Disrupting the Status Quo:

Investigational Therapies in Advanced Prostate Cancer

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Disclosures

- Eisai: Advisory board
- Johnson and Johnson: Advisory board

Outline

- Background and status quo
- Novel androgen receptor targeting agents
  - PROTACS
  - CYP11A1 Inhibitors
  - RIPTAC
- Extracellular targeting agents
  - Novel radioligand therapies
  - BiTE therapy
  - Antibody drug conjugates

Androgen deprivation has been gold standard since 1941

1941 – Androgen Deprivation Era

- Bilateral orchiectomy causes regression of metastatic prostate cancer
- Charles Huggins would ultimately win the Nobel Prize

1985 – Chemical Castration Era

- Development of GnRH agonists including leuprolide and goserelin
- Later introduction of first-generation anti-androgens
- Chemotherapy though palliative in nature

2004 – Taxane Era

- Docetaxel became first cytotoxic agent to prolong life in CRPC

2010 – ARPI Era

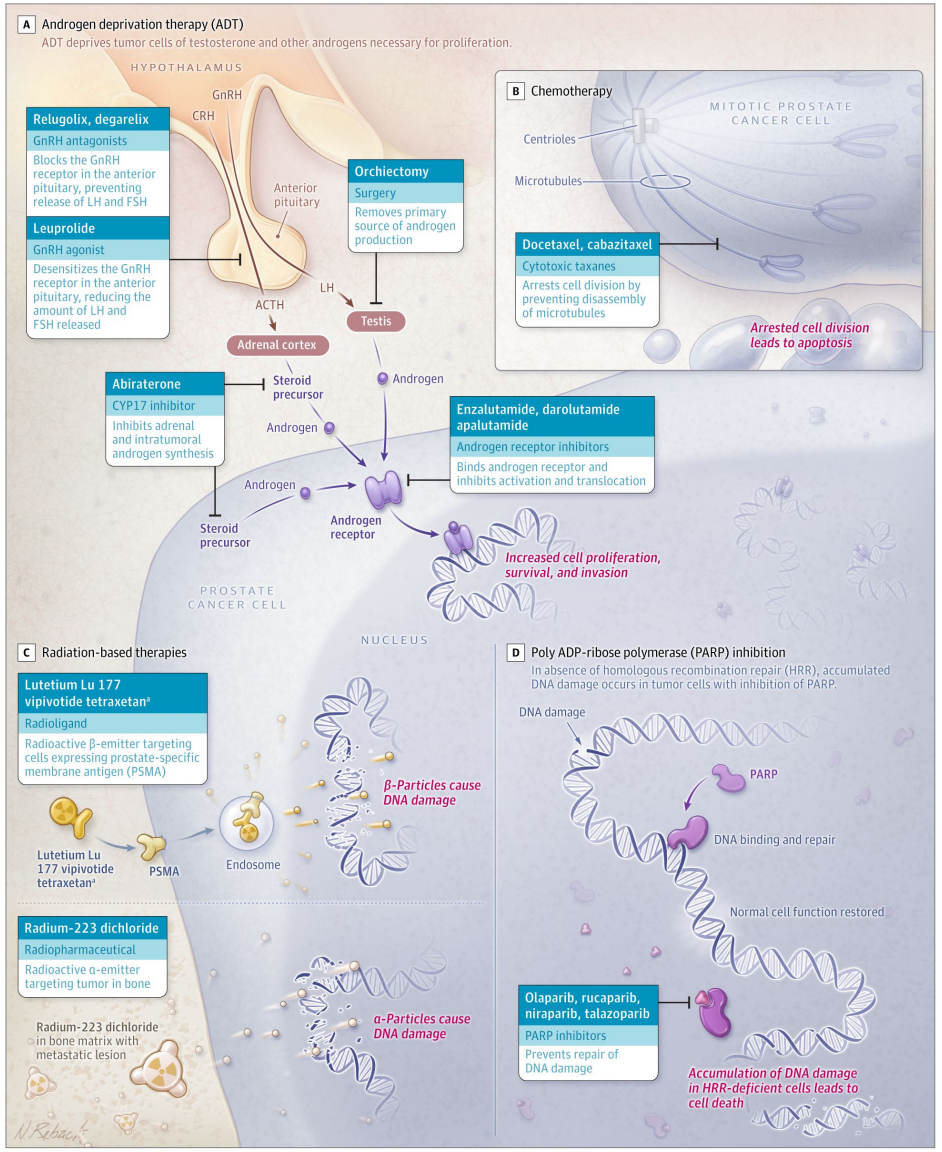
- Abiraterone acetate first approved post-docetaxel CRPC
- Abiraterone, enzalutamide, apalutamide, and darolutamide ultimately moved to earlier disease space

2020 Targeted Era

- Olaparib approved for HRR deficient CRPC
- Pluvicto received FDA approval in 2022, targeting PSMA

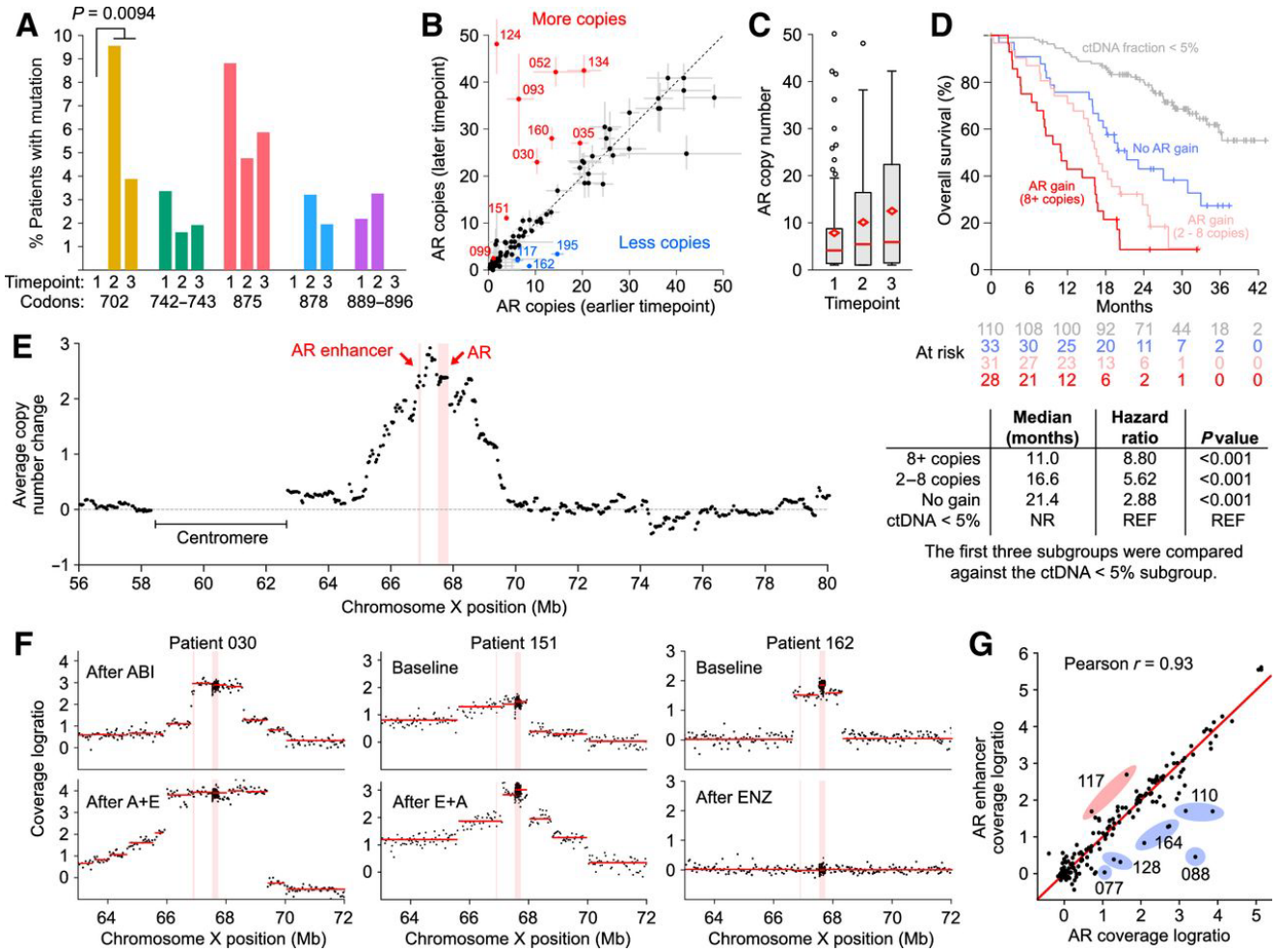
Current therapeutic landscape

- Androgen deprivation therapy
  - GnRH agonists; GnRH antagonistis; orchiectomy
- Androgen receptor signaling inhibitors (ARSI)
  - CYP17 inhibition; AR antagonists
- Chemotherapy
  - Docetaxel and Mitoxantrone
- Radiopharmaceuticals
  - Ra223 and Lutetium Lu177 vipivotide tetraxetan
- PARP inhibitors
  - Olaparib, rucaparib, niraparib, talazoparib



Raychaudhuri R, Lin DW, Montgomery RB. Prostate Cancer: A Review. JAMA. 2025;333(16):1433–1446. doi:10.1001/jama.2025.0228

CRPC is still driven by aberrant AR activation



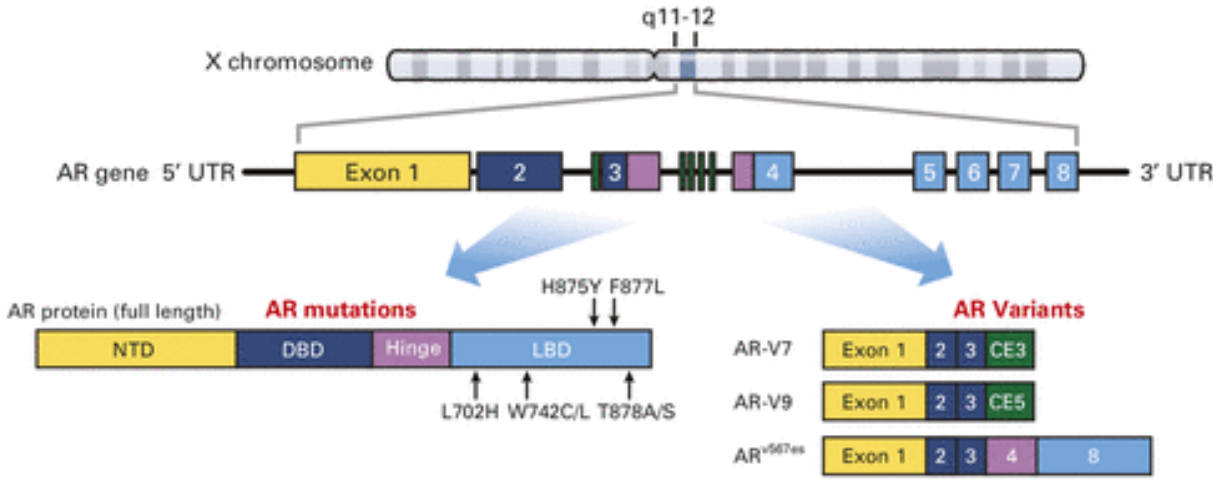
	Median (months)	Hazard ratio	*P* value
8+ copies	11.0	8.80	<0.001
2–8 copies	16.6	5.62	<0.001
No gain	21.4	2.88	<0.001
ctDNA < 5%	NR	REF	REF

The first three subgroups were compared against the ctDNA < 5% subgroup.

Annala M, Taavitsainen S, Khalaf DJ, et al. Evolution of castration-resistant prostate cancer in ctDNA during sequential androgen receptor pathway inhibition. *Clin Cancer Res*. 2021;27(16):4610-4623. doi:10.1158/1078-0432.CCR-21-1625

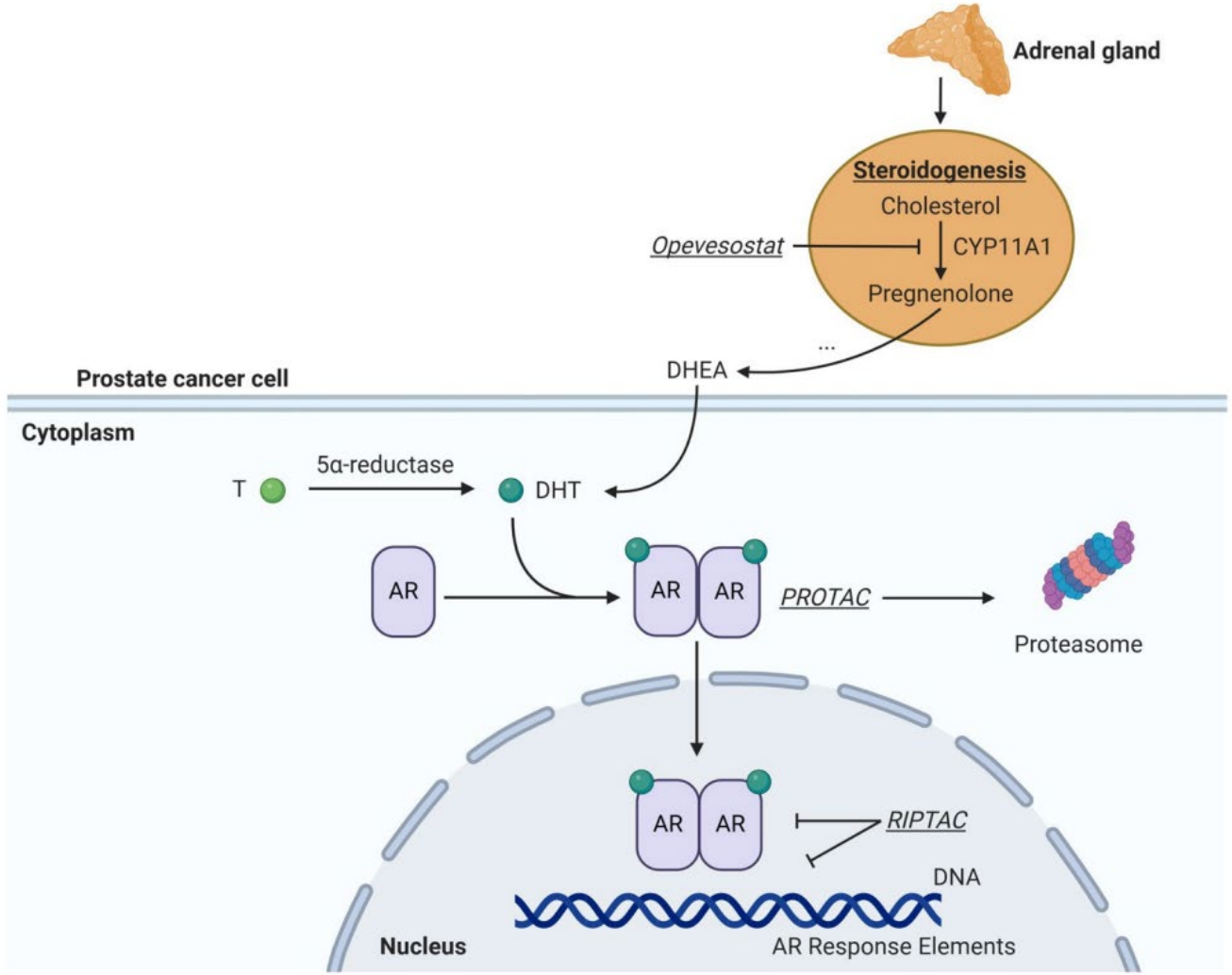
Common resistance mechanisms to ARSI therapy

Mechanism	Notes
AR amplification	Most common
AR LBD mutations (e.g., L702H, F877L)	Enables resistance via ligand promiscuity
AR truncating rearrangements	Escape via ligand-independence
AR splice variants (AR-V7)	Biomarker of poor response to switch ARSI
Neuroendocrine differentiation	AR-independent escape route
Glucocorticoid receptor upregulation	GR mimics AR function
PI3K/AKT activation (PTEN loss)	Promotes survival signals
DNA repair defects	Enables other therapies (PARP inhibitors)



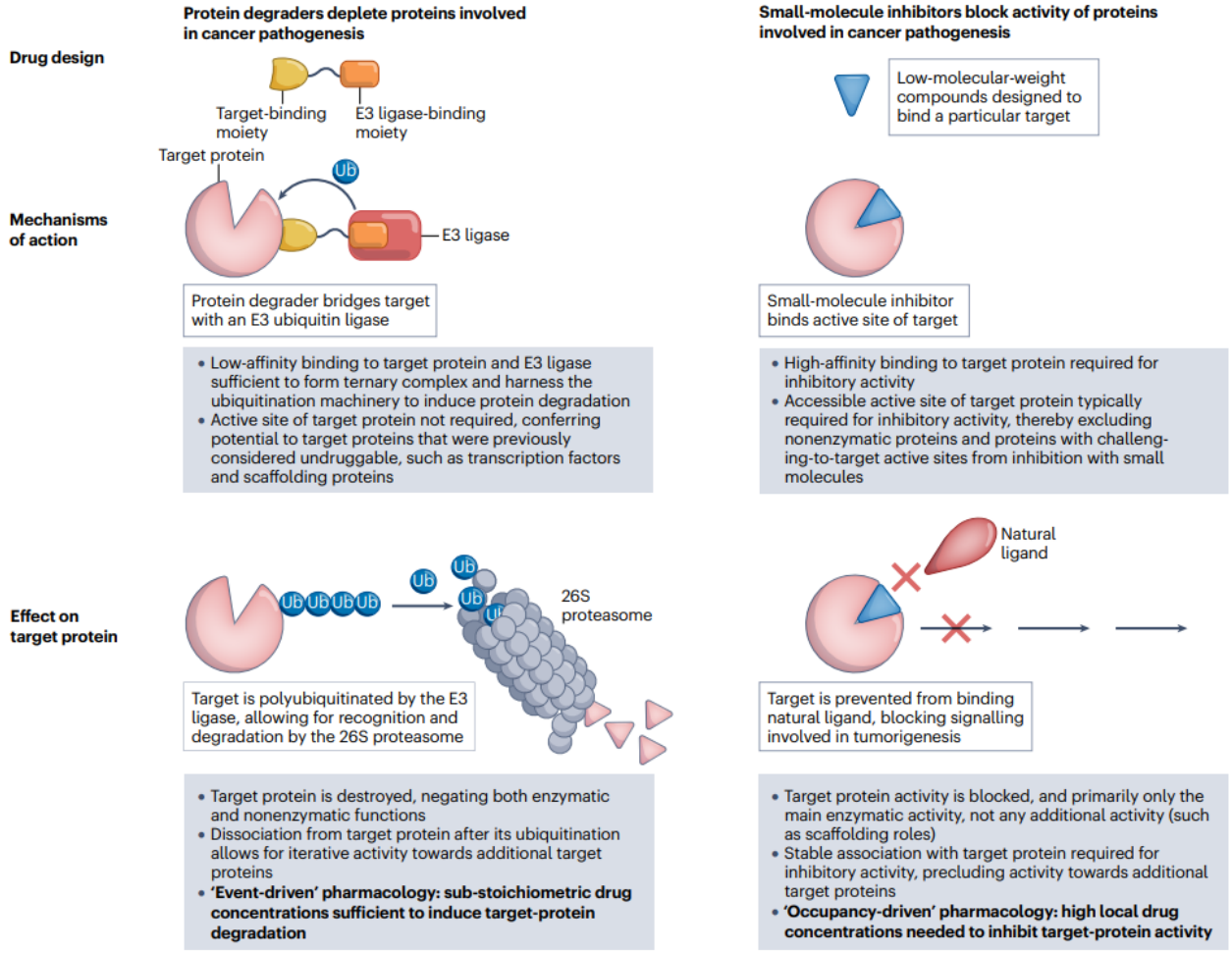
Dai C, Dehm SM, Sharifi N. Targeting the Androgen Signaling Axis in Prostate Cancer. *J Clin Oncol*. 2023;41(26):4267-4278. doi:10.1200/JCO.23.00433

(Next) next-generation AR targeting drugs



Grewal K, Dorff TB, Mukhida SS, Agarwal N, Hahn AW. Advances in Targeted Therapy for Metastatic Prostate Cancer. *Curr Treat Options Oncol*. 2025;26(6):465-475. doi:10.1007/s11864-025-01323-7

PROteolysis TArgeting Chimera (PROTAC)



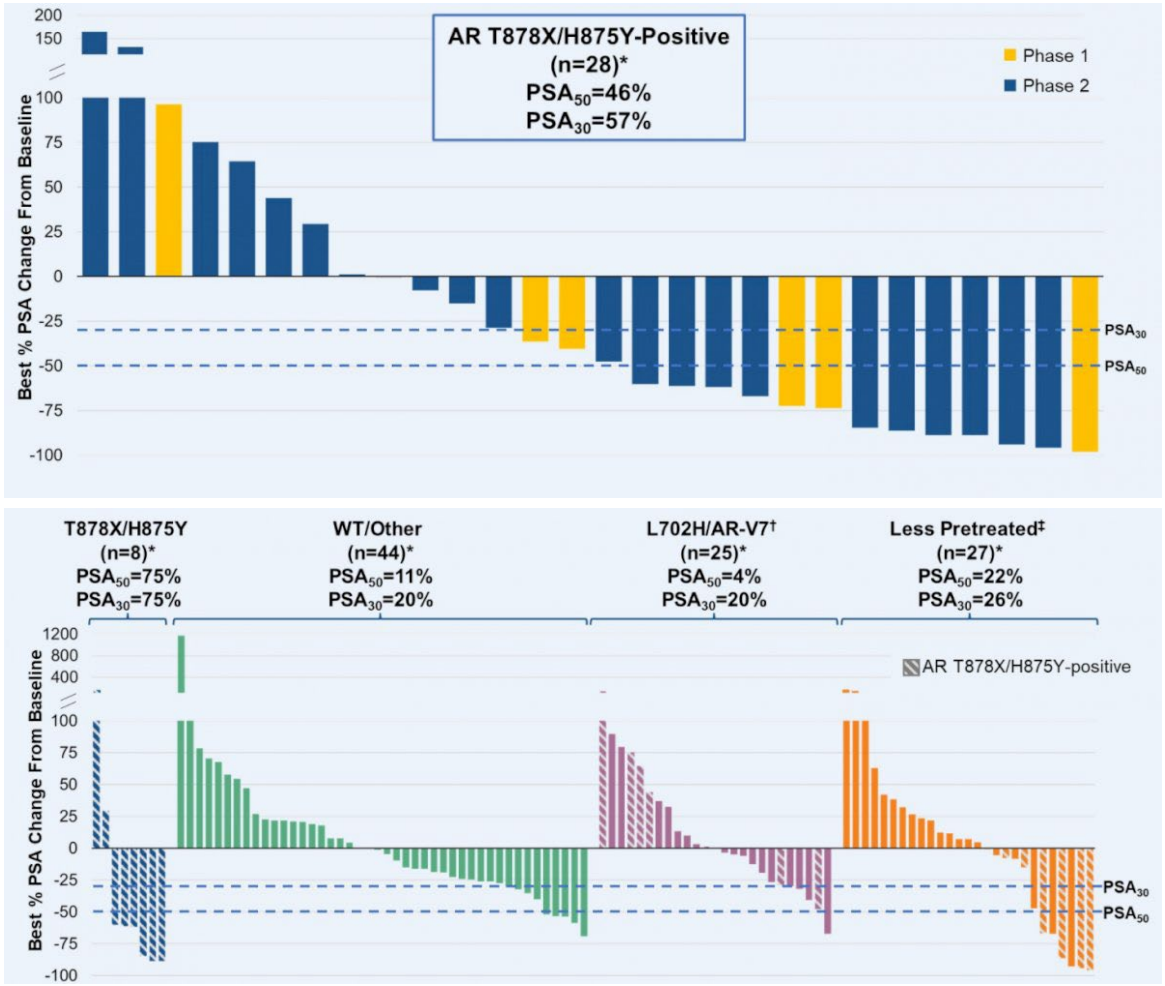
AR degradation via clinical PROTACs is at the vanguard of this novel therapeutic mechanism in oncology

Chirnomas D, Hornberger KR, Crews CM. Protein degraders enter the clinic - a new approach to cancer therapy. *Nat Rev Clin Oncol*. 2023;20(4):265-278. doi:10.1038/s41571-023-00736-3

Early phase efficacy signals are encouraging

- ARV-110 (Bavdegalutamide)[1]
  - First to enter clinical trials
  - Potent response in AR T878X/H875Y AR-LBD
  - Poor response in AR-V7 or L702H
- ARV-766 (Luxdegalutamide)[2]
  - Phase I data presented at ASCO 2024
  - PSA 50 in AR-LBD selected cohort: 50%
- HP-518[3]
- BMS-986365[4]
  - "Ligand directed degrader" – dual AR degradation and antagonism

ARV-110 PSA response rates (GU ASCO 2022)

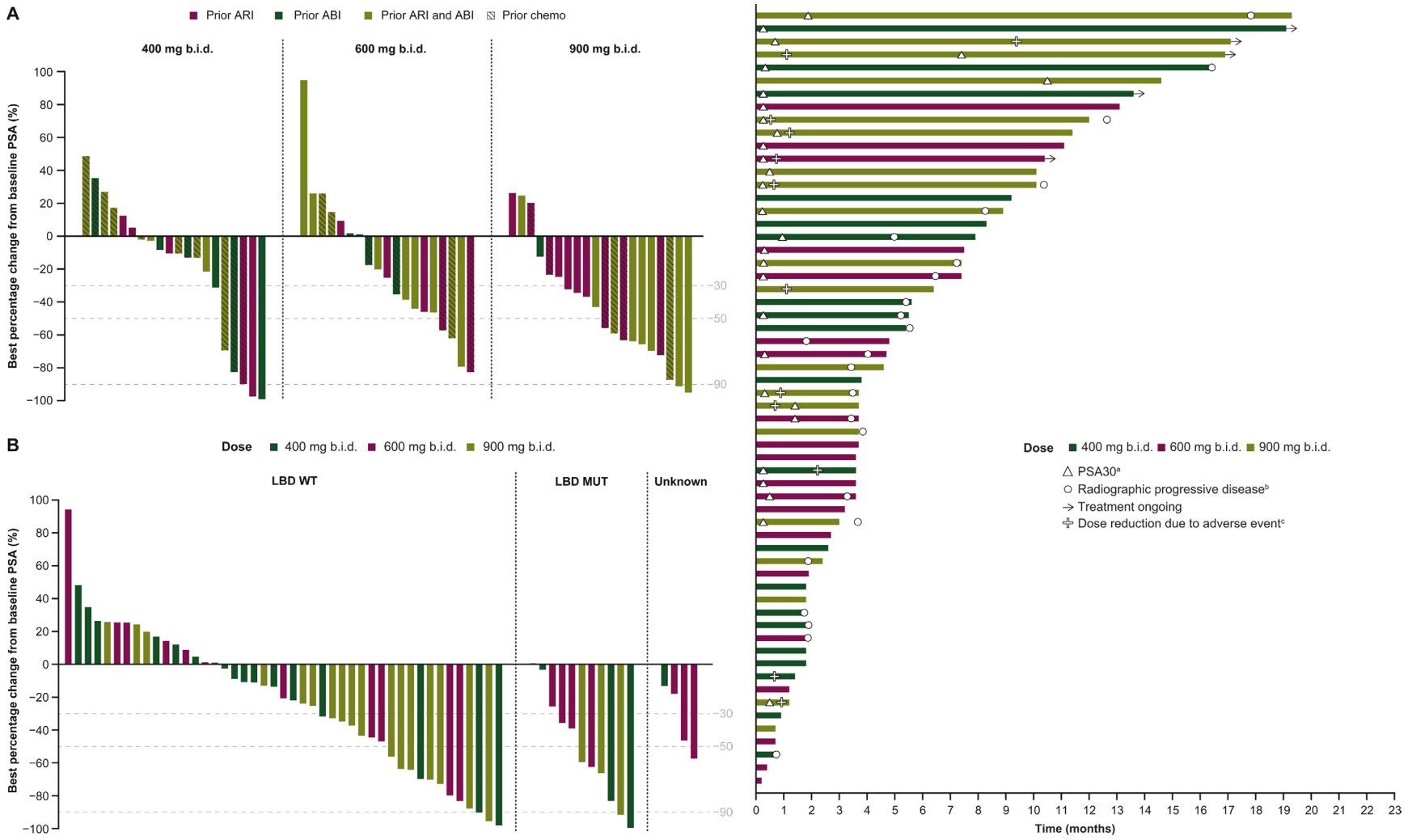


1. Xin et al. J Clin Oncol 40, 2022 (suppl 6; abstr 17)
2. J Clin Oncol 42, 2024 (suppl 16; abstr 5011)
3. Arun Azad et al. *J Clin Oncol* **42**, 124-124(2024).
4. Rathkopf D et al *Ann Oncol*. 2025;36(1):76-88. doi:10.1016/j.annonc.2024.09.005

Early phase efficacy signals are encouraging

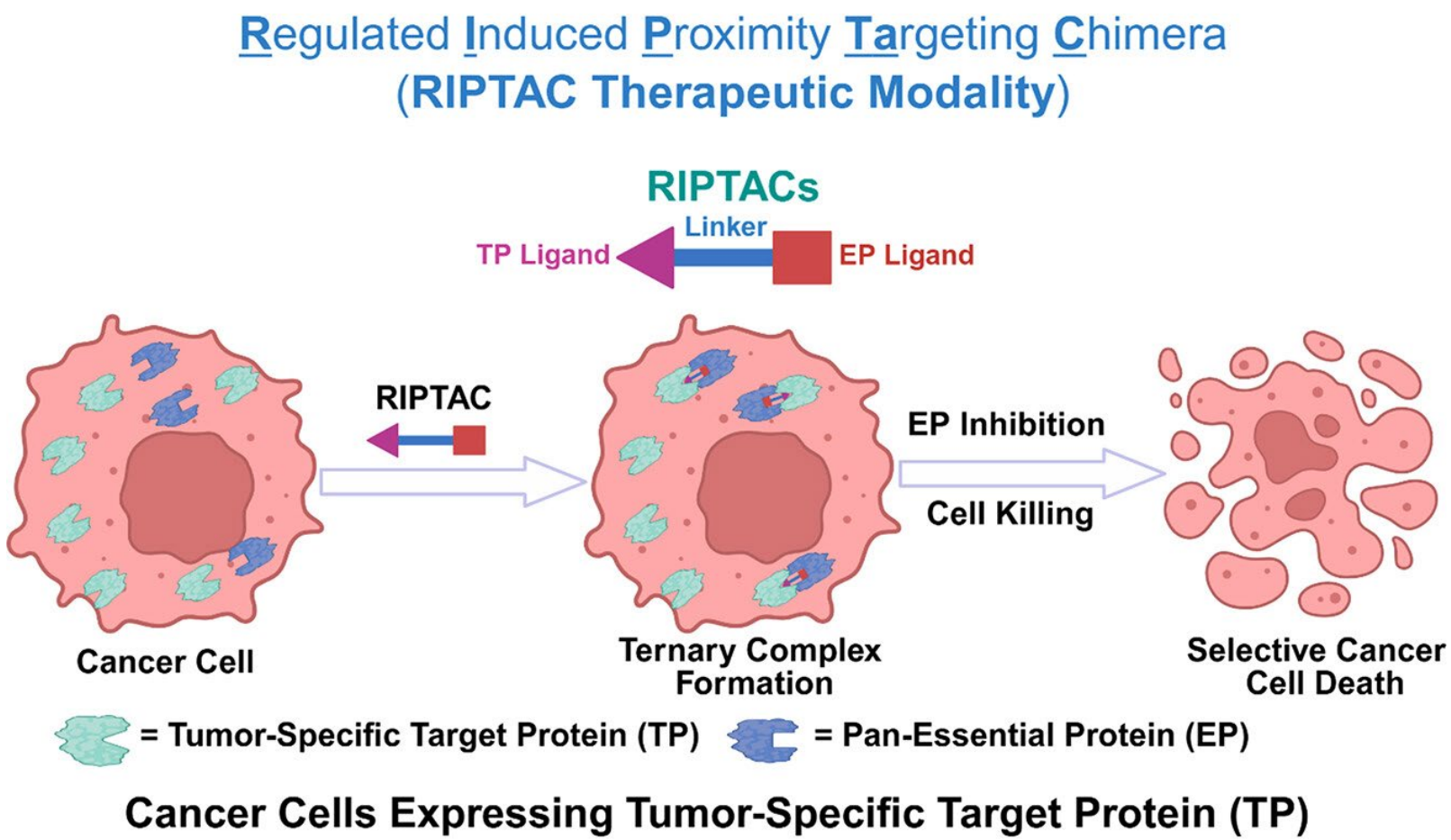
BMS-986365

- PSA50:
  - 50% (900mg bid)
  - 27% (AR wt)
  - 55% (AR LBD)
- MTD not reached
- No grade 4/5 TRAE
- 1 DLT for QTc prolongation
- Common AE:
  - QT prolongation
  - Bradycardia
  - Nausea



Rathkopf D et al *Ann Oncol*. 2025;36(1):76-88. doi:10.1016/j.annonc.2024.09.005

RIPTAC – Another emerging technology to target AR



Ma Z, Zhang C, Shen Q, Zhou J. RIPTACs for Precision Cancer Therapy: A Novel Modality with the Inspiration of HLD-0915 as the First Candidate in Clinical Trials. *J Med Chem*. 2025;68(11):10503-10506. doi:10.1021/acs.jmedchem.5c01250

Mullard A. Induced proximity pushes beyond protein degraders, as first RIPTAC moves into the clinic. *Nat Rev Drug Discov*. 2025;24(4):235-237. doi:10.1038/d41573-025-00037-7

CYP11A1 Inhibitor – Opevesostat/MK5684/ODM-208

- CYP11A1 – Starts steroidogenesis through conversion of cholesterol to pregnenolone
- Opevesostat inhibits CYP11A1 – effectively shutting off all adrenal steroidogenesis
- Adrenal insufficiency is an expected on target effect – require fludrocortisone/

CYPIDES Phase I/II trial – significant toxicity noted

- In phase I 36.2% of patients experience adrenal insufficiency
- Significant dose de-escalation needed to arrive at RP2D
- In phase II, AI occurred in 13.3% (6.7% grade III AI)
- Other common side effects included anemia, fatigue, dypsnea etc

Table 2. Summary of Treatment-Emergent Adverse Events and a List of Adverse Events (Regardless of Causality) Occurring in Greater Than or Equal to 15% of Patients in Either the Phase 1 or Phase 2 Cohort by Preferred Term and Maximum National Cancer Institute Common Terminology Criteria for Adverse Events (Version 4.03) Grade.*

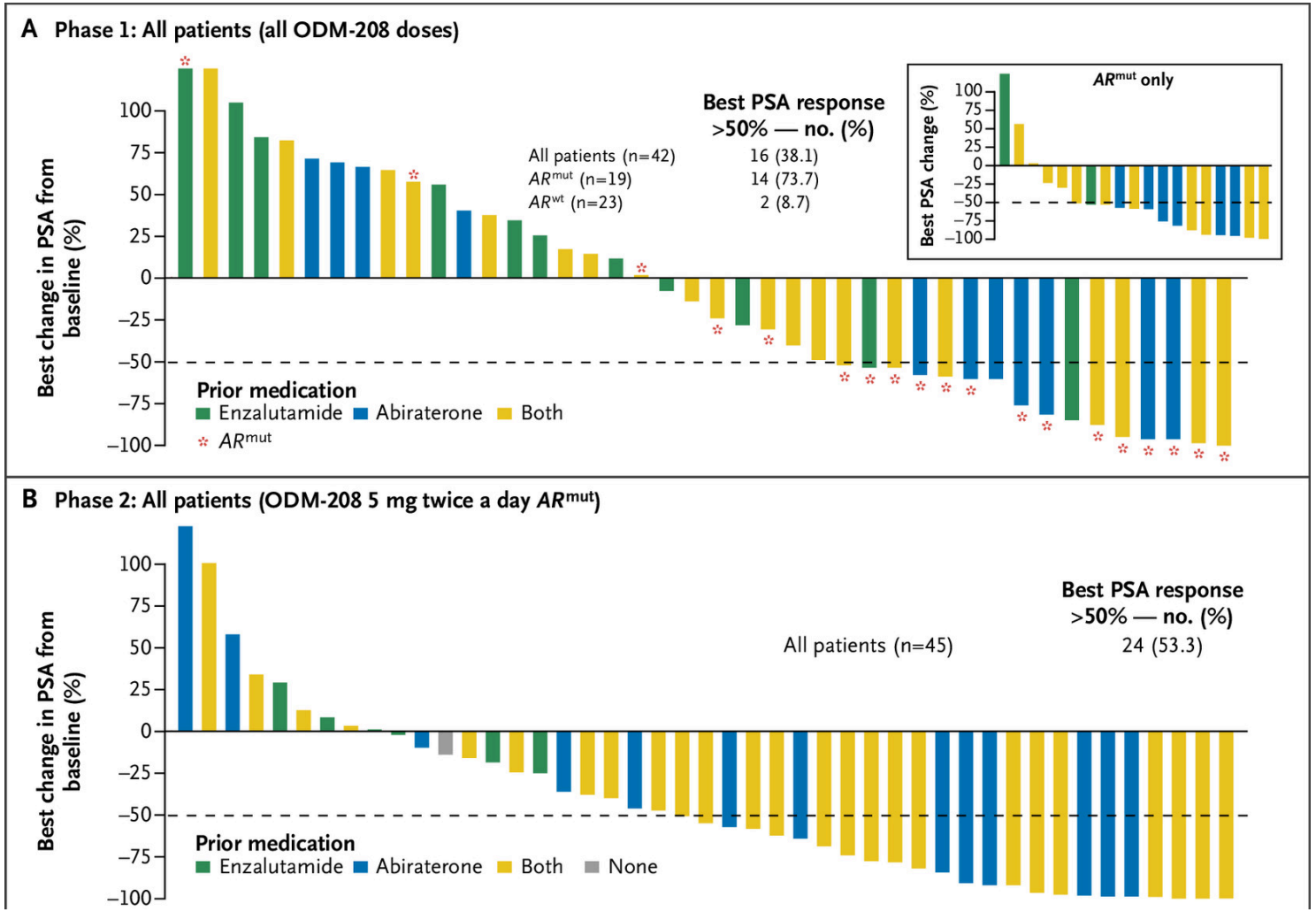
Adverse Events by Preferred Term	Phase 1 (All Dose Cohorts Combined; N=47), n (%)	Phase 2 (5 mg Twice a Day; N=45), n (%)
All adverse events	47 (100.0)	45 (100)
Grade ≥3	33 (70.2)	36 (80.0)
Related to ODM-208	44 (93.6)	38 (84.4)
Grade ≥3	21 (44.7)	10 (22.2)
Serious adverse events	29 (61.7)	29 (64.4)
Related to ODM-208	19 (40.4)	6 (13.3)
Serious adrenal insufficiency–like events†	16 (34.0)	3 (6.7)
Adverse events leading to permanent discontinuation	20 (42.6)	10 (22.2)
Adverse events leading to ODM-208 interruption	26 (55.3)	20 (44.4)
No. of patients who died	2 (4.3)	10 (22.2)
Deaths related to ODM-208	0	0

Table 3. Adverse Events Occurring in More Than 15% of Patients at Any Grade in Either the Phase 1 or Phase 2 Cohort by Preferred Term.*

	Phase 1, No. (%)		Phase 2, No. (%)	
Adverse Events by Preferred Term	Any Grade	Grade ≥3	Any Grade	Grade ≥3
All	47 (100.0)	33 (70.2)	45 (100)	36 (80.0)
Adrenal insufficiency	17 (36.2)	15 (31.9)	6 (13.3)	3 (6.7)
Anemia	16 (34.0)	7 (14.9)	17 (37.8)	6 (13.3)
Asthenia	14 (29.8)	2 (4.3)	13 (28.9)	2 (4.4)
Fatigue	14 (29.8)	0	17 (37.8)	3 (6.7)
Dyspnea	6 (12.8)	0	12 (26.7)	2 (4.4)
Muscle spasms	14 (29.8)	0	8 (17.8)	1 (2.2)
Hyponatremia	15 (31.9)	6 (12.8)	10 (22.2)	2 (4.4)
Hyperkalemia	13 (27.7)	1 (2.1)	9 (20.0)	1 (2.2)
Edema peripheral	10 (21.3)	0	12 (26.7)	0

Fizazi, K. , Bernard-Tessier, A. , Roubaud, G. , Utriainen, T. , Barthélémy, P. , Fléchon, A. , van der Voet, J. , Gravis, G. , Ratta, R. , Jones, R. , Parikh, O. , Tanner, M. , Antonarakis, E. S. , Baldini, C. , Peters, N. , Garratt, C. , Ikonen, T. , Pohjanjousi, P. , Joensuu, H. & Cook, N. (2024). Targeted Inhibition of CYP11A1 in Castration-Resistant Prostate Cancer. *NEJM Evidence, 3* (1), doi: 10.1056/ EVIDoa2300171.

CYPIDES Phase I/II trial – promising efficacy signal



Opevesostat is being evaluated in two phase III trials for mCRPC (OMAHA-3 and OMAHA-4)

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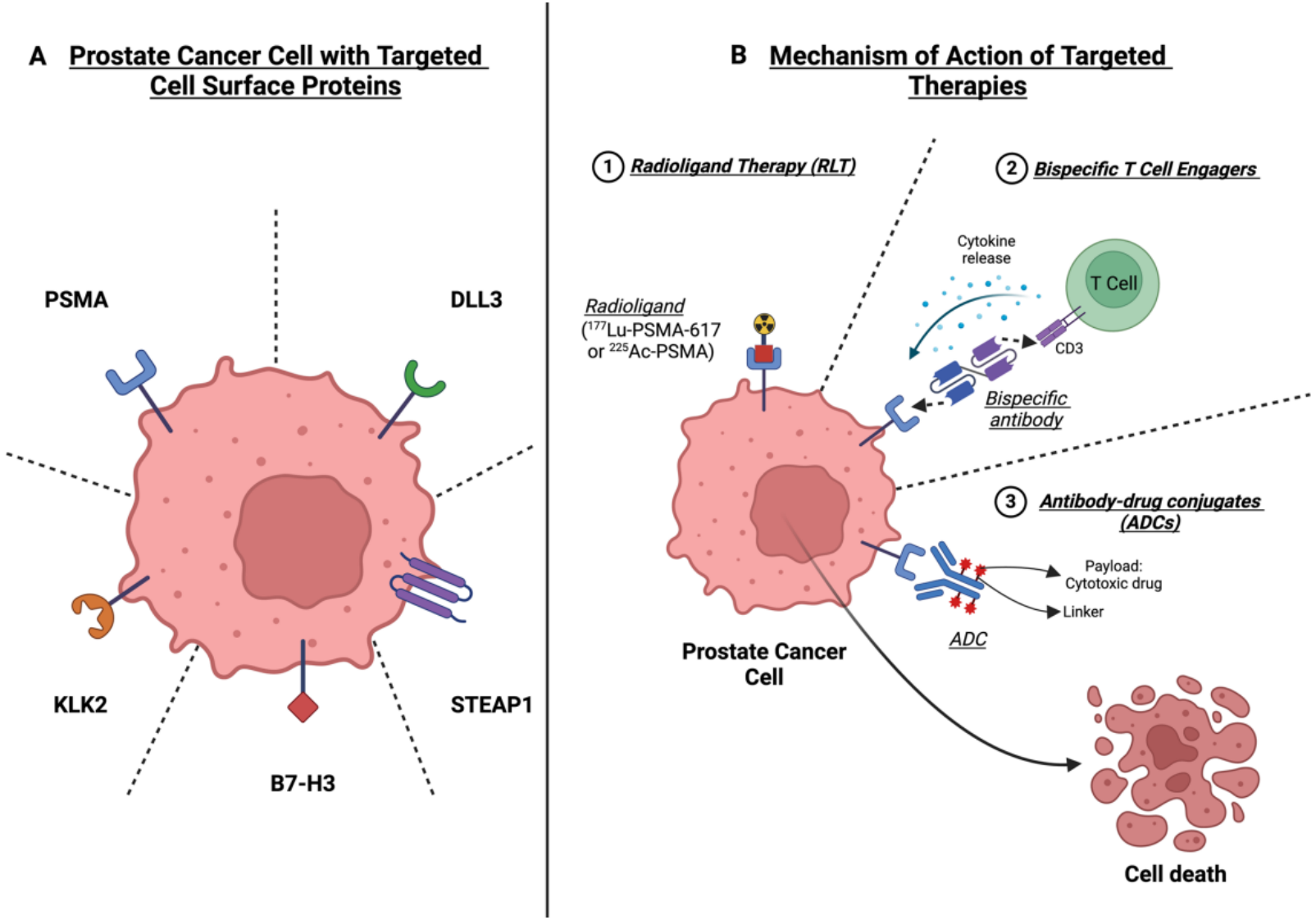
Beyond the AR - targeting the cell surface



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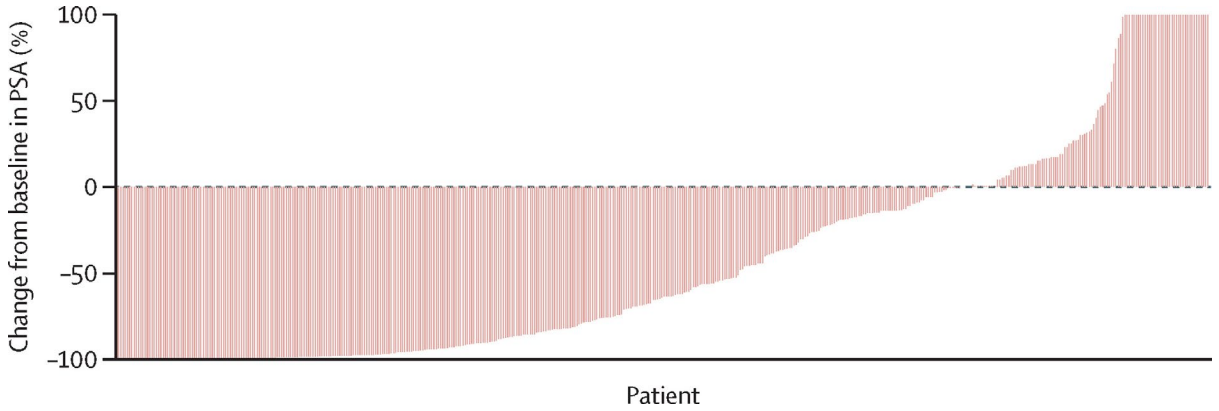
Multiple 225-Ac based RLT trials are in progress

NCT (or Identifier)	Agent	Sponsor	Patient Population / Indication
NCT04597411	**^{225}Ac-PSMA-617**	Endocyte	Men with PSMA-positive prostate cancer (mCRPC ± prior ^{177}Lu-PSMA)
NCT05983198	**^{225}Ac-PSMA-R2**	Novartis	Patients with mHSPC and mCRPC with PSMA-positive disease (some with prior therapies)
NCT06229366	**^{225}Ac-PSMA-62**	Eli Lilly and Company	Oligometastatic hormone-sensitive and metastatic castration-resistant prostate cancer
NCT06402331	**^{225}Ac-PSMA-I&T** (FPI-2265)	Fusion Pharmaceuticals	PSMA-positive mCRPC, previously treated with ^{177}Lu-PSMA radioligand therapy
NCT06052306	**^{225}Ac-macropa-pelgifatamab** (BAY 3546828, ^{225}Ac-pelgi)	Bayer	Advanced metastatic castration-resistant prostate cancer (mCRPC)
NCT04576871	**^{225}Ac-J591** (anti-PSMA antibody)	Weill Medical College of Cornell University	mCRPC patients with progressive disease
NCT06549465	**^{225}Ac Rosopatamab tetraxetan**	Convergent Therapeutics	PSMA-positive prostate cancer (participants with or without prior therapy)
NCT04644770	**^{225}Ac-DOTA-h11B6** (JNJ-69086420, targets hK2)	Janssen Research & Development, LLC	Advanced prostate cancer (targeting human kallikrein-2, hK2)

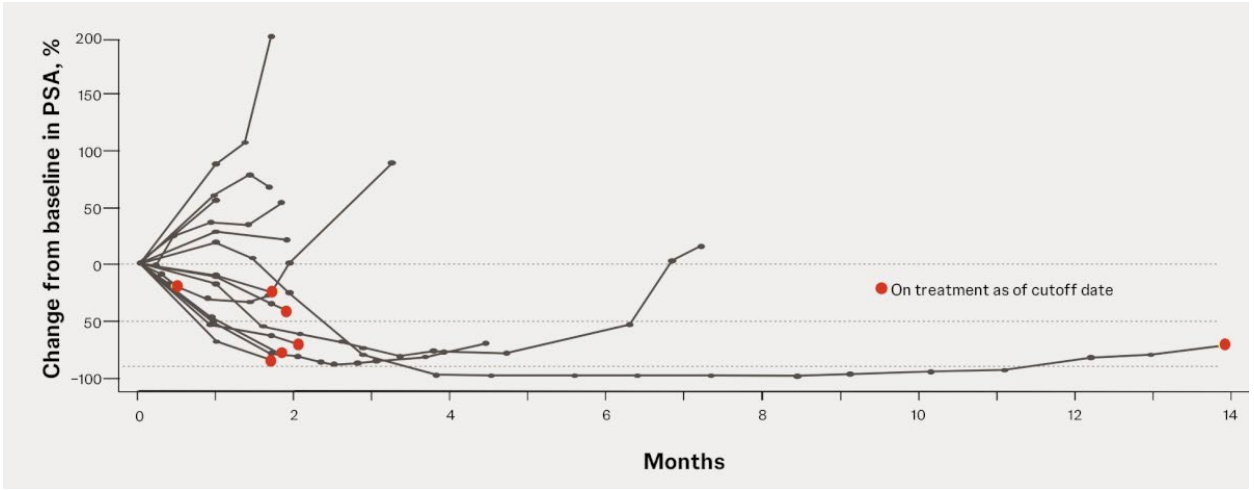
Actinium agents have shown encouraging efficacy

- WARMTH trial[1]
  - Multicenter retrospective trial
  - 488 patients treated with at least one cycle of ^{225}Ac-PSMA RLT
  - Treated on compassionate use indication



PSA50 achieved in 57% of patients

- JNJ-69086420[2]
  - First in class anti-hK2 antibody-based RLT with ^{225}Ac payload
  - Significant toxicity – 61.4% grade III AE; TEAE of note included hematologic toxicity and ILD (9%)
  - PSA50 was 45.6% with several remarkably durable responses



Adaptive dosing with lifetime cap may mitigate toxicity

1. Sathekge MM, Lawal IO, Bal C, et al. Actinium-225-PSMA radioligand therapy of metastatic castration-resistant prostate cancer (WARMTH Act): a multicentre, retrospective study. Lancet Oncol. 2024;25(2):175-183. doi:10.1016/S1470-2045(23)00638-1
2. Michael J. Morris et al. A phase 1 study of JNJ-69086420 (JNJ-6420), an actinium-225 (225Ac) -labeled antibody targeting human kallikrein 2 (hK2), for metastatic castration-resistant prostate cancer (mCRPC).. J Clin Oncol 42, 5010-5010(2024).DOI:10.1200/JCO.2024.42.16_suppl.5010

Non-PSMA targeted BiTE are in further development

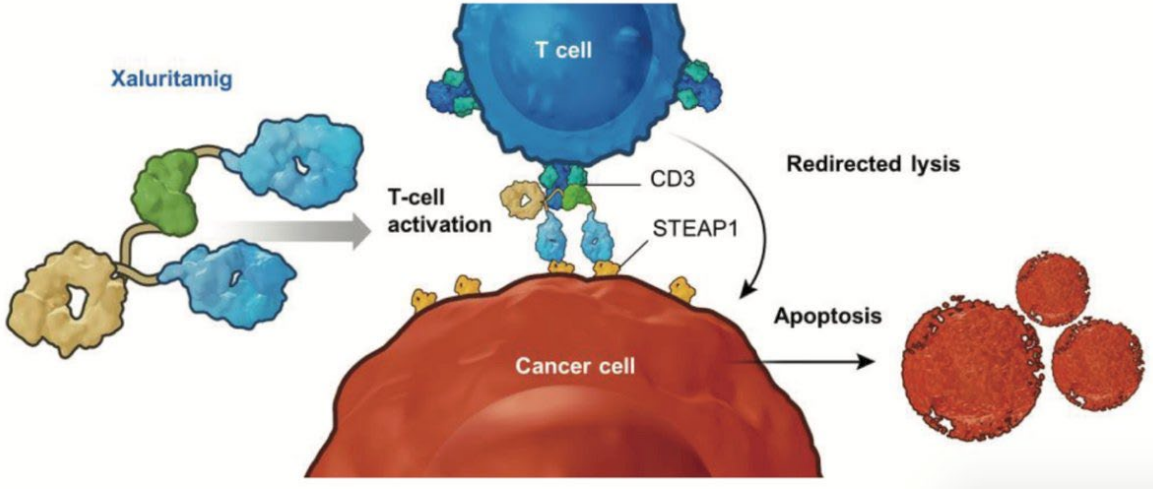
Target	Therapy	n	Clinical Activity	Safety	Notes	Year
PSMA	Pasotuxizumab	47	• PSA50: 30% (SC) • PSA 50: 33% (cIV)	• Fever 85%;; CRS 6% • Grade 3+ AE: 53%	Included SC and cIV cohort.s Short-lived responses due to anti-drug antibodies	2021
PSMA	JNJ-081	39	• “Transient” PSA declines • 0% ORR	• Fever 69%; CRS 66.7% (no grade 3+) • Serious TEAE 46.2%	Limited sustained response. Significant anti-drug antibodies for SC dosing	2023
PSMA	Acapatamab (AMG 160)	133	• PSA50: 30.4% • ORR 7.4% • mbPFS: 3.3 mos	• CRS: 98.2% (grade 3+ 16.1%) • Serious TEAE 27.1%	Lack of sustained response. Significant anti-drug antibodies	2024
STEAP1	Xaluritamig (AMG 509)	97	• PSA50: 49% • ORR 24%	• CRS 72% (4% grade 3+) • Serious TEAE: 57%	Phase III trial in progress: XALute NCT06691984.	2024
KLK2	JNJ-78278343 (Pasritamig)	174	• PSA50 42.4% (RP2D) • mPFS 6.77 mos (RP2D)	• CRS 24.7% (RP2D cohort only had 8.9% all grade I) • Grade 3+ TEAE 9.2%	Excellent safety profile	2025
DLL3	Tarlatamab	40	• ORR 10% • rPFS 3.5 mos (DLL3+)	• CRS 82.5% (5% grade 3+) • Grade 3+ TRAE 45%	Limited activity in NEPC	2025

1. Hummel HD, Kufer P, Grüllich C, et al. Pasotuxizumab, a BiTE®immune therapy for castration-resistant prostate cancer: Phase I, dose-escalation study findings. Immunotherapy. 2021;13(2):125-141. doi:10.2217/imt-2020-0256
2. Lim EA, Schweizer MT, Chi KN, et al. Phase 1 Study of Safety and Preliminary Clinical Activity of JNJ-63898081, a PSMAand CD3 Bispecific Antibody, for Metastatic Castration-Resistant Prostate Cancer. Clin Genitourin Cancer. 2023;21(3):366-375. doi:10.1016/j.clgc.2023.02.010
3. Dorff T, Horvath LG, Autio K, et al. A Phase I Study of Acapatamab, a Half-life Extended, PSMA-Targeting Bispecific T-cell Engager for Metastatic Castration-Resistant Prostate Cancer. *Clin Cancer Res*. 2024;30(8):1488-1500. doi:10.1158/1078-0432.CCR-23-2978
4. Kelly WK, Danila DC, Lin CC, et al. Xaluritamig, a STEAP1 × CD3 XmAb 2+1 Immune Therapy for Metastatic Castration-Resistant Prostate Cancer: Results from Dose Exploration in a First-in-Human Study. *Cancer Discov*. 2024;14(1):76-89. doi:10.1158/2159-8290.CD-23-0964
5. Stein MN, Vinceneux A, Robbrecht D, et al. Pasritamig, a First-in-Class, Bispecific T-Cell Engager Targeting Human Kallikrein 2, in Metastatic Castration-Resistant Prostate Cancer: A Phase I Study. *J Clin Oncol*. 2025;43(22):2515-2526. doi:10.1200/JCO-25-00678
6. Aggarwal R, Rottey S, Bernard-Tessier A, et al. Safety and Efficacy of Tarlatamab in Patients with Neuroendocrine Prostate Cancer: Results from the Phase 1b DeLLpro-300 Study. *Clin Cancer Res*. 2025;31(18):3854-3863. doi:10.1158/1078-0432.CCR-25-1211

STEAP-1: A novel cell surface target in prostate cancer

- Six-transmembrane epithelial antigen of the prostate 1
- Expressed in 77% to 83% of metastases; often associated with poor survival
- Low to no expression in normal tissue
- Xaluritamig is a novel humanized bi-specific 2+1 TCE
- Two identical humanized anti-STEAP1 fragment antigen binding domains and an anti-CD3 domain

Figure 1: Xaluritamig (AMG 509): XmAb® 2+1 T-cell engager designed to facilitate T-cell-mediated lysis of STEAP1-expressing cells[1-3]



1598P Xaluritamig, a STEAP1 x CD3 XmAb 2+1 immune therapy, in patients (pts) with metastatic castration-resistant prostate cancer (mCRPC): Initial results from dose expansion cohorts in a phase I study Kelly, W.K. et al. Annals of Oncology, Volume 35, S963 - S964. Presented by Dr. Kelly 2024 European Society of Medical Oncology (ESMO) Annual Congress. September 13th and 17th 2024. Barcelona, Spain

Phase Ib randomized dose expansion presented at ESMO 2024

Primary objectives: Safety and tolerability
Secondary objectives: PK, preliminary antitumor activity
Exploratory objectives: PD, immunogenicity

Key inclusion criteria:
- mCRPC progressing on prior novel hormonal therapy and 1–2 taxane regimens*
- ECOG PS 0–1
- Adequate organ function

Key exclusion criteria:
- Histology other than adenocarcinoma
- Active autoimmune disease

Part 1: FIH Monotherapy

Dose exploration

MTD

Dose expansion randomized 1:1:1

Planned Target Dose (mg)	Cycle 1 Doses (mg)				Cycle 2+ Dose (mg)
	D1	D8	D15	D22	
0.75	**0.1**	**0.3**	**0.75**	**0.75**	C2D1+ = **0.75** QW
1.5	**0.1**	**0.3**	**1.0**	**1.5**	C2D1+ = **1.5** QW
1.5	**0.1**	**0.3**	**1.0**	**1.5**	C2D1+ = **1.5** Q2W

C1D1 and C1D8 equivalent doses across all cohorts.

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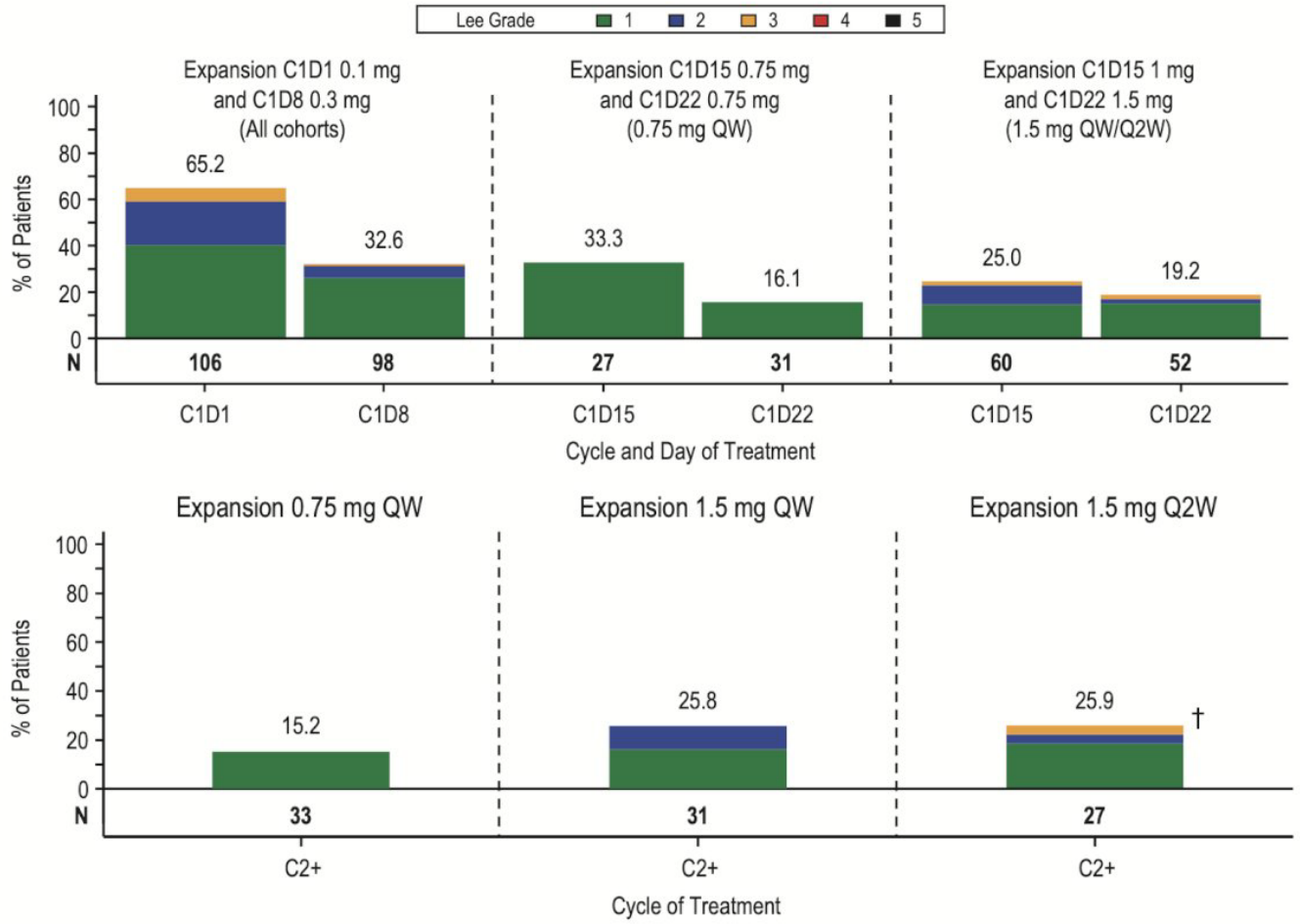
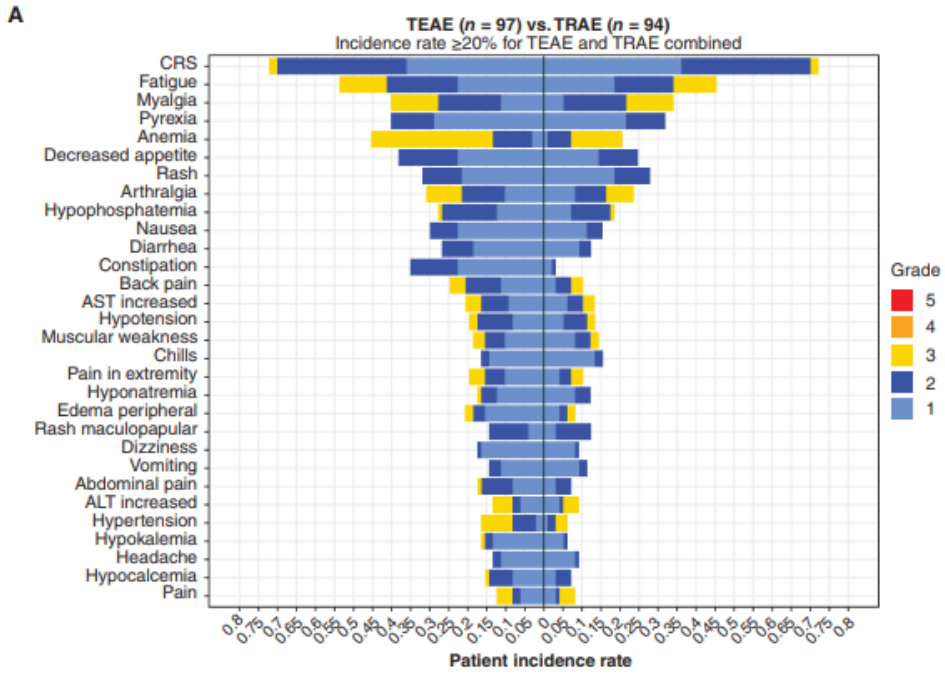
CRS was common, but generally low grade during C1

Figure 3: CRS in Cycle 1 (top) and Cycle 2 and Beyond (bottom)





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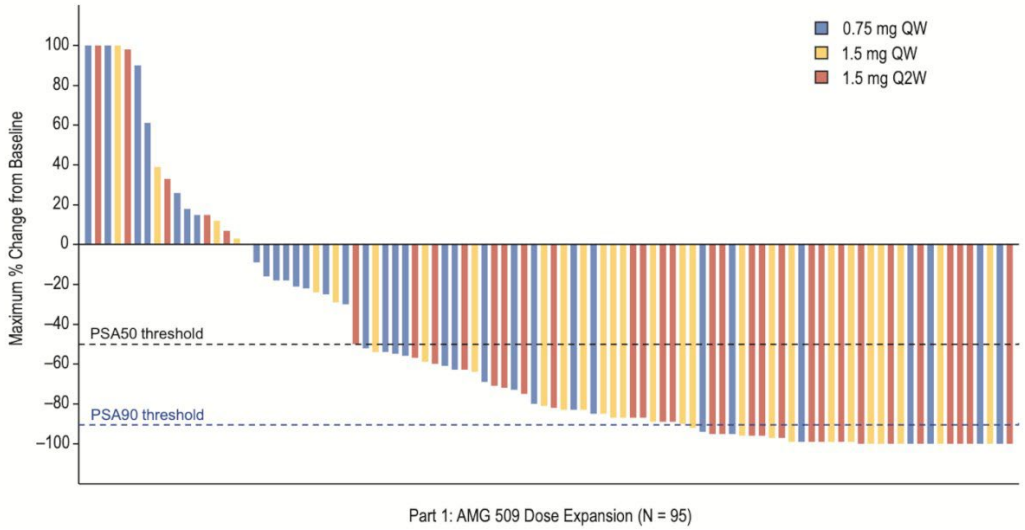
Efficacy signal good- moving to phase III

Figure 5: Waterfall Plot of Maximum PSA Reduction



Xaluritamig efficacy summary

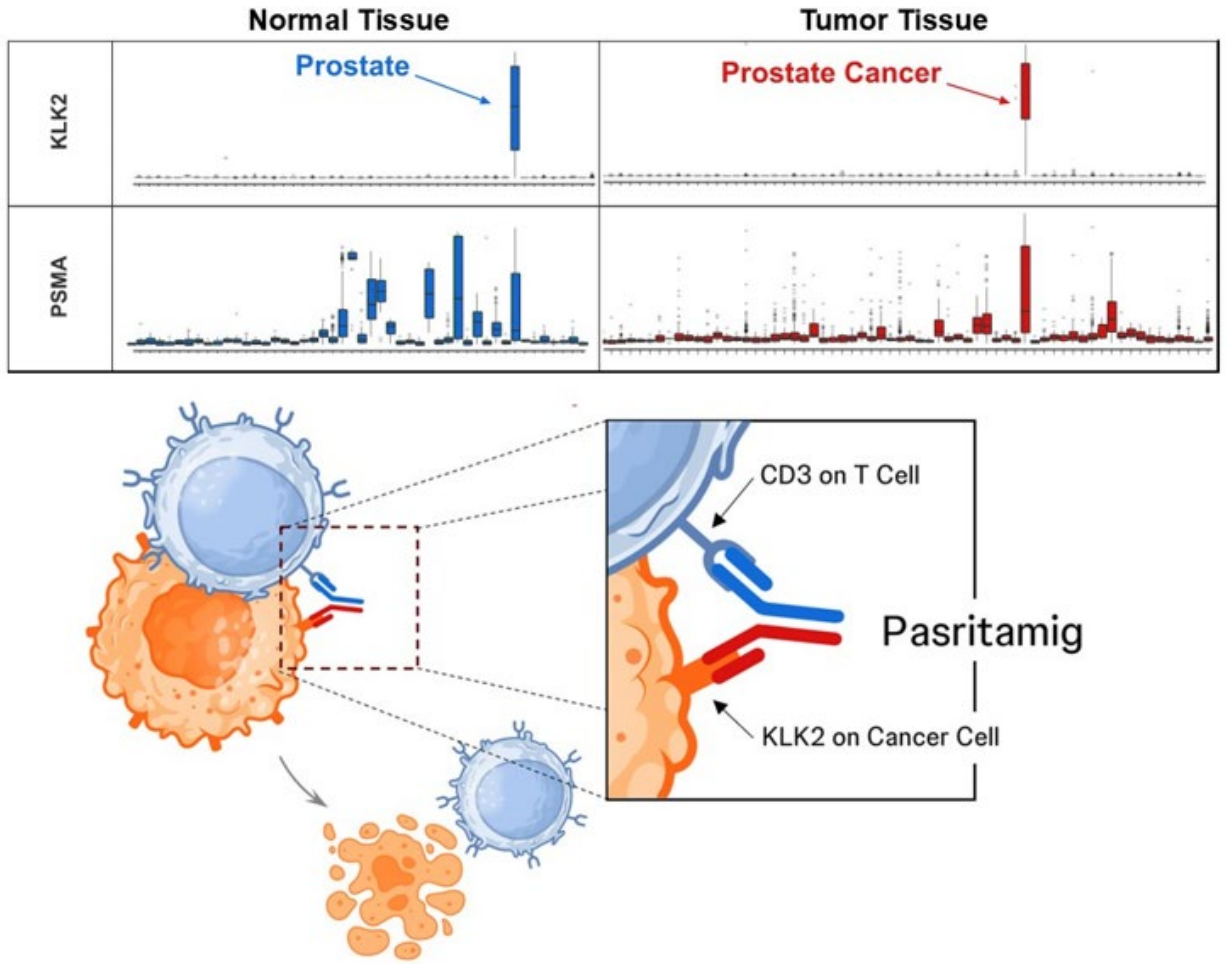
Table 3: Comparison of Efficacy Outcomes Among the 0.75 mg QW, 1.5 mg QW, and 1.5 mg Q2W Regimens

	0.75 mg QW	1.5 mg QW	1.5 mg Q2W	Dose Expansion Total
Prostate-specific antigen (PSA) evaluable	**N = 33**	**N = 30**	**N = 32**	**N = 95**
PSA50 response confirmed, n (%)	12 (36.4)	18 (60.0)	17 (53.1)	47 (49.5)
PSA90 response confirmed, n (%)	7 (21.2)	9 (30.0)	11 (34.4)	27 (28.4)
RECIST evaluable	**N = 27**	**N = 21**	**N = 21**	**N = 69**
Confirmed response (partial or complete response), n (%)	**4 (14.8)**	**4 (19.0)**	**6 (28.6)**	**14 (20.3)**
Confirmed complete response, n (%)	0 (0.0)	0 (0.0)	1 (4.8)	1 (1.4)
Confirmed partial response, n (%)	4 (14.8)	4 (19.0)	5 (23.8)	13 (18.8)
Stable disease, n (%)	10 (37.0)	14 (66.7)	10 (47.6)	34 (49.3)
Progressive disease, n (%)	12 (44.4)	1 (4.8)	4 (19.0)	17 (24.6)
Not evaluable, n (%)	1 (3.7)	2 (9.5)	1 (4.8)	4 (5.8)

Ongoing XALute trial – phase II study of xaluritamig vs cabazitaxel or hormone switch after progression on taxane and novel ARPI. NCT06691984.

Pasritamig targets KLK2 – a novel target

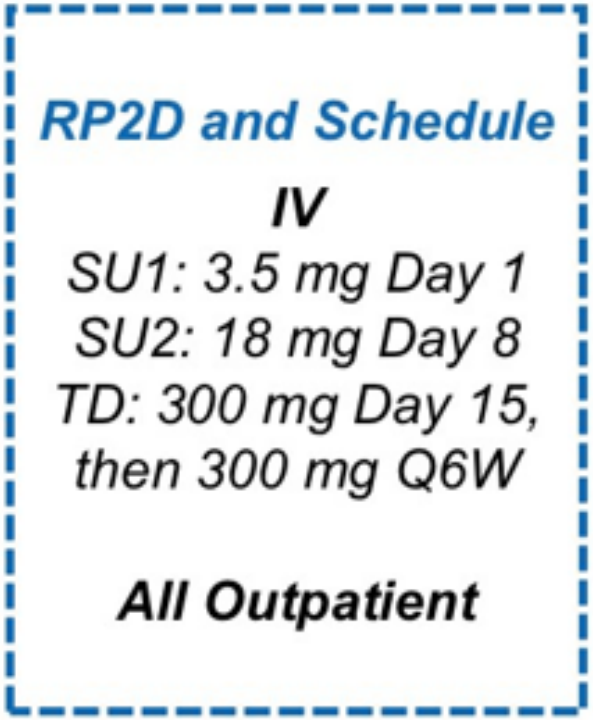
- KLK2 is trypsin-like serine protease with high homology and coexpression with PSA/KLK3 gene
- High expression in prostate cells and prostate cancer cells
- Attractive novel target for cellular therapies



Capucine Baldini et al. Phase 1 study results of JNJ-78278343 (pasritamig) in metastatic castration-resistant prostate cancer (mCRPC).. *J Clin Oncol* **43**, 5017-5017(2025).DOI:10.1200/JCO.2025.43.16_suppl.5017. Presented by C. Baldini at ASCO Annual Meeting: May30-June3; Chicago, IL

RP2D dose selected will be done all outpatient

- Initial dosing started SC with steroid premedication
- Step up dosing introduced to mitigate CRS
- Transitioned to IV dosing to achieve higher doses with fewer injections
- IV dosing chosen for RP2D based on improved safety and efficacy profile



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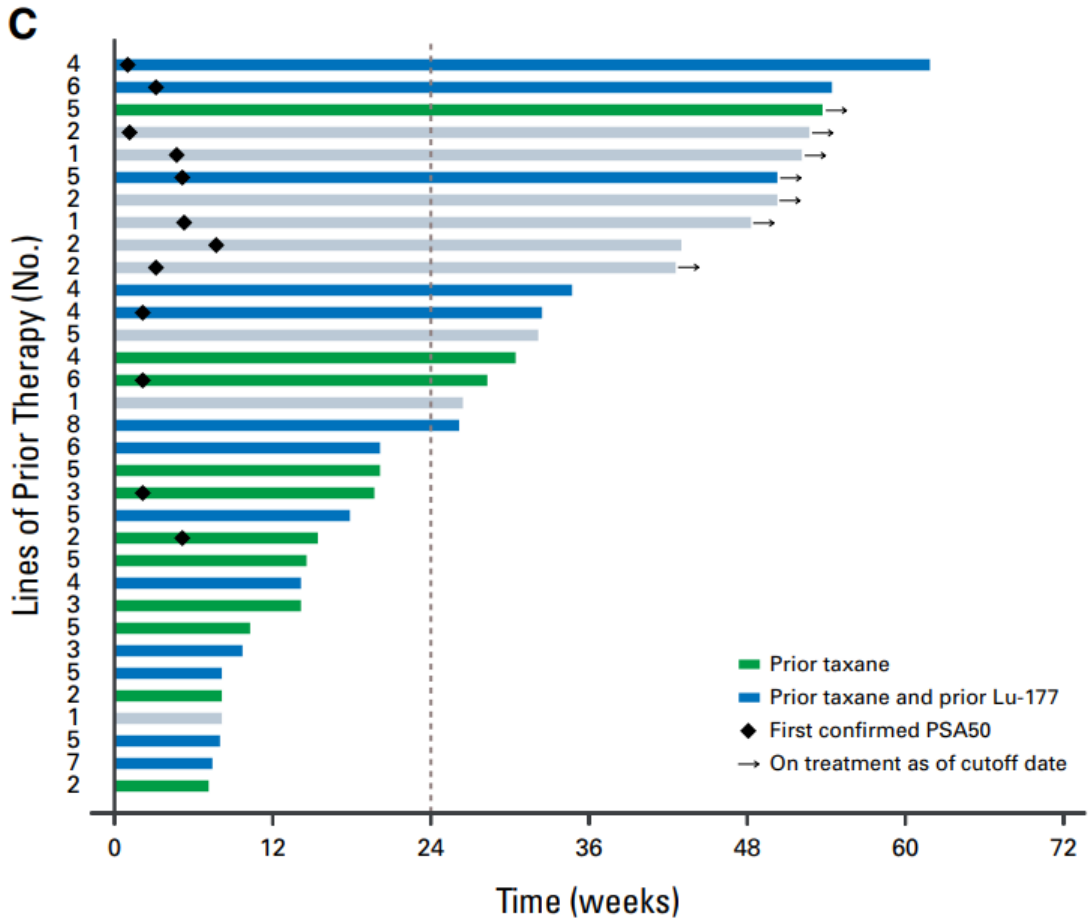
Safety profile is favorable

Adverse Event	All-Treated Population, No. (%)			RP2D Safety Population,[a] No. (%)
	Total (N = 174)	SC (n = 102)	IV (n = 72)	Total (n = 45[a])
Participants with ≥one TEAE	171 (98.3)	102 (100.0)	69 (95.8)	42 (93.3)
Serious TEAEs	57 (32.8)	41 (40.2)	16 (22.2)	8 (17.8)
Grade ≥3 TEAEs	79 (45.4)	51 (50.0)	28 (38.9)	15 (33.3)
TEAEs leading to treatment discontinuation	4 (2.3)	3 (2.9)	1 (1.4)	0
TEAEs leading to death	2 (1.1)	2 (2.0)	0	0
Participants with ≥one TRAE	144 (82.8)	94 (92.2)	50 (69.4)	27 (60.0)
Serious TRAEs	12 (6.9)	10 (9.8)	2 (2.8)	2 (4.4)
Grade ≥3 TRAEs	17 (9.8)	11 (10.8)	6 (8.3)	2 (4.4)
TRAEs leading to treatment discontinuation	1 (0.6)	1 (1.0)	0	0
TRAEs leading to death	0	0	0	0
TRAEs in ≥5% of participants by preferred term				
Injection-site reaction[b]	89 (51.1)	87 (85.3)	2 (2.8)	1 (2.2)
Fatigue	47 (27.0)	34 (33.3)	13 (18.1)	7 (15.6)
CRS	43 (24.7)	31 (30.4)	12 (16.7)	4 (8.9)
Grade 1	37 (21.3)	28 (27.5)	9 (12.5)	4 (8.9)
Grade 2	6 (3.4)	3 (2.9)	3 (4.2)	0
Infusion-related reaction[c]	22 (12.6)	7 (6.9)	15 (20.8)	11 (24.4)
Nausea	13 (7.5)	9 (8.8)	4 (5.6)	2 (4.4)
Decreased appetite	11 (6.3)	8 (7.8)	3 (4.2)	1 (2.2)
Headache	10 (5.7)	5 (4.9)	5 (6.9)	2 (4.4)
Diarrhea	8 (4.6)	4 (3.9)	4 (5.6)	1 (2.2)
Lymphopenia	7 (4.0)	2 (2.0)	5 (6.9)	0
Asthenia	6 (3.4)	6 (5.9)	0	0

Stein MN, Vinceneux A, Robbrecht D, et al. Pasritamig, a First-in-Class, Bispecific T-Cell Engager Targeting Human Kallikrein 2, in Metastatic Castration-Resistant Prostate Cancer: A Phase I Study. *J Clin Oncol*. 2025;43(22):2515-2526. doi:10.1200/JCO-25-00678

Efficacy signal is favorable



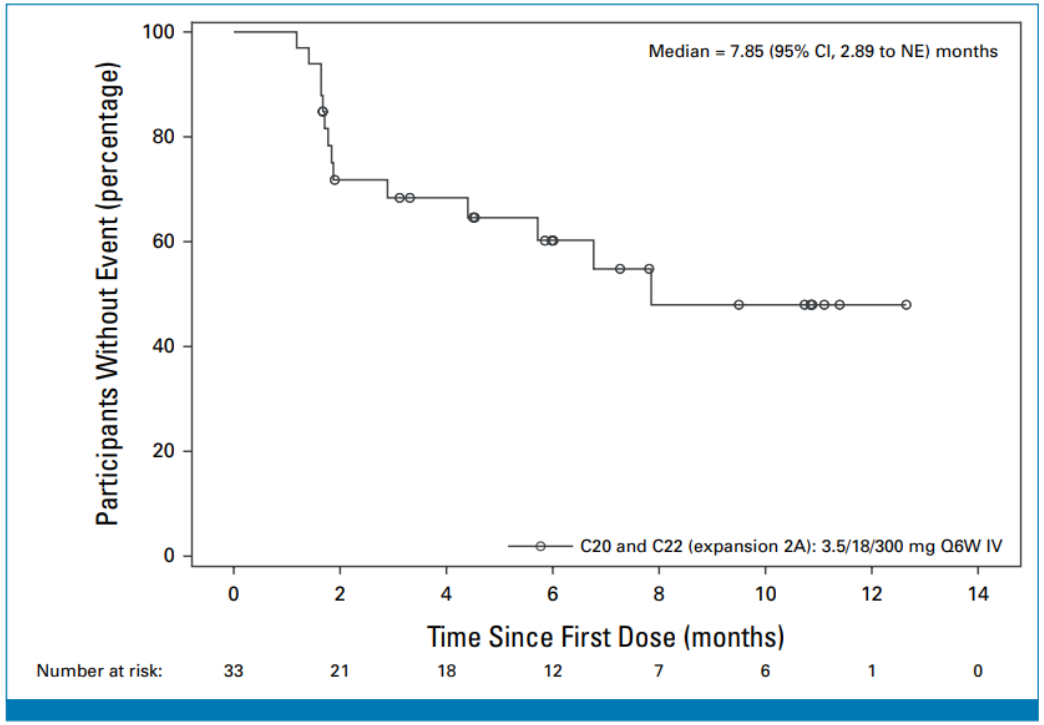


FIG 1. Kaplan-Meier plot of radiographic progression-free survival in the RP2D efficacy population (n = 33). RP2D efficacy population consists of participants in the all-treated population who received IV 3.5 mg on day 1, 18 mg on day 8, 300 mg on day 15, and then 300 mg once every 6 weeks (C20 and C22). C, cohort; IV, intravenous; NE, not estimable; Q6W, once every 6 weeks; RP2D, recommended phase II dose.

In the RP2D population, PSA50 was 42.4% with rPFS 7.82 months

Stein MN, Vinceneux A, Robbrecht D, et al. Pasritamig, a First-in-Class, Bispecific T-Cell Engager Targeting Human Kallikrein 2, in Metastatic Castration-Resistant Prostate Cancer: A Phase I Study. *J Clin Oncol*. 2025;43(22):2515-2526. doi:10.1200/JCO-25-00678

Antibody drug conjugates – remain a work in progress

- PSMA Targeted ADCs (MLN2704, PSMA-ADC, MEDI3776)
  - Relatively low efficacy signal in early phase clinical trial
  - Limited by neurotoxicity, skin toxicity, and myelotoxicity
- STEAP1-targeted ADC (DSTP30865)
  - PSA50 14% with acceptable safety profile at RP2D 2.4mg/kg q3 weeks
- B7-H3 targeted ADC (DS-7300, MGC-018)
  - Promising early responses in mCRPC and other solid tumors
- Overall not as well developed a pipeline

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7. DOI:10.1200/JCO.2021.39.15_suppl.2631

Thanks!