

21st Annual Miami Cancer Meeting

MCM

Tampa Bay Edition

Fostering Multidisciplinary Care in the
Era of Complex Cancer Treatments

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January 10 – 12, 2025

JW Marriott Tampa Water Street
Tampa, Florida

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Advances in Castration- Resistant Prostate Cancer

Mayer Fishman, MD PhD

Tampa General Hospital Cancer Institute

Collaborative Associate Professor,

University of South Florida Morsani College of
Medicine

Cancer Center of South Florida

Session V
12:10 pm – 1:10 pm

Genitourinary Session

Session Chair:

Mayer Fishman, MD, PhD | TGH Cancer Institute

12:10 pm – 12:25 pm **Updates in the Management of Kidney and Bladder Cancer**
Pedro Barata, MD, MSc, FACP | University Hospitals Seidman Cancer Center

12:25 pm – 12:40 pm **Advances in Castration-Resistant Prostate Cancer**
Mayer Fishman, MD, PhD | TGH Cancer Institute

12:40 pm – 1:10 pm **Complex Genitourinary Cases: Optimal Management**
Moderator: Mayer Fishman, MD, PhD | TGH Cancer Institute
Case Presenter: Roberto Ochoa, MD | The Oncology Institute

12:40-12:50pm **Case #1**

12:50-1:00pm **Case #2**

1:00-1:10pm **Case #3**

Panel: Barata, Fishman



CANCER CENTER
OF **SOUTH FLORIDA**



**CANCER
INSTITUTE**

What is the oldest prostate cancer citation?

William Belfield

Article [Talk](#)

From Wikipedia, the free encyclopedia

William T. Belfield (June 1, 1856 – October 4, 1929) was an American [urologist](#) who is credited with having performed the first intentional [prostatectomy](#) (via the suprapubic route) in 1885, 1886 or 1887 at [Cook County Hospital](#). It is possible he only performed a partial prostatectomy.^{[1][2]} The British surgeon Arthur Fergusson McGill (1850–1890) performed a similar procedure very close to this time, but McGill ultimately recognized Belfield as having been first.^[3]

Belfield was born in [St. Louis, Missouri](#) in 1856 but spent much of his childhood in Chicago.^[4] He earned his medical doctorate from [Rush Medical College](#) in Chicago in 1877^[5] and later became its chair of the department of urology in 1883.^[5] He traveled through Europe obtaining further surgical experience after graduating from medical school. He was instrumental in reporting the discovery of [Mycobacterium tuberculosis](#) by [Robert Koch](#) in the United States and was an early champion of the discipline of microbiology. He was the sixth president of the [American Urological Association](#).^{[6][7]}



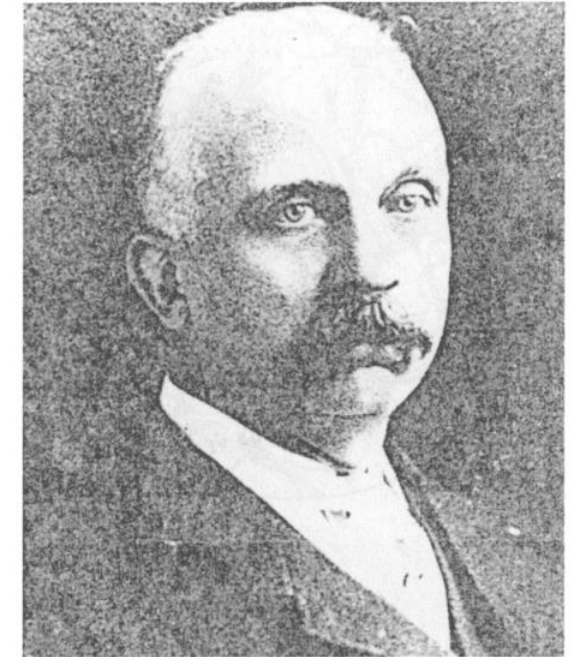
William Belfield

Born	June 1, 1856 St. Louis, Missouri
Died	October 4, 1929 Chicago, Illinois
Occupation	urologist

Figure 1 (Portrait of William T. Belfield, M.D., 1856-1929)

William T. Belfield, M.D., 1856-1929. Bacteriology captured Belfield's interest in the late 1870's and early 1880's. After publishing the first original general bacteriology book in English (1883), he became a leading surgeon and first president of the Chicago Urological Society (1903). For a portrait of Belfield as a young man see [Unrivaled Chicago](#) (1896), page 101. Henry Gradle, M.D., 1855-1911, called the Little Giant by some of his friends, looks directly and searchingly at the viewer in the portrait owned by the Chicago Historical Society. By 1870 Greene V. Black, M.D., D.D.S., 1836-1915, was balding and had adopted the full beard and mustache he wore until the end of his life (Pappas 1983, fig. 21).

Source of WTB portrait: *Ill. Med. J.*, 137 (Jan. 1970): 54-59.



Belfield WT. Report of a Case of Cancer of the Prostate. *Chic Med J Exam.* 1887 Dec;55(6):435. PMID: 37618880; PMCID: PMC9888171.

REPORT OF A CASE OF CANCER OF THE PROSTATE.

ALSO, BY W. T. BELFIELD, M. D.

Hans J—, aged forty-eight years, was admitted to the Cook County Hospital, suffering from unduly frequent and somewhat painful urination, symptoms which had existed for some three months. On two occasions blood had been observed in the urine. Examination *per rectum* showed a slightly enlarged though symmetrical prostate, along the center of which, instead of the normal depression, was a slight protuberance. By the microscope we found in the urine a few blood corpuscles. A tumor of the prostate, either papillomatous or malignant, was diagnosed; the latter seemed more probable, because the quantity of blood in the urine was altogether too slight for the benignant variety. Efforts to entangle and bring away shreds of the supposed growth in the eye of a metallic catheter, failed. May 7th, the bladder was explored by supra-pubic incision, and a malignant villous growth was found growing from the left side of the prostate, the villi projecting an inch or more into the bladder. These were removed with forceps and spoon and the base cauterized. Recovery ensued without notable event, and for eight weeks the urinary function seemed almost normal; then the former symptoms began again and steadily increased in severity. The growth finally entirely filled the bladder and involved the abdominal wall, producing a small fistulous opening, and constituting a tumor which could be plainly outlined above the symphysis pubis and through the rectum, apparently filling the pelvis. Death occurred October 8th. Only the glands in the immediate vicinity of the bladder were found to be carcinomatous, and no secondary growths in other organs were discovered. The kidneys contained numerous miliary abscesses, a condition often consequent upon chronic cystitis.

- [Report of a Case of Cancer of the Prostate.](#)
1 **Belfield WT.**
Cite Chic Med J Exam. 1887 Dec;55(6):435.
PMID: 37618880 [Free PMC article.](#) No abstract available.
Share

- [Report of a Case of Nephrolithotomy.](#)
2 **Belfield WT.**
Cite Chic Med J Exam. 1887 Dec;55(6):434-435.
PMID: 37618878 [Free PMC article.](#) No abstract available.
Share

- [Case of Enciphaloid Cancer of Kidney.](#)
3 **Belfield WT.**
Cite Chic Med J Exam. 1878 Apr;36(4):347-349.
PMID: 37617364 [Free PMC article.](#) No abstract available.
Share

- [Case of Acute Hepatitis.](#)
4 **Belfield WT.**
Cite Chic Med J Exam. 1878 Apr;36(4):337-338.
PMID: 37617346 [Free PMC article.](#) No abstract available.
Share

- [Case of Tuberculous Ulceration of the Intestine.](#)
5 **Belfield WT.**
Cite Chic Med J Exam. 1878 Apr;36(4):351-352.
PMID: 37617356 [Free PMC article.](#) No abstract available.
Share

- [Case of Amyloid Degeneration of Liver, Spleen, and Kidney.](#)
6 **Belfield WT.**
Cite Chic Med J Exam. 1878 Apr;36(4):342-344.
PMID: 37617355 [Free PMC article.](#) No abstract available.
Share

- Presented with hematuria x 2-3 months
- Resected by suprapubic incision
- Died 5 months later
- Sounds like urothelial cancer
- It is good to be the chairman

Did you ever like the term “castration-resistant?”

- Me neither
- Clearly most men with prostate cancer who need low testosterone as part of their therapy are not being castrated
- Treating with GnRH agonists or antagonists leads to low circulating testosterone, generally in the castration range, but those levels are variable.
- Now, with many treatment plans including an antiandrogen agent early on, the ambiguity that mixes patients into the same category patients with progression on:
 - GnRH monotherapy,
 - combination GnRH and bicalutamide,
 - combination GnRH and abiraterone,
 - or combination GnRH and apalutamide or enzalutamide or darolutamide

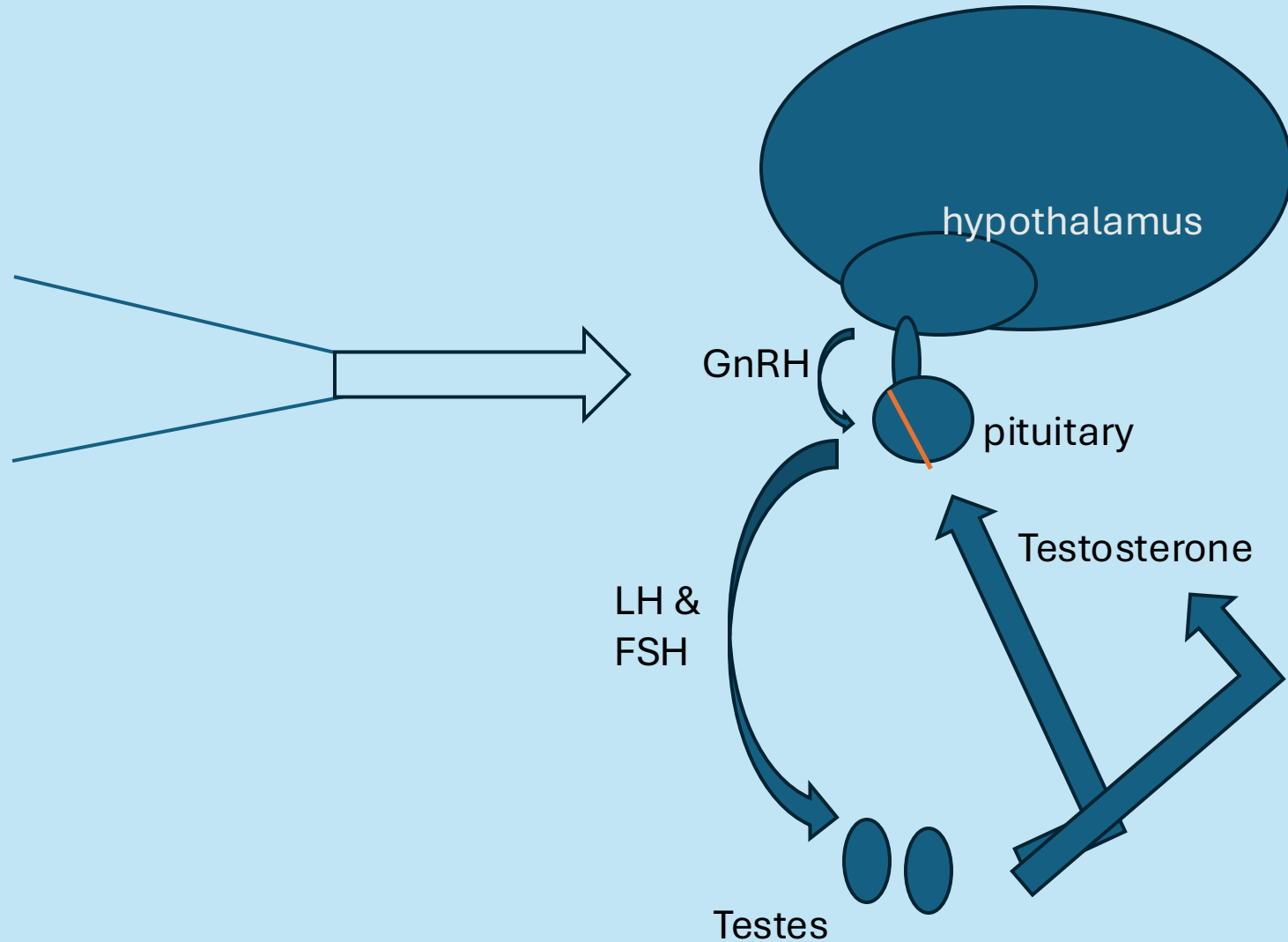
Hypothalamus – Pituitary – Gonad axis

Agonists:

- Leuprolide
- Goserelin

Antagonists

- Degarelix
- Relugolix

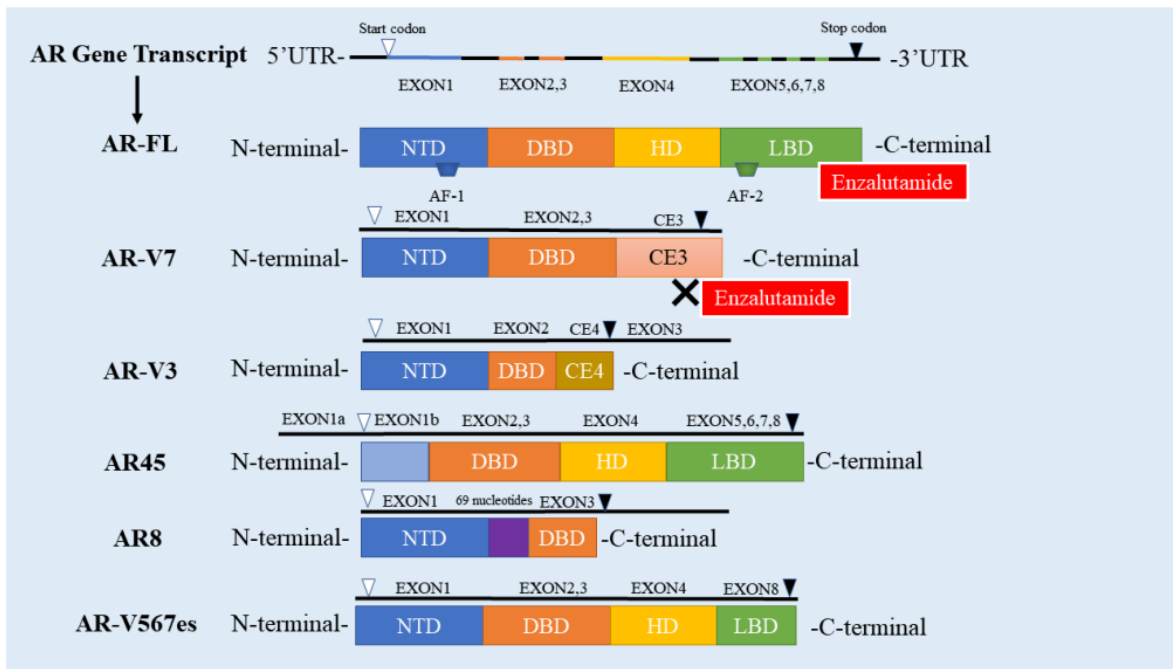


So what is a better term for what we see?

(“Castrate resistant” used to be what was thought was happening)

Some different molecular contexts of prostate cancer dependence:

- Dependent on circulating testosterone
- Independent of circulating testosterone, but dependent on intact AR protein
- Independent of circulating testosterone and dependent on a testosterone-independent AR protein (Such as ARv7)
- Independent of testosterone, and independent of any AR protein



Domain structure of AR, the androgen receptor protein

Figure 1. The Structure of AR-FL and AR-Vs. The human AR gene contains eight exons; AR has four domains, including NTD, DBD, HD and LBD. Exon 1 encodes NTD, DBD is encoded by exons 2 and 3, exon 4 encodes HD, and LBD is encoded by exons 5,6,7,8; AR-V7 has no LBD, so enzalutamide cannot bind to AR-V7; The DBD domain of AR-V3 is only encoded by exon 2, and lacks zinc finger; AR45 starts coding from exon 1b and lacks the NTD domain; The DBD domain formed by AR8 is only encoded by exon 3 and is not functional. AR8 inserts 69 nucleotides upstream of exon 3; AR-V567es does not contain exon 5,6,7; UTR: Untranslated Region; AR-FL: full-length androgen receptor; AR-V: androgen receptor splicing variant; NTD: N-end domain; DBD: DNA binding; HD: hinge domain; LBD: ligand binding domain; CE3: recessive exon 3; AF: Activate the function.

Zheng, Z.; Li, J.; Liu, Y.; Shi, Z.; Xuan, Z.; Yang, K.; Xu, C.; Bai, Y.; Fu, M.; Xiao, Q.; et al. The Crucial Role of AR-V7 in Enzalutamide-Resistance of Castration-Resistant Prostate Cancer. *Cancers* 2022, 14, 4877. <https://doi.org/10.3390/cancers14194877>

One aspect of molecular description of PC is by what the AR lesions are.

AR pathway drugs

GnRH agonists

- leuprolide
- goserelin
- others

GnRH antagonists

- Degarelix
- Relugolix (oral)

AR medications (with OS improvement in metastatic hormone sensitive PC trials)

- enzalutamide
- apalutamide
- darolutamide

17 α -hydroxylase/C17,20-lyase (CYP17) inhibitor

- abiraterone

Investigational AR examples:

- miRNA targeting (decreased translation)*
- Enhanced proteolysis of AR
- Blockade of N-terminal of AR

* Nobel.org: microRNA 2024 **Nobel Prize** in Physiology or Medicine jointly to Victor Ambros and Gary Ruvkun



Several non-AR pathway drugs available

Taxanes

Docetaxel

Cabazitaxel

Platinum + taxane

Immunotherapy

Sipuleucel-T

Pembrolizumab

Radioactive

Radium (223Ra)

Lutetium (177Lu) vipivotide tetraxetan

Target metastatic lesion XRT

PARP inhibitor medications

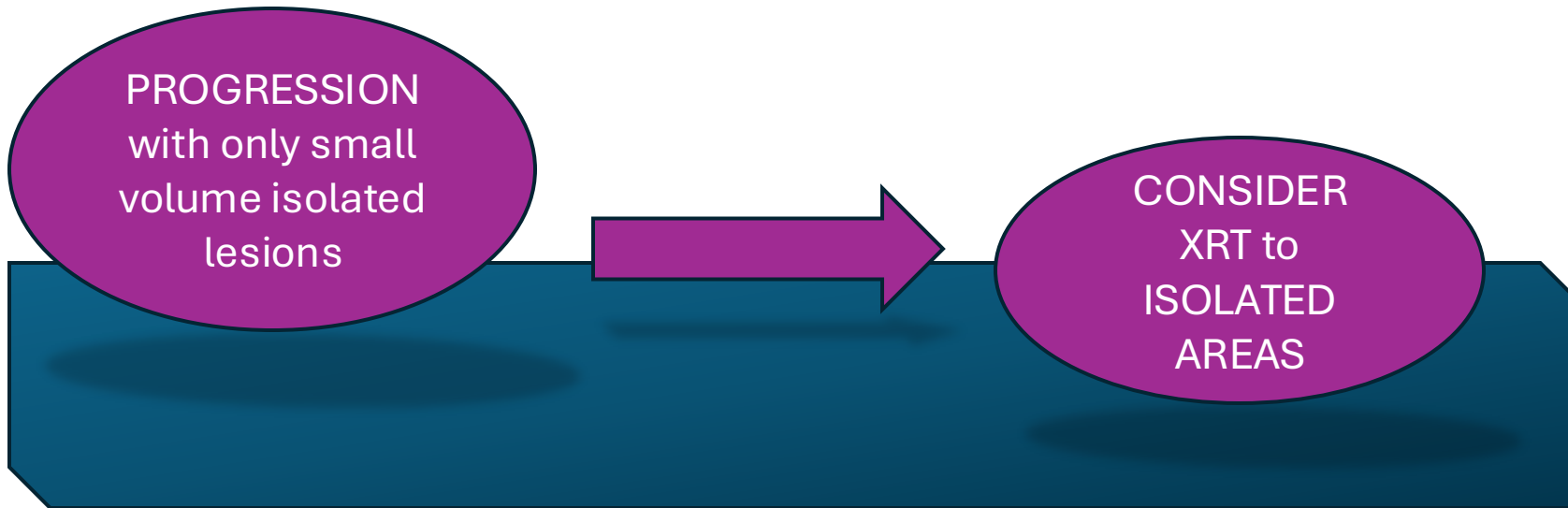
Rucaparib

Olaparib

Talazoparib

Niraparib

Some of the easy decisions (1):

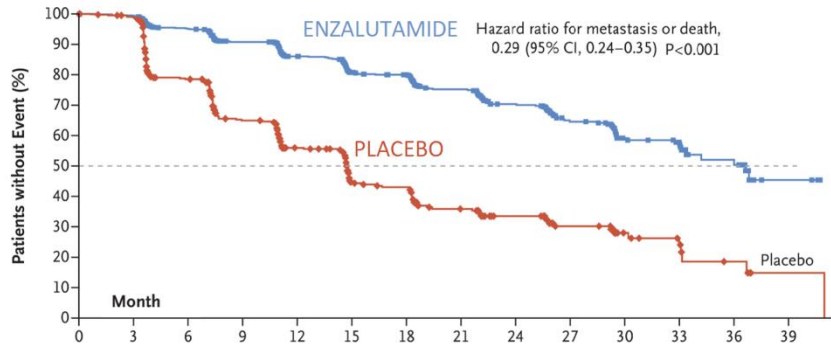


- Delay need for systemic agents
- Unknown demonstrable impact on overall survival
- Newer experiences will have PSMA-PET/CT, not conventional imaging for target identification

Deek MP, Phillips RM, Tran PT. Local Therapies in Oligometastatic and Oligoprogressive Prostate Cancer. Semin Radiat Oncol. 2021 Jul;31(3):242-249.

Some of the easy decisions (2):

CRPC, no mets on conventional scan



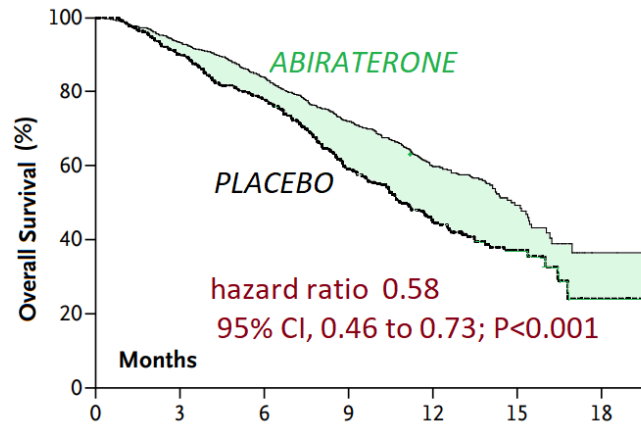
No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	
Enzalutamide	933	865	759	637	528	431	418	328	237	159	87	77	31	4	0
Placebo	468	420	296	212	157	105	98	64	49	31	16	11	5	1	0

CRPC, mets on conventional scan. Progressed through GnRH monotherapy

PROGRESSION on GnRH monotherapy



CONSIDER COMBINATION GnRH & AR MEDICATION



No. at Risk	0	3	6	9	12	15	18
Abiraterone acetate	797	736	657	520	282	68	2
Placebo	398	355	306	210	105	30	3

Hussain M, Fizazi K, Saad F, et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med. 2018 Jun 28;378(26):2465-2474.

de Bono JS, Logothetis CJ, Molina A, et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med. 2011 May 26;364(21):1995-2005.

FACTORS AT PROGRESSION AFFECTING THE LEVEL OF RISK/BENEFIT BALANCE

- Original Gleason score (grade group)

- Latency since prior treatment

- Anatomic pattern

- No visible on PSMA-PET CT

- No visible disease on bone scan & conventional CT

- Regional lymph nodes only

- Multiple level nodes; bulky nodes

- Small volume bone lesions

- Many or symptomatic bone lesions

- Visceral spread

“biochemical recurrence”

Age

General frailty

Specific comorbidities

Neuropathy

Coronary artery disease

Other malignancies

PARP inhibition:

Major impact is for those with DNA mismatch repair defect phenotype

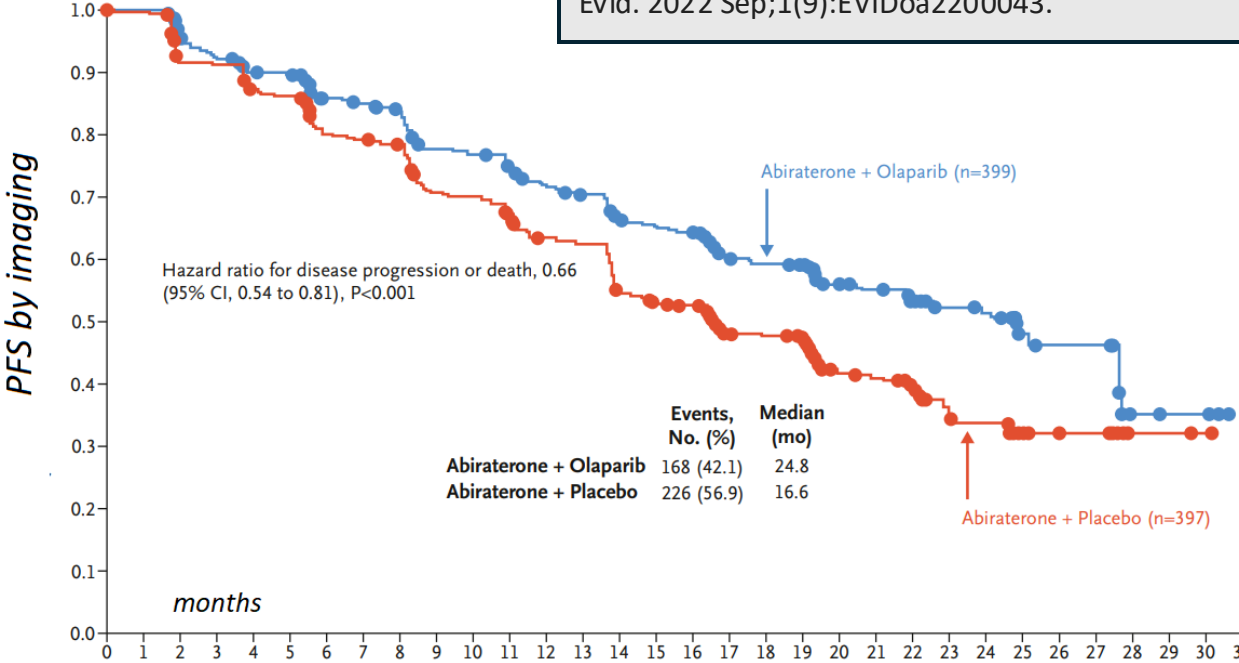
Any positive test is sufficient:
 Germline
 Original tumor
 Recent tumor
 Blood for ctDNA

BRCA2 consistently:
 most frequent
 largest impact

May be more of a stabilization than major response

Pills can be appealing over IV

Clarke NW, Armstrong AJ, Thiery-Vuillemin A et al. Abiraterone and Olaparib for Metastatic Castration-Resistant Prostate Cancer. NEJM Evid. 2022 Sep;1(9):EVIDoA2200043.



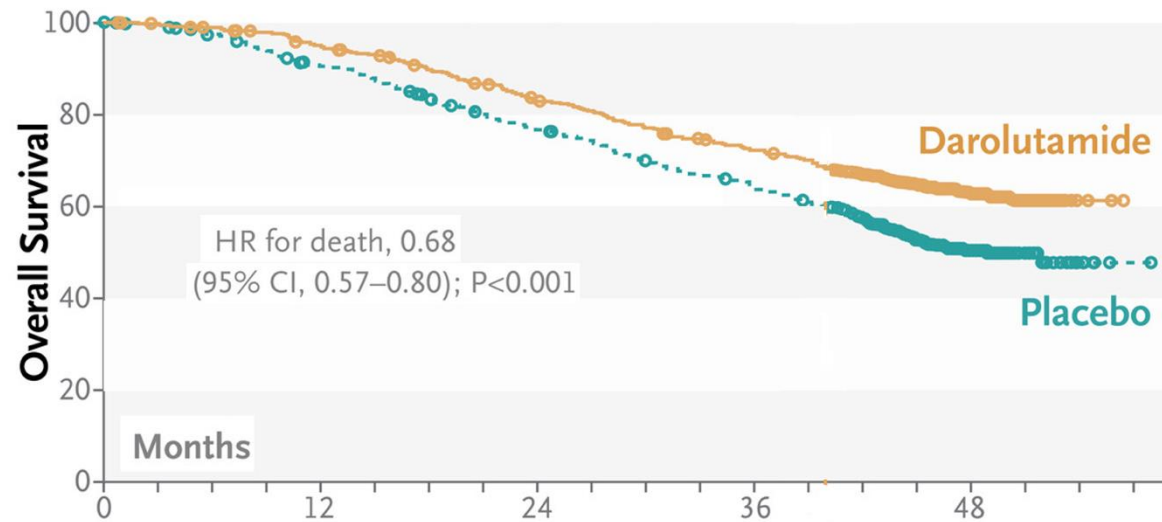
			<i>FDA label</i>
BRCA1	BRCA2		niraparib and abiraterone (combo pill)
BRCA1	BRCA2		rucaparib
BRCA1	BRCA2		olaparib and abiraterone
BRCA1	BRCA2	ATM1	olaparib

There are no direct comparative data

TAXANES: A few contexts:

ARASENS:

Docetaxel, GnRH, darolutamide

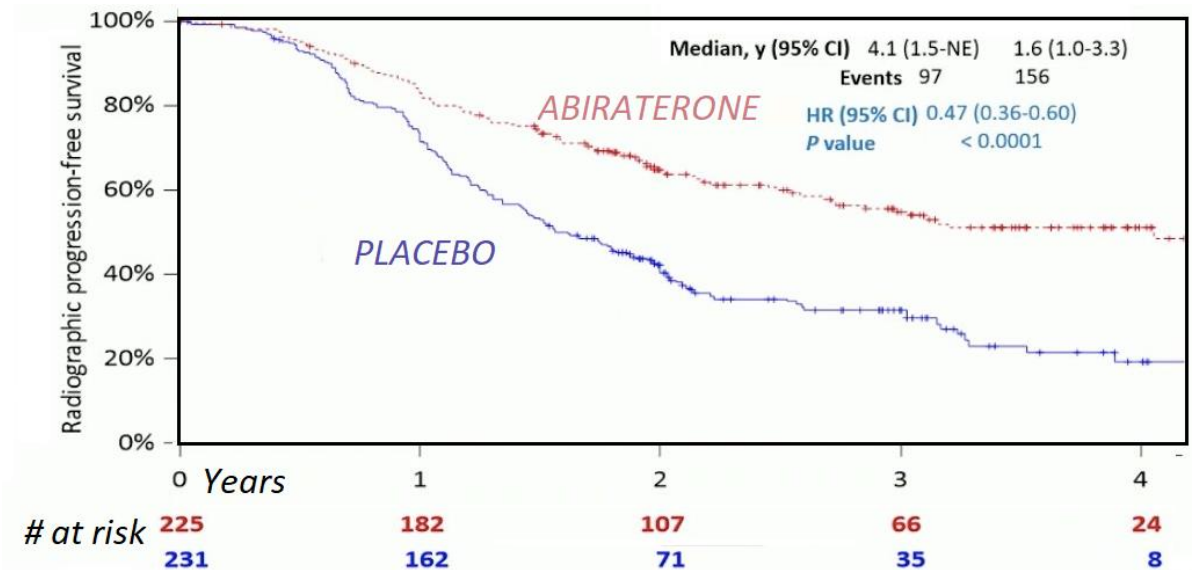


Smith M, Hussain M, Saad F et al. Darolutamide and Survival in Metastatic, Hormone-Sensitive Prostate Cancer. *N Engl J Med* 2022;386:1132-1142

INITIAL TRIPLET THERAPY of METASTATIC CSPC

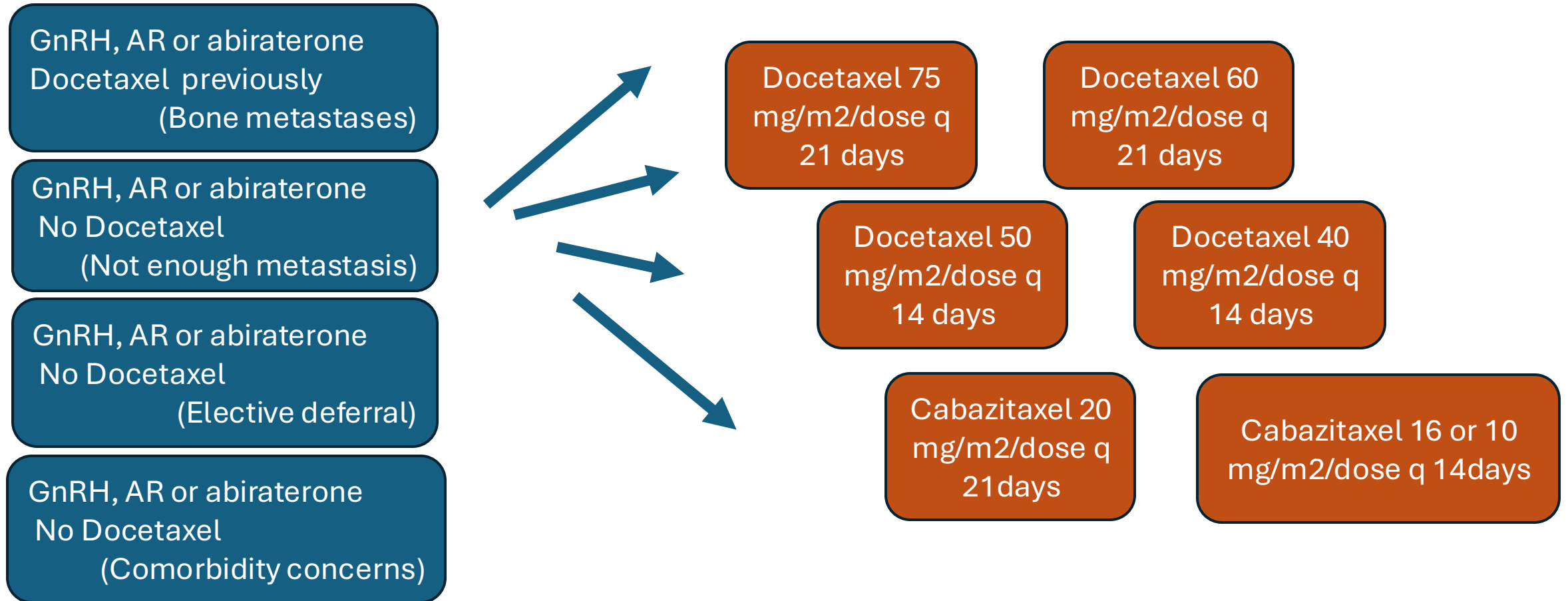
PEACE-1 (docetaxel & high-volume subset):

Docetaxel, GnRH, abiraterone/prednisone

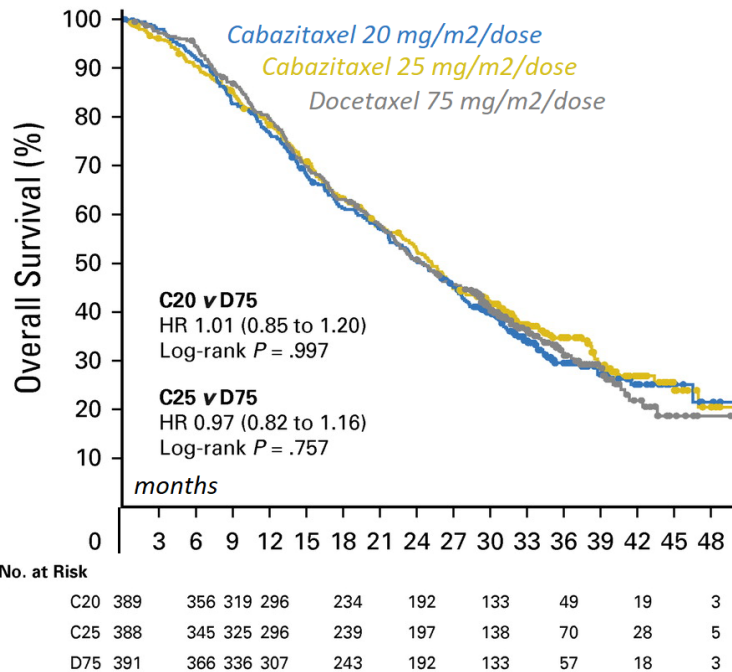


Fizazi K, Foulon S, Carles J et al. Abiraterone plus prednisone added to androgen deprivation therapy and docetaxel in de novo metastatic castration-sensitive prostate cancer (PEACE-1): a multicentre, open-label, randomised, phase 3 study with a 2 × 2 factorial design. *Lancet*. 2022 Apr 30;399(10336):1695-1707.

Taxanes as initial salvage for metastatic progression despite GnRH and AR: Several contexts to consider:



Taxanes: Cabazitaxel, and de-escalated schedules



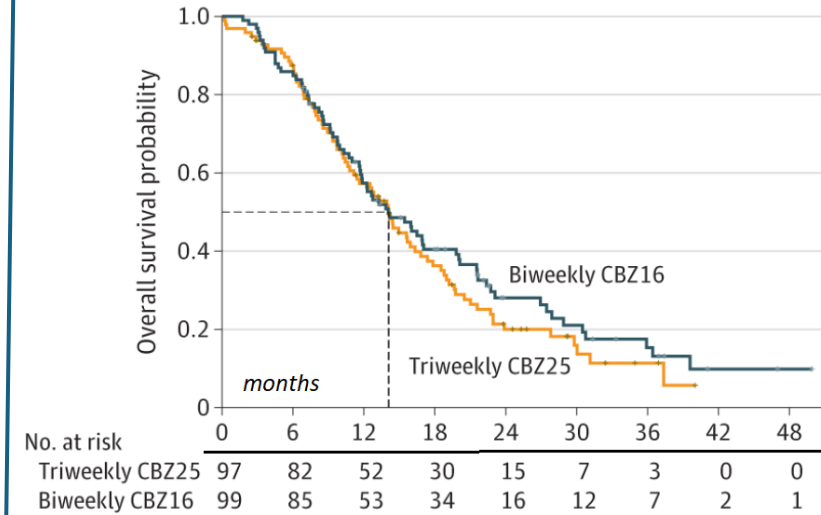
Oudard S, Fizazi K, Sengeløv L, et al. Cabazitaxel Versus Docetaxel As First-Line Therapy for Patients With Metastatic Castration-Resistant Prostate Cancer: A Randomized Phase III Trial-FIRSTANA. *J Clin Oncol.* 2017 Oct 1;35(28):3189-3197

**Docetaxel 50 mg/m² q14d
Instead of 75 mg/m² q 21d**

Hervonen P, Joensuu H, Joensuu T et al. Biweekly docetaxel is better tolerated than conventional three-weekly dosing for advanced hormone-refractory prostate cancer. *Anticancer Res.* 2012 Mar;32(3):953-6.

**TREATMENT
EMERGENT
ADVERSE
EVENTS >5%**

	Docetaxel 75 mg/m ² (%)		Cabazitaxel 25 mg/m ² (%)	
	All grades	Grade 3/4	All grades	Grade 3/4
Febrile neutropenia	8.3	8.3	12	12
Neutropenic infection	4.9	4.1	6.1	5.9
Diarrhea	37	2.3	49.9	5.6
Stomatitis	13.7	0.8	6.6	0.3
Hematuria	3.6	0.3	25.1	3.6
Peripheral neuropathy	25.1	2.1	12.3	0
Peripheral edema	20.4	1.6	7.7	0.3
Alopecia	39	0	13	0
Nail disorders	9	0.3	0.8	0



**Cabazitaxel 16 mg/m² q14d
Instead of 25 mg/m² q 21d**

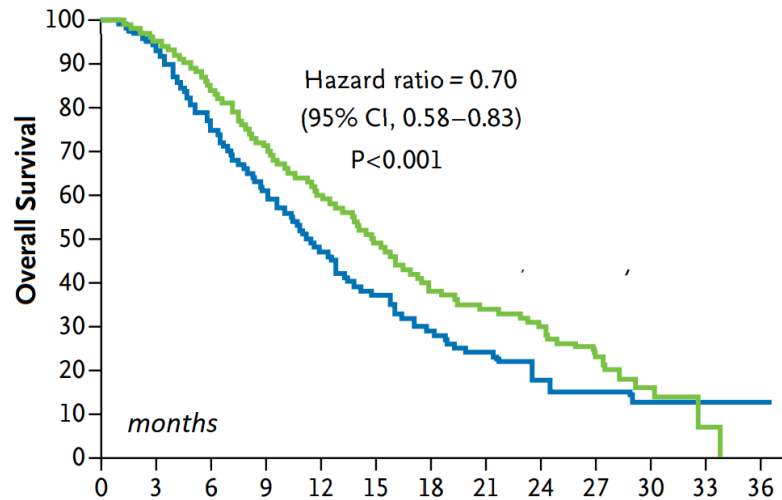
Oudard S, Ratta R, Voog Et al. Biweekly vs Triweekly Cabazitaxel in Older Patients With Metastatic Castration-Resistant Prostate Cancer: The CABASTY Phase 3 Randomized Clinical Trial. *JAMA Oncol.*

CABASTY

Radioactive intravenous treatments

Radium:

Docetaxel or not docetaxel eligible
 ALSYMPCA 2013. Only bone-only



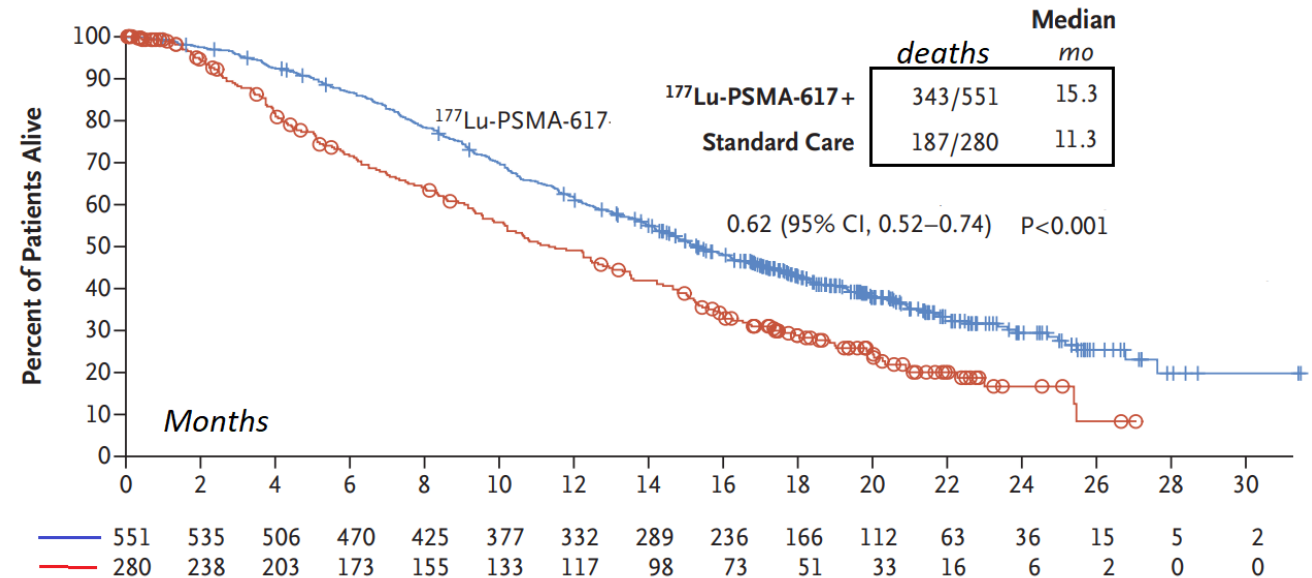
Radium-223

Placebo

614	578	504	369	274	178	105	60	41	18	7	1	0
307	288	228	157	103	67	39	24	14	7	4	2	1

Parker C, Nilsson S, Heinrich et al ALSYMPCA Investigators. Alpha emitter radium-223 and survival in metastatic prostate cancer. N Engl J Med. 2013 Jul 18;369(3):213-23.

Lutetium (177Lu) vipivotide tetraxetan: Docetaxel previously



Sartor O, de Bono J, Chi KN, et al and VISION Investigators. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. N Engl J Med. 2021 Sep 16;385(12):1091-1103

Very small
phase 2
study

(20 vs 20)

How about CRPC Lutetium treatment without prior docetaxel? (not on-label at present)

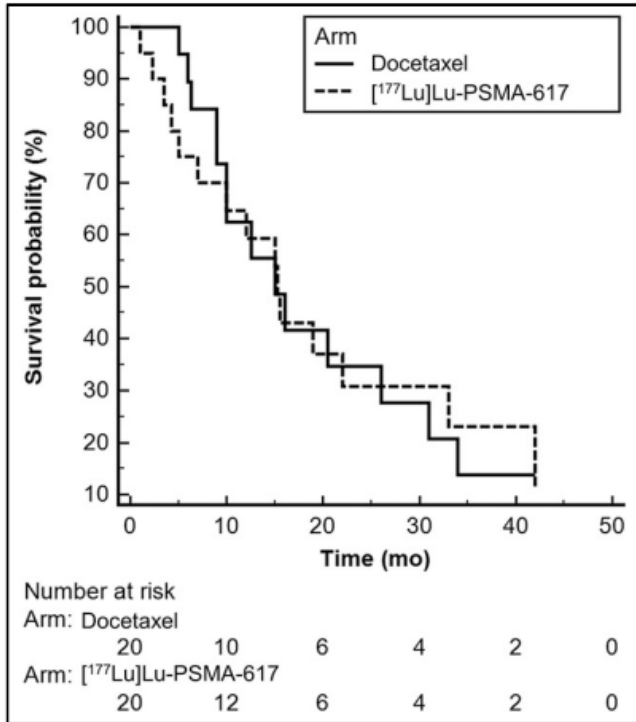
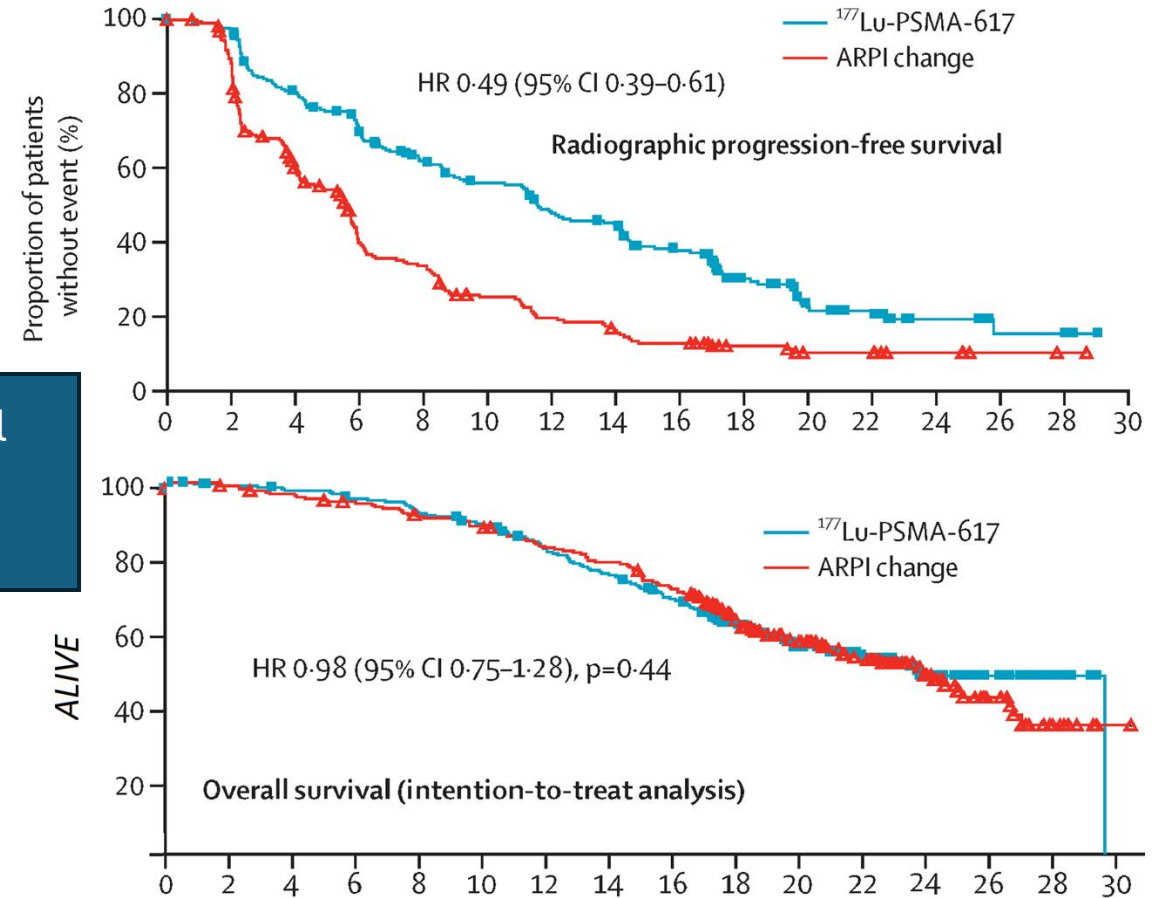


FIGURE 1. Kaplan-Meier curves for OS in intention-to-treat analysis.

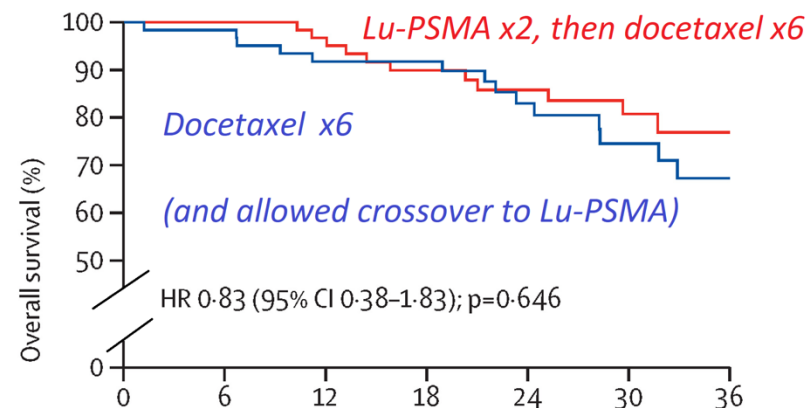
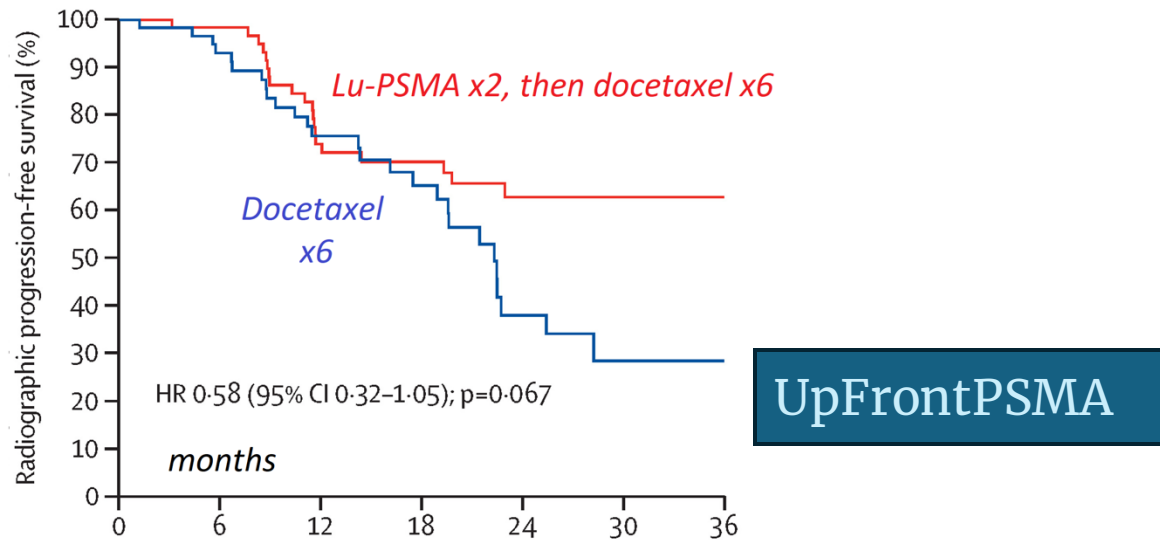
Satopathy S, Mittal BR, Sood A et al. [177Lu]Lu-PSMA-617 Versus Docetaxel in Chemotherapy-Naïve Metastatic Castration-Resistant Prostate Cancer: Final Survival Analysis of a Phase 2 Randomized, Controlled Trial. J Nucl Med. 2023 Nov;64(11):1726-1729.

Registrational
phase III trial
PSMAfore)

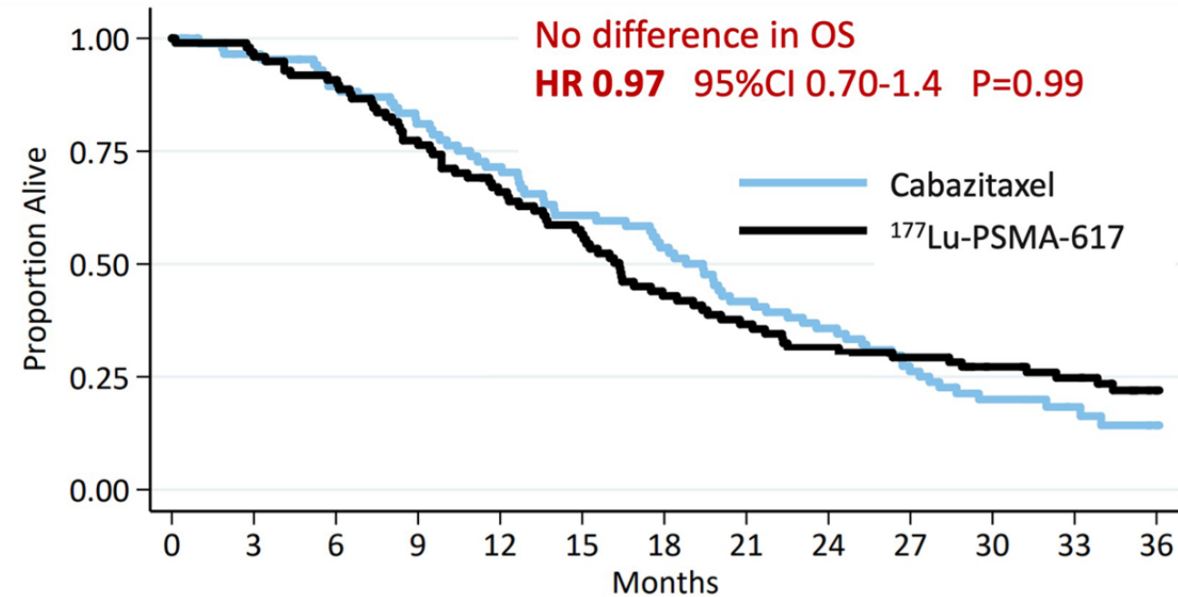


Morris MJ, Castellano D, Herrmann K et al. . 177Lu-PSMA-617 versus a change of androgen receptor pathway inhibitor therapy for taxane-naive patients with progressive metastatic castration-resistant prostate cancer (PSMAfore): a phase 3, randomised, controlled trial. Lancet. 2024 Sep 28;404(10459):1227-1239.

How about Lutetium mCSPC treatment and then docetaxel? (not on-label)



Azad AA, Bressel M, Tan H, et al. Sequential [¹⁷⁷Lu]Lu-PSMA-617 and docetaxel versus docetaxel in patients with metastatic hormone-sensitive prostate cancer (UpFrontPSMA): a multicentre, open-label, randomised, phase 2 study. Lancet Oncol. 2024 Oct;25(10):1267-1276.



Number at risk

Cabazitaxel	101	82	75	68	60	51	45	35	30	22	14	9	6
Lu-PSMA	99	94	88	75	63	54	41	35	30	28	23	20	11

How about Lutetium vs cabazitaxel with prior docetaxel?

TheraP

Hofman MS, Emmett L, Sandhu S et al. [¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial. Lancet. 2021 Feb 27;397(10276):797-804. (Figure from 2024 update at ASCO)

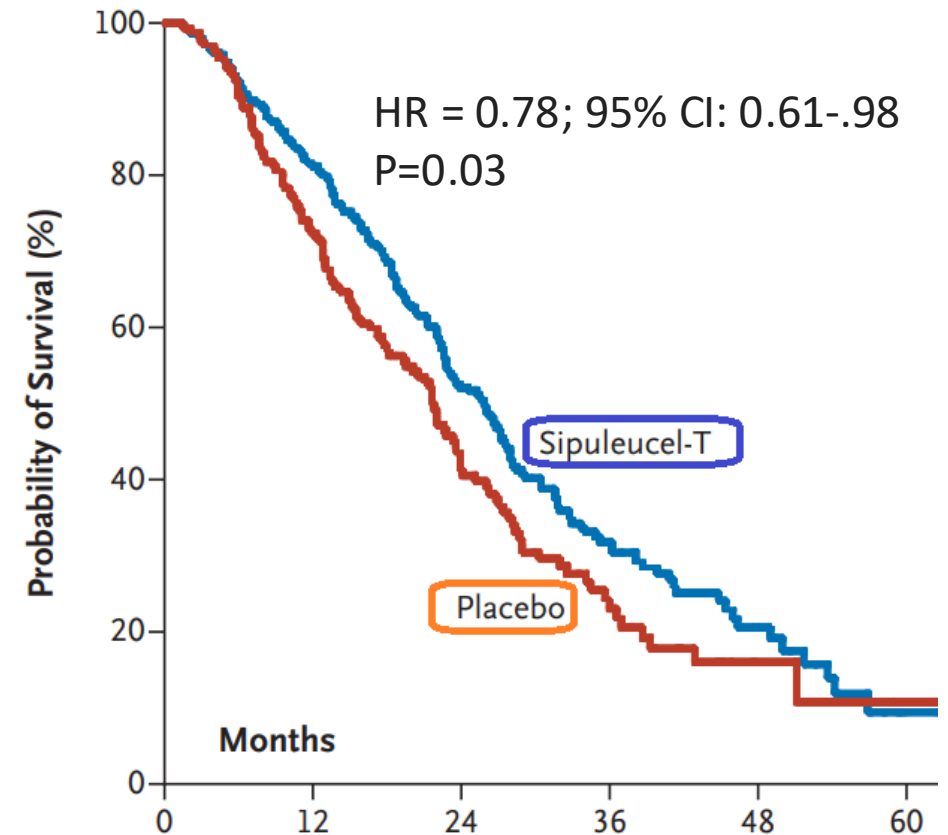
Immunotherapy: Sipuleucel-T

Stringent enrollment criteria

- No bone pain
- No visceral lesions
- No data on CRPC then sipuleucel-T or sipuleucel-T with AR or abiraterone is better
- No anticipated PSA pattern change
- Original trial: Most of the benefit in bottom PSA quartile <23
- Useful vs controversial.

IMPACT

Kantoff PW, Higano CS, Shore ND, et al. . Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med. 2010 Jul 29;363(5):411-22.

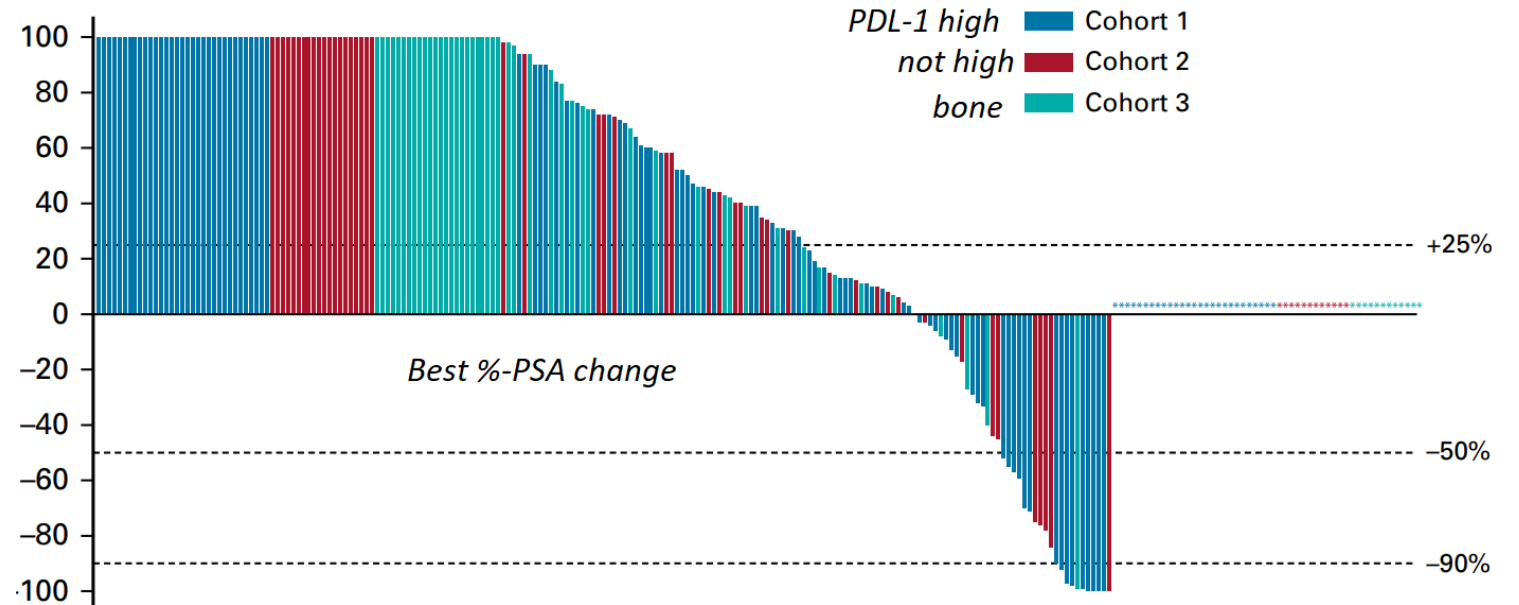
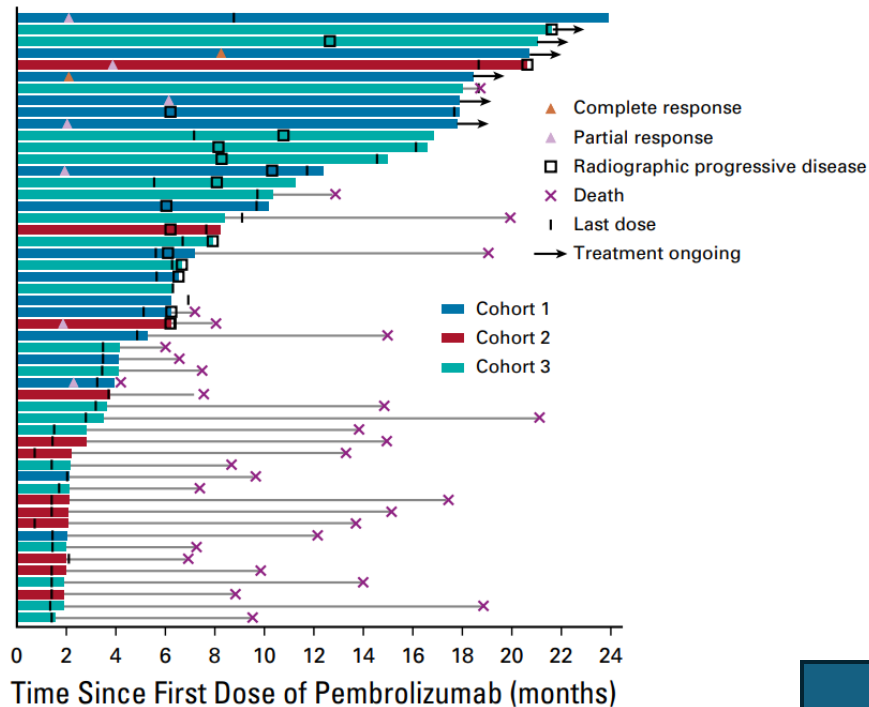


Sipuleucel-T	341	274	129	49	14	1
Placebo	171	123	55	19	4	1

Immunotherapy: Pembrolizumab (technically on label for high-PD-L1)

KEYNOTE
199

- 3 cohort CRPC noncomparative study:



Antonarakis ES, Piulats JM, Gross-Goupil Met al. Pembrolizumab for Treatment-Refractory Metastatic Castration-Resistant Prostate Cancer: Multicohort, Open-Label Phase II KEYNOTE-199 Study. J Clin Oncol. 2020 Feb 10;38(5):395-405.

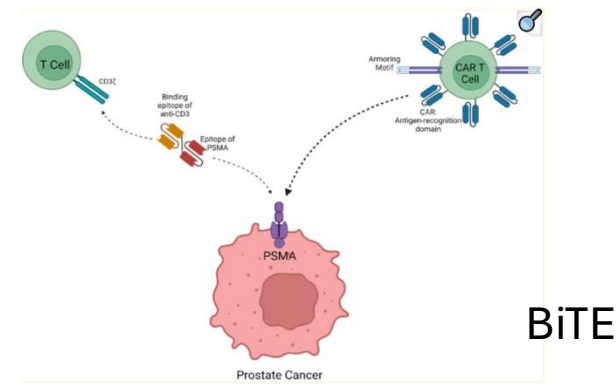
No data yet on comparative OS; or optimal patient selection

Investigational immunotherapies: CAR-T and bispecific antibodies

CAR-T for prostate cancer treatment

Table 1. Ongoing studies evaluating PSMA-targeted CAR T-cell therapy.

Trial	Intervention	Sample size	Endpoints	Study phase	Estimated completion
NCT04227275	CART-PSMA-TGFβRDN	50	DLT, AE profile, ORR (PSA response), T-cell expansion/persistence	Phase I	November 2026
NCT01140373	Autologous anti-PSMA CAR T-cells	13	DLT, bone metastasis response, quantitative CTC, PSA response, T-cell expansion/persistence	Phase I	June 2023
NCT03089203	CART-PSMA-TGFβRDN	19	TRAE, ORR (RECIST 1.1/PCWG2), PSA response, OS, PFS	Phase I	December 2038
NCT04249947	P-PSMA-101 CAR T-cells	60	TRAE/DLT, ORR (RECIST, iRECIST, PCWG2)	Phase I	September 2036
NCT04429451	4SCAR-PSMA T-cells	100	TRAE/DLT, ORR (RECIST 1.1), OS, PFS, 4SCAR-PSMA T-cell expansion/persistence	Phase I/II	December 2024
NCT04633148	UniCAR02 T-cells (TmPSMA)	39	TRAE/DLT, MTD, RP2D, ORR (irRECIST), OS, PFS, PSA response, quantitative CTC	Phase I	December 2023
NCT04768608	Non-viral PD1 integrated anti-PSMA chimeric antigen receptor T-cells	18	TRAE, PSA response, ORR (RECIST 1.1, PCWG3), T-cell expansion/persistence	Phase I	January 2024
NCT03692663	Anti-PSMA CAR NK cell (TABP EIC)	9	TRAE, PK, PD, PSA response, PFS	Phase I	June 2024
NCT05354375	PSMA-targeted CAR T-cells	20	TRAE, ORR, PFS, OS	Phase I	November 2026
NCT05489991	Dually armored CAR T-cells (TmPSMA-02)	114	AE/TRAE, DLT, ORR (RECIST 1.1), PSA response, T-cell expansion/persistence, HRQoL	Phase I/II	January 2032
NCT05656573	CART-PSMA cells	20	AE/TRAE, T-cell expansion/persistence, OS, PFS, PSA response, cytokine profile, peripheral T-cell immune profile, quantitative CTC, quantitative ctDNA/cfDNA	Phase I	December 2025



Trial	Intervention	Sample size	Endpoints	Study phase	Estimated completion
NCT04740034	PSMA × CD3 BiTE (AMG 340)	130	DLT, TRAE, PK, ORR, OS, PFS, PSA response	Phase I	September 2024
NCT05441501	PSMA × CD3 BiTE (JNJ-80038114)	90	AE, DLT, PK, PSA response, antidrug antibody quantification, ORR (PCWG3)	Phase I	March 2025
NCT04839991	Trispecific Humabody® T-cell enhancer (CB307)	70	TRAE, PFS, PK, ORR (RECIST 1.1), PSA response	Phase I	September 2025
NCT03972657	PSMA × CD3 BiTE (REGN5678) + Cempilimab	216	TRAE, DLT, PK, ORR (PCWG3), PSA response, quantitative CTC, antidrug antibody quantification	Phase I/II	February 2025
NCT05125016	PSMA × CD3 BiTE (REGN4336) ± Cempilimab	199	DLT, TRAE, PK, ORR (PCWG3), PSA response, antidrug antibody quantification	Phase I	August 2026
NCT04104607	PSMA × CD3 BiTE (CC1)	86	AE, antidrug antibody quantification, PK, cytokine profile, PSA response, ORR (RECIST), OS, PFS, HRQoL	Phase I	August 2023
NCT05369000	PSMA-targeting (Gammabody) bispecific γδ-T cell engager (LAVA-1207)	66	AE, DLT, ORR (iRECIST), PK, whole blood LAVA-1207 – Vγ9Vδ2-T cell affinity, antidrug antibody quantification	Phase I/IIa	March 2024
NCT03792841	PSMA × CD3 HLE BiTE (AMG160; acapatamab)	212	DLT, TRAE, PK, ORR (PCWG3), PSA response, quantitative CTC	Phase I	May 2025

A lot more studies than I thought.
Support clinical trial! Nice survey here:

Zarrabi KK, Narayan V, Mille P et al.. Bispecific PSMA antibodies and CAR-T in metastatic castration-resistant prostate cancer. Ther Adv Urol. 2023 Jun

Summary: What to do?

Anatomically isolated progression:

- Consider focal XRT

Still on GnRH monotherapy:

- Usually add an AR or abiraterone

Test for PARP eligibility:

- About 1/6
- Add-on, or add-on and switch AR medication

Prior docetaxel, but not too recent:

- Consider taxane again

Taxane side effect concerns

- Consider modified lower dose plan

Bone-only pattern,

- 5+ lesions (before or after docetaxel):
- Consider Radium course

Any significant PSMA positive pattern:

- (after docetaxel):
- Consider Lutetium course

Selected patients for immunotherapy

- Sipuleucel-T (asymptomatic, low PSA, no visceral mets)

Pembrolizumab (? Criteria; if molecular tests)

- Consider CAR-T trials
- Consider Bispecific trials

Other trials

Other factors

Anemia: May be a barrier for:

- Docetaxel
- Cabazitaxel
- Radium
- Lutetium-PSMA
- PARP inhibitors
- Clinical trials

Neuropathy:

- Avoid Docetaxel
- Cabazitaxel may be OK

Neuroendocrine (small cell) prostate cancer (more “castrate irrelevant” than “castrate refractory”):

For most treatment can consider carboplatin+ etoposide

Frailty:

- May have limited escalation options.
- QOL over PSA

Thank you!

Adult learners get ready:
Cases are next

