

Systemic Therapy in Patients With Metastatic Castration-Resistant Prostate Cancer: ASCO Living Guideline, Version 2026.1

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ABSTRACT

Living guidelines are developed for selected topic areas with rapidly evolving evidence that drives frequent change in recommended clinical practice. Living guidelines are updated on a regular schedule by a standing expert panel that systematically reviews the health literature on a continuous basis, as described in the *ASCO Guidelines Methodology Manual*. ASCO Living Guidelines follow the *ASCO Conflict of Interest Policy Implementation for Clinical Practice Guidelines*. Living Guidelines and updates are not intended to substitute for independent professional judgment of the treating clinician and do not account for individual variation among patients. See appendix for disclaimers and other important information ([Appendix 1](#) and [Appendix 2](#)). Updates are published regularly and can be found at www.asco.org/genitourinary-cancer-guidelines.

ACCOMPANYING CONTENT

-  [Article, 10.1200/JCO-25-00007](#)
-  [Appendix](#)
-  [Data Supplement](#)

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BACKGROUND

In 2025, ASCO launched the living clinical practice guideline on systemic therapy in patients with metastatic castration-resistant prostate cancer (CRPC). Based on new evidence, this version of the systemic therapy in patients with metastatic CRPC (mCRPC) living guideline provides updated recommendations based on latest evidence. Refer to [Appendix Table A1](#) (online only) for a list of Expert Panel members, [Appendix Table A2](#) for the full list of recommendations, and revised [Appendix Figures A1-A4](#) for the updated algorithms. [Appendix Table A3](#) presents the summary of findings table. The ASCO Guidelines Methodology Manual (available at www.asco.org/guideline-methodology) and Supplement provide additional information.

RESULTS

As of August 1, 2025, a total of 204 references have been identified as eligible for the living systematic review which included 21 new or updated references since the first

iteration of the guideline. Reports from six phase III clinical trials were deemed relevant for further review by the Expert Panel ([Appendix Table A1](#)): TALAPRO-2,^{1,2} EORTC 1333/PEACE-3,³ CONTACT-02,^{4,5} KEYNOTE-641,⁶ KEYNOTE-921,⁷ and MAGNITUDE.⁸ Of these, four were new studies (EORTC 1333/PEACE-3, CONTACT-02, KEYNOTE-641, KEYNOTE-921), two were updates of previously published studies (TALAPRO-2 and MAGNITUDE). One additional trial (PSMAfore⁹) was re-reviewed in light of the recent US Food and Drug Administration (FDA) approval of lutetium-177-PSMA-617 (¹⁷⁷Lu-PSMA-617) before docetaxel therapy. Evidence supporting unchanged recommendations is reviewed in the previous publication of this guideline.¹⁰

UPDATED RECOMMENDATIONS

Patients Previously Treated With ADT Alone in Castration-Sensitive or Nonmetastatic CRPC Setting and Whose Disease Has Progressed to mCRPC

See revised [Fig A1](#): Algorithm for patients previously treated with androgen deprivation therapy (ADT) alone.

Recommendation 1.1.3

The Panel recommends either enzalutamide or chemotherapy using docetaxel for patients with visceral disease (lung and/or liver metastases) and regardless of homologous recombination repair (HRR) alterations (please refer to 1.1.1 and 1.1.2 for preferred recommendations in patients with HRR alterations; Evidence quality: High; Strength of recommendation: Strong).

The panel recommends abiraterone with prednisone, darolutamide, apalutamide, or cabazitaxel in selected patients (see Practical Information; Evidence quality: Low; Strength of recommendation: Conditional).

Practical information for recommendation 1.1.3.

Although there are limited data for abiraterone with prednisone, darolutamide, or apalutamide for patients with visceral disease in the mCRPC setting, these agents can be used as alternatives if there are concerns about side effects or drug interactions. Cabazitaxel may be used if allergic reactions or toxicity like peripheral neuropathy which precludes the use of docetaxel. The choice between an androgen receptor pathway inhibitor (ARPI) and chemotherapy may depend on the patient's health, their ability to tolerate chemotherapy, the presence of symptoms and/or visceral disease, accessibility, cost, and the patient's preference, especially if they are averse to chemotherapy.

Recommendation 1.1.4

The Panel recommends docetaxel, abiraterone plus prednisone, enzalutamide with radium 223, or sipuleucel-T for patients with mCRPC without visceral metastases. The panel recommends radium 223 monotherapy for patients with symptomatic bone-only disease (lymph node <3 cm; Evidence quality: Moderate; Strength of recommendation: Strong).

Practical information for recommendation 1.1.4.

Unless contraindicated, the use of bone-protecting agents is strongly recommended in all patients receiving radium 223 (See Principle of Practice, item 6). Symptomatic disease is defined as consistent use of pain medications or undergoing external-beam radiation therapy for cancer-related bone pain. The Panel recommends educating patients and caregivers regarding the lack of benefit in objective intermediate measurable end points (prostate-specific antigen [PSA] levels, radiographic changes) associated with the use of sipuleucel-T. Enzalutamide monotherapy instead of enzalutamide with radium is an option in the presence of visceral metastasis or contraindications to abiraterone or radium 223.

Patients Previously Treated With ADT and an ARPI and Whose Disease Has Progressed to mCRPC

See revised [Fig A2](#): Algorithm for patients previously treated with ADT and an ARPI.

Recommendation 1.2.2.1

The Panel recommends using docetaxel chemotherapy, radium 223, or ¹⁷⁷Lu-PSMA-617 (for patients with a prostate-specific membrane antigen [PSMA]-positive positron emission tomography scan) for patients regardless of HRR alterations. (Evidence quality: Moderate; Strength of recommendation: Strong)

Practical information for recommendation 1.2.2.1.

Cabazitaxel may be offered to selected patients if they have an allergic reaction or toxicity like peripheral neuropathy which precludes the use of docetaxel.

Recommendation 1.2.3

The Panel recommends sipuleucel-T or local therapies per Recommendations 1.1.4 or 1.1.7, respectively, for selected patients. (Evidence quality: Moderate; Strength of recommendation: Conditional).

Patients Previously Treated With ADT and Docetaxel and Whose Disease Has Progressed to mCRPC

See [Fig A3](#): Algorithm for patients previously treated with ADT and docetaxel.

Recommendation 1.3.2

The Panel recommends either an ARPI such as abiraterone with prednisone or enzalutamide, or enzalutamide with radium 223, or chemotherapy with cabazitaxel (for patients regardless of HRR alterations). (Evidence quality: Moderate; Strength of recommendation: Strong; Conditional for radium 223 with enzalutamide).

Practical information for recommendation 1.3.2.

The Panel recommends either abiraterone with prednisone, enzalutamide, enzalutamide with radium 223, or cabazitaxel. Which treatment is offered depends on the patient's clinical status, presence or absence of symptoms from metastatic disease, cost and drug availability, and ability to tolerate therapy. Docetaxel rechallenge may be offered to patients with a favorable response to docetaxel (patients who received initial docetaxel therapy and achieved a favorable PSA nadir and durable response before clinical or radiologic progression) in the castration-sensitive prostate cancer setting.

Patients Previously Treated With ADT, ARPI, and Docetaxel and Whose Disease Has Progressed to mCRPC

See [Fig A4](#): Algorithm for patients previously treated with ADT, ARPI, and docetaxel.

Recommendation 1.4.1

The Panel recommends ¹⁷⁷Lu-PSMA-617 for PSMA-positive disease or radium 223 for PSMA-negative disease or

chemotherapy using cabazitaxel. (Evidence quality: Moderate; Strength of recommendation: Strong)

Evidence Review

Overall survival (OS) and radiographic progression-free survival (rPFS) analysis for the combination of talazoparib with enzalutamide versus placebo with enzalutamide on the phase III TALAPRO-2^{1,2} trial were updated. Median OS at 52.5 months of follow-up was significantly improved for talazoparib with enzalutamide (45.8 months, 95% CI, 39.4 to 50.8) compared with 37.0 months (95% CI, 34.1 to 40.4) for the enzalutamide arm. The improvement in OS was statistically significant for patients with HRR deficiency (hazard ratio [HR], 0.55 [95% CI, 0.36 to 0.83]; $P = .0035$) while not statistically significant for patients without HRR deficiency (HR, 0.88 [95% CI, 0.71 to 1.08]; $P > .22$).

In the randomized phase III PSMAfore⁹ clinical trial, ¹⁷⁷Lu-PSMA-617 (7.4 GBq once every 6 weeks for six cycles) was compared with ARPI switch therapy in 468 patients with taxane-naïve CRPC. The median rPFS was 9.3 months for ¹⁷⁷Lu-PSMA-617 versus 5.5 months for the ARPI change with a HR of 0.41 (95% CI, 0.29 to 0.56), $P < .001$. The median OS was similar 23.7 months for ¹⁷⁷Lu-PSMA-617 and 23.8 months for ARPI change arm with a HR of 0.91 (95% CI, 0.72 to 1.14; $P = .2$). A large proportion of patients, 57%, on the ARPI change arm crossed over to receive ¹⁷⁷Lu-PSMA-617. PSA response rate and overall response rates were significantly higher in the ¹⁷⁷Lu-PSMA-617 arm compared with the ARPI change arm. Dry mouth, fatigue, nausea, diarrhea, and cytopenias were common side effects associated with ¹⁷⁷Lu-PSMA-617. ¹⁷⁷Lu-PSMA-617 delayed worsening of health-related quality of life, pain, and symptomatic skeletal metastases.

KEYNOTE-921⁷ is a large phase III clinical trial which compared the combination of pembrolizumab with docetaxel with docetaxel alone in 1,030 patients with mCRPC whose disease progressed on ADT and ARPI. The addition of pembrolizumab to docetaxel did not improve OS (19.6 months [95% CI, 18.2 to 20.9] v 19.0 months [95% CI, 17.9 to 20.9]) or rPFS (8.6 months [95% CI, 8.3 to 10.2] v 8.3 months [95% CI, 8.2 to 8.5]) compared with docetaxel alone.

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In the PEACE-3³ trial, a combination of radium 223 (six cycles once every 4 weeks) with enzalutamide was compared with enzalutamide alone in 446 patients with metastatic castrate-resistant prostate cancer with bony and nodal metastatic disease. Patients with visceral metastatic disease were excluded, and the use of bone protective agents (zoledronic acid or denosumab) was mandatory. Median rPFS was significantly better for the combination; 19.4 months (95% CI, 0.54 to 0.87) compared with 16.4 months (95% CI, 13.8 to 19.2) for enzalutamide (HR, 0.69 [95% CI, 0.54 to 0.87]; $P = .0009$). The median OS was 42.3 (95% CI, 32.8 to 54.4) months with the combination of radium 223 with enzalutamide compared with 35 months (95% CI, 28.8 to 38.9) with enzalutamide (HR, 0.69 [95% CI, 0.52 to 0.90]; $P = .0031$). Final OS analysis is currently pending. Hypertension, fatigue, bone fractures, and cytopenias were common side effects associated with the use of radium 223 with enzalutamide.

The panel acknowledges results of the phase III CONTACT-02^{4,5} clinical study which evaluated the combination of cabozantinib with atezolizumab compared with ARPI switch therapy. In patients with mCRPC with measurable extrapelvic soft tissue metastases, cabozantinib with atezolizumab was associated with improved PFS 6.3 months versus 4.2 months for ARPI switch. Median OS was not statistically improved (HR, 0.89 [95% CI, 0.72 to 1.10]; $P = .3$) with cabozantinib and atezolizumab (median 14.8 months [95% CI, 1.4 to 16.7] v the ARPI switch arm 15.0 months [95% CI, 13.0 to 18.5]), and serious adverse events and discontinuation rates were higher in the cabozantinib with atezolizumab arm compared with the ARPI switch arm.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

Additional information including a supplement, clinical tools, and resources can be found at www.asco.org/genitourinary-cancer-guidelines. Patient information is available at www.cancer.org.

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EDITOR'S NOTE

This American Society of Clinical Oncology (ASCO) Living Clinical Practice Guideline provides recommendations, with review and analysis of the relevant literature for each recommendation. Additional information, including links to patient information at www.cancer.org, is available at www.asco.org/genitourinary-cancer-guidelines.

EQUAL CONTRIBUTION

M.-E.T. and R.A.P. were Expert Panel Co-Chairs.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI <https://doi.org/10.1200/JCO-25-02693>.

REFERENCES

- Agarwal N, Azad A, Carles J, et al: Final overall survival (OS) with talazoparib (TALA)+ enzalutamide (ENZA) as first-line treatment in unselected patients with metastatic castration-resistant prostate cancer (mCRPC) in the phase 3 TALAPRO-2 trial. *J Clin Oncol* 43, 2025 (suppl 5; LBA18)
- Liu G, Mu XJ, Fizazi K, et al: Abstract CT231: Identification of a novel agnostic predictive multiomic signature via elastic net/machine Learning in TALAPRO-2 (TP-2), a phase 3 study of talazoparib (TALA)+ enzalutamide (ENZA) vs placebo (PBO)+ ENZA as first-line (1L) treatment in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). *Cancer Res* 84:CT231, 2024 (suppl 7)
- Tombal B, Choudhury A, Saad F, et al: Enzalutamide plus radium-223 in metastatic castration-resistant prostate cancer: Results of the EORTC 1333/PEACE-3 trial. *Ann Oncol* 36:1058-1067, 2025
- Agarwal N, Azad A, Carles J, et al: CONTACT-02: Phase 3 study of cabozantinib (C) plus atezolizumab (A) vs second novel hormonal therapy (NHT) in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC). *J Clin Oncol* 42, 2024 (suppl 4; abstr 18)
- Agarwal N, Azad AA, Carles J, et al: Cabozantinib plus atezolizumab in metastatic prostate cancer (CONTACT-02): Final analyses from a phase 3, open-label, randomised trial. *Lancet Oncol* 26: 860-876, 2025
- Graff JN, Burotto M, Fong PC, et al: Pembrolizumab plus enzalutamide versus placebo plus enzalutamide for chemotherapy-naive metastatic castration-resistant prostate cancer: The randomized, double-blind, phase III KEYNOTE-641 study. *Ann Oncol* 36:976-987, 2025
- Petrylak DP, Ratta R, Matsubara N, et al: Pembrolizumab plus docetaxel versus docetaxel for previously treated metastatic castration-resistant prostate cancer: The randomized, double-blind, phase III KEYNOTE-921 trial. *J Clin Oncol* 43:1638-1649, 2025
- Chi KN, Castro E, Attard G, et al: Niraparib and abiraterone acetate plus prednisone in metastatic castration-resistant prostate cancer: Final overall survival analysis for the phase 3 MAGNITUDE trial. *Eur Urol Oncol* 8:986-998, 2025
- Morris MJ, Castellano D, Herrmann K, et al: ¹⁷⁷Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): A phase 3, randomised, controlled trial. *Lancet (London, England)* 404:1227-1239, 2024
- Garje R, Riaz IB, Naqvi SAA, et al: Systemic therapy in patients with metastatic castration-resistant prostate cancer: ASCO guideline update. *J Clin Oncol* 43:2311-2334, 2025
- Sanders JJ, Temin S, Ghoshal A, et al: Palliative care for patients with cancer: ASCO guideline update. *J Clin Oncol* 42:2336-2357, 2024

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST**Systemic Therapy in Patients With Metastatic Castration-Resistant Prostate Cancer: ASCO Living Guideline, Version 2025.1**

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APPENDIX 1. GUIDELINE DISCLAIMER

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APPENDIX 2. GUIDELINE AND CONFLICTS OF INTEREST

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TABLE A1. Systemic Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer Guideline Expert Panel Membership

Name	Affiliation	Area of Expertise
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(continued on following page)

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TABLE A1. Systemic Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer Guideline Expert Panel Membership (continued)

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TABLE A2. All Recommendations

Principles of Practice	Practice Statement	
<i>General Note.</i> The following recommendations (strong or conditional/weak) and terminology (see the Data Supplement, online only) represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible		
Principles of practice	1. mCRPC is defined as castrate levels of testosterone (<50 ng/mL or 1.7 nmol/L) with evidence of either new or progressive metastatic disease on radiologic assessment or two consecutive rising PSA levels (minimal start value is 1.0 ng/mL) in the setting of existing metastatic disease	
	2. The Panel recommends both germline and somatic testing for patients with metastatic prostate cancer at the earliest available opportunity. Additional recommendations and discussion regarding the same are available in the Germline and Somatic Genomic Testing for Metastatic Prostate Cancer: ASCO Guideline (Yu EY et al: J Clin Oncol 43:748-758, 2025)	
	3. The Panel recommends personalizing treatment based on prior therapies received during castration-sensitive setting, while also accounting for each patient's clinical status, cancer-related symptoms and signs, therapy-related toxicities, potential drug interactions, cost, and drug availability	
	4. The Panel recommends continuation of ADT (or surgical castration) to maintain castrate levels of testosterone for every patient with mCRPC	
	5. The Panel recommends early integration of palliative and supportive care teams for symptom management and to review goals of care for patients with mCRPC. Additional information on the same is available in the Palliative Care for Patients With Cancer: ASCO Guideline Update (Sanders et al ¹¹)	
	6. The Panel recommends the use of bone-protective agents like denosumab (RANK ligand inhibitor) or zoledronic acid (bisphosphonate) for patients with bone metastases to lower the risk of SREs. Additional recommendations on the same are available in the Bone Health and Bone-Targeted Therapies for Prostate Cancer: ASCO Endorsement of a Cancer Care Ontario Guideline (Saylor PJ, et al: J Clin Oncol 38:1736-1743, 2020)	
	7. Limited randomized clinical trial data exist for optimal sequencing of therapies for patients with mCRPC, as certain therapies studied in the mCRPC setting are now being used earlier during castration-sensitive disease	
Clinical Question	Recommendation	
For patients previously treated with ADT alone in castration-sensitive or nonmetastatic CRPC setting and whose disease has progressed to metastatic CRPC, the panel recommends (Fig A1: Algorithm for patients previously treated with ADT alone)	1.1.1. The Panel recommends HRR testing before initiation of systemic therapy (see the Germline and Somatic Genomic Testing for Metastatic Prostate Cancer: ASCO Guideline; Yu EY et al: J Clin Oncol 43:748-758, 2025). If positive for <i>BRCA1/2</i> alterations, then preferred options include either of niraparib + abiraterone, olaparib + abiraterone, or talazoparib + enzalutamide. (Evidence quality: Moderate; Strength of recommendation: Strong) <i>Practical Information for Recommendation 1.1.1:</i> The Panel recommends personalized treatment based on therapies received during castration-sensitive setting, while also accounting for each patient's clinical status, therapy-related toxicities, potential drug interactions, cost, and drug availability as per Principles of Practice Recommendation 3	
	1.1.2. The Panel suggests the combination of talazoparib and enzalutamide for patients with any of the other HRR alterations (<i>PALB2, ATM, ATR, CHEK2, FANCA, RAD51C, NBN, MLH1, MRE11A, CDK12</i>). (Evidence quality: Low, pending further follow up data; Strength of recommendation: Conditional) <i>Practical Information for Recommendation 1.1.2:</i> Responses vary according to individual genes, but the strongest responses are seen in patients with <i>PALB2</i> and <i>CDK12</i> alterations in post hoc subgroup analyses	
	1.1.3. The Panel recommends either enzalutamide or chemotherapy using docetaxel for patients with visceral disease (lung and/or liver metastases) and regardless of HRR alterations (please refer to 1.1.1 and 1.1.2 for preferred recommendations in patients with HRR alterations). (Evidence quality: High; Strength of recommendation: Strong) The panel recommends abiraterone with prednisone, darolutamide, apalutamide, or cabazitaxel in selected patients (see Practical Information; Evidence quality: Low; Strength of recommendation: Conditional) <i>Practical Information for Recommendation 1.1.3:</i> Although there are limited data for abiraterone with prednisone, darolutamide, or apalutamide for patients with visceral disease in the mCRPC setting, these agents can be used as alternatives if there are concerns about side effects or drug interactions. Cabazitaxel may be used if allergic reactions or toxicity like peripheral neuropathy which precludes the use of docetaxel. The choice between an ARPI and chemotherapy may depend on the patient's health, their ability to tolerate chemotherapy, the presence of symptoms and/or visceral disease, accessibility, cost, and the patient's preference, especially if they are averse to chemotherapy	
	1.1.4. The Panel recommends docetaxel, abiraterone plus prednisone, enzalutamide with radium, or sipuleucel-T for patients with mCRPC without visceral metastases. The panel recommends radium 223 monotherapy for patients with symptomatic bone-only disease (lymph node <3 cm; Evidence quality: Moderate; Strength of recommendation: Strong) <i>Practical Information for Recommendation 1.1.4:</i> Unless contraindicated, the use of bone-protecting agents is strongly recommended in all patients receiving radium 223 (See Principle of Practice, item 6). Symptomatic disease is defined as consistent use of pain medications or undergoing external-beam radiation therapy for cancer-related bone pain. The Panel recommends educating patients and caregivers regarding the lack of benefit in objective intermediate measurable end points (PSA levels, radiographic changes) associated with the use of sipuleucel-T. Enzalutamide monotherapy instead of enzalutamide with radium is an option in the presence of visceral metastasis or contraindications to abiraterone or radium 223	
	1.1.5. The Panel recommends pembrolizumab for patients with MSI-high or dMMR after progression on other agents listed previously. (Evidence quality: Moderate; Strength of recommendation: Strong) <i>Practical Information for Recommendation 1.1.5:</i> For patients with tumor mutational burden-high (TMB-H ≥10 mut/Mb), the Panel recommends considering other therapeutic options listed previously before utilization of pembrolizumab, given modest clinical benefit	
	1.1.7. The Panel suggests metastasis-directed therapy in the form of radiation or surgical resection after a multidisciplinary evaluation in selected patients with oligometastatic progression. (Evidence quality: Low; Strength of recommendation: Conditional)	
	For patients previously treated with ADT and an ARPI and whose disease has progressed to metastatic CRPC (Fig A2: Algorithm for patients previously treated with ADT and an ARPI)	1.2.1. The Panel recommends using olaparib monotherapy for patients with <i>BRCA1/2</i> alterations. (Evidence quality: Moderate; Strength of recommendation: Strong) <i>Practical Information for Recommendation 1.2.1:</i> Rucaparib may be offered as an alternative to olaparib for selected patients based on clinical judgment and patient preferences, pending availability
		1.2.2. The Panel suggests olaparib monotherapy for patients with any of the other HRR alterations. (Evidence quality: Very Low; Strength of recommendation: Conditional) <i>Practical Information for Recommendation 1.2.2:</i> Patients with <i>BRCA1, BRCA2, CDK12, and PALB2</i> gene alterations experienced the greatest benefit with PARP inhibitors. The data supporting continuation of ARPI with a PARP inhibitor are limited. A second ARPI can be considered based on clinical judgment, patient comorbidities, and factors for slowly progressive disease determined by slowly rising PSA without any radiologic progression or cancer-related symptoms. The Panel suggests referring to Recommendation 1.2.2.1 for alternate options
		1.2.2.1. The Panel recommends using docetaxel chemotherapy, radium 223, or ¹⁷⁷ Lu-PSMA-617 (for patients with a PSMA-positive PET scan) for patients regardless of HRR alterations. (Evidence quality: Moderate; Strength of recommendation: Strong) <i>Practical Information for Recommendation 1.2.2.1:</i> Cabazitaxel may be offered to selected patients if they have an allergic reaction or toxicity like peripheral neuropathy which precludes the use of docetaxel
		1.2.3. The Panel recommends sipuleucel-T or local therapies per Recommendations 1.1.4 or 1.1.7, respectively, for selected patients. (Evidence quality: Moderate; Strength of recommendation: Conditional)

(continued on following page)

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TABLE A2. All Recommendations (continued)

Principles of Practice	Practice Statement
For patients previously treated with ADT and docetaxel and whose disease has progressed to metastatic CRPC (Fig A3: Algorithm for patients previously treated with ADT and docetaxel)	1.3.1. The Panel recommends following Recommendations 1.1.1 and 1.1.2 for patients with HRR alterations. (Evidence quality: Moderate to Low; Strength of recommendation: Strong)
	1.3.2. The Panel recommends either an ARPI such as abiraterone with prednisone or enzalutamide, or enzalutamide with radium 223, or chemotherapy with cabazitaxel (for patients regardless of HRR alterations). (Evidence quality: Moderate; Strength of recommendation: Strong; Conditional for radium 223 with enzalutamide)
	<i>Practical Information for Recommendation 1.3.2:</i> The Panel recommends either abiraterone with prednisone, enzalutamide, enzalutamide with radium 223, or cabazitaxel. Which treatment is offered depends on the patient's clinical status, presence or absence of symptoms from metastatic disease, cost and drug availability, and ability to tolerate therapy. Docetaxel rechallenge may be offered to patients with a favorable response to docetaxel (patients who received initial docetaxel therapy and achieved a favorable PSA nadir and durable response before clinical or radiologic progression) in the CSPC setting
For patients previously treated with ADT, ARPI, and docetaxel and whose disease has progressed to metastatic CRPC (Fig A4: Algorithm for patients previously treated with ADT, ARPI, and docetaxel)	1.4.1. The Panel recommends ¹⁷⁷ Lu-PSMA-617 for PSMA-positive disease or radium 223 for PSMA-negative disease or chemotherapy using cabazitaxel. (Evidence quality: Moderate; Strength of recommendation: Strong)
	1.4.2. The Panel recommends olaparib monotherapy for patients with HRR alterations. (Evidence quality: Moderate; Strength of recommendation: Strong)
	<i>Practical Information for Recommendation 1.4.2:</i> As it has demonstrated a PFS benefit, rucaparib may be offered as an alternative to olaparib for selected patients with BRCA1/2 alterations based on clinical judgment and patient preferences, pending availability
	1.4.3. The Panel also recommends radium 223 or pembrolizumab for specific situations outlined earlier (as per Recommendations 1.1.4 and 1.1.5). (Evidence quality: Moderate; Strength of recommendation: Strong)
What are the treatment options for de novo or treatment-emergent small cell neuroendocrine carcinoma of the prostate? (Fig 5: Algorithm for treatment options for de novo or treatment-emergent small cell neuroendocrine carcinoma of the prostate) ¹⁰	1.4.4. The Panel suggests clinical trials, cabazitaxel + carboplatin, carboplatin monotherapy, best supportive care, and hospice care for patients with disease progression despite previously mentioned options. (Evidence quality: Low [cabazitaxel + carboplatin]; Low [carboplatin monotherapy]; NA [best supportive care and hospice care]; Strength of recommendation: Conditional)
	2.1. The Panel recommends using cisplatin or carboplatin plus etoposide for first-line systemic therapy as per Systemic Therapy for Small-Cell Lung Cancer: ASCO-Ontario Health (Cancer Care Ontario) Guideline (Khurshid H, et al: J Clin Oncol 41:5448-5472, 2023; Evidence quality: Low; Strength of recommendation: Strong)
	2.2. The Panel suggests carboplatin plus cabazitaxel for patients with small cell neuroendocrine prostate cancer or those with deleterious alterations in two or more of TP53, RB1, and PTEN genes. (Evidence quality: Low; Strength of recommendation: Conditional)
	2.3. The Panel recommends enrollment in clinical trials after progression on platinum-based chemotherapy for eligible patients. (Evidence quality: NA; Strength of recommendation: Strong)
How to assess for response while on systemic therapy for mCRPC?	<i>Practical Information for Recommendation 2.3:</i> Broad NGS testing at the time of disease progression may aid assessment of clinical trial eligibility
	2.3.1. In selected patients, the Panel suggests up-front chemotherapy (carboplatin and/or cisplatin plus etoposide) with immunotherapy followed by maintenance immunotherapy, lurbinectedin, topotecan, and tarlatamab may be used based on extrapolation from studies for small cell lung cancer. Prospective clinical studies for these agents for small cell prostate cancer are lacking and use of these agents should be considered on a case-by-case basis only. (Evidence quality: Very Low; Strength of recommendation: Conditional)
	<i>Practical Information for Recommendation 2.3.1:</i> Clinicians should consider the possibility of treatment-emergent small cell or neuroendocrine carcinoma or an aggressive variant prostate cancer in patients with exclusively predominant visceral metastases with low PSA, predominant lytic bone lesions, bulky (≥5 cm) lymphadenopathy, rapid disease progression within 6 months of initiation of hormonal therapy, and alterations in any two of the three tumor suppressor genes TP53, RB1, and PTEN
What scans are recommended for response assessment?	3.1. The Panel recommends using a combination of (1) clinical assessments to evaluate the tolerability of cancer therapy and cancer-related symptoms, (2) blood tests including PSA, CBC with differential, and CMP, and (3) radiologic assessments to determine if patients are benefiting from systemic therapy. (Evidence quality: NA; Strength of recommendation: Strong)
	<i>Practical Information for Recommendation 3.1:</i> The use of rising PSA alone to determine disease progression in mCRPC, without evidence of clinical or radiographic progression is not recommended
What scans are recommended for response assessment?	3.2.1. The Panel recommends use of Tc99 bone scan and CT CAP to define progression for patients with mCRPC. These radiologic assessments can be performed every 3-6 months or in patients with rising PSA levels and/or evidence of clinical progression. (Evidence quality: Moderate; Strength of recommendation: Strong)
	<i>Practical Information for Recommendation 3.2.1:</i> The Panel suggests PCWG3 (Scher HI, et al: J Clin Oncol 33:5000, 2015) criteria be referred to in the clinical decision-making process. Currently, the role of PSMA PET-CT is limited to identify PSMA-expressing tumors for patients who will benefit with ¹⁷⁷ Lu-PSMA-617. In selected patients, PSMA PET can be used to stage patients with a rising PSA and concern for progression not visualized on conventional imaging. Prospective data on using PSMA PET scans for response assessment are still emerging, and at this time, the Panel does not recommend their routine use

NOTE. The strength of the recommendation is defined as follows. Strong: In recommendations for an intervention, the desirable effects of an intervention outweigh its undesirable effects. In recommendations against an intervention, the undesirable effects of an intervention outweigh its desirable effects. All or almost all informed people would make the recommended choice for or against an intervention. Conditional/weak: In recommendations for an intervention, the desirable effects probably outweigh the undesirable effects, but appreciable uncertainty exists. In recommendations against an intervention, the undesirable effects probably outweigh the desirable effects, but appreciable uncertainty exists. Most informed people would choose the recommended course of action, but a substantial number would not.

Abbreviations: ¹⁷⁷Lu-PSMA-617, lutetium-177-PSMA-617; ADT, androgen-deprivation therapy; ARPI, androgen receptor pathway inhibitor; CAP, chest, abdomen, and pelvis; CMP, comprehensive metabolic panel; CRPC, castration-resistant prostate cancer; CSPC, castration-sensitive prostate cancer; CT, computed tomography; dMMR, mismatch repair-deficient; HRR, homologous recombination repair; mCRPC, metastatic castration resistant prostate cancer; MSI-high, microsatellite instability-high; NA, not applicable; NGS, next-generation sequencing; PARP, poly(ADP-ribose) polymerase; PCWG, Prostate Cancer Working Group; PET, positron emission tomography; PFS, progression-free survival; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RANK, receptor activator of nuclear factor-kappa B; SRE, skeletal-related event; TMB-H, tumor mutational burden-high.

TABLE A3. Summary of Findings Table

Outcome	Relative Effect, HR (95% CI)	Absolute Risk Estimates			Quality of Evidence	Trials Used
		Risk With Control	Risk With Intervention	Risk Difference (95% CI)		
Summary of findings with certainty of evidence for phase III trials in which patients received prior ADT only						
Patients with <i>BRCA1/2</i> alterations						
PARPi + ARPI						
OS	0.53 (0.29 to 0.95)	556 per 1,000	349 per 1,000	206 fewer per 1,000 (346 fewer to 18 fewer)	Moderate ^a	MAGNITUDE, TALAPRO-2, PROpel
PFS	0.33 (0.18 to 0.59)	808 per 1,000	420 per 1,000	388 fewer per 1,000 (551 fewer to 186 fewer)	Moderate ^a	MAGNITUDE, TALAPRO-2, PROpel
Talazoparib + enzalutamide						
OS	0.50 (0.32 to 0.78)	667 per 1,000	423 per 1,000	244 fewer per 1,000 (370 fewer to 91 fewer)	High	TALAPRO-2
PFS	0.26 (0.16 to 0.42)	667 per 1,000	248 per 1,000	418 fewer per 1,000 (505 fewer to 297 fewer)	High	TALAPRO-2
Patients with HRR alterations other than <i>BRCA1/2</i>						
Talazoparib + enzalutamide						
OS	0.73 (0.52 to 1.02)	609 per 1,000	496 per 1,000	113 fewer per 1,000 (223 fewer to 7 more)	Moderate ^b	TALAPRO-2
PFS	0.65 (0.47 to 0.91)	617 per 1,000	464 per 1,000	153 fewer per 1,000 (254 fewer to 35 fewer)	High	TALAPRO-2
Patients without HRR alterations						
Enzalutamide + radium						
Overall population:						
OS	0.69 (0.52 to 0.90)	576 per 1,000	447 per 1,000	129 fewer per 1,000 (216 fewer to 38 fewer)	High	EORTC 1333/PEACE-3
PFS	0.69 (0.54 to 0.87)	714 per 1,000	579 per 1,000	136 fewer per 1,000 (223 fewer to 51 fewer)	High	EORTC 1333/PEACE-3
Patients who did not receive docetaxel previously						
PFS	0.64 (0.48 to 0.84)	717 per 1,000	554 per 1,000	163 fewer per 1,000 (263 fewer to 63 fewer)	High	EORTC 1333/PEACE-3
Summary of findings with certainty of evidence for phase III trials in which patients received prior ADT + docetaxel						
Patients without HRR alterations						
Enzalutamide + radium						
Patients who had docetaxel previously						
PFS	0.86 (0.57 to 1.31)	708 per 1,000	653 per 1,000	55 fewer per 1,000 (204 fewer to 93 fewer)	Low ^c	EORTC 1333/PEACE-3

Abbreviations: ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; HR, hazard ratio; HRR, homologous recombination repair; OS, overall survival; PFS, progression-free survival.

^aSerious indirectness because of differences in the trial designs and receipt of prior therapy.

^bSerious imprecision because of null effect indicating both clinical benefit and harm.

^cVery serious imprecision because of small sample size and null effect indicating both clinical benefit and harm.

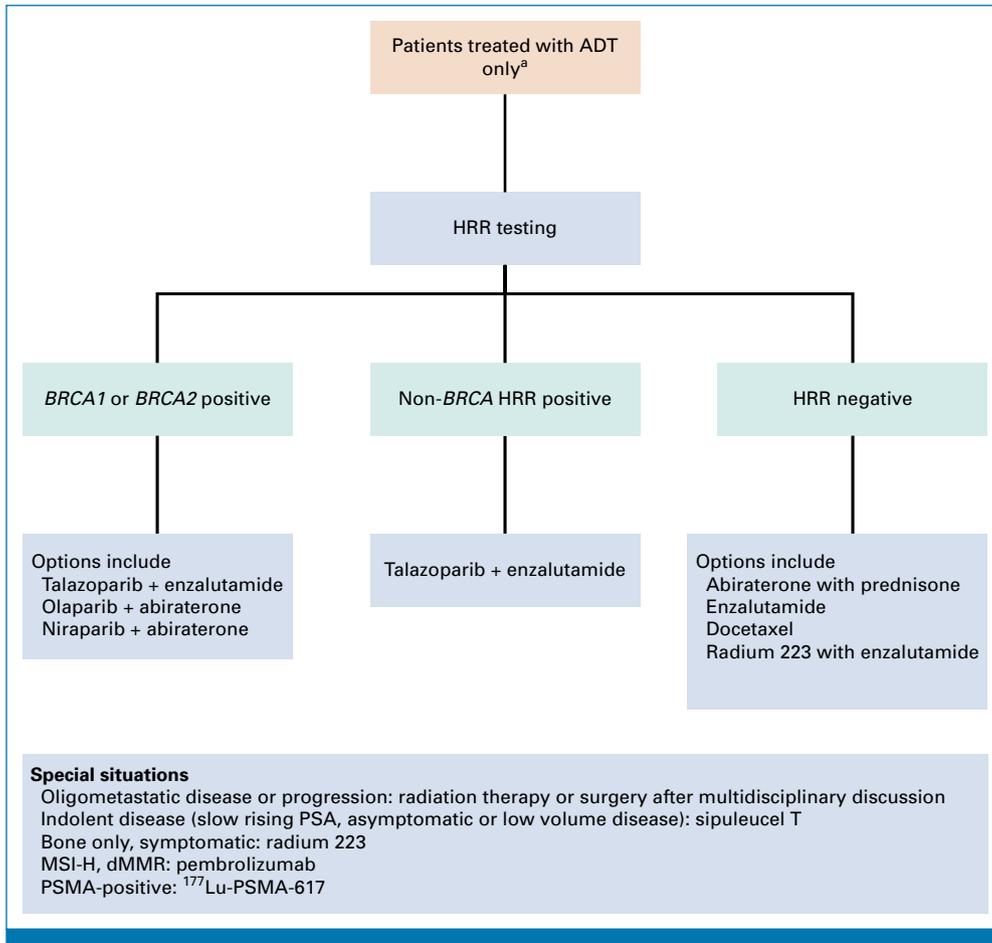


FIG A1. Algorithm for patients previously treated with ADT alone. ^aOptions listed are preferred options. ¹⁷⁷Lu-PSMA-617, lutetium-177-PSMA-617; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; dMMR, mismatch repair deficient; HRR, homologous recombination repair; MSI-H, microsatellite instability high; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen.

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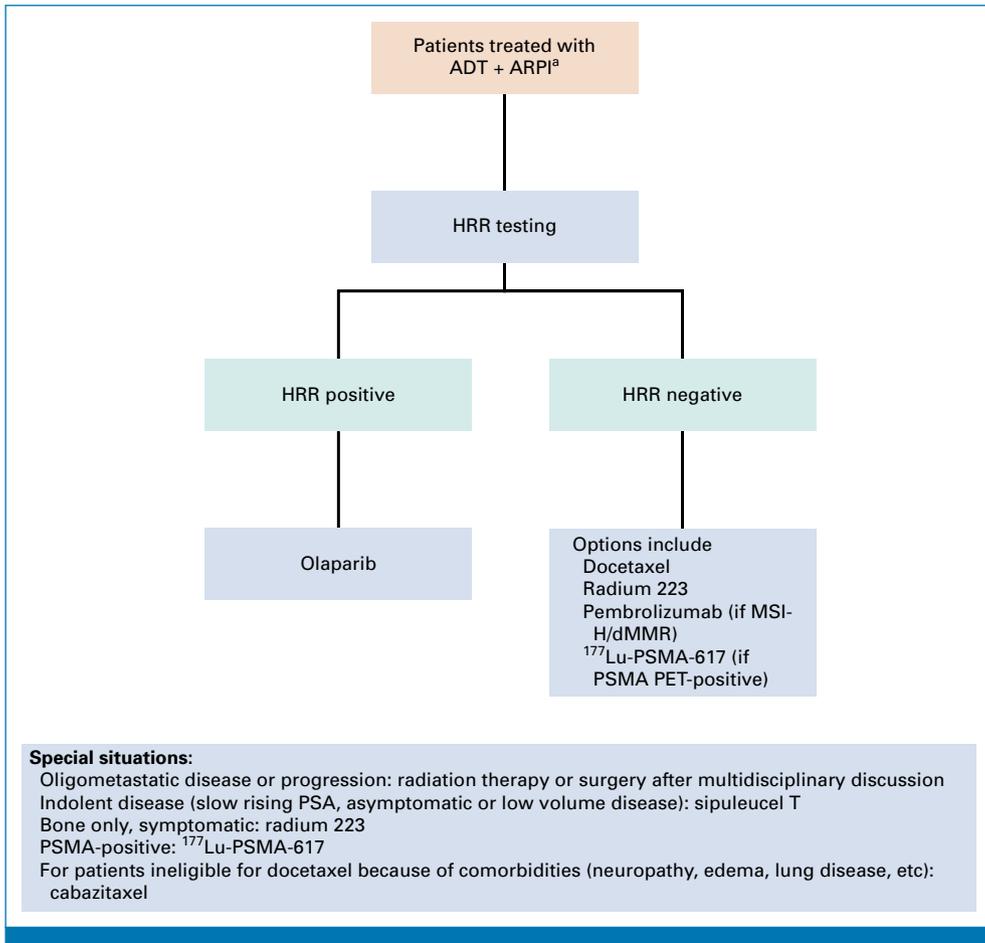


FIG A2. Algorithm for patients previously treated with ADT and an ARPI. ^aOptions listed are preferred options. ¹⁷⁷Lu-PSMA-617, lutetium-177-PSMA-617; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; dMMR, mismatch repair deficient; HRR, homologous recombination repair; MSI-H, microsatellite instability high; PET, positron emission tomography; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen.

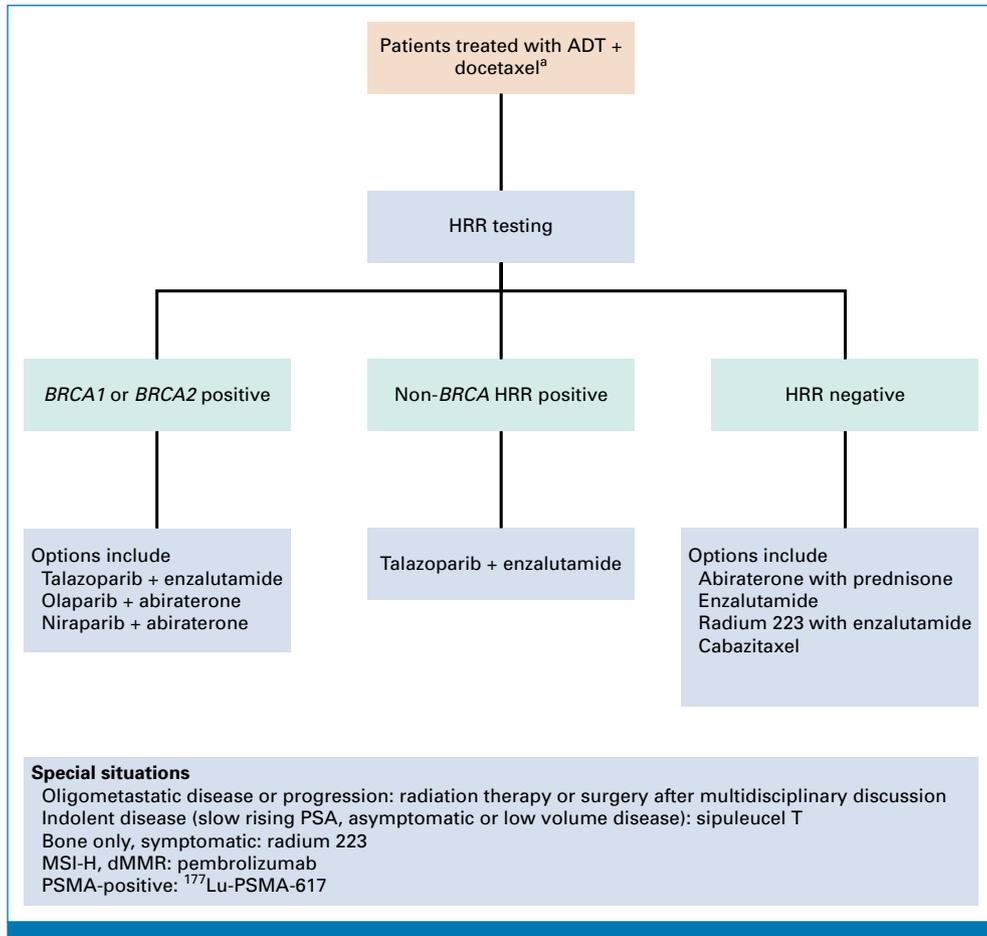


FIG A3. Algorithm for patients previously treated with ADT and docetaxel. ^aOptions listed are preferred options. ¹⁷⁷Lu-PSMA-617, lutetium-177-PSMA-617; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; dMMR, mismatch repair deficient; HRR, homologous recombination repair; MSI-H, microsatellite instability high; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen.

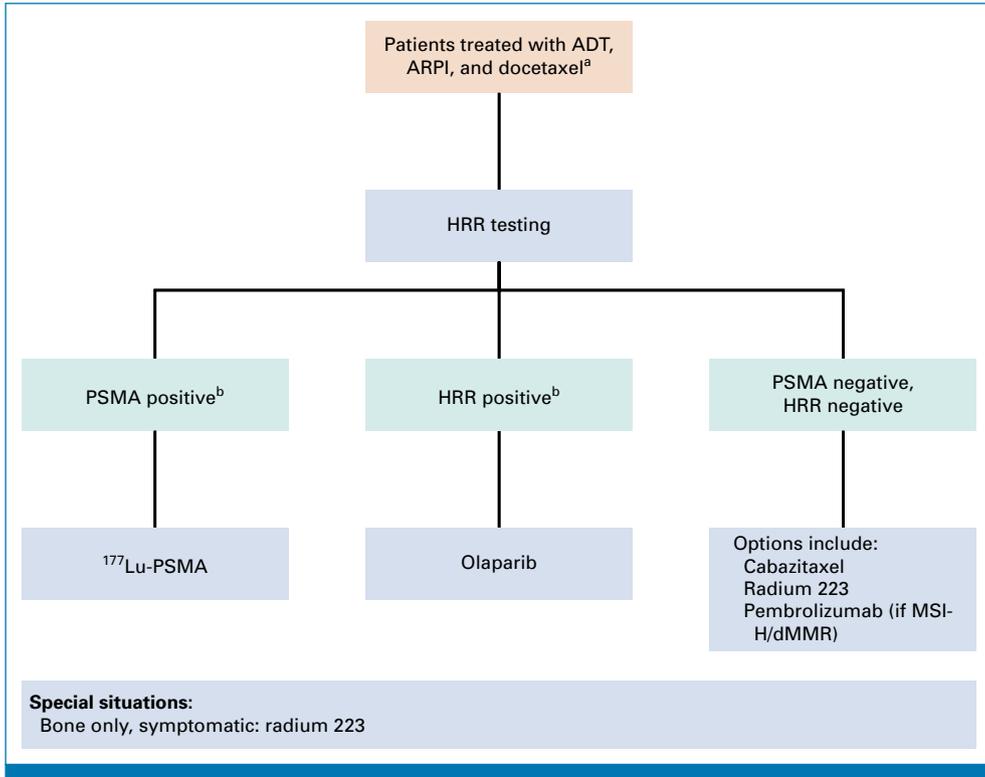


FIG A4. Algorithm for patients previously treated with ADT, ARPI, and docetaxel. ^aOptions listed are preferred options. ^bIndependent of other biomarkers. ¹⁷⁷Lu-PSMA-617, lutetium-177-PSMA-617; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; dMMR, mismatch repair deficient; HRR, homologous recombination repair; MSI-H, microsatellite instability high; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen.