
Led to treatment discontinuation	49 (10.0)	5 (1.0)
Treatment-related AEs	386 (79.1)	265 (53.4)
Grade 3–5	92 (18.9)	6 (1.2)
Led to treatment discontinuation	86 (17.6)	3 (0.6)
Led to death	0	0

[a]Serious AEs were AEs that were life-threatening, required hospitalization, resulted in death or persistent/significant disability/incapacity, or were judged as serious per investigator.
As-treated population included all participants who received ≥1 dose of study treatment. Median duration (range) of treatment was 11.1 (0.0–14.3) months with pembro and 11.1 (0.0–15.4) months with placebo.
Data cutoff date: December 14, 2020.

Treatment-Related AEs with Incidence ≥5%, As-Treated Population



As-treated population included all participants who received ≥1 dose of study treatment. No treatment-related deaths occurred. Data cutoff date: December 14, 2020.

Summary and Conclusions

- Adjuvant pembrolizumab post nephrectomy demonstrated a statistically significant and clinically meaningful improvement in DFS vs placebo
  - Additional follow-up is planned for the key secondary endpoint of OS
- Benefit was consistent across subgroups, including the M1 NED population, potentially extending the use of pembrolizumab to these patients
- Safety results were in line with expectations and no new safety signals were observed
  - Low incidence of high-dose corticosteroid treatment for immune-mediated AEs
- KEYNOTE-564 is the first positive phase 3 study of an adjuvant immunotherapy in RCC
- Pembrolizumab is a potential new standard of care for patients with RCC in the adjuvant setting

2021 ASCO ANNUAL MEETING

Health-Related Quality-of-life Analysis From the Phase 3 CLEAR Trial of Lenvatinib Plus Pembrolizumab or Everolimus vs Sunitinib for Patients With Advanced Renal Cell Carcinoma

Robert Motzer[1], Camillo Porta[2], Boris Alekseev[3], Sun Young Rha[4], Toni Choueiri[5], Maria Jose Mendez-Vidal[6], Sung-Hoo Hong[7], Anil Kapoor[8], Jeffrey C. Goh[9], Masatoshi Eto[10], Jinyi Wang[11], Janice Pan[12], Alemseged Ayele Asfaw[13], Cixin Steven He[12], Kalgi Mody[12], David Cella[14]

[1]Memorial Sloan Kettering Cancer Center; New York, NY, USA; [2]San Matteo University Hospital Foundation, Pavia, Italy; [3]P.A. Herzen Moscow Oncological Research Institute, Moscow, Russia; [4]Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Maimonides Institute for Biomedical Research of Cordoba (IMIBIC) Hospital Universitario Reina Sofía, Córdoba, Spain; [7]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, South Korea; [8]McMaster University Hamilton, Ontario, Canada; [9]ICON Research, South Brisbane & University of Queensland, St Lucia, Queensland, Australia; [10]Kyushu University, Fukuoka, Japan; [11]RTI Health Solutions, Research Triangle Park, NC, USA; [12]Eisai Inc., Woodcliff Lake, NJ, USA; [13]Merck & Co., Inc., Kenilworth, NJ, USA; [14]Northwestern University, Chicago, IL, USA.

June 7, 2021

Abstract #4502

Introduction

- The phase 3 CLEAR study compared lenvatinib (LEN) + pembrolizumab (PEMBRO) or LEN + everolimus (EVE) vs sunitinib (SUN) in the first-line treatment of patients with advanced renal cell carcinoma (RCC)[1,2]
- LEN + PEMBRO demonstrated significant improvements in PFS, OS, and ORR vs SUN[1,2]
- LEN + EVE demonstrated significant improvements in PFS and ORR vs SUN[1,2]
- The safety profiles of both combinations were consistent with each drug's known profile and generally manageable, as needed, through dose modifications[1,2]
- Here we report health-related quality-of-life (HRQoL) results

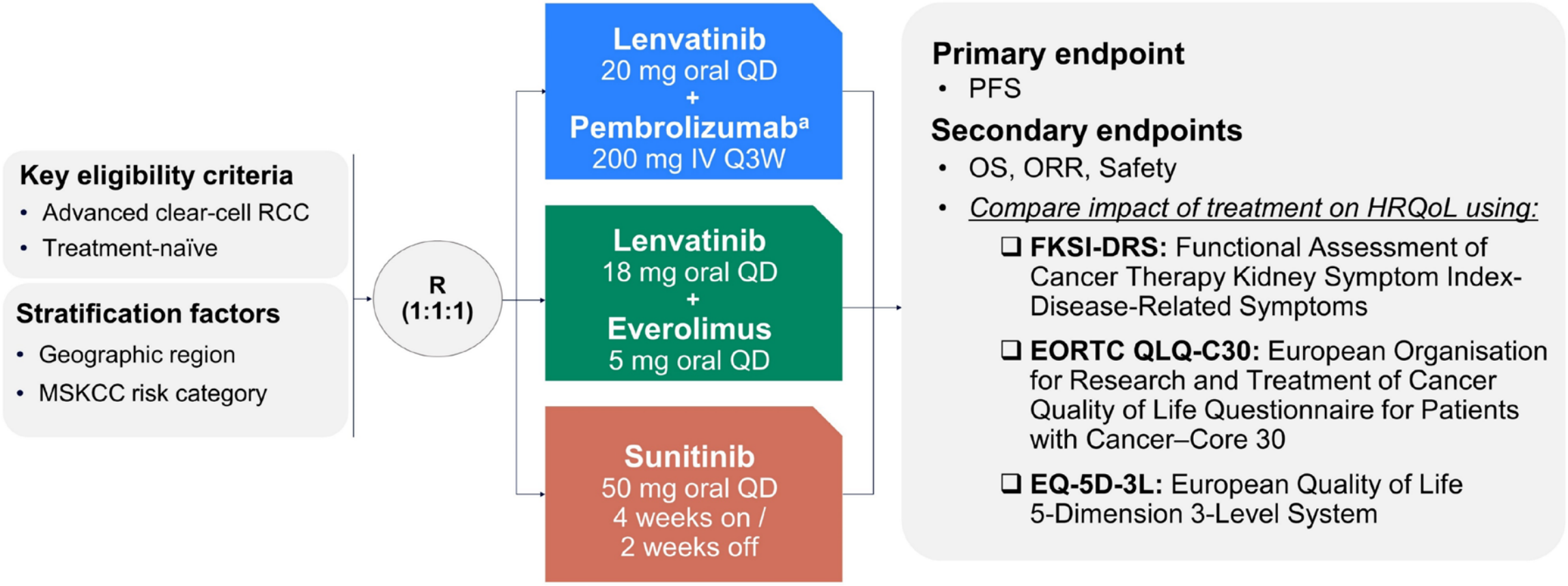
1. Motzer R et al. *N Engl J Med*. 2021;384:1289-1300. 2. Motzer R et al. Oral presentation at ASCO-GU. February 11-13, 2021. Abstract #269.
ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Efficacy Summary

	LEN + PEMBRO n = 355	LEN + EVE n = 357	SUN n = 357
Median PFS, mo (95% CI)	23.9 (20.8–27.7)	14.7 (11.1–16.7)	9.2 (6.0–11.0)
Stratified HR (95% CI) vs SUN	**0.39 (0.32–0.49)**	**0.65 (0.53–0.80)**	--
P-value	< 0.001	< 0.001	--
Median OS, mo (95% CI)	NR (33.6–NE)	NR (NE)	NR (NE)
Stratified HR (95% CI) vs SUN	**0.66 (0.49–0.88)**	**1.15 (0.88–1.50)**	--
P-value	0.005	0.3	--
Objective response rate, %	**71.0**	**53.5**	**36.1**
Complete response, %	16.1	9.8	4.2
Median duration of treatment, mo (range)	17.0 (0.1, 39.1)	11.0 (0.1, 40.0)	7.8 (0.1, 37.0)

Motzer R et al. *N Engl J Med*. 2021;384:1289-1300.
CI, confidence interval; HR, hazard ratio; NE, not estimable; NR, not reached.

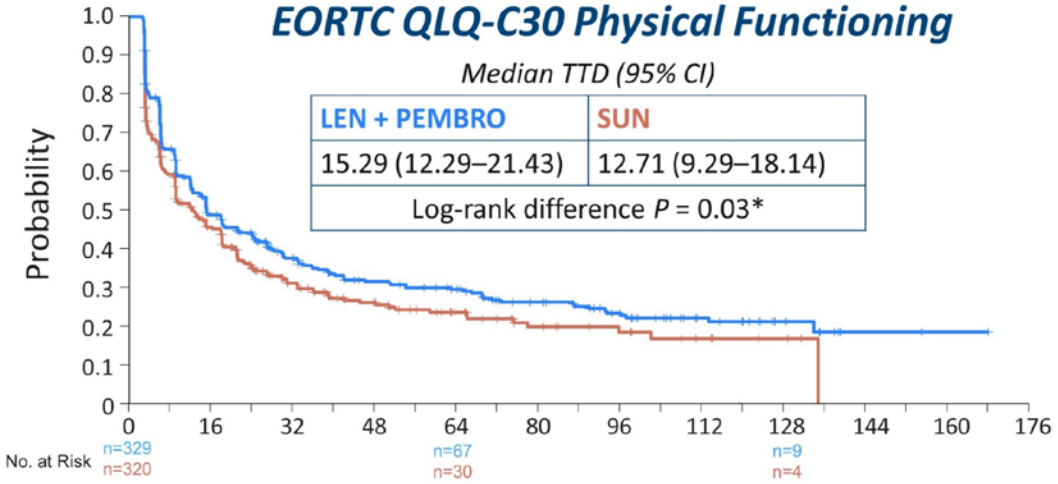
Study Design



[a]Patients could receive a maximum of 35 pembrolizumab treatments.
HRQoL, Health-related quality of life; MSKCC, Memorial Sloan Kettering Cancer Center; R, randomization.

Time to First Deterioration[a]: LEN + PEMBRO vs SUN

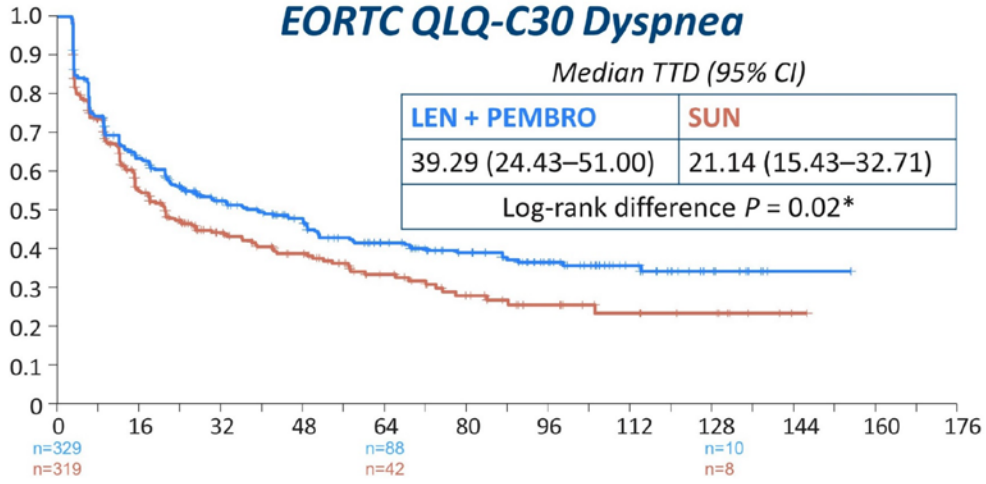
EORTC QLQ-C30 Physical Functioning



Median TTD (95% CI)

LEN + PEMBRO	SUN
15.29 (12.29–21.43)	12.71 (9.29–18.14)
Log-rank difference *P* = 0.03*	

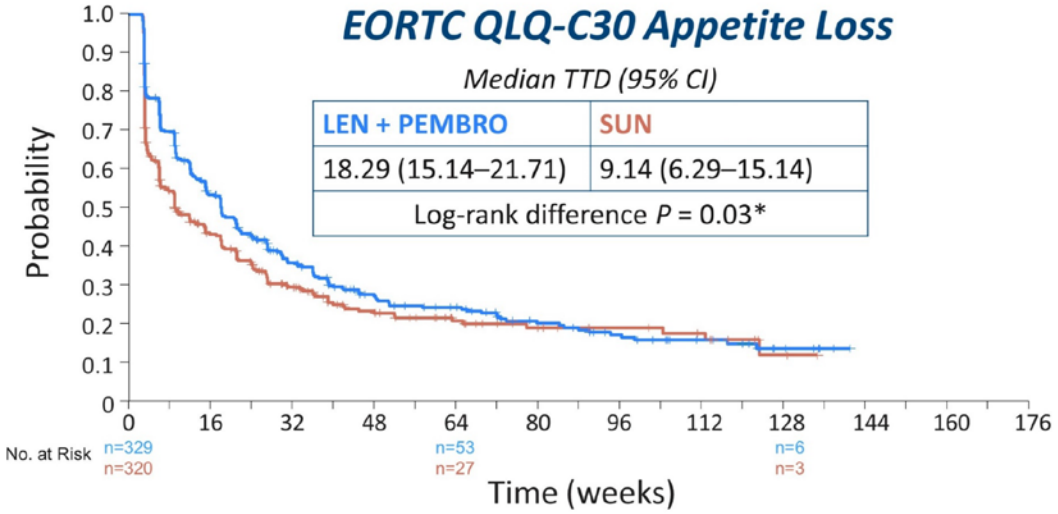
EORTC QLQ-C30 Dyspnea



Median TTD (95% CI)

LEN + PEMBRO	SUN
39.29 (24.43–51.00)	21.14 (15.43–32.71)
Log-rank difference *P* = 0.02*	

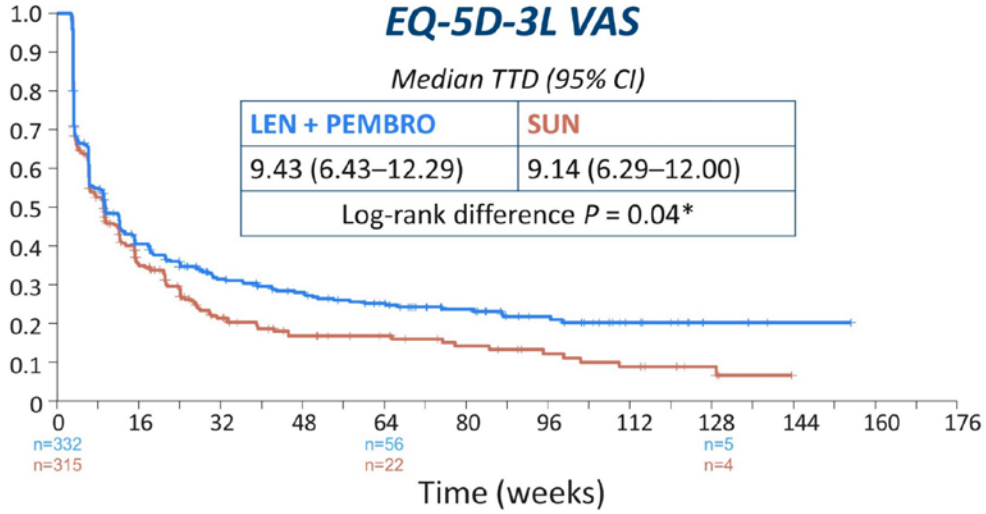
EORTC QLQ-C30 Appetite Loss



Median TTD (95% CI)

LEN + PEMBRO	SUN
18.29 (15.14–21.71)	9.14 (6.29–15.14)
Log-rank difference *P* = 0.03*	

EQ-5D-3L VAS



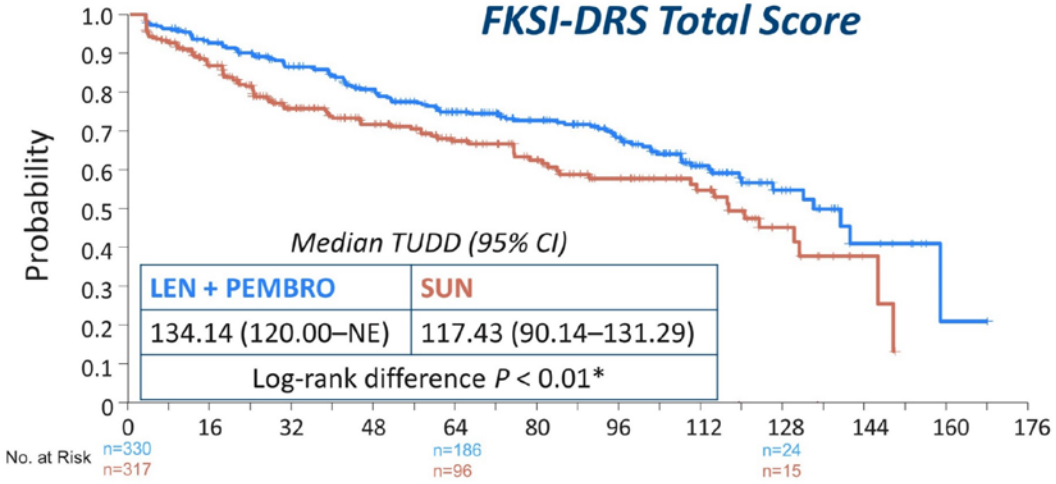
Median TTD (95% CI)

LEN + PEMBRO	SUN
9.43 (6.43–12.29)	9.14 (6.29–12.00)
Log-rank difference *P* = 0.04*	

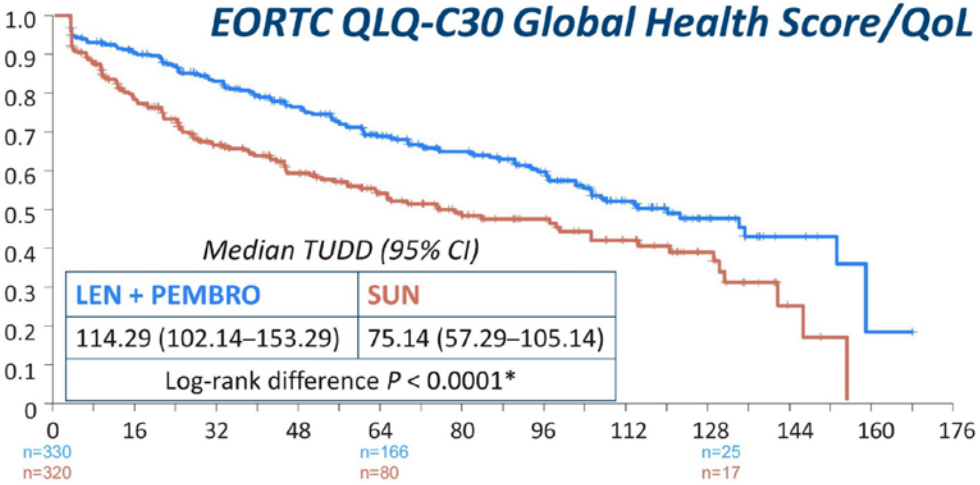
[a]The number of weeks between randomization and the first deterioration event. *Statistically significant log-rank difference of distribution of time to first deterioration for LEN + PEMBRO vs SUN ($P < 0.05$). TTD, time to first deterioration.

Time Until Definitive Deterioration[a]: LEN + PEMBRO vs SUN

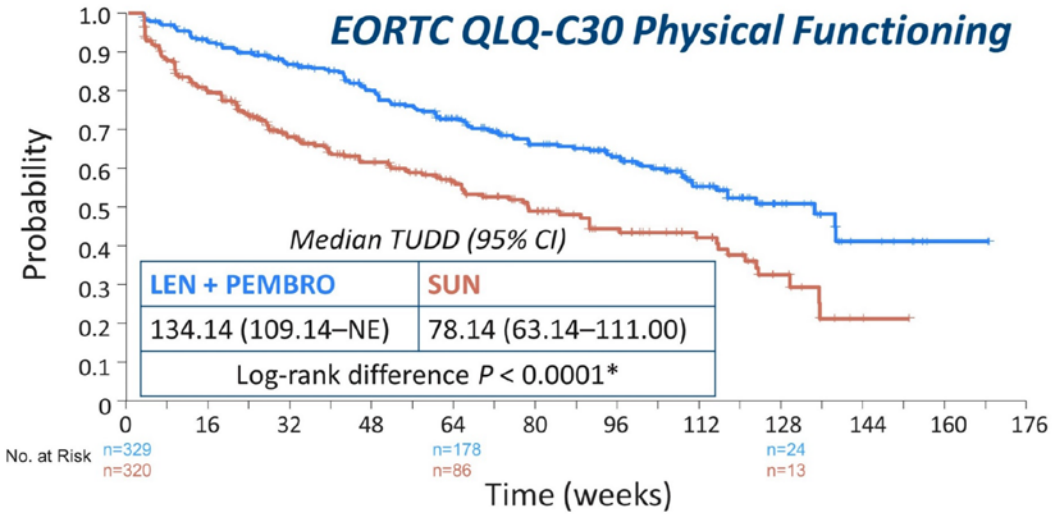
FKSI-DRS Total Score



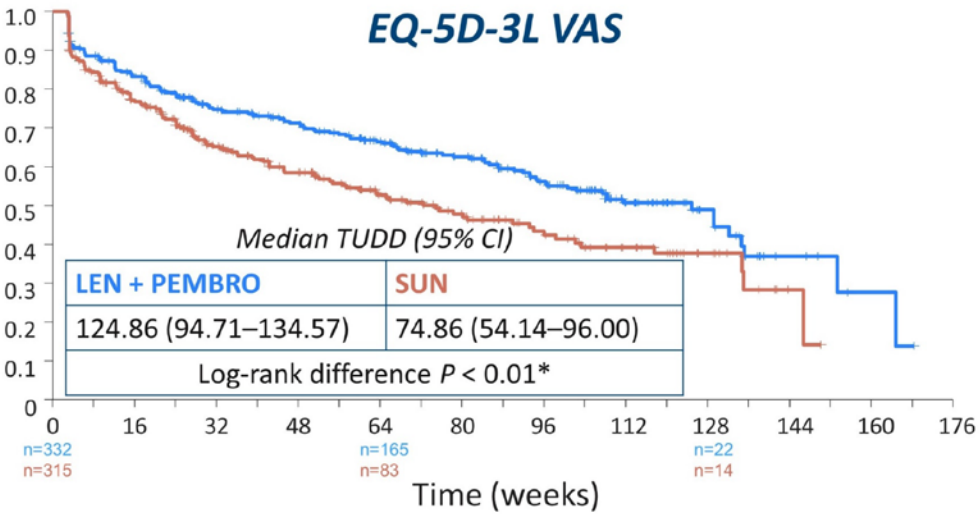
EORTC QLQ-C30 Global Health Score/QoL



EORTC QLQ-C30 Physical Functioning



EQ-5D-3L VAS



[a]The number of weeks between randomization and the earliest deterioration event with no subsequent recovery above the deterioration threshold or no subsequent HRQoL assessment data. *Statistically significant log-rank difference of distribution of time until definitive deterioration for LEN + PEMBRO vs SUN ($P < 0.05$). TUDD, time until definitive deterioration.

Conclusions

- LEN + PEMBRO demonstrated similar or improved HRQoL and disease-related symptom scores supporting its tolerability compared with SUN
- LEN + EVE resulted in similar or worse HRQoL and symptom scores compared with patients treated with SUN
- Efficacy, safety, and HRQoL results from the CLEAR trial support LEN + PEMBRO as first-line therapy for patients with advanced RCC

Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426.

First Author: Brian I. Rini

Key Eligibility Criteria

- Advanced/metastatic RCC
- No prior systemic therapy for advanced RCC.
- Karnofsky performance status (KPS) ≥ 70%

Exclusion criteria

- Prior treatment with immune checkpoint inhibitors, anti-VEGF, or anti-mTOR
- CNS metastatses

RANDOMIZED 1:1

Pembrolizumab 200 mg IV (q3 weeks) + Axitinib 5 mg orally BID. (N=432)

Sunitinib 50 mg orally once daily (N=429)

Efficacy endpoints

Primary:

- PFS per RECIST 1.1
- OS

Secondary:

- ORR per RECIST 1.1
- DCR per RECIST 1.1
- Duration of Response (DOR) per RECIST 1.1
- Adverse Events
- PFS Rate (12, 18 and 24 months)
- OS Rate (12, 18, and 24 months)
- Time to True Deterioration (TTD) of the FKSI-DRS
- Least Squares (LS) Mean Change From Baseline to Week 54 in the EORTC QLQ-C30

www.ClinicalTrials.gov (NCT02194842)

Pembrolizumab (pembro) plus axitinib (axi) versus sunitinib as first-line therapy for advanced clear cell renal cell carcinoma (ccRCC): Results from 42-month follow-up of KEYNOTE-426.

- Median duration of follow-up was 42.8 mo (range, 35.6-50.6).
- Compared with sunitinib, pembro + axi improved OS (median: 45.7 vs 40.1 mo; HR, 0.73 [95% CI, 0.60-0.88]; P<0.001) and PFS (median: 15.7 vs 11.1 mo; HR, 0.68 [95% CI, 0.58-0.80]; P<0.0001).
- The 42-mo OS rate was 57.5% with pembro + axi vs 48.5% with sunitinib; the 42-mo PFS rate was 25.1% with pembro + axi vs 10.6% with sunitinib.
- For pembro + axi vs sunitinib, ORR was 60.4% vs 39.6% (P<0.0001); CR rate was 10.0% vs 3.5%;
- Median DOR was 23.6 mo (range 1.4+ to 43.4+) vs 15.3 mo (range, 2.3-42.8+).
- Subsequent anticancer therapy was administered to 47.2% of pts in pembro + axi arm vs 65.5% of pts in sunitinib arm.
- No new safety signals were observed.

2021 ASCO ANNUAL MEETING

Phase 3 study of ^{177}Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION)

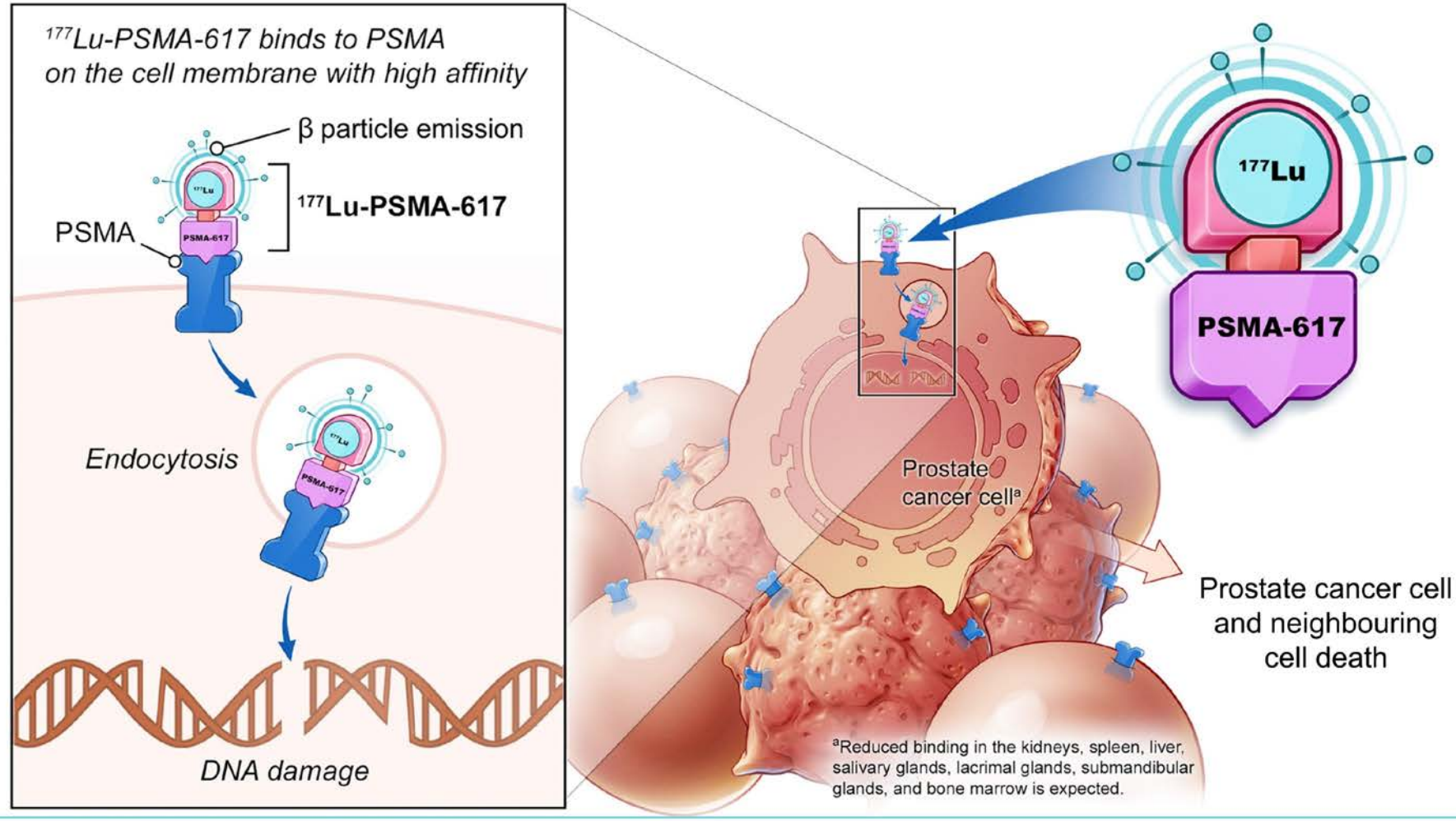
Presenter: Michael J. Morris, Memorial Sloan Kettering Cancer Center

Co-authors: J. de Bono, K. N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S. T. Tagawa, L. T. Nordquist, N. Vaishampayan, G. El-Haddad, C. H. Park, T. M. Beer, W. J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R. A. Messmann, B. J. Krause, O. Sartor, for the VISION investigators

6 June 2021

Study funded by Endocyte, Inc., a Novartis company

^{177}Lu-PSMA-617 targeted radioligand therapy



Open-label study of protocol-permitted standard of care ± ^{177}Lu-PSMA-617 in adults with PSMA-positive mCRPC

Eligible patients

- Previous treatment with both
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

2:1

Protocol-permitted SOC + ^{177}Lu-PSMA-617
7.4 GBq (200 mCi) every 6 weeks
4 cycles, increasable to 6

Protocol-permitted SOC alone

Treatment → Follow-up → Final analysis

- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

Prespecified endpoints: alternate primary, key secondary and other secondary

Alternate primary endpoints

- Radiographic progression-free survival (rPFS) per PCWG3
- Overall survival (OS)

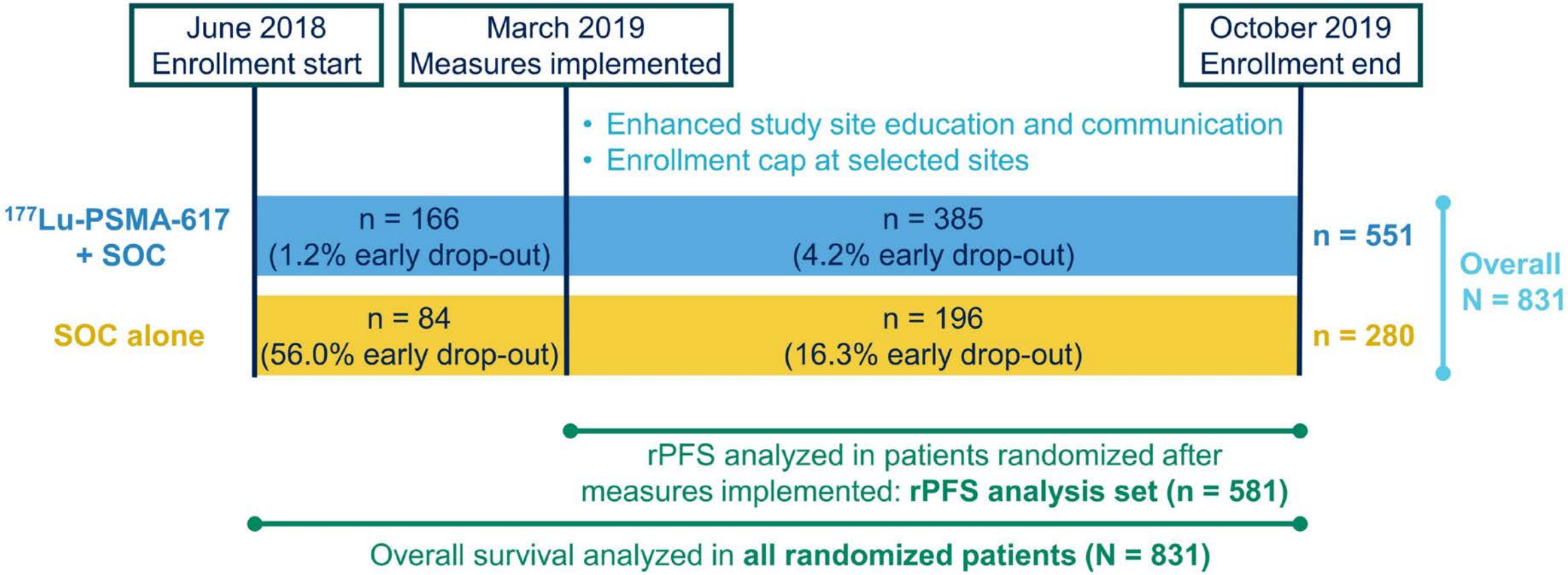
Key secondary endpoints

- Time to first symptomatic skeletal event (SSE)
- RECIST v1.1 overall response rate
- RECIST v1.1 disease control rate

Other secondary endpoints

- Safety and tolerability
- Biomarkers including PSA
- Health-related quality of life and pain

To reduce effect of drop-out on radiographic endpoints, primary analyses used different sets



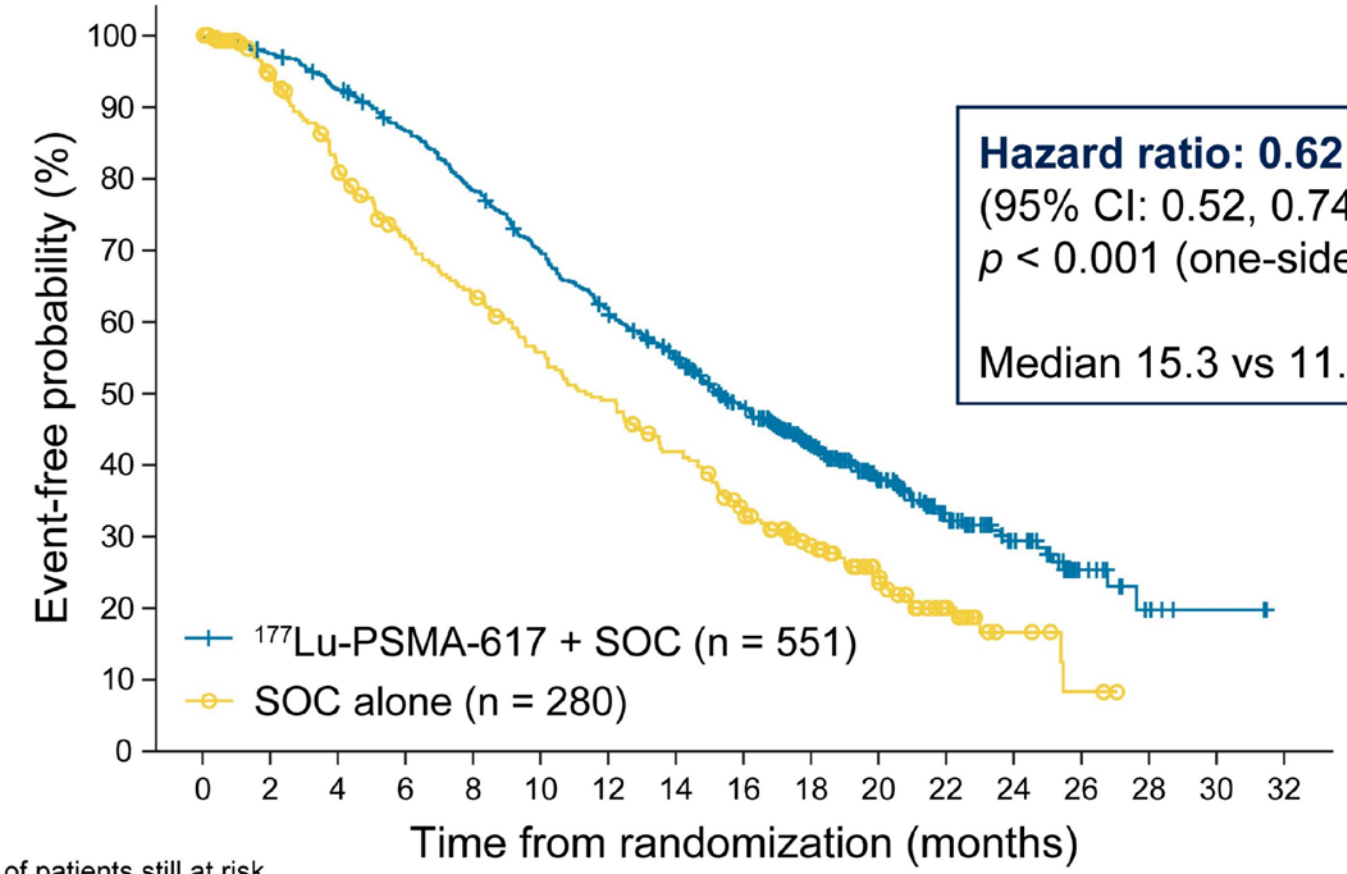
Baseline characteristics were well balanced across treatment arms and the two analysis sets

	rPFS analysis set (n = 581)		All randomized (N = 831)	
	^{177}Lu-PSMA-617 + SOC (n = 385)	SOC alone (n = 196)	^{177}Lu-PSMA-617 + SOC (n = 551)	SOC alone (n = 280)
Age, median (range)	71.0 (52–94)	72.0 (51–89)	70.0 (48–94)	71.5 (40–89)
Race, n (%)				
White	336 (87.3)	166 (84.7)	486 (88.2)	235 (83.9)
Black/African-American	29 (7.5)	14 (7.1)	34 (6.2)	21 (7.5)
Asian	6 (1.6)	9 (4.6)	9 (1.6)	11 (3.9)
ECOG status, n (%)				
0 or 1	352 (91.4)	179 (91.3)	510 (92.6)	258 (92.1)
2	33 (8.6)	17 (8.7)	41 (7.4)	22 (7.9)
Site of disease, n (%)				
Lung	35 (9.1)	20 (10.2)	49 (8.9)	28 (10.0)
Liver	47 (12.2)	26 (13.3)	63 (11.4)	38 (13.6)
Lymph node	193 (50.1)	99 (50.5)	274 (49.7)	141 (50.4)
Bone	351 (91.2)	179 (91.3)	504 (91.5)	256 (91.4)

Primary endpoints: ^{177}Lu-PSMA-617 prolonged OS

Primary analysis

All randomized patients
(N = 831)



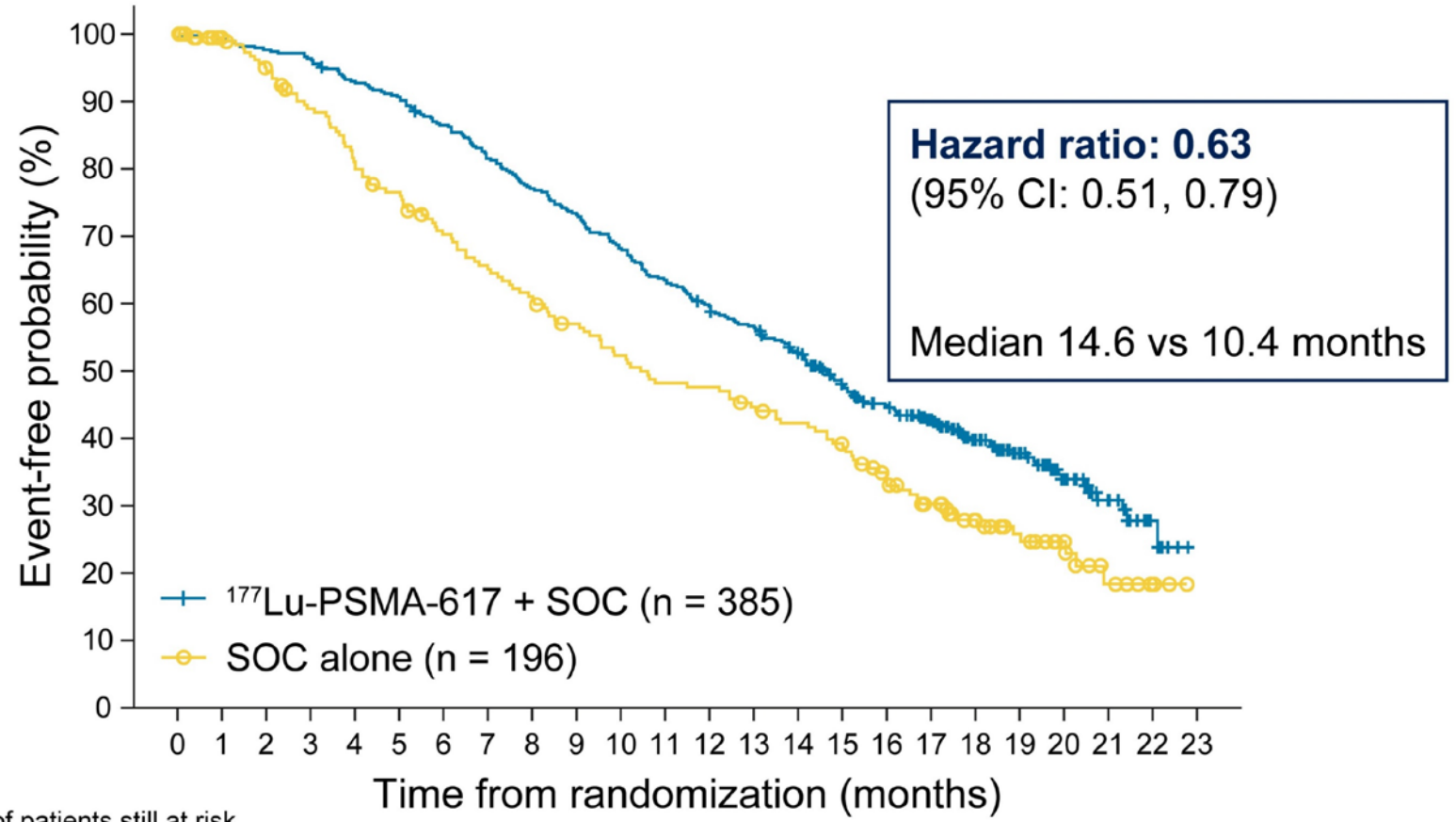
Number of patients still at risk

^{177}Lu-PSMA-617 + SOC	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
SOC alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

^{177}Lu-PSMA-617 prolonged OS in the rPFS analysis set

Additional analysis

rPFS analysis set (n = 581)

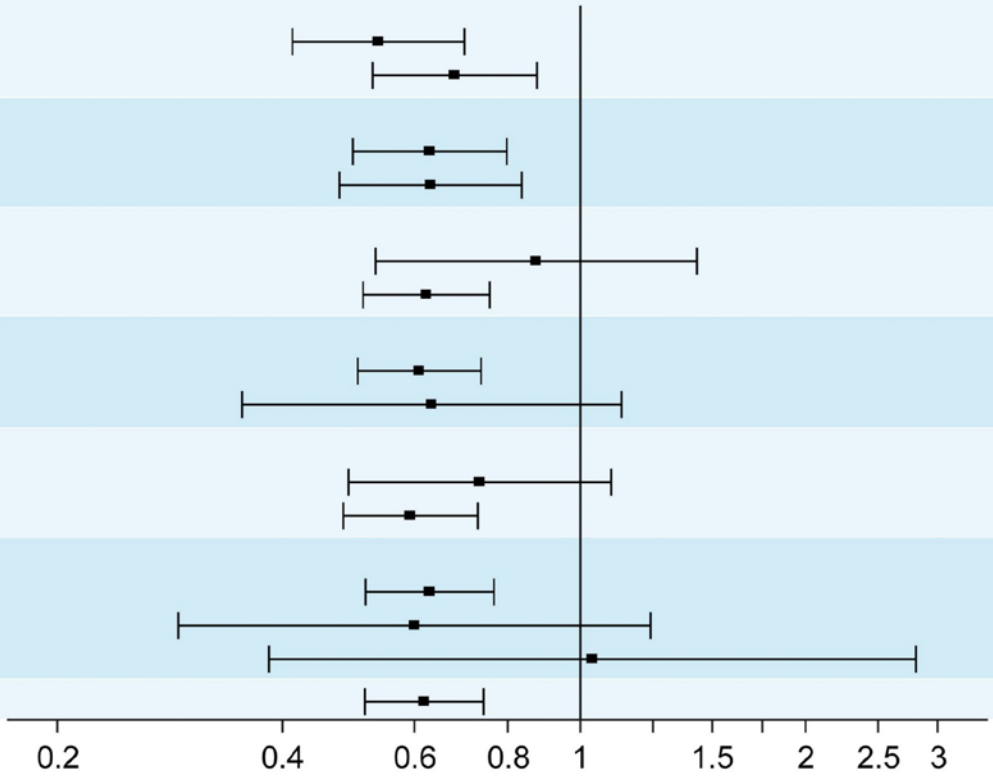


Number of patients still at risk

^{177}Lu-PSMA-617 + SOC	385	382	376	371	357	348	331	312	295	281	261	243	227	215	196	169	151	128	89	68	44	24	7	0
SOC alone	196	181	171	158	144	135	122	113	106	97	89	82	81	75	70	64	51	42	30	23	15	7	3	0

Overall survival was generally consistent across prespecified stratification factor subgroups

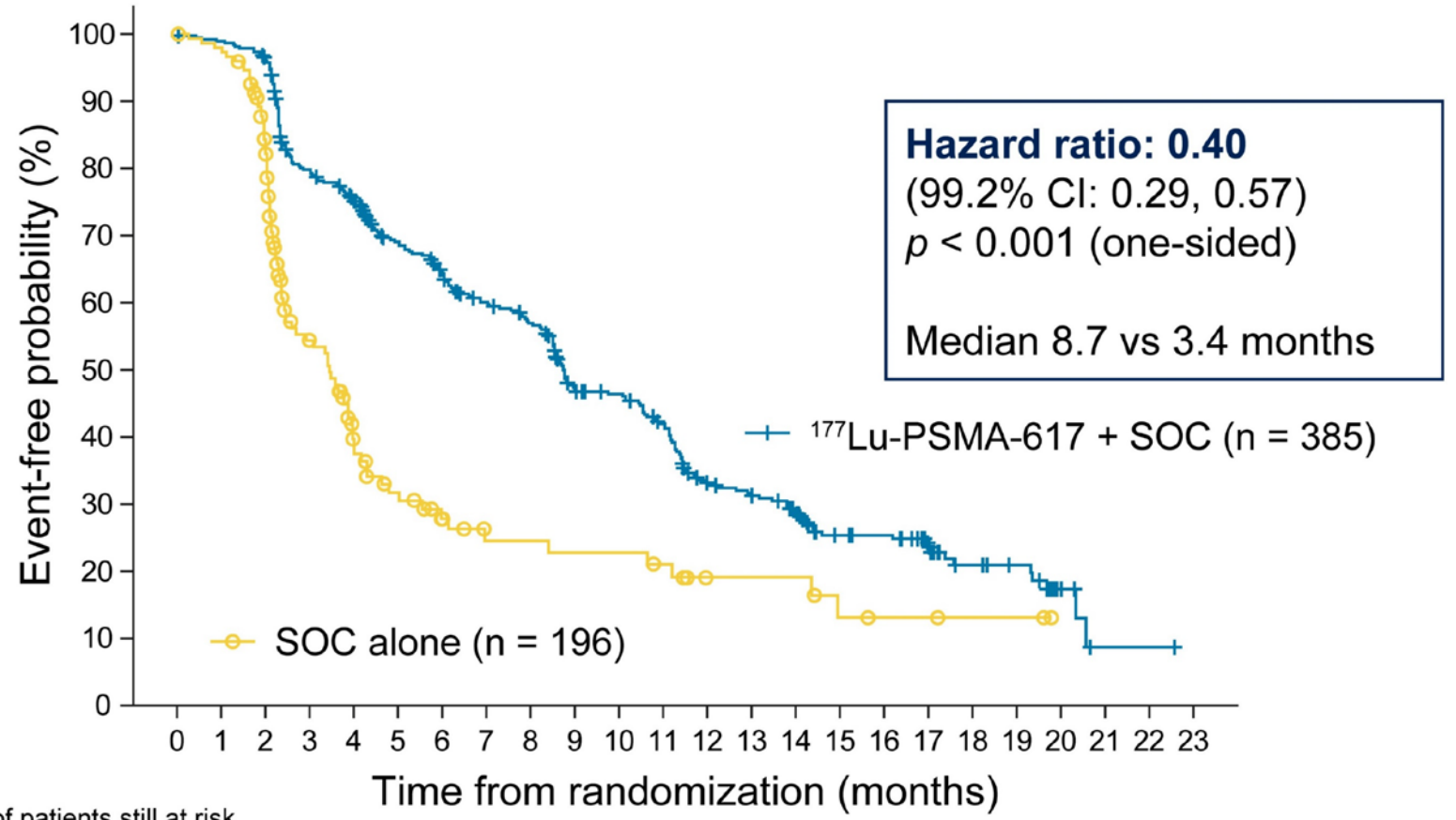
Subgroup	^{177}Lu-PSMA-617 + SOC (n = 551)	SOC alone (n = 280)	Hazard ratio (95% CI)
Androgen receptor pathway inhibitors as part of planned SOC			
Yes	243	146	0.54 (0.41, 0.70)
No	308	134	0.68 (0.53, 0.87)
LDH			
≤ 260 IU/L	368	182	0.63 (0.50, 0.80)
> 260 IU/L	182	97	0.63 (0.48, 0.84)
Liver metastases			
Yes	48	34	0.87 (0.53, 1.43)
No	503	246	0.62 (0.51, 0.76)
ECOG score			
0 or 1	510	258	0.61 (0.50, 0.74)
2	41	22	0.63 (0.35, 1.13)
Age			
< 65 years	145	60	0.73 (0.49, 1.10)
≥ 65 years	406	220	0.59 (0.48, 0.73)
Race			
White	486	235	0.63 (0.52, 0.77)
African American or Black	34	21	0.60 (0.29, 1.24)
Asian	9	11	1.04 (0.38, 2.81)
All patients	551	280	0.62 (0.52, 0.74)



Primary endpoints: ^{177}Lu-PSMA-617 improved rPFS

Primary analysis

rPFS analysis set (n = 581)



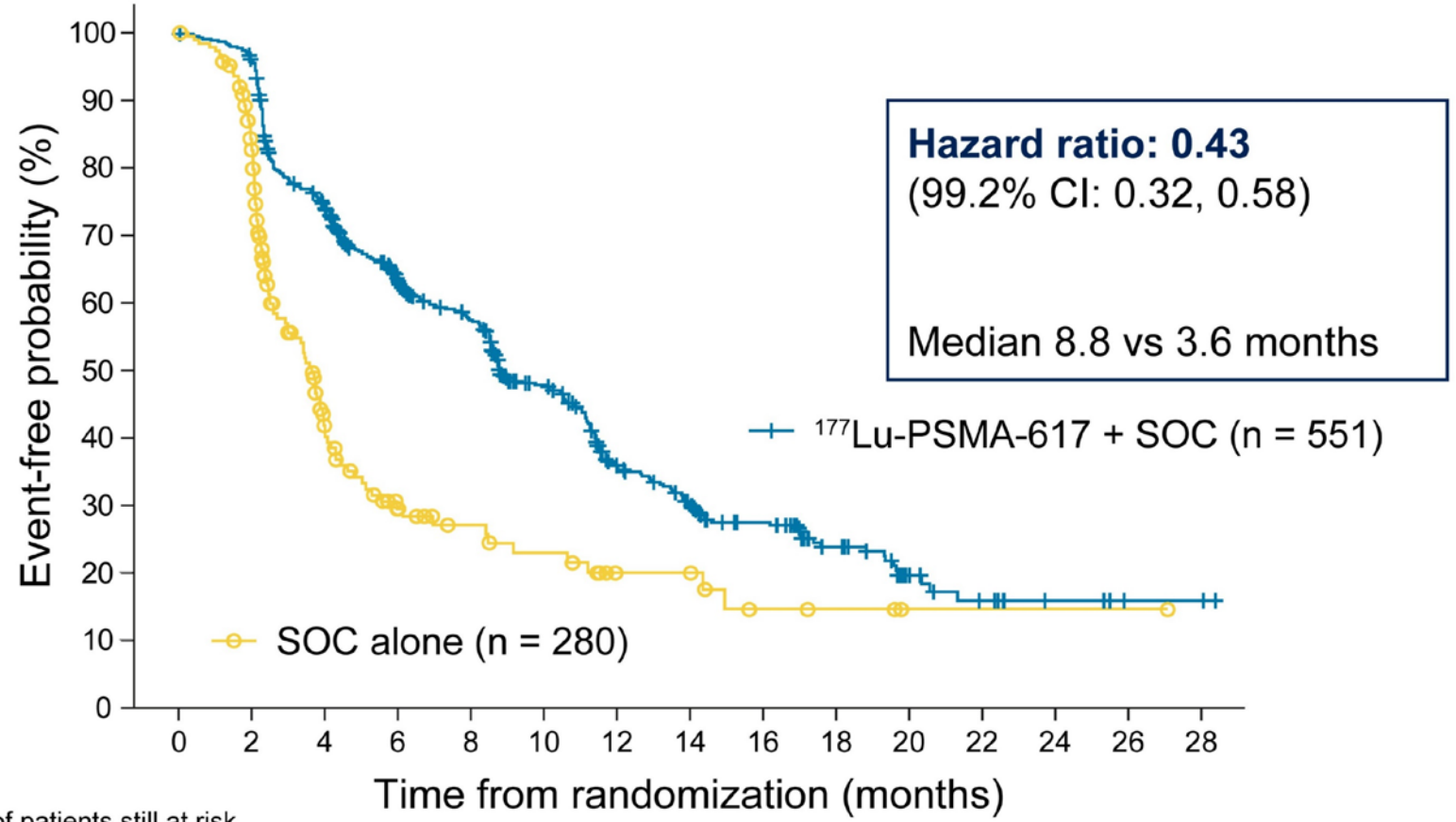
Number of patients still at risk

^{177}Lu-PSMA-617 + SOC	385	373	362	292	272	235	215	194	182	146	137	121	88	83	71	51	49	37	21	18	6	1	1	0
SOC alone	196	146	119	58	36	26	19	14	14	13	13	11	7	7	7	4	3	3	2	2	0	0	0	0

^{177}Lu-PSMA-617 improved rPFS in the OS analysis set

Additional analysis

All randomized patients
(N = 831)

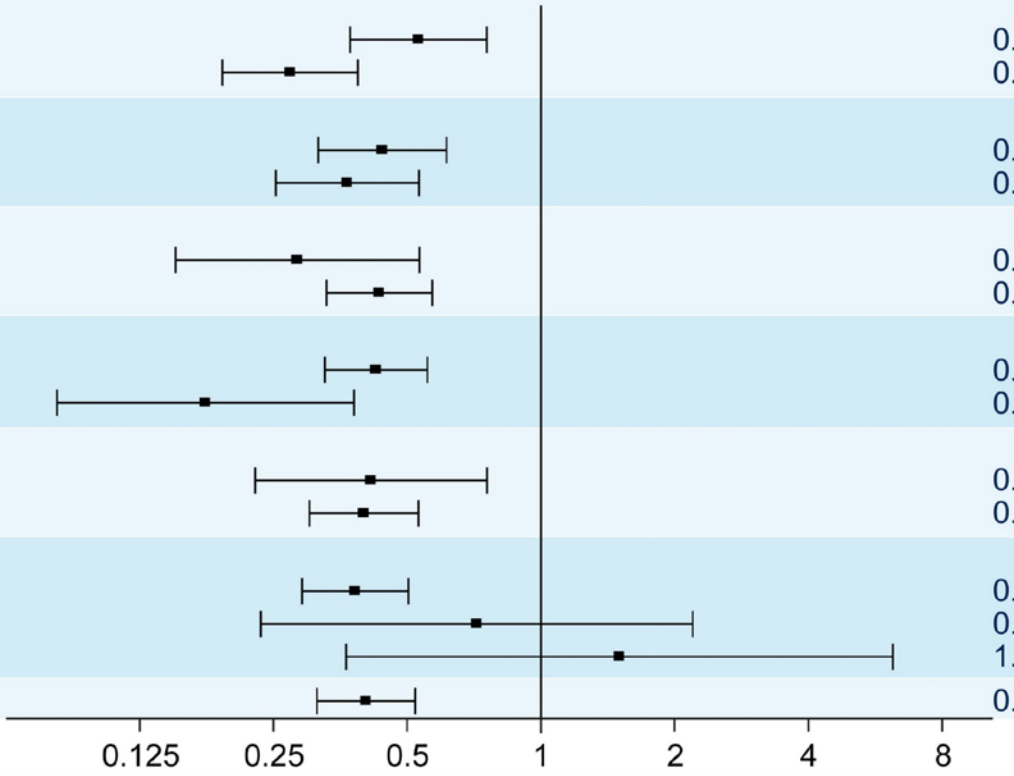


Number of patients still at risk

^{177}Lu-PSMA-617 + SOC	551	510	382	289	246	180	118	92	68	38	18	11	5	2	2
SOC alone	280	150	50	27	20	16	9	9	4	3	1	1	1	1	0

rPFS was generally consistent across prespecified stratification factor subgroups

Subgroup	^{177}Lu-PSMA-617 + SOC (n = 385)	SOC alone (n = 196)	Hazard ratio (95% CI)
Androgen receptor pathway inhibitors as part of planned SOC			
Yes	170	107	0.53 (0.37, 0.76)
No	215	89	0.27 (0.19, 0.39)
LDH			
≤ 260 IU/L	244	120	0.44 (0.32, 0.61)
> 260 IU/L	140	75	0.37 (0.25, 0.53)
Liver metastases			
Yes	37	22	0.28 (0.15, 0.53)
No	348	174	0.43 (0.33, 0.57)
ECOG score			
0 or 1	352	179	0.43 (0.33, 0.56)
2	33	17	0.18 (0.08, 0.38)
Age			
< 65 years	96	39	0.42 (0.23, 0.76)
≥ 65 years	289	157	0.40 (0.30, 0.53)
Race			
White	336	166	0.38 (0.29, 0.50)
African American or Black	29	14	0.72 (0.23, 2.20)
Asian	6	9	1.50 (0.36, 6.19)
All patients	385	196	0.40 (0.31, 0.52)



Treatment-emergent adverse events grouped as topics of interest: no unexpected or concerning safety signals

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

Treatment-emergent adverse events grouped as topics of interest: no unexpected or concerning safety signals

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VISION study conclusions

- Adding ^{177}Lu-PSMA-617 to safely combinable standard of care in patients with mCRPC after androgen receptor pathway inhibition and chemotherapy
    - Extended overall survival
    - Delayed radiographic disease progression
- ^{177}Lu-PSMA-617 was well tolerated
- These findings warrant adoption of ^{177}Lu-PSMA-617 as a new treatment option in patients with mCRPC

Poster Number 5073

Real-world utilization of advanced therapies and racial disparity among patients with metastatic castration-sensitive prostate cancer (mCSPC): a Medicare database analysis

Stephen J. Freedland, MD[1]; Neeraj Agarwal, MD[2]; Krishnan Ramaswamy, PhD[3]; Rickard Sandin, PhD[4]; David Russell, MD[3]; Agnes Hong, PharmD, MS[5]; Hongbo Yang, PhD[6]; Wei Gao, PhD[6]; Kaitlin Hagan, ScD[6]; Daniel J. George, MD[7]

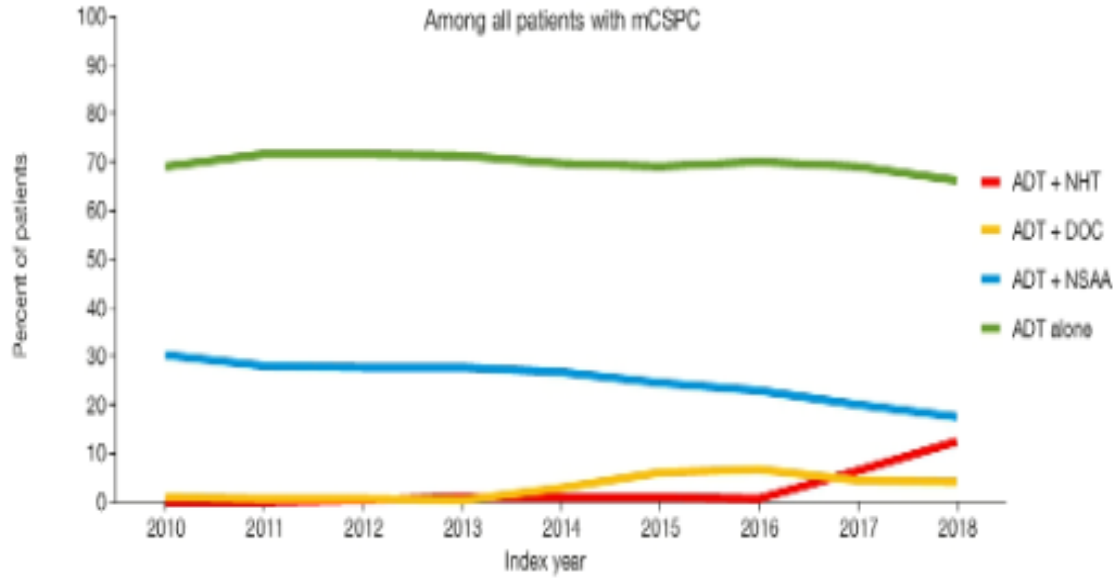
[1]Cedars-Sinai Medical Center, Los Angeles, CA, USA and the Durham VA Medical Center, Durham, NC, USA; [2]Huntsman Cancer Center, University of Utah (NCI-CCC), Salt Lake City, UT, USA; [3]Pfizer, New York, NY, USA; [4]Pfizer, Sollentuna, Sweden; [5]Astellas Pharma, Northbrook, IL, USA; [6]Analysis Group, Inc., Boston, MA, USA; [7]Duke Cancer Institute, Durham, NC, USA

FIRST-LINE TREATMENT DISTRIBUTION OVER TIME

- During 2010–2018, the proportion of patients treated with ADT + NSAA (30.3%–17.4%) and ADT alone (68.9%–66.0%) decreased while use of ADT + DOC (0.8%–4.1%) and ADT + NHT (0%–12.4%) increased (**Figure 2a**)
- Similar trends were observed among patients with visceral metastases (**Figure 2b**), although DOC use was more prevalent compared with the overall cohort

Figure 2. 1L treatment among patients with mCSPC (2010–2018)

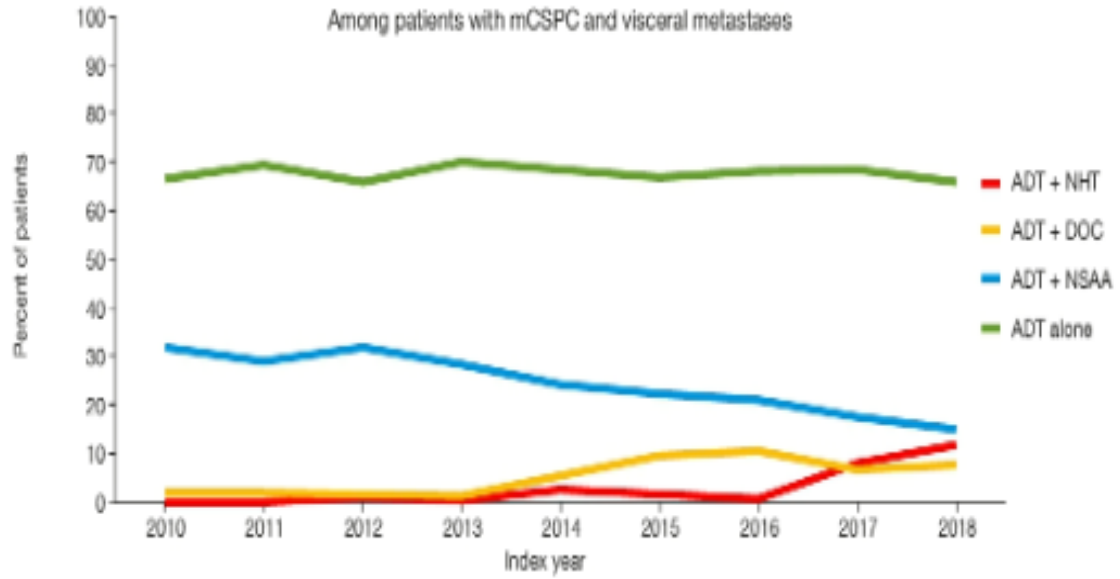
2A



	2010	2011	2012	2013	2014	2015	2016	2017	2018
ADT + NHT	0.0%	0.0%	0.3%	0.8%	0.8%	0.9%	0.6%	6.3%	12.4%
ADT + DOC	0.8%	0.7%	0.5%	0.3%	2.8%	5.9%	6.7%	4.5%	4.1%
ADT + NSAA	30.3%	27.8%	27.6%	27.6%	26.7%	24.3%	22.8%	20.1%	17.4%
ADT alone	68.9%	71.5%	71.6%	71.3%	69.7%	68.9%	69.9%	69.2%	66.0%

Among patients with mCSPC and visceral metastases

2B



	2010	2011	2012	2013	2014	2015	2016	2017	2018
ADT + NHT	0.0%	0.0%	0.9%	0.3%	2.3%	1.5%	0.5%	7.8%	11.8%
ADT + DOC	2.0%	1.8%	1.5%	1.3%	5.4%	9.5%	10.3%	6.6%	7.6%
ADT + NSAA	31.6%	29.0%	31.7%	28.3%	24.0%	22.3%	21.1%	17.3%	14.8%
ADT alone	66.4%	69.3%	65.8%	70.1%	68.2%	66.8%	68.2%	68.3%	65.7%

FIRST-LINE TREATMENT DISTRIBUTION BY RACE

- Compared to the overall population, a similar trend in treatment distribution over time was observed by race (**Figure 3**)
- The rate of treatment intensification with ADT + NHT was higher among non-Hispanic White (6.2% in 2017 to 13.0% in 2018) and Hispanic (6.2% in 2017 to 12.4% in 2018) patients than among Black patients (6.3% in 2017 to 8.3% in 2018) while the rates of treatment intensification with ADT + DOC were similar
- From the GLM (adjusted for age and metastatic site), the odds of treatment intensification was 40% lower among Black patients and 32% lower among Hispanic patients than non-Hispanic White patients (**Figure 4**)

Figure 3. 1L treatment among patients with mCSPC, by race (2010–2018)

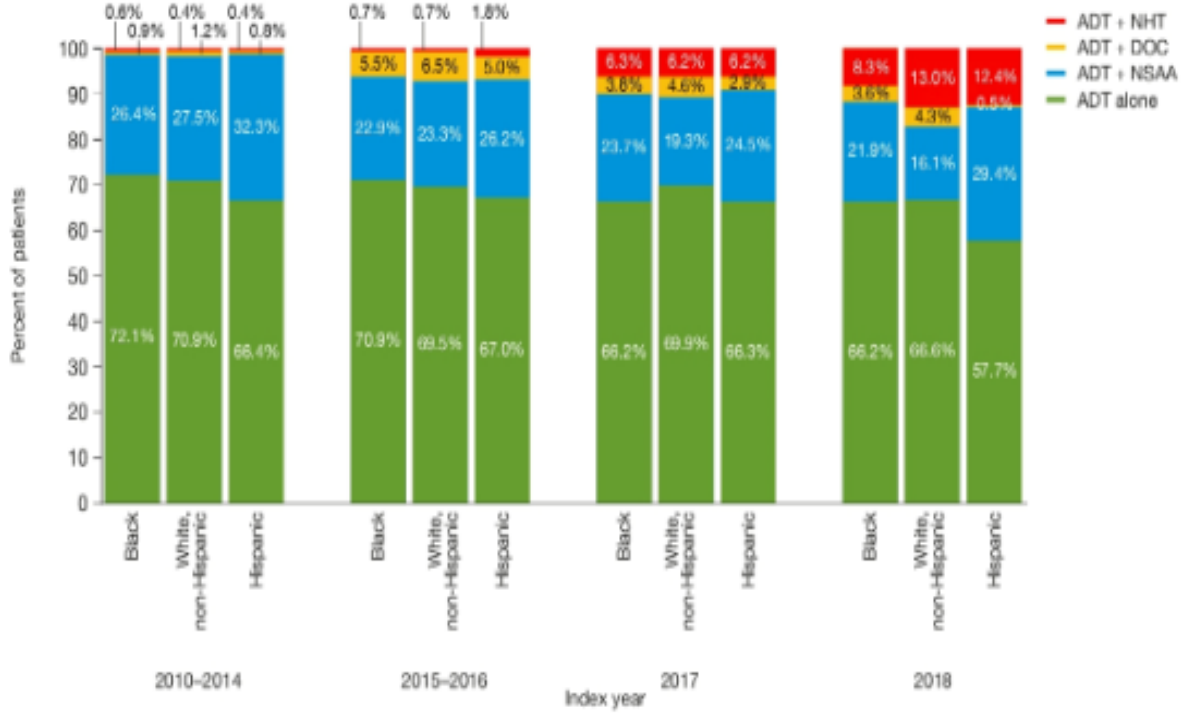
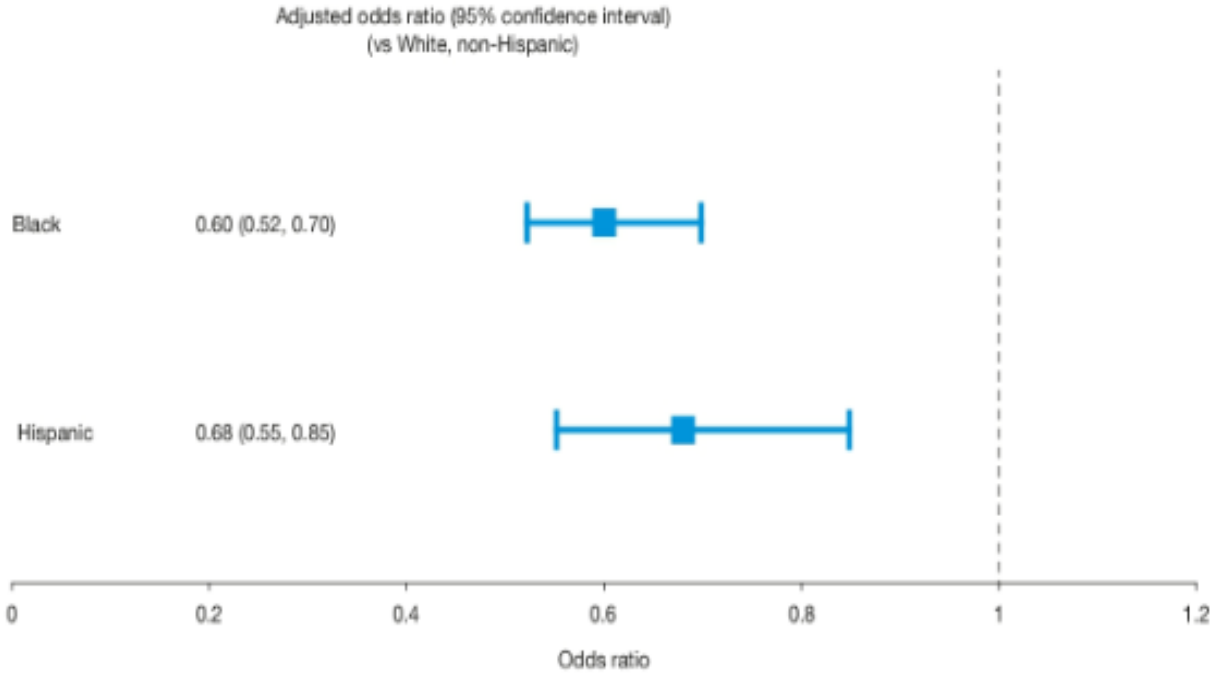


Figure 4. Comparison of treatment intensification across race adjusted for age and site of metastasis



Conclusions

- In this large and nationally representative sample of US patients with mCSPC, less than one-third of patients received treatment intensification by 2018, possibly due to patient/disease characteristics, physician awareness, therapeutic inertia, or cost
- This lack of intensification was also manifested among patients with visceral metastases, highlighting an area of concern
- Importantly, there was less frequent treatment intensification among Black vs non-Hispanic White patients. Further study is required to elucidate underlying reasons for this racial disparity

5072

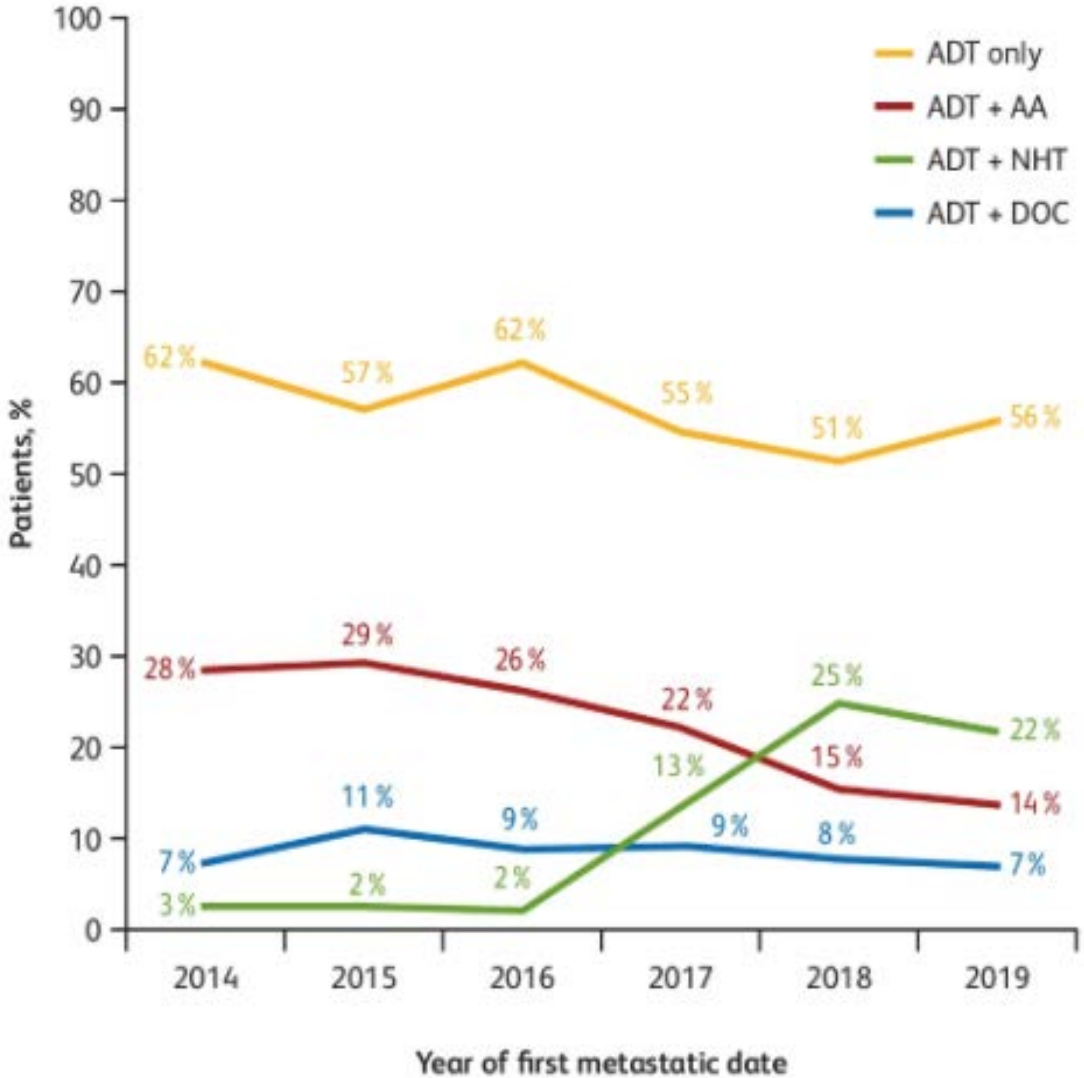
Real-World First-Line Treatment Patterns in Patients With Metastatic Castration-Sensitive Prostate Cancer in a U.S. Health Insurance Database

Umang Swami, MD,[1] Agnes Hong, PharmD, MS,[2] Nader N. El-Chaar, PhD, MSCI,[2] David Nimke, DrPH, MPH,[2] Krishnan Ramaswamy, PhD,[3] Elizabeth J. Bell, PhD, MPH,[4] Rickard Sandin, PhD,[5] Neeraj Agarwal, MD[1]

[1]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [2]Astellas Pharma Inc., Northbrook, IL, USA; [3]Pfizer Inc., New York, NY, USA; [4]Optum, Eden Prairie, MN, USA; [5]Pfizer AB, Sollentuna, Sweden

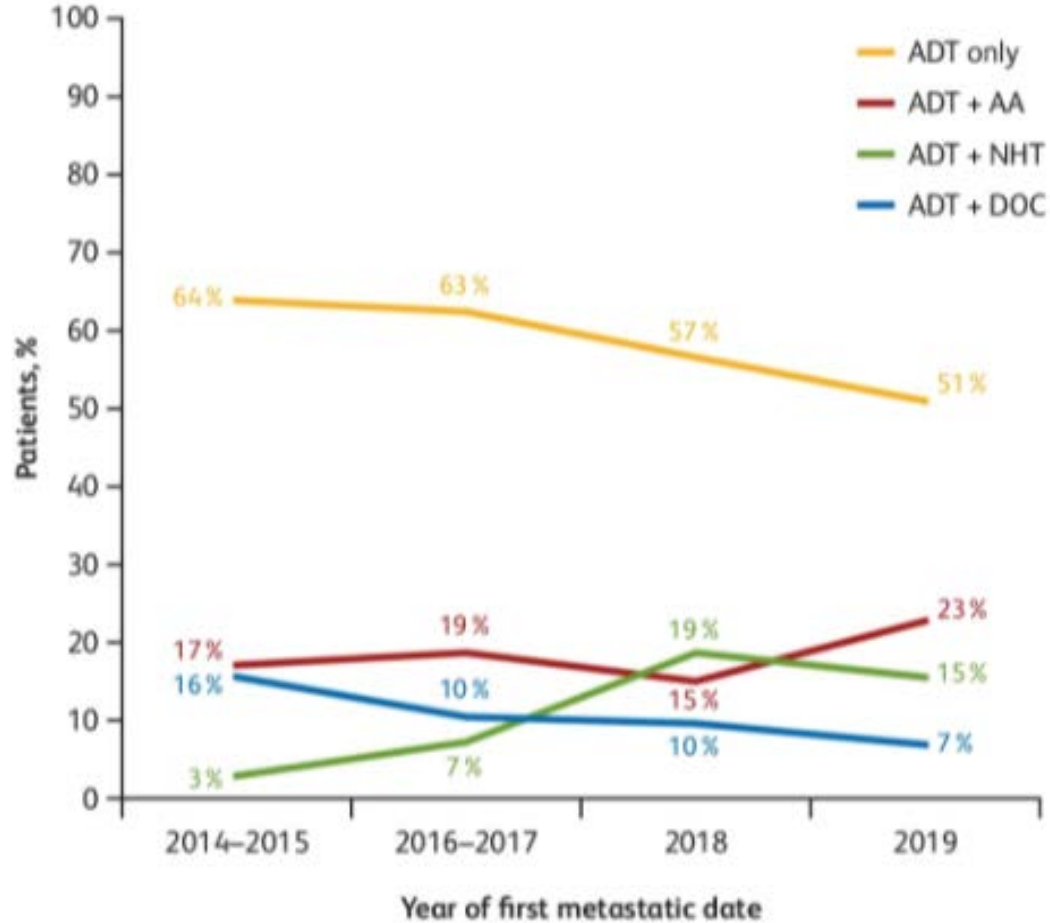
Abstract #5073

Figure 2. Treatment Trends Among Insured Patients With mCSPC



Patients receiving ADT + DOC + NHT are not included on the graph due to the small sample size.
AA=first-generation antiandrogen; ADT=androgen deprivation therapy; DOC=docetaxel; mCSPC=metastatic castration-sensitive prostate cancer; NHT=novel hormonal therapy.

Figure 3. Treatment Trends Among Insured Patients with mCSPC and Visceral Metastases



Patients receiving ADT + DOC + NHT are not included on the graph due to the small sample size. "Any visceral metastases" includes patients with the following metastases: visceral; bone and visceral; node and visceral; and bone, node, and visceral.
AA=first-generation antiandrogen; ADT=androgen deprivation therapy; DOC=docetaxel; mCSPC=metastatic castration-sensitive prostate cancer; NHT=novel hormonal therapy.

Conclusion

- Despite level 1 evidence demonstrating improved survival with intensified treatment (androgen deprivation therapy [ADT] plus docetaxel [DOC] or novel hormonal therapies [NHTs]), this study shows its underutilization in patients with mCSPC, including in patients with visceral metastases

Future Direction

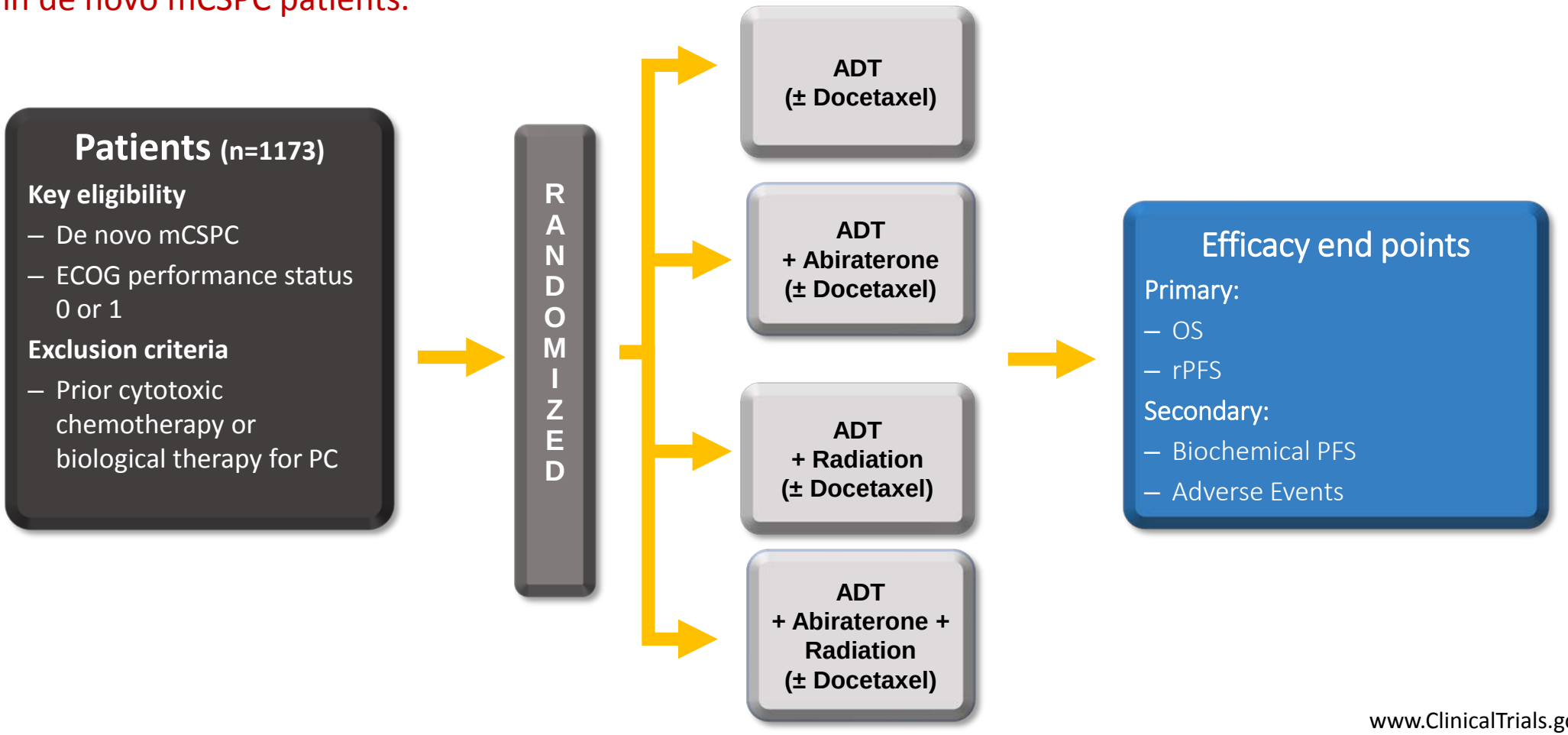
- Further studies are needed to identify the reasons for the underutilization of intensified treatments

ASCO Annual Meeting 2021: Abstract #5000

A phase 3 trial with a 2x2 factorial design of abiraterone acetate plus prednisone and/or local radiotherapy in men with de novo metastatic castration-sensitive prostate cancer (mCSPC): First results of PEACE-1.

Presenting Author: Karim Fizazi

Hypothesis: To investigate the clinical benefit of adding docetaxel, abiraterone acetate or radiation therapy to ADT in de novo mCSPC patients.



www.ClinicalTrials.gov: (NCT02567409)

PEACE-1: First Results and Conclusions

- Median age was 67, high volume 57%; median follow-up 3.5 years
- rPFS:
  - significantly improved with abiraterone in the overall population (HR: 0.54 (0.46-0.64), p<0.0001; medians: 2.2 vs 4.5 years)
  - and in ADT+ docetaxel arms (HR: 0.50 (0.40-0.62), p<0.0001; medians: 2.0 vs 4.5 years)
- Other outcomes favored abiraterone arm & arms that included docetaxel
- Safety signals as expected

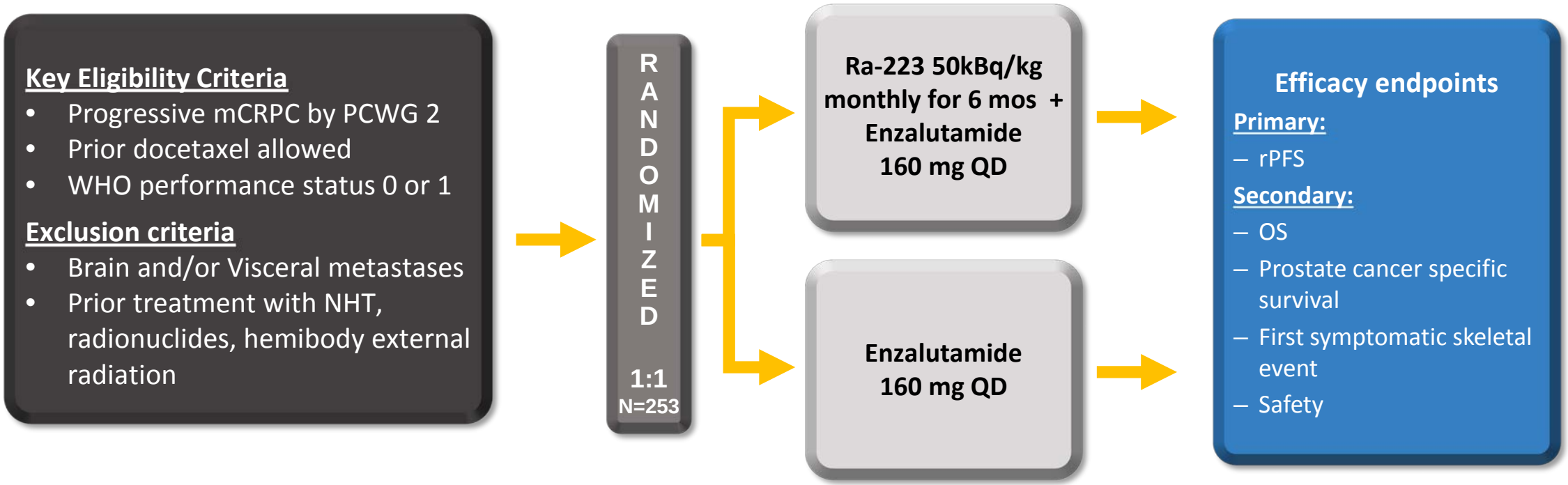
Conclusions: Adding abiraterone to ADT + docetaxel significantly improved rPFS in *de novo* metastatic prostate cancer, with about 2.5 years of absolute benefit in medians, and no meaningful additional short-term toxicity (no significant OS benefit yet)

ASCO Annual Meeting 2021: Abstract #5002

Decreased fracture rate by mandating bone protecting agents in the EORTC 1333/PEACEIII trial combining Ra223 with enzalutamide versus enzalutamide alone: An updated safety analysis.

Presenting Author: Silke Gillessen

Hypothesis: *To investigate the fracture rates after mandating bone protecting agents in mCRPC patients receiving enzalutamide with or without Ra223*



www.ClinicalTrials.gov (NCT02194842)

ASCO Annual Meeting 2021: Abstract #5002

EORTC 1333/PEACEIII trial : An updated safety analysis.

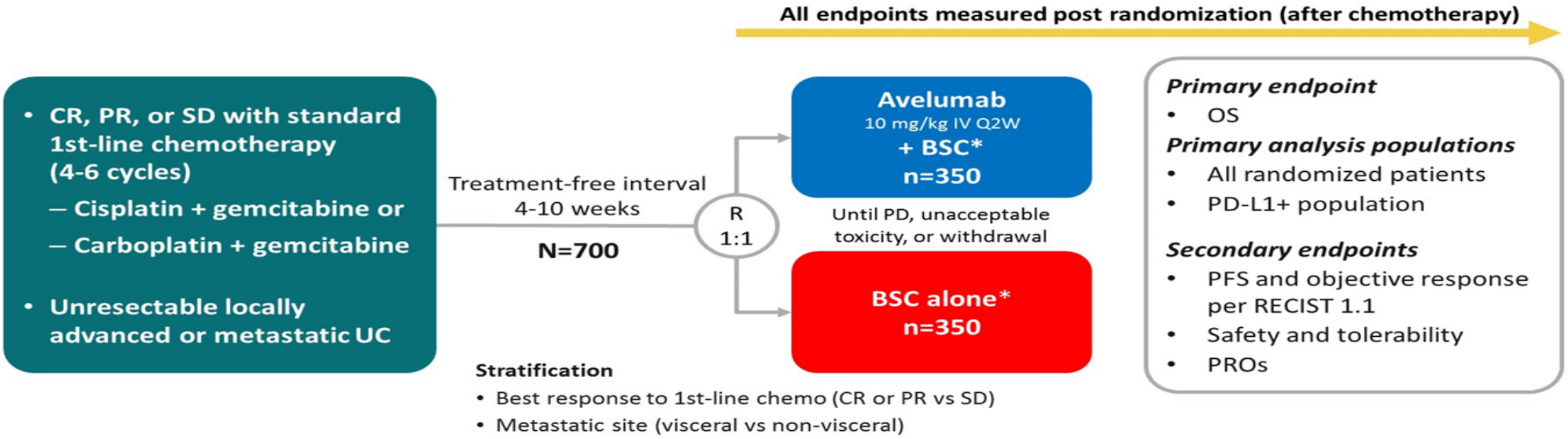
Cumulative incidence (%) of fractures (95% CI).

	Received Bone Protecting Agents		No Bone Protecting Agents	
	Enza+Ra223 (N=82)	Enza (N=87)	Enza+Ra223 (N=36)	Enza (N=32)
At 1 year	2.8 (0.5-8.8)	3.9 (1.0-10.1)	37.1 (21.3-53.0)	15.8 (5.6-30.7)
At 1.5 years	2.8 (0.5-8.8)	3.9 (1.0-10.1)	45.9 (28.6-61.6)	22.3 (9.6-38.2)

Conclusions: In the absence of bone protecting agents (BPA), the risk of fracture is increased when Ra223 is added to enzalutamide. In both arms, the risk remains almost abolished by a preventive continuous administration of BPA, thus stressing the importance of complying to international recommendations in terms of giving BPA to patients with mCRPC

Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC): Analysis of clinical & genomic subgroups from the JAVELIN Bladder 100 trial (abstract 4520; Powles et al.)

JAVELIN Bladder 100 study design (NCT02603432)



PD-L1+ status was defined as PD-L1 expression in ≥25% of tumor cells or in ≥25% or 100% of tumor-associated immune cells if the percentage of immune cells was >1% or ≤1%, respectively, using the Ventana SP263 assay; 358 patients (51%) had a PD-L1–positive tumor

BSC, best supportive care; **CR,** complete response; **IV,** intravenous; **PR**, partial response; **PRO**, patient reported outcome; **Q2W,** every 2 weeks; **R**, randomization; **RECIST 1.1,** Response Evaluation Criteria in Solid Tumors version 1.1; **SD**, stable disease

*BSC (eg, antibiotics, nutritional support, hydration, or pain management) was administered per local practice based on patient needs and clinical judgment; other systemic antitumor therapy was not permitted, but palliative local radiotherapy for isolated lesions was acceptable

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma

T. Powles, S.H. Park, E. Voog, C. Caserta, B.P. Valderrama, H. Gurney, H. Kalofonos, S. Radulović, W. Demey, A. Ullén, Y. Loriot, S.S. Sridhar, N. Tsuchiya, E. Kopyltsov, C.N. Sternberg, J. Bellmunt, J.B. Aragon-Ching, D.P. Petrylak, R. Laliberte, J. Wang, B. Huang, C. Davis, C. Fowst, N. Costa, J.A. Blake-Haskins, A. di Pietro, and P. Grivas

JAVELIN Bladder 100: ASCO 2021 New Data

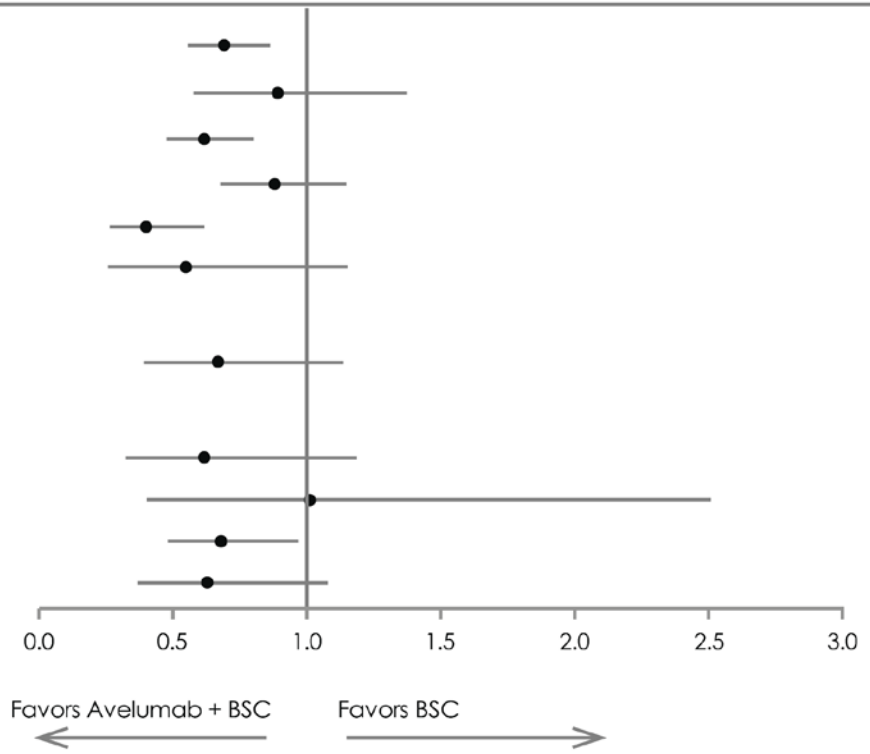
Study/Short Title	Abstract Title	Authors	Session/Abstract
JAV Bladder 100 Additional Subgroups	Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC): analysis of clinical and genomic subgroups from the JAVELIN Bladder 100 trial	Powles T, Petrylak DP, Park SH, Sridhar SS, Caserta C, Theiry-Vuillemin A, Lee HL, Bellmunt J, Yamamoto Y, Aragon-Ching JB, Huang B, Ching K, Davis C, di Pietro A, Loriot Y, Grivas P	Poster Discussion Session Title: Poster Discussion Session, Genitourinary Cancer—Kidney and Bladder On-Demand Session Abstract #: 4520
JAV Bladder 100 Tx-free Interval	Avelumab first-line (1L) maintenance for advanced urothelial carcinoma (UC) in the JAVELIN Bladder 100 trial: subgroup analysis by duration of treatment-free interval (TFI) from end of chemotherapy to start of maintenance	Sridhar SS, Powles T, Loriot Y, Climent Duran MA, Gupta S, Tsuchiya N, Bamias A, Ardizzoni A, Ullen A, Huang B, Nuno C, Laliberte RJ, di Pietro A, Sternberg CN, Grivas P	e-Poster Presentation Session Title: Poster Session: Genitourinary Cancer—Kidney and Bladder Abstract #: 4527
JAV Bladder 100 End of Next-line Therapy	Avelumab first-line (1L) maintenance plus best supportive care (BSC) vs BSC alone for advanced urothelial carcinoma (UC): analysis of time to end of next-line therapy in JAVELIN Bladder 100	Grivas P, Park SH, Voog E, Kopyltsov E, Gurney H, Borges Muniz DQ, Rolland F, Als AB, Valderrama BP, Wang J, Costa N, Laliberte RJ, di Pietro A, Powles T, Bellmunt J	e-Poster Presentation Session Title: Poster Session: Genitourinary Cancer—Kidney and Bladder Abstract #: 4525

JAVELIN Bladder 100 clinical and TCGA subgroups

Abstract 4520, Powles T et al.

Forest plot of OS based on BICR in subgroups of interest

Subgroup	No. of events/no. of patients Avelumab + BSC	BSC	HR for OS (95% CI)*
All patients (stratified†)	145/350	179/350	0.69 (0.556, 0.863)
Upper tract	47/106	38/81	0.89 (0.578, 1.373)
Lower tract	98/244	141/269	0.62 (0.477, 0.802)
Metastatic disease	110/216	115/215	0.88 (0.678, 1.147)
LA and unresectable disease	35/133	63/133	0.40 (0.265, 0.617)
Lymph node-only disease‡	13/48	16/39	0.55 (0.259, 1.152)
1L gemcitabine + carboplatin (PD-L1+ tumors)	27/74	29/54	0.67 (0.393, 1.137)
TCGA			
Basal squamous	17/45	23/44	0.62 (0.326, 1.187)
Luminal	13/30	9/25	1.01 (0.403, 2.509)
Luminal infiltrated	57/143	75/143	0.68 (0.481, 0.968)
Luminal papillary	25/61	31/63	0.63 (0.370, 1.079)

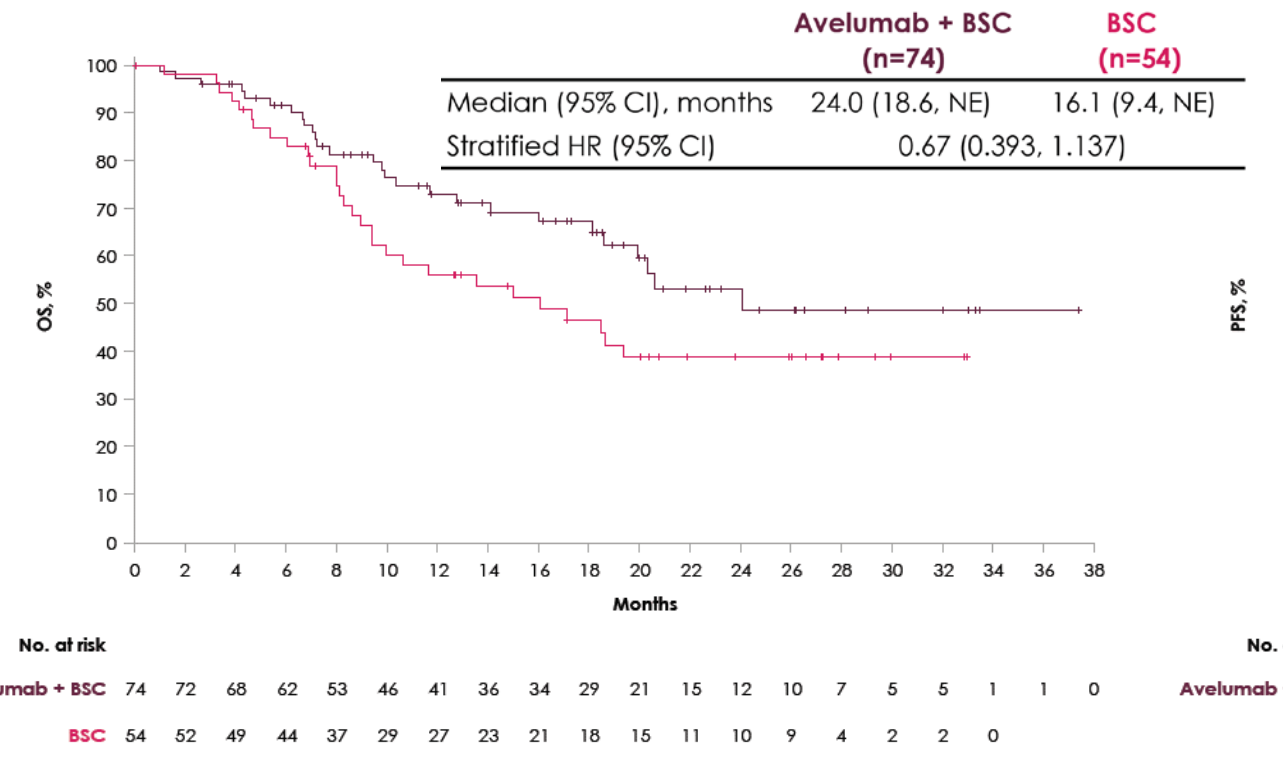


*HRs and CIs were calculated using a Cox proportional hazards model.
†Stratified by best response to 1L chemotherapy (complete or partial response vs stable disease) and metastatic disease site (visceral vs nonvisceral).
‡Post chemotherapy.
1L, first line; BICR, blinded independent central review; BSC, best supportive care; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; TCGA, The Cancer Genome Atlas.

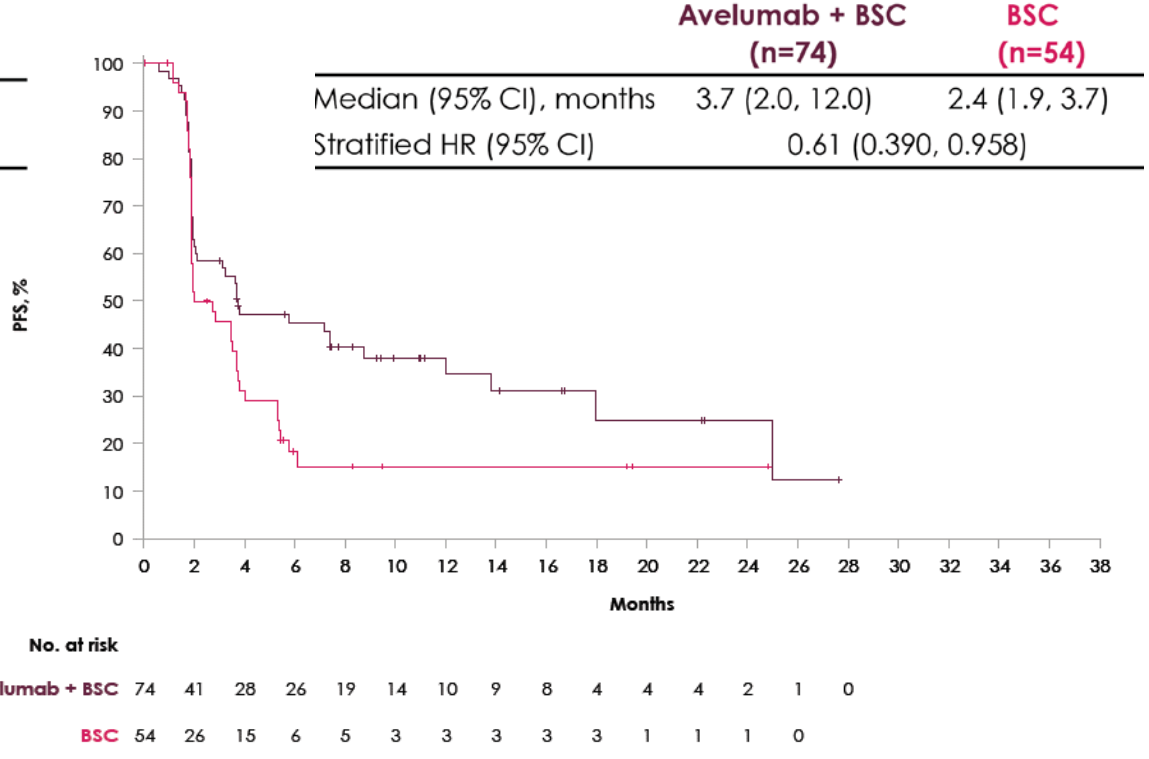
JAVELIN Bladder 100 clinical and TCGA subgroups

Abstract 4520, Powles T et al.

OS in patients with PD-L1+ tumors who received 1L gemcitabine + carboplatin



PFS in patients with PD-L1+ tumors who received 1L gemcitabine + carboplatin

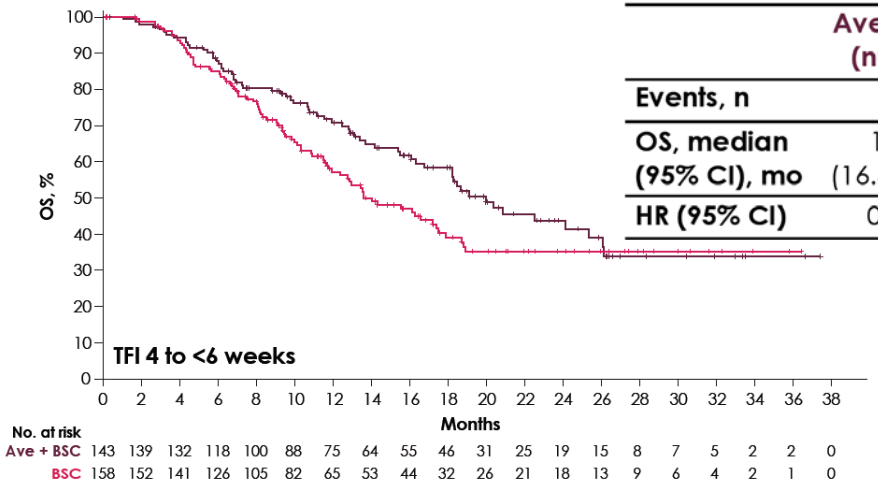


1L, first line; BSC, best supportive care; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression-free survival.

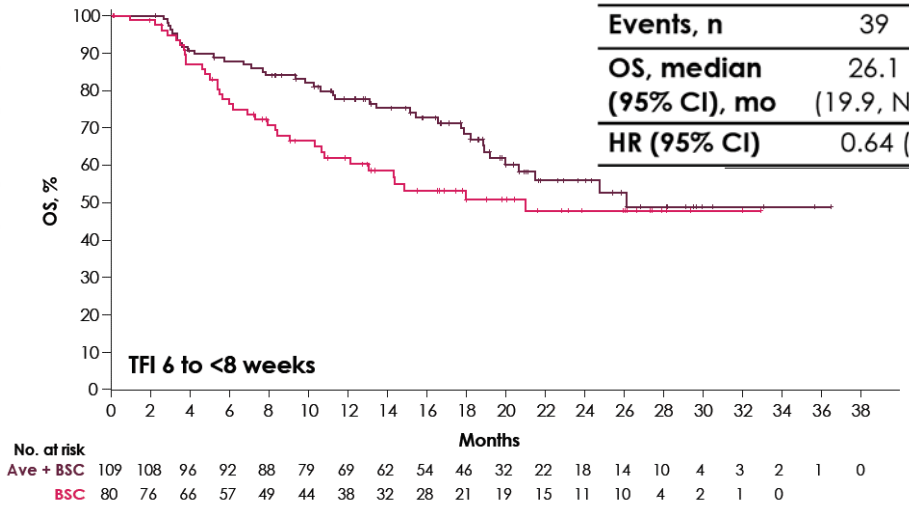
JAVELIN Bladder 100 treatment-free interval analyses

Abstract 4527, Sridhar SS et al.

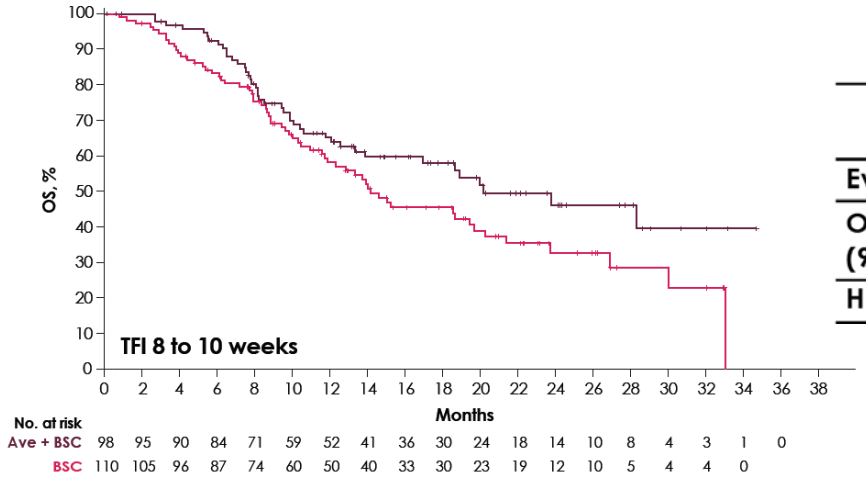
OS by duration of TFI before maintenance



	Ave + BSC (n=143)	BSC (n=158)
Events, n	64	81
OS, median (95% CI), mo	19.9 (16.3, 25.3)	13.5 (11.7, 17.4)
HR (95% CI)	0.76 (0.546, 1.059)	



	Ave + BSC (n=109)	BSC (n=80)
Events, n	39	35
OS, median (95% CI), mo	26.1 (19.9, NE)	21.0 (10.7, NE)
HR (95% CI)	0.64 (0.404, 1.021)	



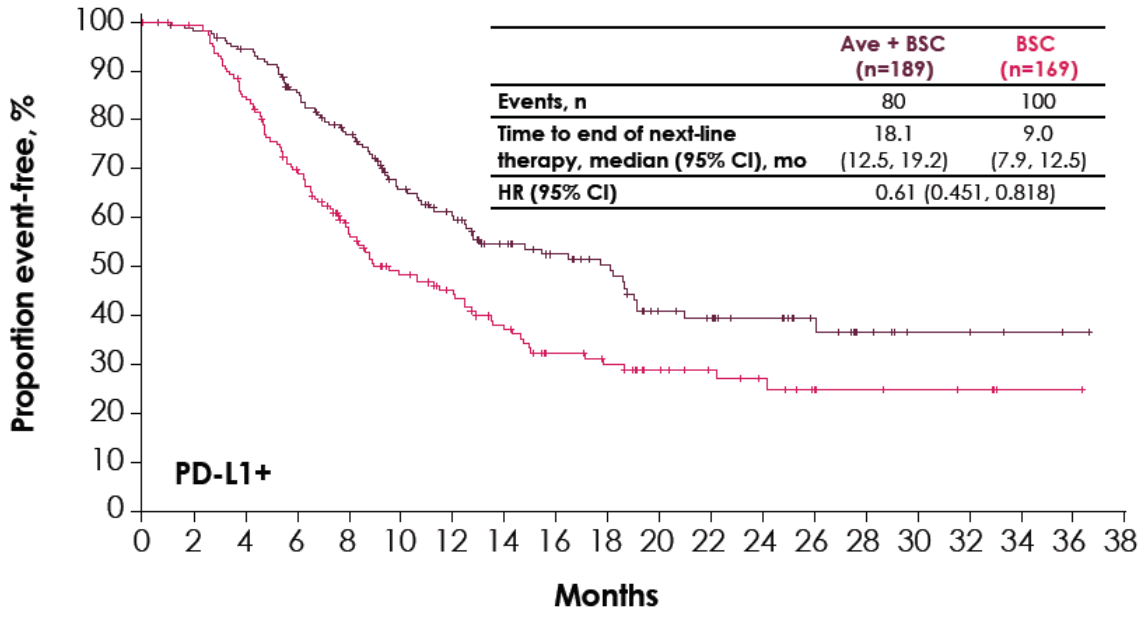
	Ave + BSC (n=98)	BSC (n=110)
Events, n	42	62
OS, median (95% CI), mo	20.1 (13.8, NE)	14.1 (11.7, 19.6)
HR (95% CI)	0.70 (0.468, 1.035)	

Ave, avelumab; BSC, best supportive care; HR, hazard ratio; NE, not estimable; OS, overall survival; TFI, treatment-free interval.

JAVELIN Bladder 100 time to end of next-line therapy

Abstract 4525, Grivas P et al.

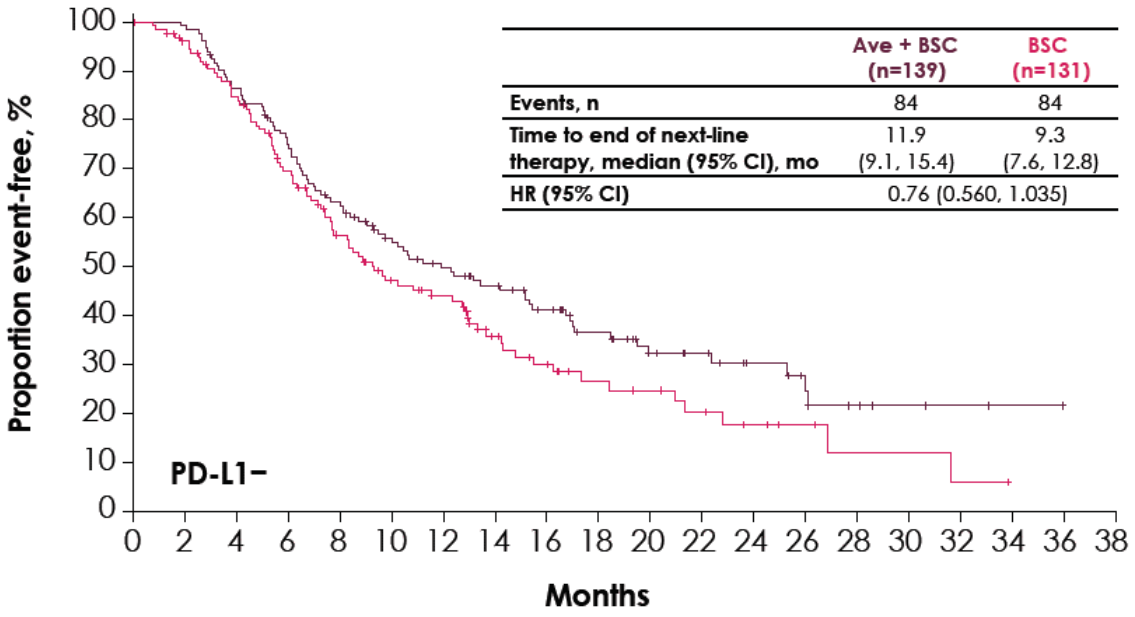
Time to end of next-line therapy in patients with PD-L1+ or PD-L1− tumors



	Ave + BSC (n=189)	BSC (n=169)
Events, n	80	100
Time to end of next-line therapy, median (95% CI), mo	18.1 (12.5, 19.2)	9.0 (7.9, 12.5)
HR (95% CI)	0.61 (0.451, 0.818)	

No. at risk

Ave + BSC	189	158	150	132	114	89	75	57	49	43	30	27	22	14	8	4	4	2	1	0
BSC	169	156	132	105	77	61	52	40	30	26	19	15	12	8	6	5	4	1	1	0



	Ave + BSC (n=139)	BSC (n=131)
Events, n	84	84
Time to end of next-line therapy, median (95% CI), mo	11.9 (9.1, 15.4)	9.3 (7.6, 12.8)
HR (95% CI)	0.76 (0.560, 1.035)	

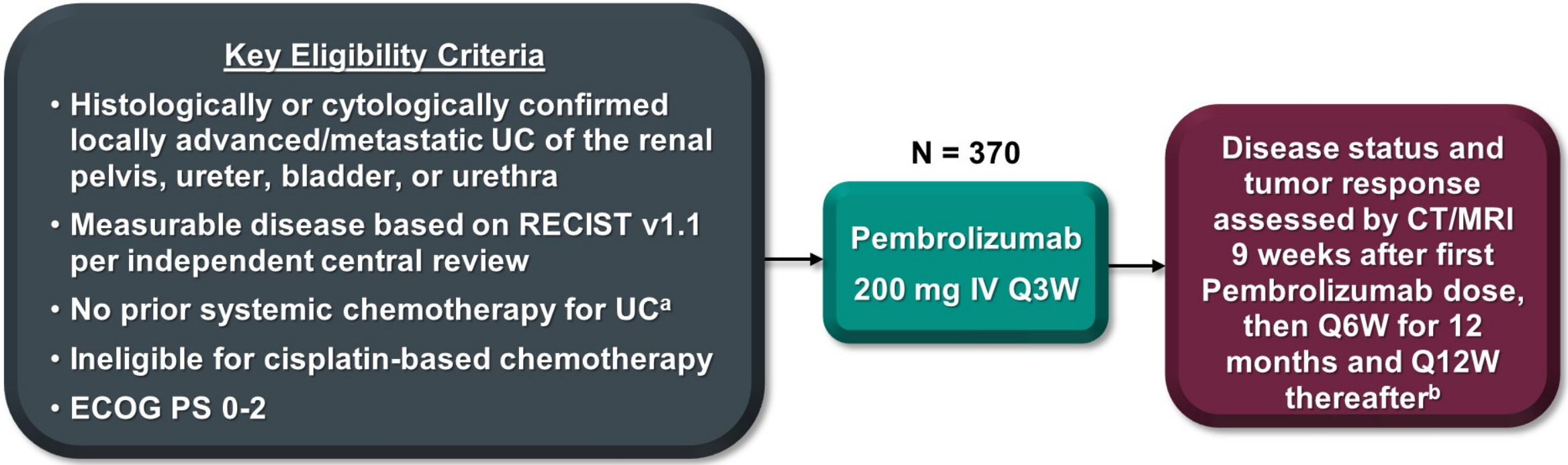
No. at risk

Ave + BSC	139	132	114	96	80	65	56	49	40	29	20	17	12	9	5	3	2	1	0	
BSC	131	119	103	82	62	47	40	26	20	14	12	9	6	4	2	2	1	0		

Time to end of next-line therapy was defined in all patients as the time from randomization until discontinuation of next treatment received after first progression, as assessed by investigator, or death from any cause, whichever occurred first; patients who did not die or receive next-line therapy were censored at last follow-up.

Ave, avelumab; BSC, best supportive care; HR, hazard ratio.

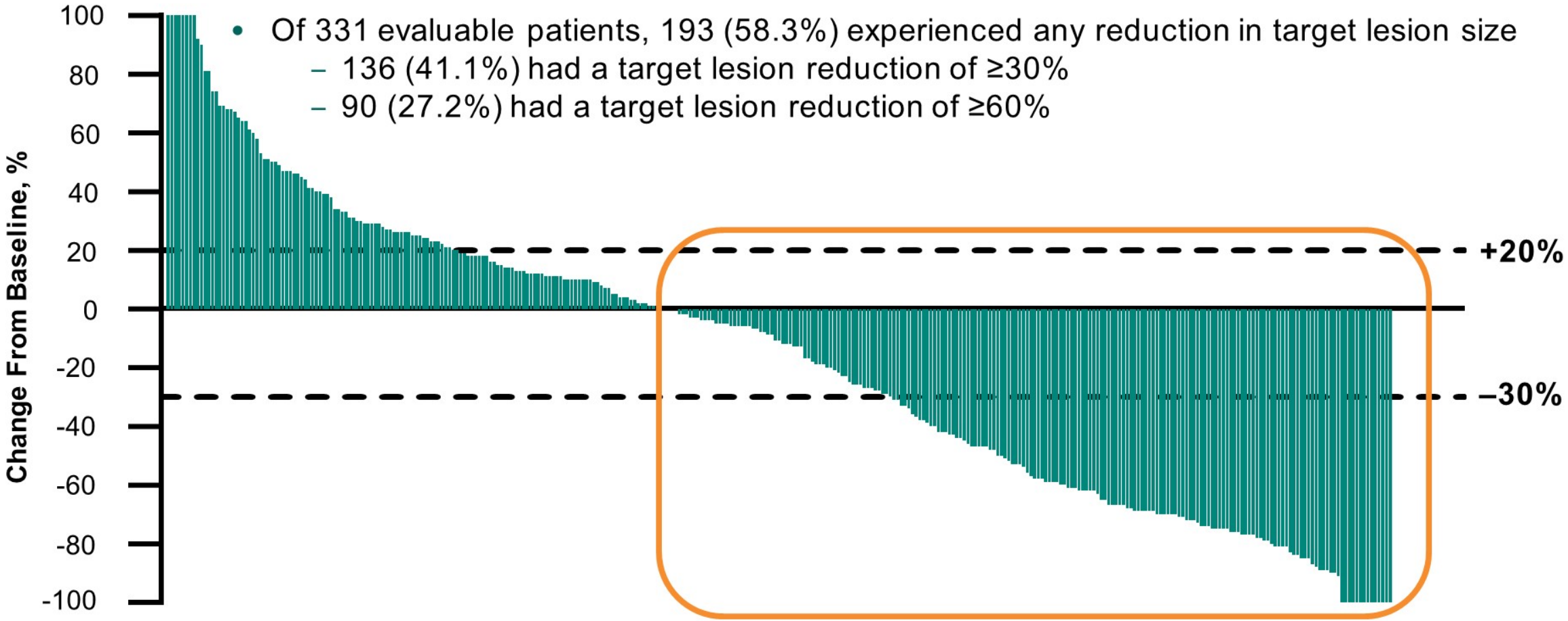
KEYNOTE-052 Study Design



- Primary end point: confirmed ORR per RECIST v1.1 by independent radiology review
- Secondary end points: PFS and DOR per RECIST v1.1 by independent radiology review, OS, safety
- End points analyzed for the overall population, patients with PD-L1 CPS ≥10 and CPS <10[c]

[a]Patients who received adjuvant/neoadjuvant platinum-based chemotherapy before/after radical cystectomy and experienced recurrence >12 months after completion were eligible to participate. [b]Until disease progression, start of new anticancer treatment, withdrawal of consent, or death. [c]CPS defined as the number of PD-L1–staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

Best Percentage Change From Baseline in Target Lesions: Overall Population[a]



[a]Patients with measurable disease at baseline and ≥1 postbaseline measurement (n = 331). Data cutoff: September 26, 2020.

Adverse Events

n (%)	Pembrolizumab N = 370
Any-grade AE	361 (97.6)
Any-grade TRAE[a]	249 (67.3)
Grade 3-5 TRAE	78 (21.1)
Serious TRAE	43 (11.6)
Death due to TRAE[b]	1 (0.3)
Discontinued[c] because of a TRAE	35 (9.5)
Discontinued because of a serious TRAE	16 (4.3)

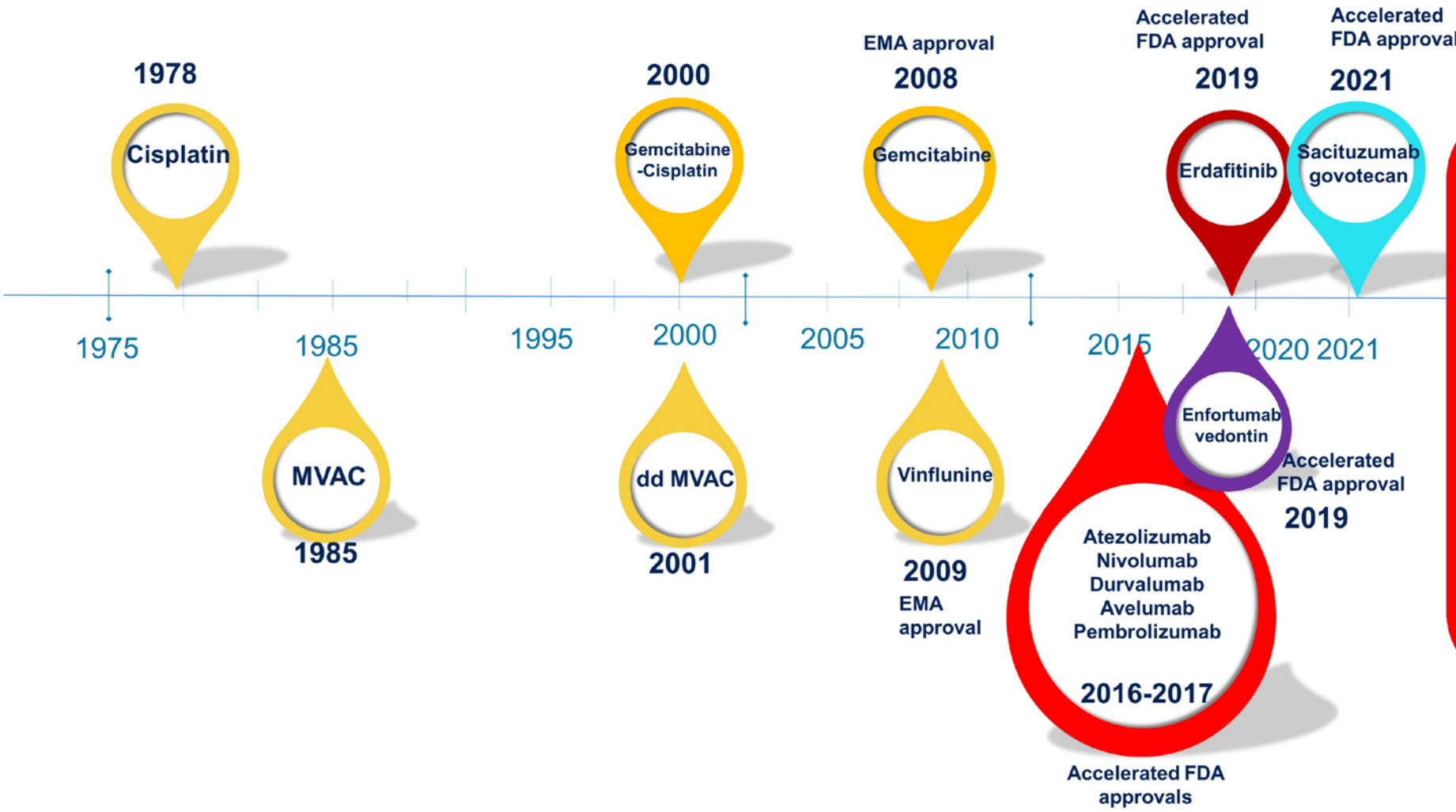
TRAEs With ≥5% Incidence	Pembrolizumab N = 370	
	Any Grade	Grade 3-5
Pruritis	68 (18.4)	3 (0.8)
Fatigue	67 (18.1)	9 (2.4)
Rash	45 (12.2)	2 (0.5)
Decreased appetite	40 (10.8)	2 (0.5)
Hypothyroidism	37 (10.0)	0 (0)
Diarrhea	34 (9.2)	4 (1.1)
Nausea	32 (8.6)	1 (0.3)

[a]Determined by investigator to be related to pembrolizumab. [b]1 death from treatment-related myositis. [c]Study medication withdrawn. Data cutoff: September 26, 2020.

Conclusions

- First-line pembrolizumab monotherapy continued to show durable antitumor activity up to 5 years after the last patient was enrolled
  - ORR: 28.9%
  - Median DOR: 33.4 months
  - Median OS: 11.3 months
- Patients with CPS ≥10 were more likely to respond than those with CPS <10, and this response was durable, supporting the current FDA indication
  - ORR: 47.3% (CPS ≥10), 20.7% (CPS <10)
  - Median DOR: NR (CPS ≥10), 21.2 months (CPS <10)
  - Median OS: 18.5 months (CPS ≥10), 9.7 months (CPS <10)
- Safety was consistent with the known profile of pembrolizumab
- These data support the use of pembrolizumab in cisplatin-ineligible patients with locally advanced or metastatic UC

Therapy Advances in Metastatic Urothelial Cancer (mUC)



2021

- **Atezolizumab and Durvalumab withdrawn for 2nd line indication in US**
- **Pembrolizumab and Atezolizumab reviewed by FDA ODAC for 1st-line indication in cis-ineligible mUC**

Advanced Urothelial Ca Treatment Algorithm

Disease State	Setting	Preferred Option	Standard Options
Metastatic, no prior chemotherapy	Cisplatin-eligible	Cisplatin/gemcitabine f/b avelumab maintenance	Cisplatin-based combination chemotherapy f/b avelumab maintenance
Metastatic, no prior chemotherapy	Cisplatin-ineligible	Gemcitabine/Carboplatin (PD-L1 low tumors in fit patients) f/b avelumab maintenance	Gemcitabine/Carboplatin f/b avelumab maintenance *Pembrolizumab* *umab* gent chemotherapy
Metastatic, prior platin chemotherapy or relapse within 1 year of perioperative cisplatin-based therapy		OR FGFRi (tumors with FGFR2/3 alterations)	umab Nivolumab
Metastatic, prior chemotherapy & immunotherapy		Antibody drug conjugate (EV; SG) OR FGFRi (tumors with FGFR2/3 alterations)	Taxane (US) Vinflunine (EU)

Clinical trials are critical throughout disease spectrum & treatment settings!

Ευχαριστώ ☺
Patient and families!

Collaborators, sponsors, institutions, foundations, colleagues, research, admin & clinical staff: Teams! @PGrivasMDPhD