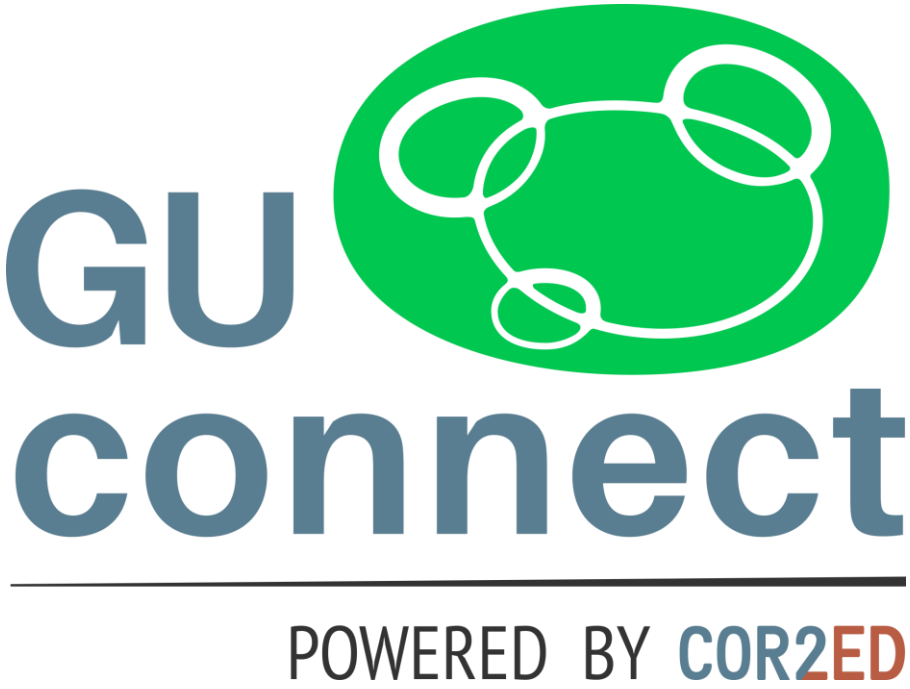
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MEETING SUMMARY
ESMO 2019, Barcelona, Spain

Prof. Neeraj Agarwal
Huntsman Cancer Institute,
University of Utah, USA

GENITOURINARY UPDATE

DISCLAIMER

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TOP 4 HIGH-IMPACT GENITOURINARY PRESENTATIONS AT ESMO 2019

PROfound:
PHASE 3 STUDY OF OLAPARIB VS ENZALUTAMIDE OR ABIRATERONE FOR mCRPC WITH HOMOLOGOUS RECOMBINATION REPAIR GENE ALTERATIONS

Hussain, et al. ESMO 2019 Abstract #LBA12

mCRPC, metastatic castration resistant prostate cancer

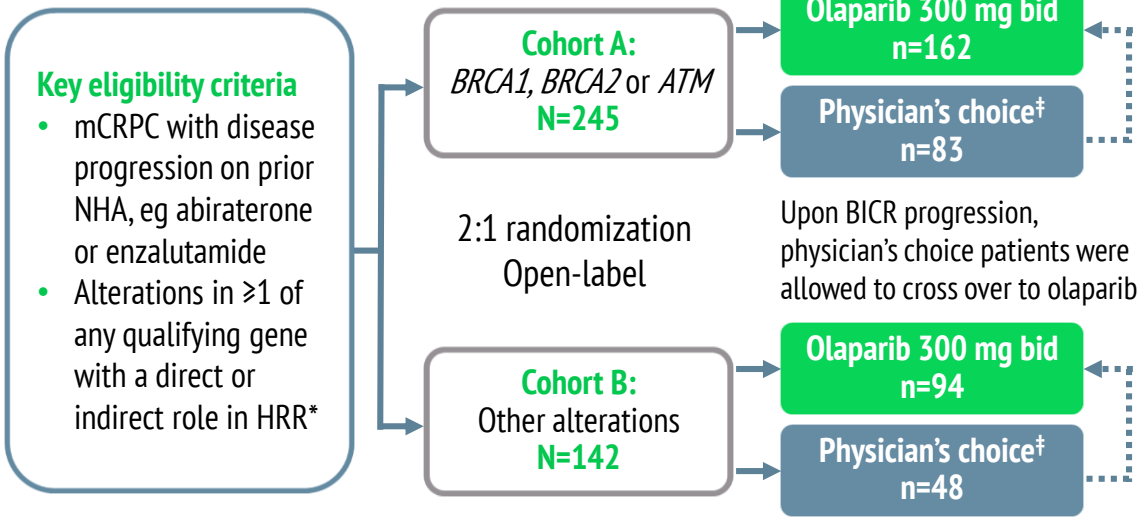
BACKGROUND

- **mCRPC is molecularly heterogenous** and **up to 30% of mCRPC harbours deleterious alterations in DNA damage repair genes**, including those with direct and indirect roles in homologous recombinant repair (HRR)[1-3]
- **These gene alterations are associated with response to PARP inhibition** of which *BRCA1, BRCA2* and *ATM* are the most well characterised[4-7]
- **Anti-tumour activity has been reported with the PARP inhibitor, olaparib,** in patients with prostate cancer harbouring HRR alterations[6,7]
- **PROfound is the first** randomised **prostate cancer trial to use biomarker selection** to identify which mCRPC patients may respond to treatment[8]

HRR, homologous recombinant repair; mCRPC, metastatic castration resistant prostate cancer; PARP, poly-ADP ribose polymerase

1. Robinson, D et al. Cell 2015; 161: 1215-28; 2. Pritchard, C et al, NEJM 2016; 375: 443-53; 3. Abida, W et al. JCO Precis Oncol 2017; 4. Abida, W et al. Ann Onc 2018; 29: abstract 793PD; 5. Smith, MR et al. JCO 2019; 37: abstract 202; 6. Mateo, J et al. NEJM 2015; 373; 1697-708; 7.Mateo, J et al. JCO 2019; 37: abstract 5005; 8. Hussain, M et al. ESMO 2019 Abstract #LBA12.

PROfound STUDY DESIGN



Primary endpoint

Radiographic progression-free survival (rPFS) in Cohort A (RECIST 1.1 & PCWG3 by BICR)

Key secondary endpoints

- rPFS in Cohorts A+B
- Confirmed radiographic objective response rate (ORR) in Cohort A
- Time to pain progression (TTPP) in Cohort AS
- Overall survival (OS) in Cohort A

*An investigational clinical trial assay, based on the FoundationOne® CDx next-generation sequencing test:-
Used to prospectively select patients harbouring alterations in *BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D* and/or *RAD54L* in their tumour tissue

‡Physicians choice of either enzalutamide (160 mg qd) or abiraterone (1000 mg qd + prednisone (5mg bid)

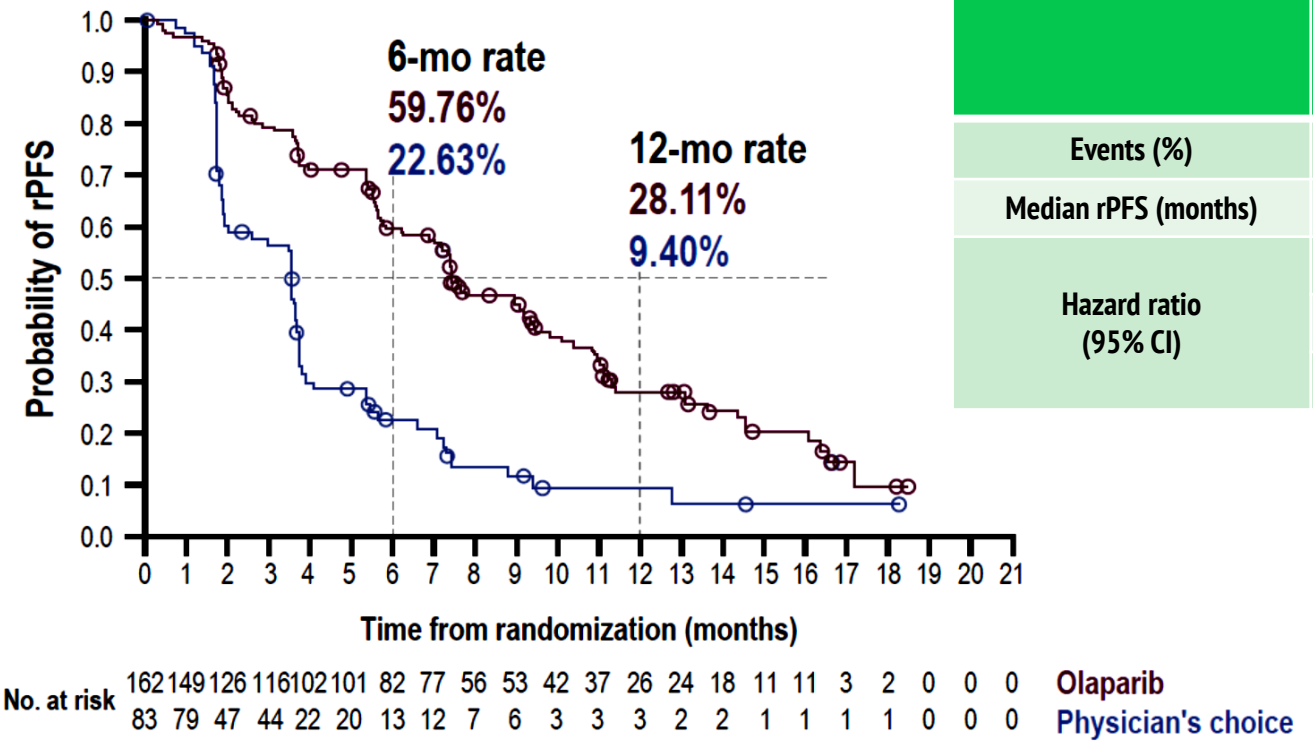
Median treatment duration was 7.4 months for olaparib and 3.9 months for enzalutamide/abiraterone.

BICR, blinded independent central review; bid, twice daily; HRR, homologous recombination repair; mCRPC, metastatic castration resistant prostate cancer; NHA, new hormonal agent; ORR, objective response rate; OS, overall survival; PCWG3, prostate cancer working group 3; qd, once daily; RECIST, response evaluation criteria in solid tumours; rPFS, radiographic progression free survival; TTPP, time to pain progression

Hussain, M et al. Presented at ESMO 2019 Abstract #LBA12.

PROfound STUDY – PRIMARY ENDPOINT

rPFS BY BICR IN PATIENTS WITH ALTERATIONS IN *BRCA1, BRCA2* OR *ATM* (COHORT A)



	Olaparib (N=162)	Physician's choice (N=83)
Events (%)	106 (65.4)	68 (81.9)
Median rPFS (months)	7.39	3.55
Hazard ratio (95% CI)	0.34	
	(0.25-0.47)	
	P<0.0001	

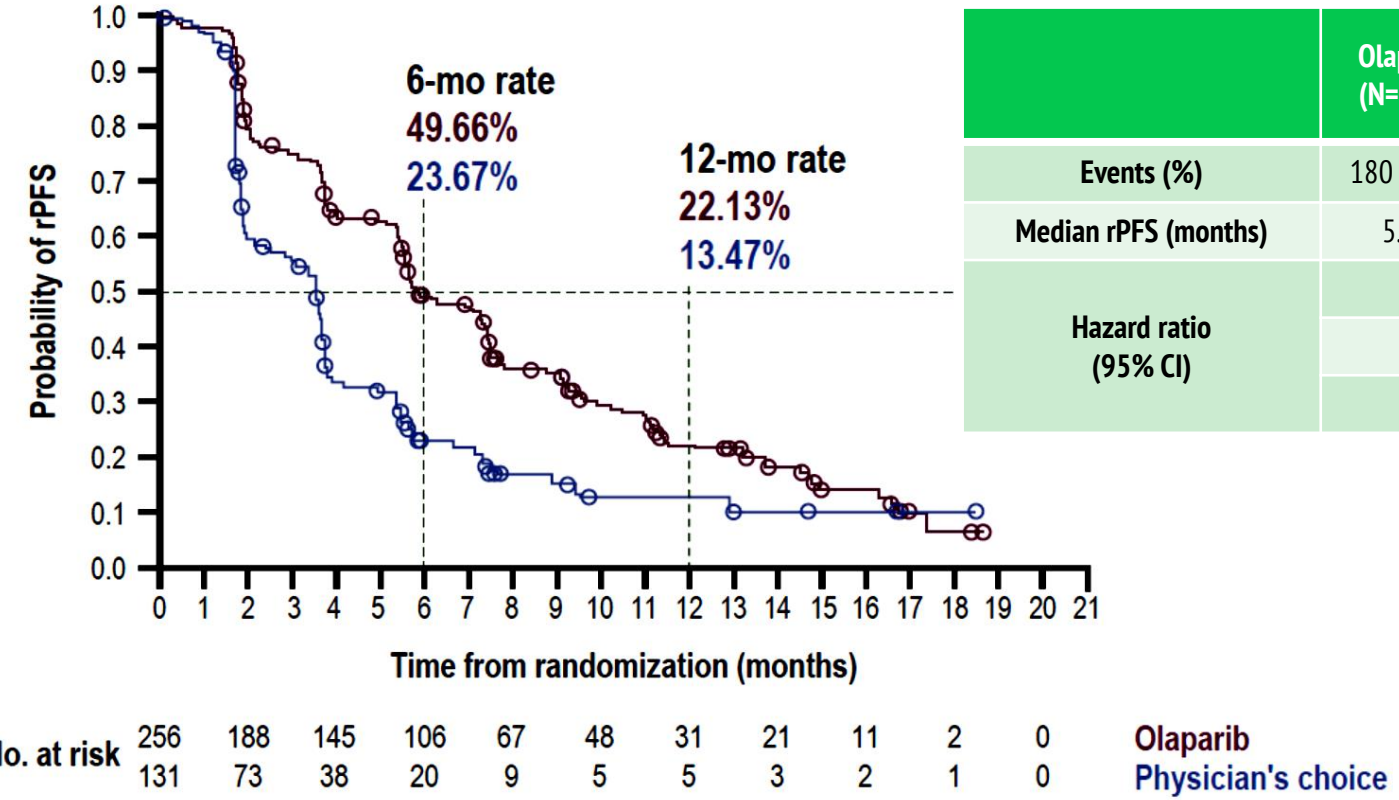
- rPFS benefit with olaparib treatment was consistent across all subgroups studied

BICR, blinded independent central review; CI, confidence interval; rPFS, radiographic progression free survival

Hussain M, et al. Presented at ESMO 2019 Abstract #LBA12.

PROfound STUDY – KEY SECONDARY ENDPOINT

rPFS BY BICR IN OVERALL POPULATION (COHORT A+B)



	Olaparib (N=256)	Physician's choice (N=131)
Events (%)	180 (70.3)	99 (75.6)
Median rPFS (months)	5.82	3.52
Hazard ratio (95% CI)	0.49	
	(0.38-0.63)	
	P<0.0001	

BICR, blinded independent central review; CI, confidence interval; rPFS, radiographic progression free survival

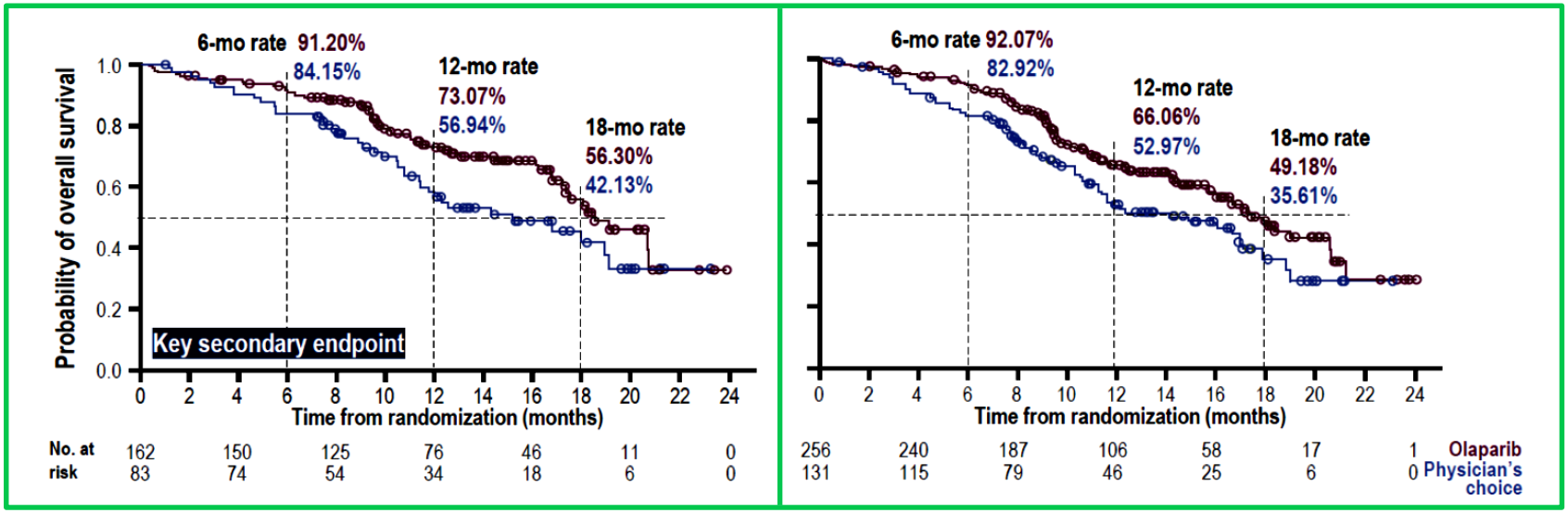
Hussain M, et al. Presented at ESMO 2019 Abstract #LBA12.

PROfound STUDY – KEY SECONDARY ENDPOINT

INTERIM* OVERALL SURVIVAL

COHORT A	Olaparib (N=162)	Physician's choice (N=83)
Median OS (months)	18.50	15.11
Hazard ratio (95% CI)	0.64 (0.43-0.97) P=0.0173‡	

COHORT A+B	Olaparib (N=256)	Physician's choice (N=131)
Median OS (months)	17.51	14.26
Hazard ratio (95% CI)	0.67 (0.49-0.93) P=0.0063 (nominal)	



- Of the physician's choice arm patients who progressed, 80.6% in cohort A and 84.6% in cohort B crossed over to olaparib

*38% maturity in Cohort A; 41% maturity in Cohort A+B; final analysis planned after ~146 deaths in cohort A (60% maturity).
‡ alpha spend at interim was 0.01; statistical significance not reached
CI, confidence interval; OS, overall survival
Hussain M, et al. Presented at ESMO 2019 Abstract #LBA12.

PROfound STUDY – OTHER RESULTS

- Patients in cohort A had a confirmed ORR of 33.3% for olaparib compared to 2.3% for enzalutamide/abiraterone (OR 20.86, 95% CI: 4.18-379.18, p<0.0001)

- No advantage to olaparib for cohort B patients in terms of rPFS (BICR) (HR 0.88, 95% CI: 0.58-1.36) or in OS (HR 0.73, 95% CI: 0.45-1.23)

- Olaparib was tolerated with a safety profile consistent with that observed in other cancers

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; OR, odds ratio; ORR, objective response rate; OS, overall survival; rPFS, radiographic progression free survival

Hussain M, et al. Presented at ESMO 2019 Abstract #LBA12.

SUMMARY

- **Olaparib treatment was associated with statistically significant and clinically relevant improvements in BICR rPFS** compared to enza/abi in mCRPC patients with:-
  - Alterations in *BRCA1*, *BRCA2* and/or *ATM*
  - Alterations in any qualifying gene with a direct/indirect role in HRR

- **PROfound will establish olaparib as standard of care** for this patient population and is likely to be the first approval for a biomarker selected treatment for prostate cancer

Abi, abiraterone; BICR, blinded independent central review; enza, enzalutamide; HRR, homologous recombination repair; mCRPC, metastatic castration resistant prostate cancer

Hussain M, et al. Presented at ESMO 2019 Abstract #LBA12.

IMvigor130: A PHASE 3 STUDY OF ATEZOLIZUMAB AS MONOTHERAPY OR COMBINED WITH PLATINUM-BASED CHEMOTHERAPY (PBC) VS PLACEBO +PBC IN PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC UC

Grande, et al. ESMO 2019 Abstract #LBA14

PBC, platinum based chemotherapy; UC, urothelial cancer

BACKGROUND

- **Current standard of care** for patients with mUC is **platinum based chemotherapy** as first line treatment
- Approximately **50%** of **patients with mUC** are **ineligible for treatment with cisplatin**
- **PD-L1 and PD-1 inhibitors are the first new therapies for mUC** in those patients experiencing disease progression after first line chemotherapy OR those ineligible for any chemotherapy OR who are ineligible for cisplatin chemotherapy with a high level of PD-L1 expression by the tumours
- **Atezolizumab** is an anti-PD-L1 which is being **investigated in** the **IMvigor130** study

mUC, metastatic urothelial cancer; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

IMvigor130 STUDY DESIGN

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- Locally advanced or mUC
- No prior systemic therapy in the metastatic setting
- ECOG PS ⩽2
- 1L platinum-eligible
- N=1200
- Randomised 1:1:1

→ **Arm A**
Atezo + plt/gem

→ **Arm B**
Atezo monotherapy

→ **Arm C**
Placebo + plt/gem

Stratification factors:

- PD-L1 IC status (IC0 vs IC1 vs IC2/3)
- Bajorin risk factor score including KPS <80% vs ⩾80% and presence of visceral metastases (0 vs 1 vs 2 and/or patients with liver metastases)
- Investigator choice of plt/gem (cisplatin + gem or carboplatin + gem)

*per RECIST 1.1

Co-primary endpoints:

- INV-assessed PFS* and OS (Arm A vs C)
- OS (Arm B vs C, hierachical approach)

Key secondary endpoints:

- INV-ORR* and DOR
- PFS* amd PS (Arm B vs C; PD-L1 IC2/3 subgroup)
- Safety

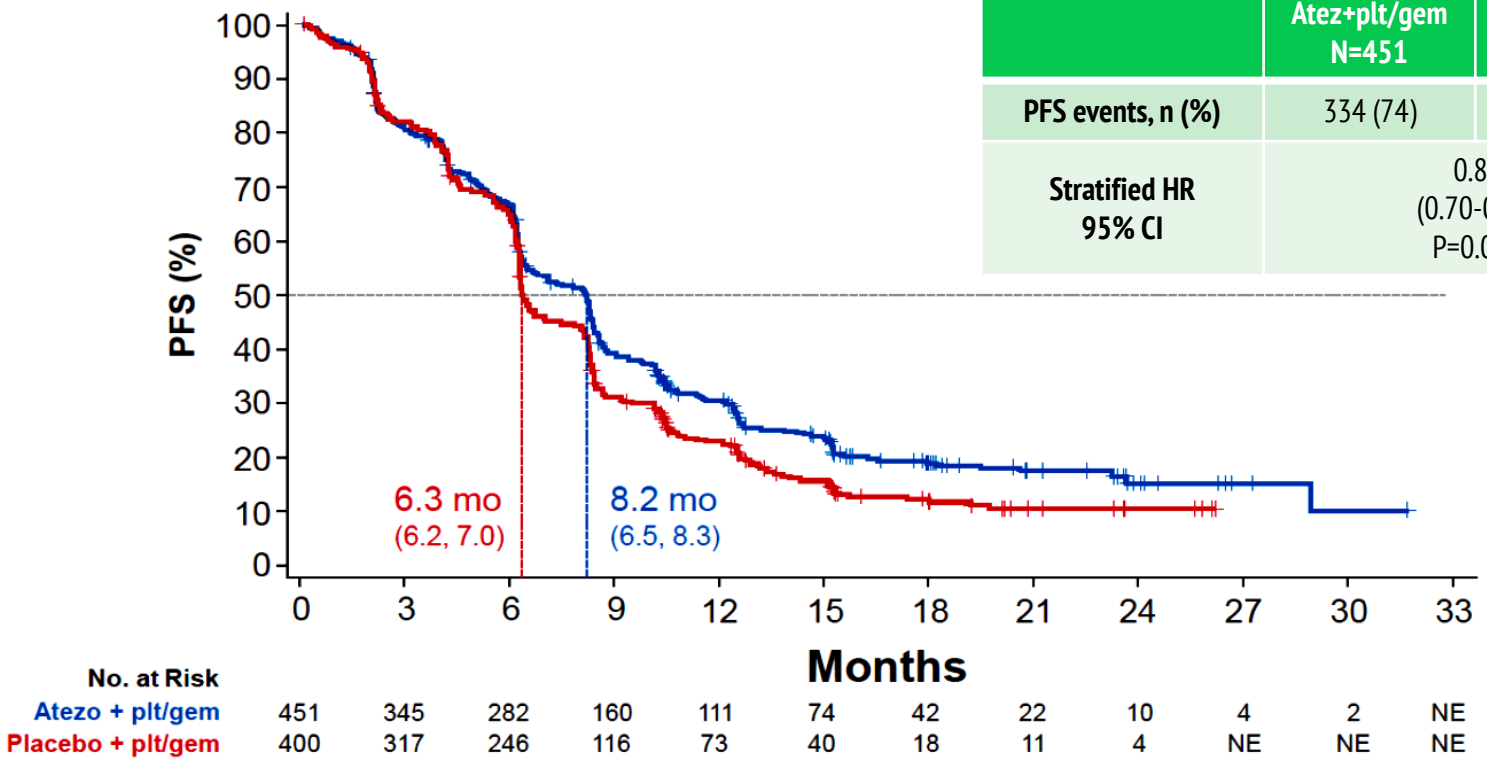
1L, first line; Atez, atezolizumab; DOR, duration of response; ECOG PS, eastern cooperative oncology group performance status; IC, tumour-infiltrating immune cells; INV, investigator; KPS, karnofsky performance status; mUC, metastatic urothelial cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1 PFS, progression free survival; plt/gem, platinum (cisplatin or carboplatin) plus gemcitabine

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

IMvigor STUDY: CO-PRIMARY ENDPOINT

FINAL PFS: ITT (ARM A VS ARM C)

	Arm A Atez+plt/gem N=451	Arm C Plb + plt/gem N=400
PFS events, n (%)	334 (74)	326 (82)
Stratified HR 95% CI	0.82 (0.70-0.96) P=0.007	



- PFS benefit with atezolizumab plus platinum/gemcitabine treatment was consistent across subgroups

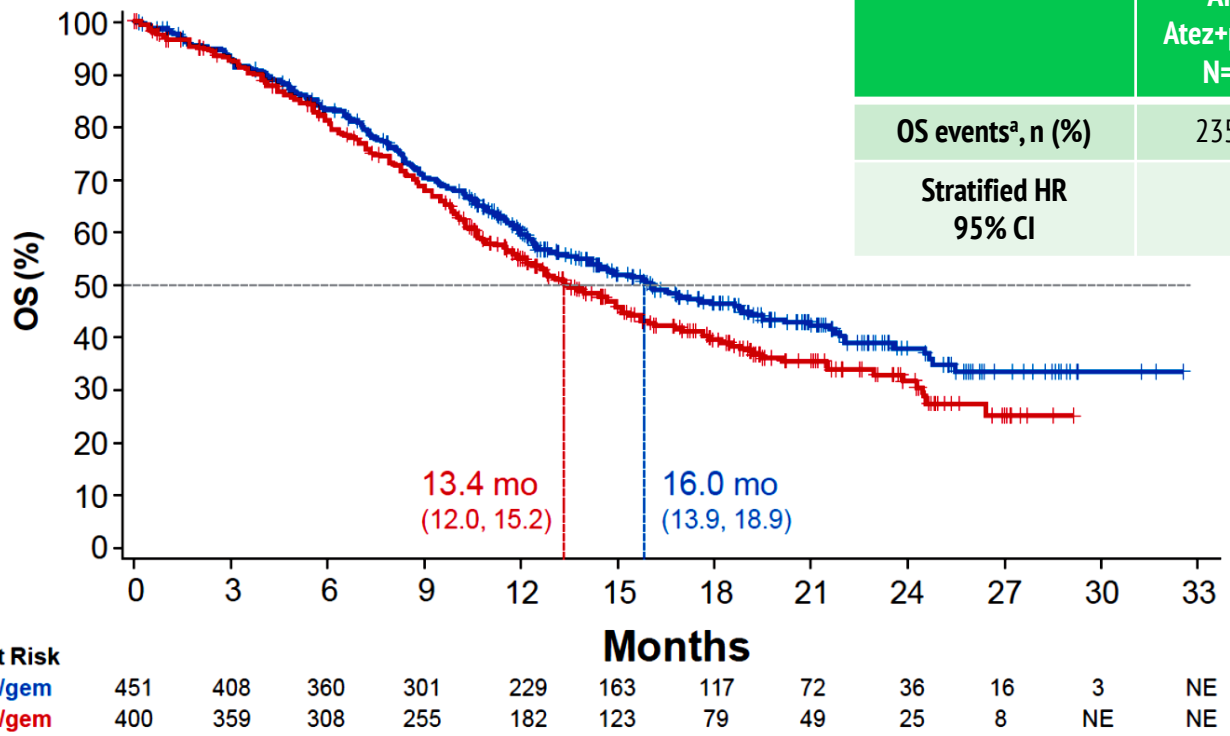
Atez, atezolizumab; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; PFS, progression free survival, Plb, placebo; plt/gem, platinum (cisplatin or carboplatin) plus gemcitabine

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

IMvigor STUDY: CO-PRIMARY ENDPOINT

INTERIM OS: ITT (ARM A VS ARM C)

	Arm A Atez+plt/gem N=451	Arm C Plb + plt/gem N=400
OS events[a], n (%)	235 (52)	228 (57)
Stratified HR 95% CI	0.83 (0.69-1.00) P=0.027[b]	



Median survival follow up of 11.8 months (all patients); [a]5% of patients from Arm A and 20% of patients from Arm C received non-protocol immunotherapy; [b]Did not cross the interim efficacy boundary of 0.007 per the O'Brien-Fleming alpha spending function

- There was a trend to OS benefit with atezolizumab plus platinum/gemcitabine treatment but the data are not mature at this point

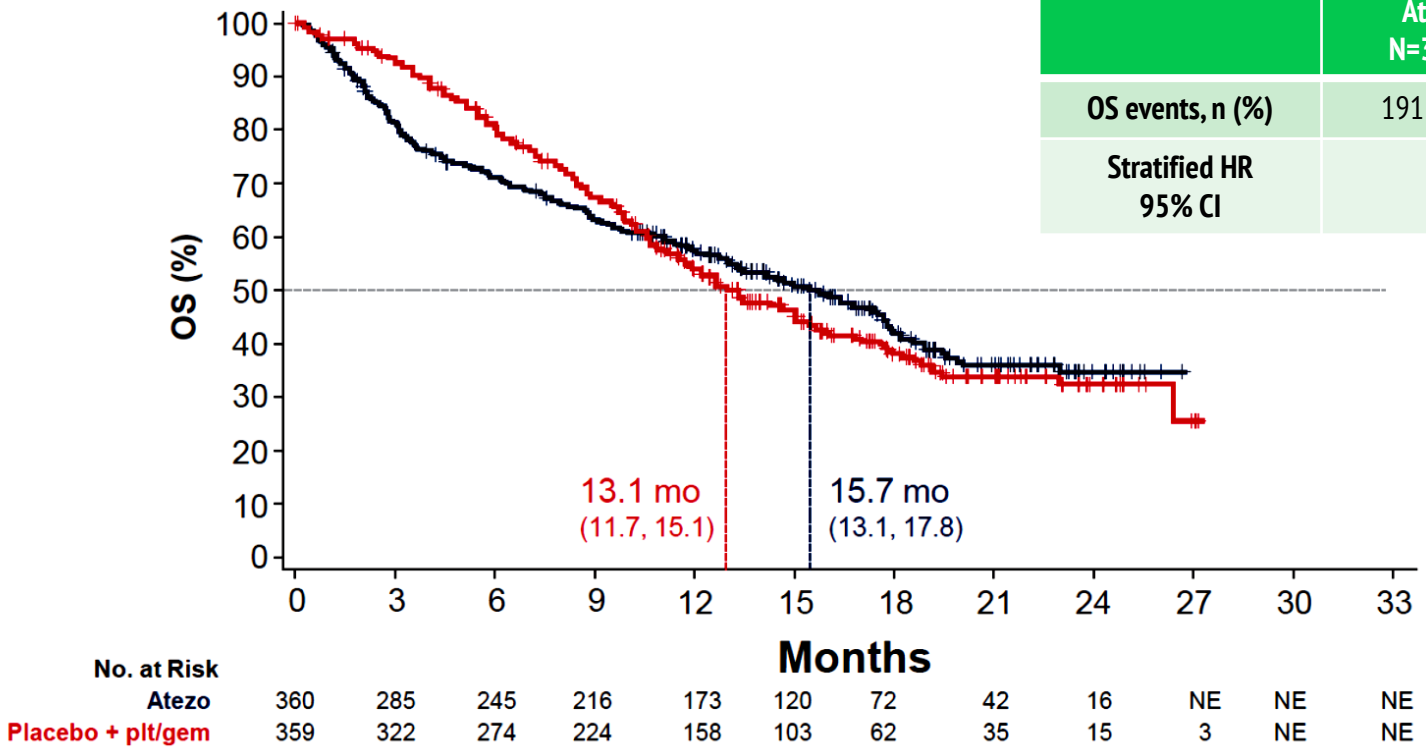
Atez, atezolizumab; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; OS, overall survival, Plb, placebo; plt/gem, platinum (cisplatin or carboplatin) plus gemcitabine

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

IMvigor STUDY: CO-PRIMARY ENDPOINT

INTERIM OS FOR MONOTHERAPY: ITT (ARM B VS ARM C)

	Arm B Atez N=360	Arm C Plb + plt/gem N=359[a]
OS events, n (%)	191 (53)	198 (55)
Stratified HR 95% CI	1.02 (0.83-1.24)	



Median survival follow up of 11.8 months (all patients); [a]Comparison only includes patients concurrently enrolled with ArmB

Atez, atezolizumab; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; OS, overall survival, Plb, placebo; plt/gem, platinum (cisplatin or carboplatin) plus gemcitabine

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

SUMMARY

- This is the **first immune checkpoint inhibitor study to demonstrate an improvement in PFS over standard of care in first line mUC**
- The **OS data was immature** at the time of this interim analysis
- The **atezolizumab + plt/gem combination** was **well tolerated** with a safety profile consistent with the individual agents
- **These data are sufficiently robust to change clinical practice and we await approval by regulatory bodies**
- Multiple other trials are currently ongoing investigating the effects of pembrolizumab, immune checkpoint combinations and switch maintenance therapies
- In the near future, these trials are likely to move immune checkpoint inhibitors from second line therapy to first line therapy in mUC

mUC, metastatic urothelial cancer; PD-L1, programmed death-ligand 1; PFS, progression free survival; plt/gem, platinum (cisplatin or carboplatin) plus gemcitabine

Grande E, et al. Presented at ESMO 2019 Abstract #LBA14.

TITAN: PHASE III STUDY OF APALUTAMIDE AND PLACEBO IN mHSPC PATIENTS RECEIVING ADT (PATIENT REPORTED OUTCOMES)

Agarwal, et al. ESMO 2019 Abstract #851PD

ADT, androgen deprivation therapy; mHSPC, metastatic hormone sensitive prostate cancer

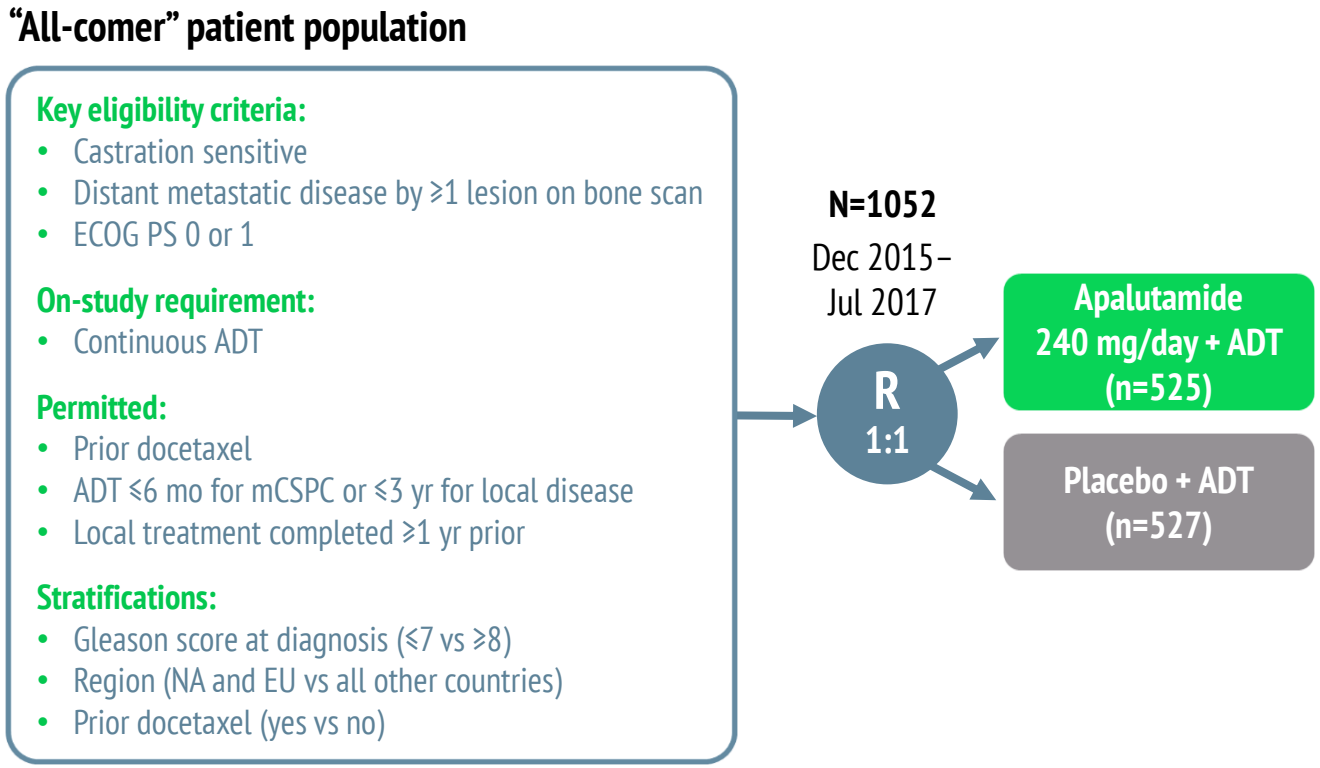
BACKGROUND

- **TITAN investigated the effect of apalutamide (androgen receptor inhibitor) in combination with ADT in men with mCSPC**
  - The addition of apalutamide to ADT improved the dual primary endpoint of rPFS and OS
  - Results of the trial led to approval of apalutamide by the FDA for mCSPC in Sept 2019[1]
- **Patient-reported outcomes were prespecified exploratory endpoints in TITAN and were assessed using the BPI-SF, BFI, FACT-P, and EQ-5D-5L**
  - BPI-SF and BFI were completed for 7 consecutive days (days −6 plus day 1 of each cycle visit), then at months 4, 8, and 12 in follow-up
  - FACT-P and EQ-5D-5L were completed during cycles 1–7, then every other cycle until the end of treatment, and at months 4, 8, and 12 in follow-up
  - Analyses were based on the intention-to-treat population

ADT, androgen deprivation therapy; BFI, brief fatigue inventory; BPI-SF, brief pain inventory-short form; EQ-5D-5L, EuroQoL 5D questionnaire 5 level; FACT-P, functional assessment of cancer therapy-prostate; FDA, food and drug administration; mCSPC, metastatic castration sensitive prostate cancer; rPFS, radiographic progression free survival; OS, overall survival

1. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-apalutamide-metastatic-castration-sensitive-prostate-cancer
Agarwal N, et al. ESMO 2019 Abstract #851PD; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

TITAN MAIN STUDY DESIGN

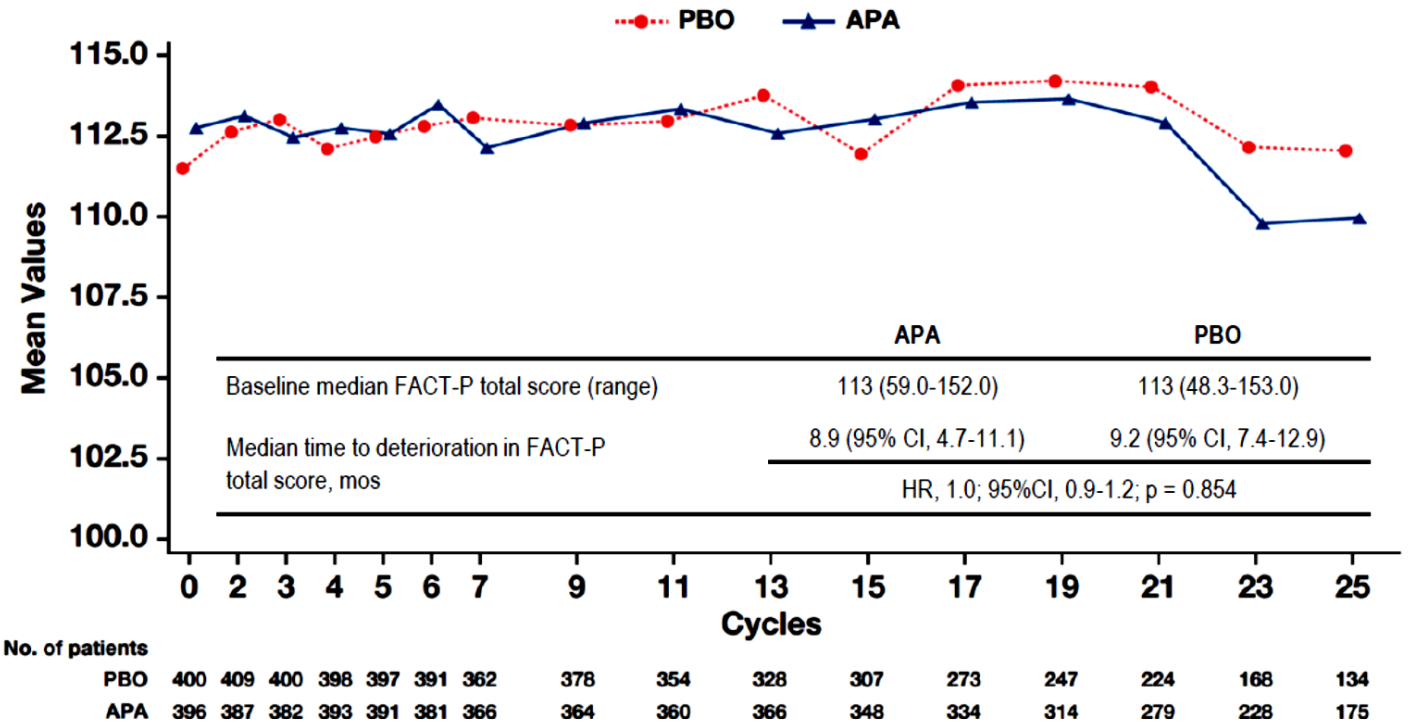


- Patient reported outcomes were pre-specified exploratory endpoints

ADT, androgen deprivation therapy; ECOG PS, eastern cooperative oncology group performance status; EU, europe; mCSPC, metastatic castration sensitive prostate cancer; NA, north america

Chi, et al. Presented at ASCO 2019, Abstract Number 5006; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

TITAN – HRQoL WAS PRESERVED WITH THE ADDITION OF APALUTAMIDE TO ADT (FACT-P)



- FACT-P values were similar with apalutamide or placebo

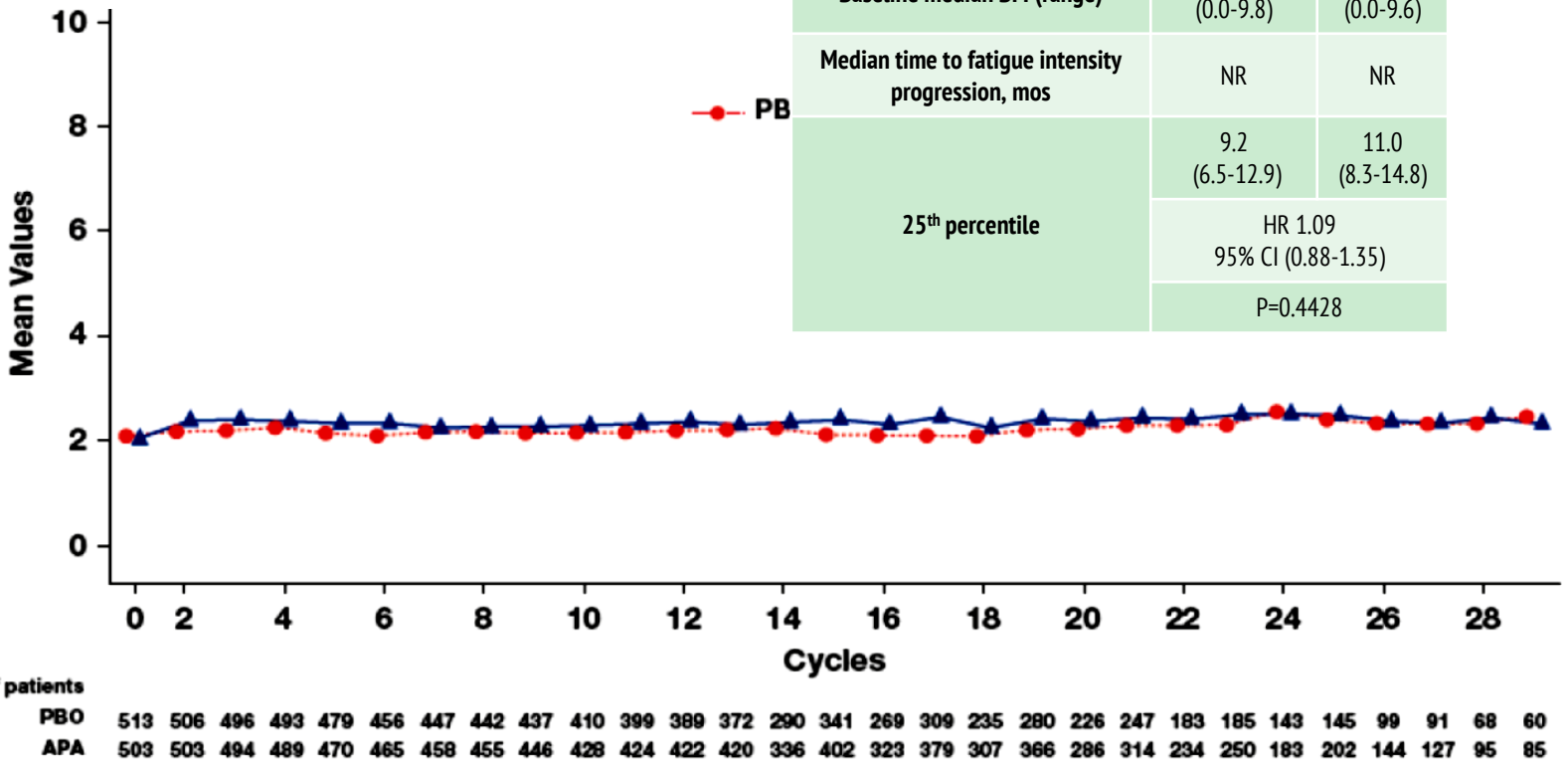
ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; FACT-P, functional assessment of cancer therapy-prostate; HR, hazard ratio; HRQoL, health related quality of life; PBO, placebo

Agarwal N, et al. ESMO 2019 Abstract #851PD; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

TITAN –ADDITION OF APALUTAMIDE TO ADT DID NOT INCREASE FATIGUE (BFI)

GROUP MEAN VALUES FOR WORST FATIGUE INTENSITY

	apalutamide	placebo
Baseline median BFI (range)	1.29 (0.0-9.8)	1.43 (0.0-9.6)
Median time to fatigue intensity progression, mos	NR	NR
25th percentile	9.2 (6.5-12.9)	11.0 (8.3-14.8)
	HR 1.09 95% CI (0.88-1.35)	
	P=0.4428	

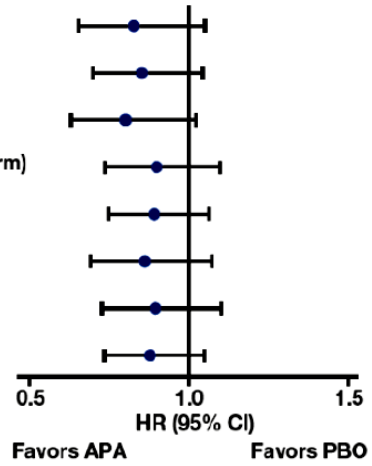


ADT, androgen deprivation therapy; APA, apalutamide; BFI, brief fatigue inventory; CI, confidence interval; HR, hazard ratio; NR, not reached; PBO, placebo

Agarwal N, et al. ESMO 2019 Abstract #851PD; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

TIME TO PAIN PROGRESSION FAVOURED APALUTAMIDE

Stratified PRO time to event end points	HR (95% CI)	Events/N APA	Events/N PBO
Pain progression (≥ 2 points to more than 4 points, minimum 1 day)	0.828 (0.653-1.049)	128/525	148/527
Pain progression (≥ 2 points, minimum 1 day)	0.853 (0.699-1.042)	182/525	207/527
Pain progression (≥ 2 points to more than 4 points, minimum 4 days)	0.803 (0.630-1.024)	120/525	143/527
Pain progression (≥ 2 points to more than 4 points, minimum 1 day no confirm)	0.899 (0.738-1.096)	190/525	207/527
Pain intensity (≥ 30%)	0.890 (0.747-1.062)	242/525	271/527
Pain intensity (≥ 2 points)	0.862 (0.692-1.074)	151/525	173/527
Pain interference	0.895 (0.728-1.100)	176/525	191/527
Average pain	0.878 (0.735-1.049)	237/525	262/527



- Results of sensitivity and exploratory analyses were consistent with time to pain progression endpoint results, with all HRs favouring apalutamide

ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; HR, hazard ratio; PBO, placebo; PRO, patient reported outcome

Agarwal N, et al. ESMO 2019 Abstract #851PD; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

SUMMARY

- The **combination of apalutamide in addition to ADT significantly improved survival outcomes** in patients with mCSPC compared with ADT alone **while maintaining HRQoL** despite additive androgen blockade

- One of the **most commonly discussed side effects of treatment with androgen receptor blockers is fatigue** and this was found to be **similar between treatment arms**

ADT, androgen deprivation therapy; HRQoL, health related quality of life; mCSPC, metastatic castration sensitive prostate cancer

Agarwal N, et al. ESMO 2019 Abstract #851PD; Agarwal, N et al. Lancet Oncology 2019:doi:10.1016/S1470-2045(19)30620-5

CARD: RANDOMISED, OPEN LABEL STUDY OF CABAZITAXEL VS ABIRATERONE OR ENZALUTAMIDE IN mCRPC

de Wit, et al. ESMO 2019 Abstract #LBA13

mCRPC, metastatic castration resistant prostate cancer

BACKGROUND

- **Several agents are approved for mCRPC but the optimal treatment sequence remains unclear**

- Prior mCRPC trials have not compared the 'new' agent with current standard therapy

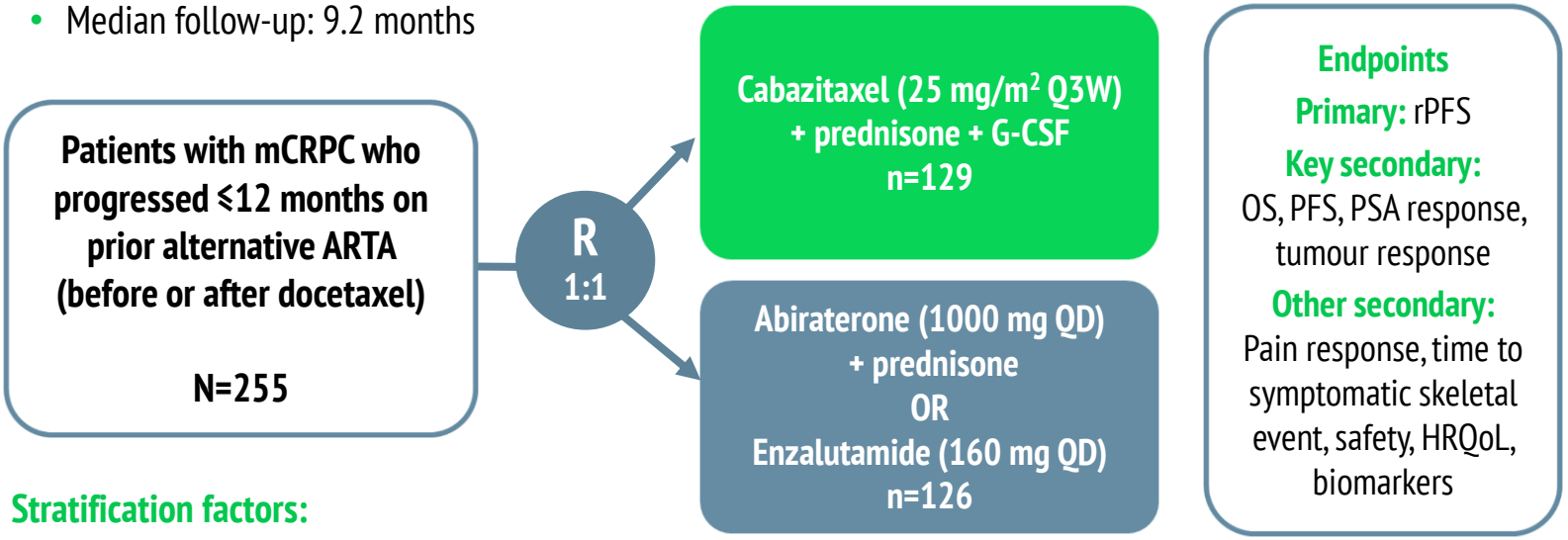
- The **CARD** trial **investigated** the **best treatment option for mCRPC** patients previously treated with docetaxel, currently progressing on an ART such as abiraterone or enzalutamide, within 12 months of starting therapy with ART:
  - Should the next treatment be an ART not already tried
  - Should the next treatment be a cytotoxic, ie. cabazitaxel

ART, androgen receptor therapy; mCRPC, metastatic castration resistant prostate cancer

de Wit R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY DESIGN

- Multicenter, randomized, open-label study
- Enrollment: Nov 2015 – Nov 2018
- Median follow-up: 9.2 months



Stratification factors:

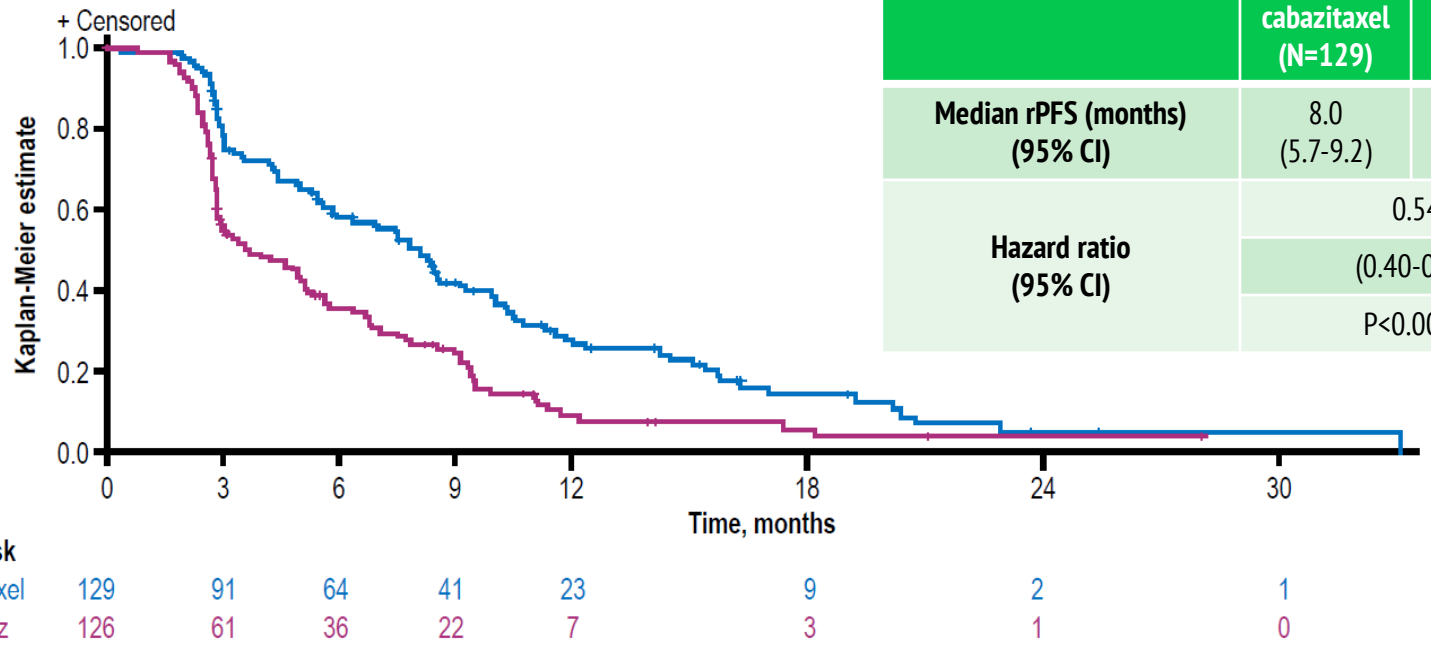
- ECOG PS (0/1 vs 2)
- Time to progression on prior alternative ARTA (0–6 vs >6–12 months)
- Timing of ARTA (before vs after docetaxel)

ARTA, androgen receptor-targeted agents; ECOG PS, eastern cooperative oncology group performance status; G-CSF, granulocyte colony stimulating factor; HRQoL, health related quality of life; mCRPC, metastatic castration resistant prostate cancer; OS, overall survival; Q3W, every three weeks; QD, once daily; (r)PFS, (radiographic)progression free survival; PSA, prostate specific antigen

de Wit,R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY – PRIMARY ENDPOINT

RADIOGRAPHIC PFS (INVESTIGATOR ASSESSED)



	cabazitaxel (N=129)	abi/enza (N=126)
Median rPFS (months) (95% CI)	8.0 (5.7-9.2)	3.7 (2.8-5.1)
Hazard ratio (95% CI)	0.54	
	(0.40-0.73)	
	P<0.0001	

- rPFS benefit observed for cabazitaxel compared to abi/enz was consistent across key subgroups, especially timing of ART with respect to receipt of docetaxel, as well as time from ART initiation to progression

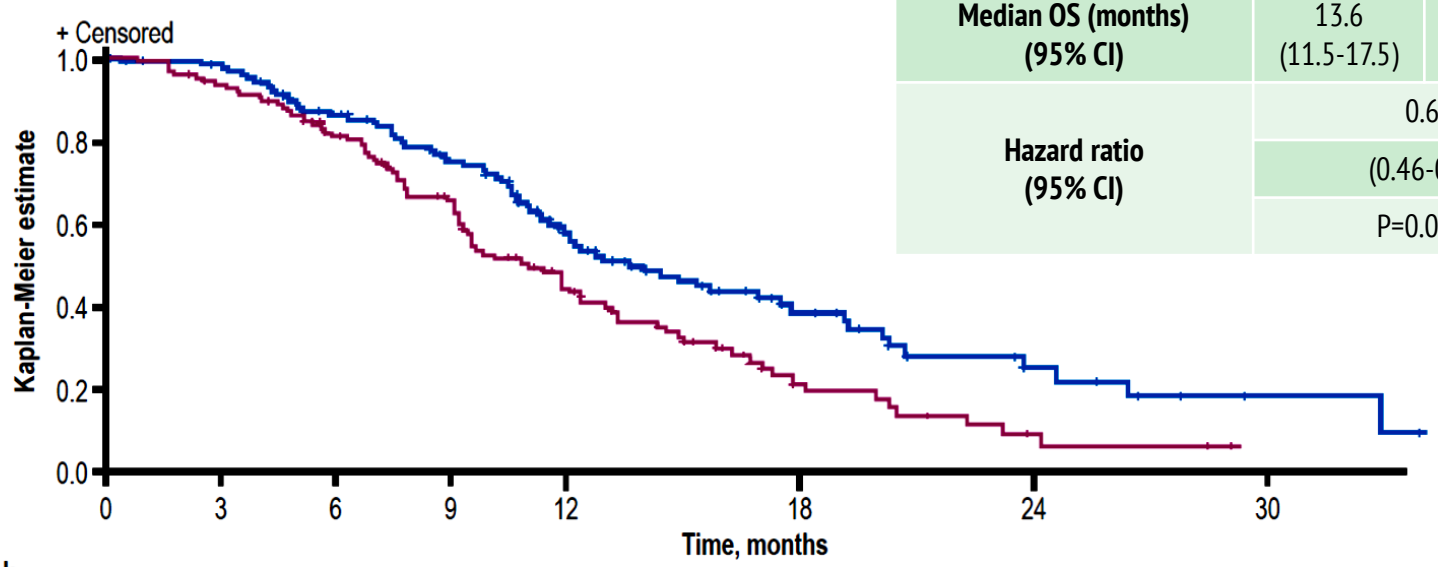
Abi, abiraterone; CI, confidence interval; enza, enzalutamide; PCWG2, prostate cancer working group 2; RECIST, response evaluation criteria in solid tumours; (r)PFS, (radiographic) progression free survival

de Wit,R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY – SECONDARY ENDPOINT

OVERALL SURVIVAL

	cabazitaxel (N=129)	abi/enza (N=126)
Median OS (months) (95% CI)	13.6 (11.5-17.5)	11.0 (9.2-12.9)
Hazard ratio (95% CI)	0.64	
	(0.46-0.89)	
	P=0.0078	



No. at risk								
Cabazitaxel	129	122	96	77	51	21	8	2
Abi or enz	126	116	88	64	39	11	3	0

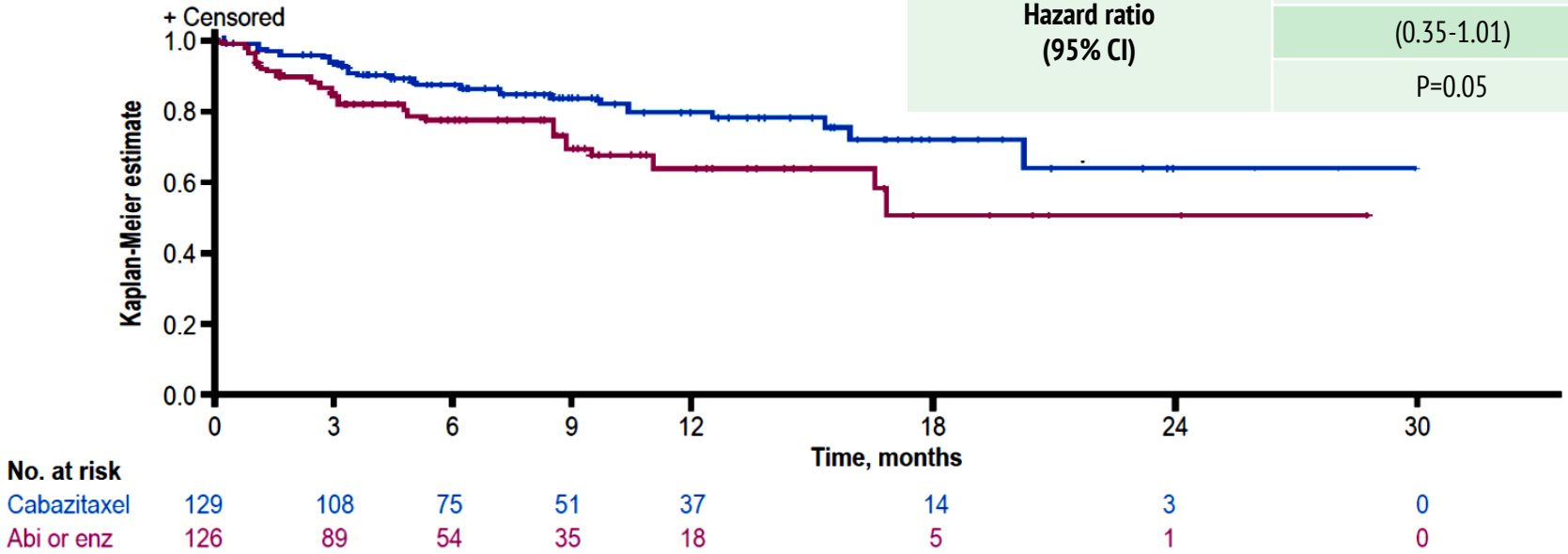
Abi, abiraterone; CI, confidence interval; enza, enzalutamide

de Wit R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD STUDY – SECONDARY ENDPOINT

TIME TO SKELETAL EVENT

	cabazitaxel (N=129)	abi/enza (N=126)
Median time to SSE (months) (95% CI)	NR (20.0-NR)	16.7 (10.8-NR)
Hazard ratio (95% CI)	0.59	
	(0.35-1.01)	
	P=0.05	



The median time to the first symptomatic skeletal event could not be evaluated (NE) in the cabazitaxel group. Tick marks indicate censored data.

Abi, abiraterone; CI, confidence interval; enza, enzalutamide; NR, not reached; SSE, symptomatic skeletal event

de Wit R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

CARD: SAFETY

MAIN GRADE ≥3 ADVERSE EVENTS*

Adverse events, n (%)	Cabazitaxel (N=126)	Abiraterone or enzalutamide (N=124)
Infections	10 (7.9)	9 (7.3)
Asthemia/fatigue	5 (4.0)	3 (2.4)
Diarrhea	4 (3.2)	0
Peripheral neuropathy	4 (3.2)	0
Renal disorders**	4 (3.2)	10 (8.1)
Febrile neutropenia	4 (3.2)	0
Spinal cord and nerve root disorders†	3 (2.4)	5 (4.0)
Musculoskeletal pain/discomfort‡	2 (1.6)	7 (5.6)
Cardiac disorders	1 (0.8)	6 (4.8)

*In ≥3% of patients in either treatment arm; **Includes acute kidney injury, renal failure and impairment, hydronephrosis, pyelocaliectasis; †Includes sciatica, radiculopathy, spinal cord compression; ‡Includes back pain, flank pain, musculoskeletal discomfort and pain, neck pain, pain in extremities.

- 98.4% patients in the cabazitaxel group vs. 94.4% in the abiraterone/enzalutamide group had an adverse event of any grade
- The incidence of serious adverse events of any grade was similar in the cabazitaxel group (38.9%) and the androgen-signaling–targeted inhibitor group (38.7%)

de Wit R, et al. ESMO 2019 Abstract #LBA13; de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

SUMMARY

- **The CARD trial addresses an unmet clinical need regarding sequencing of 3rd line treatments for progressive mCRPC patients**
- The current treatment landscape should be for fit patients to receive docetaxel and abiraterone or enzalutamide at some stage (+/- radium-223)
- The results of the **CARD trial** are in agreement with those of previous studies that have **shown poor outcomes with a second androgen signaling–targeted inhibitor**[1-5]
- Based on information presented in the CARD trial, **cabazitaxel is a new standard of care for 3rd line patients with progressive disease on prior novel androgen signaling inhibitors therapy ≤12 months of initiating therapy, and with prior docetaxel therapy**

mCRPC, metastatic castration resistant prostate cancer

1. Attard G, et al. JCO. 2018;36(25):2639-46; 2. Khalaf D, et al. JCO. 2018;36(15):5015; 3. Smith MR, et al. Eur Urol. 2017;72(1):10-13; 4. Zhang T, et al. Clin Genitoruin Cancer. 2015;13:392-9; 5. Azad AA, et al. Eur Urol. 2015;67:23-9; 6. de Wit R, et al. ESMO 2019 Abstract #LBA13; 7. de Wit R, et al; NEJM 2019: DOI: 10.1056/NEJMoa1911206.

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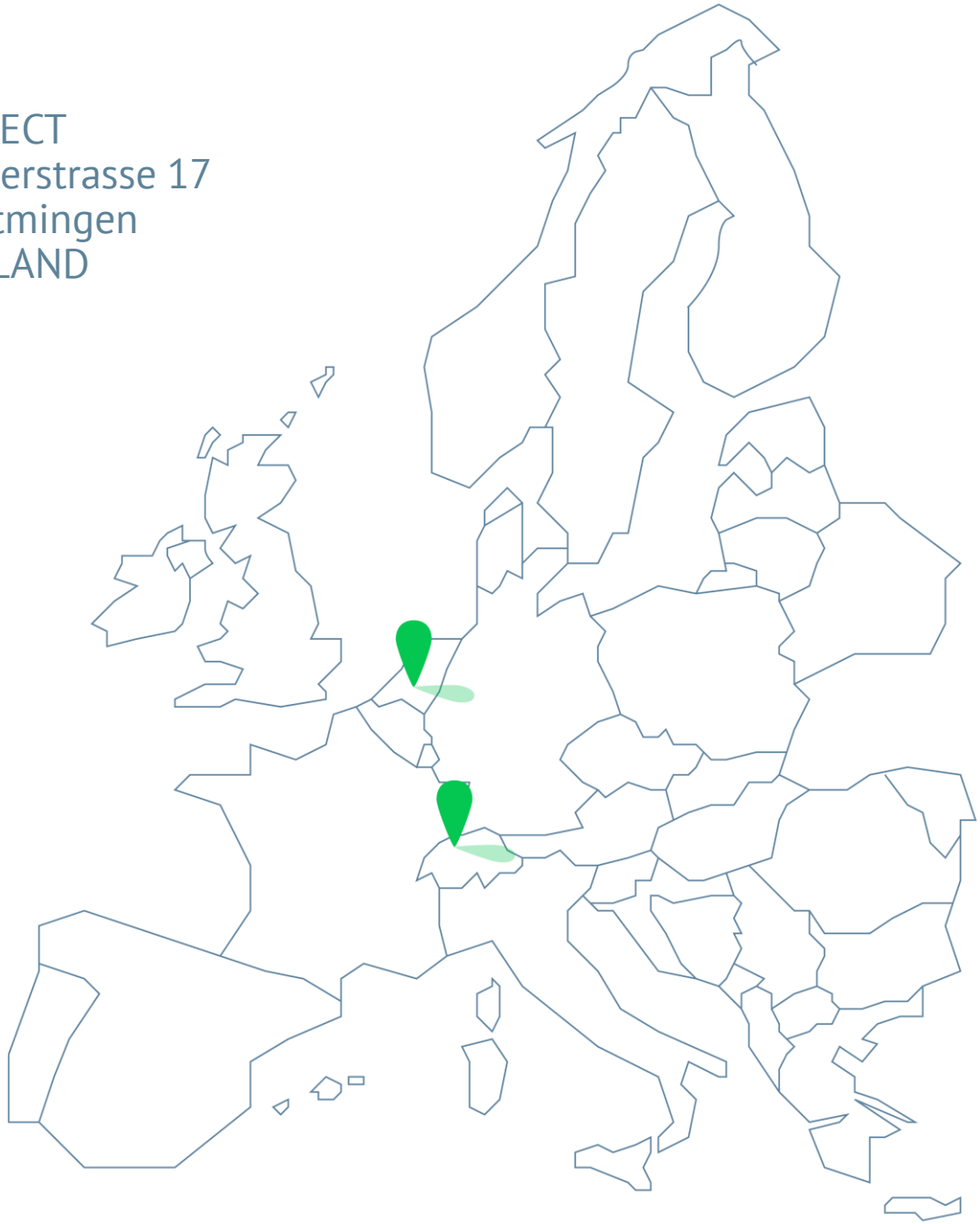

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