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OPTIMISING TREATMENT SEQUENCE FOR mCRPC AFTER INTENSIFIED THERAPY IN mCSPC

Dr Neal Shore, MD, FACS

Medical Director, Carolina Urologic Research Center, and
Chief Medical Officer, Surgical Oncology and Urology, GenesisCare, USA

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mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer

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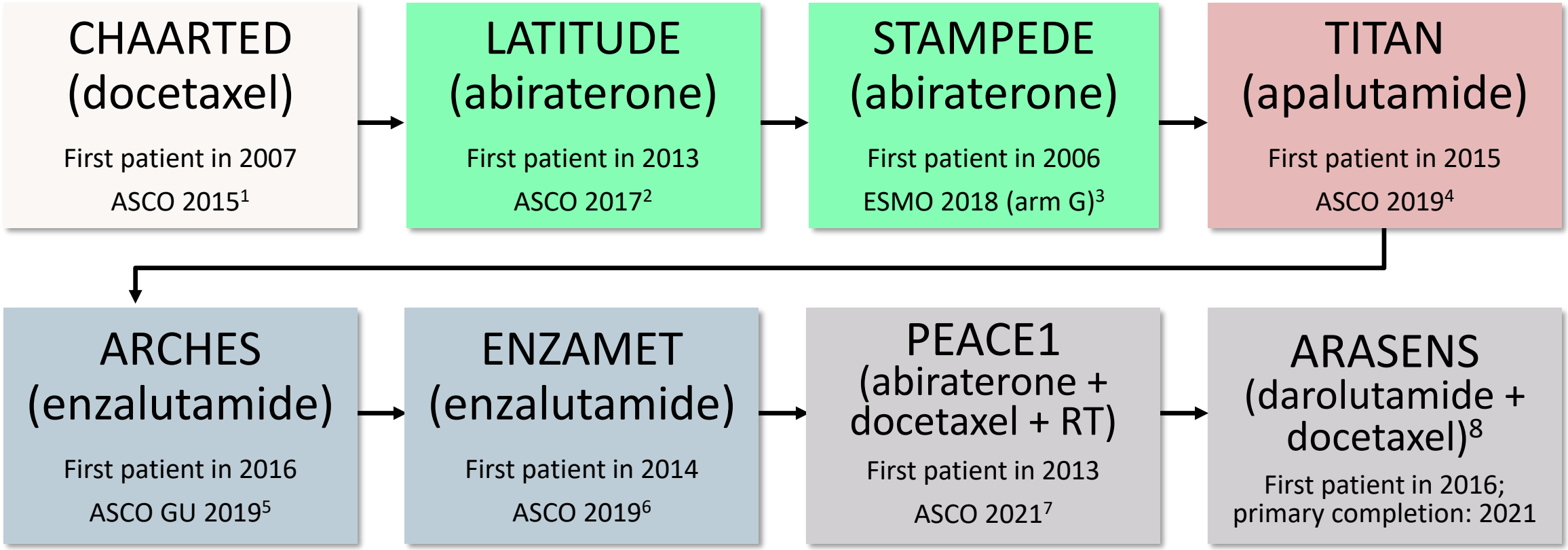
INTRODUCTION

- Androgen deprivation therapy (ADT) monotherapy for metastatic prostate cancer has been foundational, yet has limited to poor clinical outcomes
- Tumour burden, location, and biology affect overall survival
- A new standard of care for metastatic castration-sensitive prostate cancer (mCSPC) is combined therapy
  - ADT plus the early addition of either docetaxel or an androgen receptor pathway inhibitor (ARPI)
  - Despite level-1 evidence, many patients are still only receiving treatment with monotherapy ADT +/- an older ARPI
- Prior treatments, including those for mCSPC, influence future treatment decisions when the patient progresses to metastatic castration-resistant prostate cancer (mCRPC)
  - mCRPC patients may have already received treatment with an ARPI
- Cross-resistance can occur with ARPIs, so it is preferable to select subsequent therapies with a different mechanism of action
- There are several different treatments available for patients with mCRPC, and individualisation of treatment is important, considering patient preference and quality of life

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; mCRPC, metastatic castration-resistant prostate cancer; mCSPC, metastatic castration-sensitive prostate cancer

Lowrance W, et al. Advanced prostate cancer: AUA/ASTRO/SUO guideline. Available from https://www.auanet.org/guidelines/advanced-prostate-cancer. Accessed Jul 30, 2021; NCCN Clinical Practice Guidelines in Oncology – Prostate Cancer, version 2.2021. Accessed Jul 30, 2021

THE DEVELOPMENT OF NOVEL HORMONE THERAPY AND CHEMOTHERAPY IN mCSPC



Trials investigated treatments in addition to ADT

ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; GU, genitourinary; mCSPC, metastatic castration-sensitive prostate cancer; RT, radiation therapy

1. Maughan BL, et al. J Clin Oncol. 2015;33(suppl):e16079; 2. Fizazi K, et al. J Clin Oncol. 2017;35(suppl):LBA3; 3. Hoyle AP, et al. Ann Oncol. 2018;29(suppl 8):viii722;
4. Chi KN, et al. J Clin Oncol. 2019;37(15_suppl):5006; 5. Armstrong AJ, et al. J Clin Oncol. 2019;37(7_suppl):687; 6. Sweeney C, et al. J Clin Oncol. 2019;37(18_suppl):LBA2;
7. Fizazi K, et al. J Clin Oncol 39, 2021 (suppl 15; abstr 5000); 8. NCT02799602 at www.clinicaltrials.gov

mCSPC – DOCETAXEL TRIALS

Trial	Comparator	Phase; size	Primary endpoint	Results (docetaxel vs comparator)	Febrile neutropenia with docetaxel (grade ≥ 3)	Steroids?
GETUG-AFU15 2013[1]	ADT	3; 385	OS	mOS 58.9 vs 54.2 months HR 1.01, NS	7% (↓ with G-CSF)	Corticosteroids for 3 days
CHAARTED 2015[2]	ADT	3; 790	OS	mOS 57.6 vs 44.0 months HR 0.61, p<0.001	6.1%	Dexamethasone 3 doses
STAMPEDE 2016[3]	ADT	2/3; 1,776 (2 arms)	OS	mOS 81 vs 71 months HR 0.78, p=0.006	15%	Prednisolone 10 mg/day + premedication

ADT, androgen deprivation therapy; G-CSF, granulocyte colony-stimulating factor; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; (m)OS, (median) overall survival; NS, non-significant

1. Gravis G, et al. Lancet Oncol. 2013;14:149-58; 2. Sweeney C, et al. N Engl J Med. 2015;373:737-46; 3. James N, et al. Lancet. 2016;387:1163-77

mCSPC – ANDROGEN RECEPTOR-DIRECTED INTENSIFICATION

Treatment	Trial publication year	Population	Comparator	Phase; study size	Primary endpoint	Treatment vs control
Abiraterone acetate with prednisone	LATITUDE 2017	mCSPC	ADT + placebo	3; 1,199	OS	53.3 vs 36.5 months (HR: 0.66 [95% CI: 0.56-0.78], p<0.0001)
	STAMPEDE 2017	mCSPC and locally advanced prostate cancer	ADT alone	3; 1,917	OS	Estimated 83% vs 73% alive at 3 years (HR: 0.63 [95% CI: 0.52-0.76], p<0.001)
Enzalutamide	ENZAMET 2019	mCSPC	ADT + non-steroidal AR-directed therapy	3; 1,125	OS	Estimated 80% vs 72% alive at 3 years (HR: 0.67 [95% CI: 0.52-0.86], p=0.002)
	ARCHES 2019	mCSPC–stratified by CHAARTED criteria	ADT + placebo	3; 1,150	rPFS or death	NR vs 19 months (HR: 0.39 [95% CI: 0.3-0.5], p<0.001)
Apalutamide	TITAN 2019	mCSPC	ADT + placebo	3; 1,052	rPFS or death	68.2% vs 47.5% at 24 months (HR: 0.48 [95% CI: 0.39-0.60], p<0.001)
					OS	82.4% vs 73.5% alive at 24 months (HR: 0.67 [95% CI: 0.51-0.89], p=0.005)

ADT, androgen deprivation therapy; ALT, alanine aminotransferase; AR, androgen receptor; AST, aspartate aminotransferase; CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; NR, not reached; OS, overall survival; rPFS, radiographic progression-free survival

Schulte B, et al. Am Soc Clin Oncol Educ Book. 2020;40:198-207

INITIATION OF 1L TREATMENT FOLLOWING mCSPC DIAGNOSIS

mCSPC 1L regimen	Median duration to next regimen (months)	2014	2015	2016	2017	2018	2019
ADT + AA	14.3	42.6%	31.9%	31.7%	20.1%	19.8%	16.5%
ADT	8.9	20.4%	19.8%	22.0%	21.5%	15.8%	26.6%
ADT + NHT ± AA	14.3	10.2%	11.2%	14.6%	19.2%	27.7%	34.2%
ADT + DOC ± AA	10.8	8.3%	19.8%	14.6%	22.0%	17.0%	10.1%
Other treatment	n/a	18.5%	17.2%	17.1%	17.3%	19.8%	12.7%

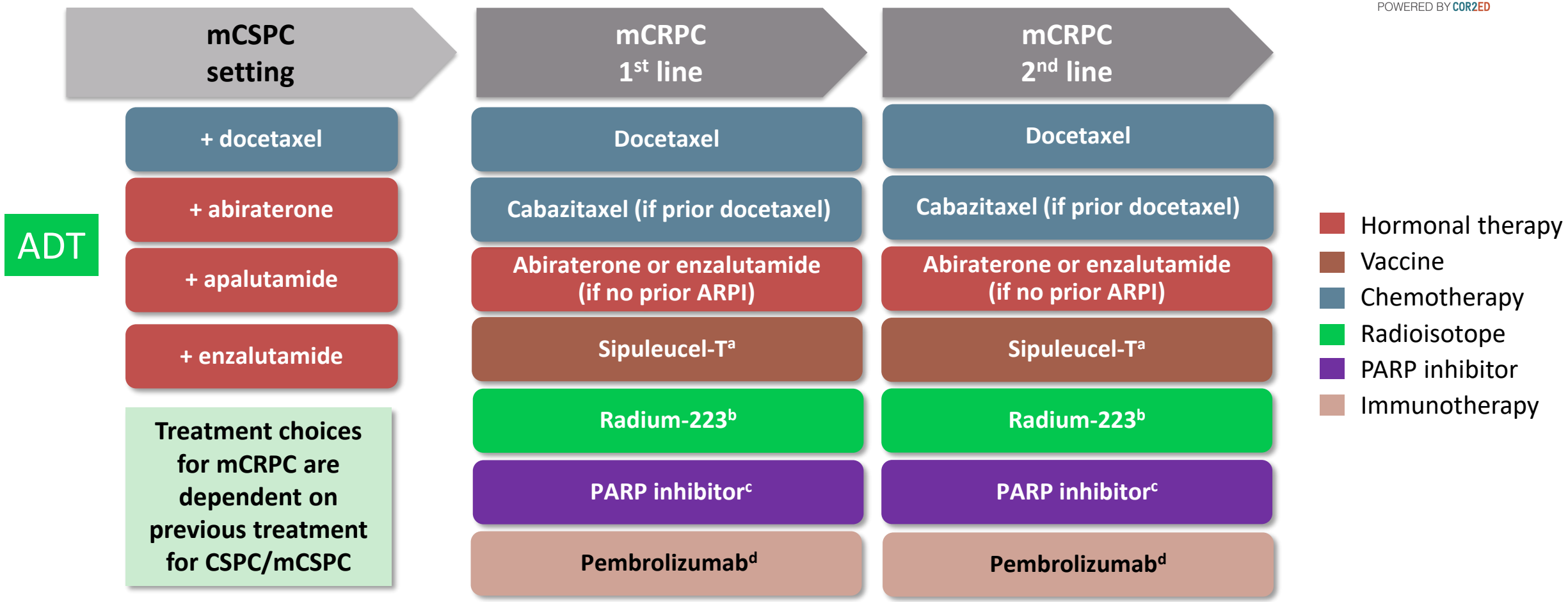
- Despite level 1 evidence, in 2019, over half of mCSPC patients treated in real-world settings did not receive 1L therapy, now known to significantly improve survival (ADT + NHT or ADT + DOC) over ADT alone
- Those who did, received shorter durations of treatment than observed in registrational trials

SOC for mCSPC patients should be ADT + docetaxel or an ARPI

1L, first line; AA, anti-androgen; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; DOC, docetaxel; mCSPC, metastatic castration-sensitive prostate cancer; NHT, novel hormonal therapies; SOC, standard of care

George D, et al. J Clin Oncol. 2021;39(suppl 15):5074

THERAPEUTIC OPTIONS IN mCRPC



Treatment options vary depending on local approvals and treatment guidelines

[a]Not recommended if visceral metastases are present; [b]For patients with symptomatic bone metastasis and no known visceral metastasis (in the EU, radium-223 should be restricted for use in patients who have had two previous treatments for metastatic prostate cancer or who cannot receive other treatments); [c]PARP inhibitor as per FDA indication: olaparib for men with *HRR* mutations, after ARPI, before or after taxane; rucaparib for men with *BRCA1* or *BRCA2* mutations after ARPI and taxane. Mutations can be germline or somatic; [d]FDA-approved for men with tumours identified as having high microsatellite instability (MSI high)

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; (m)CSPC, (metastatic) castration-sensitive prostate cancer; BRCA 1/2, breast cancer 1/2; FDA, food and drug administration; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; MSI, microsatellite instability; PARP, poly (ADP-ribose) polymerase

Adapted from Birtle A. Women for Mankind: Optimal Use of Chemotherapy in Metastatic Prostate Cancer. ESMO 2018; Cornford P, et al. Eur Urol. 2021;79:263-82; NCCN Clinical Practice Guidelines in Oncology – Prostate Cancer, version 2.2021. Accessed Jul 30, 2021

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[zz,ccc,ddd,eee]

No prior docetaxel/no prior novel hormone therapy[fff]	Prior novel hormone therapy/No prior docetaxel[fff,lll]
• Preferred regimens ▸ Abiraterone[t,ggg] (category 1[hhh]) ▸ Docetaxel[aaa,iii] (category 1) ▸ Enzalutamide[t] (category 1) •Useful in certain circumstances ▸ Sipuleucel-T[aaa,jjj] (category 1) ▸ Radium-223[kkk] for symptomatic bone metastases (category 1) •Other recommended regimens ▸ Other secondary hormone therapy[t]	• Preferred regimens ▸ Docetaxel (category 1)[aaa] ▸ Sipuleucel-T[aaa,jjj] • Useful in certain circumstances ▸ Olaparib for HRRm (category 1)[mmm] ▸ Cabazitaxel/carboplatin[aaa,nnn] ▸ Pembrolizumab for MSI-H or dMMR[aaa] ▸ Radium-223[kkk] for symptomatic bone metastases (category 1) ▸ Rucaparib for BRCAm[ooo] • Other recommended regimens ▸ Abiraterone[t,ggg] ▸ Abiraterone + dexamethasone[ggg,ppp] ▸ Enzalutamide[t] ▸ Other secondary hormone therapy[t]
Prior docetaxel/no prior novel hormone therapy[fff]	Prior docetaxel and prior novel hormone therapy[fff,lll]
• Preferred regimens ▸ Abiraterone[t, ggg] (category 1) ▸ Cabazitaxel[aaa] ▸ Enzalutamide[t] (category 1) • Useful in certain circumstances ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[aaa] ▸ Cabazitaxel/carboplatin[aaa,nnn] ▸ Pembrolizumab for MSI-H or dMMR[aaa] ▸ Radium-223[kkk] for symptomatic bone metastases (category 1) • Other recommended regimens ▸ Sipuleucel-T[aaa,jjj] ▸ Other secondary hormone therapy[t]	(All systemic therapies are category 2B if visceral metastases are present) • Preferred regimens ▸ Cabazitaxel[aaa] (category 1[hhh]) ▸ Docetaxel rechallenge[aaa,eee] • Useful in certain circumstances ▸ Olaparib for HRRm (category 1)[hhh,mmm] ▸ Cabazitaxel/carboplatin[aaa,nnn] ▸ Pembrolizumab for MSI-H or dMMR[aaa] ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[aaa] ▸ Radium-223[kkk] for symptomatic bone metastases (category 1[hhh]) ▸ Rucaparib for BRCAm[ooo] • Other recommended regimens ▸ Abiraterone[t,ggg] ▸ Enzalutamide[t] ▸ Other secondary hormone therapy[t]

BRCAm, breast cancer mutated; dMMR, deficient DNA mismatch repair; HRRm, homologous recombination repair mutated; CRPC, metastatic castration-resistant prostate cancer; MSI-H, microsatellite instability-high

NCCN Clinical Practice Guidelines in Oncology – Prostate Cancer, version 2.2021. Accessed Jul 30th, 2021

KEY PHASE 3/4 TRIALS IN mCRPC

OVERALL SURVIVAL RESULTS

Study	Treatments	N	Population	HR	95% CI; p value
TAX 327[1]	Docetaxel[a]/prednisone vs mitoxantrone/prednisone	1,006	mCRPC	0.76	0.62-0.94; p=0.009
TROPIC[2]	Cabazitaxel/prednisone vs mitoxantrone/prednisone	755	mCRPC (post docetaxel)	0.70	0.59-0.83; p<0.0001
COU-AA-301[3]	Abiraterone/prednisone vs placebo/prednisone	1,195	mCRPC (post docetaxel)	0.74	0.64-0.86; p<0.0001
COU-AA-302[4]	Abiraterone/prednisone vs placebo/prednisone	1,088	mCRPC (pre docetaxel)	0.81	0.70-0.93; p=0.0033
PREVAIL[5]	Enzalutamide vs placebo	1,717	mCRPC (pre docetaxel)	0.71	0.60-0.84; p<0.001
AFFIRM[6]	Enzalutamide vs placebo	1,199	mCRPC (post docetaxel)	0.63	0.53-0.75; p<0.001
ALSYMPCA[7]	Radium-223 vs placebo	921	mCRPC	0.70	0.58-0.83; p<0.0001
IMPACT[8]	Sipuleucel-T vs placebo	512	mCRPC (pre chemotherapy[b])	0.78	0.61-0.98; p=0.03
CARD[9]	Cabazitaxel/prednisone vs ASTI[c]	255	mCRPC (post docetaxel and post abiraterone or enzalutamide)	0.64	0.46-0.89; p=0.008
PROfound[10]	Olaparib vs ASTI[c]	387	mCRPC with HRR mutations (post abiraterone or enzalutamide and post chemotherapy[d]	0.69[e]	0.50-0.97; p=0.02

[a]3-weekly docetaxel cycle; [b]18.2% had received previous treatment with chemotherapy; [c]enzalutamide or abiraterone plus prednisone; [d]approximately 65% of patients had previously progressed on taxanes; [e]Results for cohort A of study: patients with alterations in *BRCA1, BRCA2, ATM*

ASTI, androgen signaling targeted inhibitor; ATM, ataxia telangiectasia mutated; BRCA1/2, breast cancer 1/2; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer

1. Tannock IF, et al. N Engl J Med. 2004;351:1502-12; 2. de Bono JS, et al. Lancet. 2010;376:1147-54; 3. Fizazi K, et al. Lancet Oncol. 2012;13; 983-92; 4. Ryan CJ, et al. Lancet Oncol. 2015;16:152-60; 5. Beer TM, et al. N Engl J Med. 2014;371:424-33; 6. Scher HI, et al. N Engl J Med. 2012;367:1187-97; 7. Parker C, et al. N Engl J Med. 2013;369: 213-23; 8. Kantoff PW, et al. N Engl J Med. 2010;363:411-22; 9. de Wit R, et al. N Engl J Med. 2019;381:2506-18; 10. Hussain M, et al. N Engl J Med. 2020;383:2345-57

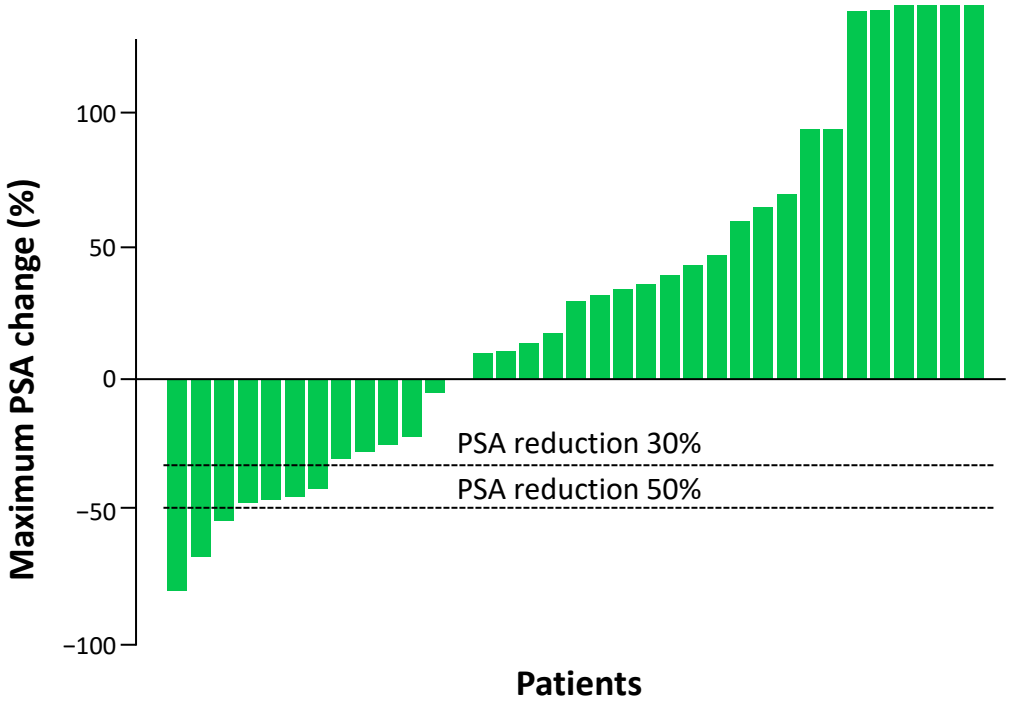
CLINICAL FACTORS TO SUPPORT TREATMENT CHOICE

- Consider prior treatments. **Novel mechanism of action preferred**
- Is the patient symptomatic or asymptomatic?
- Consider sites of metastases: visceral vs bone-only disease
- Is the patient suitable for chemotherapy?
- Is there small cell/neuroendocrine differentiation?
- Are there targetable DNA repair mutations?
- Is there microsatellite instability?
- Consider co-morbidities, quality of life, patient preference
- Are there suitable clinical trial options?

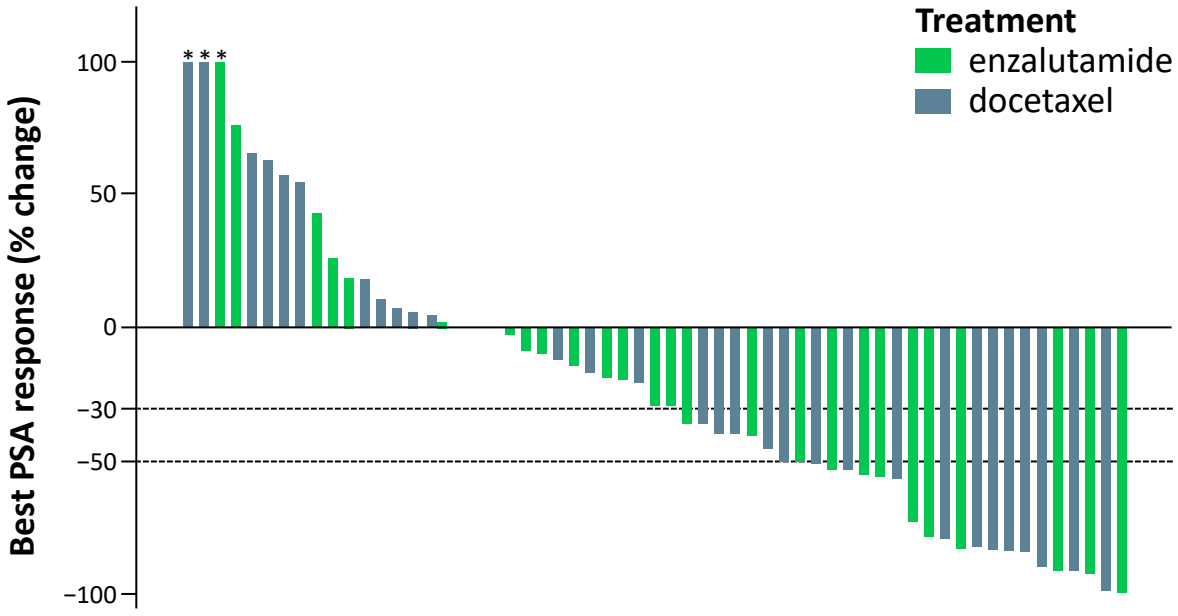
PARPi, Poly (ADP-ribose) polymerase inhibitor

SEQUENCING: MODEST EFFECTS OF ABIRATERONE AFTER ENZALUTAMIDE AND ENZALUTAMIDE AFTER ABIRATERONE

RESPONSE TO ABIRATERONE AFTER TREATMENT WITH ENZALUTAMIDE IN mCRPC PATIENTS[1]



ENZALUTAMIDE VS DOCETAXEL IN MEN WITH CRPC PROGRESSING ON ABIRATERONE[2]



*Bar is truncated because of a PSA increase > 100%

CRPC, castration-resistant prostate cancer; PSA, prostate-specific antigen

1. Loriot Y, et al. Ann Oncol. 2013;24:1807-12; 2. Suzman DL, et al. Prostate. 2014;74:1278-85

BODY OF EVIDENCE SUGGESTS LIMITED BENEFIT TO SEQUENCING AR-PATHWAY INHIBITORS

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Drug	N	≥50% PSA response	Median PFS/TTPP (months)	Median OS (months)
Enzalutamide → abiraterone + prednisone				
Attard G et al.[1a]	125	2%	5.6	Not Reported
Khalaf D et al.[2]	75	4%†	TTPP: 1.7 months[b]	24.7
Abiraterone + prednisone → enzalutamide				
Smith MR et al.[3]	33	67%	TTPP: 2.8 months	Not Reported
Zhang T et al.[4]	9	11%	3.6	8.5
Azad AA et al.[5]	47	26%	6.6	8.6
Khalaf D et al.[2]	73	36%[c]	TTPP: 3.5 months[b]	28.8

[a]Limited benefit of using abiraterone after enzalutamide in the PLATO trial – however was not the primary aim of this trial; [c]PSA ≥30% decline from baseline;
[b]Time to second PSA progression on second therapy

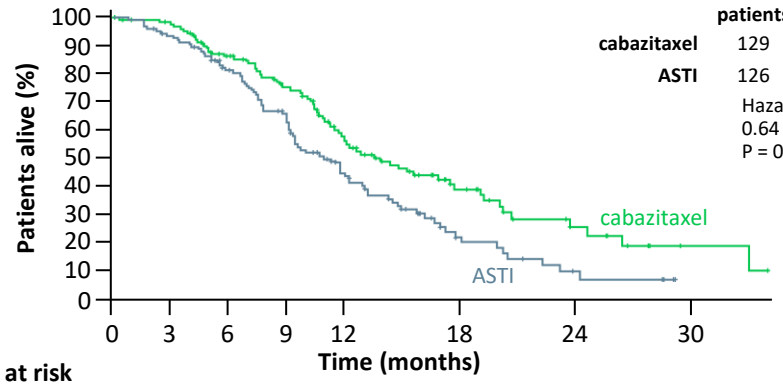
AR, androgen receptor; OS, overall survival; PFS, progression-free survival; PSA, prostate-specific antigen; TTPP, time to PSA progression

1. Attard G, et al. J Clin Oncol. 2018;36:2639-46; 2. Khalaf D, et al. Lancet Oncol. 2019;20:1730-39; 3. Smith MR, et al. Eur Urol. 2017;72:10-13;
4. Zhang T, et al. Clin Genitourin Cancer. 2015;13:392-9; 5. Azad AA, et al. Eur Urol. 2015;67:23-9

CARD: CABAZITAXEL MORE EFFECTIVE THAN ABI OR ENZA AFTER ABI OR ENZA

- Men previously treated with both docetaxel and ARPI (abi or enza)
  - Median age 70 (range 46–85) years in cabazitaxel group
  - 69% had pain progression at trial entry
- 14% of patients in ARPI treatment group had a ≥50% PSA response to second AR targeted agent
- Median PFS of 2.7 months for second AR agent

Overall survival

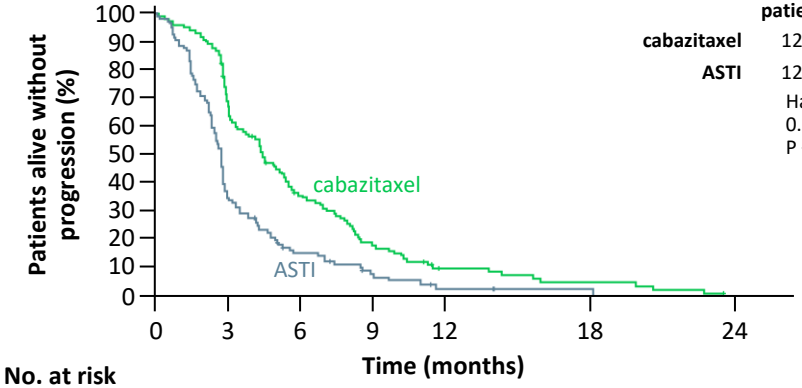


	No. of patients	Median overall survival (95% CI), months
cabazitaxel	129	13.6 (11.5–17.5)
ASTI	126	11.0 (9.2–12.9)

Hazard ratio for death
0.64 (95% CI 0.46–0.89)
P = 0.008

No. at risk								
cabazitaxel	129	122	96	77	51	21	8	2
ASTI	126	116	88	64	39	11	3	0

Progression-free survival



	No. of patients	Median progression-free survival (95% CI), months
cabazitaxel	129	4.4 (3.6–5.4)
ASTI	126	2.7 (2.4–2.8)

Hazard ratio for progression or death
0.52 (95% CI 0.40–0.68)
P < 0.001

No. at risk							
cabazitaxel	129	82	39	20	8	4	0
ASTI	126	42	16	7	2	1	0

abi, abiraterone; AR, androgen receptor; ARPI, androgen receptor pathway inhibitor; CI, confidence interval; enza, enzalutamide; PFS, progression-free survival; PSA, prostate-specific antigen

de Wit R, et al. N Engl J Med. 2019;381:2506-18

PROFOUND STUDY: PROGRESSION-FREE SURVIVAL

- Sequencing AR agents not effective
- Median PFS of 3.6 months for second ARI

Key eligibility criteria
- mCRPC with disease progression on prior NHA (e.g. abiraterone acetate or enzalutamide)
- Alterations in ≥1 of any qualifying gene with a direct or indirect role in HRR

Cohort A
BRCA1, *BRCA2*, or *ATM* alteration
(N=245)
- **Olaparib 300 mg BID (n=162)**
- **Physician's choice[a] (n=83)**

Cohort B
Other alterations
(N=142)
- **Olaparib 300 mg BID (n=94)**
- **Physician's choice (n=48)**

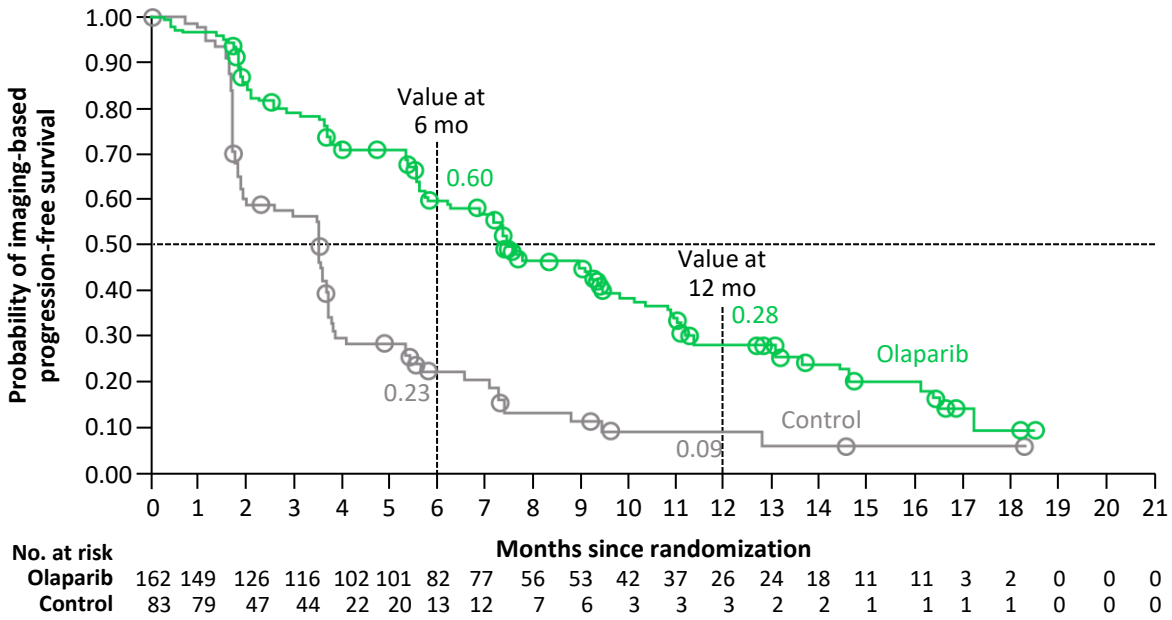
2:1 randomisation (Open label)

Upon progression by BICR, physician's choice patients were allowed to cross over to olaparib

Stratification factors
- Previous taxane
- Measurable disease

[a]Physician's choice: enzalutamide 160 mg/day, or abiraterone 1,000 mg/day + prednisone 5 mg BID

rPFS IN COHORT A (PRIMARY ENDPOINT)

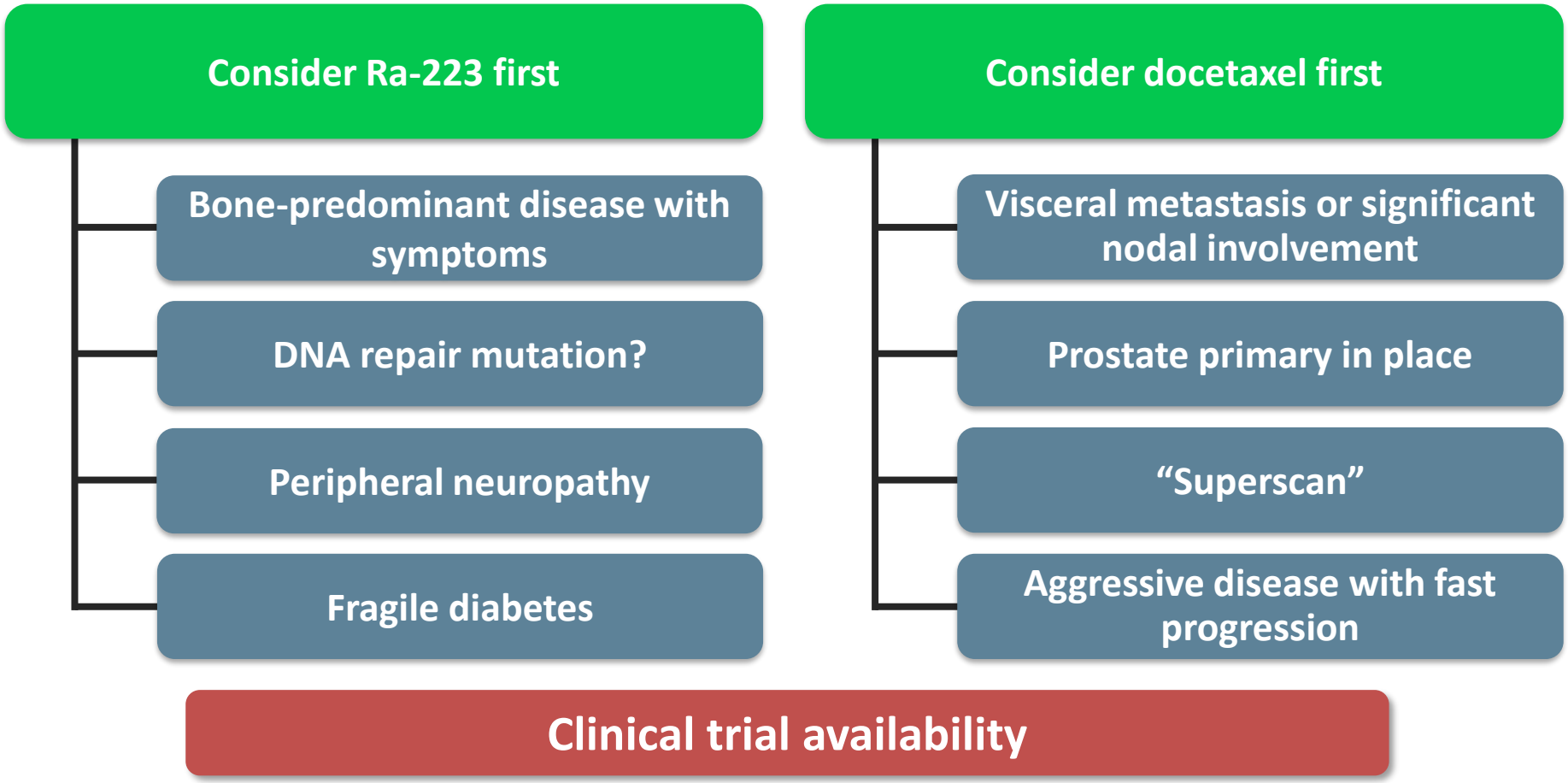


	Olaparib (n=162)	Physician's choice (n=83)
Median rPFS, months	7.4	3.6
Hazard ratio (95% CI)	0.34 (0.25–0.47) p<0.001	

AR(I), androgen receptor (inhibitor); ATM, ataxia telangiectasia mutated; BICR, blinded independent central review; BID, twice daily; BRCA1/2, breast cancer 1/2; CI, confidence interval; HRR, homologous recombination repair; mCRPC, metastatic castration-resistant prostate cancer; NHA, new hormonal agent; (r)PFS, (radiographic) progression-free survival

de Bono J, et al. N Engl J Med. 2020;382:2091-102; Hussain M, et al. Ann Oncol. 2019;30(suppl 5):v881-2 (ESMO 2019 oral presentation)

CHEMOTHERAPY VS RADIUM-223: WHICH SEQUENCE?

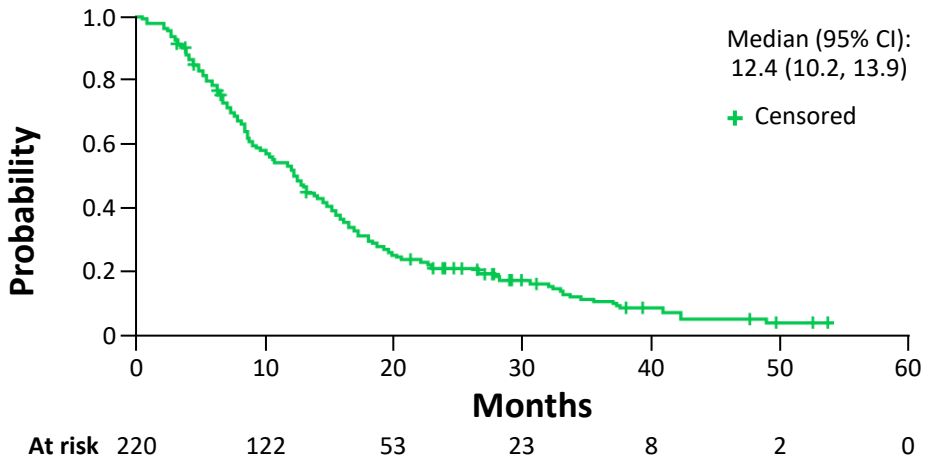


EBXRT, external beam radiation therapy; ^{177}Lu, lutetium 177; PSMA, prostate-specific membrane antigen; Ra-223, radium-223

CHEMOTHERAPY AFTER Ra-223 TREATMENT STILL PROVIDES OS BENEFIT FOR mCRPC PATIENTS (REAL-WORLD DATA)

- Longest OS was observed in the radium-223 pre-chemotherapy cohort
- OS did not differ significantly between radium-233 pre-chemotherapy or post-chemotherapy cohort, or between the radium-223 monotherapy and radium-223 combination cohorts

OS FROM RADIUM-223 INITIATION



OS FROM INITIATION OF FIRST-LINE mCRPC THERAPY

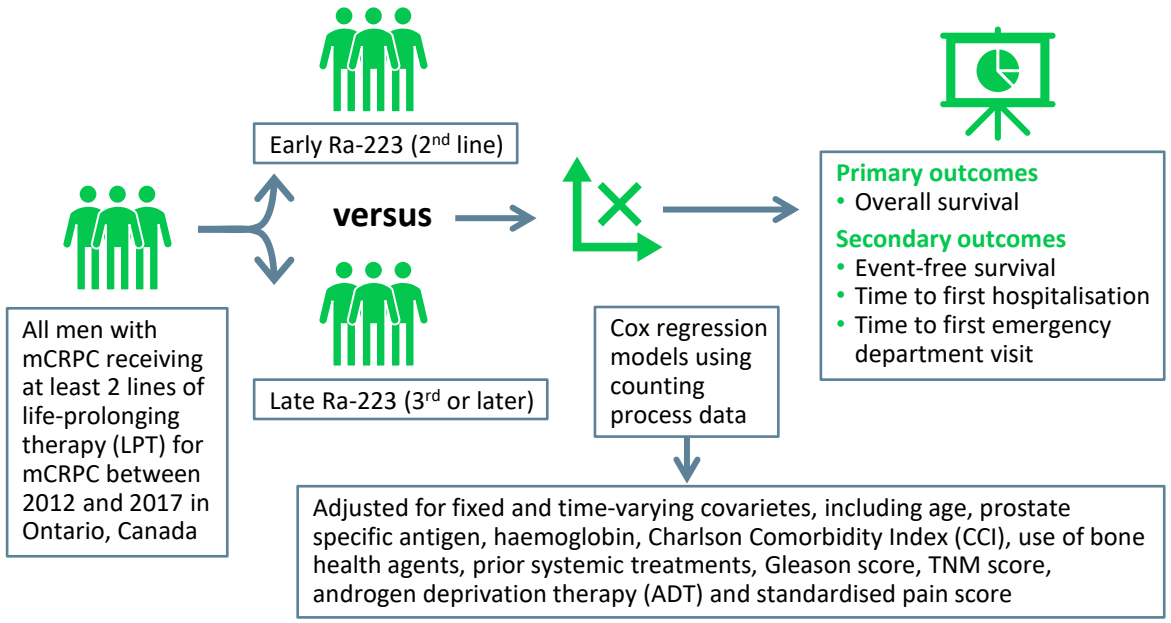
	N	Median OS, months (95% CI)
Chemotherapy subgroups		
Patients treated with chemotherapy	147	38.7 (34.4, 44.2)
Patients treated with radium-223 pre-chemotherapy	64	39.4 (33.0, 48.8)
Patients treated with radium-223 post-chemotherapy	83	37.4 (32.0, 43.5)
Radium-223 therapy subgroups		
Patients treated with radium-223 combination therapy	92	35.2 (27.9, 43.3)
Patients treated with radium-223 monotherapy	128	32.0 (26.9, 36.0)

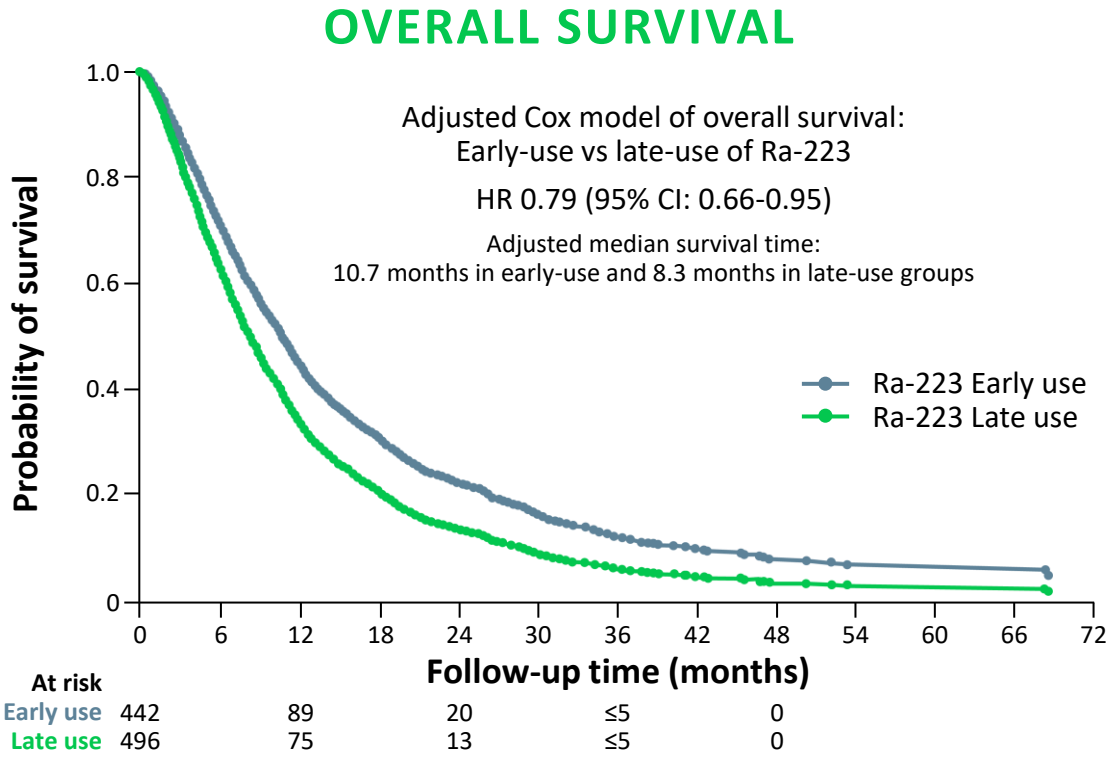
CI, confidence interval; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; Ra-223, radium-223

McKay R, J Clin Oncol. 2020;38(6_suppl):223 (poster)

Ra-223 EARLY VS LATE IN THE TREATMENT SEQUENCE (RETROSPECTIVE ANALYSIS)

- Patients who received Ra-223 in second-line versus third-line or later had better outcomes
- Patients who received Ra-223 early received less chemotherapy, but had better survival



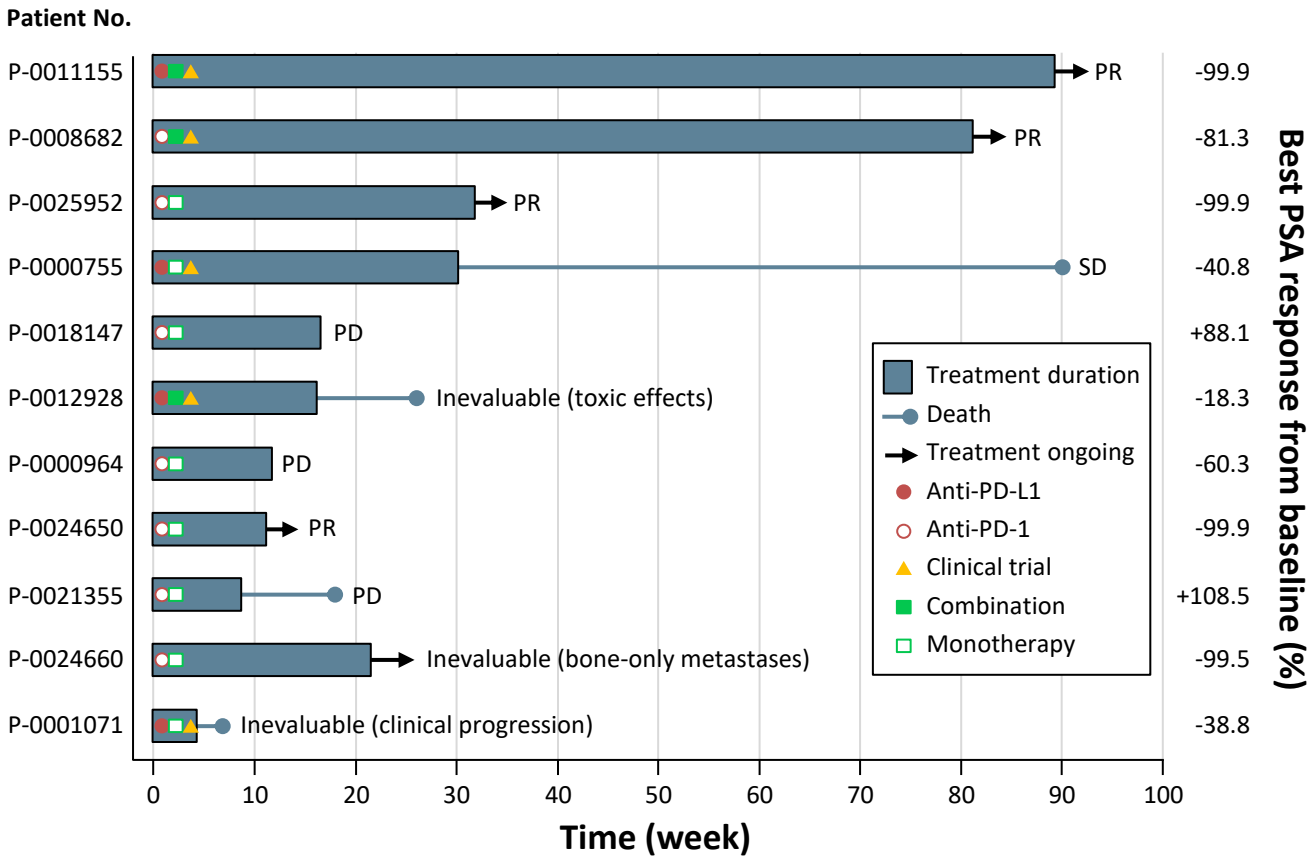


ADT, androgen deprivation therapy; CCI, Charlson Comorbidity Index; CI, confidence interval; HR, hazard ratio; LPT, life-prolonging therapy; mCRPC, metastatic castration-resistant prostate cancer; Ra-223, radium-223; TNM, tumour, node, metastasis

Mbuagbaw L, et al. J Clin Oncol. 2021;39(6_suppl):136 (Poster session)

PEMBROLIZUMAB IN MSI-HIGH PROSTATE CANCER

- 32 (3.1%) of 1,033 of prostate cancer patients tested with germline + somatic DNA sequencing had MSI-high or mismatch-repair deficient status
- 6 of 11 treated with PD-1/PD-L1 antibody therapy had a PSA decline >50%
- 8 patients were evaluable for radiographic response
- Duration of therapy ranged from 4.6 to 89 weeks or longer



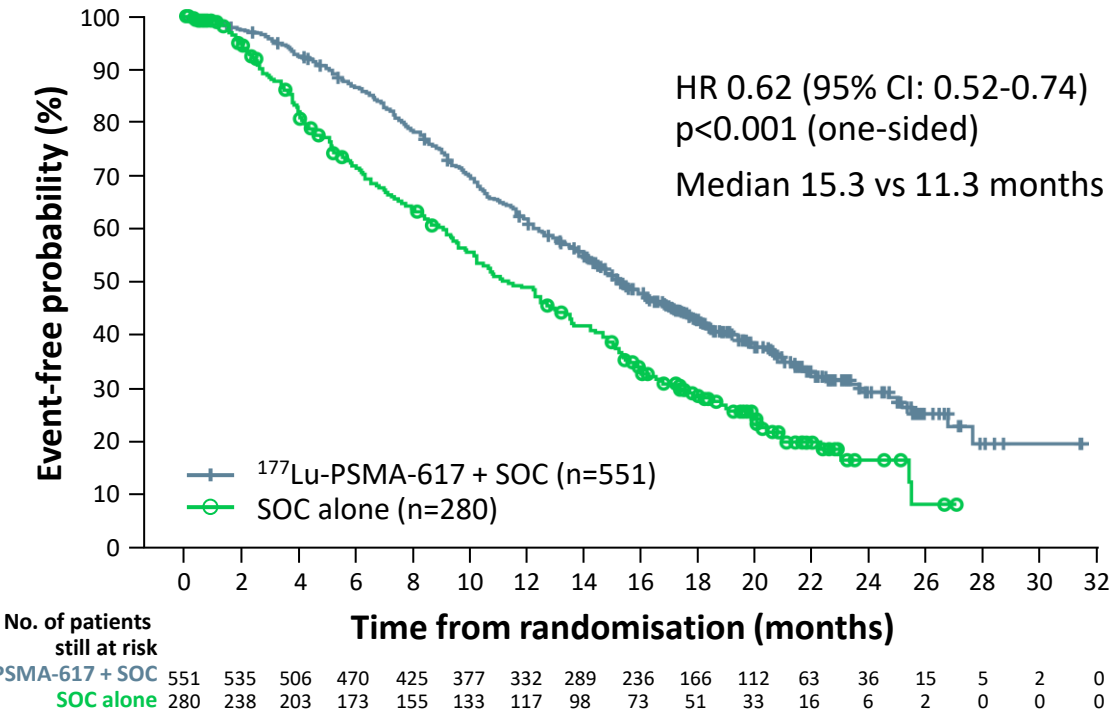
MSI, microsatellite instability; PD, progressing disease; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PR, partial response; PSA, prostate-specific antigen; SD, stable disease

Abida W, et al. JAMA Oncol. 2019;5:471-8

VISION TRIAL: ^{177}LU-PSMA-617 PROLONGS OVERALL SURVIVAL

ALTERNATE PRIMARY ENDPOINTS

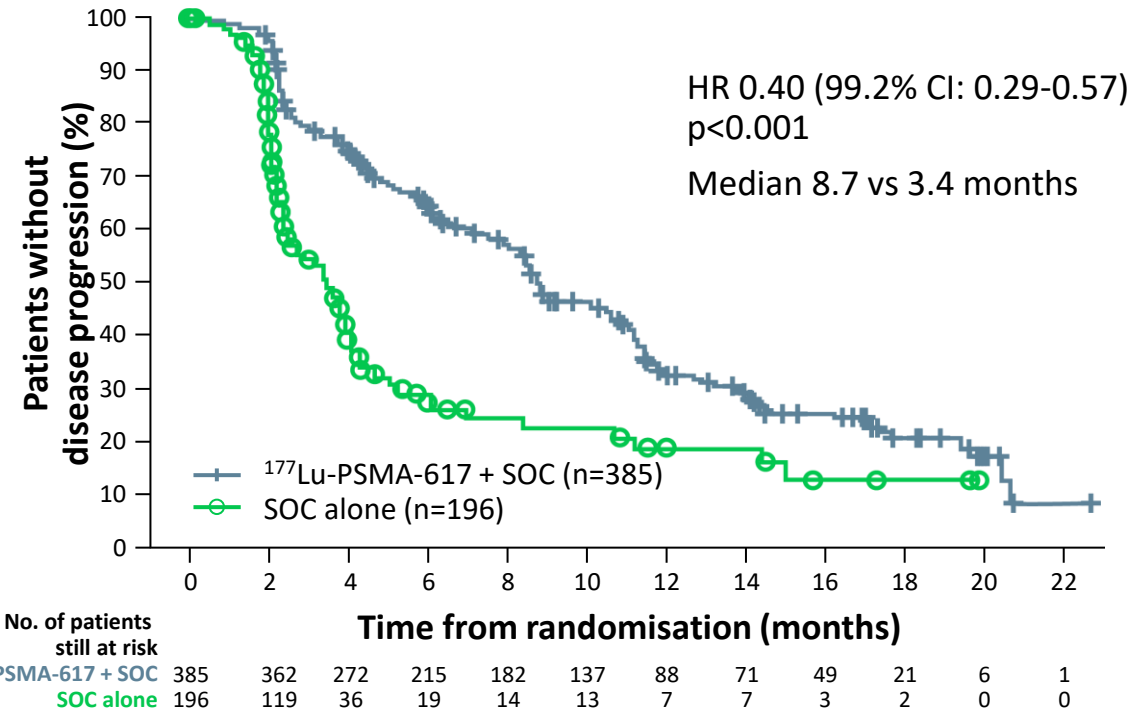
OS all randomised patients (N=831)



No. of patients still at risk

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

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



No. of patients still at risk

^{177}Lu-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; ^{177}Lu-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. DOI: 10.1056/NEJMoa2107322

CONCLUSIONS

- Standard of care for mCSPC requires consideration of early addition of either docetaxel or an AR-pathway inhibitor (abiraterone acetate, apalutamide, enzalutamide) to ADT
- Treatment decisions for mCRPC patients are dependent on the treatment previously received in the CSPC setting
- The aim is to give mCRPC patients as many novel life prolonging treatments as possible, whilst preserving quality of life
  - Sequencing treatments with different mechanism of actions is preferred

ADT, androgen deprivation therapy; AR, androgen receptor; mCRPC, metastatic castration-resistant prostate cancer; (m)CSPC, (metastatic) castration-sensitive prostate cancer

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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

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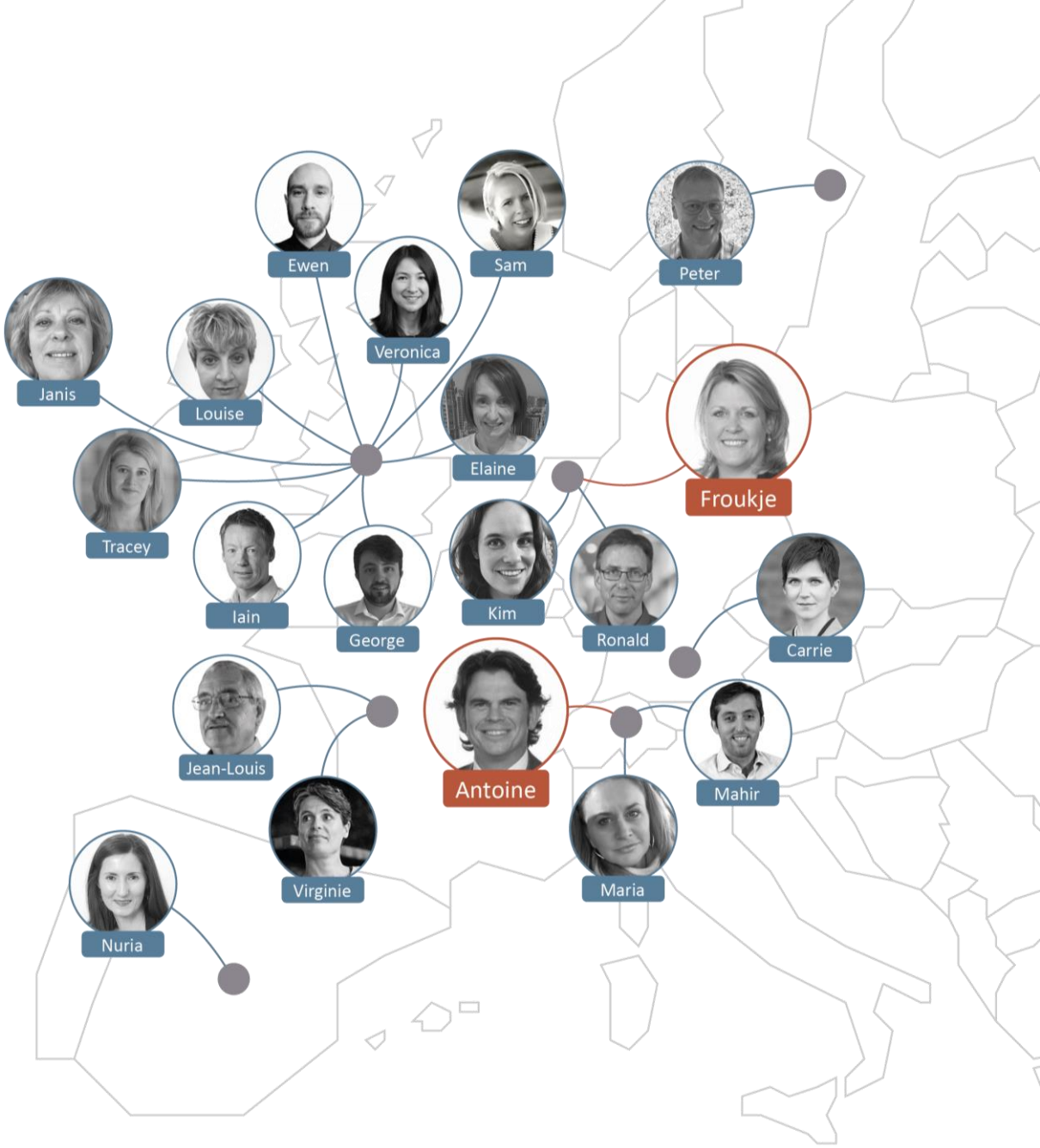

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