M1 CRPC: First and Second Line Treatment Options

Alicia K. Morgans, MD, MPH, FASCO
Associate Professor, Harvard Medical School
Director, Adult Survivorship Program
Dana-Farber Cancer Instiute
Boston, MA

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

1

Disclosures

Consulting or Advisory Role: AstraZeneca, Astellas, AAA, Bayer, BMS, Clarity, Curium, Exact Science, Johnson and Johnson, Lantheus, Merck, Novartis, Pfizer, Sumitomo Pharma, Inc., Telix, Tolmar

Research Collaborations: Astellas, Bayer, Curium, Johnson and Johnson, Lantheus, Merck, Novartis, Pfizer, Sumitomo Pharma, Inc., Telix

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

2

General Principle: Clinical Factors Still Key

- **Prior treatments - Novel mechanism of action preferred**
- Is the cancer PSMA PET positive?
- Are there visceral metastases? Bone only metastases?
- How is the cancer progressing (symptomatic/aggressive, asymptomatic)?
- Is the patient a candidate for chemotherapy?
- Is there small cell/neuroendocrine differentiation?
- Are there targetable DRD mutations, MMR mutations, or is the tumor MSI high (did I do genetic testing to look for these?)?
- Which options are available in my practice location? What limitations may the patient have (support at home, number of bathrooms/ability to distance, etc.)?
- Clinical trials?

3

M1 CRPC FIRST LINE

CLINICAL STATE	PRIOR THERAPY	
M1 CRPC	• ADT only	
M0 CRPC	• ADT plus NHT	
mHSPC	• ADT plus docetaxel plus NHT • ADT plus NHT	

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

4

National Comprehensive Cancer Network®

NCCN Guidelines Version 5.2026
Prostate Cancer

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[g,aa,jjj,kkk]

Pre-ARPI[aa,lll]	Post-ARPI[lll]/Pre-Docetaxel[aa]	Post-ARPI[lll]/Post-Docetaxel[aa]
Preferred: • Abiraterone (category 1) • Enzalutamide (category 1) **Other Recommended:** • Docetaxel[hhh] (category 1) **Useful in Certain Circumstances:** • Molecular Biomarker-Directed Therapy ▸ *BRCA* mutation ◊ Niraparib/abiraterone[mmm] (category 1) ◊ Olaparib/abiraterone[mmm] (category 1) ◊ Talazoparib/enzalutamide[mmm] (category 1) ▸ *HRRm* (other than BRCA1/2) ◊ Talazoparib/enzalutamide[mmm] (category 1) • Disease State-Specific Therapy ▸ Bone metastases ◊ Radium-223[ooo]/enzalutamide	**Preferred:** • Docetaxel[hhh] (category 1) **Useful in Certain Circumstances:** • Molecular Biomarker-Directed Therapy ▸ *BRCA* mutation ◊ Olaparib[mmm] (category 1, preferred) ◊ Rucaparib[mmm] (category 1, preferred) ◊ Niraparib/abiraterone[mmm] (category 2B) ◊ Talazoparib/enzalutamide[mmm] (category 2B) ▸ *HRRm* (other than BRCA1/2) ◊ Olaparib[mmm] ◊ Talazoparib/enzalutamide[mmm] (category 2B) • Disease State-Specific Therapy ▸ PSMA-positive metastases ◊ Lutetium Lu 177 vipivotide tetraxetan (Lu-177-PSMA-617)[qqq] ▸ Aggressive variant[iii] ◊ Cabazitaxel/Carboplatin[hhh]	**Preferred:** • Cabazitaxel[hhh] (category 1) • Docetaxel rechallenge[hhh] **Useful in Certain Circumstances:** • Molecular Biomarker-Directed Therapy ▸ *BRCA* mutation ◊ Olaparib[mmm] (category 1) ◊ Rucaparib[mmm] ▸ *HRRm* (other than *BRCA1/2*) ◊ Olaparib[mmm] ▸ Other FDA-approved agents for tissue agnostic indications[hhh] • Disease State-Specific Therapy ▸ PSMA-positive metastases ◊ Lu-177-PSMA-617[qqq] (category 1) ▸ Aggressive variant[iii] ◊ Cabazitaxel/carboplatin[hhh] ▸ Palliation for symptomatic patients unable to tolerate other therapies ◊ Mitoxantrone[hhh]

Additional Options Irrespective of Prior ARPI or Prior Docetaxel (Useful in Certain Circumstances)

• Disease State-Specific Therapy ▸ Asymptomatic without visceral metastases ◊ Sipuleucel-T[hhh,ppp] ▸ Oligometastatic[h]/Oligoprogressive disease ◊ Metastasis-directed therapy[nnn] with metastatic castration-resistant prostate cancer (mCRPC) systemic therapy ▸ Symptomatic bone-predominant metastases ◊ Radium-223[ooo] (category 1)	• Molecular Biomarker-Directed Therapy ▸ MSI-High (MSI-H)/dMMR ◊ Pembrolizumab[hhh] (category 2B)

Spratt DE, et al. NCCN Prostate Cancer V5.2026.

5

American Urological Association

American Urological Association (AUA)/
Society of Urologic Oncology (SUO)

APPROVED BY THE AUA BOARD OF DIRECTORS APRIL 2023

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

Reviewed and Updated 2023

ADVANCED PROSTATE CANCER: AUA/SUO GUIDELINE

(Published 2020; Amended 2023)

William Lowrance, MD, MPH, MBA; Rodney Breau, MSc, MD; Roger Chou, MD; Brian F. Chapin, MD; Tony Crispino; Robert Dreicer, MD, MS, MACP; David F. Jarrard, MD; Adam S. Kibel, MD; Todd M. Morgan, MD; Alicia K. Morgans, MD, MPH; William K. Oh, MD; Matt[illegible] MD, MMH[illegible]

Amendm[illegible] David F. J[illegible] C. Griffin,[illegible]

To know where to go, we must know where we have been.

METASTATIC CASTRATION RESISTANT PROSTATE CANCER

Prognosis

Clinicians SHOULD

- Obtain baseline labs and review location of metastatic disease, disease-related symptoms, and performance status
- Perform imaging at least annually in mCRPC patients without PSA progression or new symptoms
- Order PSMA PET imaging in mCRPC

Treatment (cont.)

Clinicians SHOULD (cont.)

- Recommend cabazitaxel rather than an alternative androgen pathway directed therapy in patients who received prior docetaxel and abiraterone acetate plus prednisone or enzalutamide
- Offer a PARP inhibitor to patients with deleterious or suspected deleterious [illegible]omatic HRR gene-mutated [illegible]wing prior treatment with [illegible] or abiraterone, and/or a [illegible] chemotherapy; platinum-[illegible]otherapy may be offered for [illegible] cannot use or obtain a PARP [illegible]

Clinicians SHOULD

- Offer continued ADT with abiraterone acetate plus prednisone, docetaxel, or enzalutamide in mCRPC patients who have not received prior androgen receptor pathway inhibitors
- Offer radium-223 to patients with symptoms from bony metastases from mCRPC and without known visceral disease or lymphadenopathy >3cm
- Offer ^{177}Lu-PSMA-617 to patients with progressive mCRPC having previously received docetaxel and androgen pathway inhibitor with a positive PSMA PET imaging study

- Offer pembrolizumab to patients with mismatch repair deficient or microsatellite instability high mCRPC

Clinicians MAY

- Offer sipuleucel-T to asymptomatic/ minimally symptomatic patients
- Offer cabazitaxel to patients who received prior docetaxel with or without prior abiraterone acetate plus prednisone or enzalutamide

Lowrance W, et al. J Urol. 2023.

6

M1 CRPC FIRST OR SECOND LINE

- Sipuleucel-T
- Docetaxel
- Abiraterone
- Enzalutamide
- Radium-223
- Cabazitaxel
- ^{177}Lu PSMA-617
- Pembrolizumab (select patients with MSI high, dMMR mutation)
- PARP inhibitor (plus or minus abiraterone or enzalutamide) (separate talk)

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

7

SIPULEUCEL-T

- Autologous cellular immunotherapy for men with asymptomatic or minimally asymptomatic mCRPC (FDA approval 2010)
- Intravenous infusion 3 doses every 2 weeks
- **IMPACT trial**
  - Overall survival 4.1 months longer with sipuleucel-T versus placebo (25.8 months versus 21.7 months)
  - Overall survival 13 months longer with sipuleucel-T in PSA <22.1 versus placebo (41.3 months versus 28.3 months)

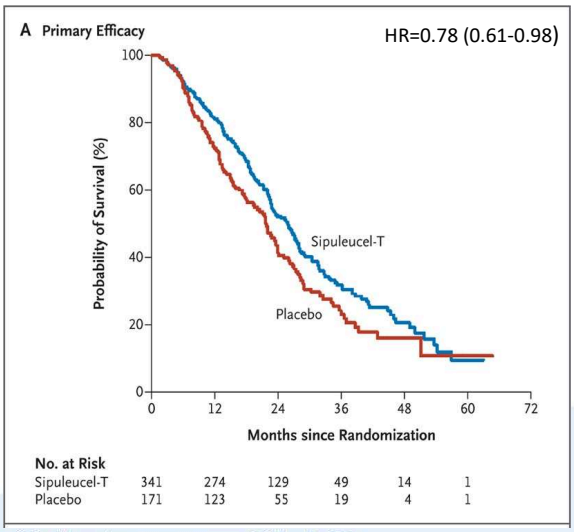
American Urological Association Education & Research, Inc.

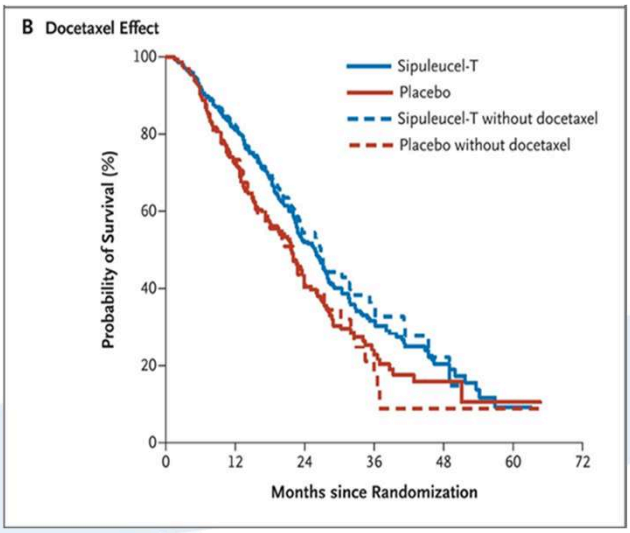
SUO Society of Urologic Oncology, Inc.

Kantoff PW et al. N Engl J Med 2010;363:411-422. Schellhammer PF et al. Urology 2013. 81:1297-302.

8

SIPULEUCEL-T





American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

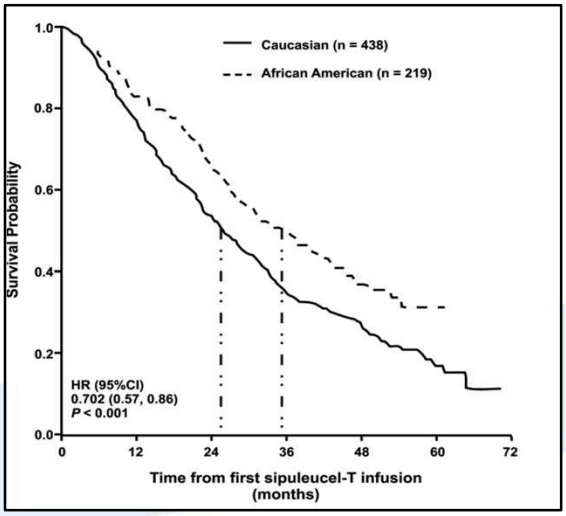
6.7% Black men enrolled

Kantoff PW et al. N Engl J Med 2010;363:411-422.

9

SIPULEUCEL-T

- **PROCEED Registry**
  - Multicenter, open-label, observational registry of 1902 patients with mCRPC
  - Nearly 12% African American men
- Overall survival longer in African American compared to Caucasian men
  - PSA-matched: HR=0.70 (95% CI:0.57-0.86, p<0.001)
  - All patients: HR=0.81 (95% CI:0.68-0.97, p=0.03)



American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Sartor O et al. Prostate Cancer and Prostatic Diseases (2020) 23:517-526.

10

SIPULEUCEL-T

Patient profile

- Asymptomatic or minimally symptomatic
- Life expectancy > 6 months
- ECOG PS status 0-1
- No liver metastasis
- Prostate adenocarcinoma

Monitor

- Acute infusion reaction
- Syncope and hypotension
- Used with caution in men with risk factors for thromboembolic events
- May require central access to administer treatment

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Sartor O et al. Prostate Cancer and Prostatic Diseases (2020) 23:517-526.

11

DOCETAXEL

- Antineoplastic agent which binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly, ultimately resulting in inhibition of mitosis (FDA approval 2004)
- Intravenous infusion 75 mg/m^2 every 3 weeks
- **TAX 327 trial:** Docetaxel plus prednisone versus mitoxantrone plus prednisone
- **SWOG 9916:** Docetaxel plus estramustine versus mitoxantrone plus prednisone

American Urological Association Education & Research, Inc.

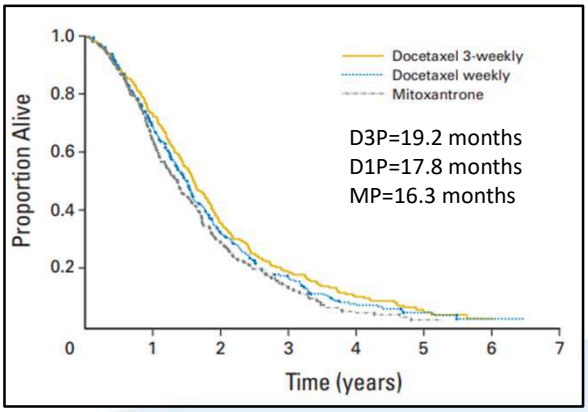
SUO Society of Urologic Oncology, Inc.

Berthold DR et al. J Clin Oncol 2008:26:242-245. Tannock IF et al. N Engl J Med 2004:351:1502-1512. Petrylak EP et al. N Engl J Med 2004:351:1513-1520..

12

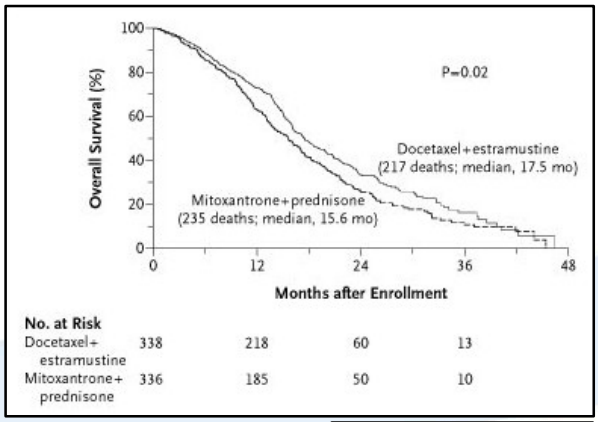
DOCETAXEL

TAX327



% Black men enrolled not reported

SWOG 9916



15 % Black men enrolled

American Urological Association Education & Research, Inc.

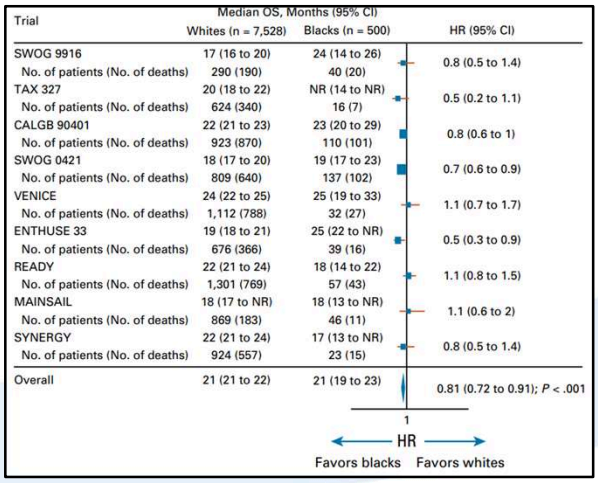
SUO Society of Urologic Oncology, Inc.

Berthold DR et al. J Clin Oncol 2008:26:242-245. Tannock IF et al. N Engl J Med 2004:351:1502-1512. Petrylak EP et al. N Engl J Med 2004:351:1513-1520..

13

DOCETAXEL

- Large meta-analysis of docetaxel regimens in mCRPC from 9 Phase 3 trials
- Of 8,820 men, 85% white, 6% black, 5% asian
- Black men younger, worse PS, higher testosterone, higher PSA
- Median OS 21 months versus 21.2 months
- Pooled multivariable HR=0.81 (95% CI, 0.72-0.91)
- Statistically significant increased OS in black versus white men



American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Halabi S et al. J Clin Oncol 37:403-410.

14

DOCETAXEL

Patient profile

- Symptomatic
- Life expectancy > 6 months
- ECOG PS status 0-2
- Bone and visceral metastasis
- Prostate adenocarcinoma

Monitor

- Hypersensitivity reactions including fatal anaphylaxis
- Monitor liver function (contraindicated if bilirubin > ULN, AST and/or ALT > 1.5 x ULN)
- Neurologic toxicities including peripheral neuropathy
- Cutaneous reactions including erythema and desquamation
- Severe fluid retention in 6.5% despite dexamethasone premedication

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Halabi S et al. J Clin Oncol 37:403-410.

15

ABIRATERONE

- Selective, irreversible inhibitor of CYP17, an enzyme critical in production of androgens by the testes, adrenal gland, and prostate tumor tissues (FDA approval 2011)
- Oral agent 1000 mg daily given with prednisone 5 mg PO BID
- **COU-AA-301:** Abiraterone versus placebo after chemotherapy
- **COU-AA-302:** Abiraterone versus placebo before chemotherapy

American Urological Association Education & Research, Inc.

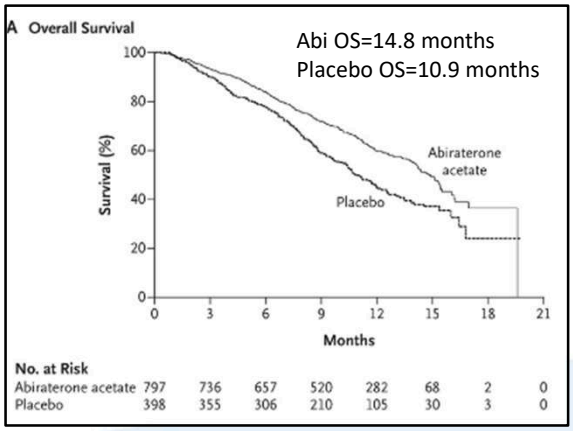
SUO Society of Urologic Oncology, Inc.

Scher HI et al. N Engl J Med 2012:367:1187-1197. Beer TM et al. N Engl J Med 2014;371:424-322. Shore ND et al. Lancet Oncol 2016:17:153-163.

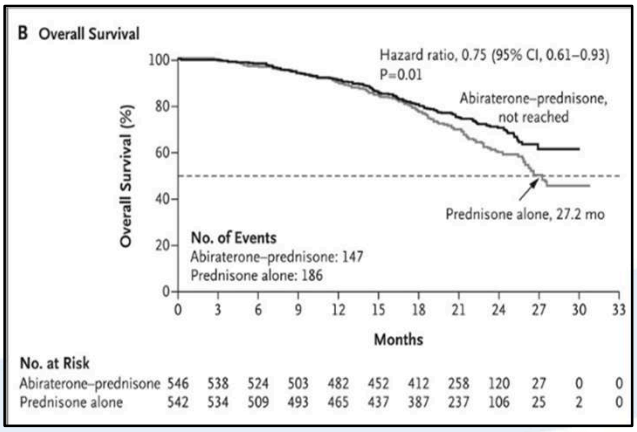
16

ABIRATERONE

COU-AA-302



COU-AA-301



American Urological Association Education & Research, Inc.

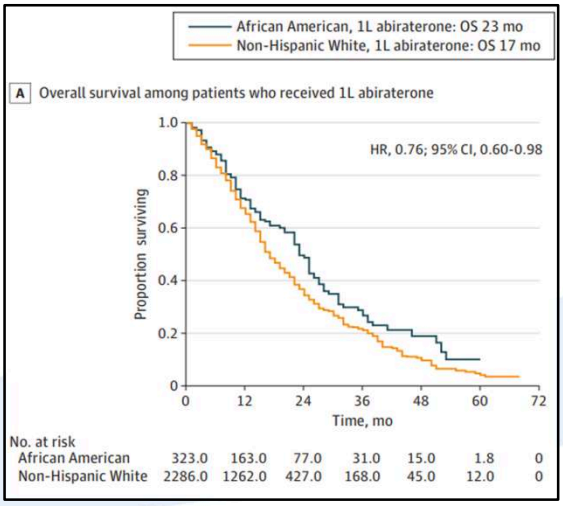
SUO Society of Urologic Oncology, Inc.

De Bono JS et al. N Engl J Med 2011:364:1995-2005. Ryan CJ et al. N Engl J Med 2013:368:138-148.

17

ABIRATERONE

- Real world, retrospective cohort study
- Flatiron Health database
- 2615 white and 404 black men, no prior chemotherapy
- Black men had higher median overall survival of 23 months compared to white men at 17 months



American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Marar M et al. JAMA Netw Open . 2022 Jan 4;5(1):e2142093.

18

ABIRATERONE

Patient profile

- Symptomatic
- Life expectancy > 6 months
- ECOG PS status 0-2
- Bone and visceral metastasis
  - No visceral metastasis in pre-chemotherapy
- Prostate adenocarcinoma

Monitor

- Signs of mineralocorticoid excess
- Hypertension
- Hypokalemia
- Peripheral edema
- Monitor liver function
- Reduce dose in patients with moderate hepatic impairment (Child-Pugh Class B)
- Taken on empty stomach (exposure increases 10-fold when taken with meals)
- Monitor drug-drug interactions (pioglitazone)

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Halabi S et al. J Clin Oncol 37:403-410.

19

ENZALUTAMIDE

- Androgen receptor inhibitor acts by competitively inhibiting androgen binding to androgen receptors, then inhibiting nuclear translocation of androgen receptors and their interaction with DNA (FDA approval 2014)
- Oral agent 160 mg daily
- **AFFIRM:** Enzalutamide versus placebo after chemotherapy
- **PREVAIL:** Enzalutamide versus placebo before chemotherapy
- ***TERRAIN:*** *Enzalutamide versus bicalutamide*
- ***STRIVE:*** *Enzalutamide versus bicalutamide*

American Urological Association Education & Research, Inc.

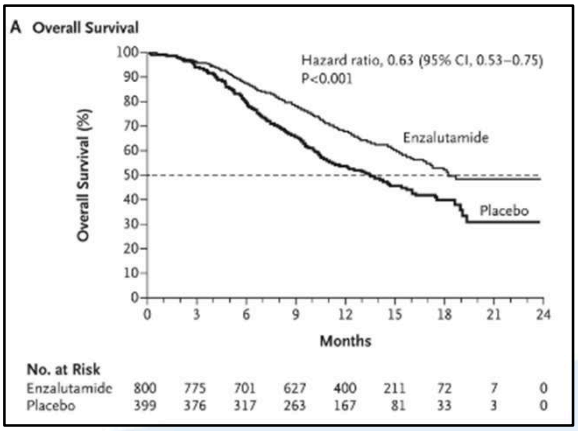
SUO Society of Urologic Oncology, Inc.

Scher HI et al. N Engl J Med 2012:367:1187-1197. Beer TM et al. N Engl J Med 2014;371:424-322. Shore ND et al. Lancet Oncol 2016:17:153-163.

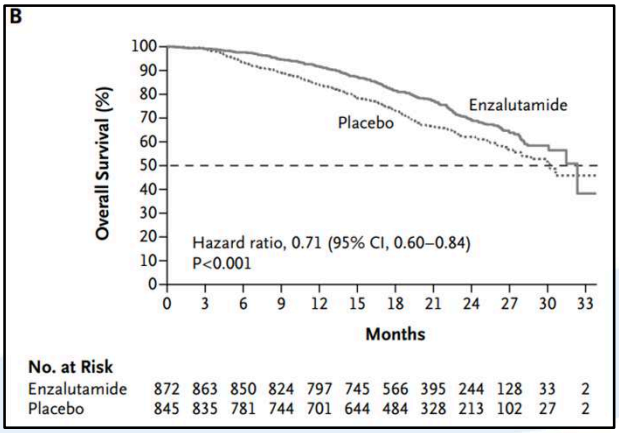
20

ENZALUTAMIDE

AFFIRM



PREVAIL



American Urological Association Education & Research, Inc.

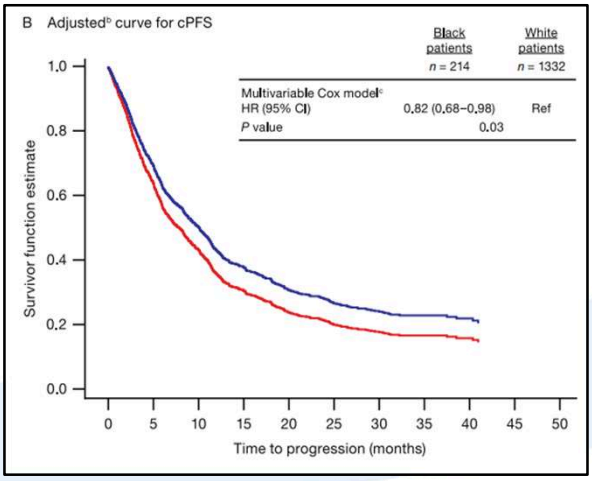
Society of Urologic Oncology, Inc.

Scher HI et al. N Engl J Med 2012:367:1187-1197. Beer TM et al. N Engl J Med 2014;371:424-322.

21

ENZALUTAMIDE

- Real world, retrospective cohort study
- InstrinsiQ Specialty Solutions database from community urology practices
- 1332 white and 214 black men, no prior chemotherapy
- Black men younger, high baseline PSA
- PSA > 50% decline similar, > 90% numerically higher trend
- Black men had better clinical progression-free survival than white men



American Urological Association Education & Research, Inc.

Society of Urologic Oncology, Inc.

Freedland SJ et al. Prostate Cancer and Prostatic Diseases 2023 26:523-530.

22

ENZALUTAMIDE

Patient profile

- Life expectancy > 6 months
- ECOG PS status 0-2
- Bone and/or visceral metastasis
- Prostate adenocarcinoma

Monitor

- Seizure occurred in 2.2% in men with predisposing factors
- Posterior reversible encephalopathy syndrome
- Ischemic heart disease
- Falls and fractures
- Drug-drug interactions
  - Major interactions: apixaban, amlodipine, tramadol, venlafaxine

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Beer TM et al. N Engl J Med 2014;371:424-322.

23

RADIUM-223

- Alpha particle-emitting radioactive therapeutic agent for mCRPC patients with symptomatic bone metastasis and no known visceral metastatic disease (FDA approval 2013)
- Injection of 50 kBq (1.35 microcurie) per kg body weight q4 weeks for 6 doses
- **ALSYMPCA:** Radium-223 versus placebo

American Urological Association Education & Research, Inc.

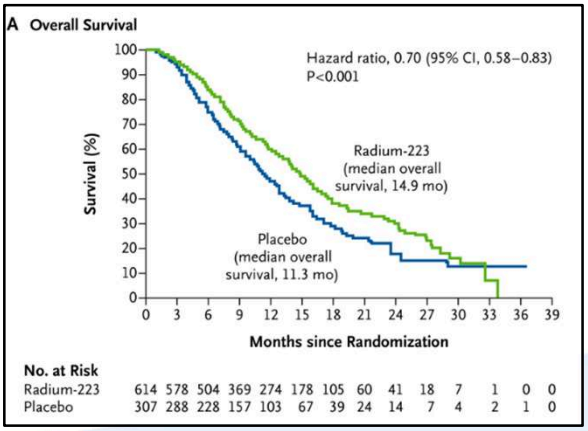
SUO Society of Urologic Oncology, Inc.

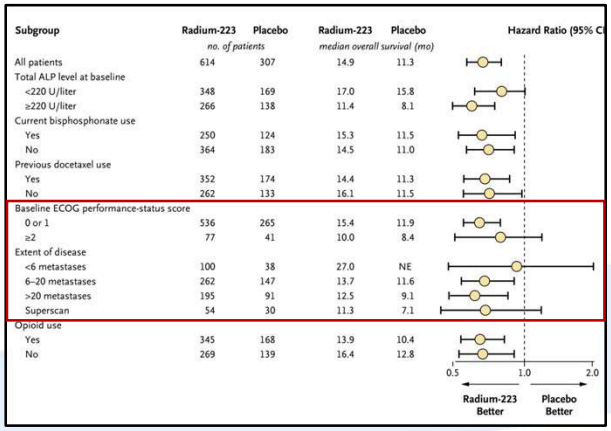
Parker C et al. N Engl J Med 2013:369:213-223.

24

RADIUM-223

ALSYMPCA





American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Parker C et al. N Engl J Med 2013:369:213-223.

25

RADIUM-223

Patient profile

- ECOG 0-2
- Symptomatic bone metastasis
- No visceral metastasis
- Lymph node involvement up to 3 cm acceptable
- Adequate bone marrow reserve
- Prostate adenocarcinoma

Monitor

- Bone marrow suppression
- Nausea, diarrhea, vomiting
- Not recommended in combination with abiraterone due to increased incidence of fractures and deaths (ERA-223)
- Radiation protection precautions

American Urological Association Education & Research, Inc.

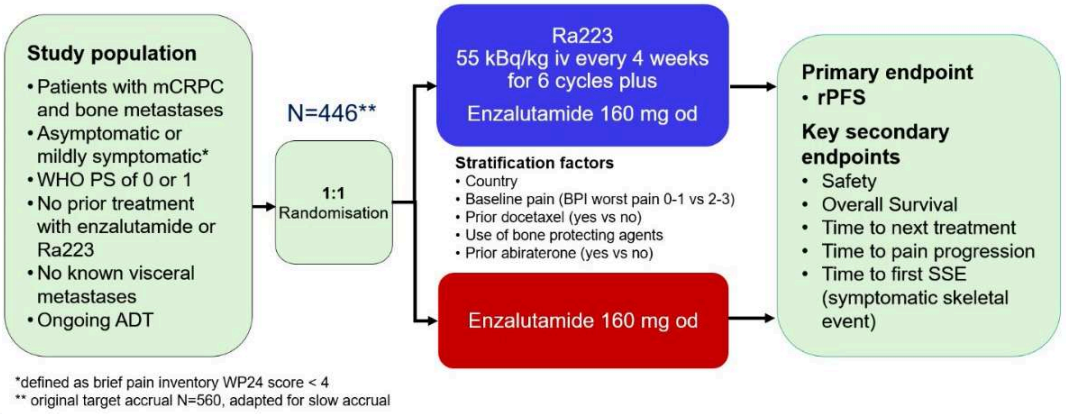
SUO Society of Urologic Oncology, Inc.

Parker C et al. N Engl J Med 2013:369:213-223. Smith M et al. Lancet Oncol 2019: 20:408-419.

26

RADIUM-223 + Enzalutamide

PEACE-3



*defined as brief pain inventory WP24 score < 4
** original target accrual N=560, adapted for slow accrual

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Use of bone protecting agents (BPA) made mandatory (after inclusion of 119 patients)

S Gillessen, ESMO 2024, LBA1

27

RADIUM-223 + Enzalutamide

PEACE-3

Baseline Characteristics

	Enza+Ra223 (N=222)	Enza (N=224)
	N (%)	N (%)
Age, Median (range) years	70.0 (43.0 - 90.0)	70.0 (47.0 - 90.0)
PSA, Median (Q25-Q75) ng/mL	25.3 (6.5 - 68.8)	23.0 (8.5 - 54.9)
WHO Performance status 0	152 (69)	154 (69)
Prior docetaxel[1]	67 (30.2)	66 (30)
Prior abiraterone[1]	4 (2)	7 (3)
Bone lesions[2]		
<10	109 (49)	105 (47)
≥10	93 (42)	99 (44)
Missing or diffuse lesions	20 (9)	20 (9)
Alkaline phosphatase		
≤ULN	127 (57)	107 (48)
>ULN	82 (37)	110 (49)
Missing	13 (6)	7 (3)
Extra-skeletal disease at baseline	77 (35)	73 (33)

(1) Prior docetaxel or abiraterone was allowed for mHSPC
(2) Per imaging guidelines, the type of bone lesions is reported by a radiologist and classified into focal, diffuse or equivocal. Only focal bone lesions can be counted.

Treatment Exposure

	Enza+Ra223	Enza
Enzalutamide treatment duration (months)		
	N=218	N=224
Median	17.3	14.0
Q25 – Q75	9.7 - 27.6	8.3 - 23.3
Radium, number of cycles		
	N=215	
< 6 cycles	25 (11.6%)	
6 cycles	189 (87.9%)	
Missing	1 (0.5%)	

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

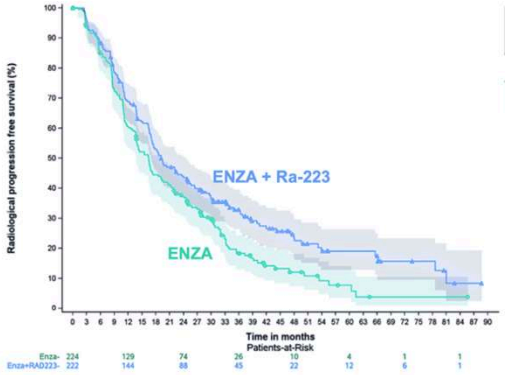
S Gillessen, ESMO 2024, LBA1

28

RADIUM-223 + Enzalutamide

PEACE-3

Primary Endpoint: Radiographic Progression-Free Survival



Arm	No. of Events/Total No.	rPFS, Median (95% CI), mo
ENZA + Ra-223	156/222	**19.19** (16.92, 24.57)
ENZA	176/224	**16.43** (13.77, 19.15)

HR (95% CI): **0.71** (0.57, 0.89)

	ENZA + Ra-223 (n = 222) (95% CI)	ENZA (n = 224) (95% CI)
6 mo	88.4 (83.3, 92.0)	84.6 (79.1, 88.8)
12 mo	68.9 (62.2, 74.7)	60.6 (53.8, 66.8)
18 mo	52.9 (45.9, 59.4)	44.5 (37.7, 51.0)
24 mo	44.1 (37.2, 50.7)	37.2 (30.7, 43.7)

Database locked on January 12, 2026 (cut off date: May 1, 2025)

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

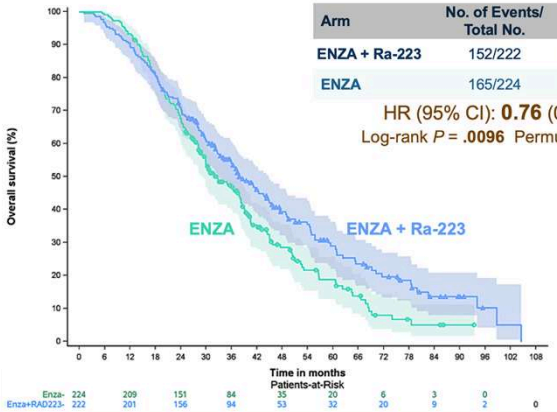
Gallardo E, et al. J Clin Oncol. 2026;44(suppl 7):abstr 15.

29

RADIUM-223 + Enzalutamide

PEACE-3

Secondary Endpoint: Final Overall Survival



Arm	No. of Events/ Total No.	OS, Median (95% CI), mo
ENZA + Ra-223	152/222	**38.21** (33.08, 44.75)
ENZA	165/224	**32.62** (29.31, 38.24)

HR (95% CI): **0.76** (0.60, 0.96)
Log-rank *P* = **.0096** Permutation: **0.0105**

- Preset level of significance at final analysis: < .0248
- Crossing of the curves (still) present at mo 18
- Only 3 pts censored < 24 mo

	ENZA + Ra-223 (n = 222) (95% CI)	ENZA (n = 224) (95% CI)
6 mo	96.8 (93.5, 98.5)	99.1 (96.5, 99.8)
12 mo	90.5 (85.9, 93.7)	92.9 (88.6, 95.6)
18 mo	81.1 (75.3, 85.6)	80.8 (74.9, 85.3)
24 mo	71.1 (64.7, 76.6)	67.7 (61.2, 73.4)
36 mo	54.2 (47.1, 60.6)	47.4 (40.6, 54.0)

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Gallardo E, et al. J Clin Oncol. 2026;44(suppl 7):abstr 15.

30

RADIUM-223 plus enzalutamide

Patient profile

- ECOG 0-2
- Asymptomatic or minimally symptomatic
- Bone metastasis
- No visceral metastasis
- Lymph node involvement
- No prior enzalutamide
- Adequate bone marrow reserve
- Prostate adenocarcinoma

Monitor

- Bone marrow suppression
- Nausea, diarrhea, vomiting
- Use bone health agent (zoledronic acid or denosumab)
- Radiation protection precautions

American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Parker C et al. N Engl J Med 2013:369:213-223. Smith M et al. Lancet Oncol 2019: 20:408-419.

31

RADIUM-223

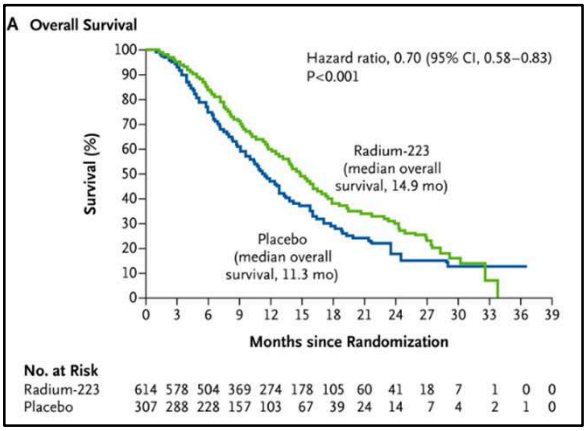
- Alpha particle-emitting radioactive therapeutic agent for mCRPC patients with symptomatic bone metastasis and no known visceral metastatic disease (FDA approval 2013)
- Injection of 50 kBq (1.35 microcurie) per kg body weight q4 weeks for 6 doses
- **ALSYMPCA:** Radium-223 versus placebo

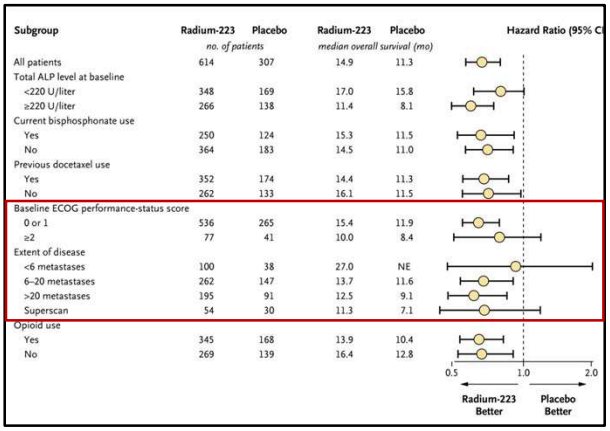
Parker C et al. N Engl J Med 2013:369:213-223.

32

RADIUM-223

ALSYMPCA





Parker C et al. N Engl J Med 2013:369:213-223.

33

^{177}Lu PSMA-617

Patient profile

- ECOG 0-2
- PSMA PET positive metastatic disease
- Adequate bone marrow reserve
- Prostate adenocarcinoma
- Ability to travel for treatment
- Independently able to manage for three days during isolation
- Has own bathroom/space

Monitor

- Bone marrow suppression
- Nausea
- Radiation protection precautions

Parker C et al. N Engl J Med 2013:369:213-223. Smith M et al. Lancet Oncol 2019: 20:408-419.

34

^{177}Lu PSMA-617

- PSMA targeted radiopharmaceutical used to treat PSMA PET positive advanced prostate cancer
- Intravenous infusion every 6 weeks up to 6 times
- **VISION:** ^{177}Lu PSMA-617 plus BSC vs BSC (post-chemotherapy)
- **PSMAfore:** ^{177}Lu PSMA-617 vs abiraterone or enzalutamide (ARPI switch) (pre-chemotherapy)
- **TheraP:** ^{177}Lu PSMA-617 vs Cabazitaxel 25 mg/m^2

American Urological Association Education & Research, Inc.

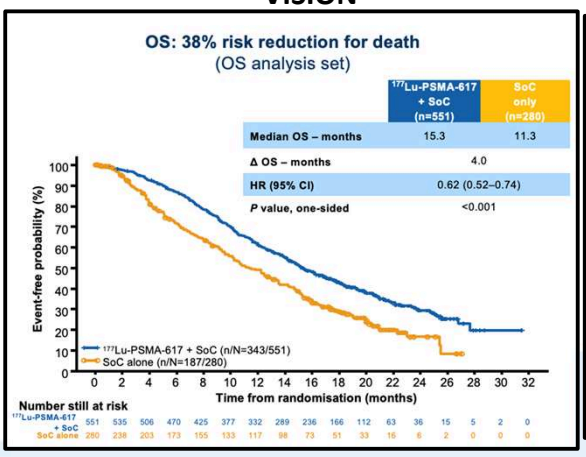
SUO Society of Urologic Oncology, Inc.

De Bono JS et al. Lancet 2010:376:1147-1154. de Wit R et al. N Engl J Med 2019;381:2506-2518. Eisenberger M et al. J Clin Oncol 2017 35:3198-3206.

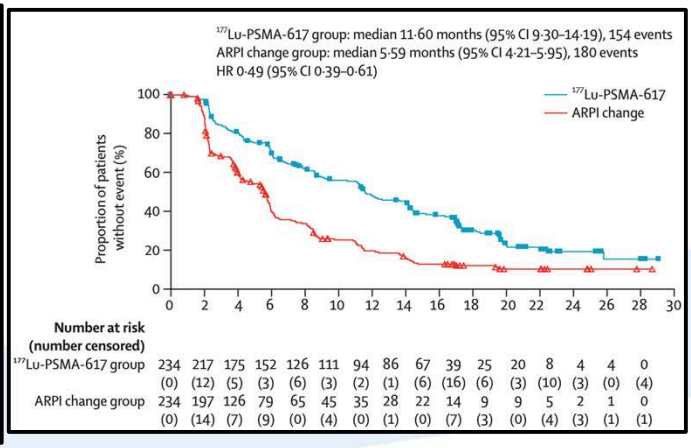
35

^{177}Lu PSMA-617

VISION



PSMAfore



American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

Sartor AO, et al. New Engl J Med. 2021. Morris M, Lancet, 2024.

36

^{177}Lu PSMA-617

Patient profile

- Received prior novel hormone therapy, before or after docetaxel
- Prefers targeted radioactivity rather than chemotherapy

Monitor

- Low blood counts
- Nausea
- Radiation safety requirements
- Dry mouth

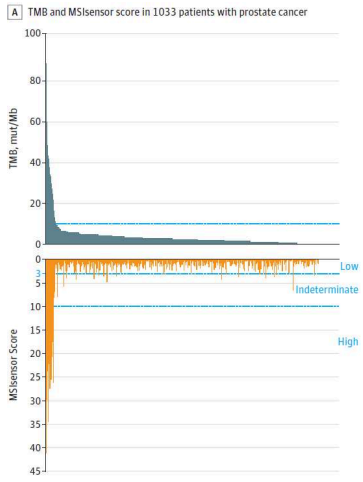
American Urological Association Education & Research, Inc.

SUO Society of Urologic Oncology, Inc.

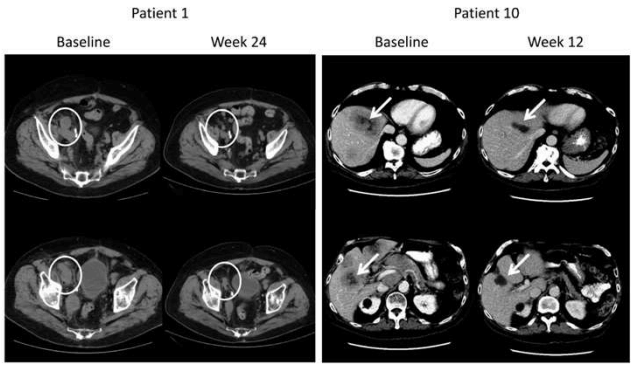
Parker C et al. N Engl J Med 2013:369:213-223. Corn PG et al. Lancet Oncol 2019;20:1432-1443.

37

Don't Forget: Pembrolizumab for MSI-H, mutations in Mismatch Repair Proteints (MSH2, MSH6, MLH2, PSM2) for mCRPC



- Approximately 2-3% of patients with prostate cancer have MSI-H tumors (left) and can have radiographic responses to pembrolizumab (right).



Abida W, et al. JAMA Oncol, 2018.

Graff J, et al. Oncotarget, 2016.

38

M1 CRPC FIRST OR SECOND LINE

- Treatment selection based on prior therapy both in mHSPC and mCRPC
- Consider patient factors including symptomatic disease, location of metastases, including presence of visceral metastases vs bone only disease, and bone marrow reserve
- Genetic testing important in determining treatment selection with PARP plus novel hormonal therapy (separate talk)
- Adverse event monitoring critical in ensuring timely dose modification and maintaining patients' quality of life

39