GU connect®

POWERED BY COR2ED

HIGHLIGHTS OF 2021 FROM GU CONNECT

Prof. David Pfister, MD

Professor and Deputy Director of The Department of Urology,
University Hospital of Cologne, Germany

DECEMBER 2021

DISCLAIMER AND DISCLOSURES

Please note: The views expressed within this presentation are the personal opinions of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GU CONNECT group.

This content is supported by an Independent Educational Grant from Bayer.

Prof. David Pfister has received financial support/sponsorship for research support, consultation or speaker fees from the following companies:

- Astellas, AstraZeneca, Bayer, Janssen, Merck, MSD, Pfizer

PROSTATE CANCER
2021 HIGHLIGHTS

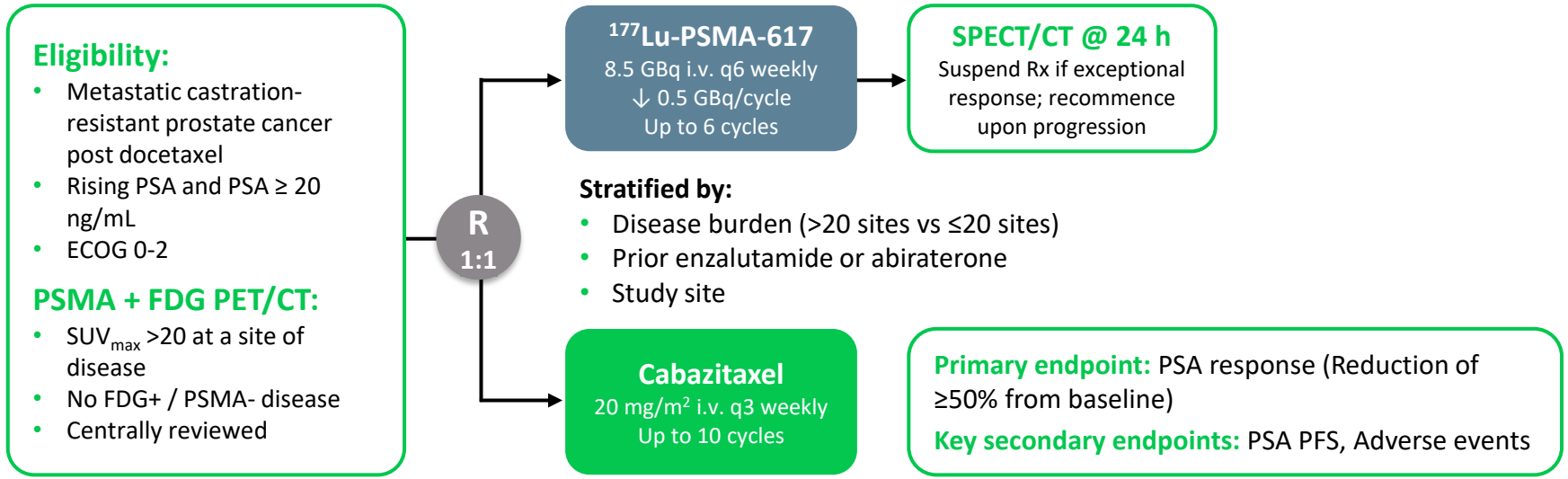
^{177}LU-PSMA-617 VS CABAZITAXEL IN mCRPC PROGRESSING AFTER DOCETAXEL: UPDATED RESULTS INCLUDING PFS AND PROs (TheraP ANZUP 1603)

Hofman M, et al.
ASCO GU 2021. Abstract #6. Oral presentation

mCRPC, metastatic castration-resistant prostate cancer; PFS, progression-free survival; PROs, patient reported outcomes

TheraP: OVERVIEW

- ^{177}Lu-PSMA-617 **(Lu-PSMA)** is a radiolabelled small molecule that delivers **therapeutic β-radiation to PSMA-expressing tumours**
- Encouraging efficacy and safety of Lu-PSMA has been observed in prior trials of mCRPC
- **TheraP is the first randomised study comparing Lu-PSMA to cabazitaxel in men with mCRPC after docetaxel**



FDG, Fluorodeoxyglucose; LuPSMA, 177Lu-PSMA-617; i.v., intravenous; mCRPC, metastatic castration resistant prostate cancer; PET/CT, positron-emission tomography-computed tomography; PFS, progression free survival; PSA, prostate specific antigen; PSMA, prostate specific membrane antigen; Rx, treatment; SUV, standardised uptake value.

Hofman MS, et al. J Clin Oncol. 2021;39 suppl 6:6 (ASCO GU 2021 oral presentation); Hofman M, et al. The Lancet. 2021;397:797-804

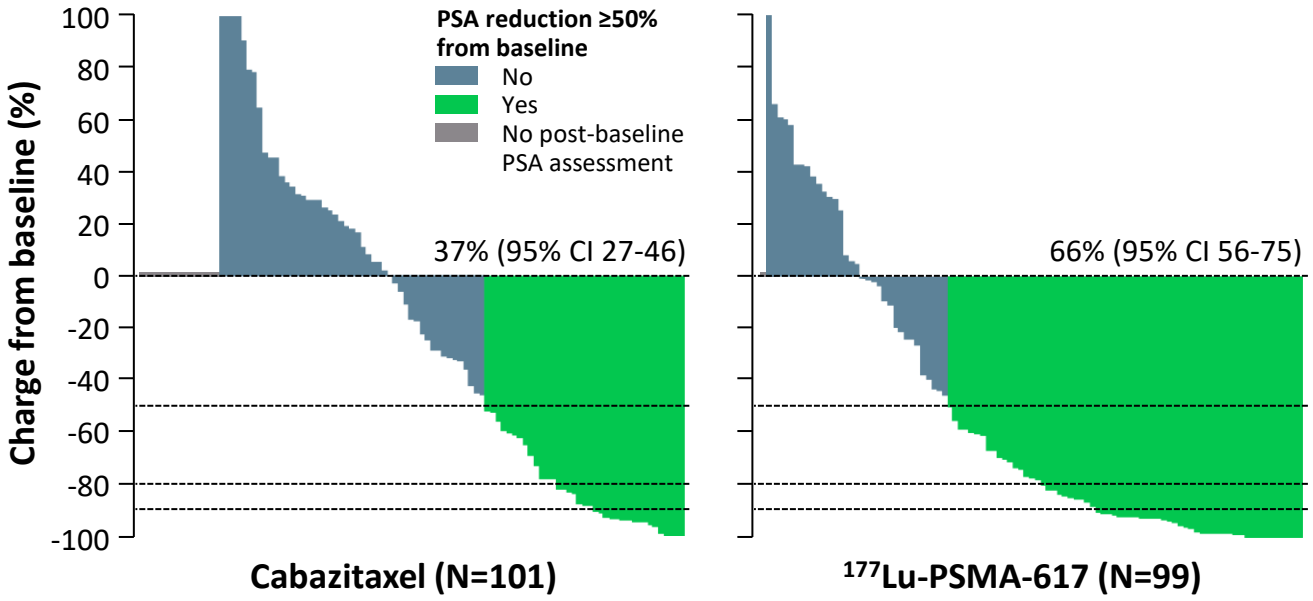
TheraP: RESULTS

BASELINE CHARACTERISTICS (ITT)

	^{177}Lu-PSMA-617 (N=99)	Cabazitaxel (N=101)
Age, years		
Mean (SD)	71.7 (7.9)	71.5 (7.0)
Median (IQR)	72.1 (66.9-76.7)	71.8 (66.7-77.3)
>20 metastases[a]	77 (78%)	79 (78%)
ECOG performance status		
0	42 (42%)	44 (44%)
1	53 (54%)	52 (52%)
2	4 (4%)	4 (4%)
Missing data	0	1 (1%)
PSA, ng/mL	93.5 (44-219)	110 (64-245)
Alkaline phosphatase, U/L	111 (83-199)	130 (79-187)
Gleason score at diagnosis		
≤7	25 (25%)	35 (35%)
≥8	53 (53%)	50 (50%)
Missing data	21 (21%)	16 (16%)
Disease stage		
Lymph node only	7 (7%)	9 (9%)
Bone metastases	90 (91%)	90 (89%)
Visceral metastases	7 (7%)	13 (13%)
Previous treatment		
Abiraterone only	21 (21%)	24 (24%)
Enzalutamide only	49 (50%)	58 (57%)
Both	21 (21%)	9 (9%)

Data are n (%), mean (SD) or median (IQR);
[a]assessed using ^{68}Ga-PSMA-11 PET-CT by central review

PRIMARY ENDPOINT – PSA RESPONSE

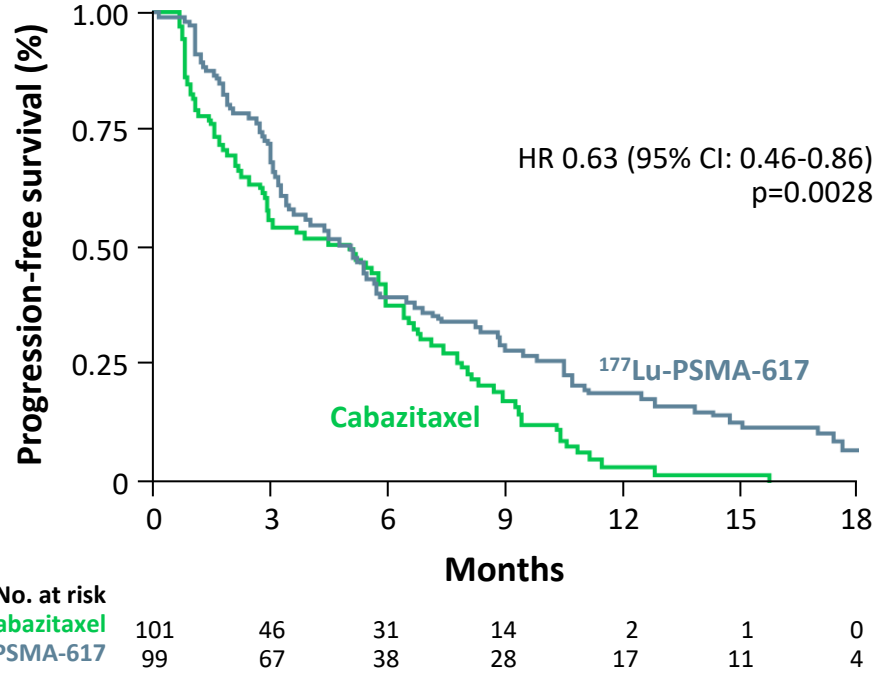


^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CI, confidence interval; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; ITT, intention-to-treat; PET, positron-emission tomography; PSA, prostate-specific antigen; SD, standard deviation

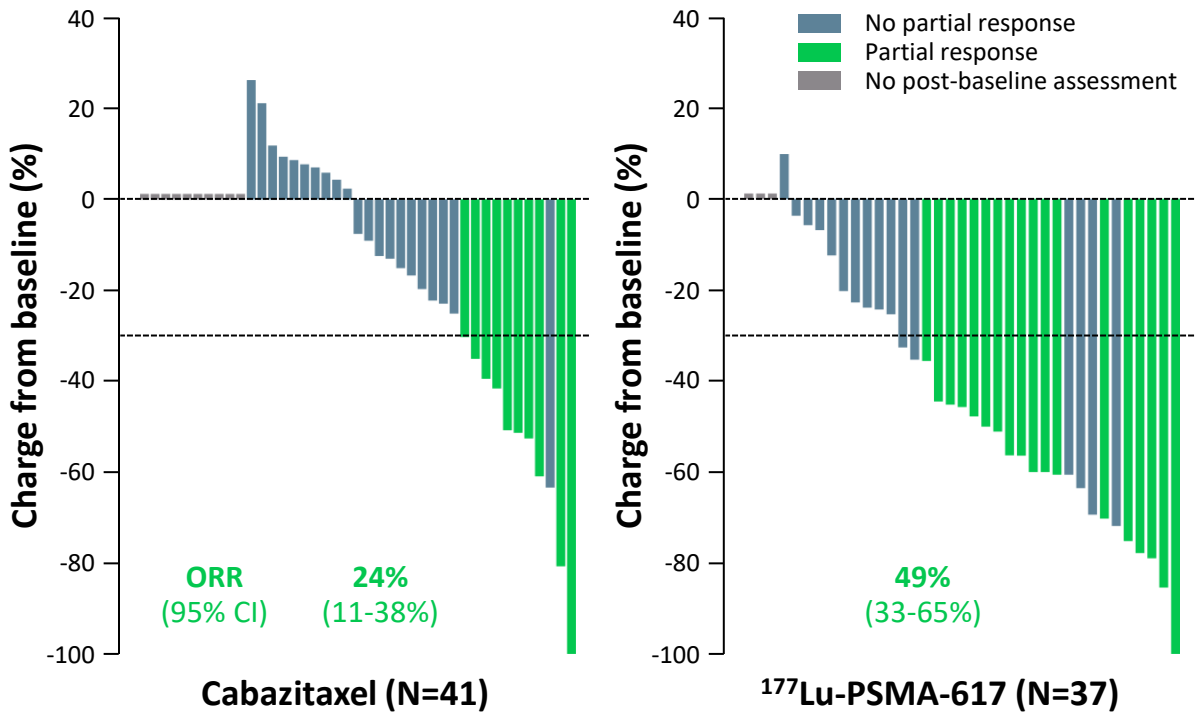
Hofman MS, et al. J Clin Oncol. 2021;39 suppl 6:6 (ASCO GU 2021 oral presentation); Hofman MS, et al. Lancet 2021;397:797-804

TheraP: RESULTS

PROGRESSION-FREE SURVIVAL (PSA AND RADIOGRAPHIC)



OBJECTIVE RESPONSE RATE (RECIST 1.1)



177Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CI, confidence interval; HR, hazard ratio; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumours

Hofman MS, et al. J Clin Oncol. 2021;39 suppl 6:6 (ASCO GU 2021 oral presentation); Hofman MS, et al. Lancet. 2021;397:797-804

TheraP: RESULTS

Term	Cabazitaxel (N=85)		Lu-PSMA (N=98)	
	G1-2 %	G3-4 %	G1-2 %	G3-4 %
Neutropenia (+/- fever)	5	13	7	4
Thrombocytopaenia	5	0	18	11
Dry mouth	21	0	60	0
Diarrhoea	52	5	18	1
Dry eye	4	0	30	0
Dysgeusia	27	0	12	0
Neuropathy (motor or sensory)	26	1	10	0
Fatigue	72	4	70	5
Nausea	34	0	40	1
Anaemia	13	8	19	8
Vomiting	12	2	12	1
TOTAL (all AEs)	40	54	54	33

Discontinuations for toxicity occurred in 1/98 (1%) Lu-PSMA vs 3/85 (4%) cabazitaxel-treated
There were no Lu-PSMA related deaths

AE, adverse event; G, grade; Lu-PSMA, ^{177}Lutetium-PSMA-617

Hofman MS, et al. J Clin Oncol. 2021;39 suppl 6:6 (ASCO GU 2021 oral presentation)

TheraP: SUMMARY

- **Lu-PSMA** demonstrated a **greater PSA50 response compared to cabazitaxel** in men with mCRPC after docetaxel
- Lu-PSMA may represent a favourable treatment option compared to cabazitaxel in a selected population with high PSMA expression
- **PFS data is immature** at the time of this analysis **but initial data is favourable**
- Improvement in **overall survival is yet to be confirmed** from this trial
- **Relatively fewer G3-4 AEs** were experienced by patients treated **with Lu-PSMA** compared to those receiving cabazitaxel

AE, adverse event; Lu-PSMA, ^{177}Lutetium-PSMA-617; mCRPC, metastatic castration resistant prostate cancer; PFS, progression free survival; PSA50, PSA ≥50% response

Hofman MS, et al. The Lancet. 2021;397:797-804

A PHASE 3 STUDY OF ^{177}LU-PSMA-617 IN PATIENTS WITH mCRPC (VISION TRIAL)

Morris MJ, et al.

ASCO 2021. Abstract #LBA4. Oral presentation

Fizazi K, et al.

ESMO 2021. Abstract # 576MO

177Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; mCRPC, metastatic castration-resistant prostate cancer

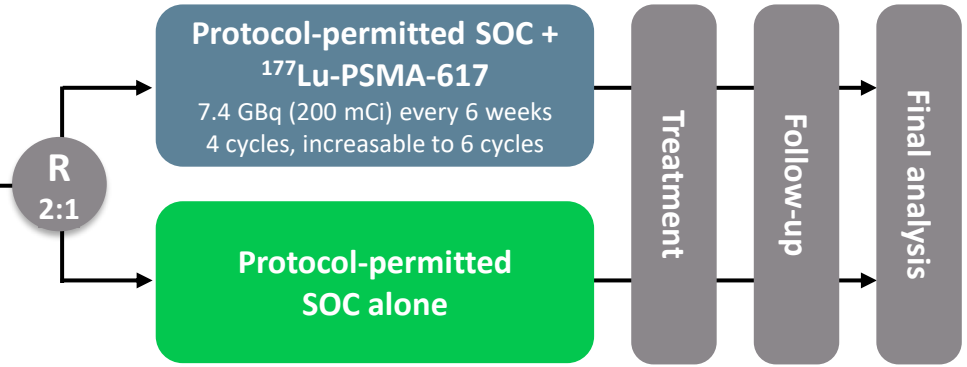
VISION: OVERVIEW

- Prostate-specific membrane antigen (PSMA) is highly expressed on the surface of prostate cancer cells, including metastatic lesions, and is only expressed on a few normal tissues such as the salivary and lacrimal glands
- Studies have confirmed that PSMA-bound imaging is highly specific for PET-based imaging of prostate cancer
- The VISION trial randomised patients with mCRPC who had ≥1 PSMA-PET positive metastatic lesion and no PSMA-negative metastatic lesions to receive either ^{177}Lu-PSMA plus ongoing standard of care or standard of care

Eligibility:

- Previous treatment with **both**
  - ≥1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted SOC planned before randomisation
  - Excluding chemotherapy, immunotherapy, radium-223, investigational drugs
- ECOG performance status 0-2
- Adequate major organ and bone marrow function
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

~87% of patients scanned met the VISION imaging criteria for PSMA-positive mCRPC



Alternate primary endpoints:

- Radiographic progression-free survival
- Overall survival

Key secondary endpoints:

- Time to first symptomatic skeletal event
- 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
  - FACT-P
  - Brief Pain Inventory – Short Form
  - EQ-5D-5L

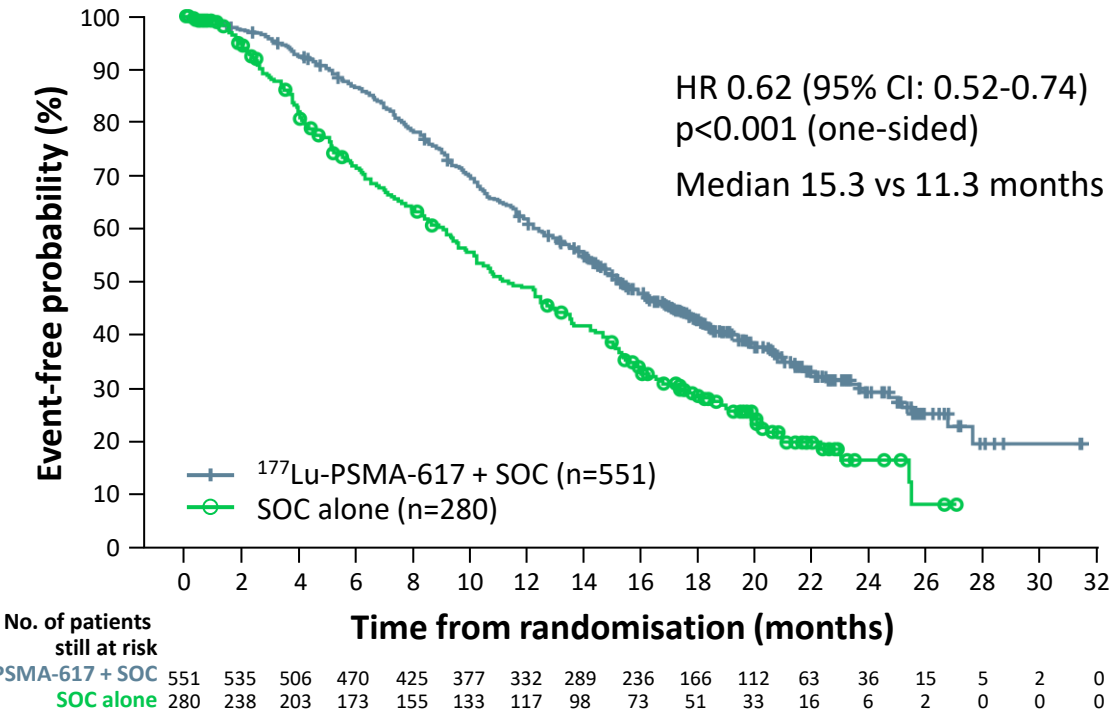
^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; EQ-5D-5L, European Quality of Life (EuroQol)–5 domain 5 level scale; FACT-P, Functional Assessment of Cancer Therapy–Prostate; mCRPC, metastatic castration-resistant prostate cancer; PET, positron-emission tomography; PSA, prostate-specific antigen; PSMA prostate-specific membrane antigen; RECIST, Response Evaluation Criteria in Solid Tumours; SOC, standard of care

Morris MJ, et al. J Clin Oncol. 2021;39 suppl 15:LBA4 (ASCO 2021 oral presentation); Sartor O, et al. N Eng J Med. 2021;385:1091-103

VISION: RESULTS

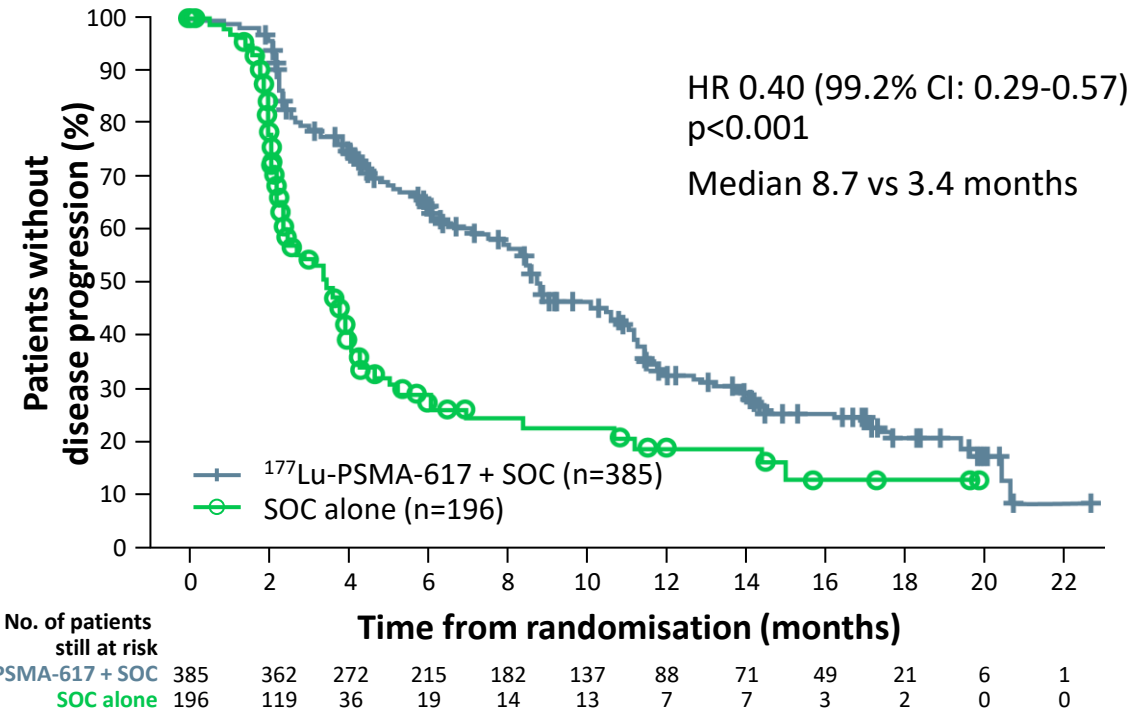
ALTERNATE PRIMARY ENDPOINTS

OS all randomised patients (N=831)



No. of patients still at risk																	
177Lu-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

Imaging-based progression-free survival (n=581)



No. of patients still at risk												
177Lu-PSMA-617 + SOC	385	362	272	215	182	137	88	71	49	21	6	1
SOC alone	196	119	36	19	14	13	7	7	3	2	0	0

CI, confidence interval; 177Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; HR, hazard ratio; OS, overall survival; rPFS, radiographic progression-free survival; SOC, standard of care

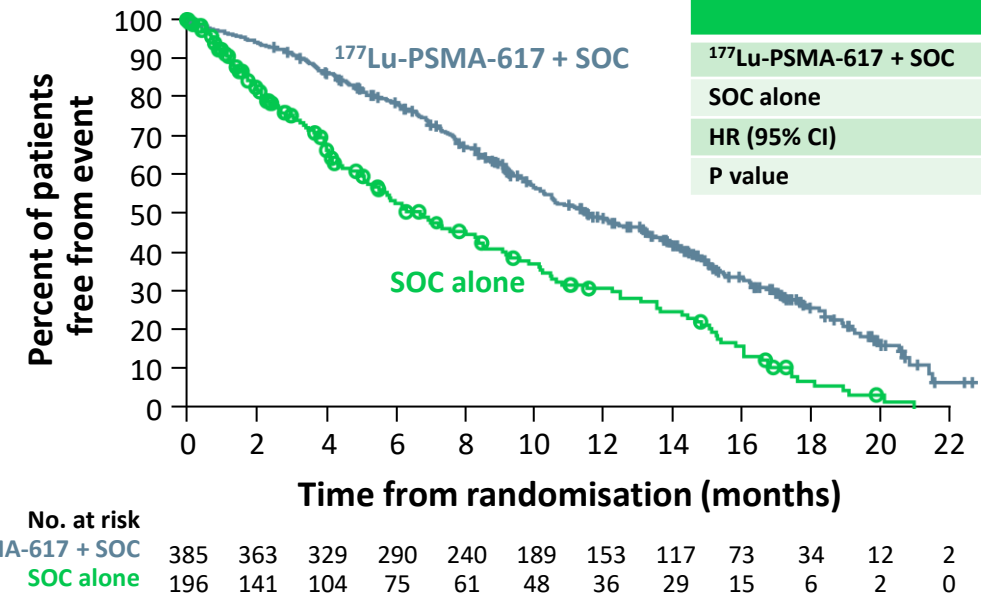
Sartor O, et al. N Engl J Med. 2021;385:1091-103

VISION: RESULTS

SECONDARY ENDPOINTS

Patients with evaluable disease at baseline	^{177}Lu-PSMA-617 + SOC (N=319)	SOC (N=120)
ORR, n (%)	95 (29.8)	2 (1.7)
	OR 24.99 (95% CI: 6.05-103.24) p<0.001	
DCR, n (%)	284 (89.0)	80 (66.7)
	OR 5.79 (95% CI: 3.18-10.55) p<0.001	

Time to first symptomatic skeletal event



	No. of events/ no. of patients	Median mo
^{177}Lu-PSMA-617 + SOC	256/385	11.5
SOC alone	137/196	6.8
HR (95% CI)	0.50 (0.40-0.62)	
P value	<0.001	

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CI, confidence interval; DCR, disease control rate; HR, hazard ratio; mo, months; OR, odds ratio; ORR, overall response rate; SOC, standard of care

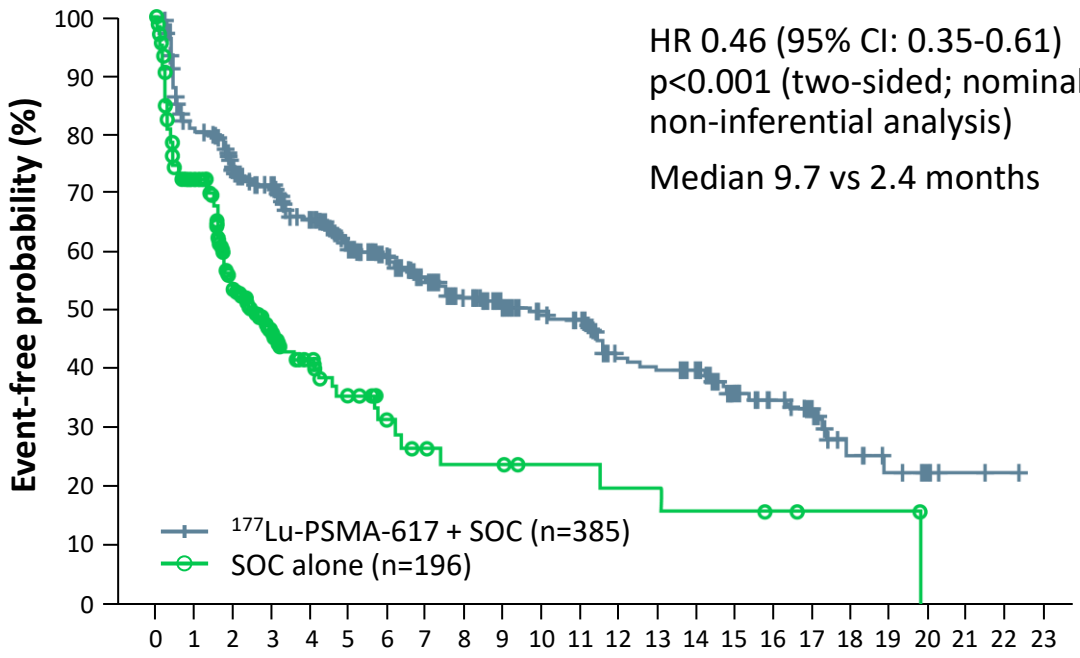
Sartor O, et al. N Engl J Med. 2021;385:1091-103

VISION: HEALTH-RELATED QUALITY OF LIFE

FACT-P TOTAL SCORE

Time to worsening favoured the ^{177}Lu-PSMA-617 arm

rPFS analysis set (N=581)



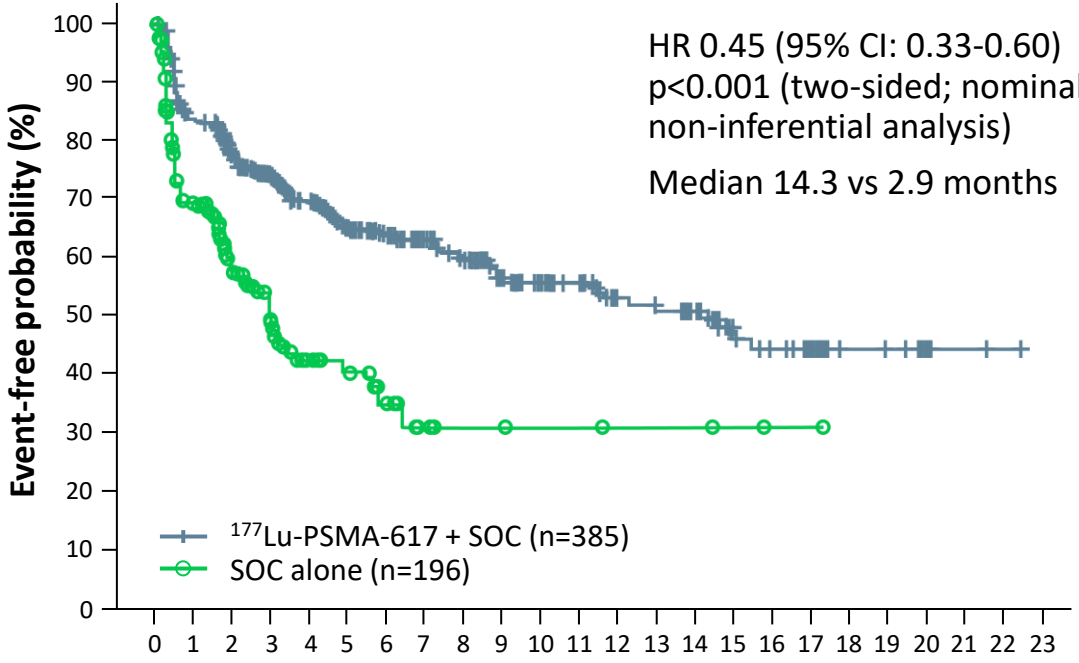
No. of patients still at risk																								
^{177}Lu-PSMA-617 + SOC	385	289	255	235	201	167	146	126	110	89	76	72	54	51	46	33	27	21	10	7	4	2	1	0
SOC alone	196	97	66	42	30	21	14	10	8	8	6	6	5	5	4	4	3	2	2	2	0	0	0	0

Time to the first occurrence of ≥10-point decrease in FACT-P total from baseline

BPI-SF PAIN INTENSITY

Time to worsening favoured the ^{177}Lu-PSMA-617 arm

rPFS analysis set (N=581)



No. of patients still at risk																								
^{177}Lu-PSMA-617 + SOC	385	296	265	238	197	162	146	129	113	87	70	66	51	48	42	24	21	15	8	6	2	2	1	0
SOC alone	196	94	65	37	25	19	12	7	5	5	4	4	3	3	3	2	1	1	0	0	0	0	0	0

Time to the first occurrence of ≥30-point or ≥2-point increase in BPI-SF pain intensity from baseline

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; BPI-SF, Brief Pain Inventory–Short Form; CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy– Prostate; HR, hazard ratio; rPFS, radiographic progression-free survival; SOC, standard of care

Sartor O, et al. N Engl J Med. 2021;385:1091-103; Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8 (ESMO 2021 oral presentation)

VISION: RESULTS

TREATMENT-EMERGENT ADVERSE EVENTS

Patients, n (%)	^{177}Lu-PSMA-617 + SOC (N=529)		SOC alone (N=205)	
	All grades	Grade 3-5	All grades	Grade 3-5
Any drug-related TEAE	451 (85.3)	150 (28.4)	59 (28.8)	8 (3.9)
Serious	49 (9.3)	43 (8.1)	5 (2.4)	5 (2.4)
Grade 5[a]	5 (0.9)	5 (0.9)	0 (0.0)	0 (0.0)
TEAEs grouped by topics of interest				
Fatigue	260 (49.1)	37 (7.0)	60 (29.3)	5 (2.4)
Bone marrow suppression	251 (47.4)	124 (23.4)	36 (17.6)	14 (6.8)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Anaemia	168 (31.8)	68 (12.9)	27 (13.2)	10 (4.9)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Dry mouth	208 (39.3)	0 (0.0)	2 (1.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	8 (1.5)	35 (17.1)	1 (0.5)
Renal effects	46 (8.7)	18 (3.4)	12 (5.9)	6 (2.9)
Second primary malignancies	11 (2.1)	4 (0.8)	2 (1.0)	1 (0.5)
Intracranial haemorrhage	7 (1.3)	5 (0.9)	3 (1.5)	2 (1.0)

[a] There were five drug-related treatment-emergent adverse events leading to death in the ^{177}Lu-PSMA-617 arm: pancytopenia, n=2; bone-marrow failure, n=1; subdural haematoma, n=1; intracranial haemorrhage, n=1

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; Lu-PSMA; SOC, standard of care; TEAE, treatment-emergent adverse event

Sartor O, et al. N Engl J Med. 2021; 385:1091-103; Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8 (ESMO 2021 oral presentation)

VISION: SUMMARY

- Radio-ligand therapy + standard of care was well tolerated in patients with advanced prostate cancer
- Time interval to worsening of quality of life and pain is increased

Take-home messages:

- Low negative side effects
- Prolonging PFS and OS
- Integration in therapy sequence of CRPC after results of randomised trials
- Improved quality of life

CRPC, castration-resistant prostate cancer; OS, overall survival; PFS, progression-free survival

Sartor O, et al. N Engl J Med. 2021;385:1091-103; Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8 (ESMO 2021 oral presentation)

A PHASE 3 TRIAL WITH A 2X2 FACTORIAL DESIGN IN MEN WITH *DE NOVO* mCSPC: OVERALL SURVIVAL WITH ABIRATERONE PLUS PREDNISONE IN PEACE-1

Fizazi K, et al.
ESMO 2021. Abstract #LBA5_PR. Oral presentation

mCSPC, metastatic castration-sensitive prostate cancer

PEACE-1: BACKGROUND AND STUDY DESIGN

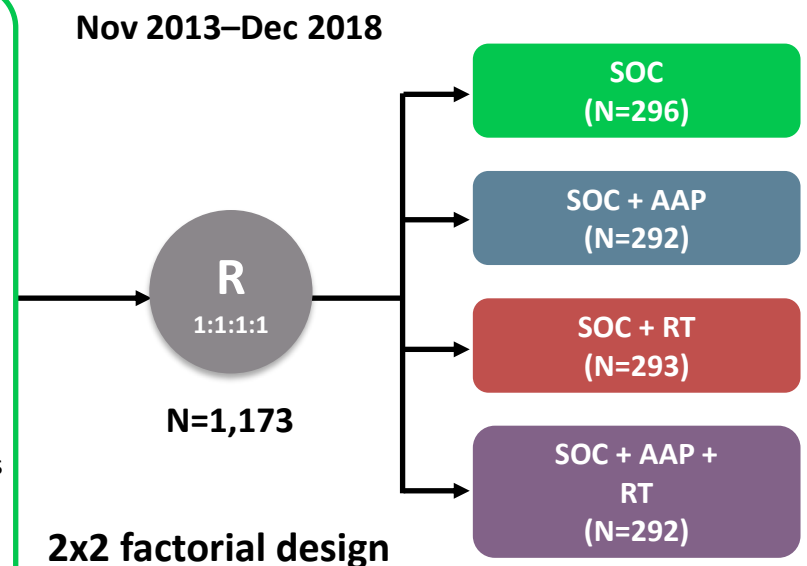
- ADT was SOC for men **with metastatic castration-sensitive prostate cancer** (mCSPC) for many years
- Since 2015, **combining ADT with either docetaxel, novel hormonal therapies, or RT** to the primary tumor (for those with low-burden metastases) was shown to improve OS and **is now the new SOC**
- **PEACE-1** evaluates whether combining these new treatments on top of ADT leads to improved outcomes

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 (lymph node vs bone vs visceral)
- Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)
- Docetaxel (yes vs no)



Co-primary
- Radiographic progression-free survival (rPFS):
  - PCWG 2 criteria
  - Imaging at least every 6 months after PSA rise
- OS

SOC = ADT and docetaxel 75 mg/m^2 every 3 weeks for 6 cycles

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; LHRH, luteinising hormone releasing hormone; mCSPC, metastatic castration-sensitive prostate cancer; OS, overall survival; PCWG 2, Prostate Cancer Working Group 2; PSA, prostate specific antigen; rPFS, radiographic progression-free survival; RT, radiotherapy; SOC, standard of care

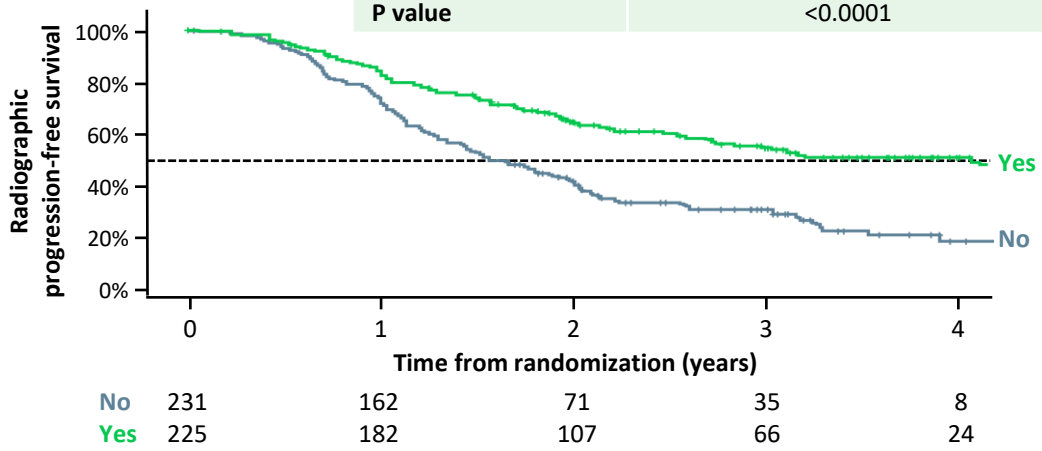
Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

PEACE-1: RESULTS

- Previous results from PEACE-1, showed that **AAP + ADT + docetaxel significantly improved rPFS** in men with mCSPC (HR 0.50; (95% CI: 0.40-0.62), p<0.0001)[1]
- Low and high volume disease data were presented at ESMO[2]

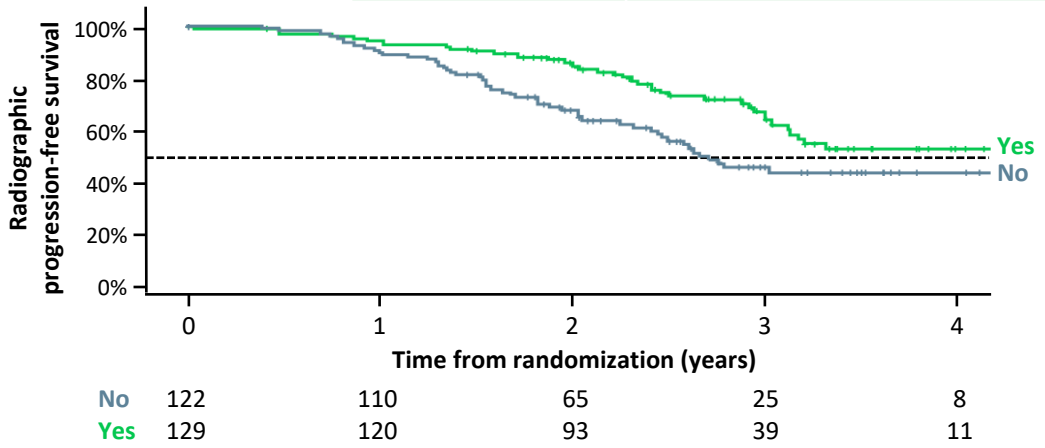
High volume

	SOC + AAP (N=225)	SOC (N=231)
Median, y (95% CI)	4.1 (2.7-NE)	1.6 (1.4-2.0)
Events	97	156
HR (95% CI)[a]	0.47 (0.36-0.60)	
P value	<0.0001	



Low volume

	SOC + AAP (N=129)	SOC (N=122)
Median, y (95% CI)	NE (3.1-NE)	1.6 (1.4-2.0)
Events	41	55
HR (95% CI)[a]	0.58 (0.39-0.87)	
P value	0.006	



[a]Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden)

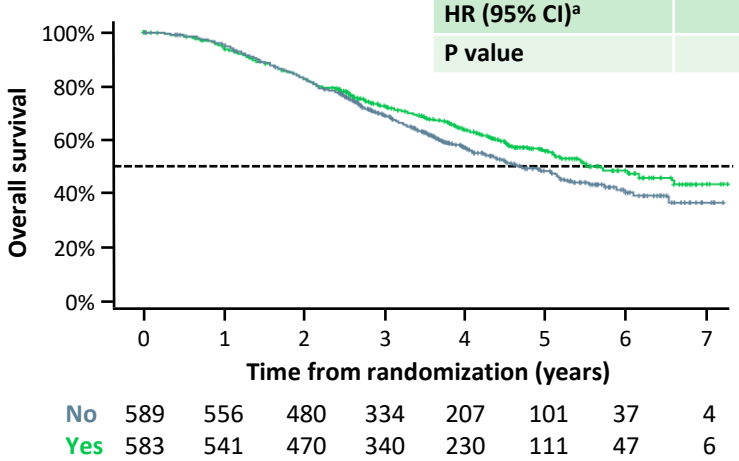
AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration sensitive prostate cancer; NE, not estimable; rPFS, radiographic progression-free survival; RXT, radiotherapy to primary tumour; SOC, standard of care

1. Fizazi K, et al. Abstract #5000. ASCO 2021; 2. Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

PEACE-1: RESULTS

OS in the overall population

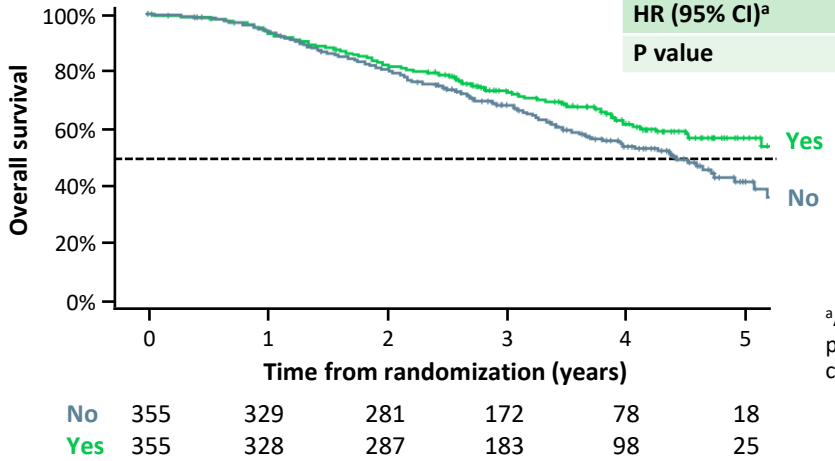
	SOC + AAP (N=583)	SOC (N=589)
Median, y (95% CI)	5.7 (5.1-NE)	4.7 (4.3-5.3)
Events	228	268
HR (95% CI)[a]	0.82 (0.69-0.98)	
P value	0.030	



[a]Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden, doxetaxel)

OS with AAP in the ADT + docetaxel (+/- RXT) population

	SOC + AAP (N=355)	SOC (N=355)
Median, y (95% CI)	NE (4.5-NE)	4.4 (3.8-4.9)
Events	121	151
HR (95% CI)[a]	0.75 (0.59-0.95)	
P value	0.017	



[a]Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden)

- **OS effect seen across subgroups**, including those with **high volume disease** (HR 0.72, 95% CI 0.55-0.95) and **low volume disease** (HR 0.83, 95% CI 0.50-1.38; data immature)
- Combination of **AAP + ADT + docetaxel was well tolerated**
  - No difference in rates of grade 3 to 5 neutropenia or febrile neutropenia
  - Grade 3 to 5 liver toxicity (6% vs 1%) and hypertension (22% vs 13%) with SOC + AAP compared to SOC alone

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; OS, overall survival; RXT, radiotherapy to primary tumour; SOC, standard of care

Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

PEACE-1: RESULTS

TREATMENTS 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)

ADT, androgen deprivation therapy; Lu-PSMA, lutetium-PSMA; nCRPC, numbers developing castration-resistant prostate cancer; PSMA, prostate-specific membrane antigen; RXT, radiotherapy; SOC, standard of care

Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

PEACE-1: RESULTS

G3-5 TOXICITY ON STUDY TREATMENTS (ADT + DOCETAXEL SAFETY POPULATION)

Toxicity, n (%)	SOC (± RXT) + abiraterone (N=346)	SOC (± RXT) (N=350)
Neutropenia	34 (10)	32 (9)
Febrile neutropenia	18 (5)	19 (5)
Liver	20 (6)	2 (1)
Hypertension	76 (22)	45 (13)
Hypokalemia	11 (3)	1 (0)
Cardiac	6 (2)	5 (1)
Fatigue	10 (3)	15 (4)
Gastro-intestinal	14 (4)	18 (5)
Grade 5	7 (2)	3 (1)

ADT, androgen deprivation therapy; g, GRADE; RXT, radiotherapy; SOC, standard of care
Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

PEACE-1: SUMMARY

- **Adding AAP to ADT plus docetaxel improve both rPFS and OS** in mCSPC men, even when 84% of mCRPC men from the control arm receive an androgen signalling inhibitor
- Toxicity was as expected – **no safety concerns** from combination treatment
- Triple therapy can be recommended

Clinical perspective:

- Benefit of a median **lifetime gain of more than 1.5 years** for mCSPC men with high volume disease (5.1 vs 3.5 years)

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer; mo, months; OS, overall survival; rPFS, radiographic progression free survival

Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S1299 (ESMO 2021 oral presentation)

ABIRATERONE ACETATE PLUS PREDNISOLONE WITHOUT ENZALUTAMIDE ADDED TO ADT COMPARED TO ADT ALONE FOR MEN WITH HIGH-RISK M0 PCa: COMBINED ANALYSIS FROM TWO COMPARISONS IN THE STAMPEDE PLATFORM PROTOCOL

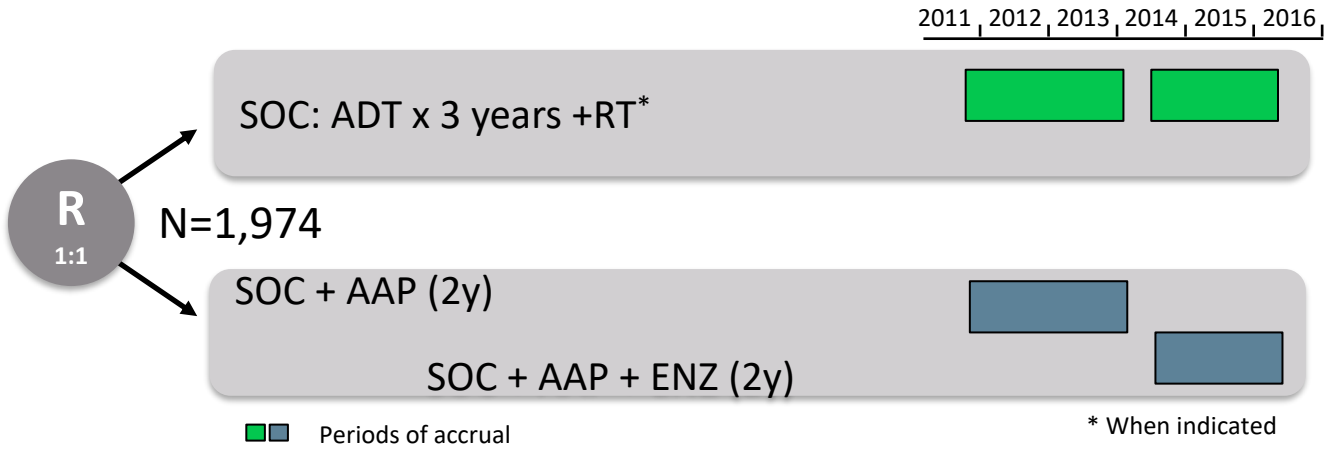
Attard G, et al.

ESMO 2021, Abstract #LBA4_PR. Oral presentation

ADT, androgen deprivation therapy; M0, non-metastatic; Pca, prostate cancer

STAMPEDE: BACKGROUND AND STUDY DESIGN

- Patients with **high-risk non-metastatic prostate cancer** (M0 PCa) are treated with androgen deprivation therapy (ADT) and local radiotherapy (RT), where indicated
- **Intensifying hormone treatment** with abiraterone acetate plus prednisone (AAP), enzalutamide (ENZ) or apalutamide (APA) **continuous to progression improves outcomes of metastatic PCa** but its efficacy in M0 PCa starting ADT is unknown
- This analysis of **STAMPEDE evaluated** whether there is a benefit for abiraterone acetate and prednisone **(AAP) in high-risk M0 PCa patients**



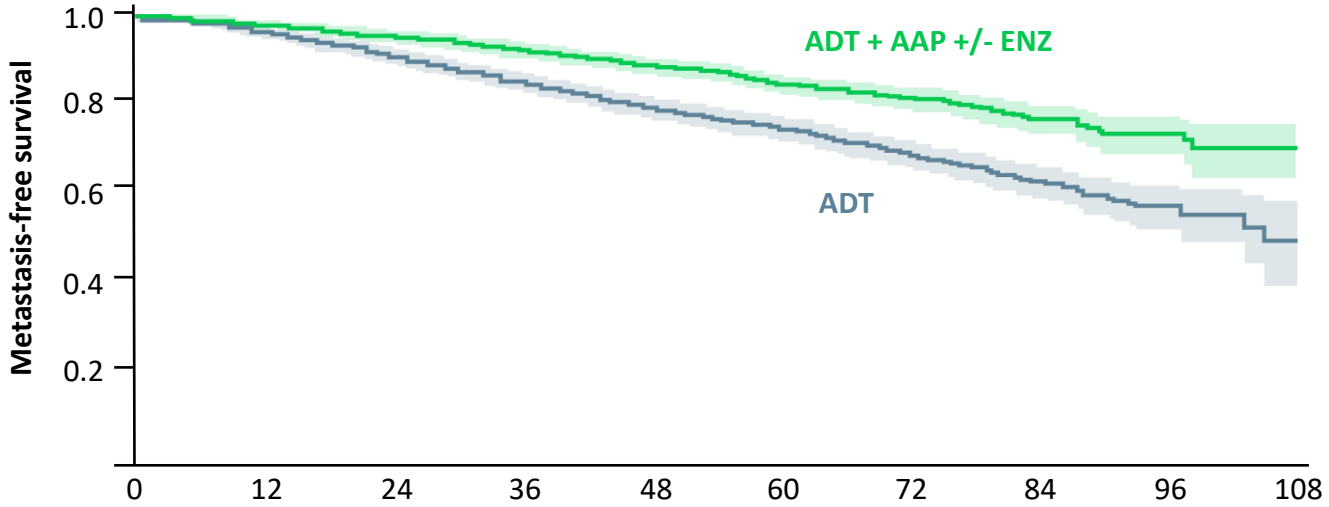
Primary endpoint: metastasis-free survival (MFS)
Secondary endpoint: Overall survival (OS)

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; APA, apalutamide; ENZ, enzalutamide; M0, non-metastatic; M1, metastatic; MFS, metastasis-free survival; OS, overall survival; PCa, prostate cancer; RT, radiotherapy; SOC, standard of care

Attard G, et al. Ann Oncol. 2021;32 suppl 5:S1298 (ESMO 2021 oral presentation)

STAMPEDE: RESULTS

METASTASIS-FREE SURVIVAL



ADT										
At-risk	988	950	894	836	767	550	329	172	53	9
Censored	0	8	11	14	26	201	387	522	632	673
Event	0	30	83	138	195	237	272	294	303	306
ADT + AAP +/- ENZ										
At-risk	986	948	917	884	839	622	369	198	71	14
Censored	0	21	28	31	45	225	460	615	737	792
Event	0	17	41	71	102	139	157	173	178	180

Kaplan–Meier estimates with 95% CI in lighter shade

Events
180 ADT + AAP +/- ENZ
306 ADT

HR:	**0.53**
95% CI:	0.44-0.64
P value:	2.9×10^{-11}

6-year MFS improved from 69% to 82%

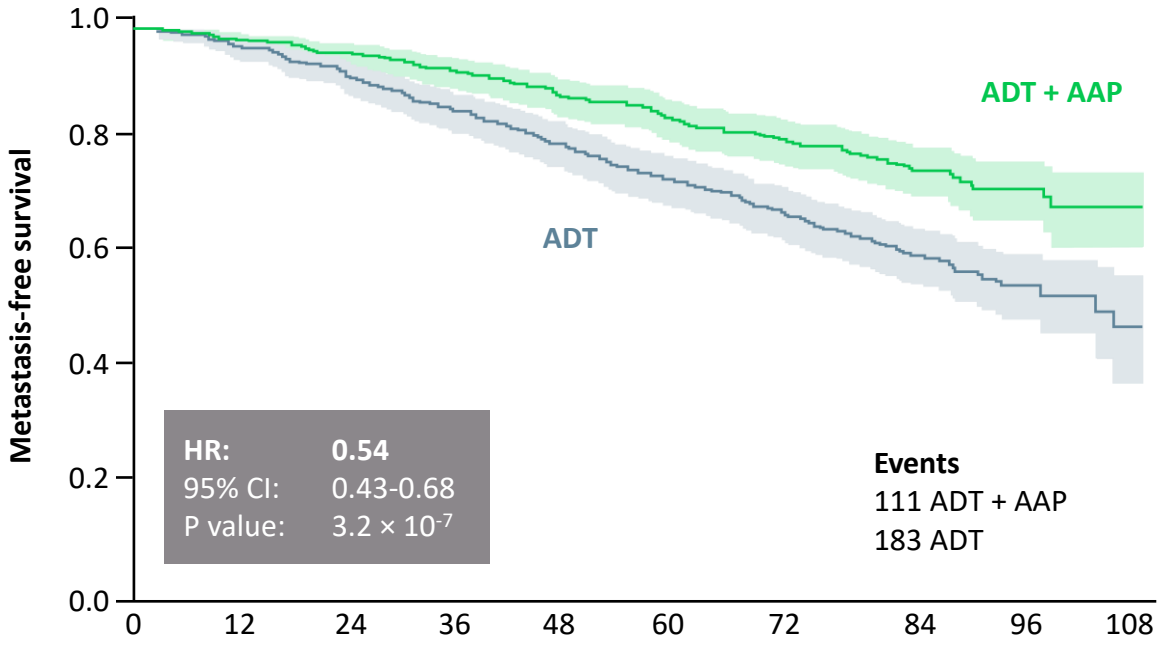
- **MFS: treatment effect was consistent** in major subgroups and between AAP and AAP + ENZ randomisation periods

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; MFS, metastasis-free survival

Attard G, et al. Ann Oncol. 2021;32 suppl 5:S1298 (ESMO 2021 oral presentation); Efstathiou, E. Discussant Abstract #LBA4_PR. ESMO 2021

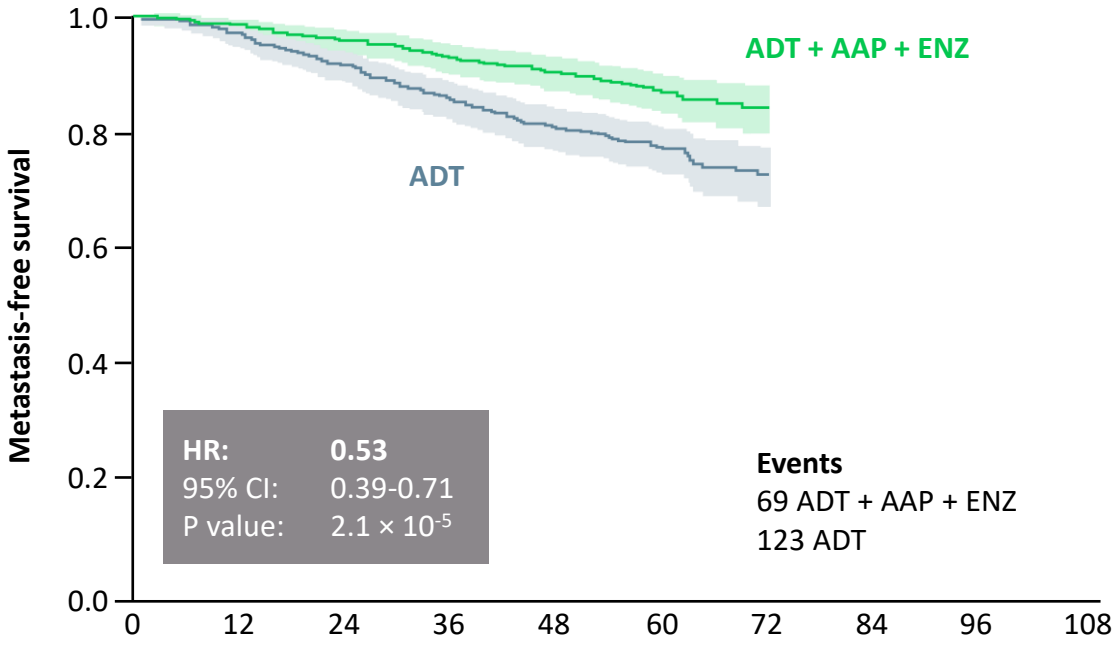
STAMPEDE: RESULTS

MFS BY RANDOMISATION PERIOD



ADT										
At-risk	455	438	411	385	351	318	266	172	53	9
Censored	0	3	4	5	8	15	40	112	222	263
Event	0	14	40	65	96	122	149	171	180	183
ADT + AAP										
At-risk	459	441	426	411	391	362	312	198	71	14
Censored	0	9	13	13	14	22	58	157	279	334
Event	0	9	20	35	54	75	89	104	109	111

Kaplan–Meier estimates with 95% CI in lighter shade



ADT							
At-risk	533	512	483	451	416	232	63
Censored	0	5	7	9	18	186	347
Event	0	16	43	73	99	115	123
ADT + AAP + ENZ							
At-risk	527	507	491	473	448	260	57
Censored	0	12	15	18	31	203	402
Event	0	8	21	36	48	64	68

Kaplan–Meier estimates with 95% CI in lighter shade

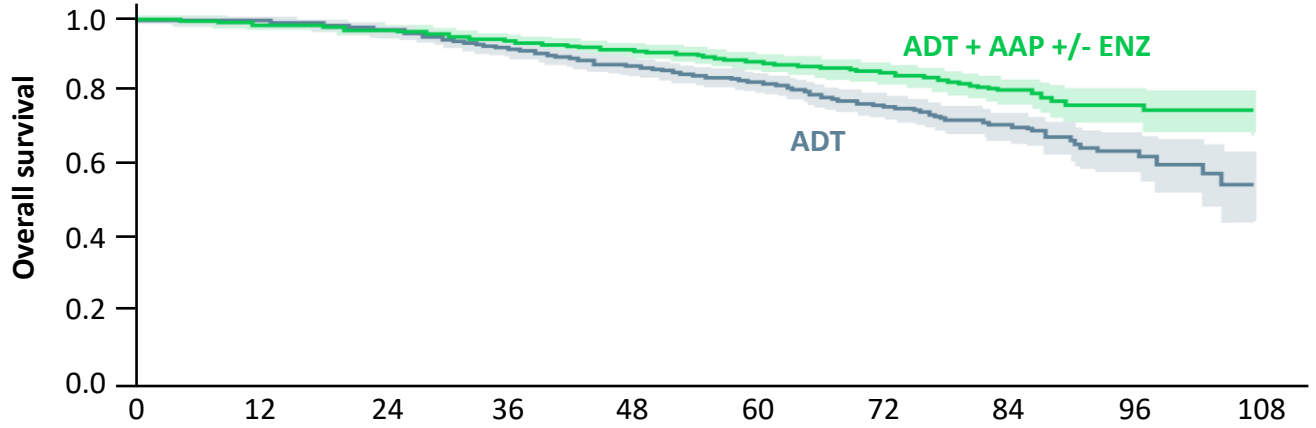
Interaction HR: 1.02 (95% CI: 0.70-1.50) p=0.908

AAP, abiraterone and prednisolone; ADT, androgen deprivation therapy; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; MFS, metastasis-free survival

Attard G, et al. Ann Oncol. 2021;32 suppl 5:S1298 (ESMO 2021 oral presentation); Efstathiou, E. Discussant abstract #LBA4_PR. ESMO 2021

STAMPEDE: RESULTS

OVERALL SURVIVAL



ADT										
At-risk	988	974	947	901	837	610	368	200	63	10
Censored	0	8	11	14	28	616	421	568	693	742
Event	0	6	30	73	123	162	199	220	232	236
ADT + AAP +/- ENZ										
At-risk	986	956	928	899	861	645	386	205	74	16
Censored	0	21	29	32	46	234	477	641	766	823
Event	0	9	29	55	79	107	123	140	146	147

Kaplan–Meier estimates with 95% CI in lighter shade

Events
147 ADT + AAP +/- ENZ
236 ADT

HR:	**0.60**
95% CI:	0.48-0.73
P value:	9.3×10^{-7}

6-year survival improved from 77% to 86%

Non-proportional hazards p=0.1

- **OS: treatment effect was consistent** between AAP and AAP + ENZ randomisation periods:
  - **ADT + AAP:** HR 0.63 (95% CI: 0.48-0.82), p=0.0005
  - **ADT + AAP + ENZ:** HR 0.54 (95% CI: 0.39-0.76), p=0.00043
    - Interaction between comparisons p=0.5

AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; OS, overall survival
Attard G, et al. Ann Oncol. 2021;32 suppl 5:S1298 (ESMO 2021 oral presentation); Efstathiou, E. Discussant Abstract #LBA4_PR. ESMO 2021

STAMPEDE: SUMMARY

- **2 years of AAP-based therapy** significantly improved MFS and OS of high-risk M0 PCa patients starting ADT and **should be considered a new standard of** care
- Adding ENZA to AAP increased toxicity but has **no apparent effect on efficacy**

Clinical perspective:

- Addressed an unmet need for high-risk M0 PCa patients
- MFS and OS results are clinically meaningful
- No quality of life data or long-term adverse event data at this stage

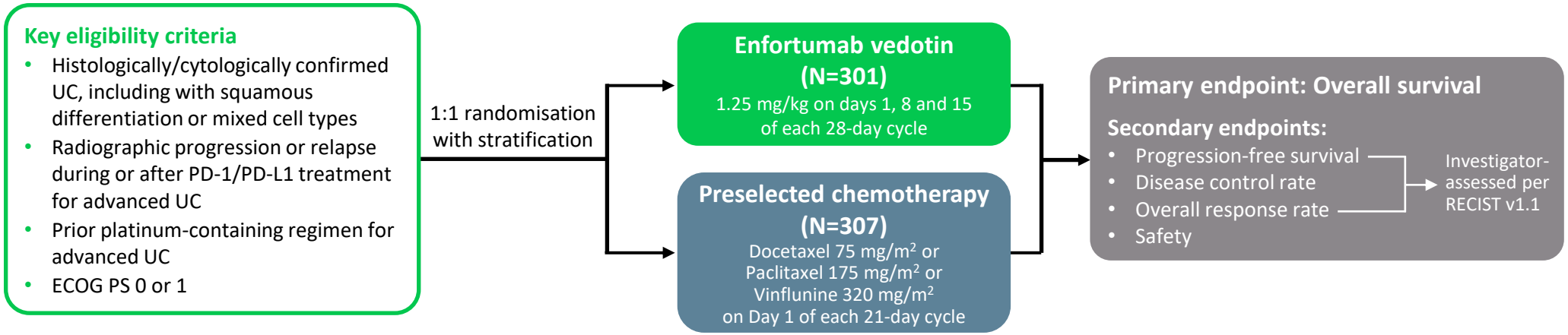
AAP, abiraterone and prednisone; ADT, androgen deprivation therapy; ENZA, enzalutamide; M0, non-metastatic; M1, metastatic; MFS, metastasis-free survival; OS, overall survival; PCa, prostate cancer

Attard G, et al. Ann Oncol. 2021;32 suppl 5:S1298 (ESMO 2021 oral presentation); Efstathiou, E. Discussant Abstract #LBA4_PR. ESMO 2021

UROTHELIAL CARCINOMA
2021 HIGHLIGHTS

EV-301: BACKGROUND AND STUDY DESIGN

- Patients with advanced urothelial carcinoma have poor overall survival after platinum-containing chemotherapy and programmed cell death protein 1 (PD-1) or programmed death ligand 1 (PD-L1) inhibitor treatment
- Enfortumab vedotin is an antibody-drug conjugate directed to nectin-4, a cell adhesion molecule highly expressed in urothelial carcinoma
- EV-301 was a phase 3 trial of enfortumab vedotin versus chemotherapy in patients with previously treated locally advanced or metastatic urothelial carcinoma



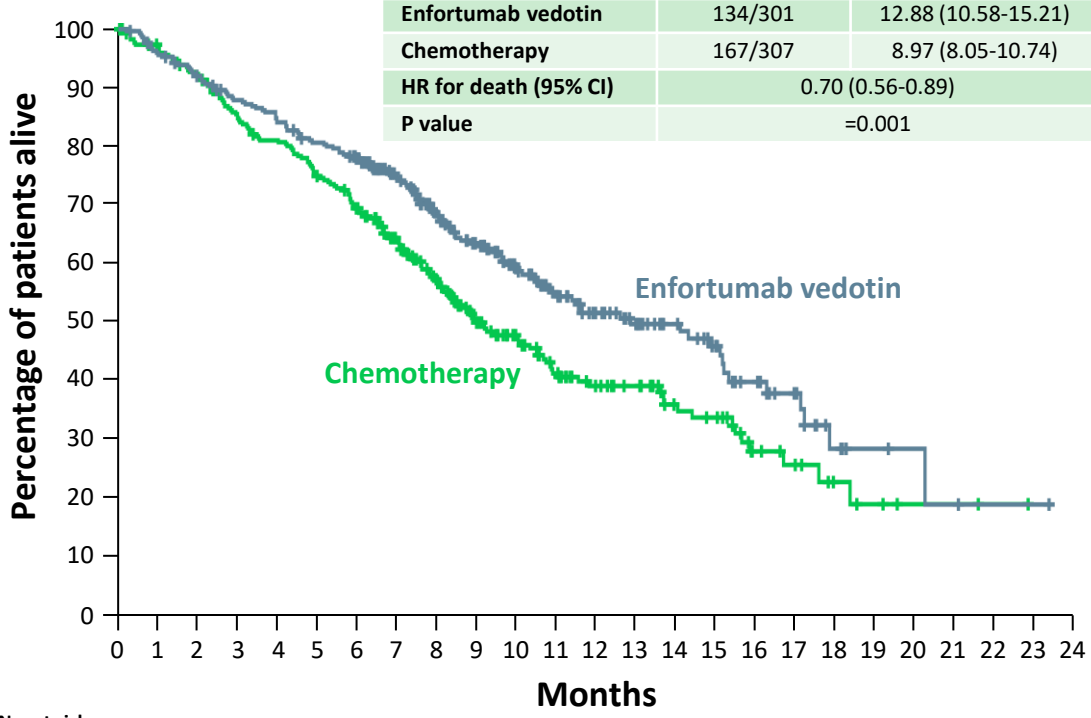
ECOG PS, Eastern Cooperative Oncology Group performance status; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumours; UC, urothelial cell carcinoma

Powles T, et al. N Engl J Med. 2021;384:1125-35; Powles T, et al. J Clin Oncol. 2021;39 suppl 6:393

EV-301: RESULTS

OVERALL SURVIVAL ACCORDING TO TREATMENT GROUP

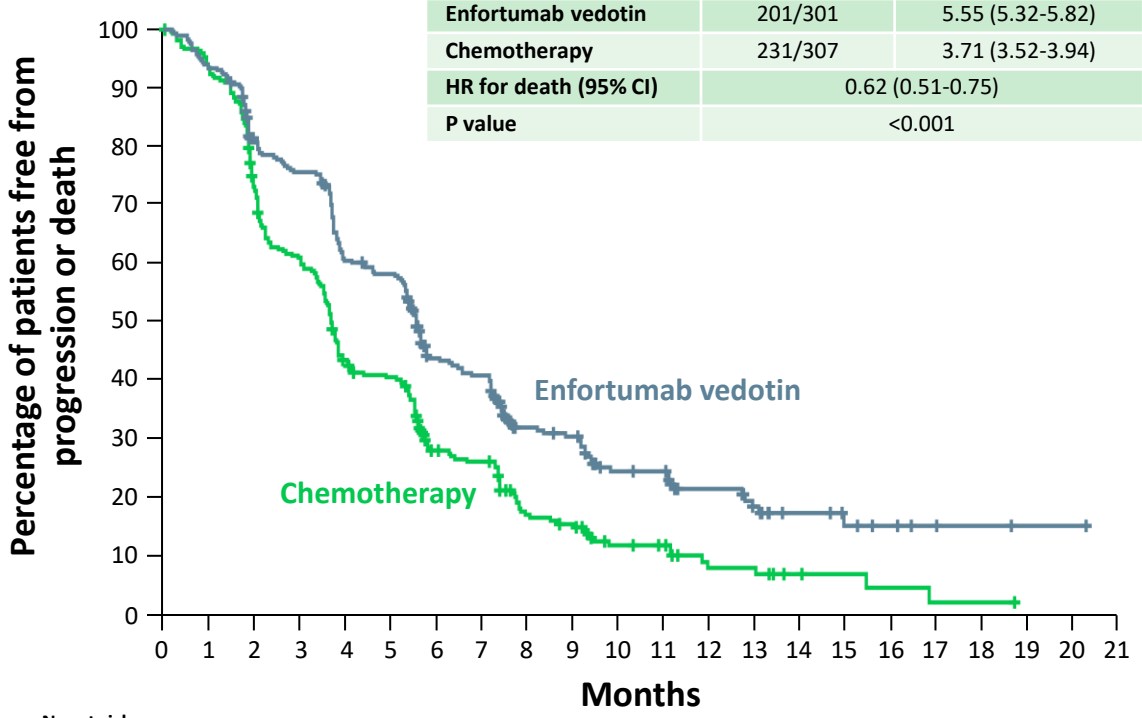
	No. of deaths/ No. of patients	Median overall survival (95% CI) mo
Enfortumab vedotin	134/301	12.88 (10.58-15.21)
Chemotherapy	167/307	8.97 (8.05-10.74)
HR for death (95% CI)	0.70 (0.56-0.89)	
P value	=0.001	



No. at risk																								
Enfortumab vedotin	301	286	272	257	246	234	222	190	158	130	105	85	63	52	42	33	23	15	7	4	3	2	1	1	0
Chemotherapy	307	288	274	250	238	219	198	163	131	101	84	66	51	44	32	29	16	11	6	4	2	2	1	0	0

PROGRESSION-FREE SURVIVAL – ITT POPULATION

	No. of deaths/ No. of patients	Median progression-free survival (95% CI) mo
Enfortumab vedotin	201/301	5.55 (5.32-5.82)
Chemotherapy	231/307	3.71 (3.52-3.94)
HR for death (95% CI)	0.62 (0.51-0.75)	
P value	<0.001	



No. at risk																								
Enfortumab vedotin	301	269	224	208	165	158	102	95	60	56	38	36	23	17	11	7	5	2	2	1	1	0		
Chemotherapy	307	259	200	166	116	107	62	57	33	29	18	16	8	8	4	3	2	1	1	0	0	0		

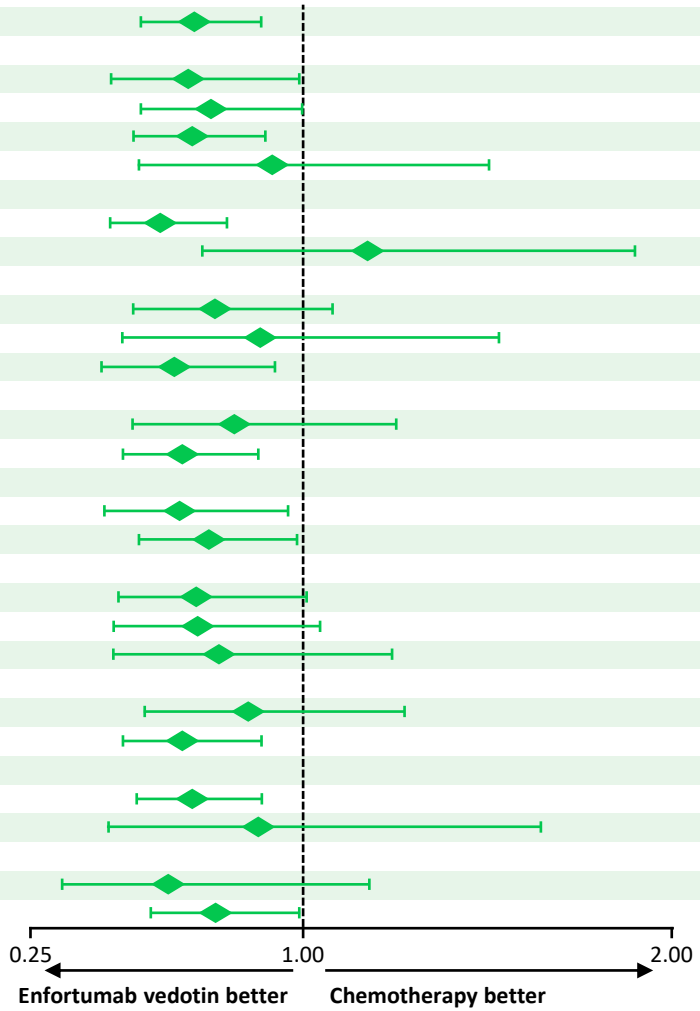
CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; mo, months

Powles T, et al. N Engl J Med. 2021;384:1125-35

EV-301: RESULTS

DEATHS ACCORDING TO SUBGROUP

Subgroup	Enfortumab vedotin	Chemotherapy	Hazard ratio (95% CI)
	No. of deaths/no. of patients		
All patients	134/301	167/307	0.70 (0.56-0.89)
Age group			
<65 yr	49/108	66/111	0.68 (0.47-0.99)
≥65 yr	85/193	101/196	0.75 (0.56-1.00)
<75 yr	109/249	128/239	0.69 (0.53-0.89)
≥75 yr	25/52	39/68	0.91 (0.55-1.51)
Sex			
Male	101/238	132/232	0.61 (0.47-0.79)
Female	33/63	35/75	1.17 (0.72-1.89)
Geographic region			
Western Europe	57/126	72/129	0.76 (0.53-1.07)
United States	25/43	25/44	0.88 (0.51-1.54)
Rest of the world	52/132	70/134	0.64 (0.45-0.92)
ECOG performance status			
0	40/120	46/124	0.81 (0.53-1.24)
1	94/181	121/183	0.67 (0.51-0.87)
Liver metastasis			
Yes	53/93	63/95	0.66 (0.46-0.96)
No	81/208	104/212	0.73 (0.55-0.98)
Preselected chemotherapy			
Paclitaxel	63/141	59/112	0.71 (0.49-1.10)
Docetaxel	41/87	67/117	0.71 (0.48-1.04)
Vinflunine	30/73	41/78	0.77 (0.48-1.24)
Primary site of tumour			
Upper urinary tract	44/98	52/107	0.85 (0.57-1.27)
Bladder or other site	90/203	115/200	0.67 (0.51-0.88)
Previous systemic therapies			
1-2	115/262	147/270	0.69 (0.54-0.88)
≥3	19/39	20/37	0.88 (0.47-1.64)
Best response among patients who previously received CPI treatment			
Response	18/61	23/50	0.63 (0.34-1.17)
No response	100/207	120/215	0.76 (0.58-0.99)



CI, confidence interval, CPI, checkpoint inhibitor; ECOG, Eastern Cooperative Oncology Group; yr, year

Powles T, et al. N Engl J Med. 2021;384:1125-35

EV-301: RESULTS

TREATMENT-RELATED ADVERSE EVENTS (SAFETY POPULATION)

Adverse event	Enfortumab Vedotin Group (N=296)		Chemotherapy Group (N=291)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Adverse event	278 (93.9)	152 (51.4)	267 (91.8)	145 (49.8)
Alopecia	134 (45.3)	0	106 (36.4)	0
Peripheral sensory neuropathy†	100 (33.8)	9 (3.0)	62 (21.3)	6 (2.1)
Pruritus	95 (32.1)	4 (1.4)	13 (4.5)	0
Fatigue	92 (31.1)	19 (6.4)	66 (22.7)	13 (4.5)
Decreased appetite	91 (30.7)	9 (3.0)	68 (23.4)	5 (1.7)
Diarrhoea	72 (24.3)	10 (3.4)	48 (16.5)	5 (1.7)
Dysgeusia	72 (24.3)	0	21 (7.2)	0
Nausea	67 (22.6)	3 (1.0)	63 (21.6)	4 (1.4)
Maculopapular rash	48 (16.2)	22 (7.4)	5 (1.7)	0
Anaemia	34 (11.5)	8 (2.7)	59 (20.3)	22 (7.6)
Decreased neutrophil count	30 (10.1)	18 (6.1)	49 (16.8)	39 (13.4)
Neutropenia	20 (6.8)	14 (4.7)	24 (8.2)	18 (6.2)
Decreased white-cell count	16 (5.4)	4 (1.4)	31 (10.7)	20 (6.9)
Febrile neutropenia	2 (0.7)	2 (0.7)	16 (5.5)	16 (5.5)

† A total of 113 patients (55 in the enfortumab vedotin group and 58 in the chemotherapy group) had preexisting peripheral neuropathy

Powles T, et al. N Engl J Med. 2021;384:1125-35

EV-301: SUMMARY

GU connect® POWERED BY COR2ED

Enfortumab vedotin:

- Had superior overall survival compared with chemotherapy in patients with advanced urothelial carcinoma who had previously received platinum-based chemotherapy and a PD-1/PD-L1 inhibitor
- Showed superior progression-free survival and response rates compared with chemotherapy
- Demonstrated a tolerable and manageable safety profile, with no new safety signals identified
- Is the first drug, beyond chemotherapy and immunotherapy, to show significant survival advantage in previously treated advanced urothelial carcinoma

PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1

Powles T, et al. N Engl J Med. 2021;384:1125-35

KEY APPROVALS: UROTHELIAL CANCER

FDA APPROVALS

FDA approves nivolumab for adjuvant treatment of urothelial carcinoma

Share Tweet Linkedin Email Print

On August 19, 2021, the Food and Drug Administration approved nivolumab (Opdivo, Bristol-Myers Squibb Co.) for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection.

This is the first FDA approval for adjuvant treatment of patients with high-risk UC. The results supporting this approval also supported the conversion of nivolumab's accelerated approval for advanced/metastatic UC to a regular approval.

Nivolumab was investigated in CHECKMATE-274 (NCT02632409), a randomized, double-blind, placebo-controlled trial in patients who were within 120 days of radical resection of UC of the bladder or upper urinary tract (renal pelvis or ureter) at high risk of recurrence. Patients were randomized (1:1) to receive nivolumab 240 mg or placebo by intravenous infusion every 2 weeks until recurrence or until unacceptable toxicity for a maximum treatment duration of 1 year.

The primary efficacy endpoint was investigator-assessed disease-free survival (DFS) in the intent-to-treat (ITT) population and in patients with tumors expressing PD-L1 ≥1%. DFS was defined as time -to- first recurrence (local urothelial tract, local non-urothelial tract, or distant metastasis), or death. At a prespecified interim analysis, a statistically significant improvement in DFS was demonstrated in patients on the nivolumab arm vs. placebo for both primary endpoints. In the ITT analysis, the median DFS was 20.8 months (95% CI: 16.5, 27.6) in patients who received nivolumab compared with 10.8 months (95% CI: 8.3, 13.9) in patients who received placebo (HR 0.70; 95% CI: 0.57, 0.86; p=0.0008). For patients with tumors expressing PD-L1 ≥1%, median DFS was not reached (95% CI: 21.2, not estimable) in those who received nivolumab vs. 8.4 months (95% CI: 5.6, 21.2) for patients who received placebo (HR 0.55; 95% CI: 0.39, 0.77; p=0.0005).

In an exploratory analysis of patients with PD-L1-negative tumors (58%), the unstratified DFS hazard ratio estimate was 0.83 (95% CI: 0.64, 1.08). OS data is immature with 33% of

FDA grants regular approval to enfortumab vedotin-ejfv for locally advanced or metastatic urothelial cancer

Share Tweet Linkedin Email Print

On July 9, 2021, the Food and Drug Administration approved enfortumab vedotin-ejfv (Padcev, Astellas Pharma US, Inc.), a Nectin-4-directed antibody and microtubule inhibitor conjugate, for adult patients with locally advanced or metastatic urothelial cancer who

- have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, or
- are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy.

FDA granted accelerated approval in December 2019 to enfortumab vedotin-ejfv for patients with locally advanced or metastatic urothelial cancer who have received a PD-1 or PD-L1 inhibitor and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting.

Trial EV-301 (NCT03474107) was an open-label, randomized, multicenter trial required to confirm the clinical benefit of the 2019 accelerated approval. This trial enrolled 608 patients with locally advanced or metastatic urothelial cancer who received a prior PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. Patients were randomized (1:1) to receive either enfortumab vedotin-ejfv (EV) 1.25 mg/kg on days 1, 8 and 15 of a 28-day cycle or investigator's choice of single-agent chemotherapy (docetaxel, paclitaxel, or vinflunine).

The primary efficacy endpoint was overall survival (OS) with key secondary efficacy endpoints of progression-free survival (PFS), and overall response rate (ORR) assessed by investigator using RECIST 1.1. Median OS was 12.9 months (95% CI: 10.6, 15.2) for patients on the EV arm (n=301) versus 9.0 months for those receiving chemotherapy

FDA grants accelerated approval to sacituzumab govitecan for advanced urothelial cancer

Share Tweet Linkedin Email Print

On April 13, 2021, the Food and Drug Administration granted accelerated approval to sacituzumab govitecan (Trodelvy, Immunomedics Inc.) for patients with locally advanced or metastatic urothelial cancer (mUC) who previously received a platinum-containing chemotherapy and either a programmed death receptor-1 (PD-1) or a programmed death-ligand 1 (PD-L1) inhibitor.

Efficacy and safety were evaluated in TROPHY (IMMU-132-06; NCT03547973), a single-arm, multicenter trial that enrolled 112 patients with locally advanced or mUC who received prior treatment with a platinum-containing chemotherapy and either a PD-1 or PD-L1 inhibitor. Patients received sacituzumab govitecan, 10 mg/kg intravenously, on days 1 and 8 of a 21-day treatment cycle.

The main efficacy endpoints were objective response rate (ORR) and duration of response (DOR), evaluated by independent review using RECIST 1.1 criteria. The confirmed ORR was 27.7% (95% CI:19.6, 36.9) with 5.4% complete responses and 22.3% partial responses. The median DOR was 7.2 months (n=31; 95% CI: 4.7, 8.6; range 1.4+, 13.7).

Most common adverse reactions (incidence >25%) in patients receiving sacituzumab govitecan are neutropenia, nausea, diarrhea, fatigue, alopecia, anemia, vomiting, constipation, decreased appetite, rash, and abdominal pain.

The recommended sacituzumab govitecan dose is 10 mg/kg once weekly on days 1 and 8 of 21-day treatment cycles until disease progression or unacceptable toxicity.

View full prescribing information for Trodelvy.

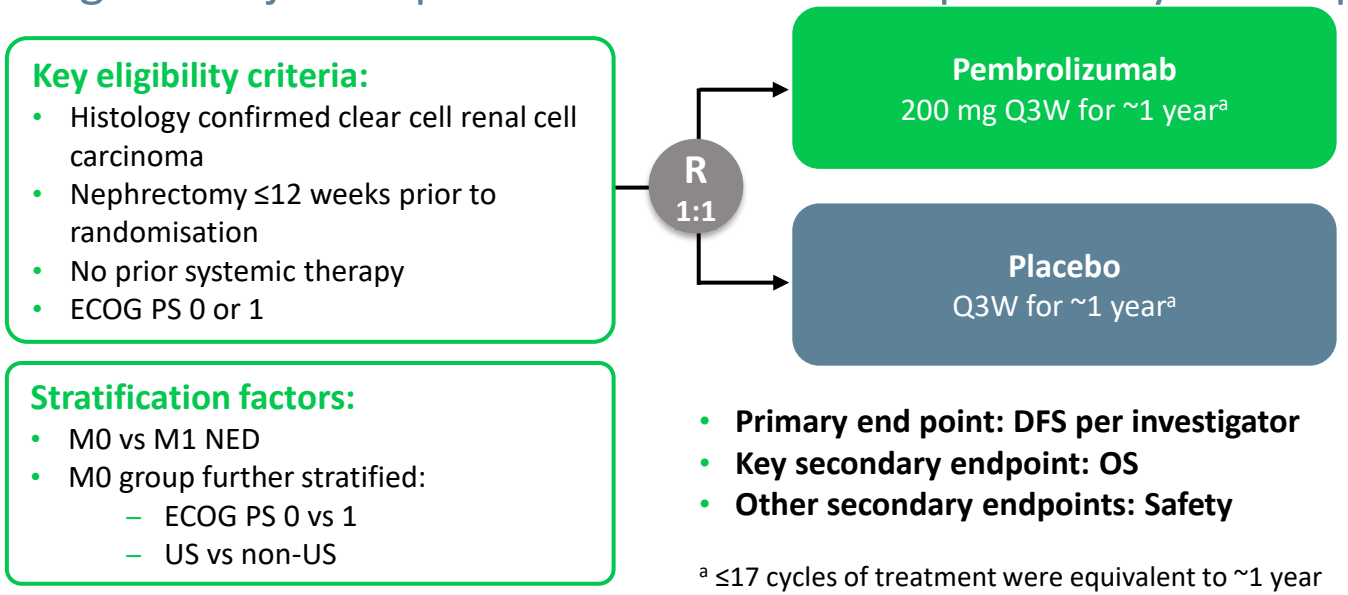
This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

www.fda.gov/drugs/. Accessed 16 November 2021

RENAL CELL CARCINOMA
2021 HIGHLIGHTS

KEYNOTE-564: BACKGROUND AND STUDY DESIGN

- Nephrectomy is the standard of care for locoregional renal cell carcinoma (RCC)
- Up to 40% of patients with locoregional RCC experience disease recurrence after surgery and develop metastasis
- KEYNOTE-564 investigated adjuvant pembrolizumab after nephrectomy in RCC patients



DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; M0, non-metastatic; M1, metastatic; NED, no evidence of disease; OS, overall survival; Q3W, every 3 weeks; RCC, renal cell carcinoma

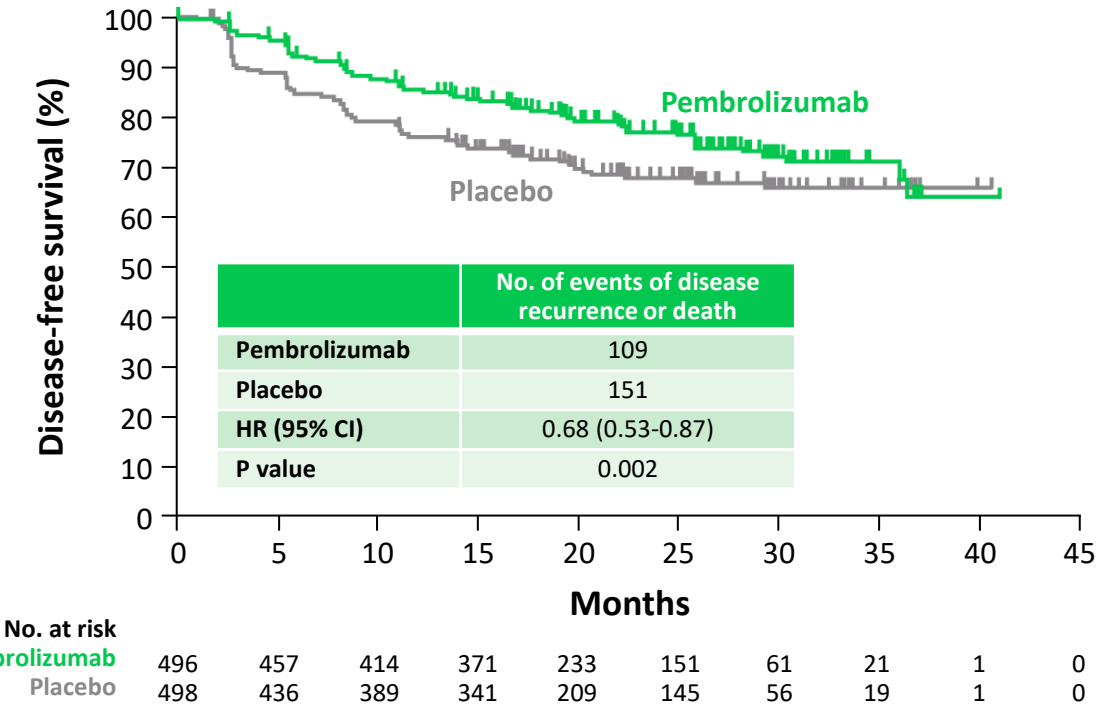
Choueiri TK, et al. J Clin Oncol. 2021;39 suppl 15:LBA5 (ASCO 2021 oral presentation); National Comprehensive Cancer Network. Kidney Cancer (Version 3.2022). https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf; Escudier B, et al. Ann Oncol. 2019;30:706-20; Smaldone MC, et al. Hematol Oncol North Am. 2011;25:765-91; Sun M, et al. Eur Urol. 2018;74:611-20; Correa AF, et al. J Clin Oncol. 2019;37:2062-71

KEYNOTE-564: RESULTS

BASELINE CHARACTERISTICS (ITT POPULATION)

Characteristic	Pembrolizumab (N=496)	Placebo (N=498)
Age		
Median (range), yr	60.0 (27-81)	60.0 (25-84)
≥65 yr, n (%)	158 (31.9)	172 (34.5)
Male sex, n (%)	347 (70.0)	359 (72.1)
ECOG performance status score of 1, n (%)	75 (15.1)	72 (14.5)
Geographic location		
North America	133 (26.8)	125 (25.1)
European Union	188 (37.9)	187 (37.6)
Rest of the world	175 (35.3)	186 (37.3)
Radical nephrectomy, n (%)	459 (92.5)	460 (92.4)
Sarcomatoid features, n (%)		
Present	52 (10.5)	59 (11.8)
Absent	417 (84.1)	415 (83.3)
Unknown	27 (5.4)	24 (4.8)
Disease risk category, n (%)		
M0, intermediate-to-high risk	427 (86.1)	433 (86.9)
M0, high risk	40 (8.1)	36 (7.2)
M1 NED	29 (5.8)	29 (5.8)
PD-L1 combined positive score, n (%)		
<1	124 (25.0)	113 (22.7)
≥1	365 (73.6)	383 (76.9)
Missing data	7 (1.4)	2 (0.4)

DFS BY INVESTIGATOR (ITT POPULATION)

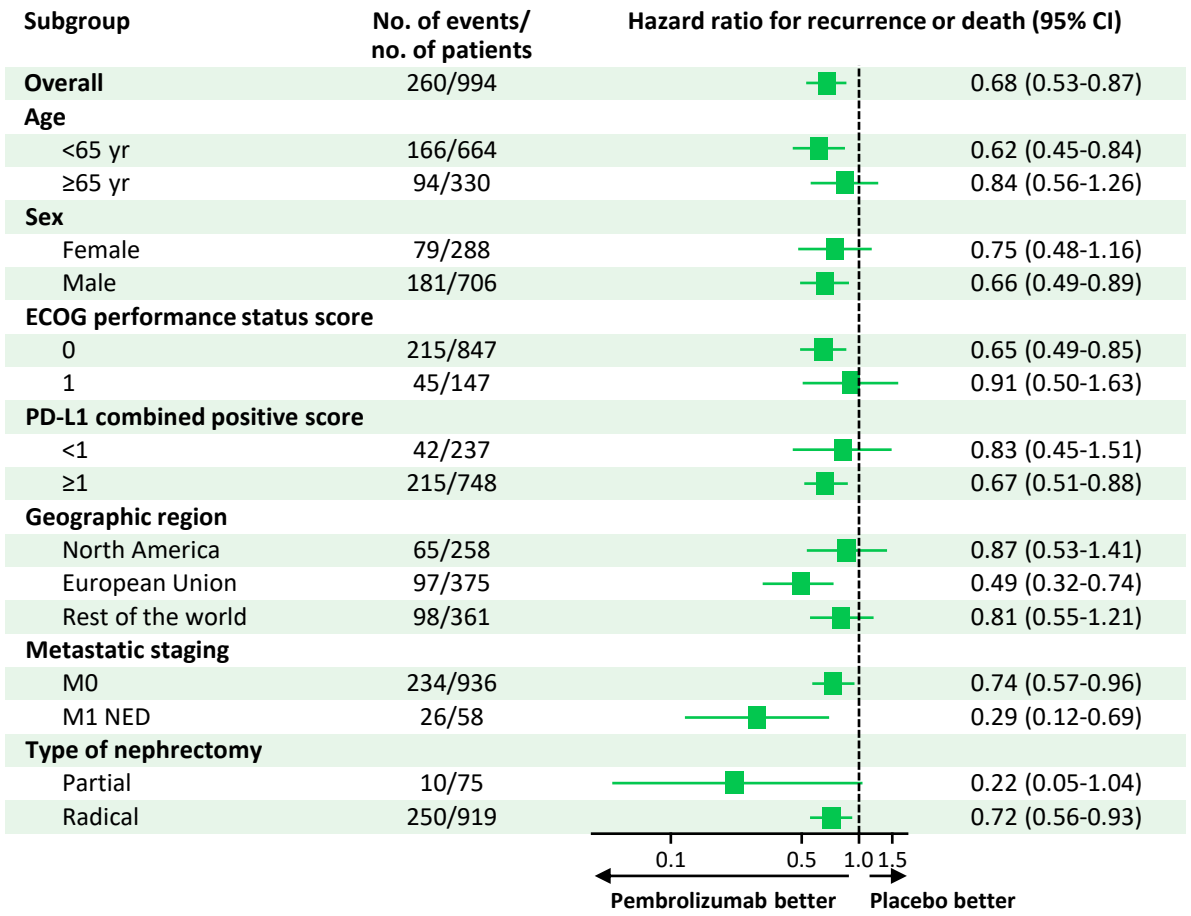


CI, confidence interval; DFS, disease-free survival; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; ITT, intention-to-treat; M0, non-metastatic; M1, metastatic; NED, no evidence of disease; PD-L1, programmed death ligand 1; yr, year

Choueiri TK, et al. J Clin Oncol. 2021;39 suppl 15:LBA5 (ASCO 2021 oral presentation); Choueiri TK, et al. N Engl J Med. 2021;385:683-94

KEYNOTE-564: RESULTS

DFS BY INVESTIGATOR IN SUBGROUPS (ITT POPULATION)



ANY CAUSE AND TRAE (AS-TREATED POPULATION)

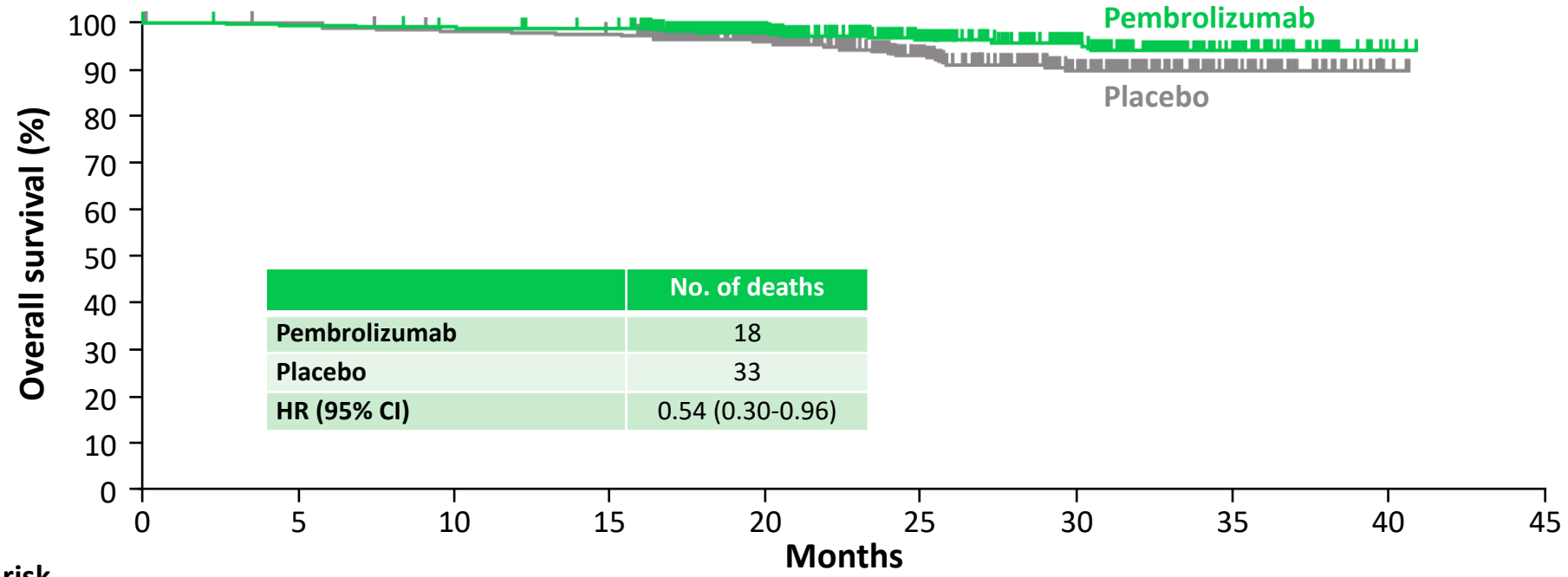
EVENT	Pembrolizumab (N=488)	Placebo (N=496)
Any-cause adverse events, n (%)		
Adverse event of any grade	470 (96.3)	452 (91.1)
Adverse event of grade 3 to 5	158 (32.4)	88 (17.7)
Discontinuation of pembrolizumab or placebo due to adverse event	101 (20.7)	10 (2.0)
Death due to adverse event	2 (0.4)	1 (0.2)
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, n (%)		
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

CI, confidence interval; DFS, disease-free survival; ECOG, Eastern Cooperative Oncology Group; ITT, intention-to-treat; M0, non-metastatic; M1, metastatic; NED, no evidence of disease; PD-L1, programmed death ligand 1; TRAE, treatment-related adverse event; yr, year

Choueiri TK, et al. J Clin Oncol. 2021;39 suppl 15:LBA5 (ASCO 2021 oral presentation); Choueiri T, et al. N Engl J Med. 2021;385:683-94

KEYNOTE-564: RESULTS

INTERIM OS DATA (ITT POPULATION)



	No. of deaths
Pembrolizumab	18
Placebo	33
HR (95% CI)	0.54 (0.30-0.96)

No. at risk										
Pembrolizumab	496	490	486	482	338	215	124	51	3	0
Placebo	498	494	485	480	336	209	117	48	3	0

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival

Choueiri TK, et al. J Clin Oncol. 2021;39 suppl 15:LBA5 (ASCO 2021 oral presentation); Choueiri T, et al. N Engl J Med. 2021;385:683-94

KEYNOTE-564: SUMMARY

- Adjuvant pembrolizumab post-nephrectomy demonstrated a statistically significant and clinically meaningful improvement in DFS compared with placebo
  - This benefit was consistent across subgroups
- Safety data were as expected with no new safety signals observed
- Pembrolizumab is a potential new standard of care for RCC patients in the adjuvant setting

DFS, disease free survival; RCC, renal cell carcinoma

Choueiri TK, et al. J Clin Oncol. 2021;39 suppl 15:LBA5 (ASCO 2021 oral presentation); Choueiri T, et al. N Engl J Med. 2021;385:683-94

KEY APPROVALS: RENAL CELL CARCINOMA

GU connect® POWERED BY COR2ED

FDA APPROVALS

FDA approves nivolumab plus cabozantinib for advanced renal cell carcinoma

Share Tweet Linkedin Email Print

On January 22, 2021, the Food and Drug Administration approved the combination of nivolumab (Opdivo, Bristol-Myers Squibb Co.) and cabozantinib (Cabometyx, Exelixis) as first-line treatment for patients with advanced renal cell carcinoma (RCC).

Efficacy was evaluated in CHECKMATE-9ER (NCT03141177), a randomized, open-label trial in patients with previously untreated advanced RCC. Patients were randomized to receive either nivolumab 240 mg over 30 minutes every 2 weeks in combination with cabozantinib 40 mg orally once daily (n=323) or sunitinib 50 mg orally daily for the first 4 weeks of a 6-week cycle (4 weeks on treatment followed by 2 weeks off) (n=328).

The trial demonstrated a statistically significant improvement in progression-free survival (PFS), overall survival (OS) and confirmed overall response rate (ORR) for patients treated with nivolumab plus cabozantinib compared with those who received sunitinib. Median PFS per blinded independent central review (BICR) was 16.6 months versus 8.3 months; HR 0.51 (95% CI: 0.41, 0.64). Median OS was not reached in either arm; HR 0.60 (95% CI: 0.40, 0.89). Confirmed ORR per BICR was 55.7% and 27.1% in the nivolumab plus cabozantinib and sunitinib arms, respectively.

The most common adverse reactions (≥ 20%) in patients receiving the combination of nivolumab and cabozantinib were diarrhea, fatigue, hepatotoxicity, palmar-plantar erythrodysaesthesia syndrome, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

The recommended dose is nivolumab 240 mg every 2 weeks (30-minute intravenous infusion) or 480 mg every 4 weeks (30-minute intravenous infusion) in combination with cabozantinib 40 mg orally once daily without food until disease progression or

FDA approves lenvatinib plus pembrolizumab for advanced renal cell carcinoma

Subscribe to Email Updates Share Tweet Linkedin Email Print

On August 10, 2021, the Food and Drug Administration approved the combination of lenvatinib (Lenvima, Eisai) plus pembrolizumab (Keytruda, Merck) for first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

The efficacy of this combination was investigated in CLEAR (Study 307/KEYNOTE-581; NCT02811861), a multicenter, open-label, randomized phase 3 trial in patients with advanced RCC in the first-line setting. Patients were enrolled regardless of PD-L1 tumor expression status. The efficacy population supporting this approval included patients randomized to lenvatinib plus pembrolizumab (n=355) compared with those randomized to single-agent sunitinib (n=357).

Progression-free survival (PFS), assessed by independent radiologic review according to RECIST 1.1, and overall survival (OS) were the major efficacy endpoints. Patients receiving pembrolizumab with lenvatinib had a median PFS of 23.9 months (95% CI: 20.8, 27.7) compared with 9.2 months (95% CI: 6.0, 11.0) for those receiving sunitinib (HR 0.39; 95% CI: 0.32, 0.49; p<0.0001). Median OS was not reached in either arm (HR 0.66; 95% CI: 0.49, 0.88; p=0.0049). The objective response rates were 71% (95% CI: 66, 76) and 36% (95% CI: 31, 41; p<0.0001); complete response rates were 16% and 4% on the combination and sunitinib arms, respectively.

The most common adverse reactions reported in ≥ 20% of patients who received lenvatinib and pembrolizumab in clinical trials are fatigue, diarrhea, musculoskeletal pain, hypothyroidism, hypertension, stomatitis, decreased appetite, rash, nausea, decreased weight, dysphonia, proteinuria, palmar-plantar erythrodysesthesia syndrome, abdominal pain, hemorrhagic events, vomiting, constipation, hepatotoxicity, headache, and acute kidney injury. Arterial thrombotic events occurred in 5% of patients in CLEAR, including myocardial infarction (3.4%) and cerebrovascular accident (2.3%).

The recommended dosages for patients with advanced RCC are lenvatinib 20 mg orally

www.fda.gov/drugs/. Accessed 16 November 2021

KEY APPROVALS: RENAL CELL CARCINOMA

FDA APPROVALS

FDA approves tivozanib for relapsed or refractory advanced renal cell carcinoma

Share | Tweet | Linkedin | Email | Print

On March 10, 2021, the Food and Drug Administration approved tivozanib (Fotivda, AVEO Pharmaceuticals, Inc.), a kinase inhibitor, for adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

Efficacy was evaluated in TIVO-3 (NCT02627963), a randomized (1:1), open-label, multicenter trial of tivozanib versus sorafenib in patients with relapsed or refractory advanced RCC who received two or three prior systemic treatments,including at least one VEGFR kinase inhibitor other than sorafenib or tivozanib. Patients were randomized to either tivozanib 1.34 mg orally once daily for 21 consecutive days every 28 days or sorafenib 400 mg orally twice a day continuously, until disease progression or unacceptable toxicity.

The main efficacy outcome measure was progression-free survival (PFS), assessed by a blinded independent radiology review committee. Other efficacy endpoints were overall survival (OS) and objective response rate (ORR).

Median PFS was 5.6 months (95% CI: 4.8, 7.3) in the tivozanib arm (n=175) compared with 3.9 months (95% CI: 3.7, 5.6) for those treated with sorafenib (HR 0.73; 95% CI: 0.56, 0.95; p=0.016). Median OS was 16.4 (95% CI: 13.4, 21.9) and 19.2 months (95% CI: 14.9, 24.2), for the tivozanib and sorafenib arms, respectively (HR 0.97; 95% CI: 0.75, 1.24). The ORR was 18% (95% CI: 12%, 24%) for the tivozanib arm and 8% (95% CI: 4%, 13%) for the sorafenib arm.

The most common (≥20%) adverse reactions were fatigue, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis. The most common grade 3 or 4 laboratory abnormalities (≥5%) were decreased sodium, increased

FDA approves pembrolizumab for adjuvant treatment of renal cell carcinoma

Share | Tweet | Linkedin | Email | Print

On November 17, 2021, the Food and Drug Administration approved pembrolizumab (Keytruda, Merck) for the adjuvant treatment of patients with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

Efficacy was evaluated in KEYNOTE-564 (NCT03142334), a multicenter, randomized (1:1), double-blind, placebo-controlled trial in 994 patients with intermediate-high or high risk of recurrence of RCC, or M1 no evidence of disease. Patients were randomized to pembrolizumab 200 mg intravenously every 3 weeks or placebo for up to 1 year until disease recurrence or unacceptable toxicity.

The major efficacy outcome measure was investigator-assessed disease-free survival (DFS), defined as time to recurrence, metastasis, or death. An additional outcome measure was overall survival (OS). A statistically significant improvement in DFS was demonstrated at a prespecified interim analysis, with 109 (22%) events in the pembrolizumab arm and 151 (30%) events in those receiving placebo (HR 0.68; 95% CI: 0.53, 0.87; p=0.0010). Median DFS was not reached in either arm. At the time of the DFS analysis, OS data were not mature, with 5% deaths in the overall population.

The most common adverse reactions (≥20%) occurring in patients on this trial were musculoskeletal pain, fatigue, rash, diarrhea, pruritus, and hypothyroidism.

The recommended pembrolizumab dose is 200 mg every 3 weeks or 400 mg every 6 weeks

www.fda.gov/drugs/. Accessed 03 December 2021

REACH GU CONNECT VIA TWITTER, LINKEDIN, VIMEO & EMAIL OR VISIT THE GROUP'S WEBSITE

https://guconnect.cor2ed.com/

Follow us on Twitter
@guconnectinfo

Follow the
GU CONNECT
group on LinkedIn

Watch us on the
Vimeo Channel
GU CONNECT

Email
sam.brightwell@cor2ed.com

GU connect®

POWERED BY COR2ED

GU CONNECT
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND

Dr. Froukje Sosef MD

+31 6 2324 3636

froukje.sosef@cor2ed.com

Dr. Antoine Lacombe Pharm D, MBA

+41 79 529 42 79

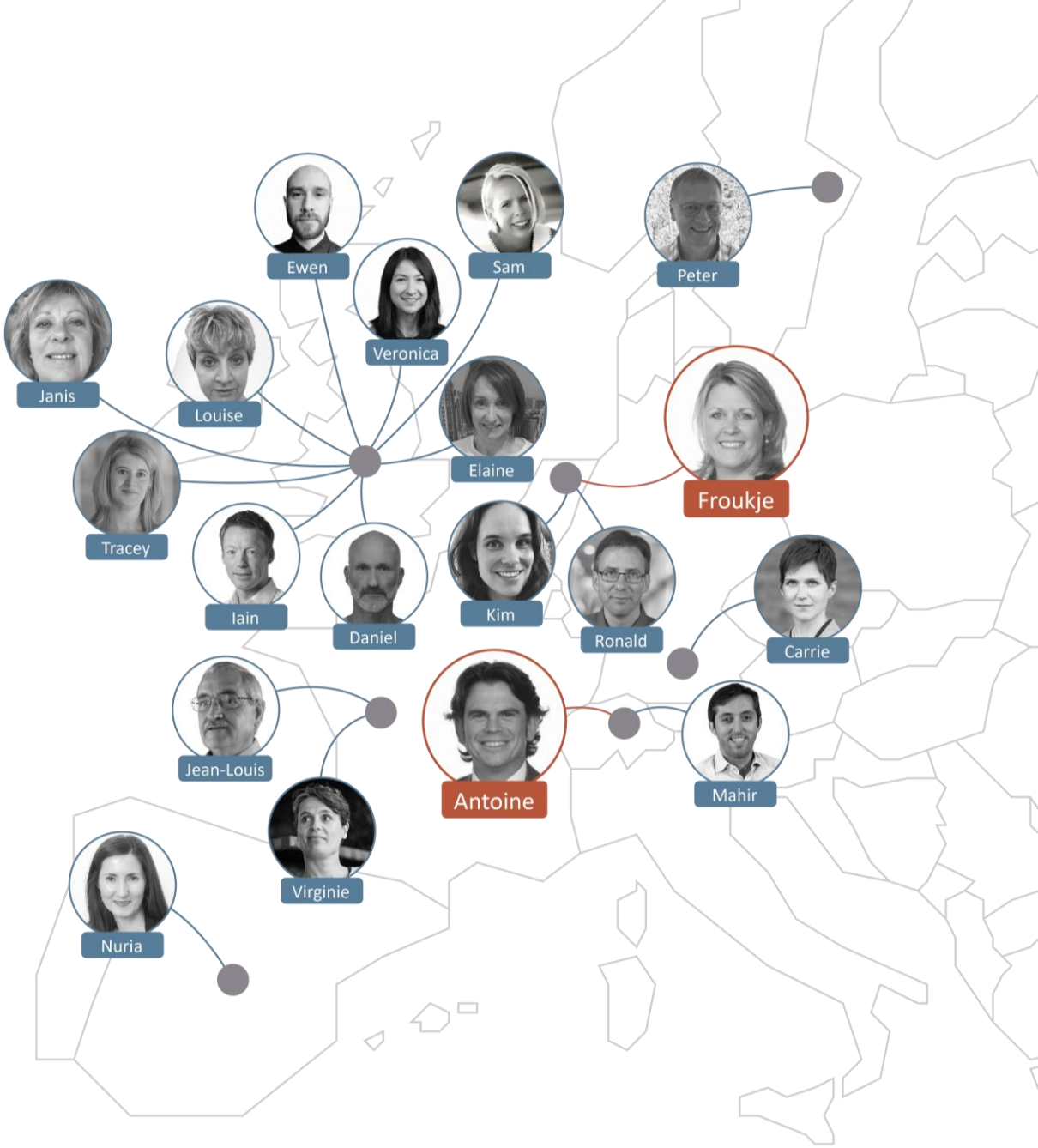
antoine.lacombe@cor2ed.com

Connect on
LinkedIn @GU CONNECT

Watch on
Vimeo @GU CONNECT

Visit us at
guconnect.cor2ed.com

Follow us on
Twitter @guconnectinfo



Heading to the heart of Independent Medical Education Since 2012