



**Post conference
meeting 2021**

Highlights in medical oncology

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Conflicts of interest



- I have no potential conflict of interest to report
- or
- I have the following potential conflict(s) of interest to report

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	Janssen
Receipt of honoraria or consultation fees:	Roche, Ipsen, MSD, BMS, Pfizer, Janssen, Astellas
Participation in a company sponsored speaker's bureau:	Roche, Ipsen, MSD, Pfizer, Janssen, Astellas, BMS
Stock shareholder:	-
Spouse/partner:	-
Other support (please specify): travel fees	Pfizer, Roche, Astellas, Ipsen



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UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

**Post conference
meeting 2021**

Prostate cancer

Hormone sensitive metastatic disease



Should we use doublet or triplet systemic therapy in upfront mHSPC?

THE PEACE 1 trial datas in 2021

PEACE 1: trial design

Key Eligibility Criteria

De novo mCSPC

Distant metastatic disease by ≥ 1 lesion on bone scan and/or CT scan

ECOG PS 0 -2

On-Study Requirement

Continuous ADT

Permitted

ADT ≤ 3 months

Stratification

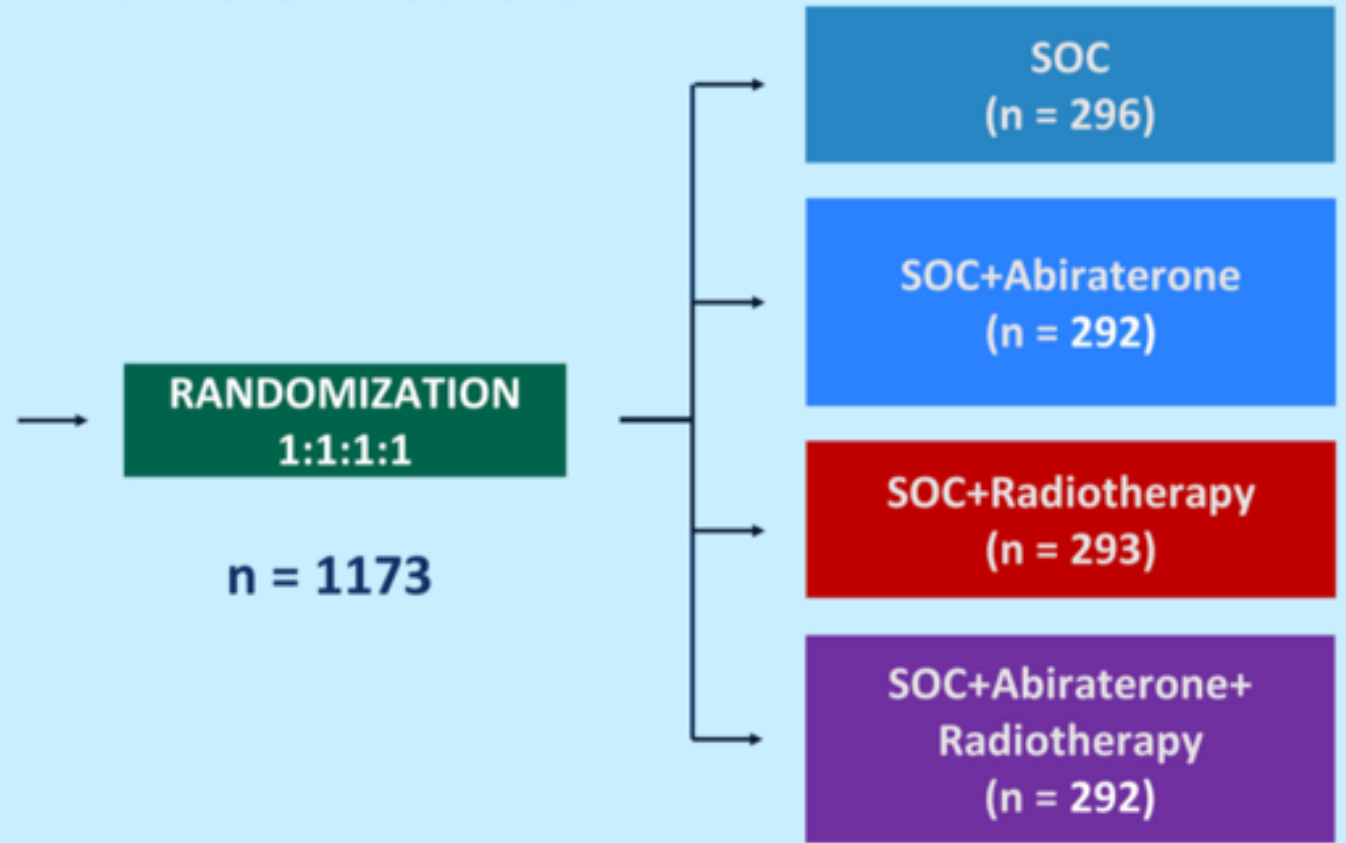
ECOG PS (0 vs 1-2)

Metastatic sites (LN vs bone vs visceral)

Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)

Docetaxel (yes vs no)

Nov 2013 – Dec 2018



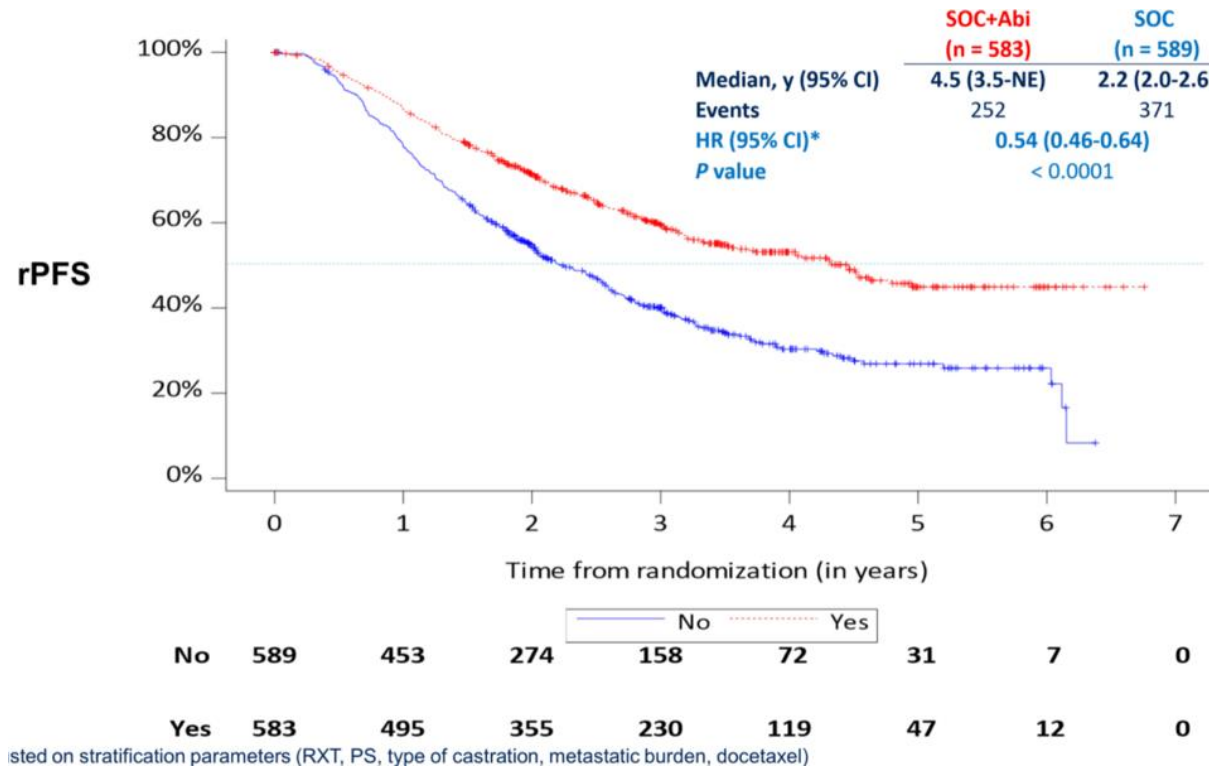
PEACE 1: population

		SOC (+/- RXT) (n = 589)	SOC (+/- RXT) + Abiraterone (n = 583)
Median age, year (IQR)		66 (59–72)	67 (61–72)
ECOG PS score, n (%)	0	412 (70)	412 (71)
	1-2	177 (30)	171 (29)
Gleason score at initial diagnosis, n (%)	≤ 7	132 (23)	144 (25)
	≥ 8	440 (77)	427 (75)
Median time from diagnosis, month (IQR)		2.3 (1.5-3.1)	2.3 (1.6-3.2)
Metastatic sites, n (%)	Lymph nodes only	52 (9)	47 (8)
	Bone without visceral	475 (81)	472 (81)
	Visceral	62 (11)	64 (11)
Disease burden, n (%)	Low	252 (43)	250 (43)
	High	334 (57)	330 (57)
Median baseline PSA, ng/mL (IQR)		11.4 (3.1-55.3)	14.2 (3.2-62.1)
Docetaxel, n (%)	Yes	355 (60)	355 (61)
	No	234 (40)	228 (39)

PEACE 1: results

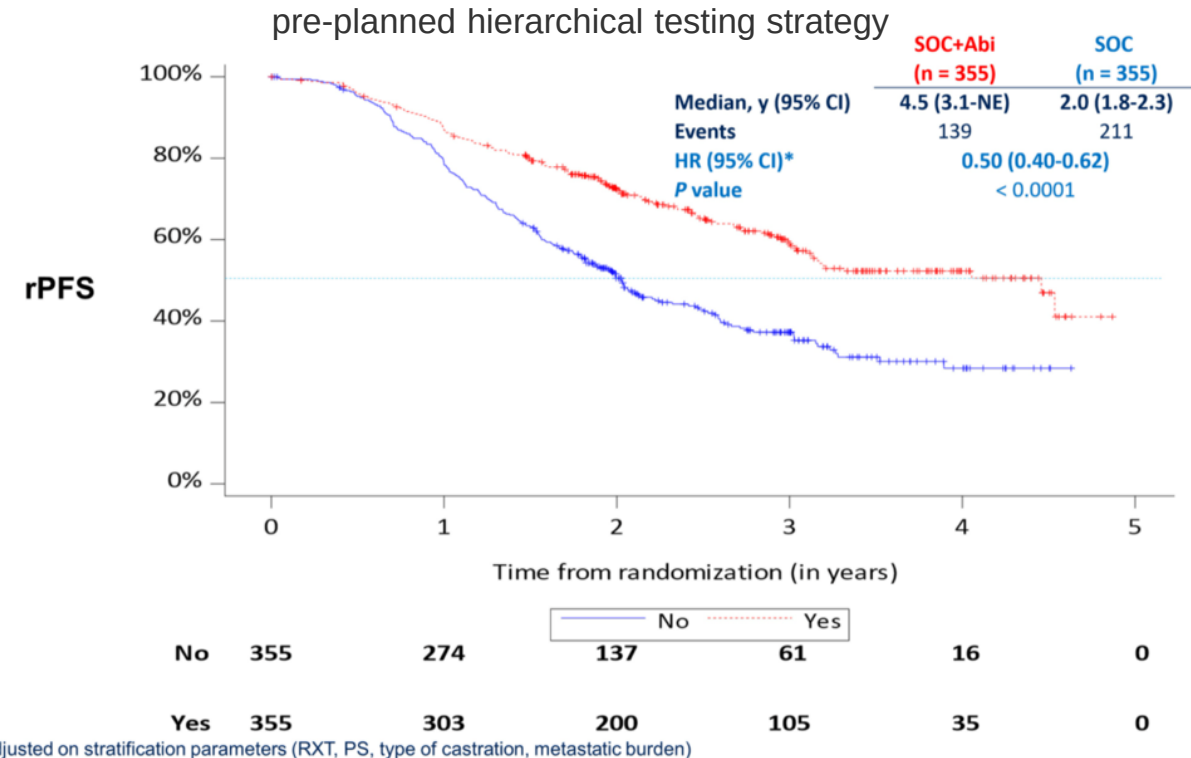
rPFS in the overall cohort

SOC: ADT
+- RT
+- Docetaxel



rPFS in patient receiving docetaxel as SOC +/- RT

pre-planned hierarchical testing strategy



PEACE-1 secondary endpoints: CRPC-Free Survival

Outcome	Abiraterone + SoC (± Radiotherapy)	SoC (± Radiotherapy)
CRPC-free survival in overall population	(n = 583)	(n = 589)
▪ Median CRPC-free survival, yr (95% CI)	3.8 (3.1-4.5)	1.5 (1.4-1.6)
▪ Events	276	453
▪ HR (95% CI)	0.40 (0.35-0.47); <i>P</i> <.0001	
CRPC-free survival in ADT + docetaxel population	(n = 355)	(n = 355)
▪ Median CRPC-free survival, yr (95% CI)	3.2 (3.0-4.5)	1.4 (1.3-1.6)
▪ Events	156	268
▪ HR (95% CI)	0.38 (0.31-0.47); <i>P</i> <.0001	

PEACE-1 secondary endpoints: Clinical PFS

Outcome	Abiraterone + SoC (± Radiotherapy)	SoC (± Radiotherapy)
Clinical PFS in overall population	(n = 583)	(n = 589)
▪ Median clinical PFS, yr (95% CI)	4.3 (3.3-4.8)	2.1 (1.8-2.4)
▪ Events	262	379
▪ HR (95% CI)	0.54 (0.46-0.63); <i>P</i> <.0001	
Clinical PFS in ADT + docetaxel population	(n = 355)	(n = 355)
▪ Median clinical PFS, yr (95% CI)	4.1 (3.0-NE)	1.9 (1.6-2.1)
▪ Events	145	217
▪ HR (95% CI)	0.50 (0.40-0.62); <i>P</i> <.0001	

Overall Survival for PEACE 1 trial

	OS (overall population) SOC+ABI (n=583)	OS (overall population) SOC (n=589)
Median, y (95% CI)	5,7 (5,1-NE)	4,7 (4,3-5,3)
HR (95%CI)	0,82 (0,69-0,98)	
P value	0,030	

	OS with abiraterone in the ADT + docetaxel (+- RT) population SOC+ABI (n=583)	OS with abiraterone in the ADT + docetaxel (+- RT) population SOC (n=589)
Median, y (95% CI)	NE (4,5-NE)	4,4 (3,8-4,9)
HR (95%CI)	0,75(0,59-0,85)	
P value	0,017	

Adjusted on stratification parameters (RT, PS, type of castration, metastatic burden)

PEACE 1: High Volume vs Low volume rPFS & OS data

	rPFS Median (years)	rPFS HR	OS Median (years)	OS HR
High volume Abi+ADT+Doce +-RT (n=225)	4,1 (2,7-NE)	0,47 (0,36-0,60) <i>P value <0,0001</i>	5,1 (3,8- NE)	0,72 (0,55-0,95) <i>P value 0,019</i>
High Volume ADT+doce +-RT (n=231)	1,6 (1,4-2,0)		3,5 (3,2-4,0)	
Low volume Abi+ADT+Doce +- RT (n=129)	NE (3,1-NE)	HR:0,58 (0,39-0,87) <i>P value 0,006</i>	NE (NE-NE)	0,83 (0,50-1,38) <i>P value 0,66</i>
Low volume ADT+Doce +- RT (n=122)	2,7 (2,5-NE)		NE (4,7-NE)	

Subsequent therapy

Treatment beyond progression ADT + docetaxel population

At least one treatment, n (%)	SOC (+/- RXT) + Abiraterone n _{CRPC} =141	SOC (+/- RXT) n _{CRPC} =263
Life-prolonging treatment	104 (74)	221 (84)
Next gen. Hormonal Therapy	65 (46)	213 (81)
Abiraterone	22 (16)	153 (58)
Enzalutamide	57 (40)	119 (45)
Docetaxel	29 (21)	25 (10)
Cabazitaxel	84 (60)	114 (43)
Radium 223	3 (2)	11 (4)
Lu-PSMA	2 (1)	3 (1)

PEACE 1: Safety



	SOC (+/- RXT) + Abiraterone (n=335)	SOC (+/- RXT) (n=336)
	n (%)	n (%)
Hematological	50 (14)	52 (15)
Neutropenia	33 (10)	31 (9)
Febrile neutropenia	16 (5)	16 (5)
Liver	20 (6)	1 (0)
Cardiac	3 (1)	3 (1)
Hypertension	43 (12)	28 (8)
Gastro-intestinal	8 (2)	15 (4)
Fatigue	6 (2)	13 (4)
Grade 5	3 (0.9)	2 (0.6)

PEACE 1 Monday morning question



The question before was:
Chemotherapy or Abiraterone?

The question now is:
Who will still needs chemotherapy upfront?

One size fits all
approach?

FIT patients with high
volume disease

Patients with poor PSA
decline after 1 month of
Abiraterone?

Arasens & Enzamet OS
are coming to help to
address the question

A microscopic image showing a dense cluster of prostate cancer cells, characterized by their irregular shapes and prominent nuclei, stained in a dark teal color. This image occupies the top portion of the slide, with a white curved border separating it from the text area below.

A New Class of Effective Therapy for Men with Metastatic Castration- Resistant Prostate Cancer: Lutetium PSMA

TheraP Clinical Trial Results

A randomised phase II trial of **¹⁷⁷Lu-PSMA-617 THERANOSTIC** versus **CABAZITAXEL CHEMOTHERAPY**

PATIENT SELECTION

MEN WITH PROSTATE CANCER
metastatic castration
resistant disease

PSMA PET IMAGING

shows prostate cancer
with PSMA

⁶⁸Ga-PSMA-11

Patients with high PSMA
enter the trial

Positron Emission
Tomography (PET)
reveals the tracers'
location with
high precision.

200 PARTICIPANTS
in 11 sites
across Australia
RANDOMISED

TRIAL



50% MEN TREATED WITH CABAZITAXEL
20mg/m² IV q3 weekly
Up to 10 cycles

50% MEN TREATED WITH ¹⁷⁷Lu-PSMA-617
8.5 GBq IV q6 weekly
↓ 0.5 GBq each cycle
Up to 6 cycles



OUTCOMES

PSA Reduction
≥ 50% from baseline



Progression Free Survival
at 12 months



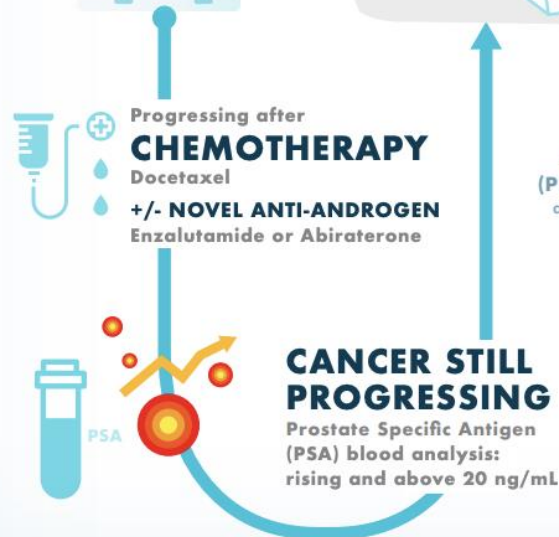
Objective Response Rate
on CT Scan (RECIST)



Troublesome Adverse Events
Grade 3-4



Patient Reported Outcomes



Prostate Specific
Membrane Antigen
(PSMA) is a protein found
abundantly on the surface
of prostate cancer cells.

Tracers are small
radiolabelled
molecules that bind
to the targeted
cancer cells.

Prostate
cancer cell

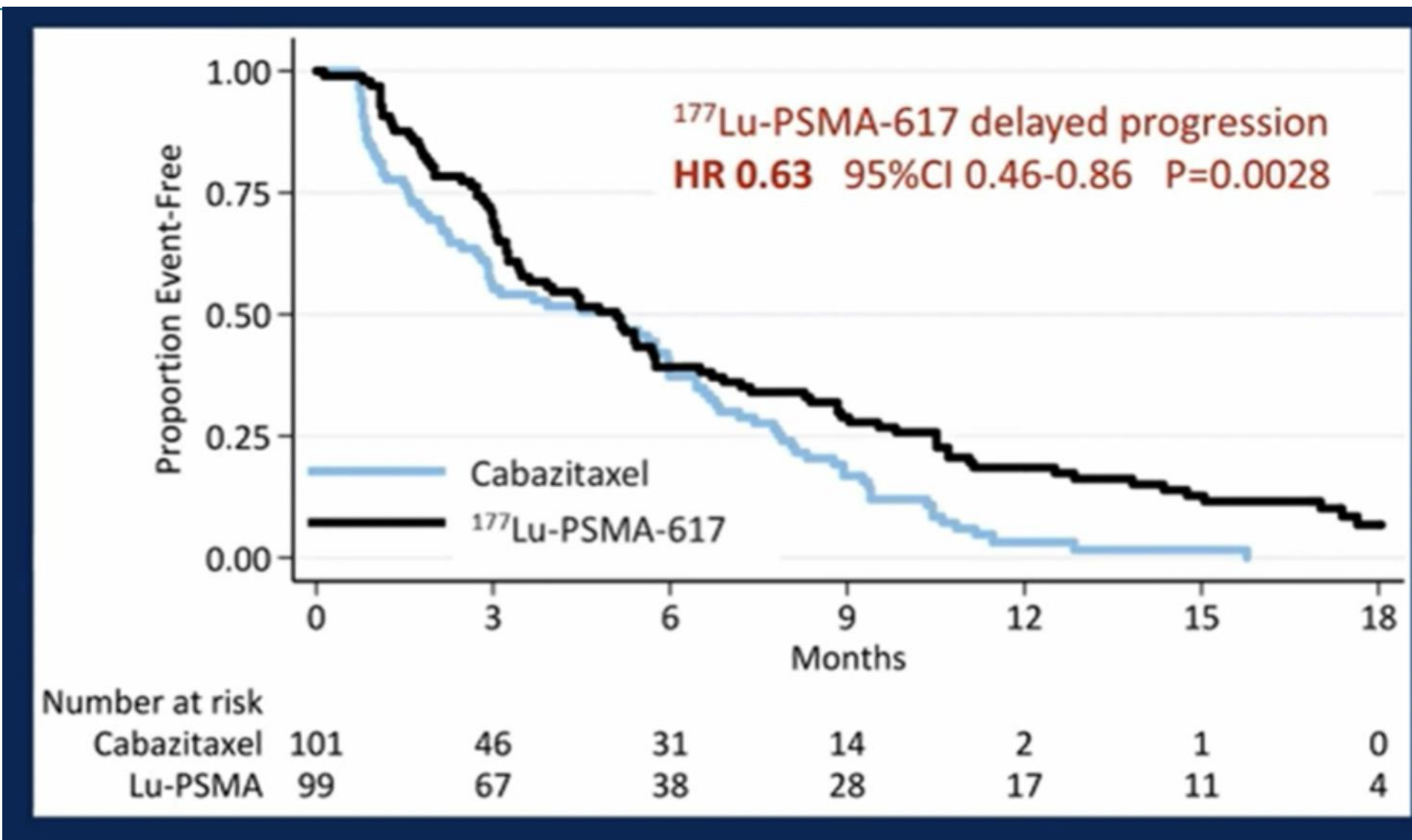
⁶⁸Ga-PSMA-11
is used for diagnostic
PET imaging

THERANOSTICS
seamlessly aligns a
diagnostic and
therapeutic tracer.

¹⁷⁷Lu-PSMA-617
is used for therapeutic
purposes. It emits
beta-radiation killing
cancer cells.

β-radiation
~ 1mm

TheraP clinical trial results on PFS



VISION phase 3 trial

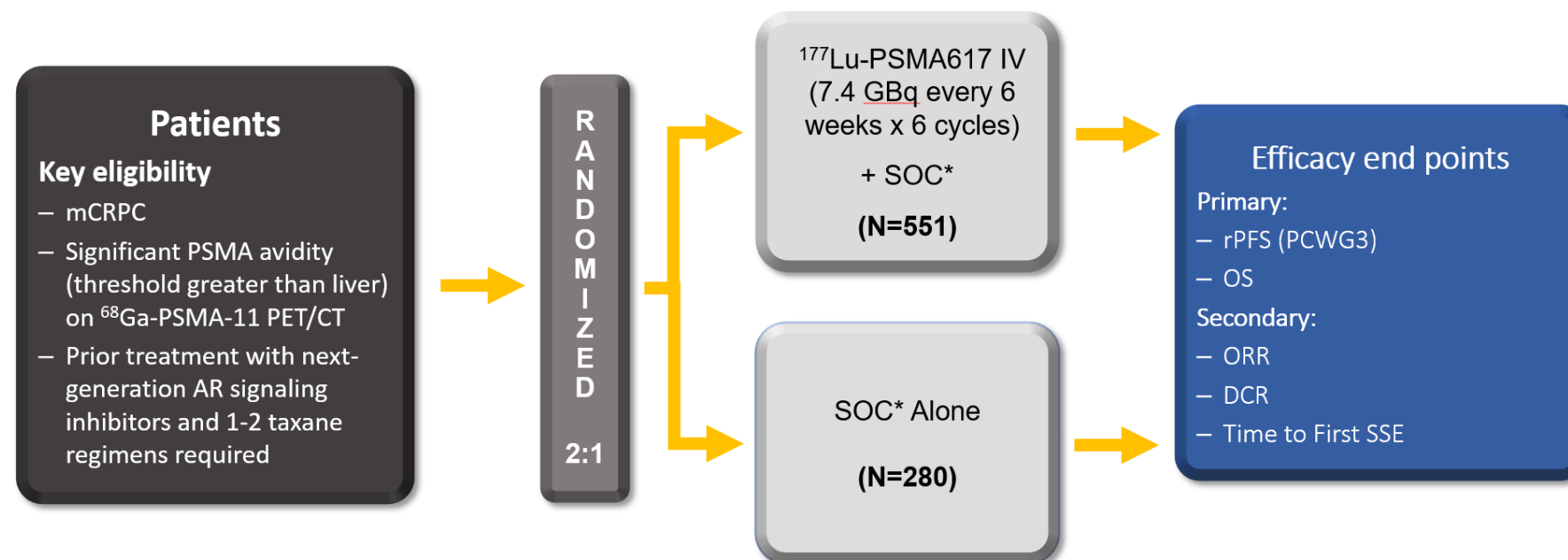


ASCO Annual Meeting 2021, Abstract #LBA4

Phase III study of lutetium-177-PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION).

Presenting Author: Michael J. Morris, MD

Hypothesis: To investigate the clinical benefit of ^{177}Lu -PSMA-617 plus SOC treatment in men with advanced-stage PSMA-positive mCRPC.



*SOC was investigator determined but excluded cytotoxic chemotherapy and radium-223

But Enza or Abi were not excluded

[www.clinicaltrials.gov/](https://www.clinicaltrials.gov/ct2/show/study/NCT03511664) (NCT03511664)



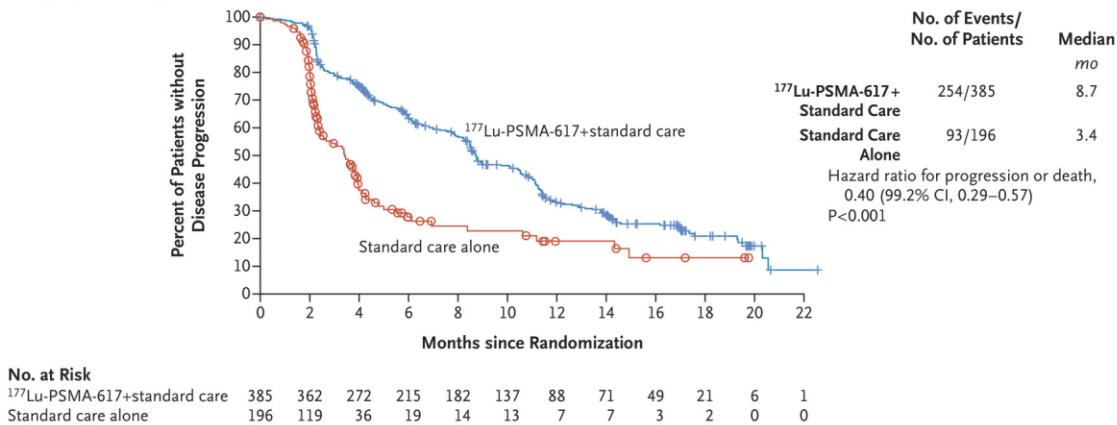
Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

Oliver Sartor, M.D., Johann de Bono, M.B., Ch.B., Ph.D., Kim N. Chi, M.D., Karim Fizazi, M.D., Ph.D., Ken Herrmann, M.D., Kambiz Rahbar, M.D., Scott T. Tagawa, M.D., Luke T. Nordquist, M.D., Nitin Vaishampayan, M.D., Ghassan El-Haddad, M.D., Chandler H. Park, M.D., Tomasz M. Beer, M.D., et al., for the VISION Investigators*

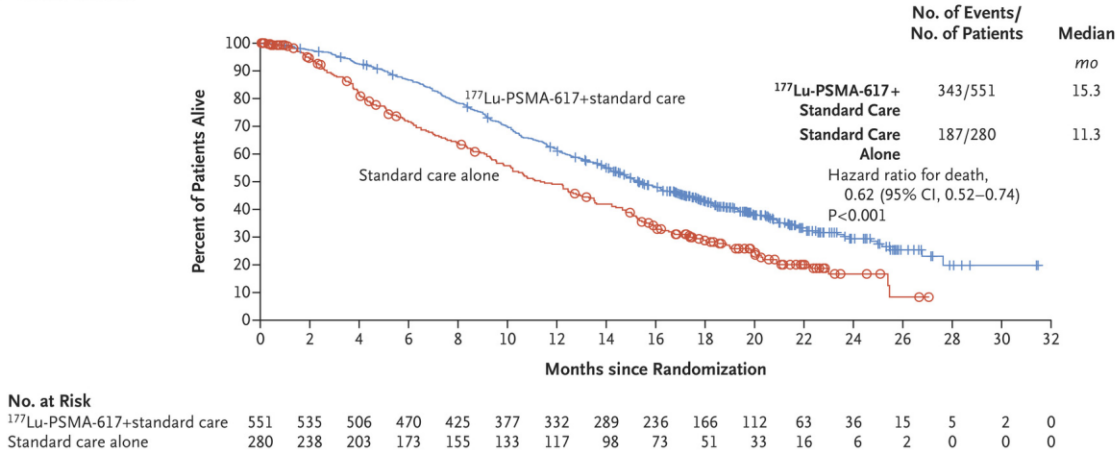
Table 1. Characteristics of the Patients at Baseline, According to Analysis Set.*

Characteristic	Analysis Set for Imaging-Based Progression-free Survival (N=581)		All Patients Who Underwent Randomization (N=831)	
	¹⁷⁷ Lu-PSMA-617 plus Standard Care (N=385)	Standard Care Alone (N=196)	¹⁷⁷ Lu-PSMA-617 plus Standard Care (N=551)	Standard Care Alone (N=280)
Median age (range) — yr	71.0 (52–94)	72.0 (51–89)	70.0 (48–94)	71.5 (40–89)
ECOG performance-status score of 0 or 1 — no. (%)†	352 (91.4)	179 (91.3)	510 (92.6)	258 (92.1)
Site of disease — no. (%)				
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)
Median PSA level (range) — ng/ml	93.2 (0–6988)	90.7 (0–6600)	77.5 (0–6988)	74.6 (0–8995)
Median alkaline phosphatase level (range) — IU/liter‡	108.0 (26–2524)	96.0 (34–1355)	105.0 (17–2524)	94.5 (28–1355)
Median LDH (range) — IU/liter‡	230.5 (119–5387)	232.0 (105–2693)	221.0 (88–5387)	224.0 (105–2693)
Median time since diagnosis (range) — yr	7.3 (0.9–28.9)	7.0 (0.7–26.2)	7.4 (0.9–28.9)	7.4 (0.7–26.2)
Gleason score at diagnosis — no. (%)§				
8–10	226 (58.7)	118 (60.2)	324 (58.8)	170 (60.7)
Unknown	28 (7.3)	19 (9.7)	42 (7.6)	24 (8.6)
Previous prostatectomy — no. (%)¶	159 (41.3)	82 (41.8)	240 (43.6)	130 (46.4)
Previous androgen-receptor–pathway inhibitor — no. (%)				
One regimen	213 (55.3)	98 (50.0)	298 (54.1)	128 (45.7)
Two regimens	150 (39.0)	86 (43.9)	213 (38.7)	128 (45.7)
More than two regimens	22 (5.7)	12 (6.1)	40 (7.3)	24 (8.6)
Previous taxane therapy — no. (%)**				
One regimen	207 (53.8)	102 (52.0)	325 (59.0)	156 (55.7)
Two regimens	173 (44.9)	92 (46.9)	220 (39.9)	122 (43.6)
Docetaxel	377 (97.9)	191 (97.4)	534 (96.9)	273 (97.5)
Cabazitaxel	161 (41.8)	84 (42.9)	209 (37.9)	107 (38.2)

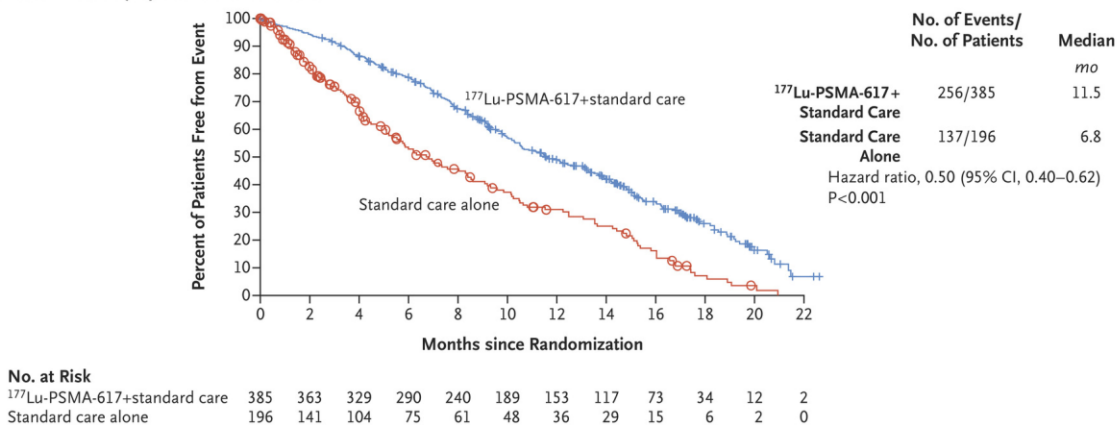
A Imaging-Based Progression-free Survival



B Overall Survival



C Time to First Symptomatic Skeletal Event



VISION: Safety



Table 2. Adverse Events.*

Event	¹⁷⁷ Lu-PSMA-617 plus Standard Care (N=529)		Standard Care Alone (N=205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	<i>number of patients (percent)</i>			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Adverse event that occurred in >12% of patients				
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Dry mouth	205 (38.8)	0	1 (0.5)	0
Nausea	187 (35.3)	7 (1.3)	34 (16.6)	1 (0.5)
Anemia	168 (31.8)	68 (12.9)	27 (13.2)	10 (4.9)
Back pain	124 (23.4)	17 (3.2)	30 (14.6)	7 (3.4)
Arthralgia	118 (22.3)	6 (1.1)	26 (12.7)	1 (0.5)
Decreased appetite	112 (21.2)	10 (1.9)	30 (14.6)	1 (0.5)
Constipation	107 (20.2)	6 (1.1)	23 (11.2)	1 (0.5)
Diarrhea	100 (18.9)	4 (0.8)	6 (2.9)	1 (0.5)
Vomiting	100 (18.9)	5 (0.9)	13 (6.3)	1 (0.5)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ¹⁷⁷ Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ¹⁷⁷ Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ¹⁷⁷ Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

Lutetium PSMA (Monday morning) September 2025? morning question



Where does it fits best in the treatment landscape?

After 1 hormonal agents and 1 or 2 chemotherapy?

No data in pts with HHR genes alterations

When will we use Ra223?

Logistical aspect may be an issue and will need time

20% set to received a second taxane post protocole

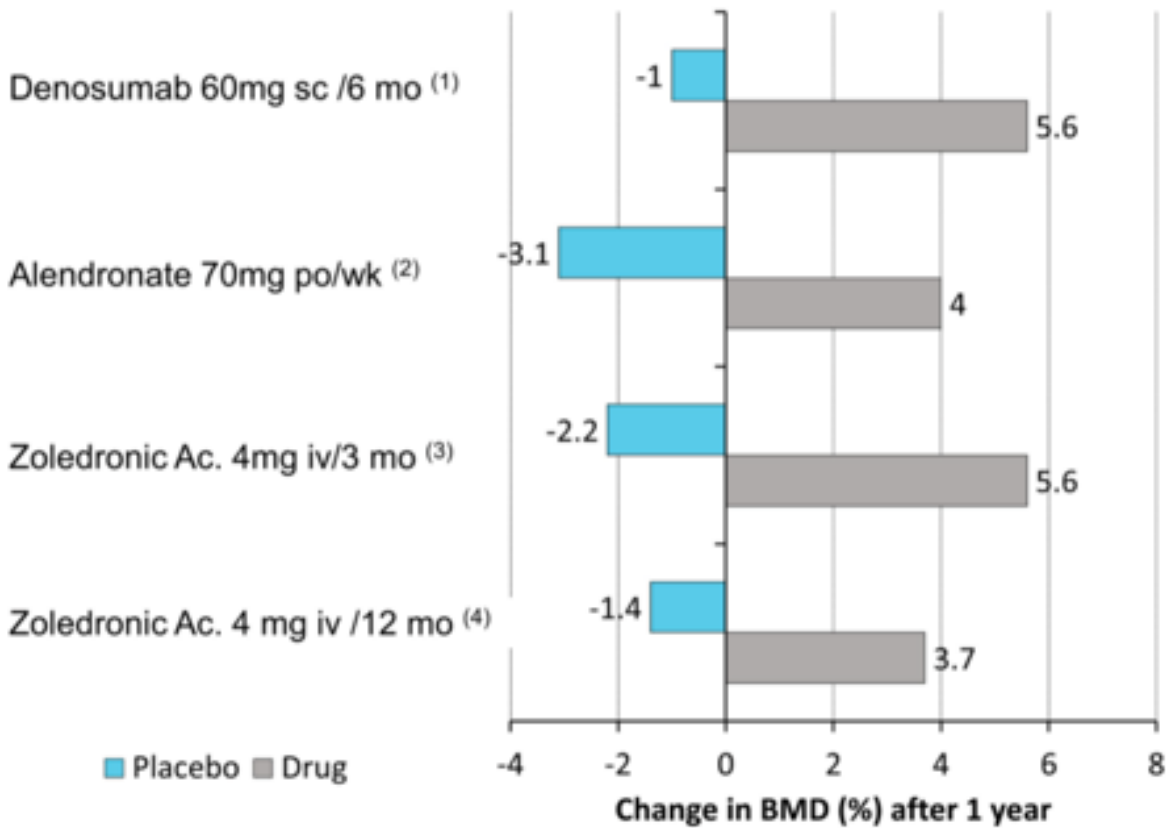


Back to basics: Bone protecting agents in mCRPC

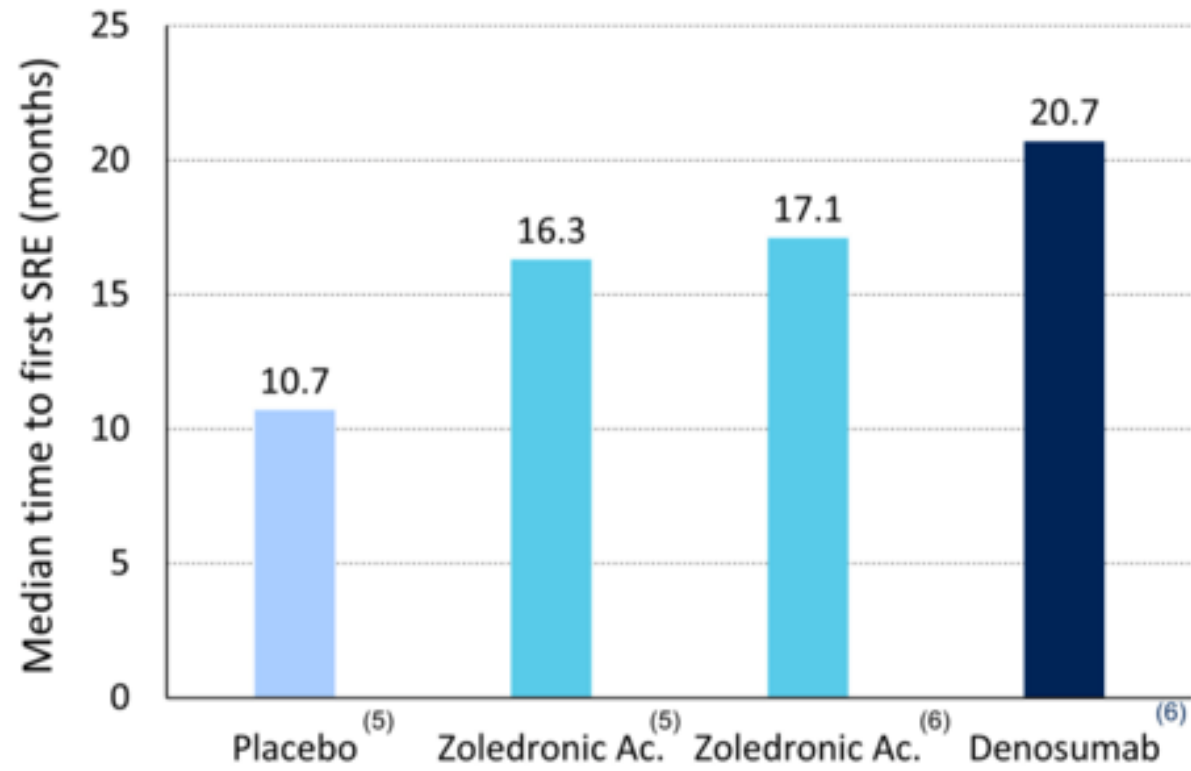
ASCO 2021: Decreased Fracture Rate by Mandating Bone Protecting Agents in the EORTC 1333/PEACEIII Trial Combining Radium-223 with Enzalutamide Versus Enzalutamide Alone: An Updated Safety Analysis



Change in BMD in non metastatic men receiving ADT

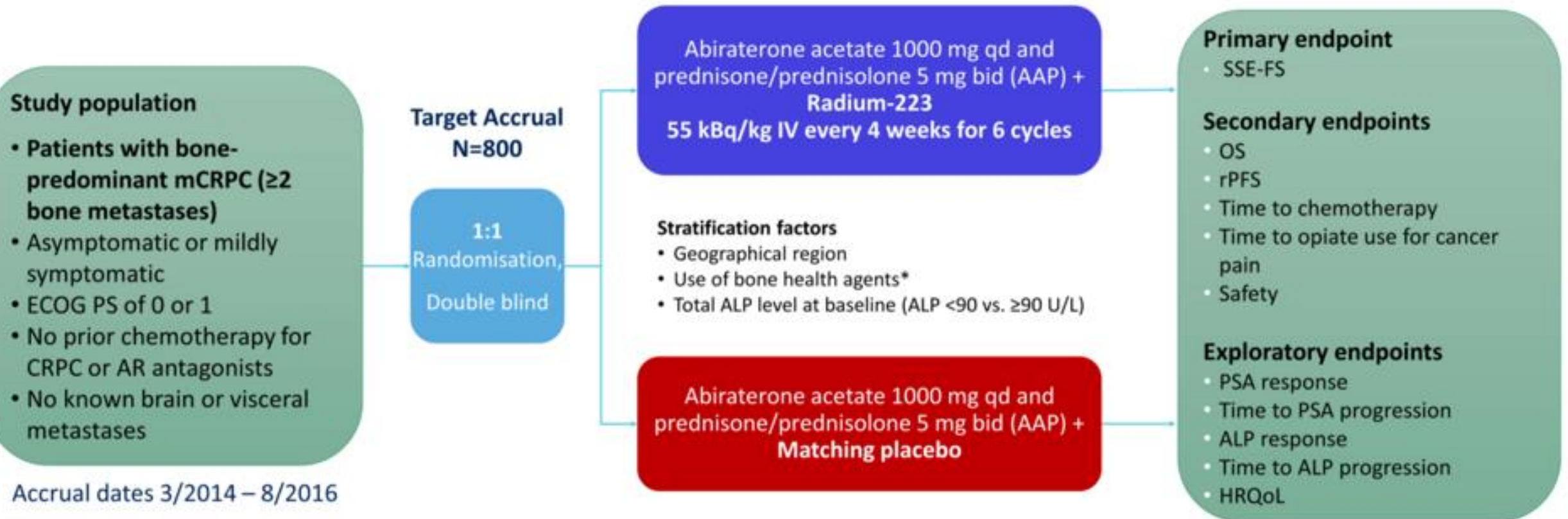


Time to first SRE in mCRPC trials^(5,6)



1. Smith et al. NEJM 2009 361(8):745-55; 2. Greenspan et al. JCO 2008 26:4426-4434; 3. Smith et al. J Urol 2003 169:2008-12; 4. Michaelson et al. JCO 2007 25:1038; 2; 5. Saad et al. JNCI 2004 6:879-82; 6. Fizazi et al. Lancet 2011 77:813-22.

ERA 223 trial results

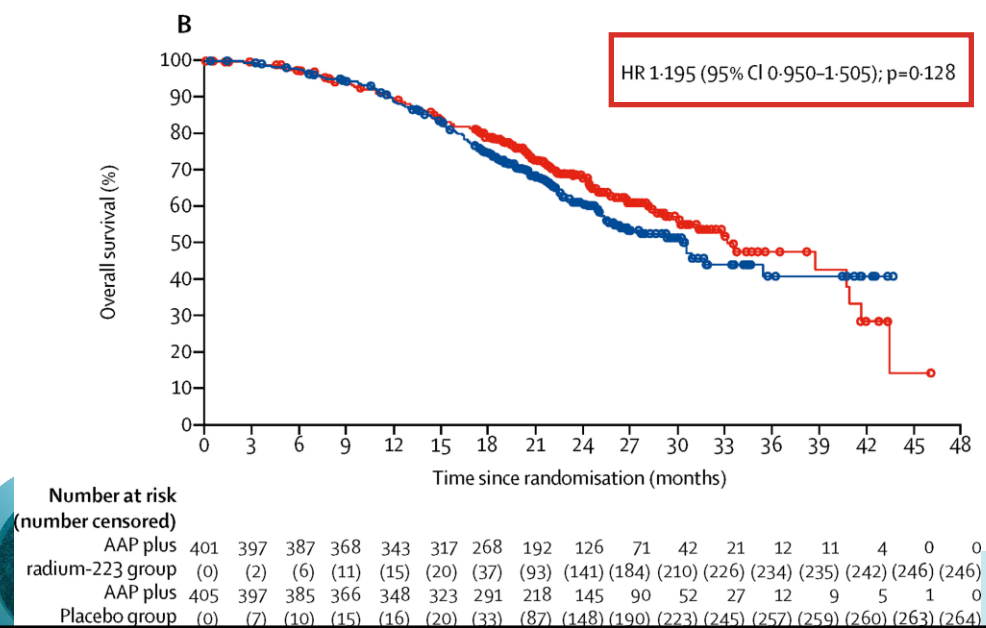
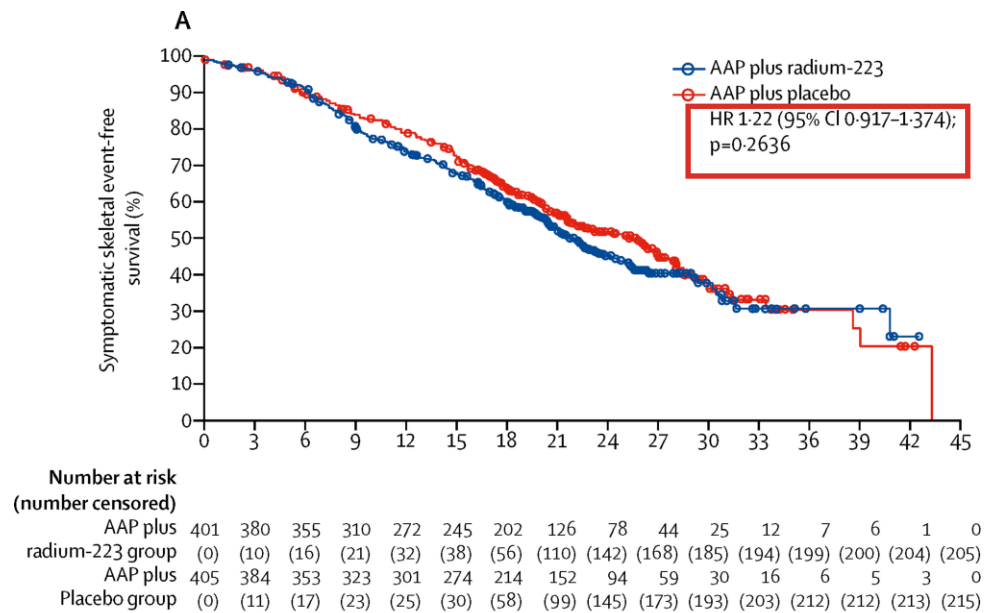


Accrual dates 3/2014 – 8/2016

Bone health agents (denosumab or bisphosphonates) only permitted in patients receiving them at baseline; Initiation during study was prohibited to prevent confounding effects.

389 events were required to detect a 39% increase in SSE-FS using a test with a 2-sided alpha of 0.05, 90% power and 1:1 randomisation

ERA 223 trial results



UNBLINDED prematurely on the recommendation of the IDMC because more fractures and deaths were observed in the AAP + radium-223 group

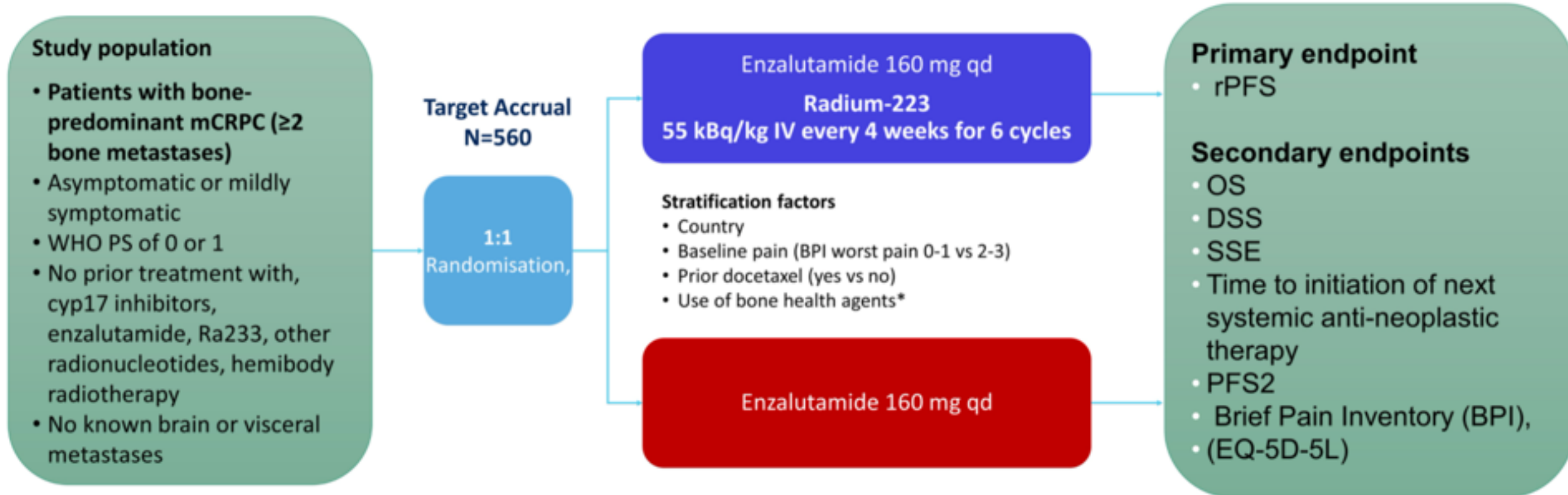
Most Frequent Treatment-Emergent Adverse Events

TEAEs in ≥15% of patients in either group, n (%)	AAP + radium-223 N=392			AAP + placebo N=394		
	All	Grade 3	Grade 4	All	Grade 3	Grade 4
Back pain	133 (34)	23 (6)	0	121 (31)*	16 (4)	0
Fatigue	89 (23)	4 (1)	0	79 (20)	6 (2)	0
Arthralgia	80 (20)	4 (1)	0	75 (19)	5 (1)	0
Fracture†	103 (26)	35 (9)	1 (0.3)	38 (10)*	12 (3)	0

Independent Review of Fracture Events*

	AAP + radium-223	AAP + placebo
Patients with ≥1 fracture, n	76	23
No bone metastasis at site of fracture, n	60	17
Type of fracture, n		
Pathological	19	6
Traumatic	27	13
Osteoporotic	37	4
Indeterminate	1	0

PEACE 3 trial



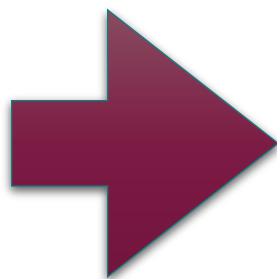
Bone health agents (denosumab or bisphosphonates) only permitted in patients receiving them at baseline; Initiation during study was prohibited to prevent confounding effects.

Amendment after ERA223 results: Bone protecting agents mandatory in each arms

Impact of ERA 223 on study design PEACE3



14
march
2018



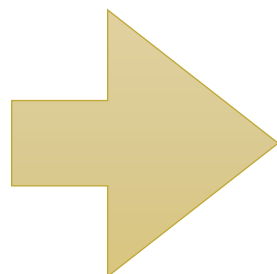
Urgent safety letter: MANDATORY use of BPA and delayed initiation of Ra 223

BPA, at the SRE preventing dose, should be used in BOTH arms of the trials

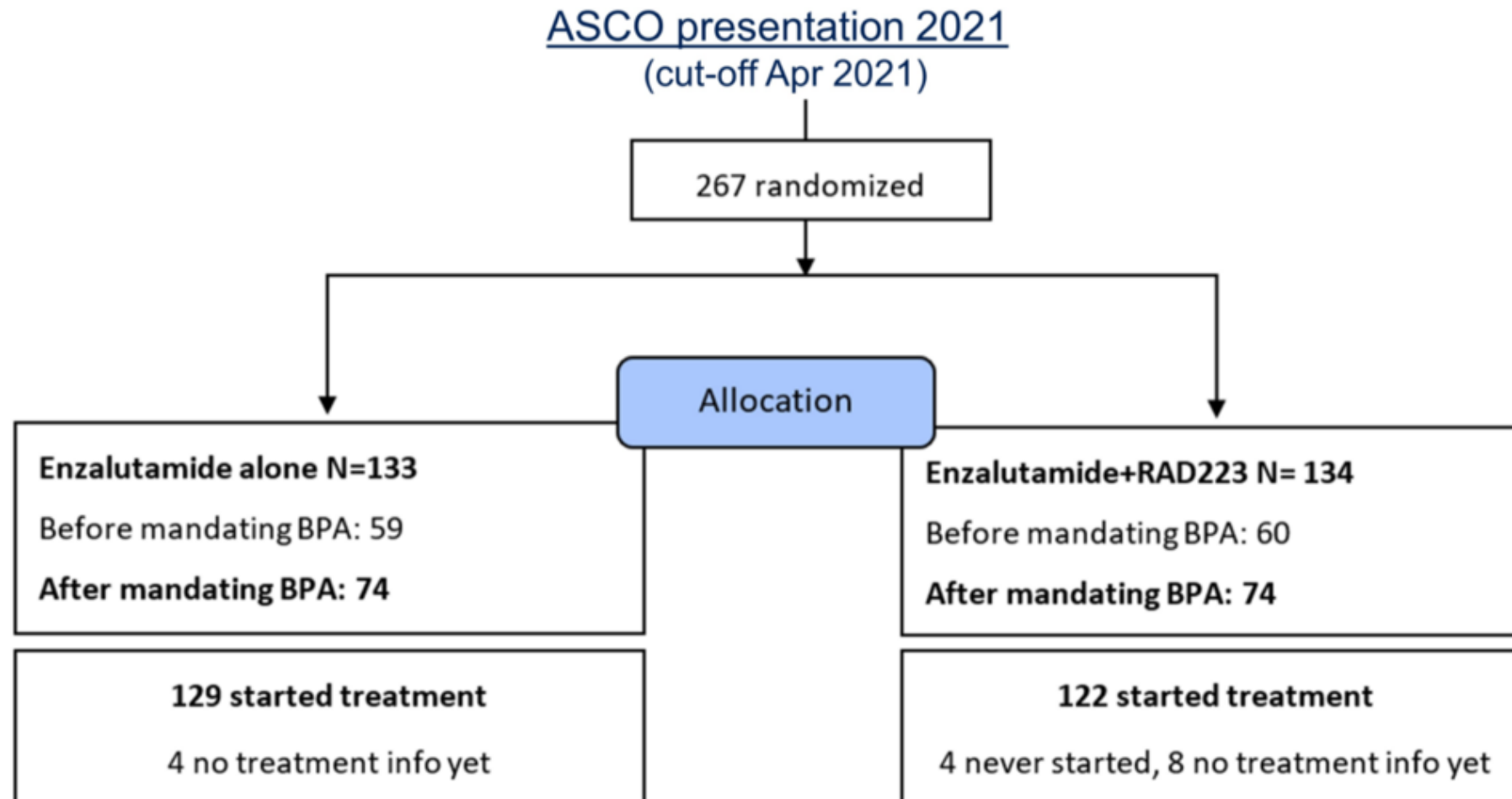
For patients starting BPA prior to randomisation, a minimum of 6wk should exist between the start date of BOA and start date of Ra 223

All skeletal events that occurred after 14 march 2018 should be promptly reported to pharmacovigilance

April
2018



PEACE 3 trial



Bones fractures and cumulative incidence in peace 3 (%)



Time point	No exposure to bone-protecting agents		Exposure to bone-protecting agents	
	ENZA+Ra-223 (N=35)	ENZA (N=32)	ENZA+Ra-223 (N=87)	ENZA (N=97)
9 mo	26	9	2.7	1.3
12 mo	37	16	2.7	2.6
15 mo	43	22	4.3	2.6
18 mo	46	22	4.3	2.6
21 mo	52	22	4.3	2.6



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UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

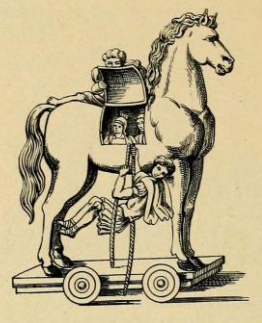
**Post conference
meeting 2021**

Urothelial cancer



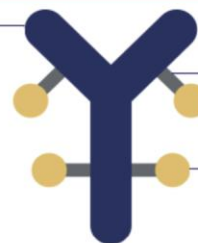
The new compounds in UC everyone should now know

ANTIBODY DRUG CONJUGATE



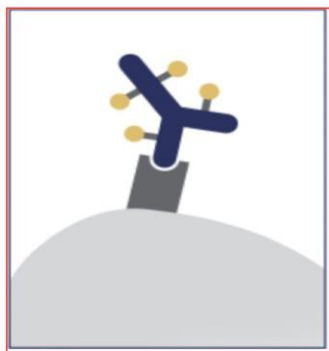
A (old) new way of delivering chemotherapy: Antibody drug conjugates

An **antibody** that attaches to a certain type of protein on the surface of a cell

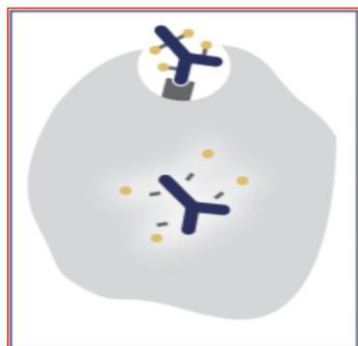


A **link** that connects the cell-killing medicine to the antibody

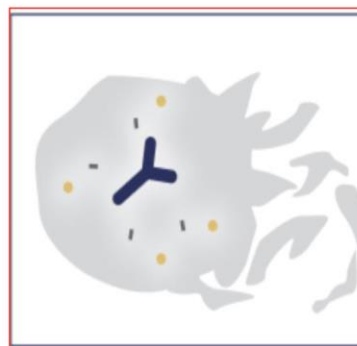
Cell-killing medicine that is released inside of the cell



ADC **binds to tumor target cell surface antigens**



The binding triggers a receptor mediated **internalization**



The internalized ADCs **release cytotoxic payloads** inside the tumor cell and leads to cell death

ADCs are an emerging class of targeted therapeutic agents with the ability to deliver a **highly cytotoxic payload** to tumour sites by utilizing the **exquisite specificity of a mAb** as a **delivery vehicle**

There are previous positive experiences in medical oncology/haematology such as brentuximab vedotin or Trastuzumab emtansine

A new way of delivering chemotherapy: Antibody drug conjugates

ADC	Targeted Ag	Payload	Linkage
Enfortumab Vedotin	Nectin-4	Monomethyl auristatin E MMAE	protease cleavable linker
Tisotumab Vedotin	Thromboplastin	MMAE	protease cleavable linker
ASG 15 ME	SLITRK6	MMAE	protease cleavable linker
Sacituzuman Govitecan	Trop-2	SN38	Hydrolisable cleavable linker
RC 48 Disitamab Vedotin	Her-2	MMAE	cathepsin cleavable linker

EV 301 phase III trial post platinum & CPIPhase 3 Trial of Enfortumab Vedotin vs Chemotherapy in Metastatic Urothelial Cancer:
Results

11.1 mo Follow-up

Docetaxel,
paclitaxel or
vinflunine

	Enfortumab vedotin (N=301)	Chemotherapy (N = 307)
OS HR=0.70 [95% CI: 0.56-0.89], 1-sided P =0.001	12.9 mo	9.0 mo
PFS HR=0.61 [95% CI: 0.50-0.75]; 1-sided P <0.00001	5.6 mo	3.7 mo
ORR P<0.001	40.6%	17.9%
DCR P<0.001	71.9%	53.4%
TRAEs	93.9%	91.8%
Serious TRAEs	22.6%	23.4%

Rates of grade ≥ 3 TRAEs were ~50% in both groups; decreased neutrophil count (13.4%) and white blood cell count (6.9%) were more common in the chemotherapy group, and maculo-papular rash (7.4%) was more common in the EV group.

Adverse Events of Special Interest

Treatment-Related Adverse Event	Enfortumab Vedotin N=296		Chemotherapy N=291	
	All Grade	Grade ≥3	All Grade	Grade ≥3
Skin Reactions^a	47%	15%	16%	1%
Rash	44%	15%	10%	0 ^c
Severe cutaneous adverse reactions ^b	20%	5%	8%	1%
Peripheral neuropathy	46%	5%	31%	2%
Sensory events	44%	4%	30%	2%
Motor events	7%	2%	2%	0
Hyperglycemia	6%	4%	0^c	0

The majority of TRAEs of special interest were mild-to-moderate in severity.

Evaluated in the safety population; displaying selected TRAEs of special interest to EV. Differences between AE rates in current and prior slide may be due to preferred term groupings. TRAE are events with a reasonable possibility of relationship to study treatment as assessed by the investigator or missing relationship.

^aEncompasses rash and severe cutaneous adverse reactions.

^bSevere cutaneous adverse reactions included the following (by Preferred Term): stomatitis, drug eruption, conjunctivitis, blister, dermatitis bullous, skin exfoliation, erythema multiforme, exfoliative rash, fixed eruption, mouth ulceration, pemphigus, and toxic skin eruption.

^cOne patient had the TRAE that is listed.

Abbreviations: EV, enfortumab vedotin; TRAE, treatment-related adverse event.

Data cut-off: July 15, 2020

PRESENTED AT:

Genitourinary
Cancers Symposium

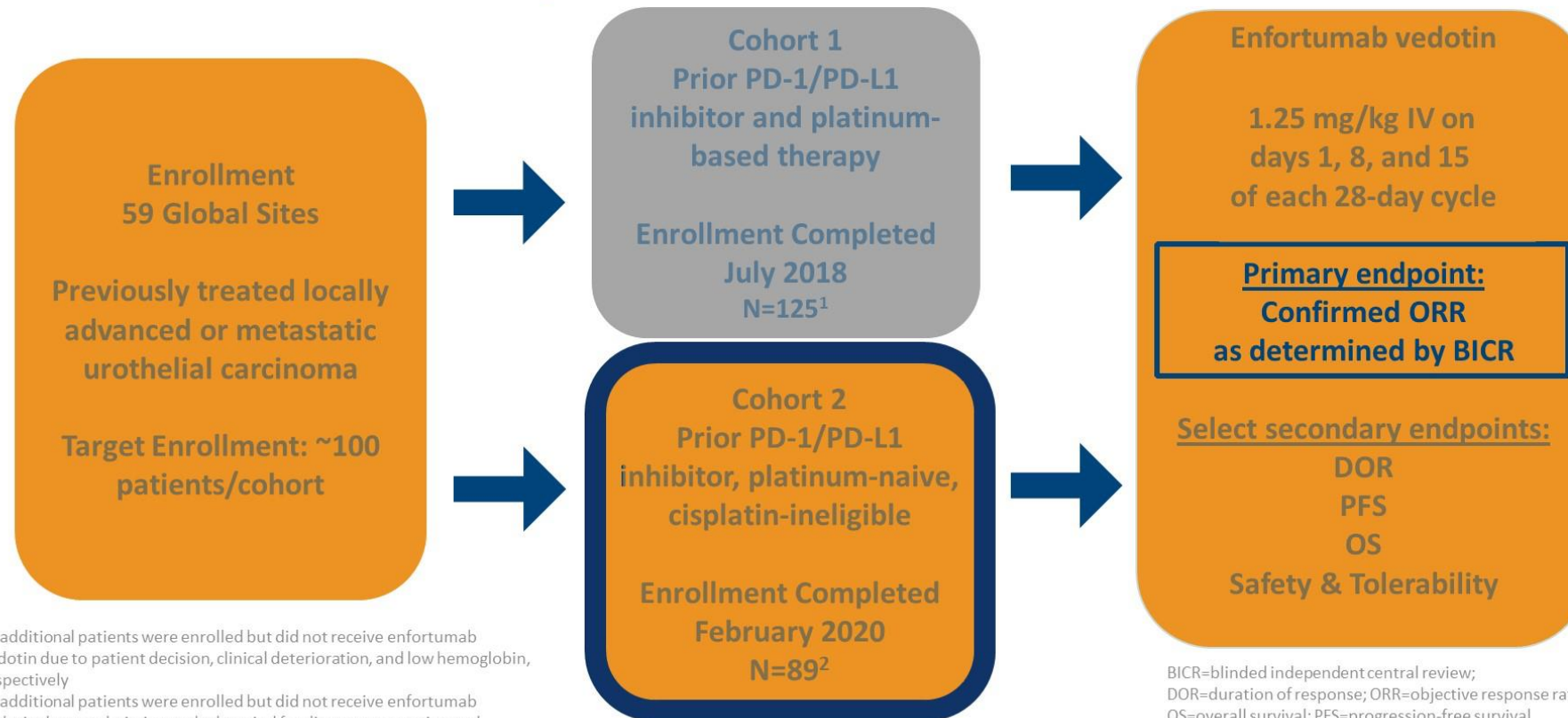
Slides are the property
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PRESENTED BY: Thomas Powles

#GU21

EV 201 phase II trial in second line post CPI

EV-201: Non-Comparative, Pivotal Phase 2 Trial



¹3 additional patients were enrolled but did not receive enfortumab vedotin due to patient decision, clinical deterioration, and low hemoglobin, respectively

²2 additional patients were enrolled but did not receive enfortumab vedotin due to admission to the hospital for disease progression and hospice care, respectively

BICR=blinded independent central review;
DOR=duration of response; ORR=objective response rate;
OS=overall survival; PFS=progression-free survival
PD-1/PD-L1=programmed cell death protein 1 inhibitor,
programmed death-ligand 1 inhibitor

EV 201 phase II trial in second line post CPI

EV-201 Cohort 2: Best Overall Response per BICR

ORR per RECIST v 1.1 assessed by BICR	Patients (N=89) %
Confirmed ORR, 95% CI ¹	52 (40.8, 62.4)
Best overall response ²	
Confirmed complete response	20
Confirmed partial response	31
Stable disease	30
Progressive disease	9
Not evaluable ³	9

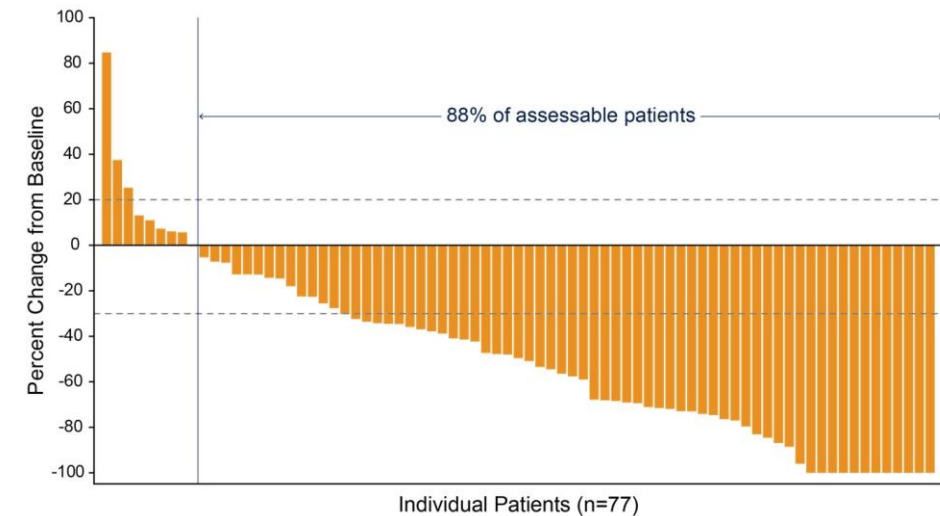
ORR = Objective Response Rate; RECIST = Response Evaluation Criteria in Solid Tumors; BICR = Blinded Independent Central Review

¹CI = Confidence Interval, Computed using the Clopper-Pearson method

²Best overall response according to RECIST v1.1. Complete response and partial response were confirmed with repeat imaging.

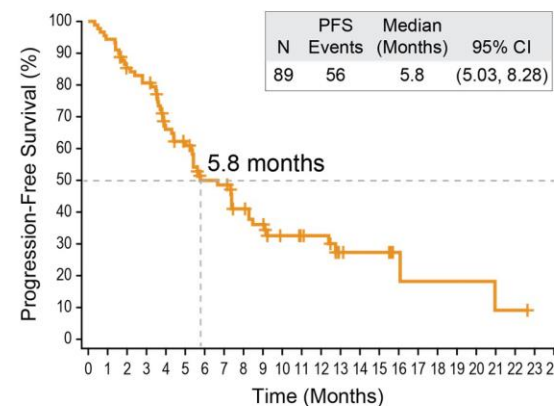
³Includes five subjects who did not have response assessment post-baseline, two subjects whose post-baseline assessment was not possible due to incomplete anatomy, and two subjects whose response cannot be assessed due to incomplete anatomy.

201 Cohort 2: Change in Tumor Measurements per BICR

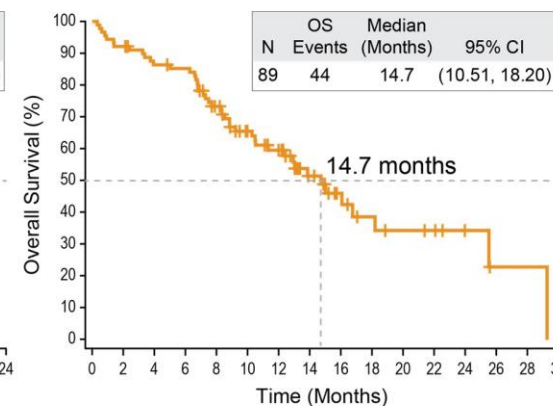


(line (n=5), incomplete assessment of target lesions post-baseline (n=1),

EV-201 Cohort 2: Progression-Free Survival and Overall Survival



No. at Risk 89 84 73 69 52 47 35 26 22 16 14 13 7 6 6 3 2 2 2 1 1



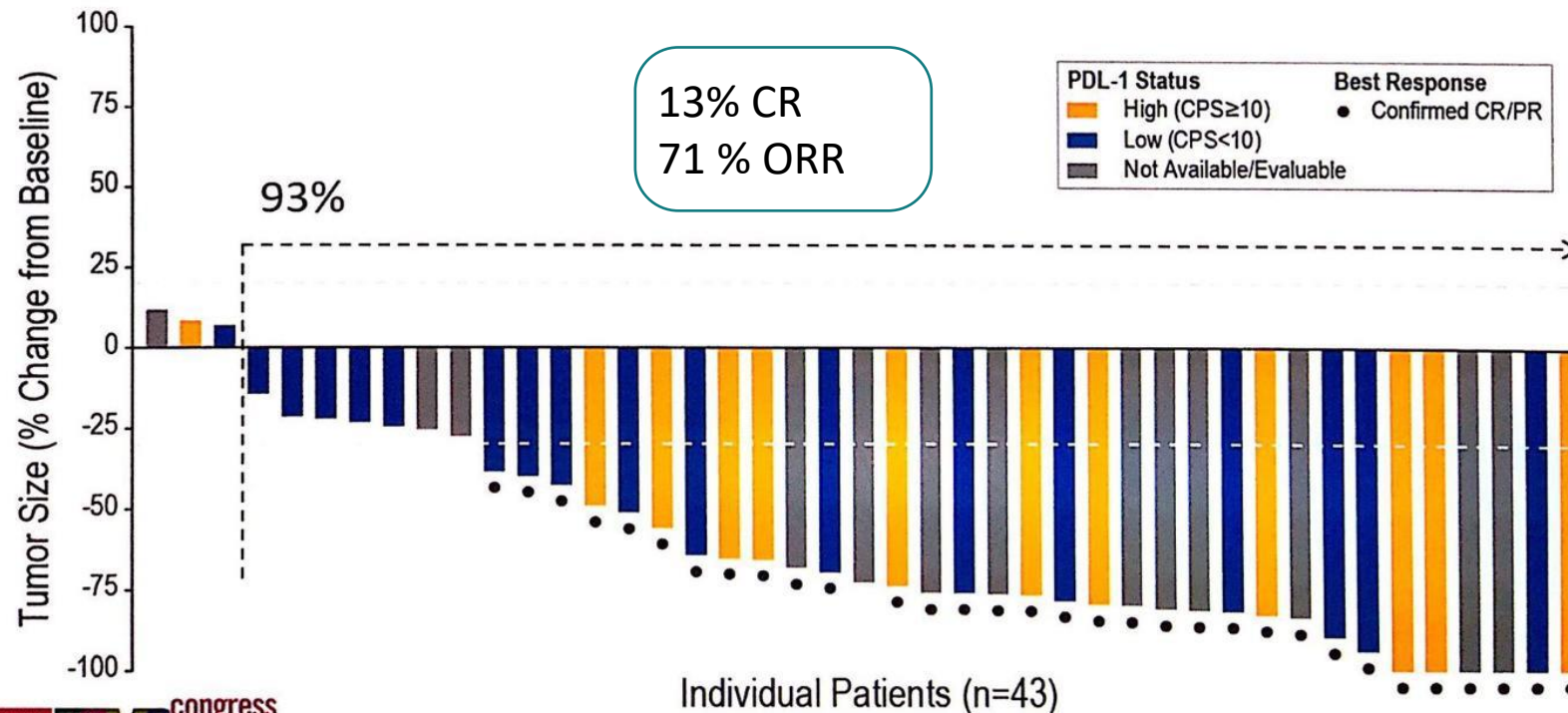
No. at Risk 89 82 75 73 58 45 37 21 13 9 7 6 3 1 1

Median follow-up: 13.4 months

Phase 1/2 trial EV103: EV & Pembrolizumab in first line cisplatin ineligible mUC

n=45

MAXIMUM PERCENT REDUCTION FROM BASELINE IN SUM OF DIAMETERS OF TARGET LESIONS PER INVESTIGATOR



BARCELONA 2019 ESMO congress

PD-L1 tested using the 22C3 PharmDx assay from Agilent/Dako

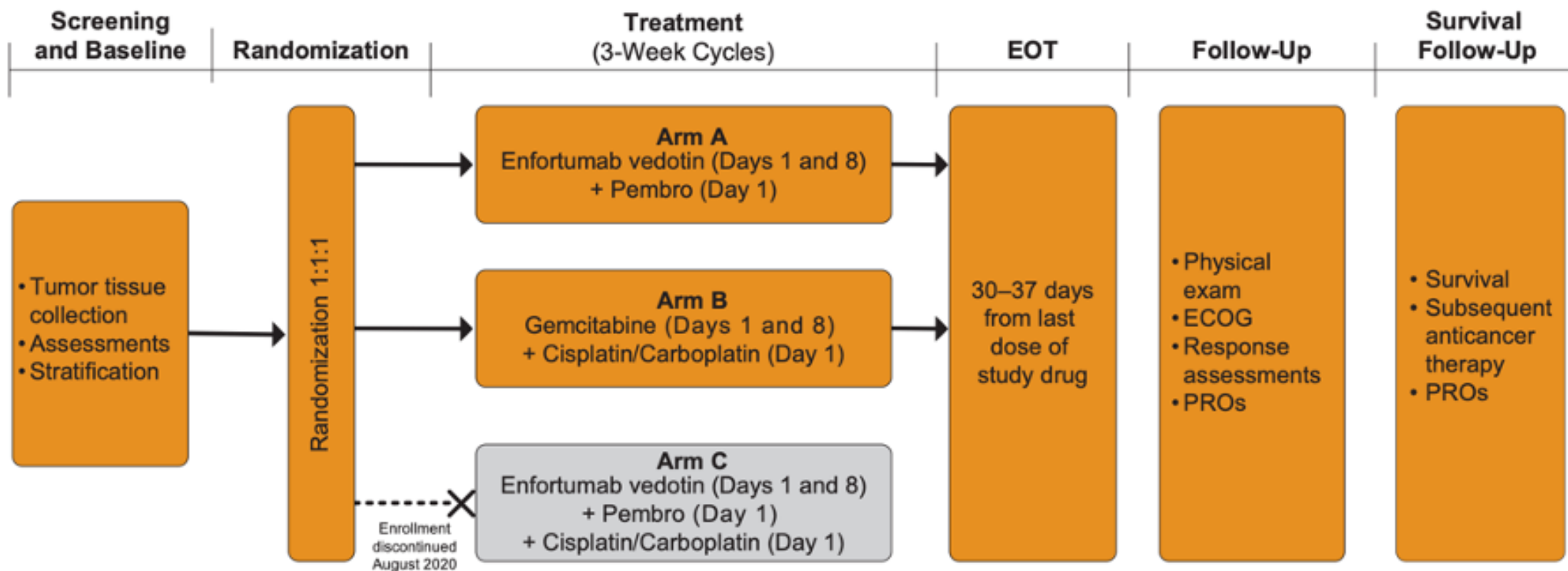
Most common grade 3 AEs (>5%):

- °Diarrhea
- °Fatigue
- °Rash

Most common adverse reaction:

- °Peripheral neuropathy
- °dysgueusia
- °nausea
- °diarrhea
- °rash
- °alopecia

EV 302 phase 3 trial is recruiting



EOT= End of Treatment; Pembro=pembrolizumab; PROs=patient reported outcomes

- Stratification Factors for Randomization: cisplatin eligibility (eligible/ineligible), liver metastases (present/absent), PD-L1 expression (high/low)
- Follow-up until disease progression, death, consent withdrawal, or study closure



Adjuvant therapy in UC?

Checkmate 274 trial

Nivolumab as adjuvant therapy

CHECKMATE 274 trial



N = 709

New

Key inclusion criteria

- Patients with ypT2-ypT4a or ypN+ MIUC who had neoadjuvant cisplatin chemotherapy
- Patients with pT3-pT4a or pN+ MIUC without prior neoadjuvant cisplatin chemotherapy and not eligible/refuse adjuvant cisplatin chemotherapy
- Radical surgery within the past 120 days
- Disease-free status within 4 weeks of dosing

Minimum follow-up, 5.9 months

Median follow-up in ITT population, 20.9 months (NIVO) and 19.5 months (PBO)

Stratification factors:

- PD-L1 status (<1% vs $\geq 1\%$)^a
- Prior neoadjuvant cisplatin-based chemotherapy
- Nodal status

R
1:1

NIVO IV
240 mg Q2W

PBO IV
Q2W

*Treat for up to
1 year of adjuvant
therapy*

Primary endpoints: DFS in ITT population and DFS in all randomized patients with tumor PD-L1 $\geq 1\%$

Secondary endpoints: NUTRFS, DSS, and OS^b

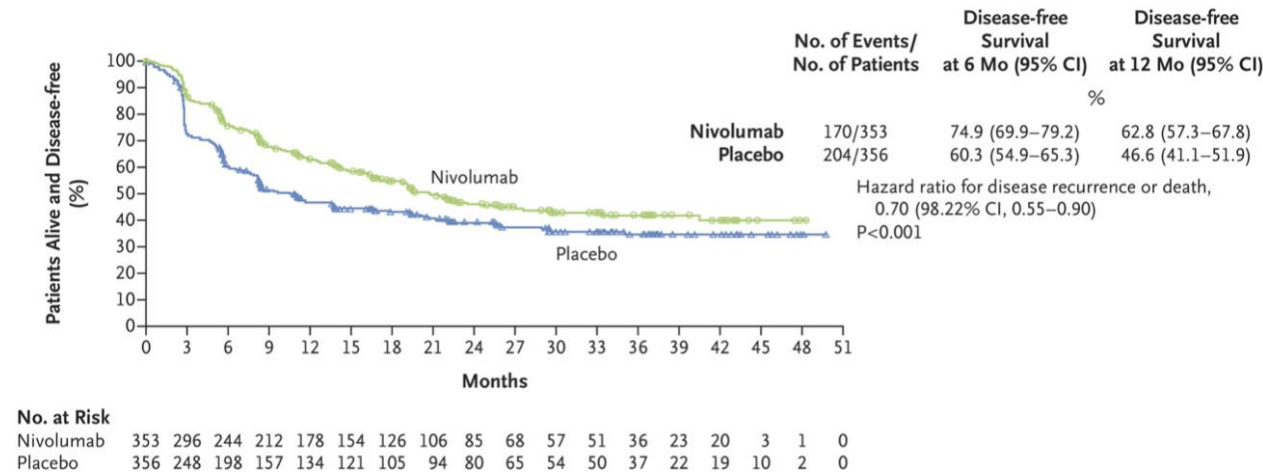
Exploratory endpoints included: DMFS, safety, HRQoL

Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Carcinoma

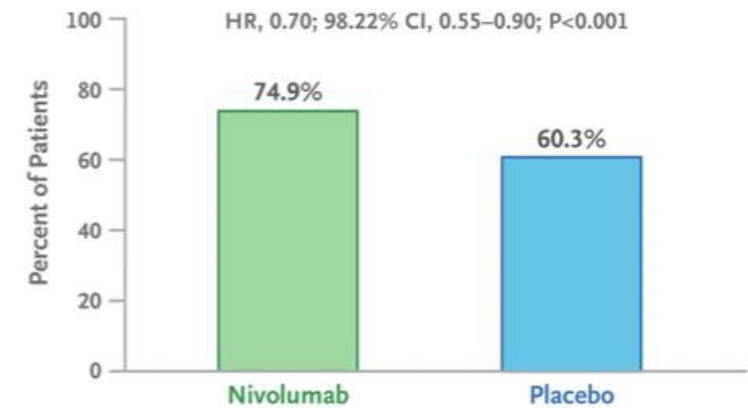
Bajorin DF et al. DOI: 10.1056/NEJMoa2034442

Disease free survival

A Intention-to-Treat Population

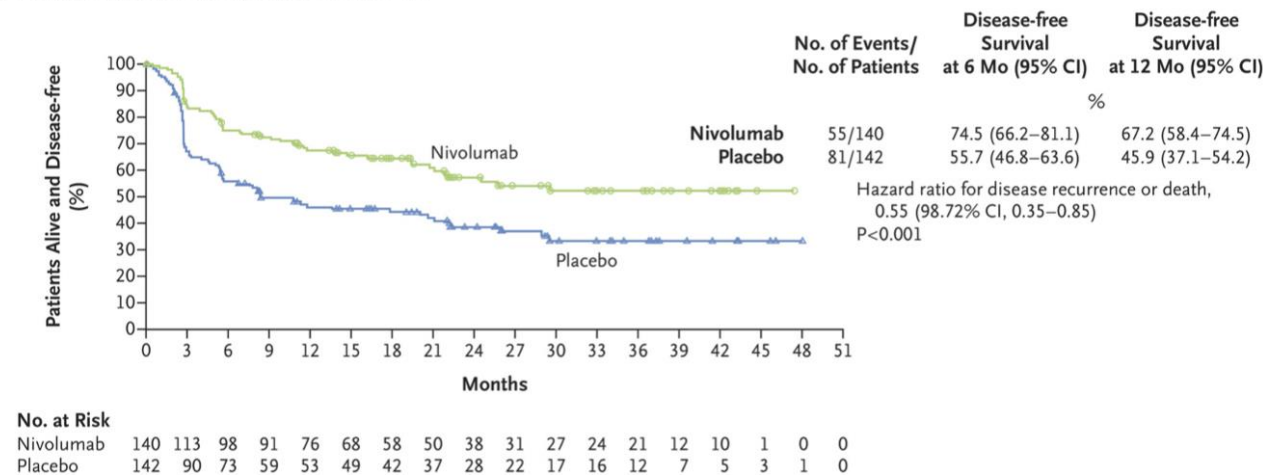


6-Month Disease-free Survival in the Intention-to-Treat Population

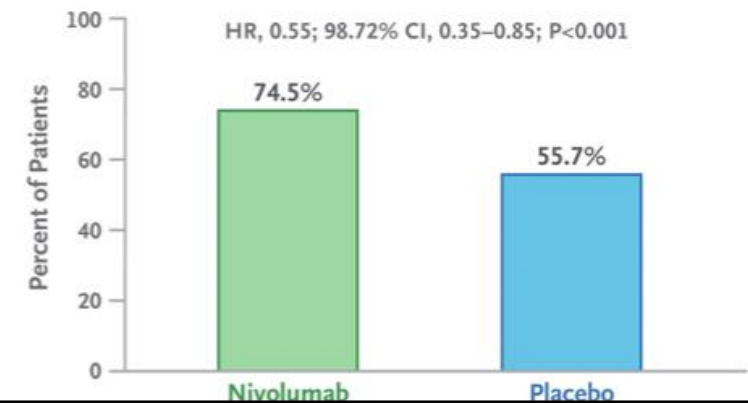


FDA
approved in
August 2021

B Patients with a PD-L1 Expression Level of ≥1%

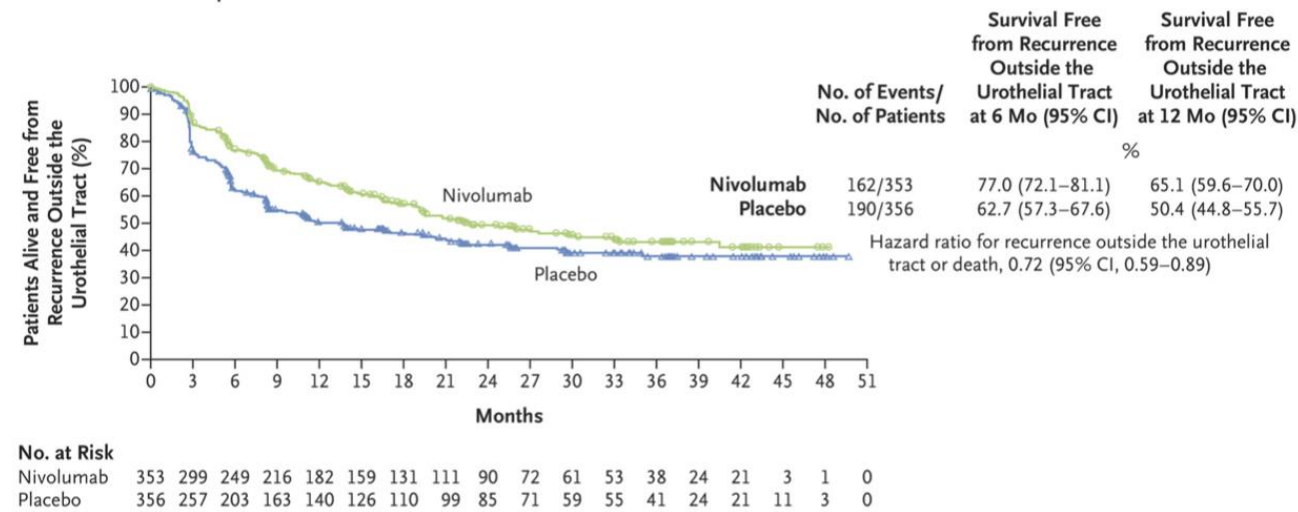


6-Month Disease-free Survival in Patients with PD-L1 of 1% or More

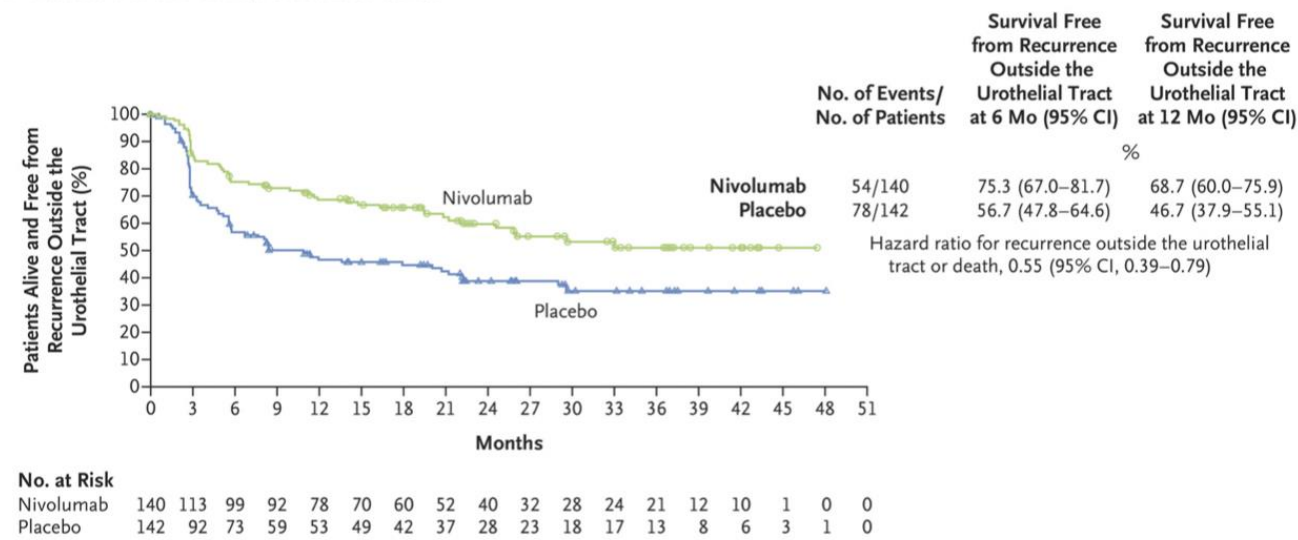


Non Urothelial tract recurrence free survival

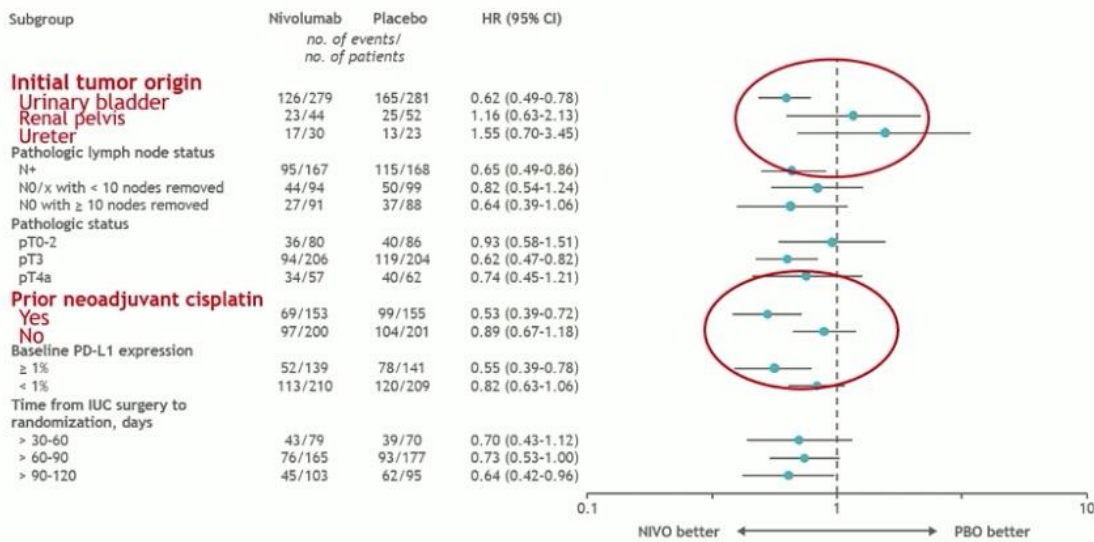
A Intention-to-Treat Population



B Patients with a PD-L1 Expression Level of ≥1%



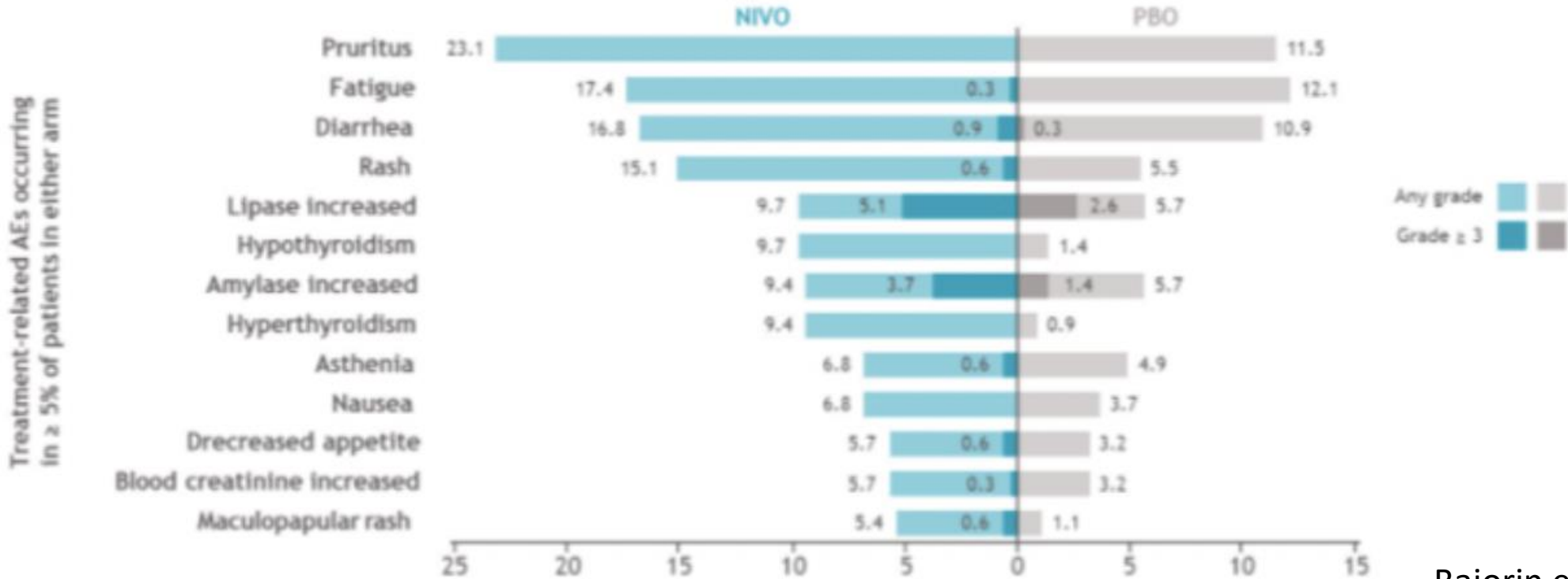
Disease-free survival in select subgroups: ITT patients



Safety profile of adjuvant nivolumab



	NIVO (N = 351) ^a		PBO (N = 348) ^a	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Any-cause AEs, %	98.9	42.7	95.4	36.8
Treatment-related AEs, ^b %	77.5	17.9	55.5	7.2
Treatment-related AEs leading to discontinuation, %	12.8	7.1	2.0	1.4



Conclusion on Adjuvant Nivolumab



Adjuvant studies

Atezolizumab/ Imvigor 010	n=800.	DFS negative
Pembrolizumab/ Ambassador	n=739	DFS ?
Nivolumab / Checkmate 234	n=800	DFS positive

FDA approved

IO boosted by prior chemo?

Need OS data

PD L1 + data
Very convincing

Superior benefit
in Bladder vs
UTUC ?

Benefit of IO
adjuvant mainly
following NAC?

Checkmate 274

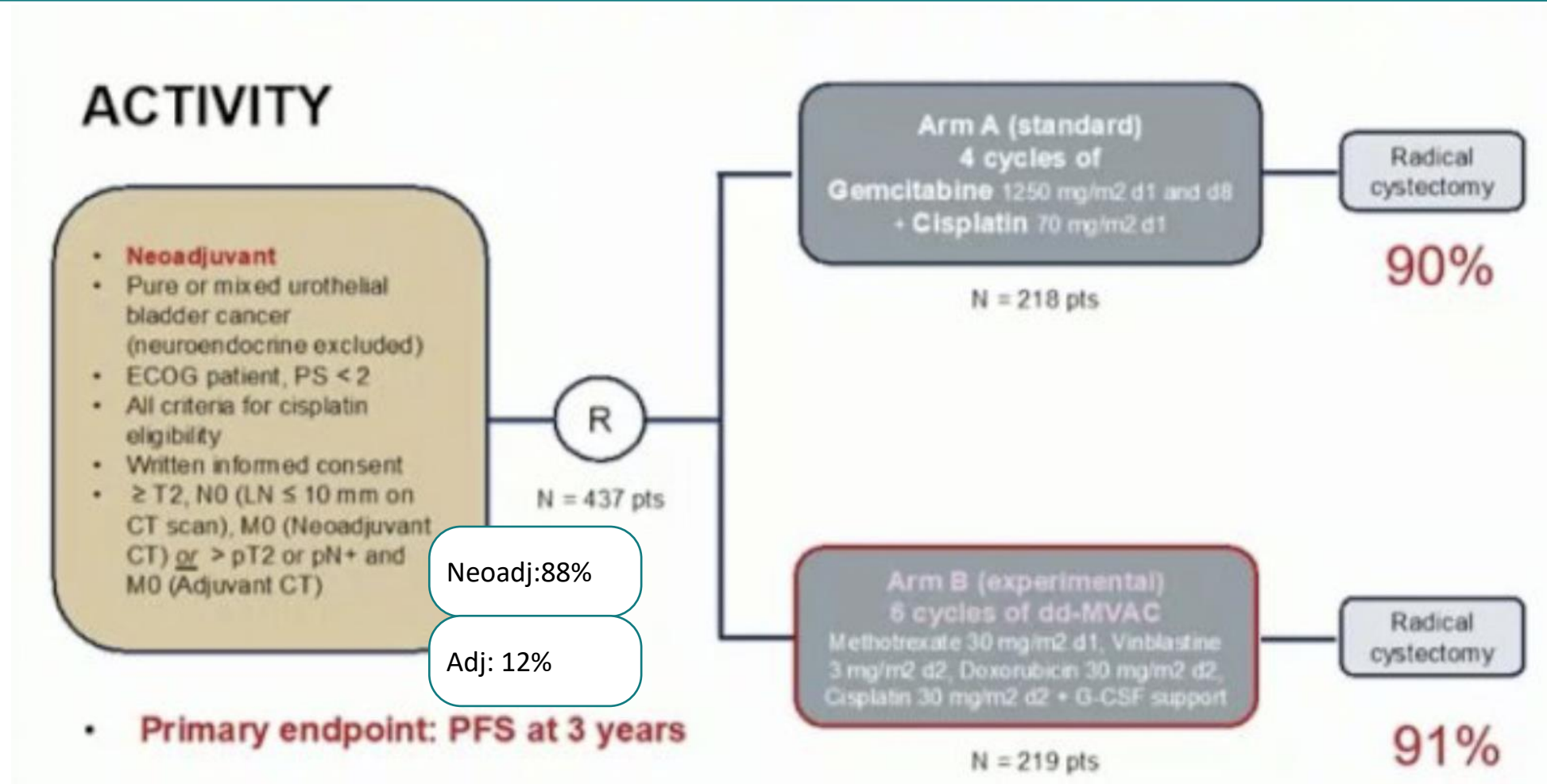
Javelin Bladder 100



Neoadjuvant: A new SOC?

VESPER phase 3 trial (GETUG)

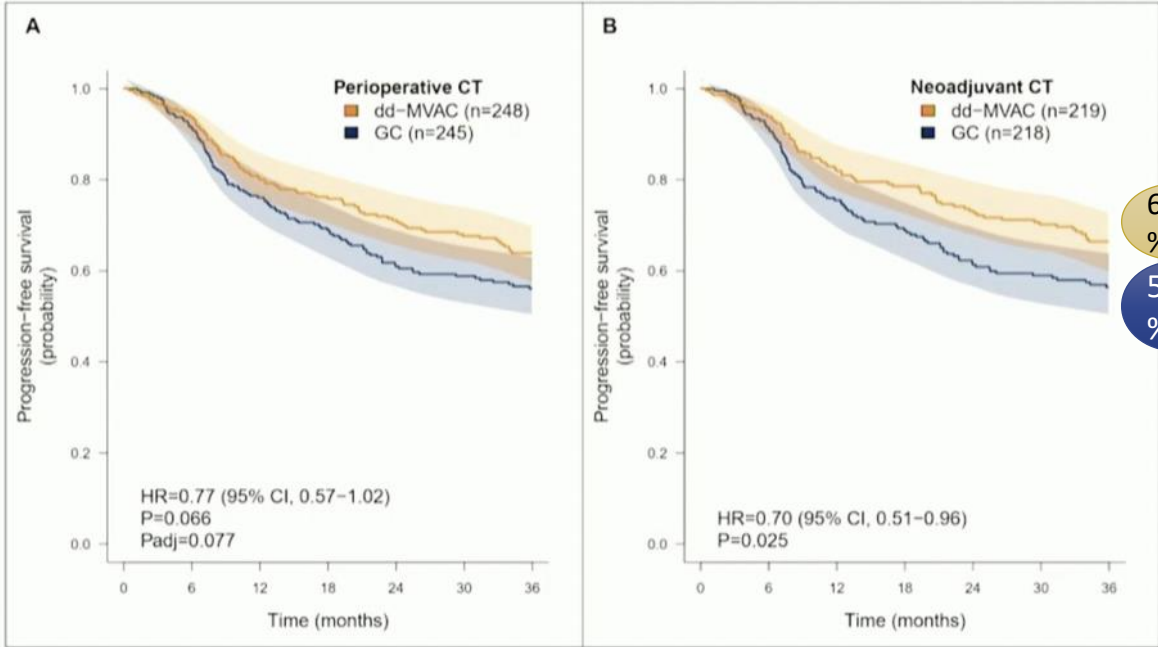
VESPER design



VESPER results

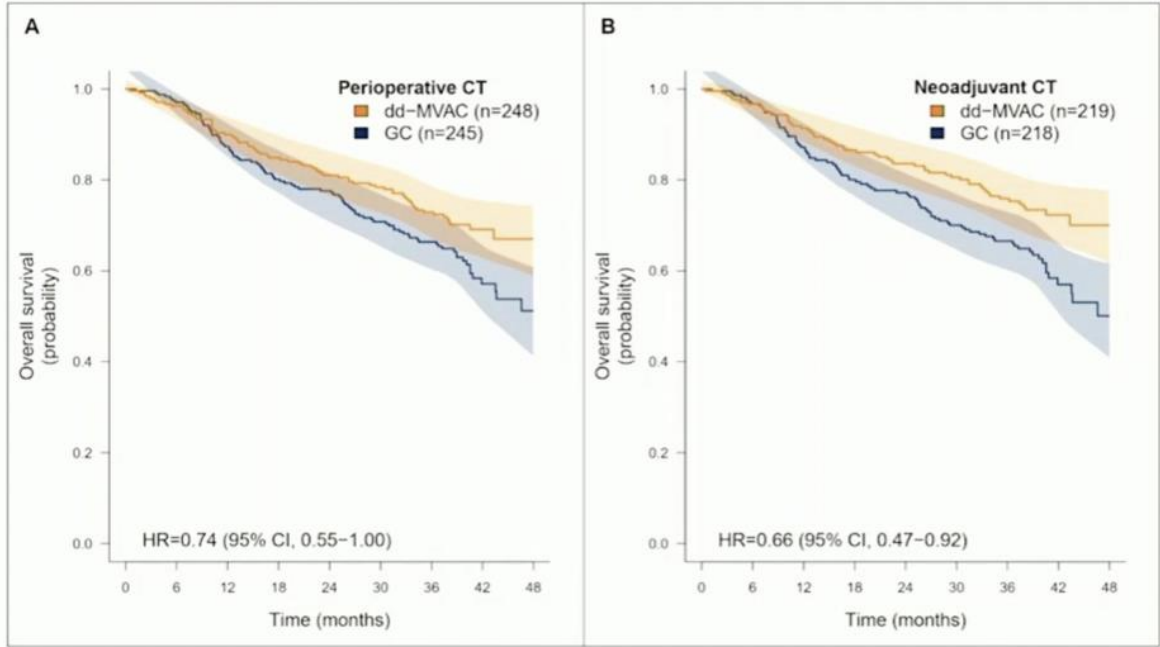


Primary endpoint: PFS



66 %
56 %

Secondary endpoint: OS



VESPER: pathological response



Pathological response (neoadjuvant CT +cystectomy performed only)		
	GC	dd-MVAC
ypT0 N0	71 (36%)	84 (42%)
ypTis,Ta or T1 and ypN0	27 (14%)	42 (21%)
ypT2 N0	26 (13%)	28 (14%)
≥ ypT3 or ypN+	73 (37%)	43 (22%)

In perspective

Dose intensity matter?

Study	VESPER	SWOG-1314	SWOG-8710	Plimack	Choueiri	Anari
	dd-MVAC (x6)	ddMVAC (x4)	dd-MVAC (x9)	AMVAC (x3)	dd-MVAC (x4)	dd-MVAC (x3)
N	219	85	153	44	39	31
ypT0 N0	42	32	38	38	26	32
ypTis,Ta or T1 and ypN0	21	24	44	16	49	13
≥ ypT2 or ypN+	36	44	56	48	51	NR

VESPER: toxicity

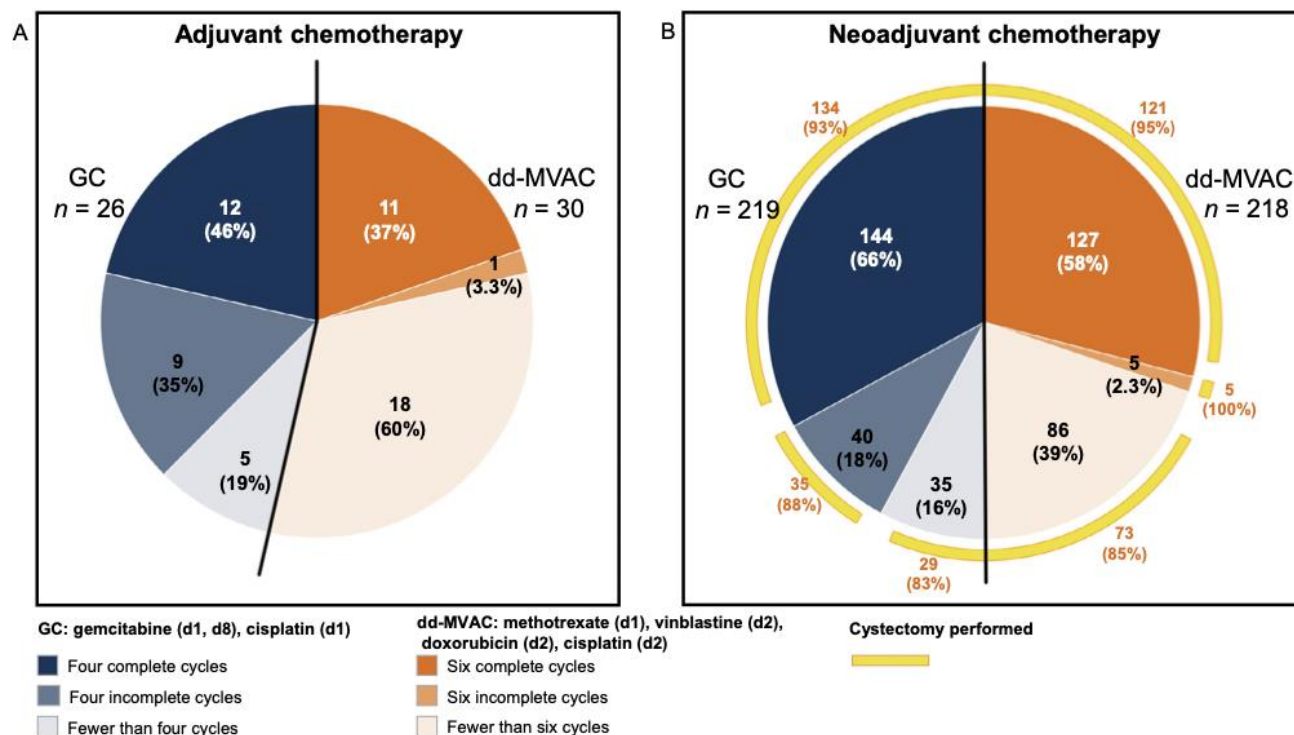


Fig. 2 – Treatment delivery in the (A) adjuvant and (B) neoadjuvant groups for the dd-MVAC and GC arms. d = day; dd-MVAC = dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; GC = gemcitabine and cisplatin.

Table 4 – CTCAE grade ≥ 3 nonhematological toxicities reported for patients of the dd-MVAC and GC arms

	GC ($n = 245$)	dd-MVAC ($n = 248$)	<i>p</i> value
Nausea/vomiting	7 (2.9%)	24 (9.7%)	0.003
Diarrhea	2 (0.81%)	3 (1.2%)	–
Asthenia	10 (4.1%)	35 (14%)	<0.001
Cardiovascular	17 (6.9%)	16 (6.5%)	>0.9
Kidney	13 (5.3%)	15 (6.0%)	0.9
Liver	13 (5.3%)	7 (2.8%)	0.2
Neuropathy	0	2 (0.81%)	–
Chemotherapy-related deaths	1	3	–

CTCAE = Common Terminology Criteria for Adverse Events; dd-MVAC = dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin; GC = gemcitabine and cisplatin.

Data are presented as frequency (percentage). Comparisons between the GC and dd-MVAC groups are performed with a chi-square test when enough events were observed. A *p* value of <0.05 would assume a statistical difference between the GC and dd-MVAC groups.

Table 3 – CTCAE grade ≥ 3 hematological toxicities reported for patients of the dd-MVAC and GC arms

	GC ($n = 245$)	dd-MVAC ($n = 248$)	<i>p</i> value
Anemia	19 (7.8%)	54 (22%)	<0.0001
Neutropenia	113 (46%)	97 (39%)	0.14
Febrile neutropenia	6 (2.4%)	16 (6.5%)	0.053
Thrombopenia	41 (17%)	49 (20%)	0.5
At least one grade ≥ 3 hematological toxicity	134 (55%)	129 (52%)	0.6



BMUC

UROLOGY - RADIATION ONCOLOGY - MEDICAL ONCOLOGY

**Post conference
meeting 2021**

Renal cell carcinoma



Adjuvant therapy in RCC?

Keynote 564 trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 19, 2021

VOL. 385 NO. 8

Adjuvant Pembrolizumab after Nephrectomy in Renal-Cell Carcinoma

T.K. Choueiri, P. Tomczak, S.H. Park, B. Venugopal, T. Ferguson, Y.-H. Chang, J. Hajek, S.N. Symeonides, J.L. Lee, N. Sarwar, A. Thiery-Vuillemin, M. Gross-Goupil, M. Mahave, N.B. Haas, P. Sawrycki, H. Gurney, C. Chevreau, B. Melichar, E. Kopyltsov, A. Alva, J.M. Burke, G. Doshi, D. Topart, S. Oudard, H. Hammers, H. Kitamura, J. Bedke, R.F. Perini, P. Zhang, K. Imai, J. Willemann-Rogerio, D.I. Quinn, and T. Powles, for the KEYNOTE-564 Investigators*

Key Eligibility Criteria

- Histologically confirmed clear cell renal cell carcinoma
- Nephrectomy ≤12 weeks prior to randomization
- No prior systemic therapy
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment

Stratification Factors

- M0 vs M1 NED
- M0 group further stratified:
 - ECOG PS 0 vs 1
 - US vs non-US

R
(1:1)

Pembrolizumab 200 mg
Q3W
for ~1 year^a

Placebo
Q3W
for ~1 year^a

- Primary end point: DFS per investigator
- Key secondary end point: OS
- Other secondary end points: Safety

Intermediate-High Risk		High Risk		M1 NED
pT2	pT3	pT4	Any pT	NED after resection of oligometastatic sites ≤1 year from nephrectomy
Grade 4 or sarcomatoid	Any grade	Any grade	Any grade	
N0	N0	N0	N+	
M0	M0	M0	M0	

Characteristic, n (%)	Pembro N = 496	Placebo N = 498	Characteristic, n (%)	Pembro N = 496	Placebo N = 498
Age, median (range), yrs	60 (27–81)	60 (25–84)	Geographic location		
Male	347 (70.0)	359 (72.1)	North America	113 (26.8)	125 (25.1)
ECOG PS			European Union	188 (37.9)	187 (37.6)
0	421 (84.9)	426 (85.5)	Rest of the world	175 (35.3)	186 (37.3)
1	75 (15.1)	72 (14.5)	PD-L1 status ^b		
Disease risk category			CPS <1	124 (25.0)	113 (22.7)
M0 intermediate-high risk	427 (86.1) ^a	433 (86.9)	CPS ≥1	365 (73.6)	383 (76.9)
M0 high risk	40 (8.1)	36 (7.2)	Missing	7 (1.4)	2 (0.4)
M1 NED	29 (5.8)	29 (5.8)	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

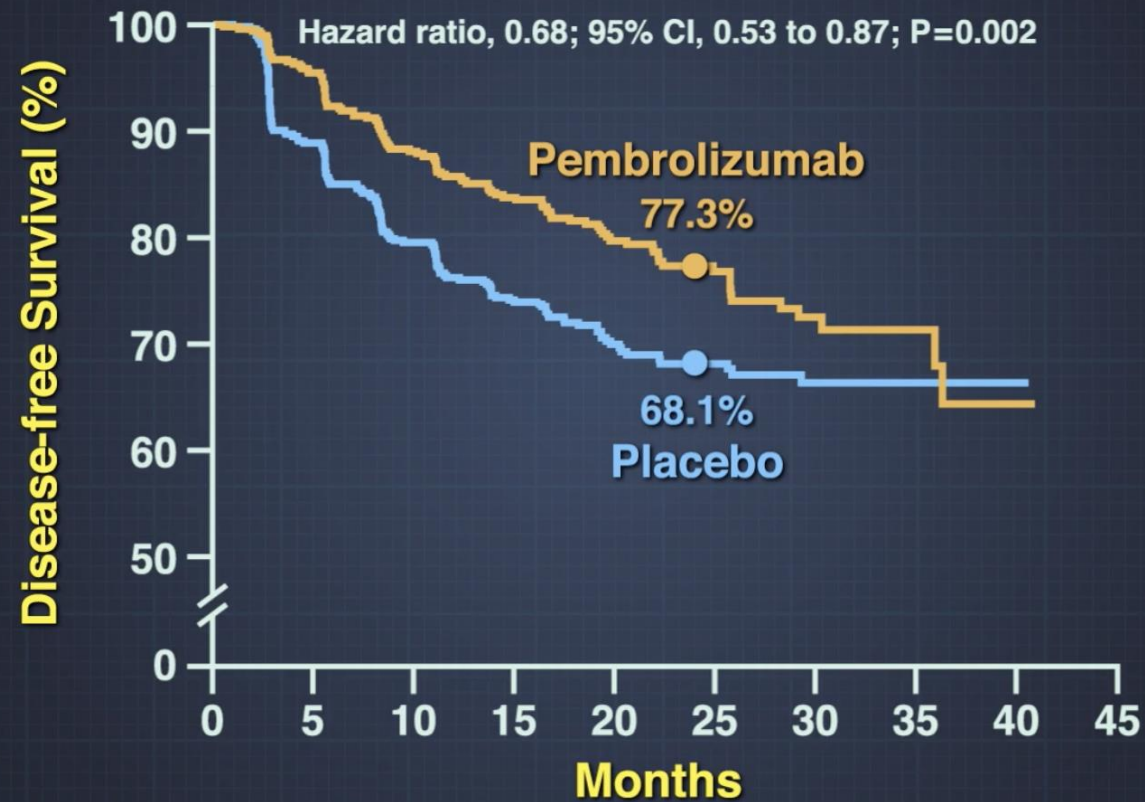
^aIncluded 5 participants with T2, grade ≤3, N0 M0 or T1 N0 M0. ^bAssessed using the PD-L1 IHC 22C3 pharmDx assay. CPS (combined positive score) is the number of PD-L1–staining cells (tumor cells, lymphocytes, and macrophages) divided by the total number of viable tumor cells, multiplied by 100. Data cutoff date: December 14, 2020.

PS, disease-free survival; Q3W, every 3 weeks.
17 cycles of treatment were equivalent to ~1 year.

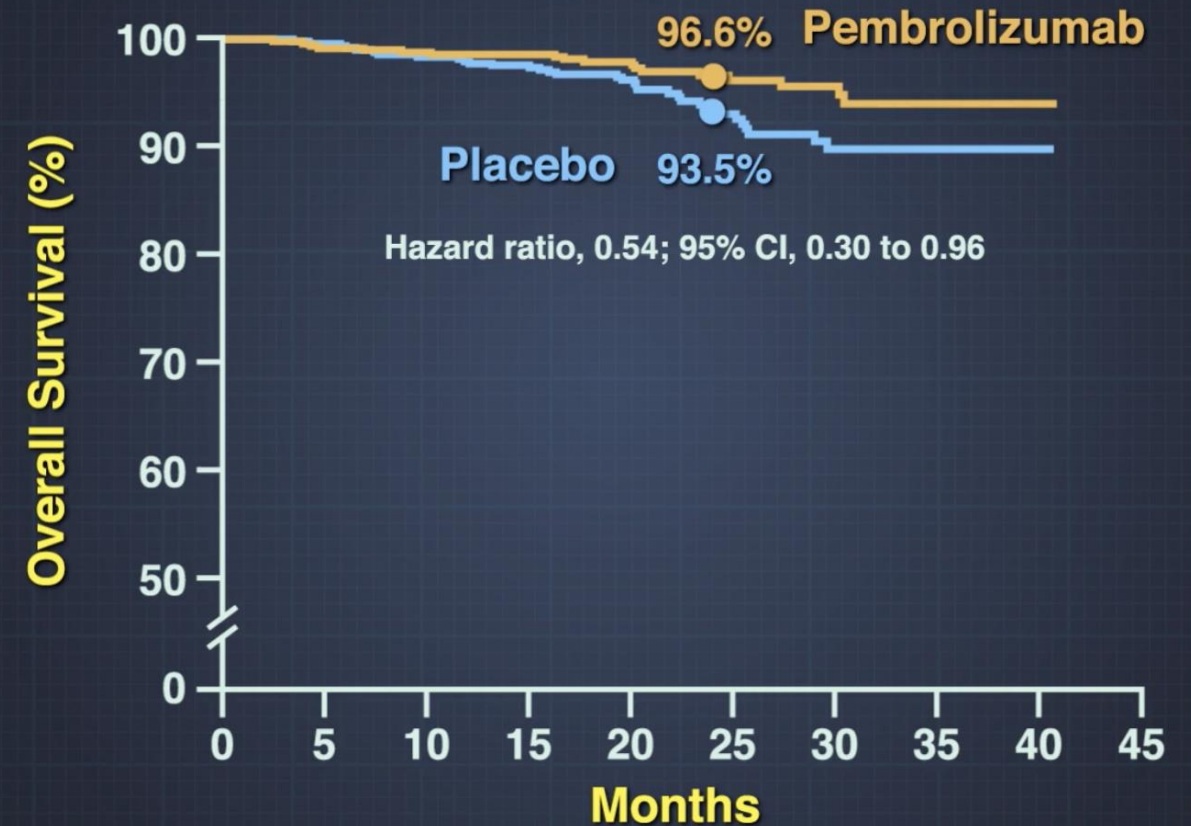
Keynote 564: results



Primary End Point — Disease-free Survival



Secondary End Point — Overall Survival



Keynote 564: safety



Table 3. Any-Cause Adverse Events with an Incidence of at Least 10% in Either Group (As-Treated Population).*

Event	Pembrolizumab (N=488)		Placebo (N=496)	
	Any Grade	Grade 3	Any Grade	Grade 3
	<i>number of patients with event (percent)</i>			
Fatigue	145 (29.7)	5 (1.0)	120 (24.2)	0
Diarrhea	124 (25.4)	8 (1.6)	111 (22.4)	1 (0.2)
Pruritus	111 (22.7)	1 (0.2)	65 (13.1)	0
Arthralgia	108 (22.1)	2 (0.4)	93 (18.8)	2 (0.4)
Hypothyroidism	103 (21.1)	1 (0.2)	18 (3.6)	0
Rash	98 (20.1)	4 (0.8)	53 (10.7)	2 (0.4)
Nausea	80 (16.4)	2 (0.4)	48 (9.7)	0
Cough	76 (15.6)	0	50 (10.1)	0
Headache	69 (14.1)	0	62 (12.5)	0
Hyperthyroidism	58 (11.9)	1 (0.2)	1 (0.2)	0
Asthenia	50 (10.2)	1 (0.2)	36 (7.3)	1 (0.2)
Increase in blood creatinine level	50 (10.2)	1 (0.2)	42 (8.5)	0
Back pain	49 (10.0)	1 (0.2)	64 (12.9)	1 (0.2)

* No adverse events of grade 4 or 5 occurred in at least 10% of the patients in either group.

Table 2. Any-Cause and Treatment-Related Adverse Events (As-Treated Population).*

Event	Pembrolizumab (N = 488)	Placebo (N = 496)
no. of patients with event (%)		
Any-cause adverse events		
Adverse event of any grade	470 (96.3)	452 (91.1)
Adverse event of grade 3 to 5	158 (32.4)	88 (17.7)
Discontinuation of pembrolizumab or placebo due to adverse event	101 (20.7)	10 (2.0)
Death due to adverse event	2 (0.4)	1 (0.2)
Serious adverse event	100 (20.5)	56 (11.3)
Discontinuation of pembrolizumab or placebo due to serious adverse event	49 (10.0)	5 (1.0)
Treatment-related adverse events, as assessed by investigator		
Adverse event of any grade	386 (79.1)	265 (53.4)
Adverse event of grade 3 to 5	92 (18.9)	6 (1.2)
Discontinuation of pembrolizumab or placebo due to adverse event	86 (17.6)	3 (0.6)
Death due to adverse event	0	0
Serious adverse event	59 (12.1)	1 (0.2)
Discontinuation of pembrolizumab or placebo due to serious adverse event	37 (7.6)	0

Other ICI adjuvant trials in progress

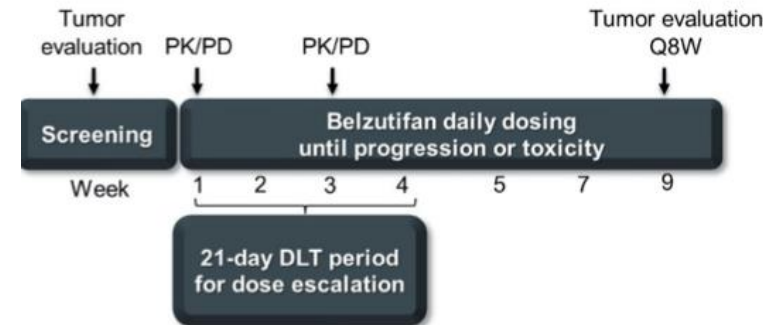
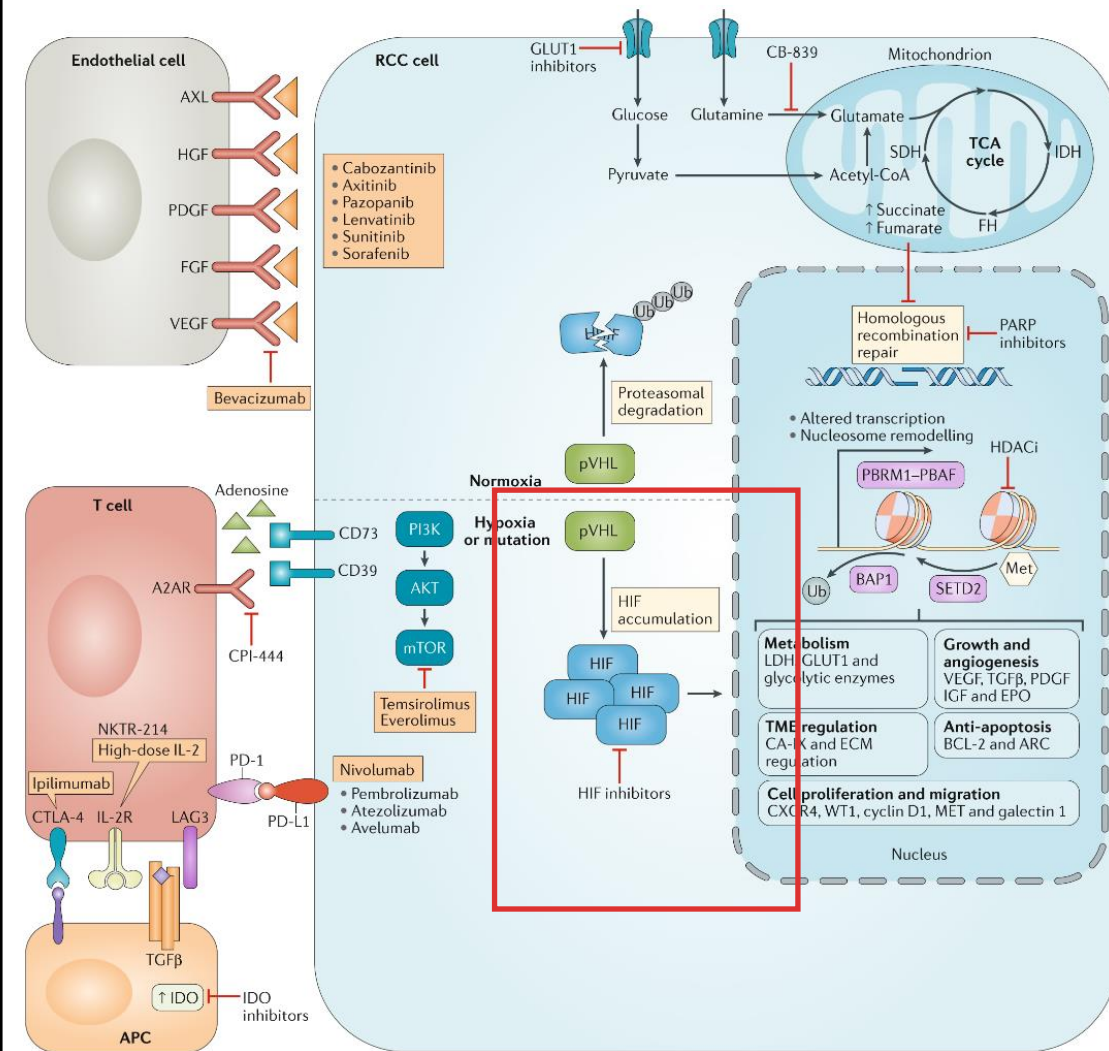
Immotion 010	n=764	Atezolizumab vs Placebo
Checkmate 914	n=800	Nivo + Ipi vs Placebo
Rampart	n=1750	Durvalumab + Tremelimumab vs Placebo
Prosper	n=766	Nivo/nephrectomy/Nivo vs Nephrectomy



A new drug is coming?

HIF 2 A inhibition in RCC data in 2021

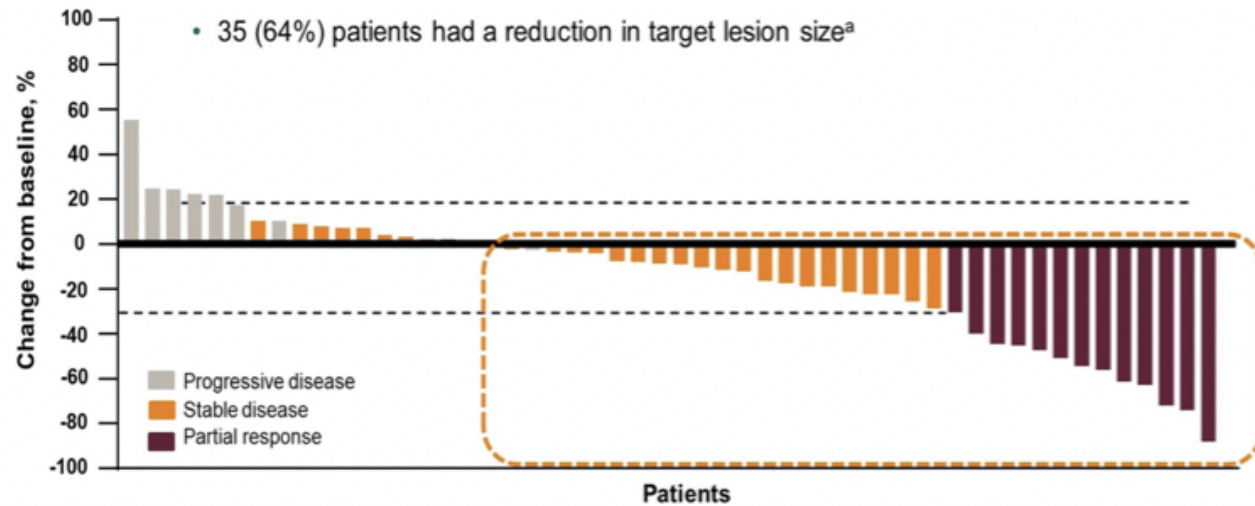
The new most promising drug: Belzutifan



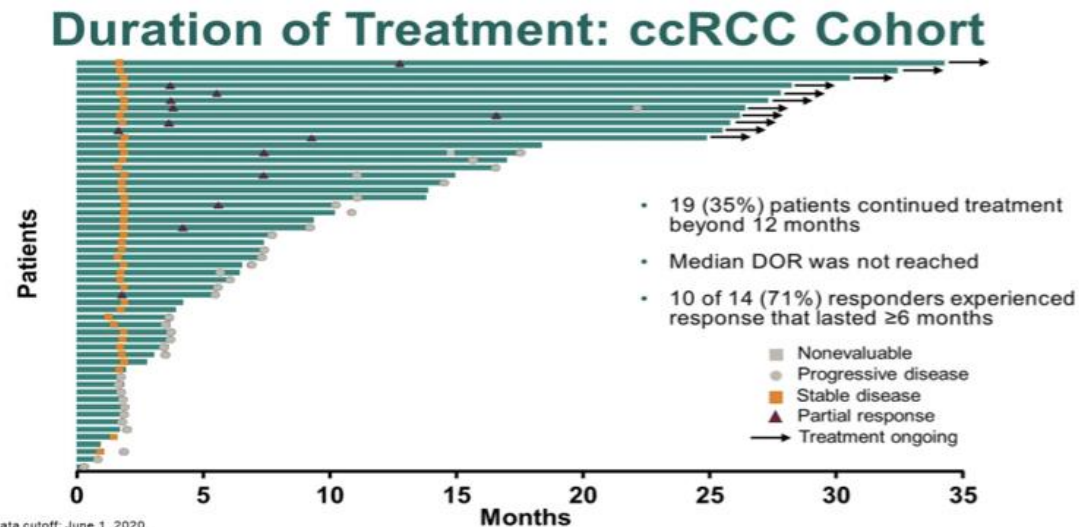
- Dose-escalation cohort for patients with advanced solid tumors
- Dose-expansion cohort for patients with advanced ccRCC who previously received ≥ 1 therapy
 - Key end points: Safety, objective response rate, duration of response

- Dose of 120 mg once daily selected for further clinical development from the dose-escalation cohort
- **55 patients with previously treated advanced ccRCC enrolled at 120 mg orally once daily in the dose-expansion cohort**
 - 44 (80%) discontinued
 - Most common reason was disease progression: 60%
 - 11 (20%) have treatment ongoing
- Median (range) follow-up:
 - 27.7 (24.8-34.3) months

HIF 2a inhibition: phase 1/2

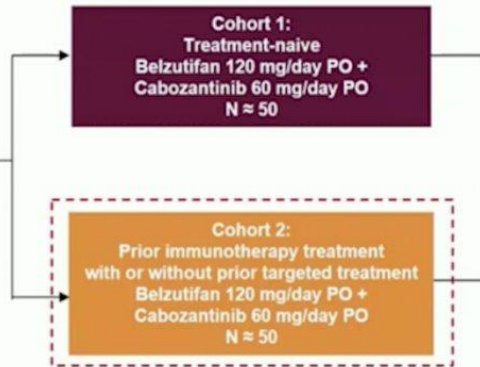


- n=55
- Median prior line: 3 (2/3:VEGF&PD1 inhibition)
- Median F up: 27,7 months
- ORR: 25%
- DCR: 80%
- mPFS:14,5 m
- Safety profile:
ANEMIA (any:76%; gr3:27%) HYPOXIA (any:31%; gr3:16%)



HIF2a inhibition in Combination: phase 1

- Key Eligibility Criteria**
- Advanced or metastatic ccRCC
 - Being treatment naive or having previously received immunotherapy and ≤ 2 regimens for locally advanced or metastatic RCC
 - ECOG PS 0 or 1
 - All IMDC risk categories (favorable/intermediate/poor) allowed



Safety and tolerability were evaluated in the first 6 participants enrolled, irrespective of cohort

- If tolerability was established, enrollment continued
- If tolerability was not established, dose was reviewed

Tumor Assessments

- Q8W after week 9 for 12 months and then Q12W thereafter

End Points

- Primary: ORR
- Secondary: PFS, TTR, DOR, OS, safety/tolerability, PK/PD

Median follow-up*

- 15.4 months (range, 8.7-30.6)

Median follow up: 11,3m

Population	ORR (CR + PR)		DCR (CR + PR + SD)	
	n/N	% (95% CI)	n/N	% (95% CI)
All patients	15/52	28.8 (17.1-43.1)	48/52	92.3 (81.5-97.9)
IMDC risk category				
Favorable	3/11	27.3 (6.0-61.0)	11/11	100 (71.5-100)
Intermediate/poor	12/41	29.3 (16.1-45.5)	37/41	90.2 (76.9-97.3)
Prior anticancer therapy				
IO only	8/28	28.6 (13.2-48.7)	26/28	92.9 (76.5-99.1)
IO/VEGF	7/24	29.2 (12.6-51.1)	22/24	91.7 (73.0-99.0)

HIF-2 α INHIBITORS: PT2385 + Nivolumab

Results from a Phase 1 Expansion Cohort of the First-in-Class Oral HIF-2 α Inhibitor PT2385 in Combination with Nivolumab in Patients with Previously-Treated Advanced RCC

Brian I. Rini¹, Leonard J. Appleman², Robert A. Figlin³, Elizabeth R. Plimack⁴, Jaime R. Merchan⁵, Keshi Wang⁶, Sanjay I. Thakkar⁷, Naseem J. Zojwalla⁸, Toni K. Choueiri⁹, David F. McDermott¹⁰

¹Cleveland Clinic, Cleveland, OH; ²University of Pittsburgh Medical Center, Pittsburgh, PA; ³Cedars-Sinai Medical Center, Los Angeles, CA; ⁴Fox Chase Cancer Center, Philadelphia, PA; ⁵University of Miami, Miami, FL;

⁶Peloton Therapeutics Inc., Dallas, TX; ⁷Dana-Farber Cancer Institute, Boston, MA; ⁸Beth Israel Deaconess Medical Center, Boston, MA, USA

Figure 2: Best Change in Tumor Size from Baseline

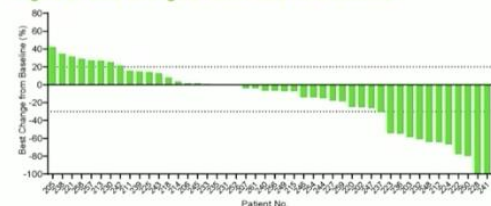
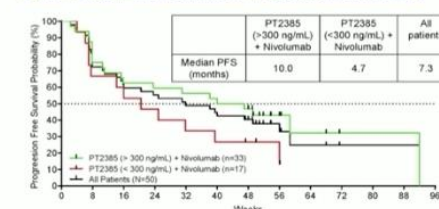


Figure 4: Kaplan-Meier Estimate of Progression Free Survival



P
D
1

Adverse Event	N=50				Total n (%)
	G 1 (%)	G 2 (%)	G 3 (%)	G 4 (%)	
Anemia	10 (20)	11 (22)	3 (6)	0 (0)	24 (48)
Fatigue	15 (30)	7 (14)	2 (4)	0 (0)	24 (48)
Nausea	14 (28)	4 (8)	1 (2)	0 (0)	19 (38)
Arthralgia	9 (18)	5 (10)	1 (2)	0 (0)	15 (30)
Diarrhea	8 (16)	5 (10)	0 (0)	0 (0)	13 (26)
Hyponatremia	11 (22)	0 (0)	1 (2)	0 (0)	12 (24)
Pain In Extremity	8 (16)	4 (8)	0 (0)	0 (0)	12 (24)
Cough	10 (20)	2 (4)	0 (0)	0 (0)	12 (24)
Dyspnea	8 (16)	3 (6)	1 (2)	0 (0)	12 (24)
Hypertension	1 (2)	10 (20)	1 (2)	0 (0)	12 (24)
Constipation	6 (12)	4 (8)	1 (2)	0 (0)	11 (22)
Decreased Appetite	4 (8)	7 (14)	0 (0)	0 (0)	11 (22)
Back Pain	5 (10)	3 (6)	3 (6)	0 (0)	11 (22)
Dizziness	10 (20)	0 (0)	1 (2)	0 (0)	11 (22)

PT2385 + Nivolumab

- N=50
- ORR: 22%; SD: 42%
- PFS: 7.3 months

Mc Dermott et al, ESMO 2021; Rini et al, ASCO GU 2019, Abs588



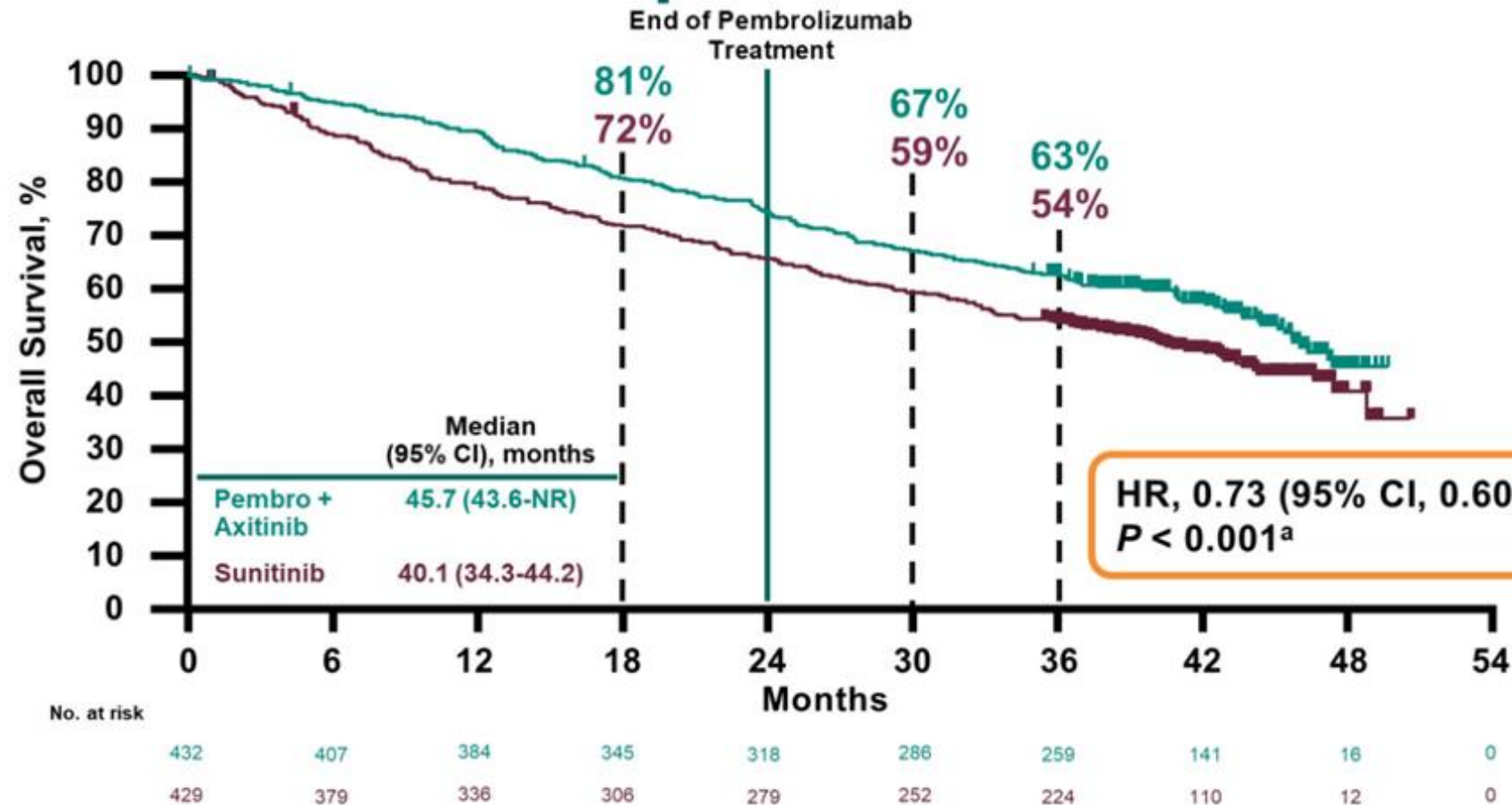
VEGF/IO combination datas in first line in 2021

A new combination and long term follow up datas

Axitinib/pembrolizumab FU 46m



OS in the ITT Population



Longest F up data for TKI/IO

Pembro was given 2 years

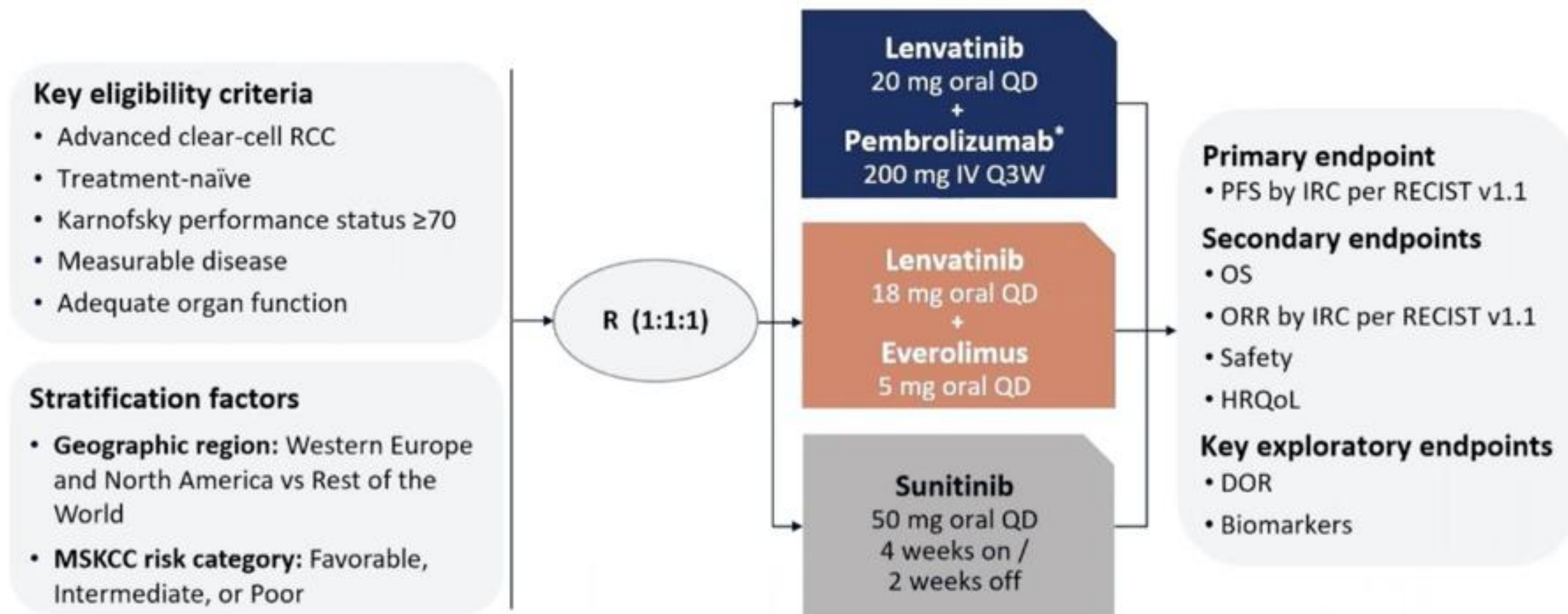
Benefit in PFS/ORR/CR maintained over time & after pembro discontinuation

HR: 0,53 at 12m F Up

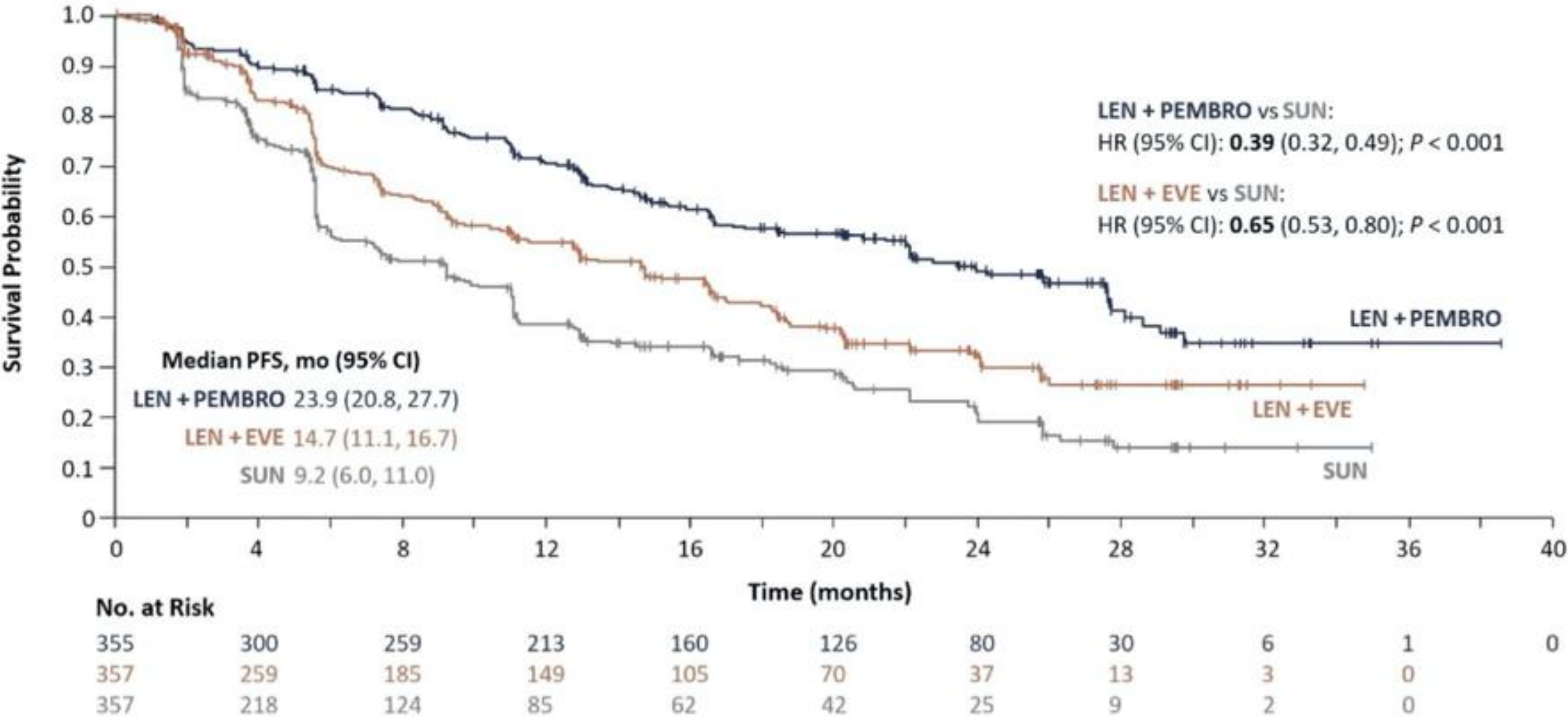
No new safety signals

^aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal P values are reported. Data cutoff: January 11, 2021.

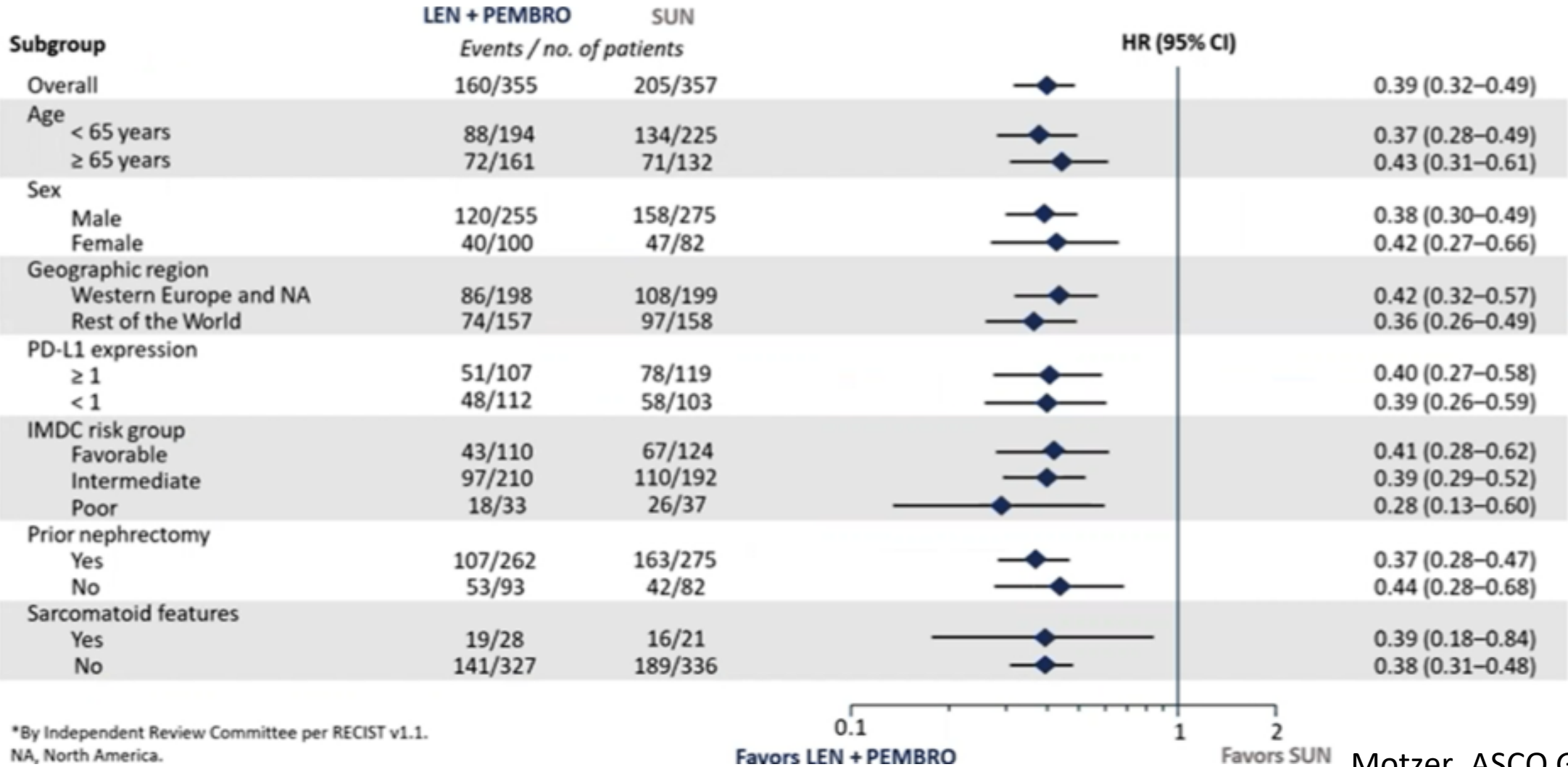
Clear trial: study design



CLEAR TRIAL primary endpoint of PFS



CLEAR trial : subgroups

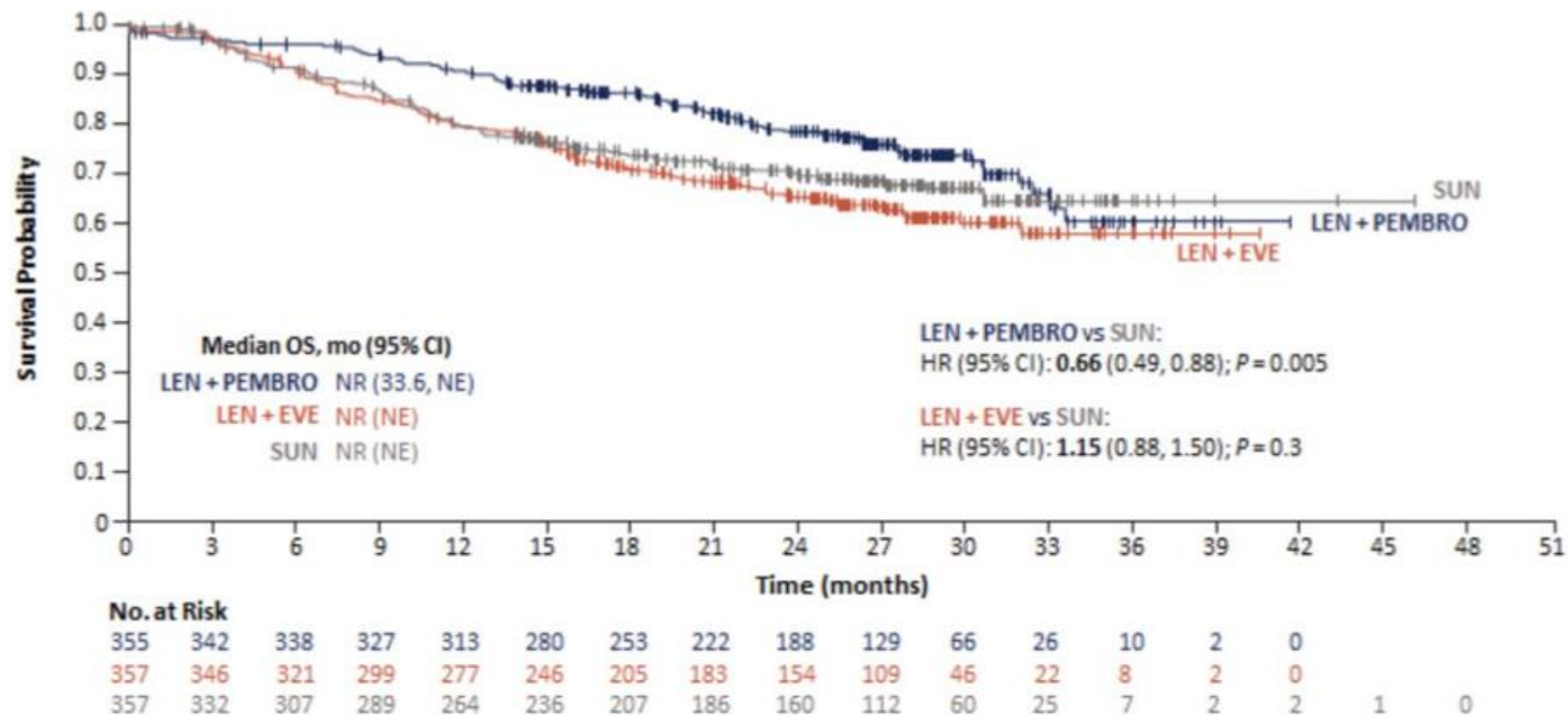


Clear trial: objective response rate

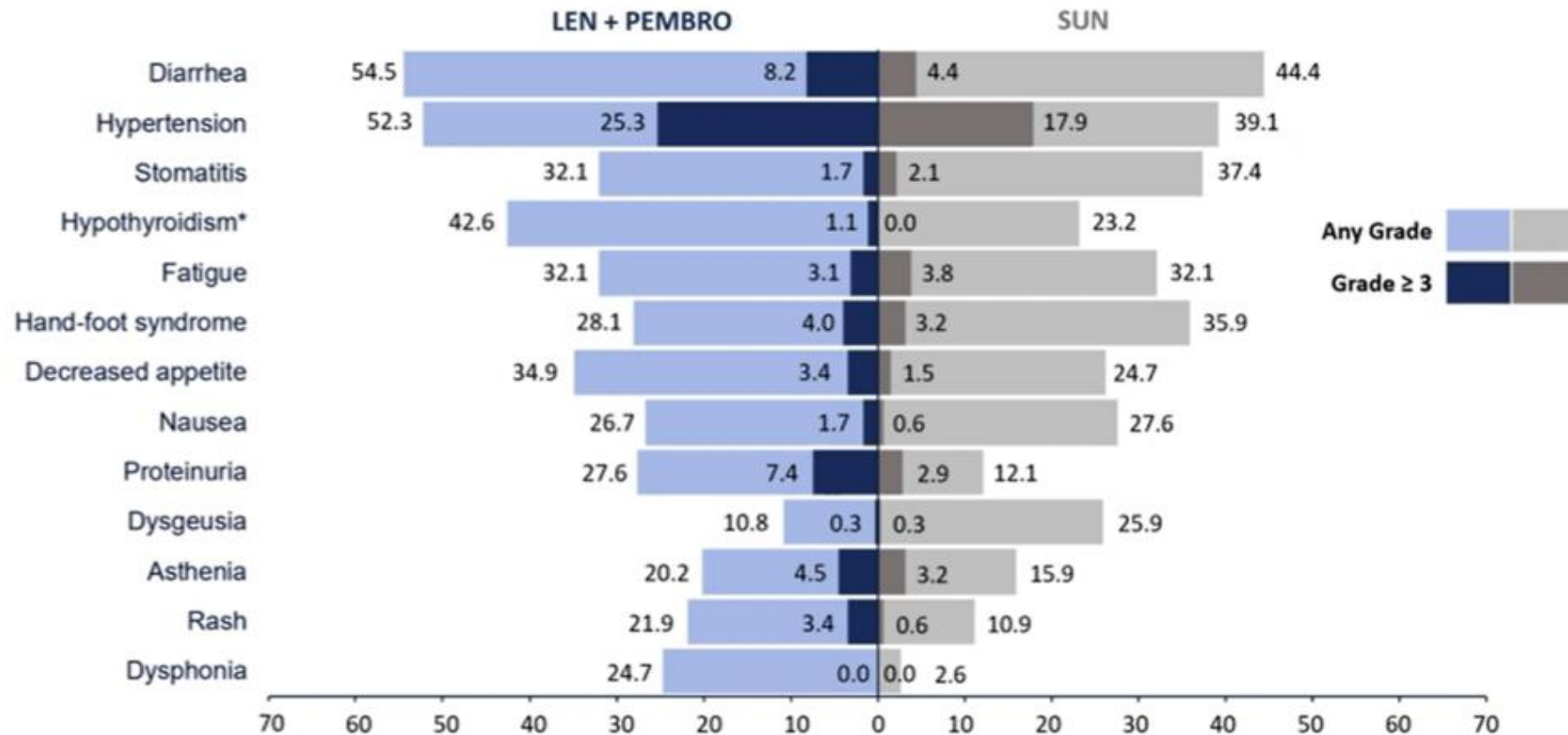


	LEN + PEMBRO (n = 355)	LEN + EVE (n = 357)	SUN (n = 357)
Objective response rate (95% CI) — %	71.0 (66.3–75.7)	53.5 (48.3–58.7)	36.1 (31.2–41.1)
Best overall response — %			
Complete response	16.1	9.8	4.2
Partial response	54.9	43.7	31.9
Stable disease	19.2	33.6	38.1
Progressive disease	5.4	7.3	14.0
Unknown / not evaluable	4.5	5.6	11.8
Relative risk versus SUN (95% CI)	1.97 (1.69–2.29)	1.48 (1.26–1.74)	--
P-value	< 0.001	< 0.001	--

CLEAR TRIAL : OS (secondary endpoint)



CLEAR TRIAL : safety



How should I treat?

Poor / intermediate prognosis

	CheckMate 214 (Ipi/Nivo) ¹ (n=550 vs n=546)	KEYNOTE-426 (Axi/Pembro) ² (n=432 vs n=429)	CheckMate 9ER (Cabo/Nivo) ³ (n=323 vs n=328)	CLEAR (Len/Pembro) ⁴ (N=355 vs n=357)
mOS, months HR (CI)	NR vs 38.4 0.69 (0.59–0.81)	NR vs 35.7 0.68 (0.55–0.85)	NR vs 29.5 0.66 (0.50–0.87)	NR vs NR 0.66 (0.49–0.88)
Landmark OS 12 mo	83% vs. 78%	90% vs. 79%	86% vs. 76%	90% vs 79% (est.)
Landmark OS 24 mo	71% vs. 61%	74% vs. 66%	72% vs 60% (est.)	79% vs. 70%
mPFS, months HR (CI)	12.2 vs 12.3 0.89 (0.76–1.05)	15.4 vs 11.1 0.71 (0.60–0.84)	17.0 vs 8.3 0.52 (0.43–0.64)	23.9 vs 9.2 0.39 (0.32–0.49)
ORR, %	39 vs 32	60 vs 40	55 vs 27	71 vs 36
CR, %	11 vs 3	9 vs 3	9 vs 4	16 vs 4
Med f/u, months	55	46	23.5	27
Prognostic risk, %				
Favorable	23	32	23	31
Intermediate	61	55	58	59
Poor	17	13	19	9
Prior nephrectomy	82%	83%	69%	74%
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)	Overall (69%) IO (48%)	Overall (40%) IO (29%)	Overall (71%) IO (53%)

1. Alligier et al. ESMO Open 2020
3. Motzer et al. ASCO GU 2021

2. Powles et al. Lancet Oncology 2020
4. Motzer et al. ASCO GU 2021.

How should I treat in first line

Intermediate or bad prognosis group

PD-1 + CTLA 4

PD-1 + VEGF

PROS

Improved OS

Mature Follow up Available

Durable responses

Potential to stop therapy

QOL during maintenance

Improved OS

High ORR
Low PD rate

Longer PFS

Lower irAE rate

CONS

Lower PFS /response rate

Higher irAE rate

Unclear AE attribution

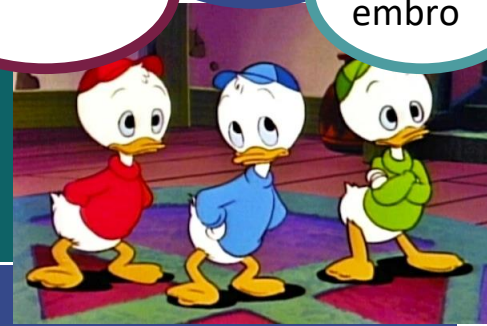
Less mature Follow up

Chronic TKI toxicity

Axi/pembr
o

Cabo/Niv
o

Lenva/P
embro





Thanks for your attention