Genitourinary Masterclass

Management of patients with advanced prostate cancer:
The latest APCCC recommendations

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Speaker disclosures

Relevant financial disclosure(s):

- Amgen, Astellas, Bayer, Janssen, MSD, Novartis, Pfizer, RedHill Biopharma
- Patent: PCPro

Relevant nonfinancial disclosure(s):

- ANZUP Board
- APCCC panelist 2022, 2024, 2025, 2026

APCCC, Advanced Prostate Cancer Consensus Conference; ANZUP, Australia and New Zealand Urogenital and Prostate; MSD, Merck Sharp & Dohme.

What is the Advanced Prostate Cancer Consensus Conference (APCCC)?

AIM: To provide an update on the current standard of advanced prostate cancer management, with a focus on situations with no high-level evidence for a specific treatment option[1]

Advanced prostate cancer is defined by APCCC as locally advanced disease, biochemical recurrence and metastatic disease[1]

For all questions for the APCCC, the panelists presume:[2,3]

- Fit patients with no treatment-limiting comorbidities
- All diagnostics tests and treatments available
- No option to enrol in clinical trial

The APCCC employs a structured voting framework with defined consensus thresholds (≥75% for consensus, ≥90% for strong consensus), ensuring transparent and robust decision-making[2,3]

APCCC, Advanced Prostate Cancer Consensus Conference.

1. APCCC. Save the date for the APCCC 2026. Available at: https://apccc.org/apccc-2026/. Last accessed: July 2025; 2. Gillessen S, et al. *Eur Urol* 2025;87:157–216; 3. Gillessen S, et al. *Eur Urol* 2023;83:267–293.

APCCC 2024 panelists

APCCC 2026
Kyu Hong Sung
South Korea

APCCC, Advanced Prostate Cancer Consensus Conference.
APCCC. Panel Members 2024. Available at: https://apccc.org/apccc-2026/panel-members-2024/. Last accessed: July 2025.

Key learning objectives

- Docetaxel in mHSPC
- Prostate radiotherapy in mHSPC
- Metastasis-directed treatment in mHSPC
- The role of PSMA-PET scan in mHSPC
- PARP inhibitors in mHSPC

mHSPC, metastatic hormone-sensitive prostate cancer; PARP, poly (ADP-ribose) polymerase; PSMA-PET, prostate-specific membrane antigen positron emission tomography.

mHSPC subgroups

Category	Definition
High volume mHSPC (High Burden, APCCC)	Meets one or both criteria (CHAARTED criteria)[1,2] • At least four bone lesions on bone scan (at least one outside vertebrae/pelvis) • Measurable visceral metastases
	Meets two out of three criteria (LATITUDE criteria, high-risk disease)[3] • At least three bone metastases • Gleason score ≥8 • Measurable visceral metastases
Low volume mHSPC (Low Burden, APCCC)	Meets one or both criteria[1,2] • Lymph node only disease outside the pelvis • At least three bone lesions on bone scan
Oligometastatic HSPC	Limited metastatic sites

APCCC, Advanced Prostate Cancer Consensus Conference; HSPC, hormone-sensitive prostate cancer; m, metastatic.

1. Sweeney CJ, et al. *N Engl J Med*. 2015;373:737–746; 2. Kyriakopoulos CE, et al. *J Clin Oncol*. 2018;36:1080–1087; 3. Fizazi K, et al. *Lancet Oncol*. 2019;20:686–700.

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Docetaxel in mHSPC

mHSPC, metastatic hormone-sensitive prostate cancer.

mHSPC – docetaxel treatment as single agent with ADT

Study	HV	OS – HV+LV	OS – LV only	OS – HV only
CHAARTED[1]	66%	HR 0.72 (95%CI: 0.59–0.89) p=0.0018	HR 1.04 (95%CI: 0.70–1.55) p=0.86	HR 0.63 (95% CI: 0.50–0.79) p<0.001
STAMPEDE[2]	56%	HR 0.81 (95% CI: 0.69–0.95) p=0.009	HR 0.76 (95% CI: 0.54–1.07) p=0.107	HR 0.81 (95% CI: 0.64–1.02) p=0.064

ADT, androgen deprivation therapy; CI, confidence interval; HV, high-volume; HR, hazard ratio; LV, low-volume; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival.

1. Kyriakopoulos CE, et al. *J Clin Oncol.* 2018;36:1080–1087; 2. Clarke NW, et al. *Ann Oncol.* 2019;30:1992–2003.

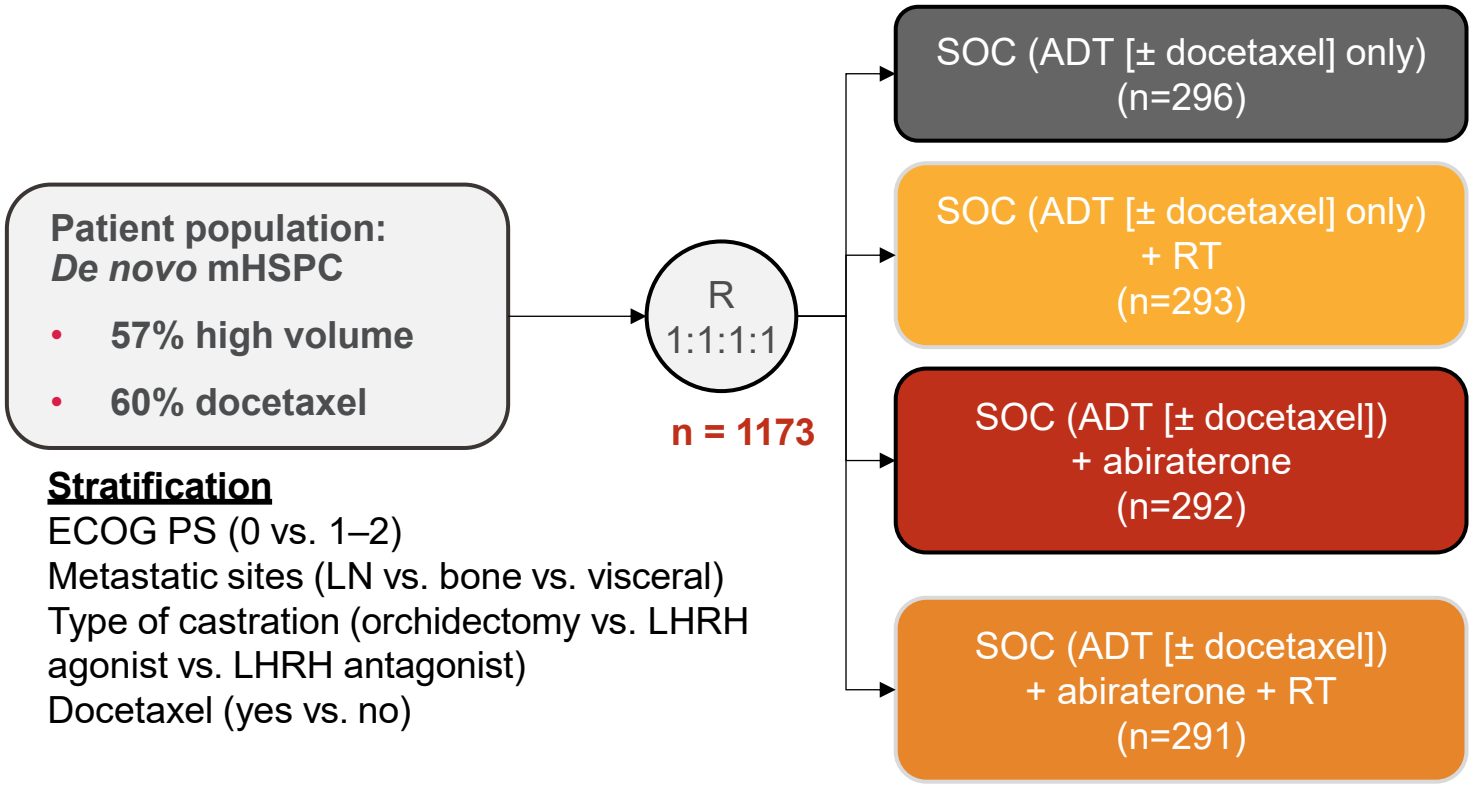
Triplet systemic therapy - ADT/docetaxel/ARPI

Trial	Total cohort number	Docetaxel treated	Investigational agent	Timing of docetaxel	Outcome
PEACE-1[1]	1172	710 (61%)	Abiraterone + prednisone	Concurrent	Improved rPFS, improved OS in HV
ENZAMET[2]	1125	503 (45%)	Enzalutamide	Concurrent	Improved OS in *de novo* HV
TITAN[3]	1052	108 (10%)	Apalutamide	Prior	NA
ARCHES[4]	1150	205 (18%)	Enzalutamide	Prior	NA
ARASENS[5]	1306	1300 (100%)	Darolutamide	Concurrent	Improved rPFS and OS

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; HV, high-volume; NA, not available; OS, overall survival; rPFS, radiographic progression-free survival.

1. Fizazi K, et al. *Lancet*. 2022;399:1695–1707; 2. Sweeney CJ, et al. *Lancet Oncol*. 2023;24:323–334; 3. Chi KN, et al. *J Clin Oncol*. 2021;39:2294–2303; 4. Armstrong AJ, et al. *J Clin Oncol*. 2019;37:2974–2986; 5. Smith MR, et al. *N Engl J Med*. 2022 Mar 24;386(12):1132–1142.

PEACE-1: Study schema



Co-primary endpoints:

- rPFS
- OS

Stratification

ECOG PS (0 vs. 1–2)
Metastatic sites (LN vs. bone vs. visceral)
Type of castration (orchidectomy vs. LHRH agonist vs. LHRH antagonist)
Docetaxel (yes vs. no)

SOC evolved 2013–2018:
ADT → ADT +/- Docetaxel → ADT + Docetaxel

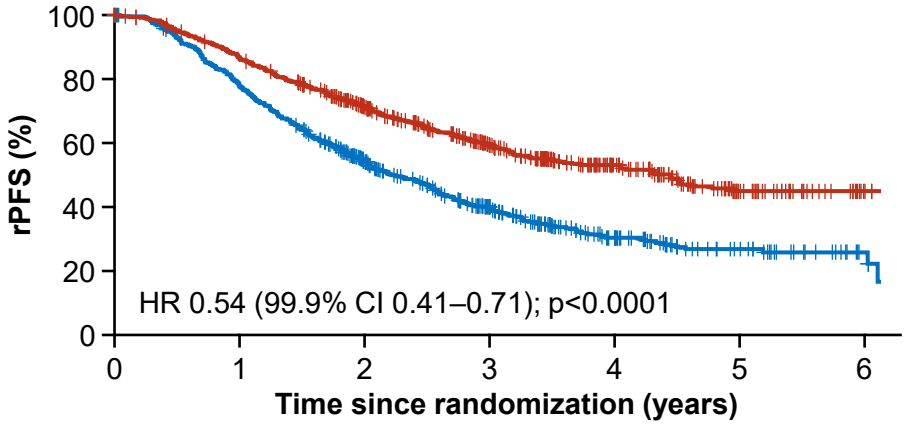
ADT, androgen deprivation therapy; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; LHRH, luteinizing hormone-releasing hormone; LN, lymph node; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; R, randomization; rPFS, radiographic progression-free survival; RT, radiotherapy; SOC, standard of care.

Fizazi K, et al. *Lancet* 2022;399:1695–1707.

PEACE-1: Outcomes

rPFS

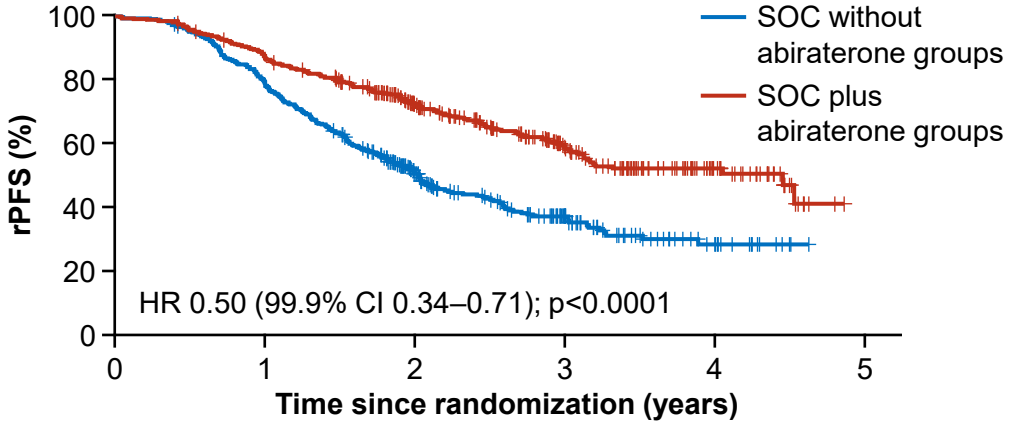
A. Overall population



Number at risk

SOC without abiraterone groups	589	453	274	158	72	31	7
SOC plus abiraterone groups	583	495	355	230	119	47	12

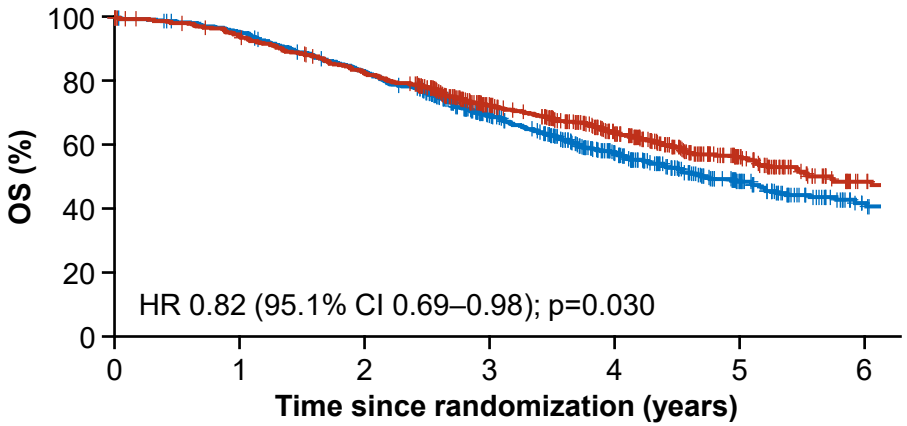
B. ADT with docetaxel population



355	274	137	61	16	0
355	303	200	105	35	0

OS

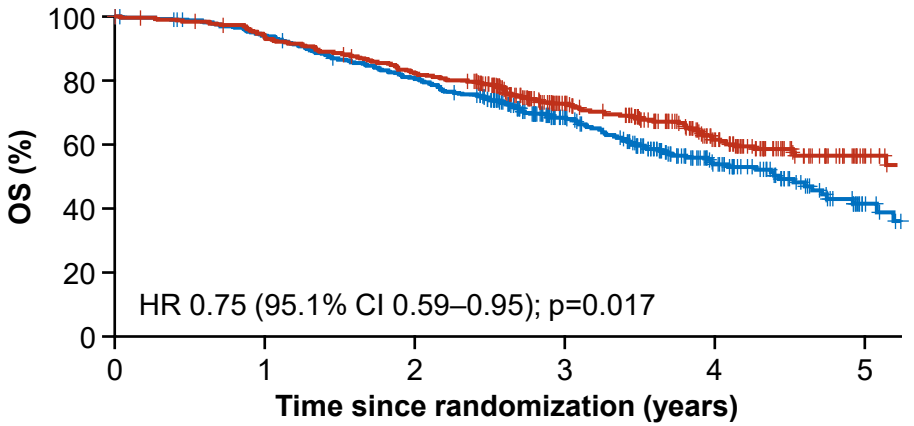
C. Overall population



Number at risk

SOC without abiraterone groups	589	556	480	334	207	101	37
SOC plus abiraterone groups	583	541	470	340	230	111	47

D. ADT with docetaxel population



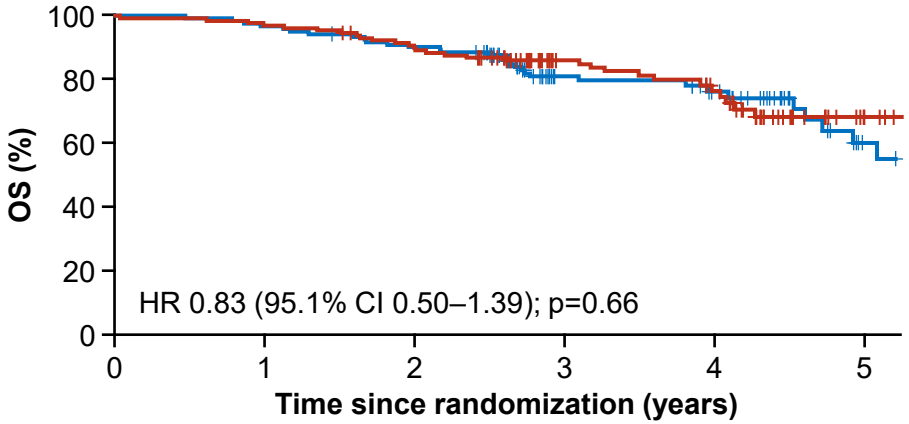
355	329	281	172	78	18
355	328	287	183	98	25

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; rPFS, radiographic progression-free survival; OS, overall survival; SOC, standard of care.

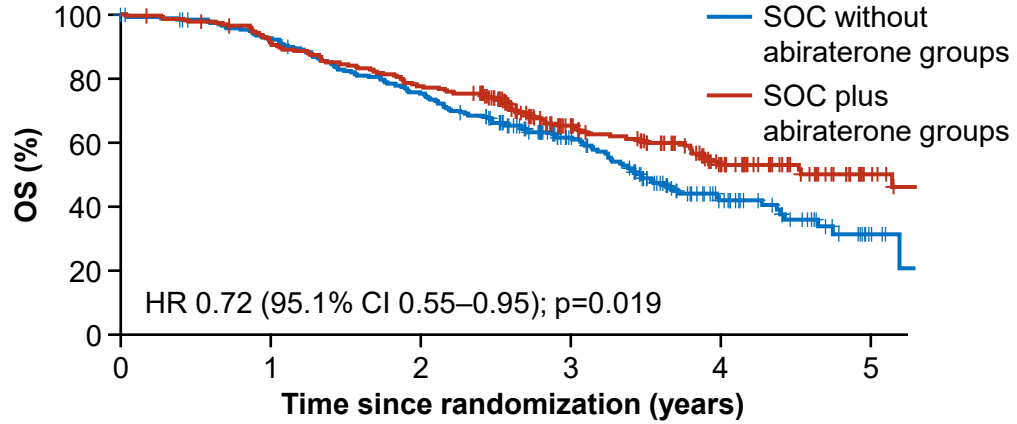
Fizazi K, et al. *Lancet* 2022;399:1695–1707.

PEACE-1: OS by disease burden

ADT with docetaxel population with low-volume metastatic burden



ADT with docetaxel population with high-volume metastatic burden



Number at risk

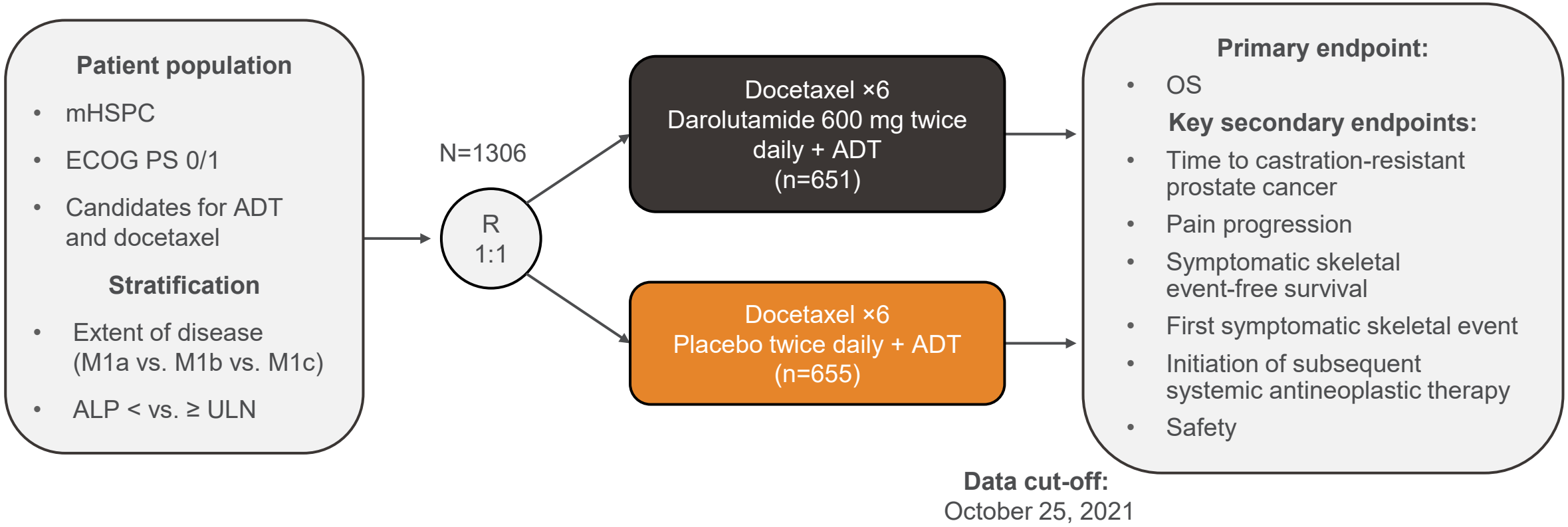
SOC without abiraterone groups	123	119	110	71	39	12
SOC plus abiraterone groups	131	127	116	80	41	9

SOC without abiraterone groups	232	210	171	101	39	6
SOC plus abiraterone groups	224	201	171	103	57	16

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; OS, overall survival; SOC, standard of care.

Fizazi K, et al. *Lancet* 2022;399:1695–1707.

ARASENS: Study schema



ADT, androgen deprivation therapy; ALP, alkaline phosphatase; ECOG PS, Eastern Cooperative Oncology Group performance status; M, metastasis; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; R, randomization; ULN, upper limit of normal.

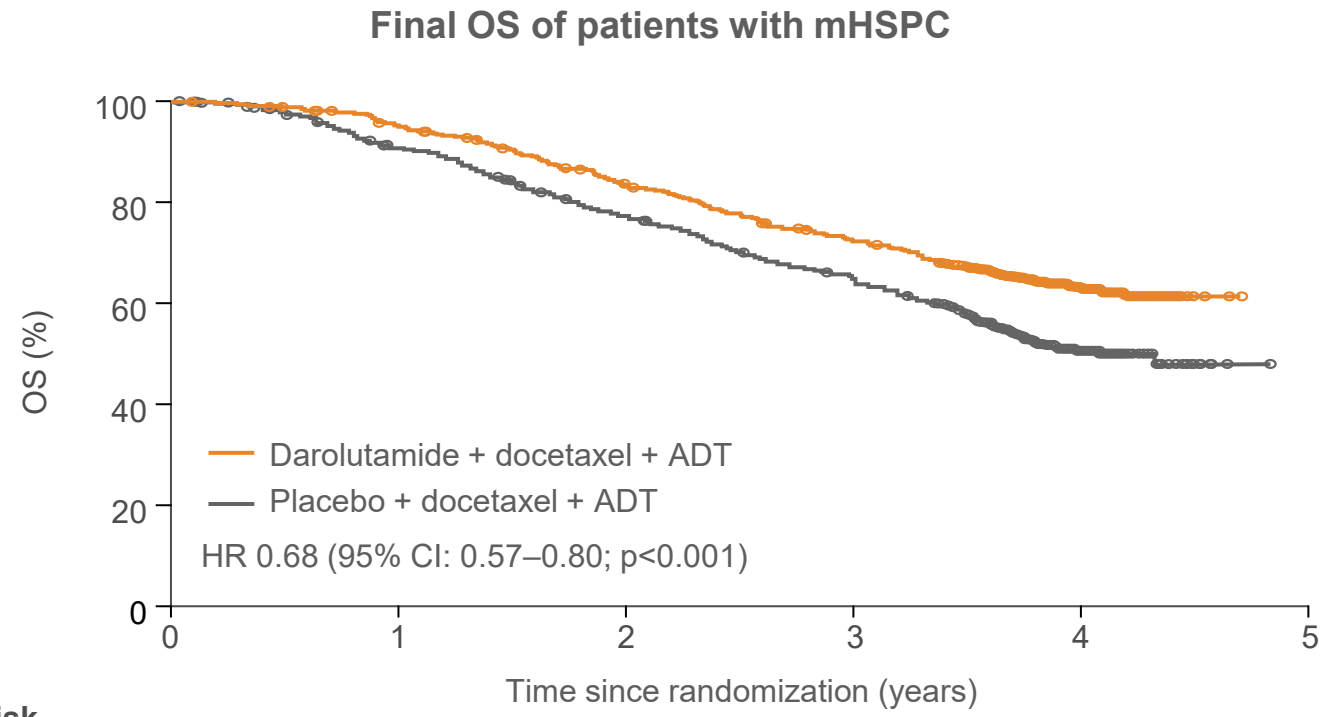
Smith MR, et al. *N Engl J Med* 2022;386:1132–1142.

ARASENS: Patient characteristics

Characteristic	Darolutamide–ADT–Docetaxel* (N=651)	Placebo–ADT–Docetaxel* (N=654)
Median age (range) – years	67 (41–89)	67 (42–86)
Gleason score at initial diagnosis – no. (%)		
<8	122 (18.7)	118 (18.0)
≥8	505 (77.6)	516 (78.9)
Data missing	24 (3.7)	20 (3.1)
Metastasis stage at initial diagnosis – no. (%)		
M1, distant metastasis	558 (85.7)	566 (86.5)
M2, no distant metastasis	86 (13.2)	82 (12.5)
MX, distant metastasis not assessed	7 (1.1)	6 (0.9)
Metastasis stage at screen – no. (%)		
M1a, nonregional lymph-node metastases only	23 (3.5)	16 (2.4)
M1b, bone metastases with or without lymph-node metastases	517 (79.4)	520 (79.5)
M1c, visceral metastases with or without lymph-node or bone metastases	111 (17.1)	118 (18.0)
Median serum PSA level (range) – ng/ml†	30.3 (0.0–9219.0)	24.2 (0.0–11,947.0)
Median serum ALP level (range) – U/liter†	148 (40–4885)	140 (36–7680)
ALP category – no. (%)†		
<ULN	290 (44.5)	291 (44.5)
≥ULN	361 (55.5)	363 (55.5)

*One patient who was randomly assigned to the placebo group but received darolutamide was included in the placebo group in the full analysis set; †These values were centrally assessed. Samples were obtained while patients were receiving ADT.
ADT, androgen deprivation therapy; ALP, alkaline phosphatase; ULN, upper limit of normal.
Smith MR, et al. *N Engl J Med* 2022;386:1132–1142.

ARASENS: OS



No. at risk

Placebo + docetaxel + ADT	654	580	488	402	107	0
Darolutamide + docetaxel + ADT	651	608	525	452	139	0

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival.

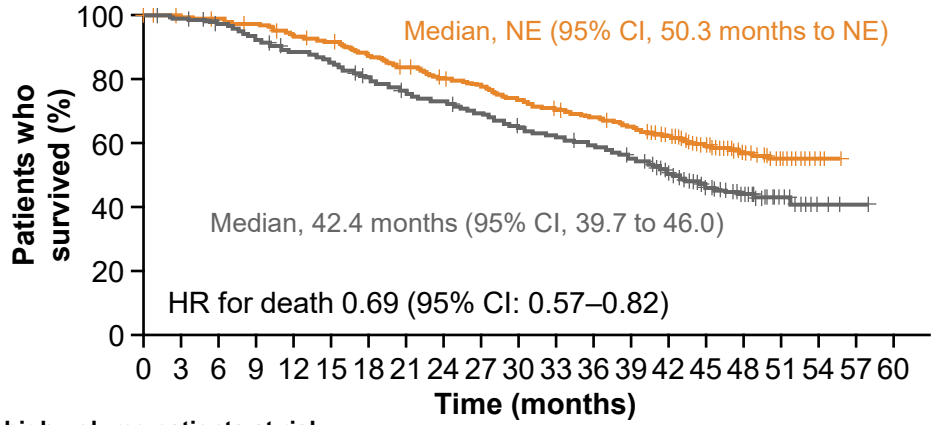
Smith MR, et al. *N Engl J Med* 2022;386:1132–1142.

ARASENS: Volume of disease

HV vs. LV (CHAARTED)[2,3]

High vs. low risk (LATITUDE)[4]

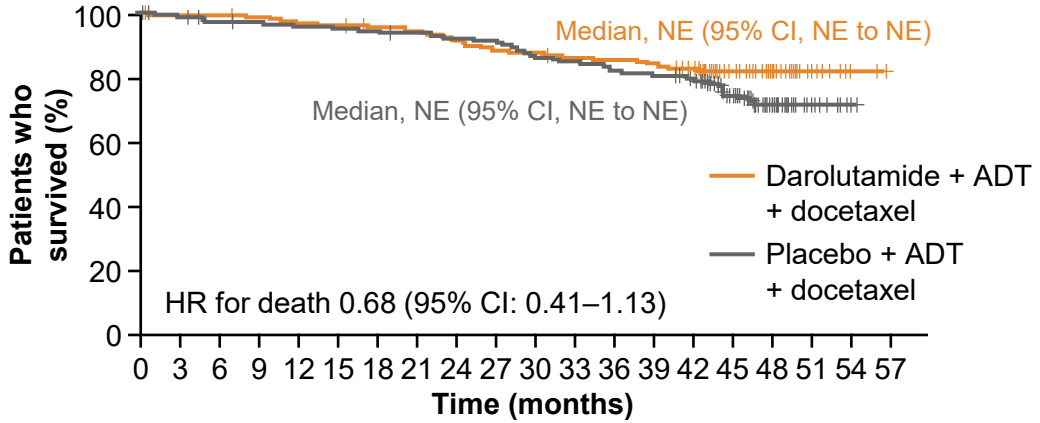
A. High-volume[1]



No. of high-volume patients at risk

Darolutamide	497	494	486	479	462	449	429	408	389	378	356	341	326	312	285	193	103	43	6	0	0
Placebo	508	502	491	469	444	430	401	378	358	341	319	304	286	269	233	153	72	23	4	1	0

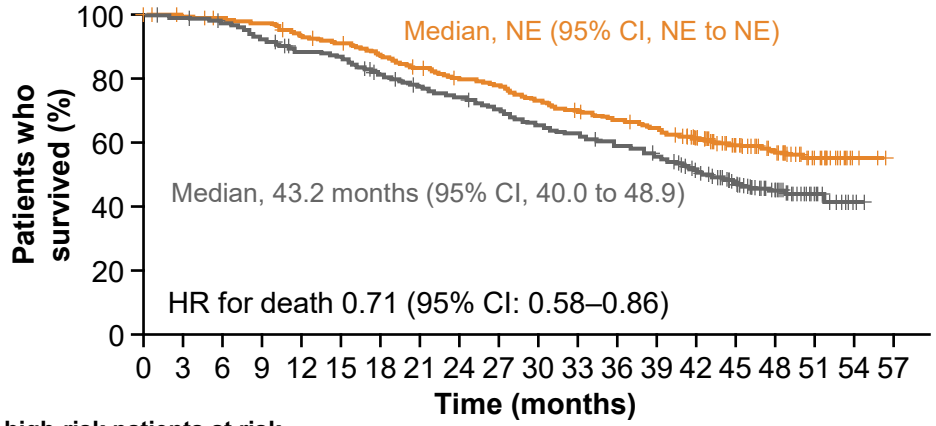
B. Low-volume[1]



No. of low-volume patients at risk

	154	151	151	148	146	144	141	140	136	131	130	127	126	124	117	74	36	13	3	0	
	146	144	139	138	136	135	134	132	130	129	122	120	116	114	107	65	35	14	2	0	

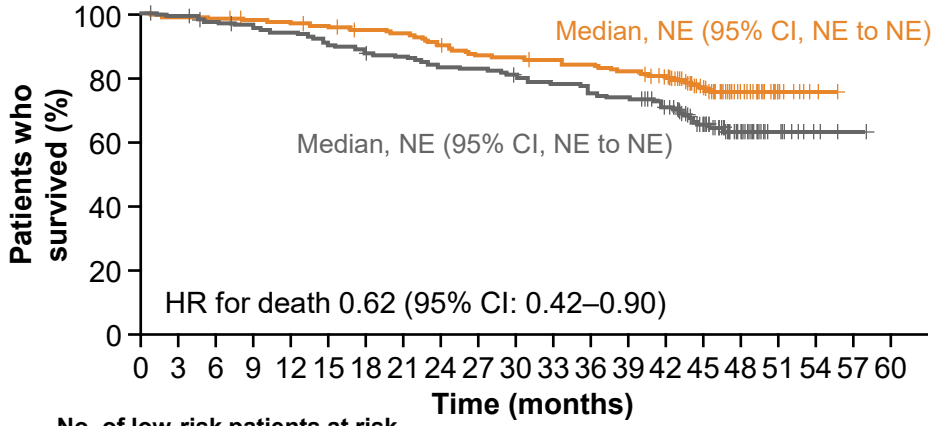
C. High-risk disease[1]



No. of high-risk patients at risk

Darolutamide	452	450	443	437	419	407	389	369	352	344	322	308	294	282	257	177	99	42	6	0	
Placebo	460	453	443	423	400	392	367	346	330	313	290	277	261	245	215	148	72	24	3	0	

D. Low-risk disease[1]



No. of low-risk patients at risk

	199	195	194	190	189	186	181	179	173	165	164	160	158	154	145	90	40	14	3	0	0
	194	193	187	184	180	173	168	164	158	157	151	147	141	138	125	70	35	13	3	1	0

High-volume disease was defined as visceral metastases and/or ≥4 bone metastases with ≥1 beyond the vertebral column/pelvis.
ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; HV, high volume; LV, low volume; NE, not estimable; OS, overall survival.

1. Hussain M, et al. *J Clin Oncol*. 2023;41:3595–3607; 2. Sweeney CJ, et al. *N Engl J Med*. 2015;373:737–746; 3. Kyriakopoulos CE, et al. *J Clin Oncol*. 2018;36:1080–1087; 4. Fizazi K, et al. *Lancet Oncol*. 2019;20:686–700.

Question for the audience

- In patients with high-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

A Yes, in the majority of patients

B Yes, but only in selected patients

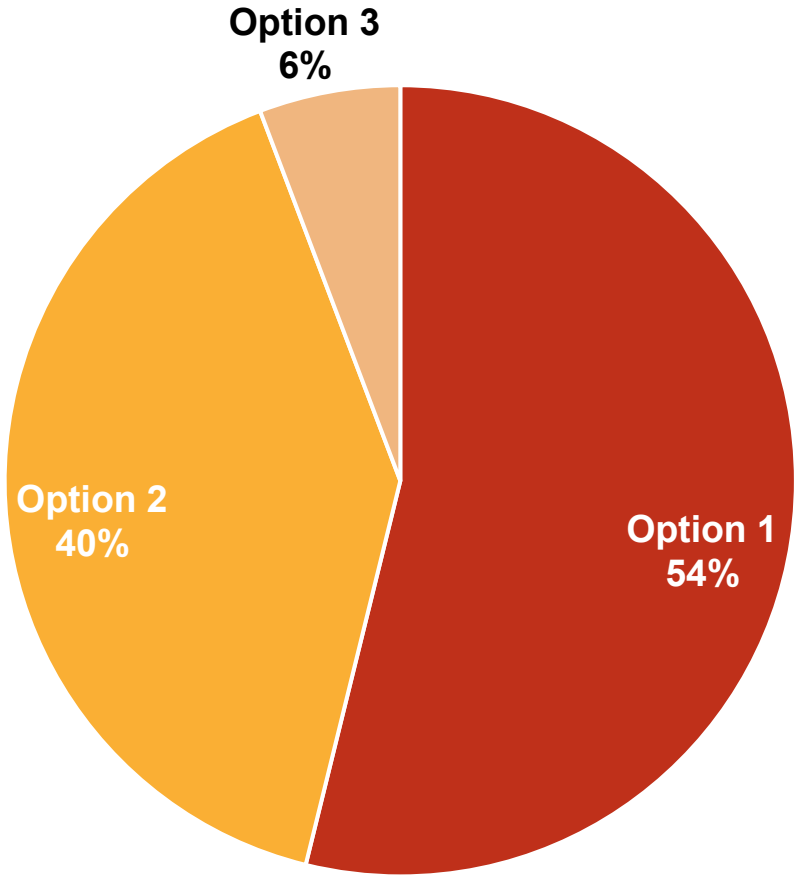
C No, I usually do not recommend this combination

D Abstain/unqualified to answer

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.

67. In patients with high-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No, I usually do not recommend this combination
4. Abstain/unqualified to answer



Option	Votes
Option 1	56
Option 2	42
Option 3	6
Abstain	2

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

Question for the audience

- If you use the triplet therapy (ADT plus docetaxel plus ARPI) only in selected patients, what is most important factor for your decision to use triplet therapy?

A Synchronous disease (vs. metachronous)

B Age (biological)

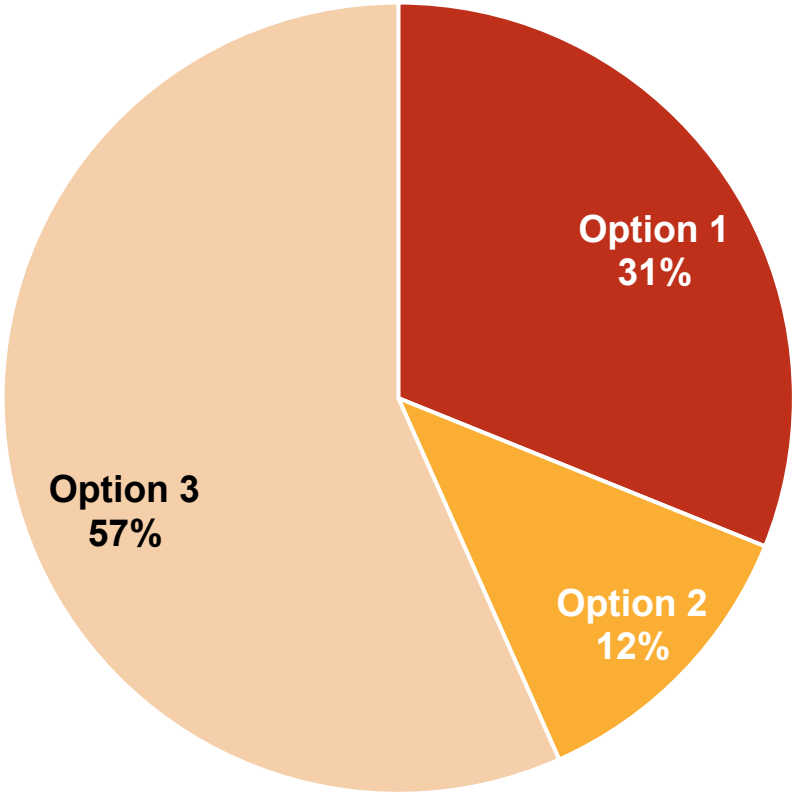
C High-volume disease (vs. low volume)

D Abstain/unqualified to answer (I did not vote for triplet therapy in selected patients)

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor.

68. If you use the triplet therapy (ADT plus docetaxel plus ARPI) only in selected patients, what is most important factor for your decision to use triplet therapy?

1. Synchronous disease (vs. metachronous)
2. Age (biological)
3. High-volume disease (vs. low volume)
4. Abstain/unqualified to answer (I did not vote for triplet therapy in selected patients)



Option	Votes
Option 1	28
Option 2	11
Option 3	51
Abstain	16

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

Question for the audience

- In patients with synchronous low-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

A Yes, in the majority of patients

B Yes, but only in selected patients

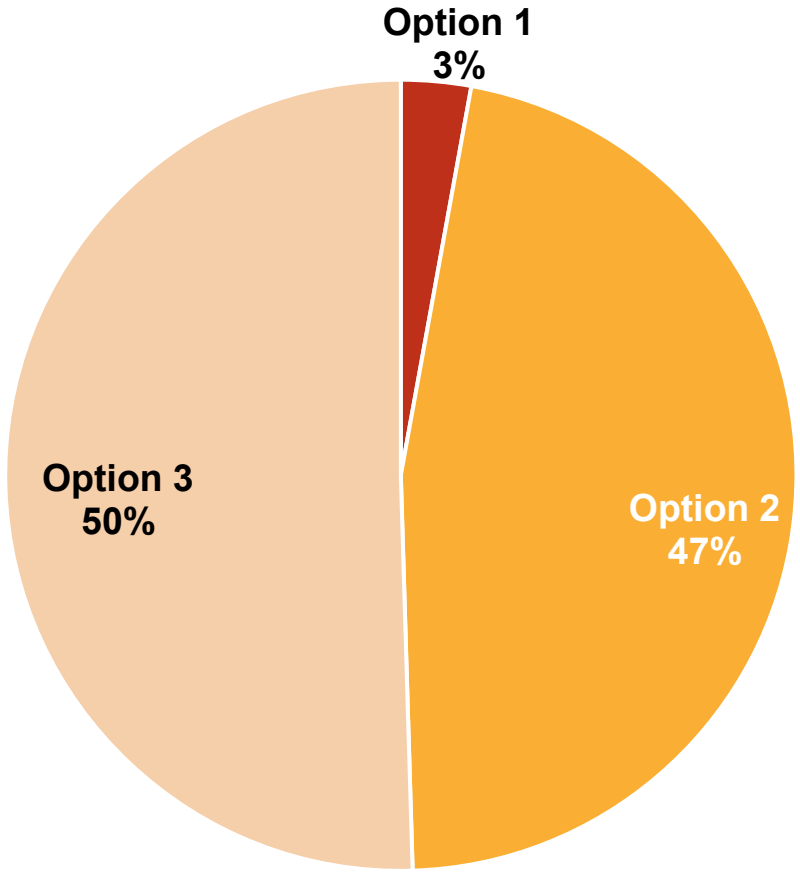
C No

D Abstain/unqualified to answer

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.

69. In patients with synchronous low-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No
4. Abstain/unqualified to answer



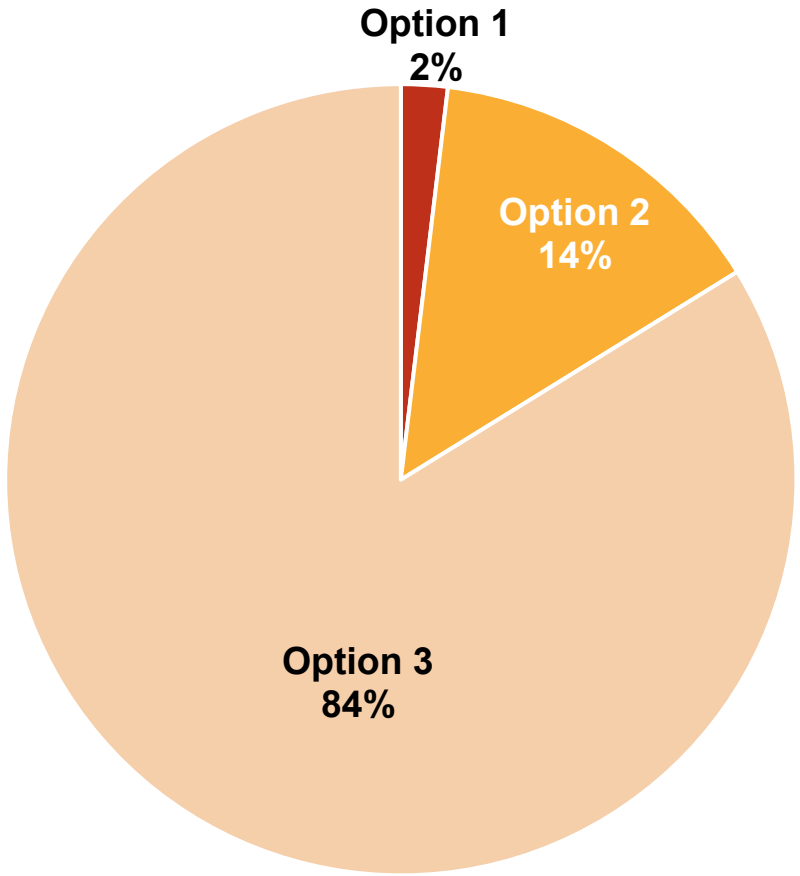
Option	Votes
Option 1	3
Option 2	49
Option 3	53
Abstain	1

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

70. In patients with metachronous low-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No
4. Abstain/unqualified to answer

CONSENSUS



Option	Votes
Option 1	2
Option 2	15
Option 3	88
Abstain	1

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

Question for the audience

- In patients with metachronous high-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

A Yes, in the majority of patients

B Yes, but only in selected patients

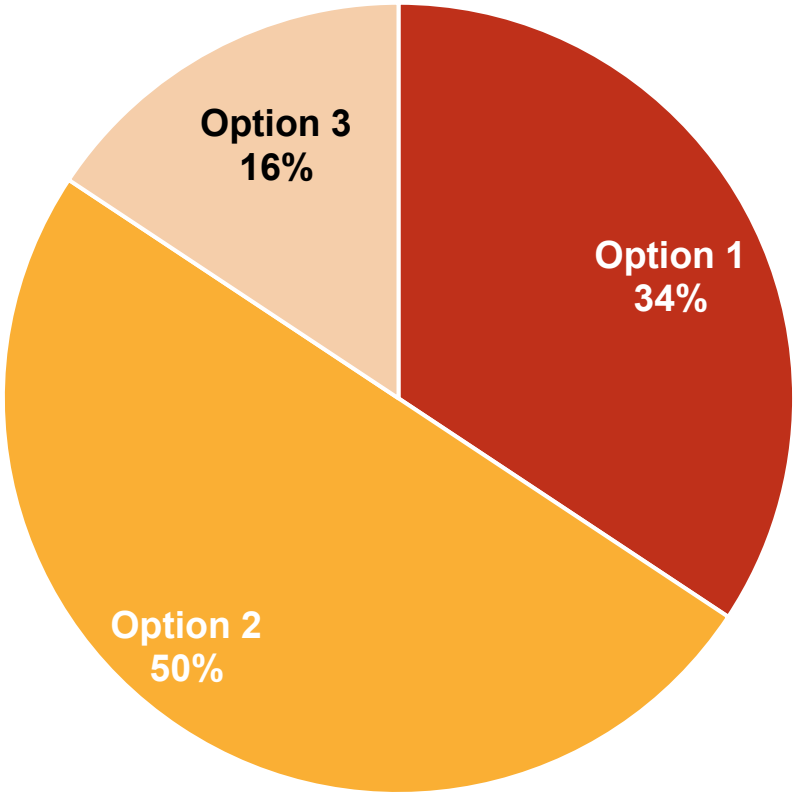
C No

D Abstain/unqualified to answer

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.

71. In patients with metachronous high-burden mHSPC that are chemotherapy fit, do you recommend the triplet therapy ADT plus docetaxel plus ARPI?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No
4. Abstain/unqualified to answer



Option	Votes
Option 1	35
Option 2	51
Option 3	16
Abstain	4

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

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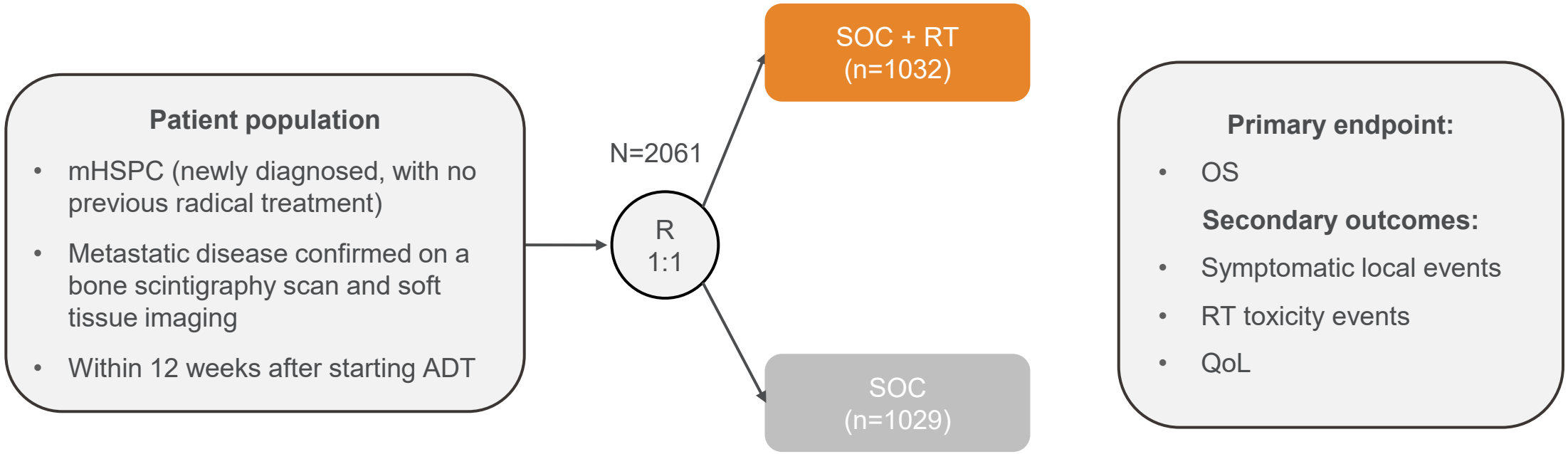
Radiotherapy in mHSPC

Controversies in low burden disease

- Radiotherapy to the prostate
- Radiotherapy to oligometastatic disease

mHSPC, metastatic hormone-sensitive prostate cancer.

STAMPEDE: Study design

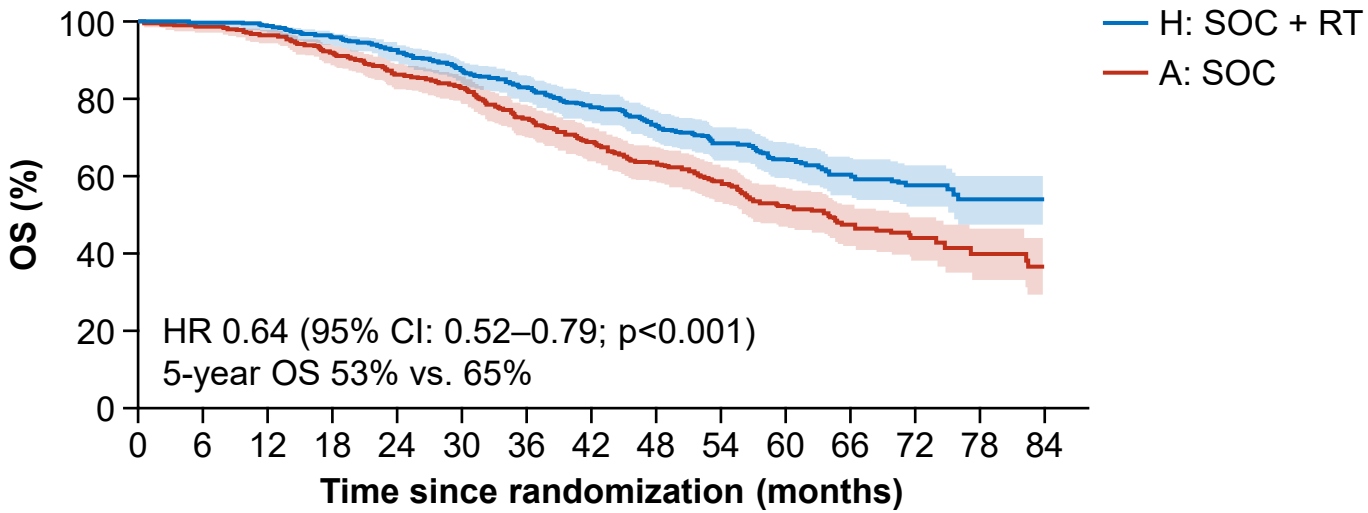


ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; R, randomization; RT, radiotherapy; QoL, quality of life; SOC, standard of care.

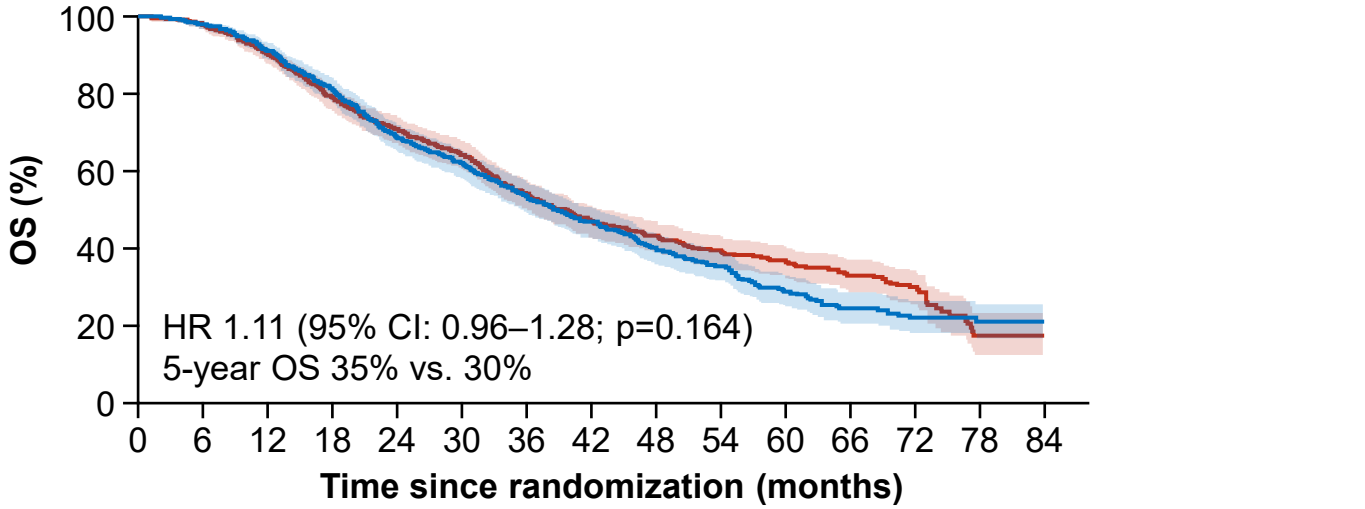
Parker CC, et al. *PLoS Med.* 2022;19:e1003998.

STAMPEDE: Treatment of the prostate

Low-volume mHSPC



High-volume mHSPC

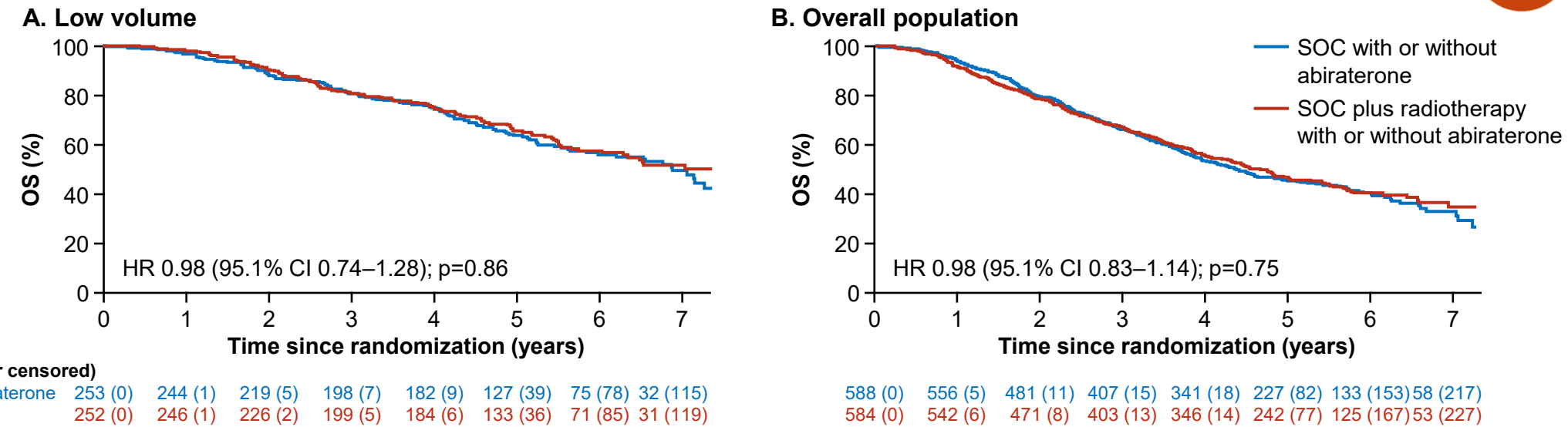


CI, confidence interval; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival.

Parker CC, et al. *PLoS Med.* 2022;19:e1003998.

PEACE-1: Treatment of the primary tumor

Overall survival

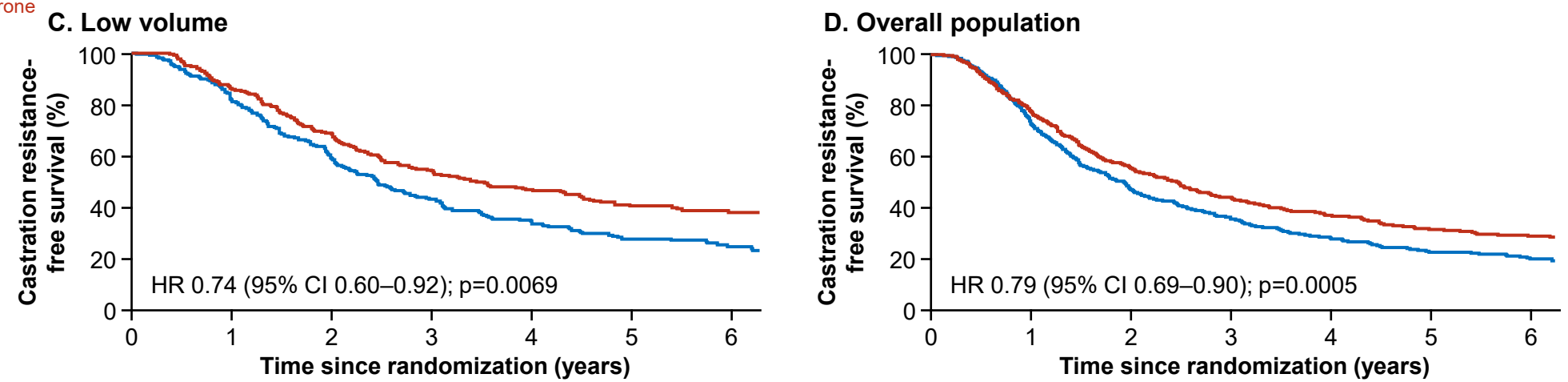


Number at risk (number censored)

SOC with or without abiraterone	253 (0)	244 (1)	219 (5)	198 (7)	182 (9)	127 (39)	75 (78)	32 (115)
SOC plus radiotherapy with or without abiraterone	252 (0)	246 (1)	226 (2)	199 (5)	184 (6)	133 (36)	71 (85)	31 (119)

SOC with or without abiraterone	588 (0)	556 (5)	481 (11)	407 (15)	341 (18)	227 (82)	133 (153)	58 (217)
SOC plus radiotherapy with or without abiraterone	584 (0)	542 (6)	471 (8)	403 (13)	346 (14)	242 (77)	125 (167)	53 (227)

Castration resistant-free survival



Number at risk (number censored)

SOC with or without abiraterone	253 (0)	206 (1)	146 (4)	106 (5)	83 (6)	56 (19)	37 (33)
SOC plus radiotherapy with or without abiraterone	252 (0)	216 (1)	172 (1)	134 (3)	115 (4)	84 (21)	51 (50)

SOC with or without abiraterone	588 (0)	424 (5)	271 (8)	204 (10)	160 (11)	107 (37)	67 (67)
SOC plus radiotherapy with or without abiraterone	584 (0)	448 (6)	320 (7)	250 (10)	210 (11)	144 (50)	81 (103)

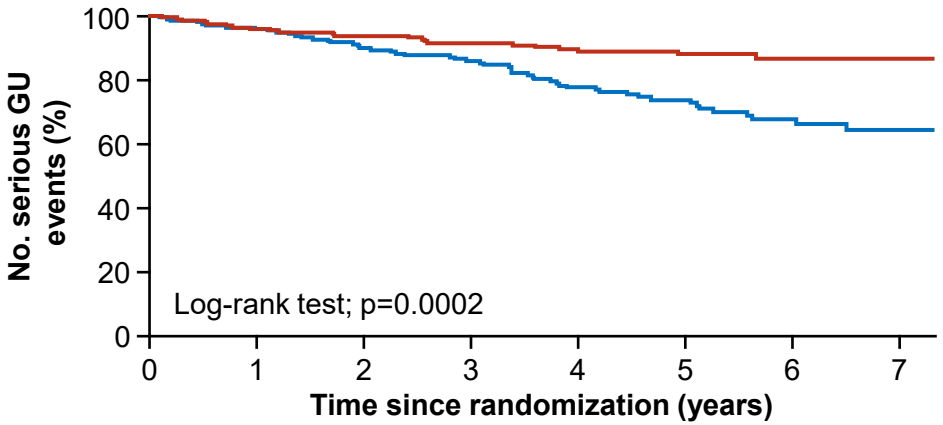
CI, confidence interval; HR, hazard ratio.

Bossi A, et al. *Lancet* 2024;404;2065–2076.

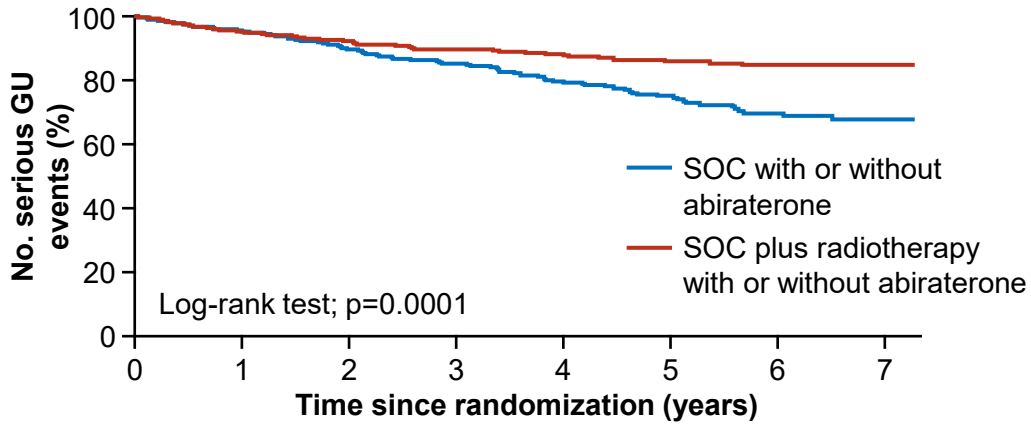
PEACE-1: Treatment of the primary tumor

Number of serious GU events

Low volume disease



Overall population



Number at risk (number censored)

SOC with or without abiraterone	200 (0)	185 (7)	162 (19)	140 (34)	119 (42)	86 (70)	46 (104)	19 (129)
SOC plus radiotherapy with or without abiraterone	198 (0)	186 (4)	169 (17)	147 (35)	134 (45)	97 (80)	55 (121)	24 (152)

SOC with or without abiraterone	458 (0)	418 (18)	350 (63)	290 (106)	235 (144)	152 (216)	84 (275)	37 (320)
SOC plus radiotherapy with or without abiraterone	451 (0)	406 (23)	346 (71)	292 (116)	246 (157)	172 (226)	90 (306)	42 (354)

RT to prostate decreased rate of:

- Urinary/suprapubic catheters
- Surgery (TURP/RP)
- Nephrostomy
- Subsequent RT to prostate

GU, genitourinary; RP, radical proctectomy; RT, radiotherapy; TURP, transurethral resection of the prostate

Bossi A, et al. *Lancet* 2024;404;2065–2076.

Question for the audience

- In patients with high-volume synchronous mHSPC without relevant local symptoms, do you recommend local radiation therapy of the primary in addition to systemic therapy?

A Yes, in the majority of patients

B Yes, but only in selected patients

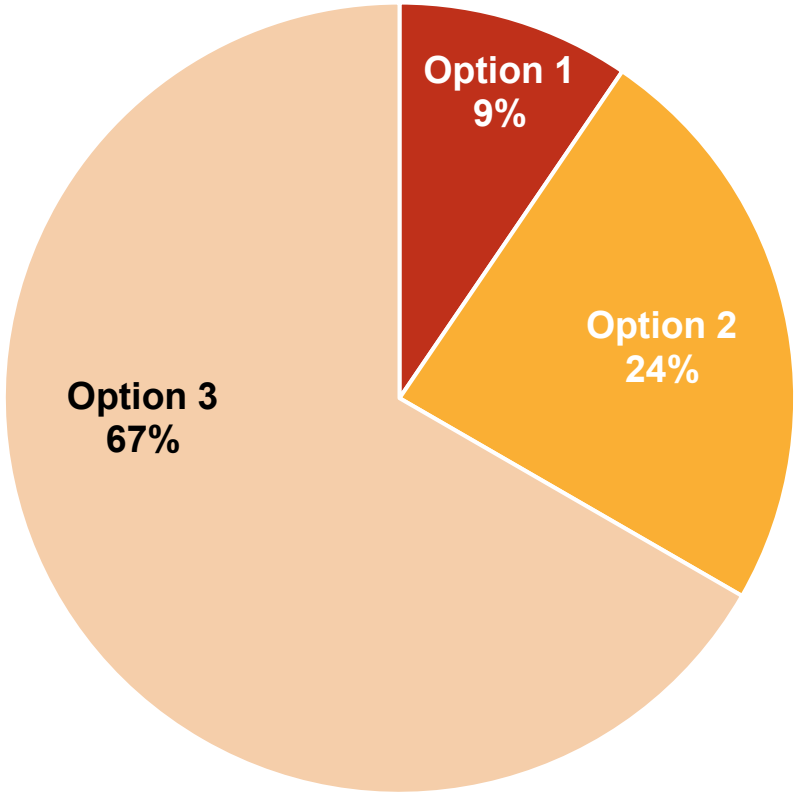
C No, I usually do not recommend RT in this situation

D Abstain/unqualified to answer

mHSPC, metastatic hormone-sensitive prostate cancer; RT, radiotherapy.

96. In patients with high-volume synchronous mHSPC without relevant local symptoms, do you recommend local radiation therapy of the primary in addition to systemic therapy?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No, I usually do not recommend RT in this situation
4. Abstain/unqualified to answer



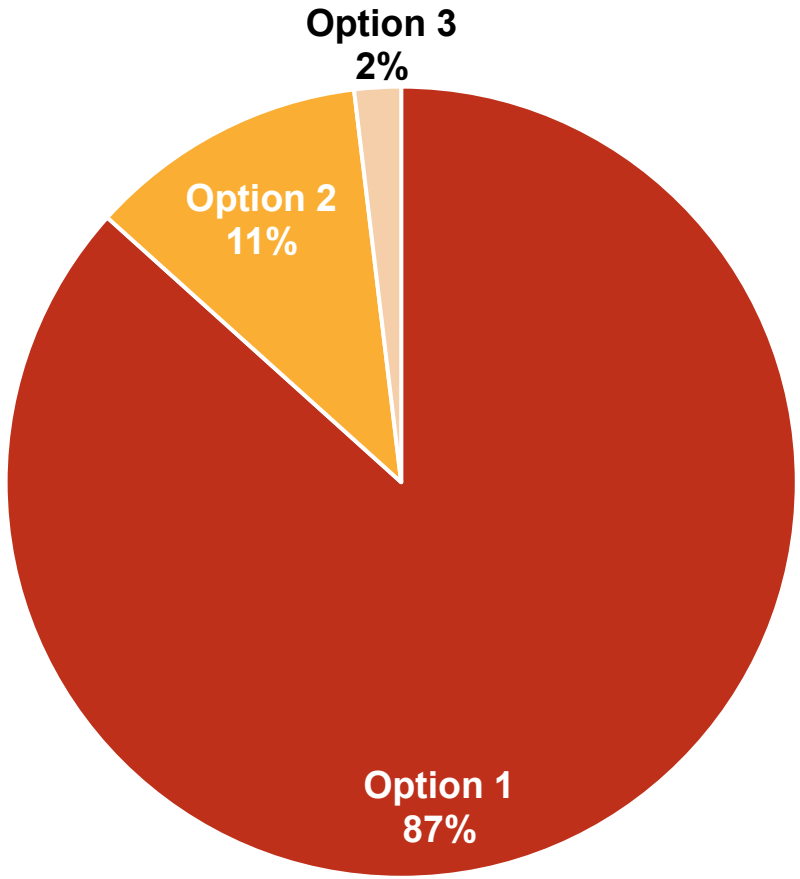
Option	Votes
Option 1	10
Option 2	25
Option 3	70
Abstain	1

mHSPC, metastatic hormone-sensitive prostate cancer; RT, radiotherapy.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

97. In patients with low-volume synchronous mHSPC without relevant local symptoms that receive ADT plus an ARPI, do you recommend local radiation therapy of the primary in addition to systemic therapy?

1. **Yes, in the majority of patients**
2. Yes, but only in selected patients
3. No, I usually do not recommend RT in this situation
4. Abstain/unqualified to answer

CONSENSUS



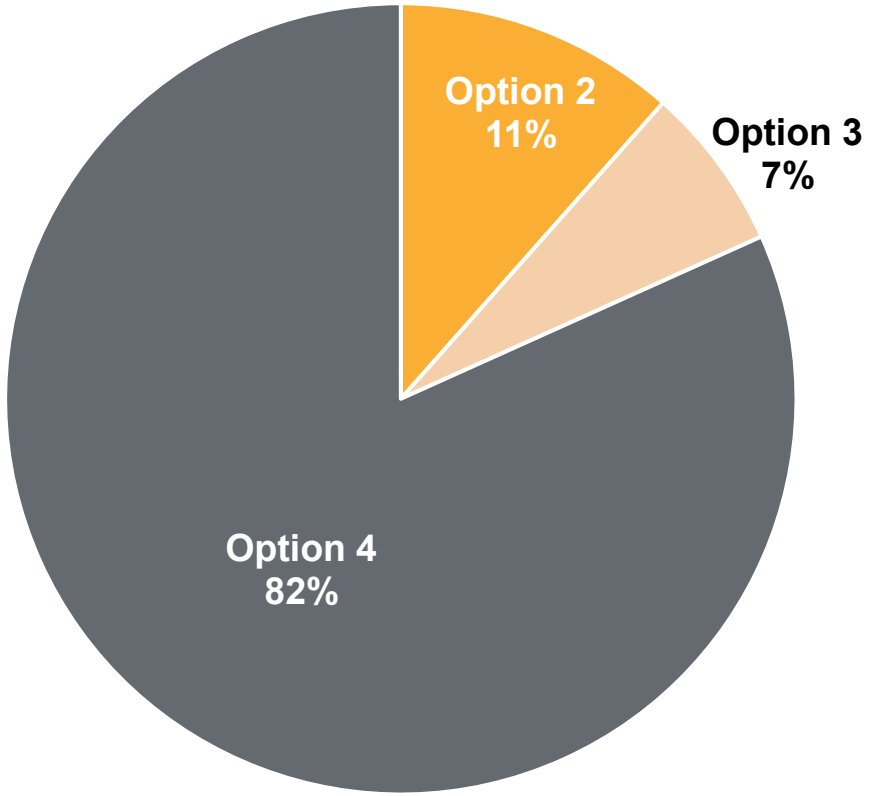
Option	Votes
Option 1	91
Option 2	12
Option 3	2
Abstain	1

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; RT, radiotherapy.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

74. In the majority of patients with synchronous low-burden mHSPC on conventional imaging, what is your treatment recommendation (regardless of the decision about metastases-directed therapy and regardless of the addition of docetaxel)?

1. ADT alone
2. ADT plus ARPI
3. ADT plus RT of the primary tumour
4. **ADT plus ARPI plus RT of the primary tumour**
5. Abstain/unqualified to answer

CONSENSUS



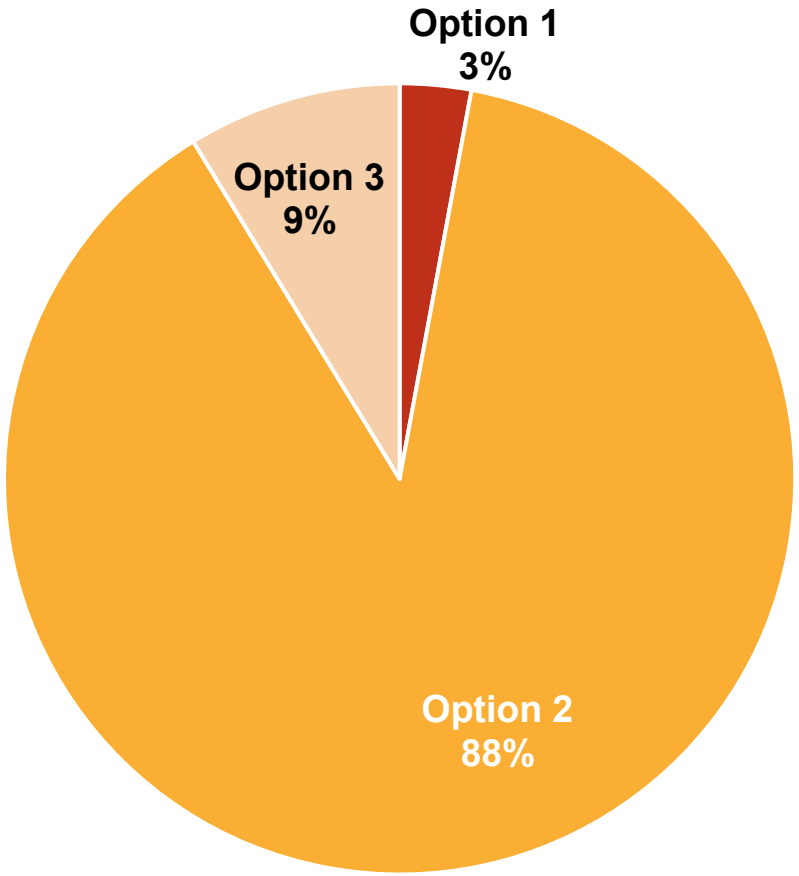
Option	Votes
Option 1	0
Option 2	12
Option 3	7
Option 4	85
Abstain	2

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; RT, radiotherapy.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

76. In the majority of patients with synchronous low-burden mHSPC on next-generation imaging and negative on conventional imaging, what is your treatment recommendation (regardless of the decision about metastases-directed therapy and regardless of the addition of docetaxel)?

1. ADT ± ARPI
2. **ADT plus RT of the primary tumour ± ARPI**
3. Treat as M0
4. Abstain/unqualified to answer

CONSENSUS



Option	Votes
Option 1	3
Option 2	91
Option 3	9
Abstain	3

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; m, metastatic; mHSPC, metastatic hormone-sensitive prostate cancer; RT, radiotherapy.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

MDT (metastasis-directed therapy)

- Four single-arm trials of LV mHSPC[1]
  - Treatment with ADT ± ARPI ± docetaxel ± prostate RT ± MDT
  - Undetectable PSA in 20–80%
- Recent meta-analysis (WOLVERINE)[2]
  - A total of 472 patients (224 SOC, 248 SOC + MDT)
  - Median follow-up 41 months; 58% HSPC

Association between MDT and outcomes

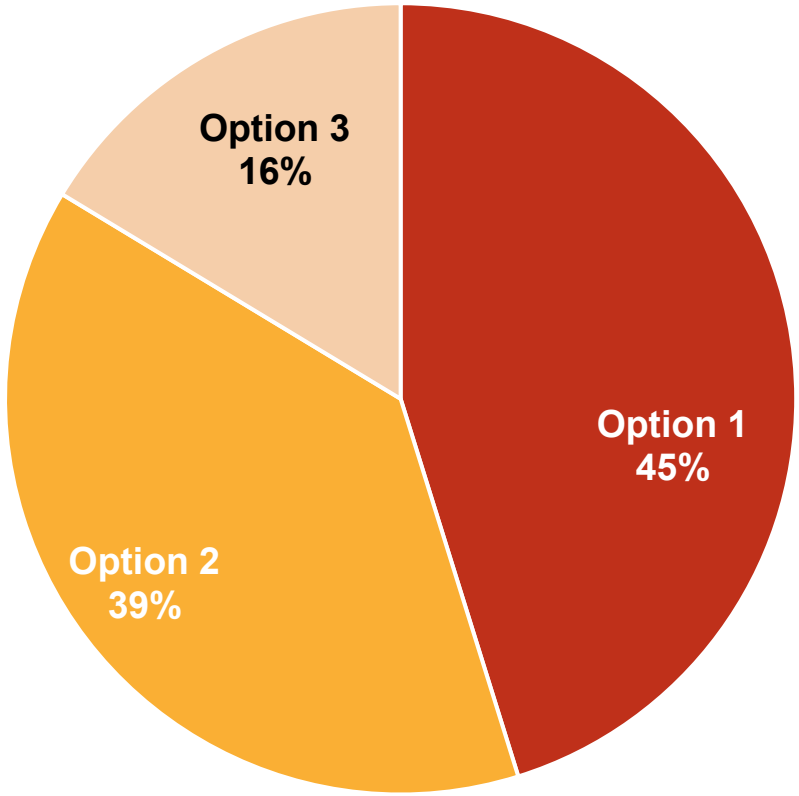
	Cox regression: HR (95% CI)	Random-effects model: HR (95% CI)
PFS	0.45 (0.35–0.58), p<0.0001	0.44 (0.35–0.57), p<0.0001
rPFS	0.59 (0.46–0.76), p<0.0001	0.60 (0.43–0.85), p=0.0039
CRFS	0.58 (0.37–0.91), p=0.020	0.58 (0.37–0.92), p=0.019
OS	0.64 (0.40–1.01), p=0.057	0.63 (0.39–1.004), p=0.051

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; CI, confidence interval; CRFS, castration-resistant free survival; HR, hazard ratio; HSPC, hormone-sensitive prostate cancer; LV, low-volume; m, metastatic; MDT, metastasis-directed therapy; OS, overall survival; PFS, progression-free survival; PSA, prostate-specific antigen; r, radiographic; RT, radiotherapy; SOC, standard of care.

1. Gillessen S, et al. *Eur Urol* 2025;87:157–216; 2. Tang C, et al. Presented at ASCO GU 2025. February 13–15 2025. San Francisco, CA (abstract number 15)

77. In patients with synchronous low-burden mHSPC on next-generation imaging and negative on conventional imaging, do you recommend additional metastases-directed therapy (if technically feasible) of all lesions?

1. Yes, in the majority of patients
2. Yes, but only in selected patients
3. No
4. Abstain/unqualified to answer

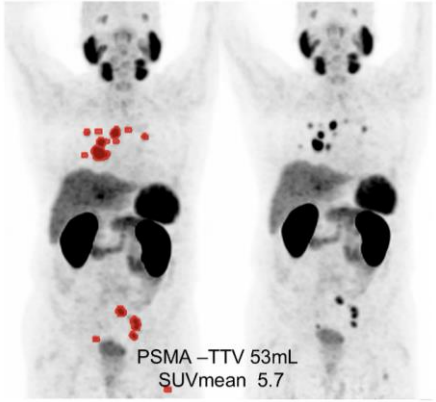


Option	Votes
Option 1	47
Option 2	40
Option 3	17
Abstain	2

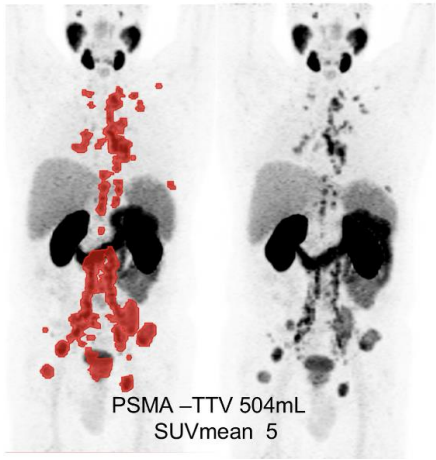
mHSPC, metastatic hormone-sensitive prostate cancer.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

PSMA-PET scan vs. conventional imaging

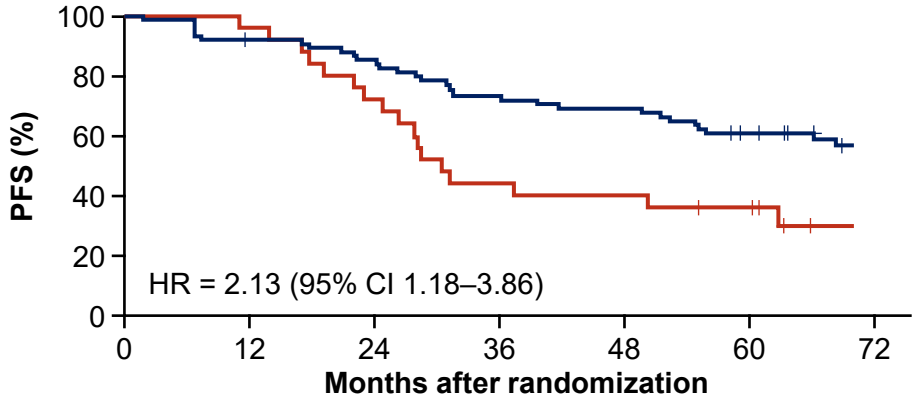
A. PSMA-PET scan with low volume nodal and bone metastases



B. PSMA-PET scan with high volume nodal and bone metastases



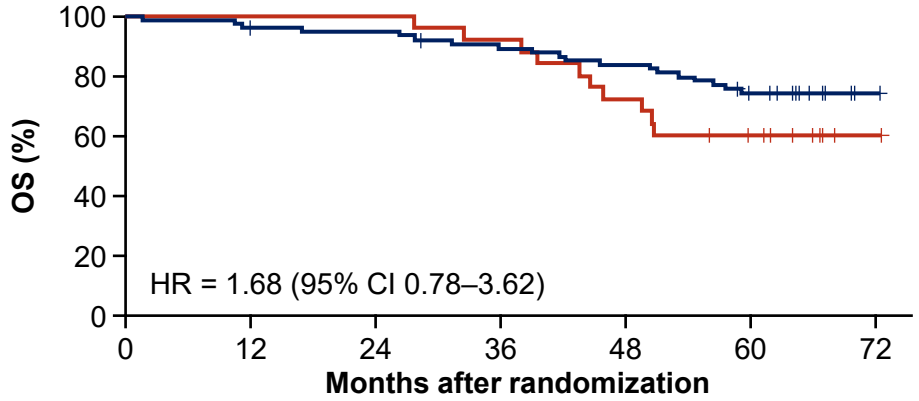
C. TTV Q4 vs. Q1–3 in PSMA-PET/CT for PFS and OS in complete cohort



Q1–3	75 (6)	68 (5)	63 (9)	53 (3)	50 (6)	42 (2)	20
Q4	25 (1)	24 (6)	18 (7)	11 (1)	10 (1)	8 (1)	3

p(interaction) = 0.78

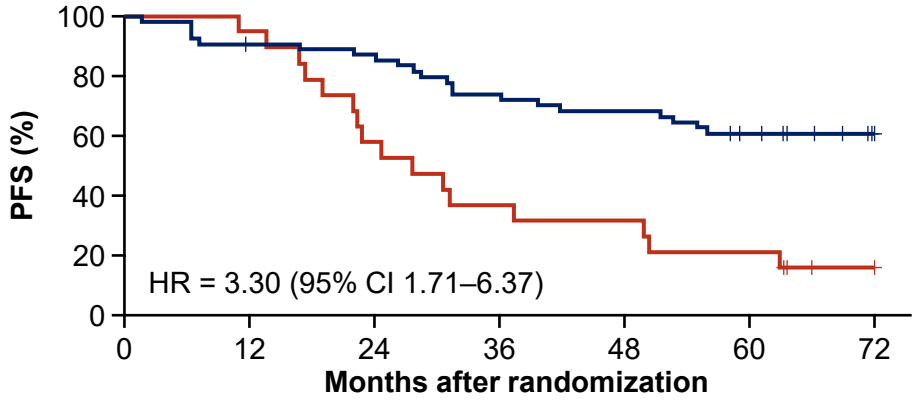
75th percentile = 71.6.g ml.



Q1–3	75 (3)	71 (1)	70 (4)	65 (4)	61 (7)	52 (0)	22
Q4	25 (0)	25 (0)	25 (2)	23 (5)	18 (3)	13 (0)	6

p(interaction) = 0.40

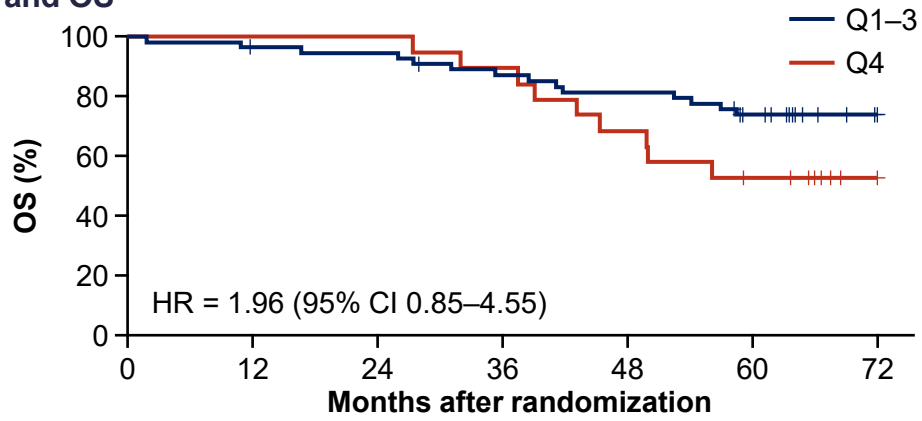
D. TTV Q4 vs. Q1–3 in CHAARTED low-volume cohort for PFS and OS



Q1–3	55 (5)	49 (2)	47 (7)	39 (3)	36 (4)	30 (0)	18
Q4	19 (1)	18 (7)	11 (4)	7 (1)	6 (2)	4 (1)	1

p(interaction) = 0.86

75th percentile = 62.4.g ml.



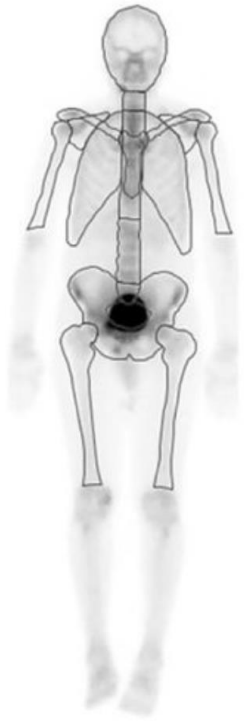
Q1–3	55 (2)	52 (1)	51 (4)	46 (3)	43 (4)	37 (0)	19
Q4	19 (0)	19 (0)	19 (2)	17 (4)	13 (3)	9 (0)	2

p(interaction) = 0.16

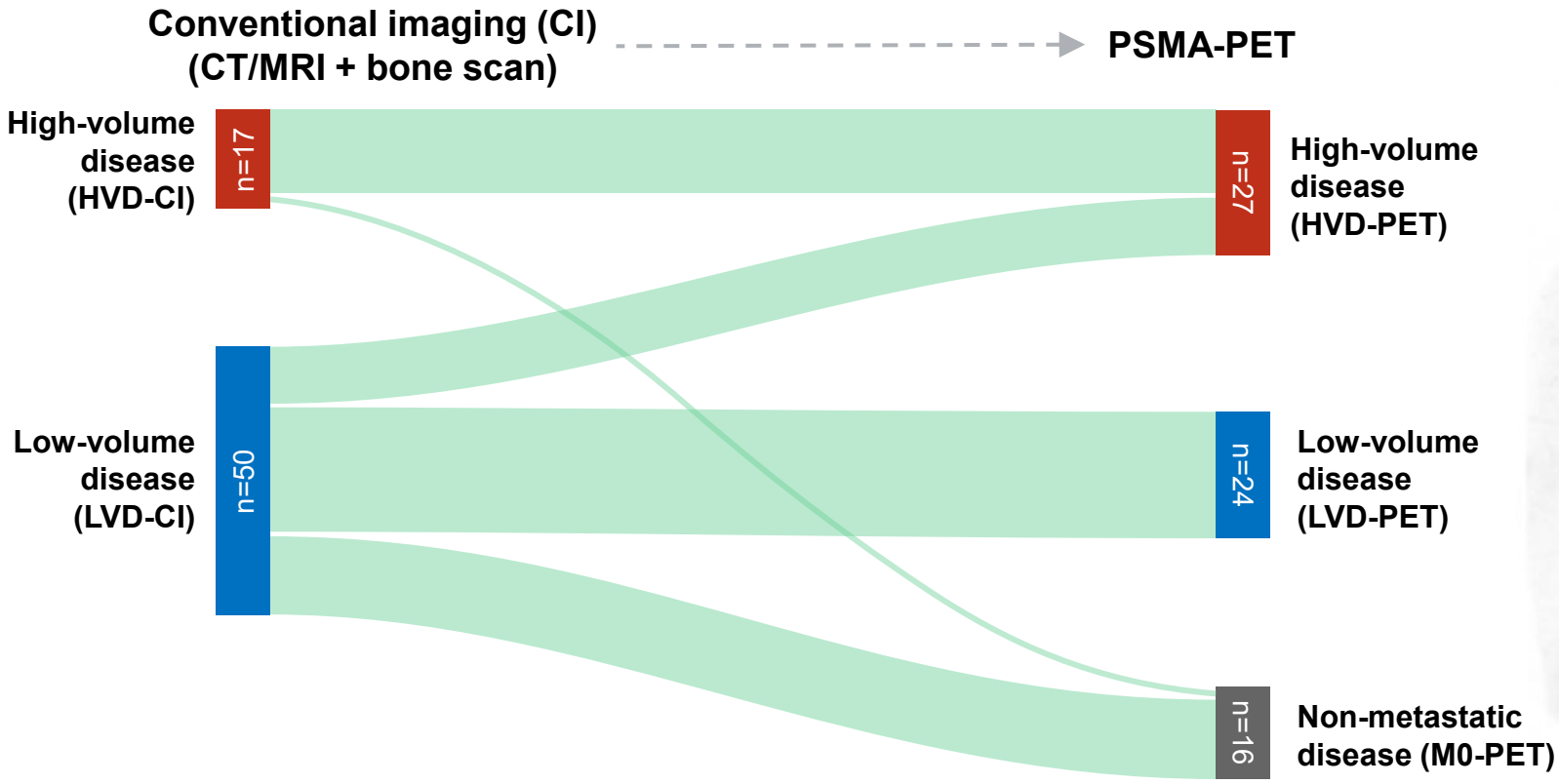
HR, hazard ratio; OS, overall survival; PFS, progression-free survival; PSMA-PET, prostate-specific membrane antigen positron emission tomography; SUV, standardized uptake value; TTV, total tumor volume.

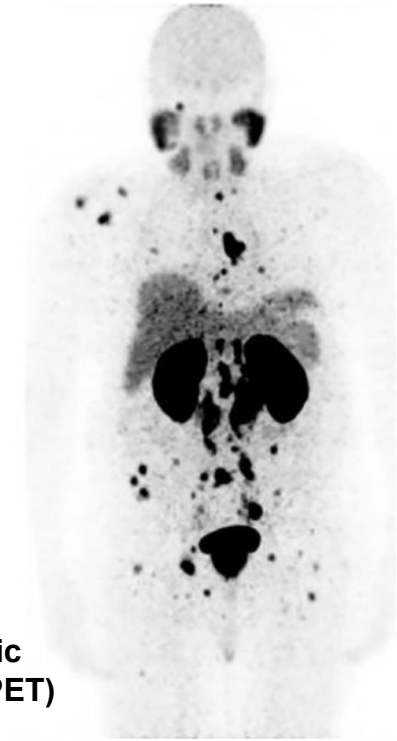
Sabahi Z, et al. ASCO 2025: Prognostic Value of PSMA PET Against CHAARTED Criteria in an ENZAMET Sub-Cohort. Available at: https://www.urotoday.com/conference-highlights/asco-2025/asco-2025-prostate-cancer/161014-asco-2025-prognostic-value-of-psma-pet-against-chaarted-criteria-in-an-enzamet-sub-cohort.html. Last accessed: July 2025.

PSMA-PET scan vs. conventional imaging



Migration between conventional imaging and PSMA PET





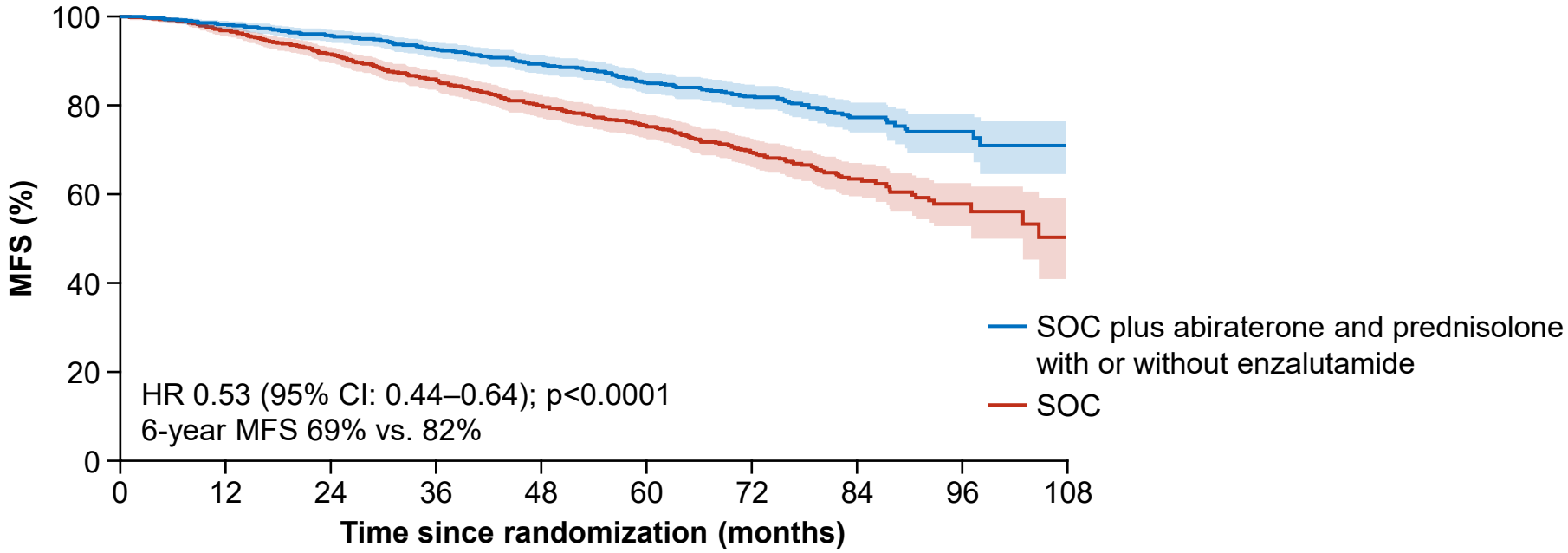
Differentiation of CHAARTED HVD vs. LVD based on PET volume
WB-PSMA-TV ≥107 ml

Low-volume | High-volume

CT, computed tomography; HVD, high-volume disease; LVD, low-volume disease; m, metastatic; MRI, magnetic resonance imaging; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; TV, tumor volume.
Unterrainer LM, et al. *J Nucl Med.* 2025;66:54–60.

STAMPEDE M0: Metastasis-free survival

Men with high-risk M0 HSPC (~40% N1)



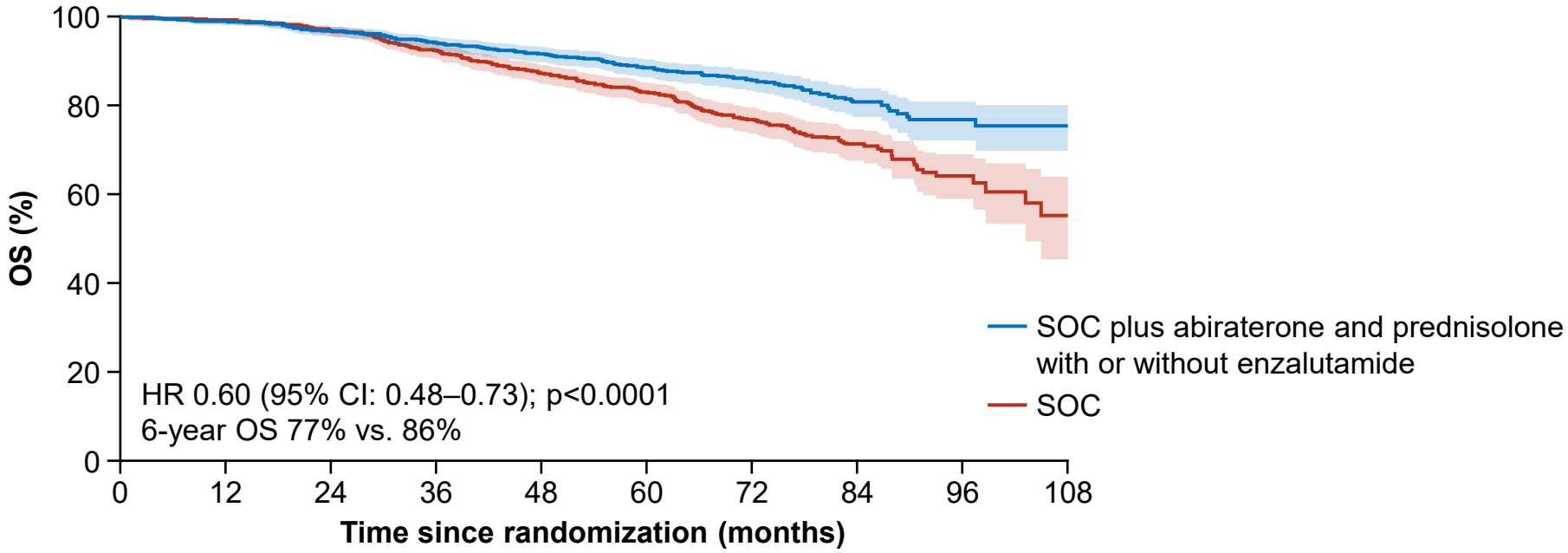
SOC plus combination therapy	At risk	986	948	917	884	839	622	369	198	71	14
	Censored	0	21	28	31	45	225	460	615	737	792
	Event	0	17	41	71	102	139	157	173	178	180
SOC	At risk	988	950	894	836	767	550	329	172	53	9
	Censored	0	8	11	14	26	201	387	522	632	673
	Event	0	30	83	138	195	237	272	294	303	306

SOC = RT + 2 years
Combination therapy = ADT +/- AAP (+/−ENZ)

AAP, abiraterone acetate plus prednisolone; ADT, androgen-deprivation therapy; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; HSPC, hormone-sensitive prostate cancer; m, metastatic; MFS, metastasis-free survival; RT, radiotherapy; SOC, standard of care.

Attard G, et al. *Lancet*. 2022;399:447–460.

STAMPEDE M0: OS



SOC plus combination therapy	**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
SOC	**At risk**	988	974	947	901	837	610	368	200	63	10
	Censored	0	8	11	14	28	216	421	568	693	742
	Event	0	6	30	73	123	162	199	220	232	236

SOC = RT + 2 years
Combination therapy = ADT +/- AAP (+/−ENZ)

AAP, abiraterone acetate plus prednisolone; ADT, androgen-deprivation therapy; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; HSPC, hormone-sensitive prostate cancer; m, metastatic; MFS, metastasis-free survival; OS, overall survival; RT, radiotherapy; SOC, standard of care.

Attard G, et al. *Lancet*. 2022;399:447–460.

Extrapolation

- Synchronous LV mHSPC diagnosed on PSMA-PET scan (especially node only)
  =
  M0 locally advanced prostate cancer on conventional imaging

LV, low-volume; mHSPC, metastatic hormone-sensitive prostate cancer; PSMA-PET, prostate-specific membrane antigen positron emission tomography.
Speaker's own experience.

Question for the audience

- For the majority of patients with low-burden synchronous mHSPC with PSMA-PET positive retroperitoneal lymph nodes what is your treatment recommendation?

A Systemic therapy alone

B Systemic therapy plus RT of the primary

C Systemic therapy plus RT of the primary and MDT

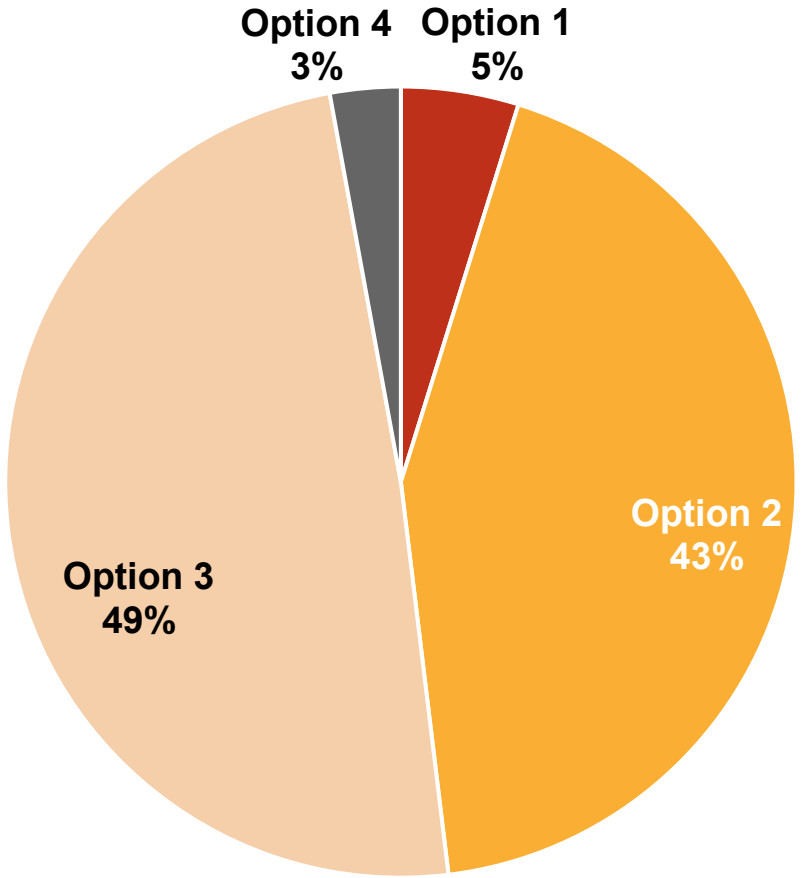
D RT of the primary and MDT without systemic therapy

E Abstain/unqualified to answer

MDT, metastases-directed therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSMA-PET, prostate-specific membrane antigen positron emission tomography; RT, radiotherapy.

73. For the majority of patients with low-burden synchronous mHSPC with PSMA-PET positive retroperitoneal lymph nodes what is your treatment recommendation?

1. Systemic therapy alone
2. Systemic therapy plus RT of the primary
3. Systemic therapy plus RT of the primary and MDT
4. RT of the primary and MDT without systemic therapy
5. Abstain/unqualified to answer



Option	Votes
Option 1	5
Option 2	45
Option 3	51
Option 4	3
Abstain	2

MDT, metastases-directed therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSMA-PET, prostate-specific membrane antigen positron emission tomography; RT, radiotherapy.
Gillessen S, et al. *Eur Urol* 2025;87:157–216.

Genitourinary Masterclass

astellas

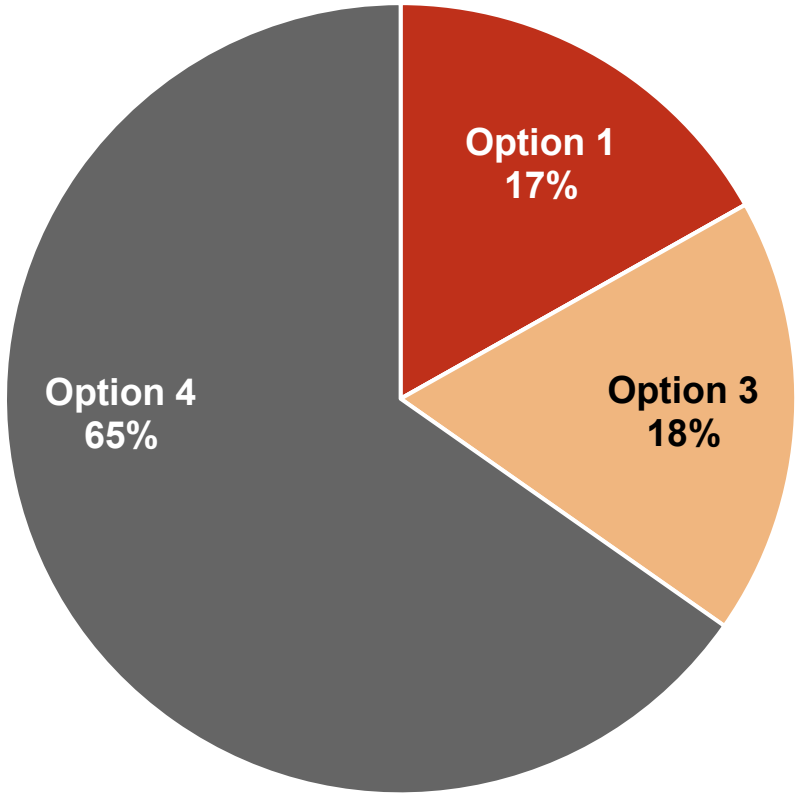
PARP inhibitors

mHSPC

mHSPC, metastatic hormone-sensitive prostate cancer; PARP, poly (ADP-ribose) polymerase.

94. In patients with synchronous mHSPC and presence of a pathogenic BRCA alteration, does this information change your treatment recommendation for the patient?

1. Yes, I recommend ADT + ARPI + Docetaxel triplet systemic therapy over ADT + ARPI doublet systemic therapy regardless of disease burden
2. Yes, I add a platinum chemotherapy to systemic therapy regardless of disease burden
3. Yes, I add a PARP inhibitor to systemic therapy regardless of disease burden
4. No
5. Abstain/unqualified to answer



Option	Votes
Option 1	16
Option 2	0
Option 3	17
Option 4	62
Abstain	11

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; BRCA, BReast CAncer gene; PARP, poly (ADP-ribose) polymerase; mHSPC, metastatic hormone-sensitive prostate cancer.

Gillessen S, et al. *Eur Urol* 2025;87:157–216.

Phase III AMPLITUDE trial

- Niraparib and abiraterone acetate plus prednisone for patients with mHSPC with alterations in HRR genes

Patient population

- mHSPC*
- Alteration in at least one HRR eligible gene: *BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, RAD54L*†
- ECOG PS 0–2

Stratification

- BRCA2 vs. CDK12 vs. all other alterations
- Prior docetaxel (yes vs. no)
- Disease volume (high vs. low)

N=696

R
1:1

PBO +
AAP (1000 mg QD + 5 mg QD)
+ ADT
(n=348)

Nira (200 mg QD) +
AAP (1000 mg QD + 5 mg QD)
+ ADT
(n=348)

Primary endpoint:

- rPFS by investigator review

Key secondary endpoints:

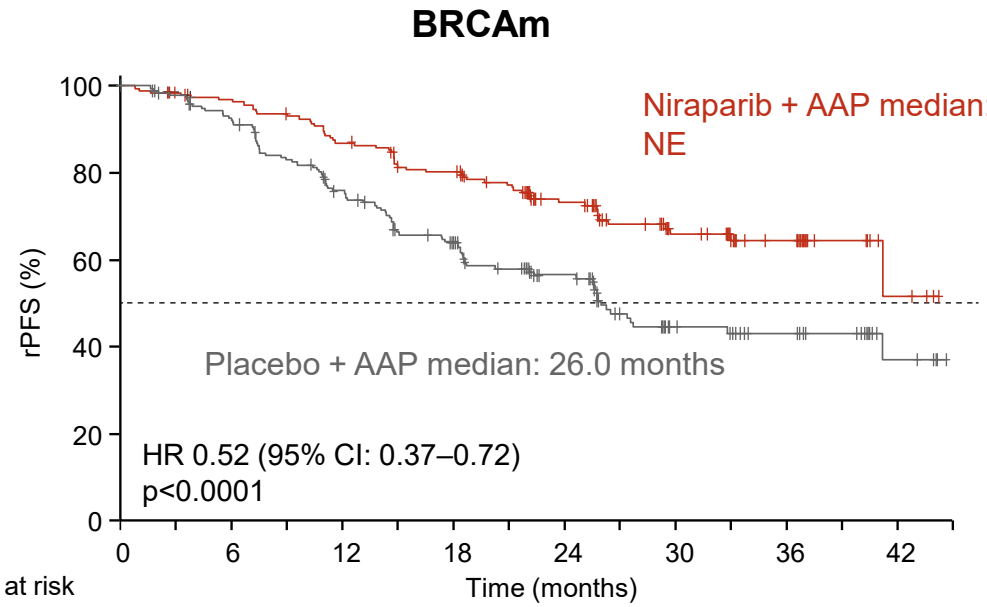
- Time to symptomatic progression
- OS
- Safety

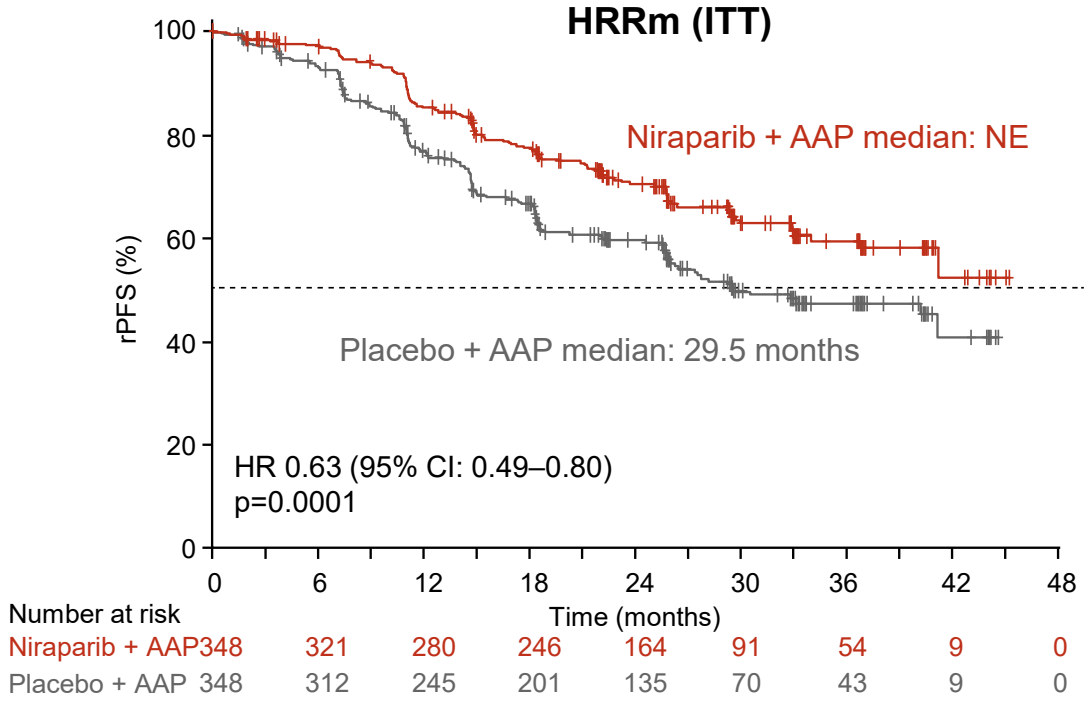
Clinical data cut-off: January 7, 2025

Niraparib is not licensed for the treatment of mHSPC; this is an investigational combination.
*Patients with lymph node-only disease are not eligible; †HRR gene panel was fixed prior to trial initiation based on MAGNITUDE trial and external data from the published literature.
AAP, abiraterone acetate plus prednisolone; ADT, androgen-deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; HRR, homologous recombination repair; mHSPC, metastatic hormone-sensitive prostate cancer; Nira, niraparib; OS, overall survival; PBO, placebo; R, randomization; rPFS, radiographic progression-free survival; RT, radiotherapy; QD, once daily.
Attard G, et al. Presented at ASCO 2025, 30 May–03 June 2025, Chicago, IL, US. abstract 5005.

AMPLITUDE trial: Primary endpoint

Primary endpoint: rPFS*





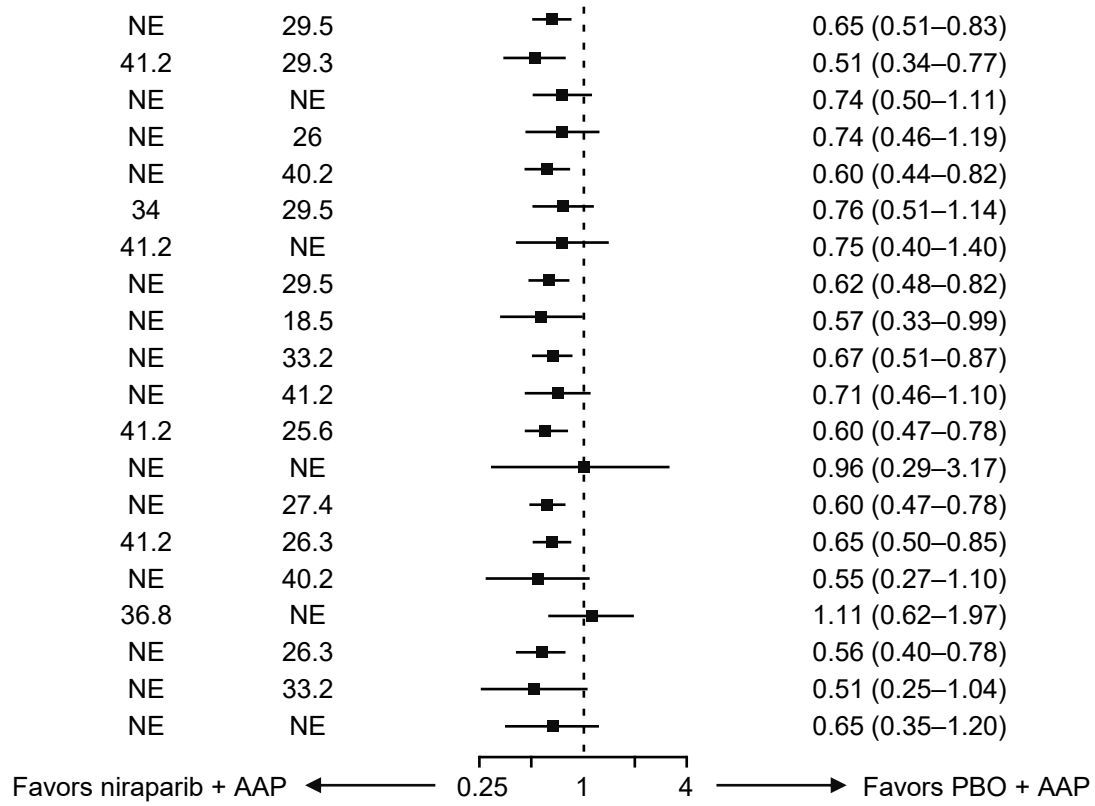
AMPLITUDE met the primary end point: Nira + AAP significantly reduced the risk of radiographic progression or death by 48% in BRCAm group and by 37% in HRR, population

Figures adapted from Attard G, et al. 2025.
Niraparib is not licensed for the treatment of mHSPC; this is an investigational combination.
*rPFS by investigator review. The results for rPFS by BICR were similar: HR 0.51 (95% CI: 0.37–0.72) and 0.61 (95% CI: 0.47–0.79) for BRCAm and HRRm groups.
AAP, abiraterone acetate plus prednisone; BICR, blinded independent central review; BRCAm, BReast CAncer gene mutation; CI, confidence interval; HR, hazard ratio; HRRm, homologous recombination repair gene mutation; ITT, intention-to-treat; NE, not estimable; rPFS, radiographic progression-free survival.
Attard G, et al. Presented at ASCO 2025, 30 May–03 June 2025, Chicago, IL, USA: Abstract LBA5006.

AMPLITUDE trial: Prespecified subgroup analysis of rPFS

Prespecified subgroup analysis of rPFS

Variable	Subgroup	Median, months		HR (95% CI)	Events/N	
		Niraparib + AAP	PBO + AAP		Niraparib + AAP	PBO + AAP
All patients		NE	29.5	0.65 (0.51–0.83)	113/348	151/348
Age	<65 years	41.2	29.3	0.51 (0.34–0.77)	35/116	62/135
	65–74 years	NE	NE	0.74 (0.50–1.11)	45/148	52/139
	≥75 years	NE	26	0.74 (0.46–1.19)	33/84	37/74
ECOG PS at baseline	0	NE	40.2	0.60 (0.44–0.82)	72/242	93/218
	≥1	34	29.5	0.76 (0.51–1.14)	41/106	58/130
Prior docetaxel use	Yes	41.2	NE	0.75 (0.40–1.40)	18/54	23/56
	No	NE	29.5	0.62 (0.48–0.82)	95/294	128/292
Visceral metastases	Yes	NE	18.5	0.57 (0.33–0.99)	22/57	30/54
	No	NE	33.2	0.67 (0.51–0.87)	91/291	121/294
Bone-only metastases at baseline	Yes	NE	41.2	0.71 (0.46–1.10)	36/146	48/154
	No	41.2	25.6	0.60 (0.47–0.78)	77/202	103/194
Metastases state at diagnosis	M0	NE	NE	0.96 (0.29–3.17)	5/32	6/36
	M1	NE	27.4	0.60 (0.47–0.78)	100/301	142/302
Disease volume at baseline	High	41.2	26.3	0.65 (0.50–0.85)	100/269	130/271
	Low	NE	40.2	0.55 (0.27–1.10)	13/79	21/77
Regions	Asia	36.8	NE	1.11 (0.62–1.97)	26/72	21/63
	Europe	NE	26.3	0.56 (0.40–0.78)	56/168	86/177
	North America	NE	33.2	0.51 (0.25–1.04)	14/45	18/44
	Rest of World	NE	NE	0.65 (0.35–1.20)	17/63	26/64

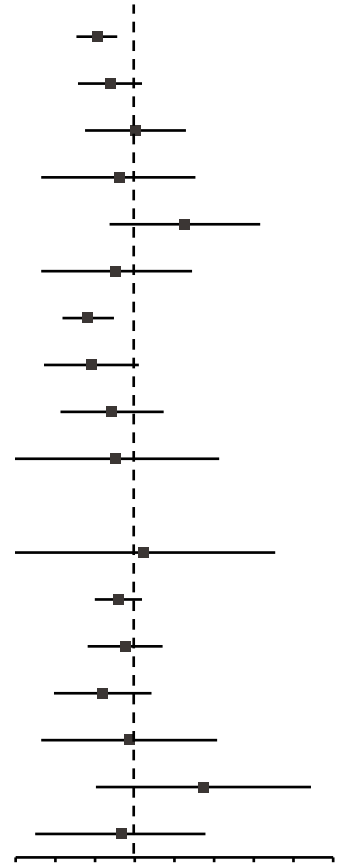


Benefit from Nira + AAP is generally consistent across prespecified subgroups

Figure adapted from Attard G, et al. 2025.
Niraparib is not licensed for the treatment of mHSPC; this is an investigational combination. Results in small subgroups should be interpreted with caution.
AAP, abiraterone acetate plus prednisone; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; NE, not estimable; Nira, niraparib; PBO, placebo.
Attard G, et al. Presented at ASCO 2025, 30 May–03 June 2025, Chicago, IL, USA: Abstract LBA5006.

AMPLITUDE trial: Subgroup analysis by BRCA and BRCA alterations

Endpoint	Subgroup	HR (95% CI)	Events/N Niraparib + AAP	Events/N PBO + AAP
rPFS	*BRCA1/2*	0.52 (0.37–0.72)	57/191	93/196
	CHEK2	0.65 (0.38–1.11)	24/72	32/76
	CDK12	1.01 (0.43–2.39)	13/28	10/28
	FANCA	0.76 (0.20–2.82)	4/15	5/15
	PALB2	2.41 (0.66–8.74)	6/9	4/13
	Other	0.72 (0.20–2.66)	6/25	4/15
Time to symptomatic progression	*BRCA1/2*	0.44 (0.29–0.68)	31/191	66/196
	CHEK2	0.47 (0.21–1.05)	9/72	18/76
	CDK12	0.68 (0.28–1.62)	9/28	12/28
	FANCA	0.71 (0.12–4.27)	2/15	3/15
	PALB2	NE (NE–NE)	1/9	2/13
	Other	1.18 (0.12–11.36)	4/25	1/15
OS*	*BRCA1/2*	0.75 (0.51–1.11)	44/191	61/196
	CHEK2	0.85 (0.45–1.59)	18/72	21/76
	CDK12	0.57 (0.25–1.31)	9/28	15/28
	FANCA	0.92 (0.20–4.12)	3/15	4/15
	PALB2	3.30 (0.52–21.21)	3/9	2/13
	Other	0.79 (0.18–3.36)	5/25	3/15



The first interim analysis (≈50% of total needed events) estimates show niraparib + AAP reduced risk of death by 25% in BRCAm group and by 21% in HRRm group

Figure adapted from Attard G, et al. 2025.
Niraparib is not licensed for the treatment of mHSPC; this is an investigational combination.
*The first interim analysis for OS was conducted when 193 patients had died (of a target of 389, an information fraction of 50%); 85 of 348 (24%) in the niraparib + AAP arm and 108 of 348 (31%) in the PBO + AAP arm.
Non-BRCA subgroups were not statistically powered for formal testing in this exploratory analysis. HRs were stratified by disease volume (high vs. low). Other: RAD54L, BRIP1, RAD51B.
AAP, abiraterone acetate plus prednisone; BRCA, BReast CAncer gene; BRCAm, BReast CAncer gene mutation; CI, confidence interval; HR, hazard ratio; HRR, homologous recombination repair gene mutation; NE, not estimable; OS, overall survival; PBO, placebo;
rPFS, radiographic progression-free survival.
Attard G, et al. Presented at ASCO 2025, 30 May–03 June 2025, Chicago, IL, USA: Abstract LBA5006.

Question for the audience

- In patients with synchronous mHSPC and presence of a pathogenic BRCA alteration, does this information change your treatment recommendation for the patient?

A Yes, I recommend ADT + ARPI + Docetaxel triplet systemic therapy over ADT + ARPI doublet systemic therapy regardless of disease burden

B Yes, I add a platinum chemotherapy to systemic therapy regardless of disease burden

C Yes, I add a PARP inhibitor to systemic therapy regardless of disease burden

D No

E Abstain/unqualified to answer

ADT, androgen deprivation therapy; ARPI; androgen receptor pathway inhibitor; BRCA, BReast CAncer gene; PARP, poly (ADP-ribose) polymerase; mHSPC, metastatic hormone-sensitive prostate cancer.

Risk stratification: Clinical summary slide

Good risk	Intermediate risk	Poor risk
(absence of any poor prognostic feature) **Good prognosis disease distribution and prior RP/XRT or M0 at first diagnosis**	**One poor prognostic factor**	**Poor prognostic disease distribution and *de novo* presentation**

Poor prognostic factors

- At least four bone metastases
- Liver metastases
- Synchronous metastatic disease (no previous local treatment)
- M1 disease within 3 months of first diagnosis

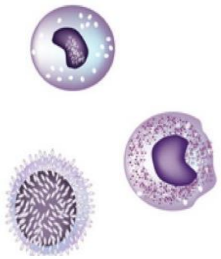
ICECaP: Intermediate Clinical Endpoints in Cancer of the Prostate
STOPCaP M1: Speed up the evaluation of therapies for mHSPC

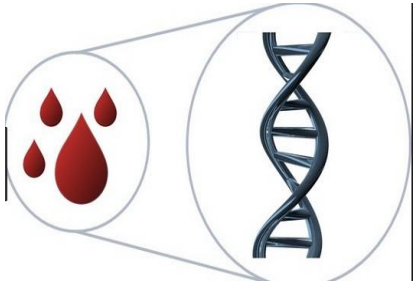
Figure presented with permission from C Sweeney.
mHSPC, metastatic hormone-sensitive prostate cancer; M, metastasis; RP, radical prostatectomy; XRT, external beam radiation.
Speaker's clinical experience.

Risk stratification: Biology of the cancer

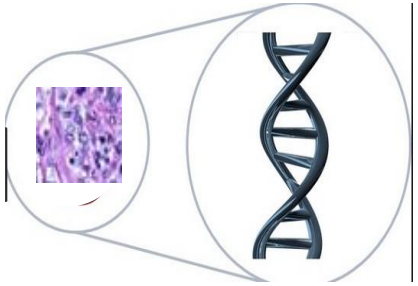
Lipid metabolism

Immune cells/ cytokines

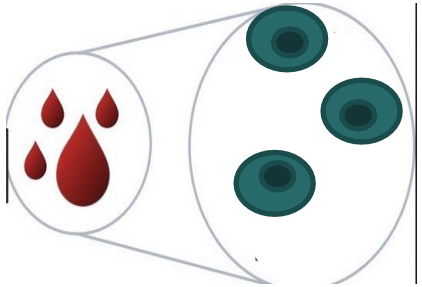




Circulating DNA



Tissue DNA/RNA



Circulating tumour cells

Images used from Stock images.
Speaker's clinical experience.

Conclusion

High Volume mHSPC

- ADT + ARPI (abiraterone/enzalutamide/apalutamide/darolutamide)
- Synchronous/high-volume/good PS: ADT + docetaxel + abiraterone or darolutamide or enzalutamide (concurrent)
- Consider RT to the primary for good responders

Low Volume mHSPC

- ADT + ARPI + RT to primary (if *de novo*)
- Consider metastasis-directed therapy for oligometastases (PET staged)

Will we be using PARPi for *BRCA1/2* mutant mHSPC?

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; PARPI, poly (ADP-ribose) polymerase inhibitor; PET, positron emission tomography; PS, performance status; RT, radiotherapy.
Speaker's clinical experience and opinion.

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