Genitourinary Masterclass

The importance of first treatment choice in advanced disease

Professor Arnulf Stenzl
Secretary General, European Association of Urology (EAU)
Senior Professor and Consultant, University of Tübingen

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Xtandi™ enzalutamide

astellas

MAT-NL-XTD-2025-00032 | July 2025

XTANDI™ (enzalutamide) indications

XTANDI is indicated, as per the EMA SmPC:

- As monotherapy or in combination with ADT for the treatment of adult men with high-risk biochemical recurrent nmHSPC who are unsuitable for salvage radiotherapy
- In combination with ADT for the treatment of adult men with mHSPC
- For the treatment of adult men with high-risk nmCRPC
- For the treatment of adult men with mCRPC who are asymptomatic or mildly symptomatic after failure of ADT and in whom chemotherapy is not yet clinically indicated
- For the treatment of adult men with mCRPC whose disease has progressed on or after docetaxel therapy

XTANDI is subject to medicinal prescription.
Astellas Pharma B.V., Sylviusweg 62, 2333 BE Leiden, The Netherlands.
ADT, androgen deprivation therapy; EMA, European Medicines Agency; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; nmCRPC, nonmetastatic castration-resistant prostate cancer; nmHSPC, nonmetastatic hormone-sensitive prostate cancer; SmPC, Summary of Product Characteristics.
XTANDI (enzalutamide). Summary of Product Characteristics.
MAT-NL-XTD-2025-00032 | July 2025

Disclosures

- The speaker has received an honorarium from Astellas for this presentation
- **Patents and royalties:**
  - Patent A290/99: Implantable incontinence device
  - Patent AT00/00001: C-Trap, implantable device to treat urinary incontinence
  - Patent 2019/8223: Risk prediction of renal cell carcinoma using proportional subtype assignments
  - Patent PCT/EP2020/056398: Method for determining RCC subtype II
- **Membership of an entity's Board of Directors:**
  - EAU

EAU, European Urology Association; RCC, renal cell carcinoma.

Patient case study report

- A 64-year-old avid biker, never seen a urologist before (except on a bike)
- PSA course: 8.05 ng/ml; repeat: 9.47 ng/ml
- Family history: Father with prostate cancer (cause of death: myocardial infarction)
- MRI: PI-RADS 4 apex, right side
- Systemic and targeted fusion Bx prostate: 8/12 with prostate cancer, Gleason score 4+4=8

- **Patient's treatment choice:** Radical prostatectomy and LAE 05/2019:
- **pT2c, N1(8/21), L1, v0, Pn1, R0, Gleason Score 4+5=9**
- **PSA** 6 weeks **post-op**: **1.3 ng/ml**

Bx, biopsy; L1, lymphatic invasion; LAE, laparoscopic assisted excision; MRI, magnetic resonance imaging; N1, nodal metastasis; PI-RADS, Prostate Index Reporting and Data System; Pn1, presence of cancer cells in regional lymph nodes; PSA, prostate-specific antigen; pT, pathological tumour score; R0, no residual tumour after resection; v0, no venous invasion.
Patient case study provided by the speaker.
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Predicted median life expectancy by age and gait speed in men aged ≥65

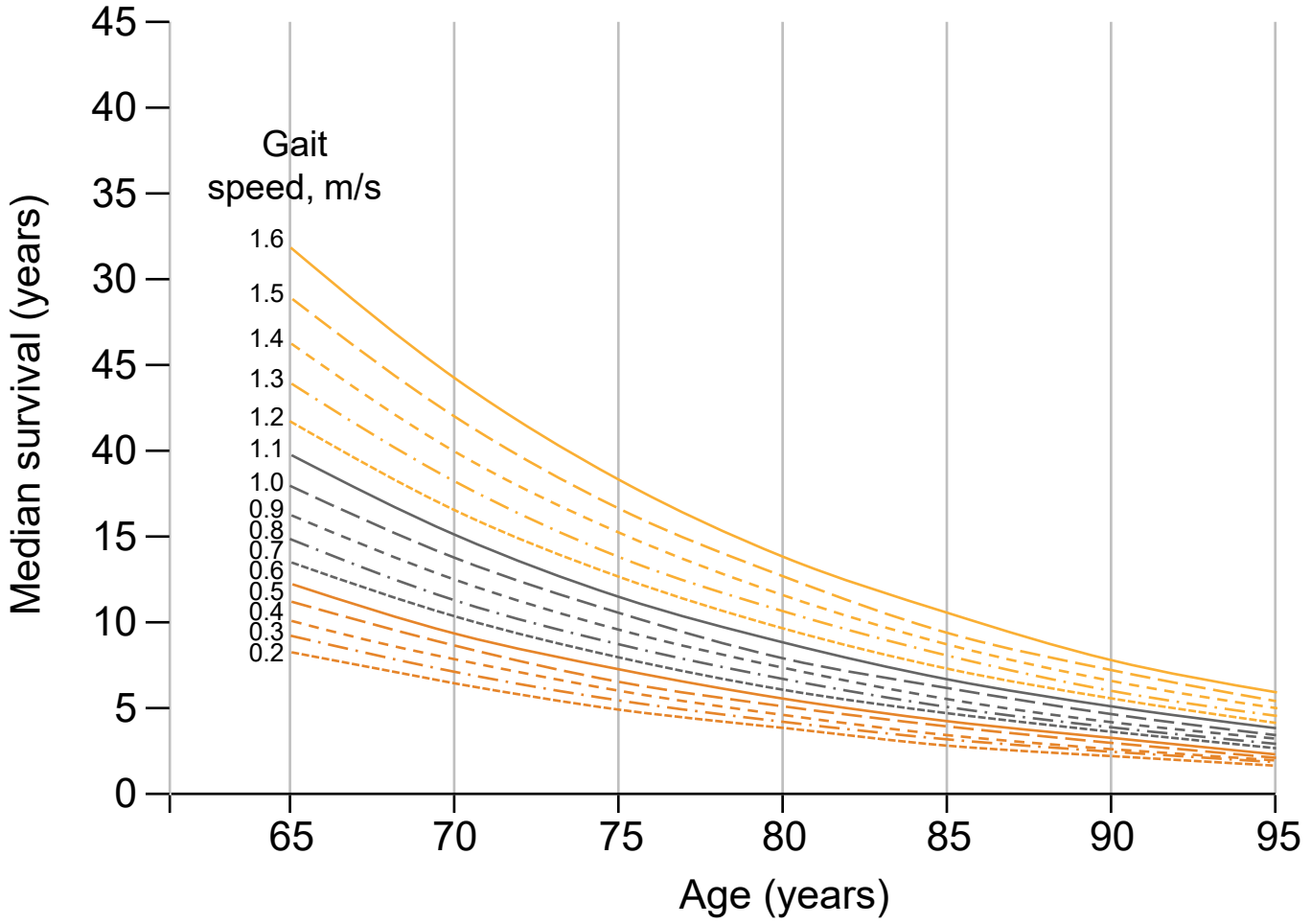


Figure adapted from Studenski S, et al., 2011.

Studenski S, et al. *JAMA* 2011;305(1):50.

Real-world evidence suggests that most patients with mHSPC are not receiving guideline-recommended treatment

- The 1st evidence of an OS benefit with ADT + ARPI for patients with mHSPC was seen in 2017[1,2]
- The 2025 EAU guidelines recommend offering ADT + ARPI for patients with mHSPC who are eligible for the regimen[3]
- However, recent real-world data have shown that 76% of patients with mHSPC are receiving treatments not recommended by guidelines[4]

Country-specific analysis of the proportion of patients with mHSPC receiving non-guideline-recommended treatments between 2018 and 2020[4]

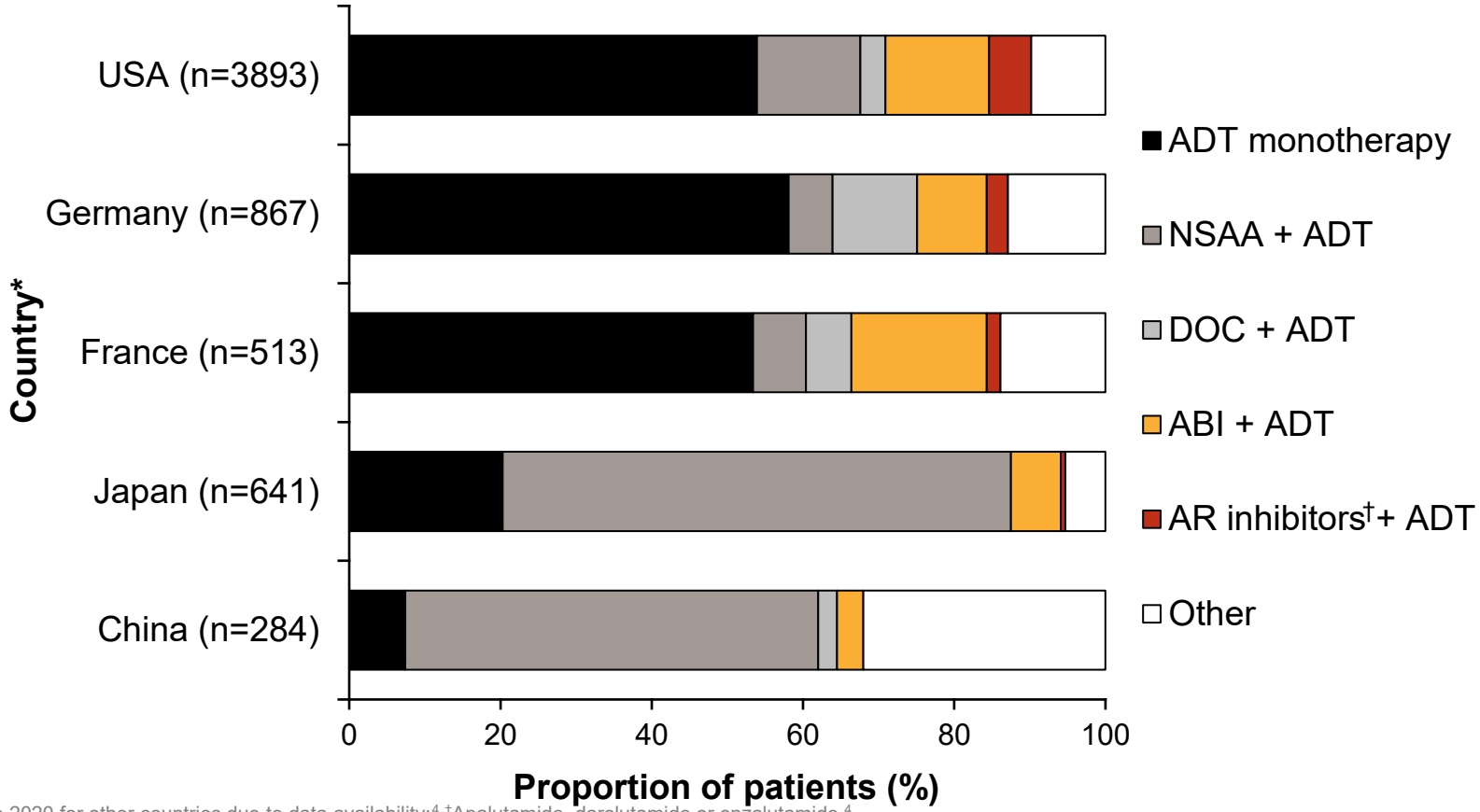


Figure adapted from Goebell PJ, et al., 2024.
*Study time frame of January 2018 through December 2019 for China vs. June 2020 for other countries due to data availability;[4] †Apalutamide, darolutamide or enzalutamide.[4]
ABI, abiraterone; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; DOC, docetaxel; mHSPC, metastatic hormone-sensitive prostate cancer; NSAA, non-steroidal anti-androgen.
1. Fizazi K, et al. *N Engl J Med* 2017;377:352–360; 2. James ND, et al. *N Engl J Med* 2017;377:338–351;
3. EAU. EAU–EANM–ESTRO–ESUR–ISUP–SIOG guidelines on prostate cancer. Available at: uroweb.org/guideline/prostate-cancer/. Last accessed: July 2025; 4. Goebell PJ, et al. *Future Oncol* 2024;20(14):903–918.

The clinical effect of ^{68}Ga-PSMA-11 PET in patients with BCR

- Intended change in treatment management in 260/382 (68%) patients
- Management pathway aligned with PET findings, i.e. local/focal therapy (44%, 54/126 patients) and towards systemic therapy or combination approaches for metastatic disease (69%, 106/153 patients)
- A total of 150 intended diagnostic tests, mostly CT scans (29%, n=43) and bone scans/NaF-PET scans (35%, n=52), were prevented by PSMA PET
- A total of 73 tests, mostly biopsies (60%, n=44) as requested by the study protocol, were triggered
- **PSMA PET --> >50% of patients with BCR had different treatment for BCR**
- **150 out of 443 tests were prevented with PSMA PET (34%)**

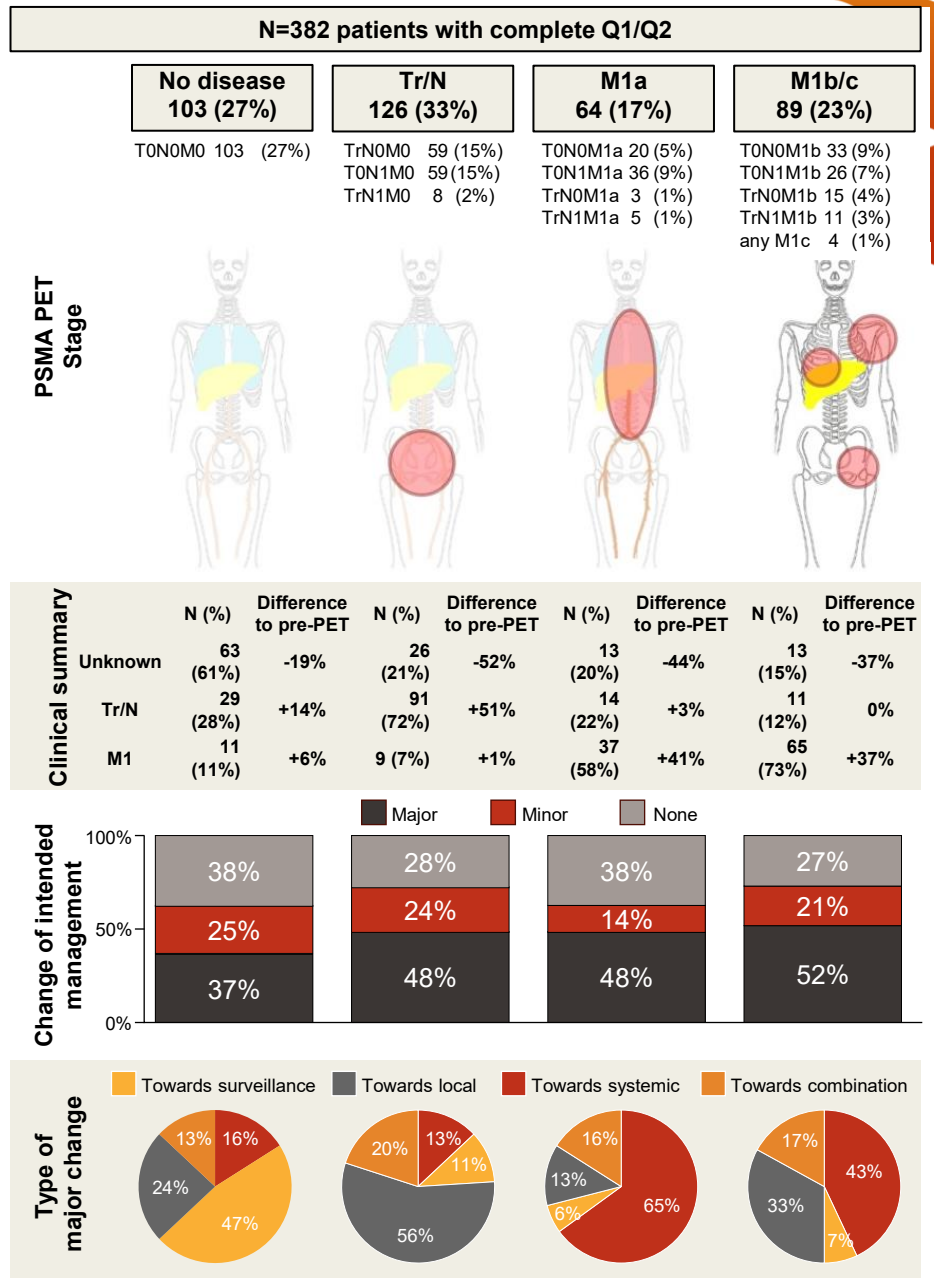


Image adapted from Fendler WP, et al., 2020.
^{68}Ga-PSMA PET, Gallium-68 prostate-specific membrane antigen positron emission tomography; BCR, biochemical recurrence; CT, computed tomography; NaF, sodium flouride; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; Q1, pre-PET questionnaire; Q2, post-PET questionnaire.
Fendler WP, et al. *J Nucl Med* 2020 Dec;61(12):1793–1799.

PSMA-PET restaging (^{68}Ga-PSMA-11)

- N=197, mixed group
- In total, a 69% change in staging:

  = 38% upstaging

  = 30% downstaging

- Influence on management* after PSMA PET-CT

57%

Impact of PSMA PET-CT imaging on staging of PCa

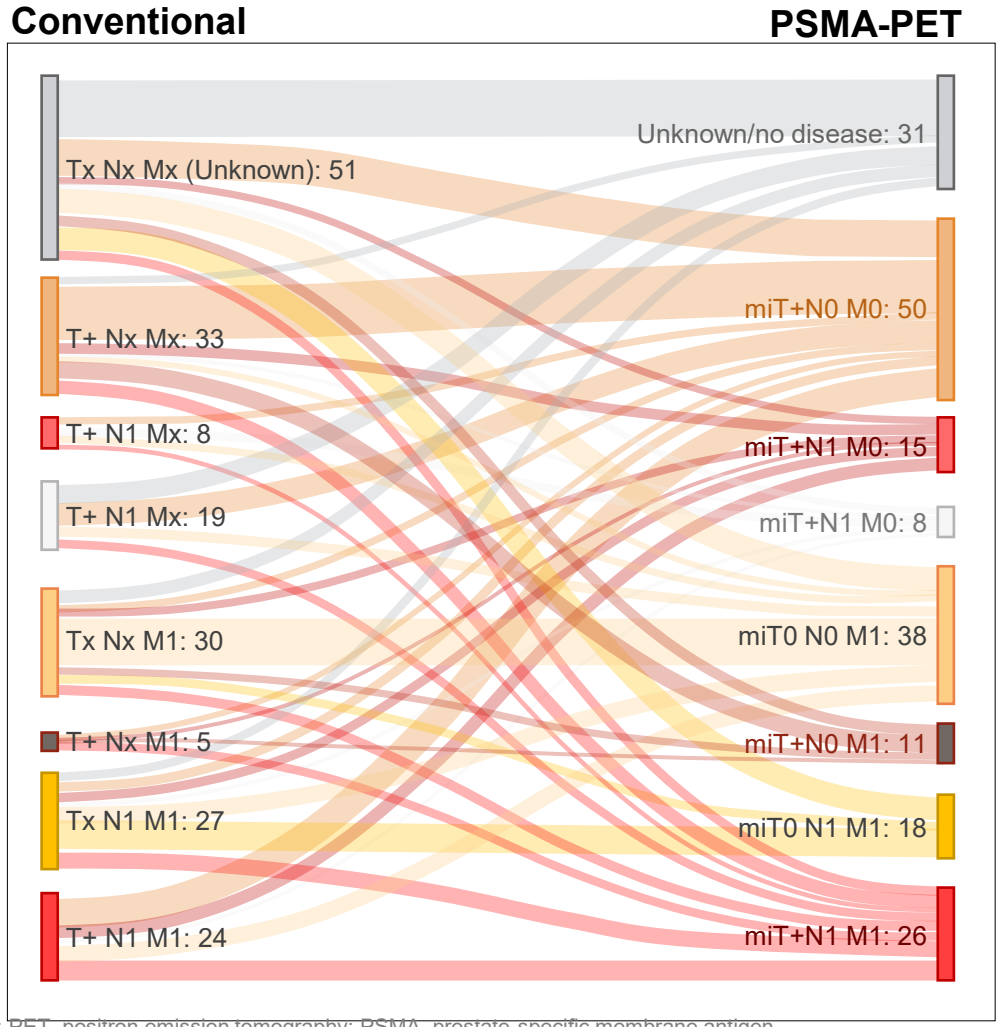


Figure adapted from Sonni I, et al., 2020.
*Change in management data available for 182/197 patients (92%).
^{68}Ga-PSMA PET, Gallium-68 prostate-specific membrane antigen positron emission tomography; CT, computed tomography; PET, positron emission tomography; PSMA, prostate-specific membrane antigen.
Sonni I, et al. *J Nucl Med* 2020;61:1153–1160.

^{68}Ga-PSMA PET positivity depending on PSA

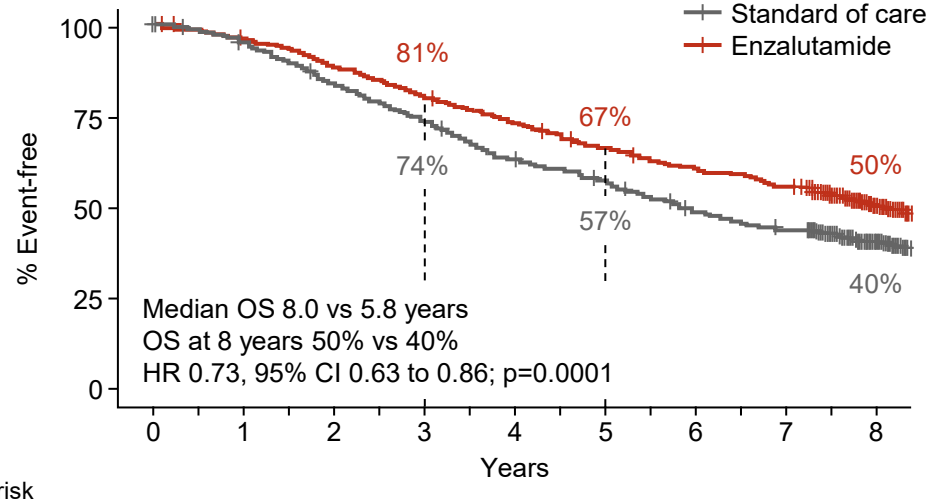
PSA (ng/ml)	^{68}Ga-PSMA PET positivity, %
<0.2	33 (CI: 16–51)
0.2–0.49	45 (CI: 39–52)
0.5–0.99	59 (CI: 50–68)
1.0–1.99	75 (CI: 66–84)
≥2.0	95 (CI: 92–97)

Table adapted from Conford P, et al., 2025.
^{68}Ga-PSMA PET, Gallium-68 prostate-specific membrane antigen positron emission tomography; CI, confidence interval; PSA, prostate-specific antigen.
Cornford P, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2025_2025-03-24-120144_rinw.pdf. Last accessed: June 2025.

Bicalutamide – challenged as the standard of care for CAB → ENZAMET: Enzalutamide + ADT vs. NSAA + ADT

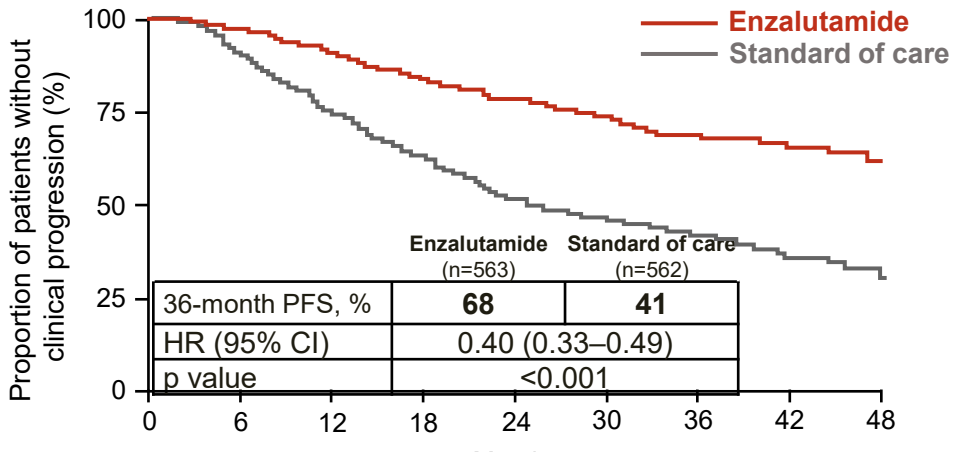
- Bicalutamide has long been shown to be inferior to castration in terms of time to treatment failure, disease progression, subjective response, and survival time[1]
- Enzalutamide had an OS and clinical PFS benefit compared with the standard of care treatment arm (bicalutamide, nilutamide or flutamide) for mHSPC[2,3]

OS*—ENZAMET trial† (mHSPC)[3]



No. at risk									
Standard of care	562	531	468	408	347	312	254	237	129
Enzalutamide	563	541	499	451	410	369	336	309	165

Clinical PFS‡—ENZAMET trial† (mHSPC)[2]



No. at risk									
Enzalutamide	563	547	507	468	424	284	156	84	36
Standard care	562	512	418	346	272	182	96	50	17

Figure (left) adapted from Zhang AY, et al., 2025;[3] Figure (right) adapted from Davis ID, et al., 2019.[2]

*Data cut-off: 30 June 2024; †ENZAMET was not powered to analyse the results of OS in individual subgroups. Therefore, an improvement in OS cannot be demonstrated formally in any subgroup, including patients with mHSPC taking XTANDI + LHRH therapy with or without concomitant docetaxel; ‡Clinical PFS was determined by results on imaging, symptoms, signs or changes in therapy; ‡ Data cut-off: February 28, 2019.

2L, second-line; ADT, androgen deprivation therapy; CAB, complete androgen blockade; CI, confidence interval; HR, hazard ratio; LHRH, luteinising hormone releasing hormone; mHSPC, metastatic hormone-sensitive prostate cancer; NSAA, non-steroidal anti-androgen; OS, overall survival; PFS, progression-free survival.

1. Bales GT, et al. *Urology* 1996;47:38-43; 2. Davis ID, et al. *N Engl J Med* 2019;381:121-131; 3. Zhang AY, et al. Poster presented at ASCO 2025. 30 May–03 June 2025, Chicago, IL, USA. Abstract 5090.

LATITUDE trial[1]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer

Karim Fizazi, M.D., Ph.D., NamPhuong Tran, M.D., Luis Fein, M.D., Nobuaki Matsubara, M.D., Alfredo Rodriguez-Antolin, M.D., Ph.D., Boris Y. Alekseev, M.D., Mustafa Özgüroğlu, M.D., Dingwei Ye, M.D., Susan Feyerabend, M.D., Andrew Protheroe, M.D., Ph.D., Peter De Porre, M.D., Thian Kheoh, Ph.D., Youn C. Park, Ph.D., Mary B. Todd, D.O., and Kim N. Chi, M.D., for the LATITUDE Investigators*

STAMPEDE trial[2]

ORIGINAL ARTICLE

Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy

N.D. James, J.S. de Bono, M.R. Spears, N.W. Clarke, M.D. Mason, D.P. Dearnaley, A.W.S. Ritchie, C.L. Amos, C. Gilson, R.J. Jones, D. Matheson, R. Millman, G. Attard, S. Chowdhury, W.R. Cross, S. Gillessen, C.C. Parker, J.M. Russell, D.R. Berthold, C. Brawley, F. Adab, S. Aung, A.J. Birtle, J. Bowen, S. Brock, P. Chakraborti, C. Ferguson, J. Gale, E. Gray, M. Hingorani, P.J. Hoskin, J.F. Lester, Z.I. Malik, F. McKinna, N. McPhail, J. Money-Kyrle, J. O'Sullivan, O. Parikh, A. Protheroe, A. Robinson, N.N. Srihari, C. Thomas, J. Wagstaff, J. Wylie, A. Zarkar, M.K.B. Parmar, and M.R. Sydes, for the STAMPEDE Investigators*

NEJM, 2017

TITAN trial[3]

ORIGINAL ARTICLE

Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D., Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D., Axel S. Merseburger, M.D., Mustafa Özgüroğlu, M.D., Hirotsugu Uemura, M.D., Dingwei Ye, M.D., Kris Deprince, M.D., et al., for the TITAN Investigators*

NEJM, 2019

ARCHES trial[4]

original report

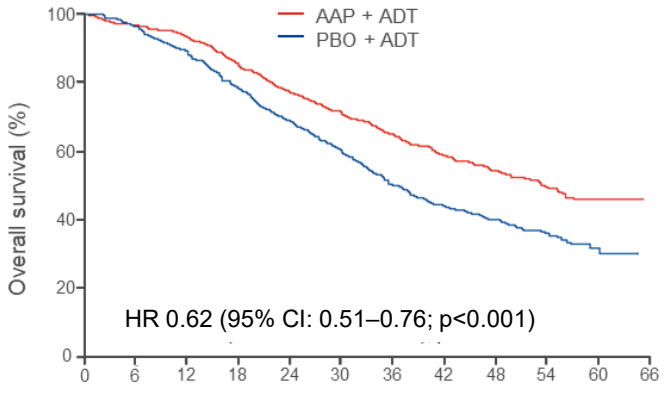
ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer

Andrew J. Armstrong, MD, ScM[1]; Russell Z. Szmulewitz, MD[2]; Daniel P. Petrylak, MD[3]; Jeffrey Holzbeierlein, MD[4]; Arnauld Villers, MD[5]; Arun Azad, MBBS, PhD[6]; Antonio Alcaraz, MD, PhD[7]; Boris Alekseev, MD[8]; Taro Iguchi, MD, PhD[9]; Neal D. Shore, MD[10]; Brad Rosbrook, MS[11]; Jennifer Sugg, MS[12]; Benoit Baron, MS[13]; Lucy Chen, MD[12]; and Arnulf Stenzl, MD[14]

JCO, 2019

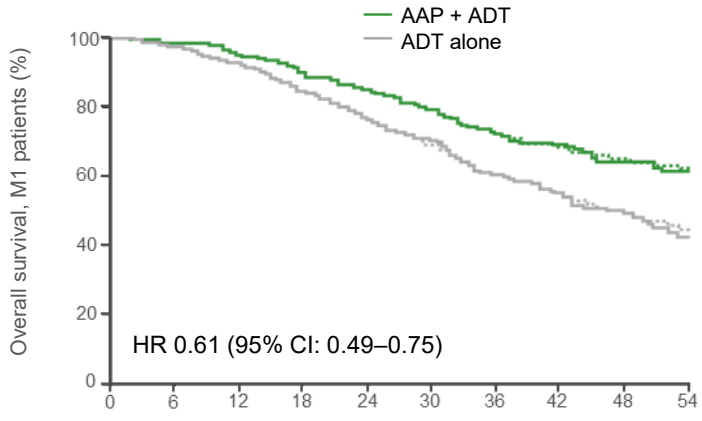
1. Fizazi K, et al. *N Engl J Med* 2017;377:352–360; 2. James ND, et al. *N Engl J Med* 2017;377:338–351; 3. Chi KN, et al. *N Engl J Med* 2019;381:13–24; 4. Armstrong AJ, et al. *J Clin Oncol* 2019;37:2974–2986.

LATITUDE trial[1]



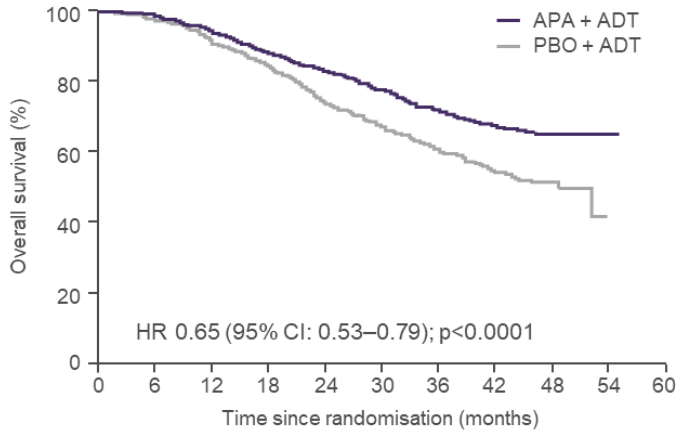
No. at risk (no. censored)												
AAP + ADT	597	565 (14)	529 (28)	479 (34)	425 (42)	389 (46)	351 (50)	311 (57)	240 (106)	124 (105)	40 (282)	0 (322)
Placebo plus ADT	602	564 (17)	505 (34)	432 (47)	368 (58)	315 (37)	256 (74)	220 (79)	165 (114)	69 (197)	23 (237)	0 (259)

STAMPEDE trial[2]



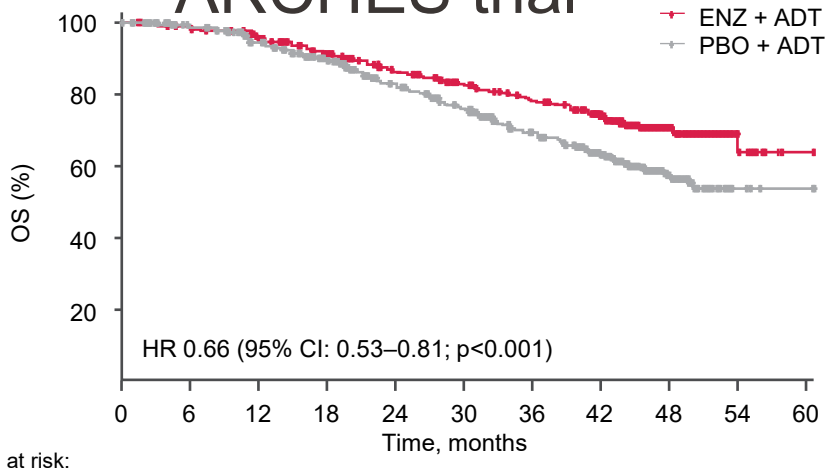
No. at risk (no. of deaths)									
AAP + ADT	500	(22)	469	(50)	415	(57)	256	(18)	81
ADT alone	502	(35)	460	(80)	371	(73)	215	(23)	60

TITAN trial[3]



No. at risk												
Apalutamide	525	513	489	452	425	394	362	227	52	3	0
Placebo	527	510	474	436	374	339	301	181	43	0	0

ARCHES trial[4]



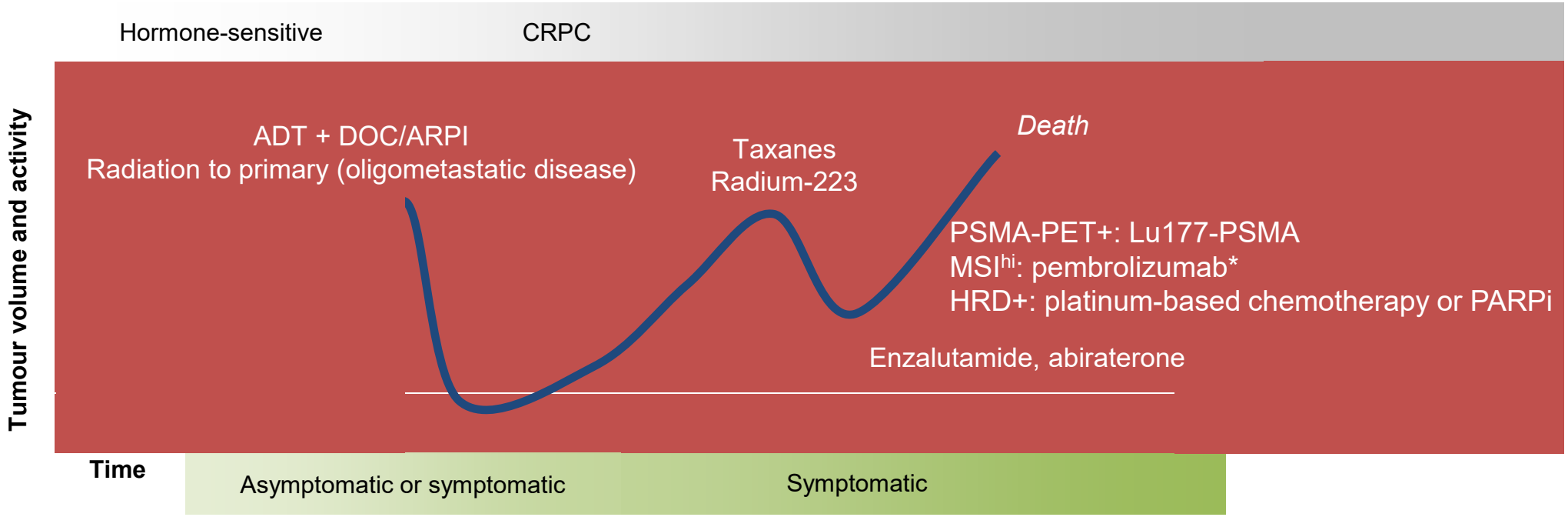
No. at risk:												
ENZ + ADT	574	559	535	498	457	427	396	316	120	17	1
PBO + ADT	576	548	511	468	404	363	322	232	80	4	1

Data shown are for illustrative purposes only, and direct comparisons should not be drawn. Figures adapted from the respective references.[1-4]

AAP, abiraterone acetate + prednisolone; ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; ENZ, enzalutamide; HR, hazard ratio; PBO, placebo.

1. Fizazi K, et al. *N Engl J Med* 2017;377:352–360; 2. James ND, et al. *N Engl J Med* 2017;377:338–351 ;3. Chi KN, et al. *N Engl J Med* 2021;39:2294–2303; 4. Armstrong AJ, et al. *J Clin Oncol* 2022;40:1616–1622.

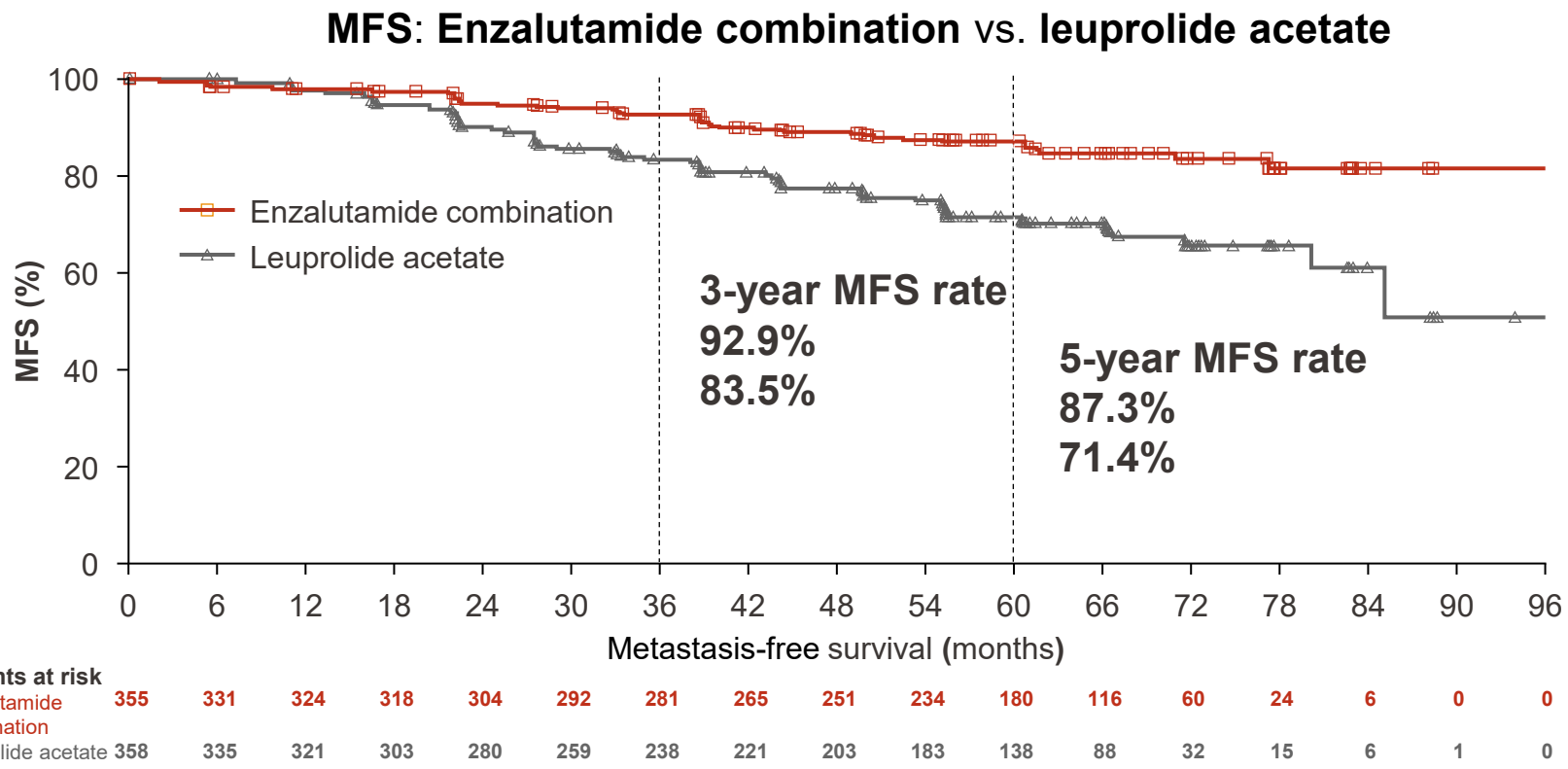
De novo mHSPC --> shorter time: rPFS, OS



- Key trials: STAMPEDE, LATITUDE, CHAARTED, ARCHES, TITAN
  - Earlier use of potent AR-targeted therapy changes the algorithm for subsequent therapies
  - Integration of chemotherapy with hormonal therapies, such as ADT or novel AR-targeted therapies

*Not approved in the EU.
ADT, androgen deprivation therapy; AR, androgen receptor; ARPI, androgen receptor pathway inhibitor; CRPC, castration-resistant prostate cancer; DOC, docetaxel; HRD, homologous recombinant deficiency; mHSPC, metastatic hormone-sensitive prostate cancer; MSI^{hi}, microsatellite instability – high; PARPi, poly (ADP-ribose) polymerase inhibitor; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; rPFS, radiographic progression-free survival.
Speaker's opinion.

The 1L treatment in mHSPC has the greatest clinical outcome: Learnings from nmHSPC



	Enzalutamide combination (n=355)	Leuprolide acetate (n=358)
Median follow-up, months	60.7	60.6
Events, n (%)	45 (13)	92 (26)
Per BICR, median MFS (95% CI), months	NR (NR)	NR (85.1–NR)

HR (95% CI): 0.42 (0.31–0.61); p<0.0001

EMBARK (N=1068)

Randomised Phase III study

High-risk BCR nmHSPC after local therapy

Patient population

- PSA ≥1 ng/ml (post-RP)
- PSA ≥2 ng/ml nadir (post-RT)
- PSADT ≤9 months
- T ≥150 ng/dl
- No distant mets (bone scan, CT or MRI)

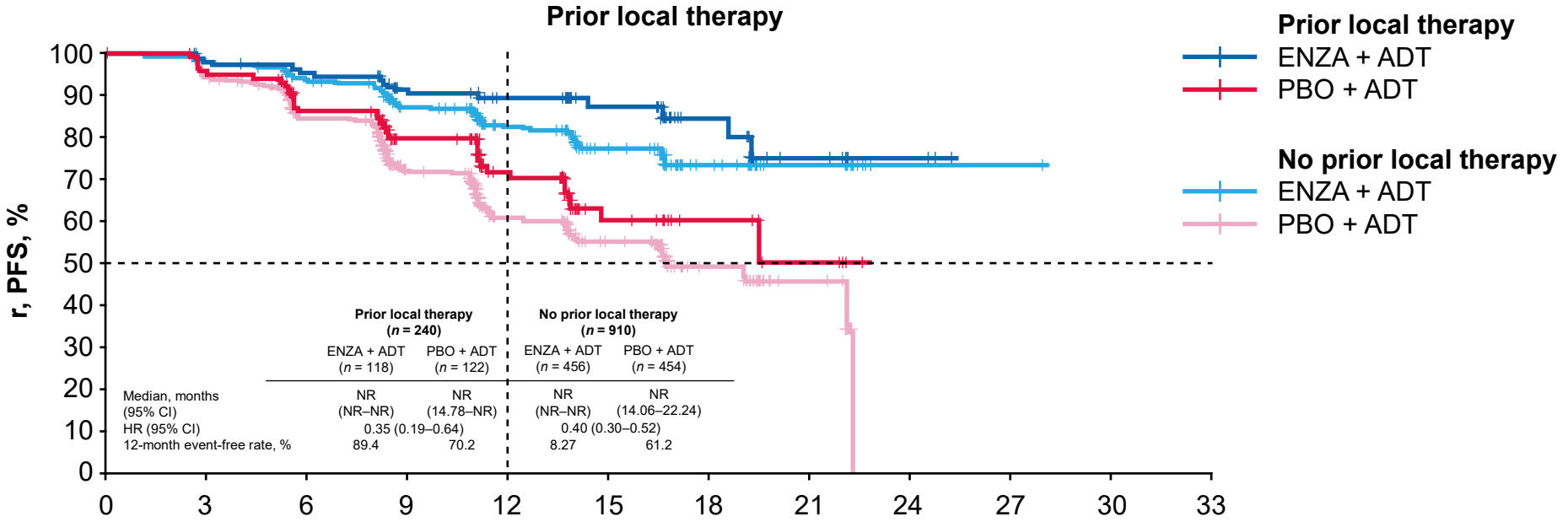
A consistent treatment effect was seen for investigator-assessed MFS: HR 0.47 (95% CI: 0.37–0.67); p<0.0001

Figure adapted from Freedland SJ, et al., 2023.

1L, first-line; BCR, biochemical recurrence; BICR, blinded independent committee review; CI, confidence interval; CT, computed tomography; HR, hazard ratio; MFS, metastasis-free survival; mHSPC, metastatic hormone-sensitive prostate cancer; MRI, magnetic resonance imaging; nmHSPC, non-metastatic hormone-sensitive prostate cancer; NR, not reached; PSA, prostate-specific antigen; PSADT, prostate -specific antigen doubling time; RP, radical prostatectomy; RT, radiotherapy; T, testosterone.

Freedland SJ, et al. *N Engl J Med* 2023;389:1453–1465.

In mHSPC, the risk of a rPFS event was reduced with enzalutamide + ADT compared with placebo + ADT, regardless of prior local treatment



Number at risk

Prior local therapy												
ENZA + ADT	118	113	108	81	63	44	19	10	3	0	0	0
PBO + ADT	122	110	99	74	46	21	10	4	0	0	0	0
No prior local therapy												
ENZA + ADT	456	403	385	289	193	100	43	13	1	1	0	0
PBO + ADT	454	401	346	240	145	85	29	6	0	0	0	0

Figure adapted from Azad AA< et al., 2022.
*Local treatment was defined as a previous radical prostatectomy and/or radiation of the prostate area.
ADT, androgen deprivation therapy; CI, confidence interval; ENZA, enzalutamide; HR, hazard ratio; NR, not reached; PBO, placebo; rPFS, radiographic progression-free survival.
Azad AA, et al. *Prostate Cancer Prostatic Dis* 2022;25;274–282.

Diabetes and the Prostate: Elevated Fasting Glucose, Insulin Resistance and Higher Levels of Adrenal Steroids in Prostate Cancer

by Stefan Zoltán Lutz [1,2,3], Jörg Hennenlotter [4], Andras Franko [1,2,5], Corinna Dannecker [1,2], Louise Fritsche [1,2], Konstantinos Kantartzis [1,2,5], Róbert Wagner [2,3,5], Andreas Peter [1,2,6], Norbert Stefan [1,2,5], Andreas Fritsche [1,2,5], Tilman Todenhöfer [4], Arnulf Stenzl [4], Hans-Ulrich Häring [1,2,5] and Martin Heni [1,2,6,7,*]

J. Clin. Med. 2022;11:6762

	Control		Prostate cancer			
	Mean	SEM	Mean	SEM	p	P adjusted for age/BMI
Age, years	63.68	0.77	63.47	0.78	0.94	-
BMI, kg/m^2	26.88	0.33	26.73	0.34	0.76	-
Insulin, fasting, pmol/L	78.09	4.8	90.84	4.89	0.004	0.0004
C-peptide, fasting, pmol/L	529.07	22.17	552.5	22.6	0.28	0.13
C-peptide, 120 mins, pmol/L	2528.69	102.23	2366.45	103.71	0.41	0.45
Non-esterified fatty acid, mg/dL	579/.1	25.32	566.44	25.57	0.34	0.35
Triglyceride, mg/dL	130.59	5.79	95.41	5.93	<0.0001	<0.0001
Cholesterol, mg/dL	205.55	3.68	195.36	3.97	0.07	0.06
HDL-cholesterol, mg/dL	51.72	1.14	52.41	1.23	0.74	0.84
LDL-cholesterol, mg/dL	123.32	3.29	118.36	3.55	0.37	0.36
C-reactive protein, mg/dL	0.14	0.1	0.32	0.14	0.45	0.36
Intrahepatic lipids, %	6.14	0.88	5.95	0.72	0.15	0.21
AUC C-peptide 0-120/AUC glucose 0-120	261.97	8.05	267.75	8.25	0.42	0.66
AUC C-peptide 0-30/AUC glucose 0-130	153.11	5.39	156.67	5.49	0.47	0.47
Testosterone, nmol/L	13.06	0.46	13.28	0.46	0.98	0.9

Table adapted from Lutz S, et al., 2022.[1]

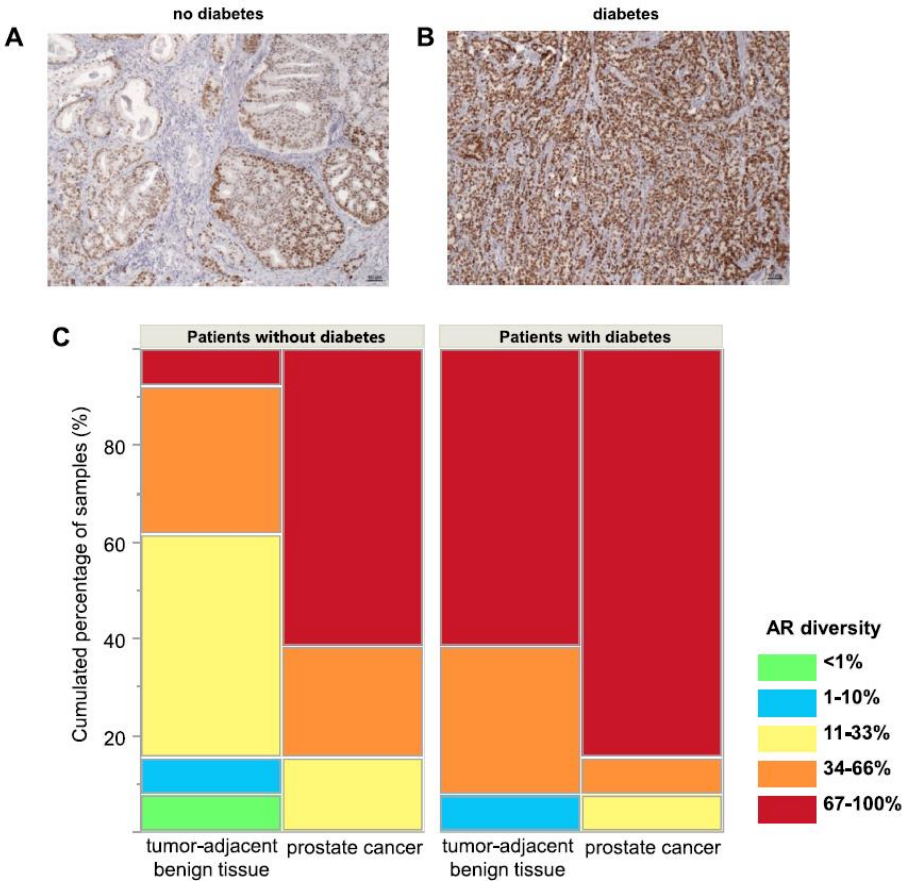
AUC, area under the curve; BMI, body mass index; HDL, high density lipoprotein; LDL, low density lipoprotein; SEM, standard error of the mean.

1. Lutz S, et al. *J Clin Med* 2022;11:6762; 2. Lutz S, et al. *Mol Metab* 2018;8:158–166.

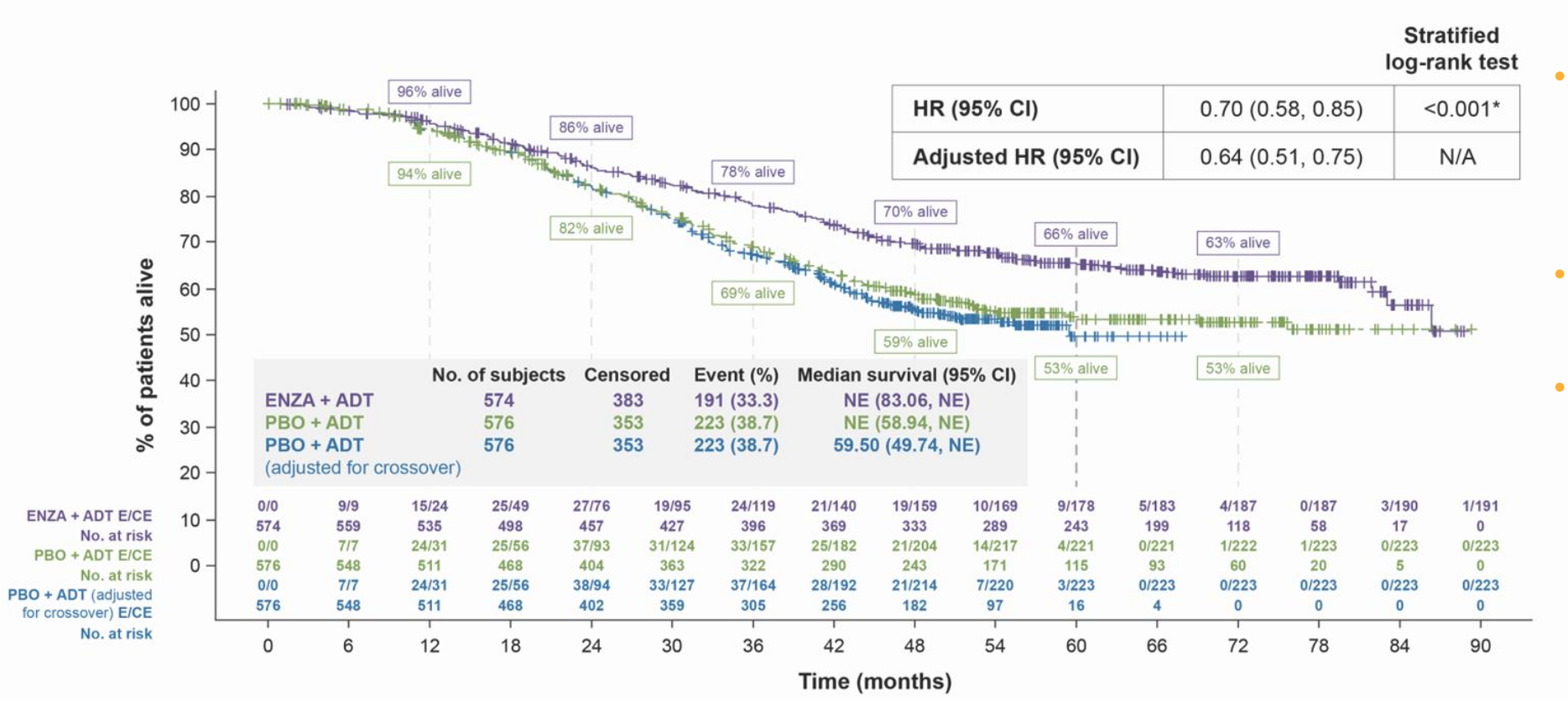
Androgen receptor overexpression in prostate cancer in type 2 diabetes

Stefan Zoltán Lutz [1,2,3], Jörg Hennenlotter [4], Marcus Oliver Scharpf [5], Corinna Sailer [2,3], Louise Fritsche [2,3], Vera Schmid [1,2,3], Konstantinos Kantartzis [1,2,3], Robert Wagner [1,2,3], Rainer Lehmann [1,2,3], Lucia Berti [2,3,6], Andreas Peter [1,2,3], Harald Staiger [2,3,7], Andreas Fritsche [1,2,3], Falko Fend [5], Tilman Todenhöfer [4], Arnulf Stenzl [4], Hans-Ulrich Häring [1,2,3,*], Martin Heni [1,2,3]

Mol Metab. 2018; 8:158–16



ARCHES: Overall survival (ITT)

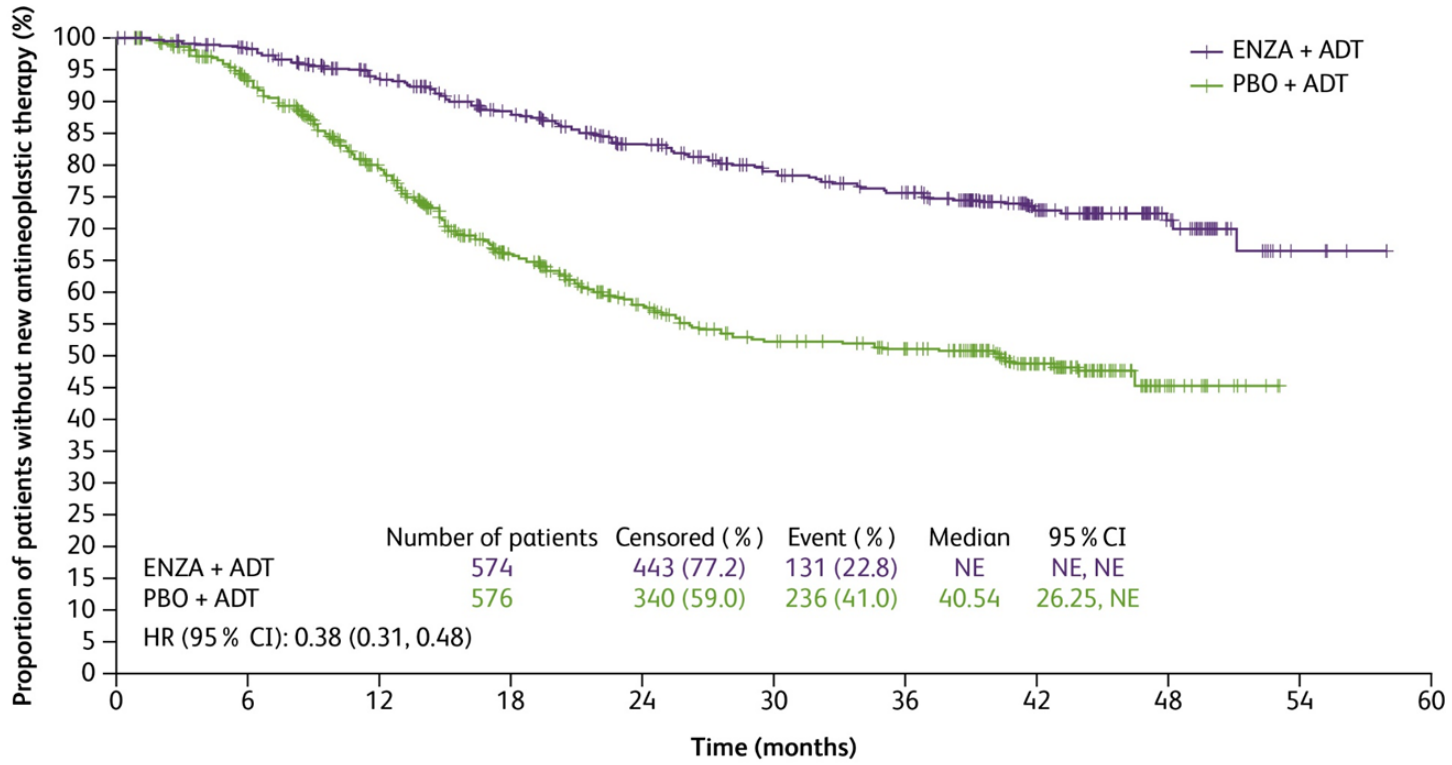


- As of July 31, 2024: 637 deaths (ENZA + ADT, 191; PBO + ADT, 223; PBO + ADT adjusted for crossover, 223) were observed
- Median follow-up time: 61.4 months
- Median treatment duration:
  - ENZA + ADT: 41.7 months
  - PBO + ADT: 13.8 months
  - PBO + ADT crossover: 44.2 months

- **Enzalutamide + ADT significantly improved overall survival by 30% vs. placebo + ADT (p <0.001)**

Figure adapted from Armstrong AJ, et al., 2025.
ADT, androgen deprivation therapy; CI, confidence interval; ENZA, enzalutamide; HR, hazard ratio; ITT, intent-to-treat; NE, not evaluable; PBO, placebo.
Armstrong AJ, et al. Presented at ASCO 2025, May 30–June 3, 2025. 5005.
MAT-NL-XTD-2025-00032 | July 2025

Time to subsequent antineoplastic therapy (ITT)



Patients at risk											
ENZA + ADT	574	542	487	432	378	341	313	193	59	3	0
PBO + ADT	576	507	396	275	210	175	159	104	20	0	0

First antineoplastic therapy for prostate cancer after treatment discontinuation

First antineoplastic PCa therapy	ENZA + ADT	PBO + ADT*
Overall, n	131	221
Docetaxel, n (%)	48 (8.4)	71 (12.3)
Abiraterone, n (%)	26 (4.5)	42 (7.3)
ENZA, n (%)	7 (1.2)	61 (10.6)
Bicalutamide/flutamide, n (%)	8 (1.4)	23 (4.0)
Cabazitaxel, n (%)	11 (1.9)	6 (1.0)
Sipuleucel-T, n (%)	4 (0.7)	6 (1.0)
Radium, n (%)	6 (1.0)	4 (0.7)
Other, n (%)	23 (4.0)	12 (2.1)

- Inclusive of crossover (n=184), 42% of patients who were initially treated with PBO + ADT received ENZA + ADT, with a total of 70% of patients initially treated with PBO + ADT receiving any proven life-prolonging therapy subsequent to study treatment

Figure and Table adapted from Armstrong AJ, et al., 2022.
*Excludes medications started after open-label enzalutamide.
ADT, androgen deprivation therapy; CI, confidence interval; ENZA, enzalutamide; HR, hazard ratio; ITT, intent-to treat; NE, not evaluable; PBO, placebo; PCa, prostate cancer.
Armstrong AJ, et al. *J Clin Oncol* 2022;40:1616–1622.
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Radiographic progression with and without prostate-specific antigen rise in patients with advanced prostate cancer treated with enzalutamide

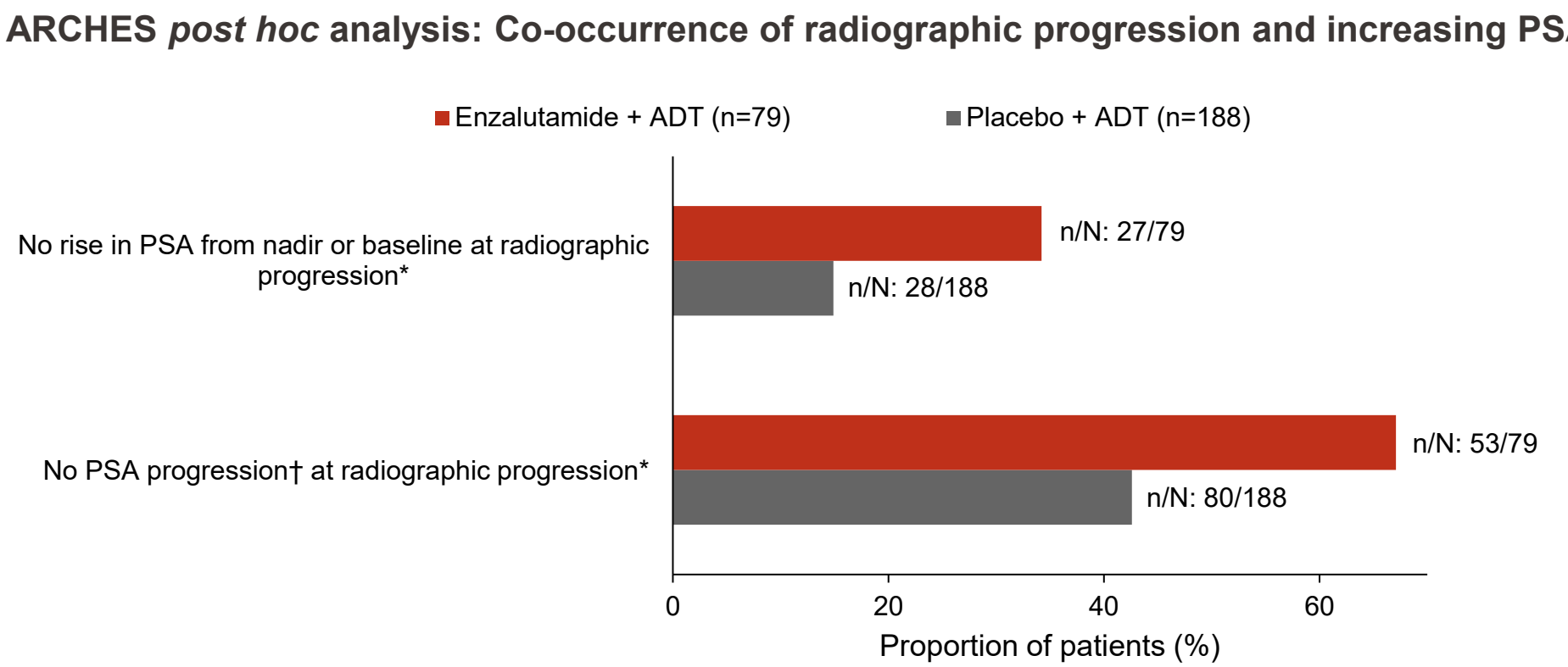
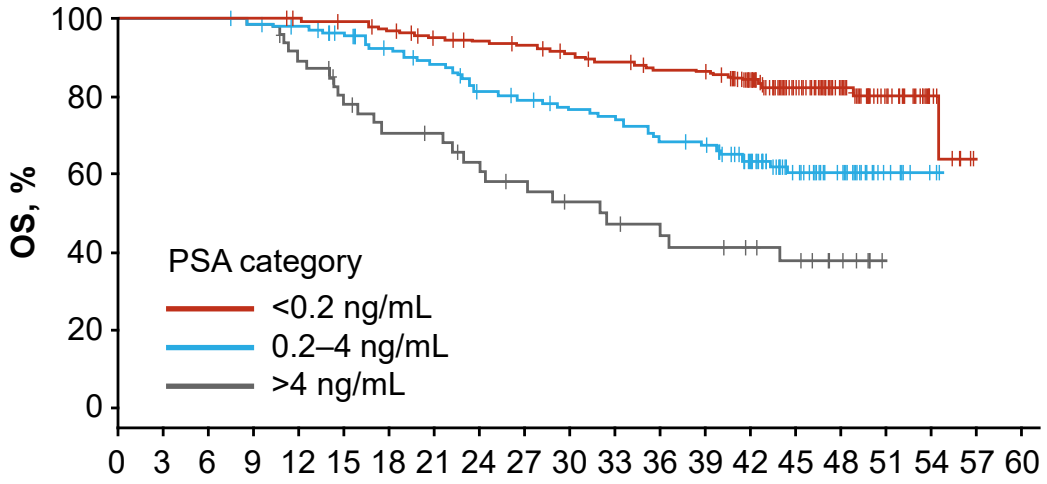


Figure adapted from Armstrong AJ, et al., 2022.
*Radiographic progression was assessed by independent central review or death (defined as death from any cause within 24 weeks from study drug discontinuation), whichever occurred first.
†PSA progression was defined as a ≥25% increase and an absolute increase of ≥2 ng/mL above the nadir, confirmed by a second consecutive value at least 3 weeks later.ADT, androgen deprivation therapy; PSA, prostate-specific antigen; rPD, radiographic progressive disease.
Armstrong AJ, et al. Poster presented at ASCO 2022, 3–7 June 2022, Chicago, IL, USA:5072.
MAT-NL-XTD-2025-00032 | July 2025

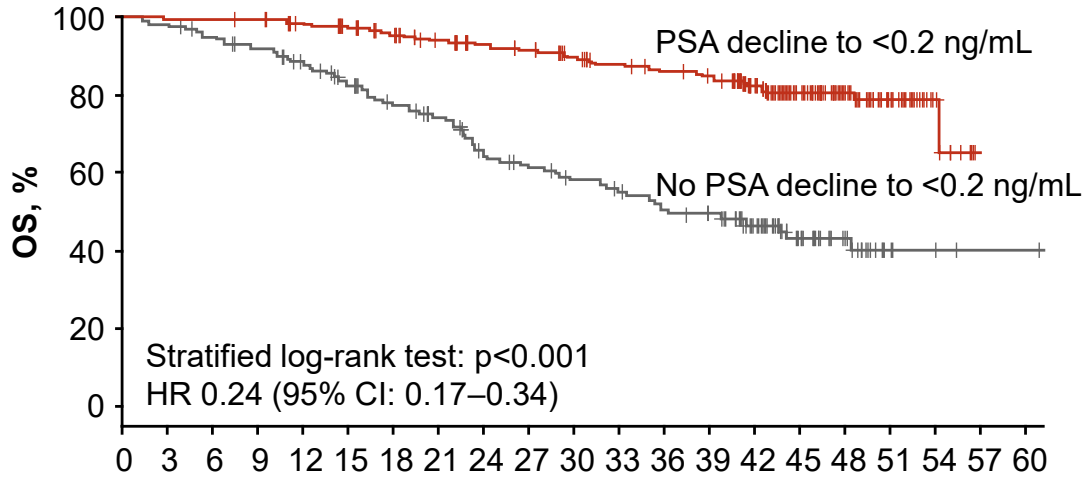
Results: Efficacy (OS) with enzalutamide + ADT

OS based on detectable PSA level at 6 months



<0.2 ng/mL																					
No. of events/ cumulative events	0/0	0/0	0/0	0/0	2/2	1/3	5/8	5/13	2/15	4/19	5/24	6/30	4/34	2/36	6/42	3/45	0/45	2/47	0/47	1/48	0/48
No. at risk	278	278	278	278	274	271	265	256	252	247	239	232	226	223	187	115	67	25	7	0	8
0.2-4 ng/mL																					
No. of events/ cumulative events	0/0	0/0	0/0	2/2	1/3	3/6	5/11	4/15	9/24	3/27	3/30	3/33	7/40	1/41	5/46	2/48	0/48	0/48	0/48	0/48	0/48
No. at risk	140	140	140	136	133	127	119	114	103	99	94	91	84	81	59	37	22	11	2	0	0
>4 ng/mL																					
No. of events/ cumulative events	0/0	0/0	0/0	0/0	5/5	5/10	3/13	0/13	4/17	1/18	2/20	2/22	1/23	1/24	0/24	1/25	0/25	0/25	0/25	0/25	0/25
No. at risk	47	47	47	47	41	34	30	29	24	22	19	17	15	14	12	10	4	0	0	0	0

OS: Detectable vs. undetectable PSA at 6 months



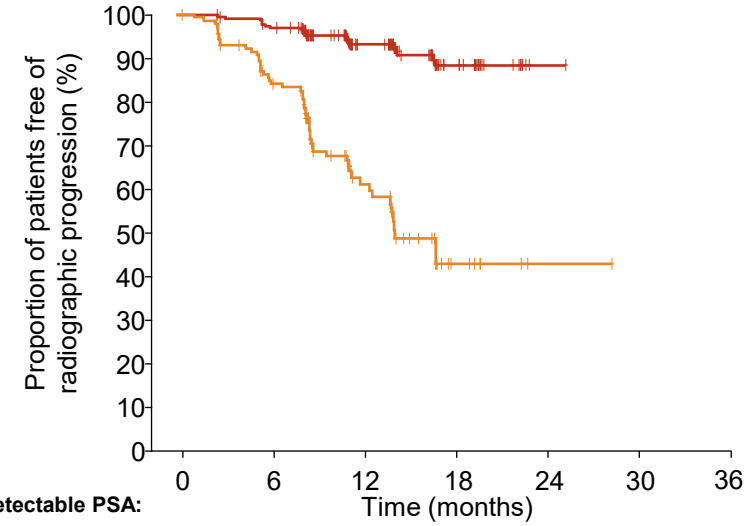
PSA decline to <0.2 ng/mL																					
No. of events/ cumulative events	0/0	1/1	½	0/2	3/5	2/7	6/13	6/19	3/22	5/27	5/32	7/39	6/45	3/48	8/56	5/61	0/61	2/63	0/63	1/64	0/64
No. at risk	348	347	346	345	339	335	327	315	310	304	295	285	277	271	226	142	84	34	8	0	0
No PSA decline to <0.2 ng/mL																					
No. of events/ cumulative events	0/0	2/2	5/7	5/12	6/18	9/27	7/34	4/38	14/52	3/55	5/60	4/64	6/70	1/71	4/75	2/77	0/77	1/78	0/78	0/78	0/78
No. at risk	159	157	150	144	135	121	111	104	87	82	75	70	63	60	42	25	15	4	3	1	1

Figures adapted from: Azad AA, et al., 2025.
ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio;; OS, overall survival; PSA, prostate-specific antigen.
Azad AA, et al. *JAMA Network Open* 2025;8:e258751.

Results for enzalutamide + ADT

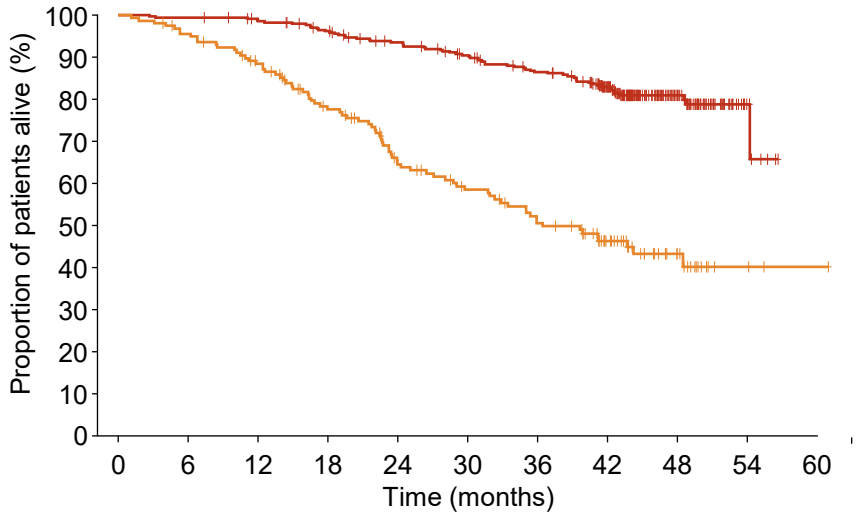
rPFS*

Undetectable PSA	Patients, n	Median	95% CI	HR (95% CI)
Yes	348	NE	(NE, NE)	0.14
No	159	14.00	(12.39– NE)	(0.09–0.23)



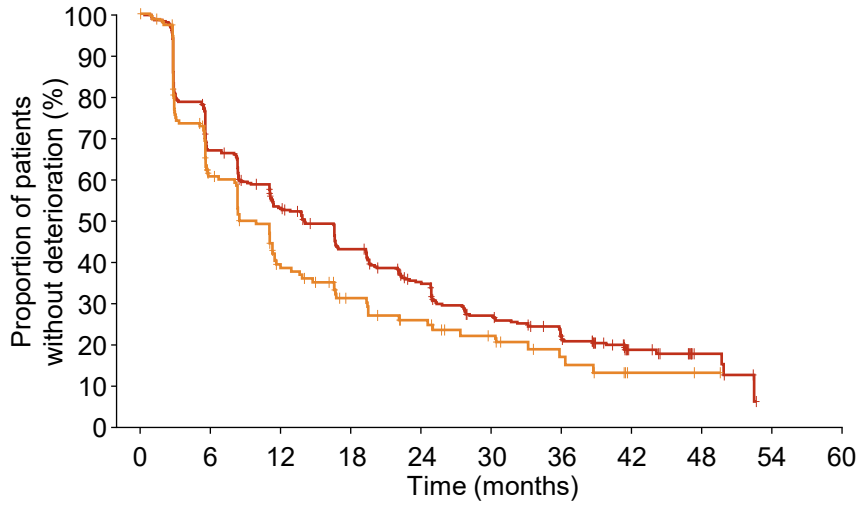
OS*

Undetectable PSA	Patients, n	Median	95% CI	HR (95% CI)
Yes	348	NE	(54.21–NE)	0.24
No	159	36.44	(29.73– 48.46)	(0.17–0.34)



Time to First Deterioration in FACT-P Total Score†‡

Undetectable PSA	Patients, n	Median	95% CI	HR (95% CI)
Yes	348	14.06	(11.14–16.69)	0.78
No	159	9.89	(8.21–11.50)	(0.62–0.98)



Undetectable PSA:								
Patients at risk	Yes	348	320	175	44	1	0	0
	No	159	113	42	7	1	0	0

Yes	348	346	339	327	310	295	277	226	84	8	0
No	159	150	135	111	87	75	63	42	15	3	1

Yes	348	222	169	133	102	74	56	22	7	0	0
No	159	81	45	30	22	15	9	2	1	0	0

- **Patients in the ENZA + ADT arm who reached undetectable levels of PSA had significantly reduced radiographic disease progression and risk of death vs. patients who did not reach undetectable levels of PSA**
- **Deterioration in overall QoL was delayed in this group compared with patients with detectable PSA levels after treatment**
- **A stepwise multivariate analysis identified initial diagnosis (M0 vs. M1: OR 4.33; p=0.0013) and baseline PSA levels (≤median** or >median: OR 3.34; p<0.0001) as predictors of undetectable PSA levels in the ENZA + ADT arm**

Figures adapted from Azad AA, et al., 2025.

*The data cut-off date for rPFS is 14 October 2018, whereas the data cut-off date for OS is 28 May 2021; †The data cut-off for time to first deterioration of FACT-P is 21 May 2021; ‡The deterioration of QoL is defined as a decrease of ≥10 points in the total FACT-P score from the baseline. In patients with QoL deterioration, the time to deterioration of QoL is defined as the time interval from the date of randomisation to the first date a decline of ≥10 points from the baseline in the total FACT-P score is recorded. In patients without FACT-P progression, the time to deterioration of QoL will be censored on the date the last FACT-P total score is calculable. **Median value of baseline PSA levels in the ENZA + ADT arm was 7.2 ng/ml.

ADT, androgen deprivation therapy; CI, confidence interval; ENZA, enzalutamide; FACT-P, Functional Assessment of Cancer Therapy-Prostate; HR, hazard ratio; M0, non-metastatic; M1, metastatic; NE, not estimable; OR, odds ratio; PSA, prostate-specific antigen; QoL, quality of life; rPFS, radiographic progression-free survival. Azad AA, et al. *JAMA Network Open* 2025;8:e258751.

Enzalutamide was associated with rPFS benefits in patients with mHSPC, irrespective of disease volume and/or risk

rPFS in subgroups stratified by volume of disease and risk[1]

rPFS	ENZ + ADT N (E)	PBO + ADT N (E)	HR (95% CI)
Overall population[1]	**574 (91)**	**576 (201)**	**0.39 (0.30–0.50)**
Volume: Secondary subgroup analysis*[1,2]			
Low-volume disease	220 (14)	203 (47)	0.25 (0.14–0.46)
High-volume disease	354 (77)	373 (154)	0.43 (0.33–0.57)
Risk: *Post hoc* analysis†[2]			
Low risk	275 (35)	281 (76)	0.42 (0.28–0.62)
High risk	261 (55)	250 (122)	0.34 (0.25–0.47)

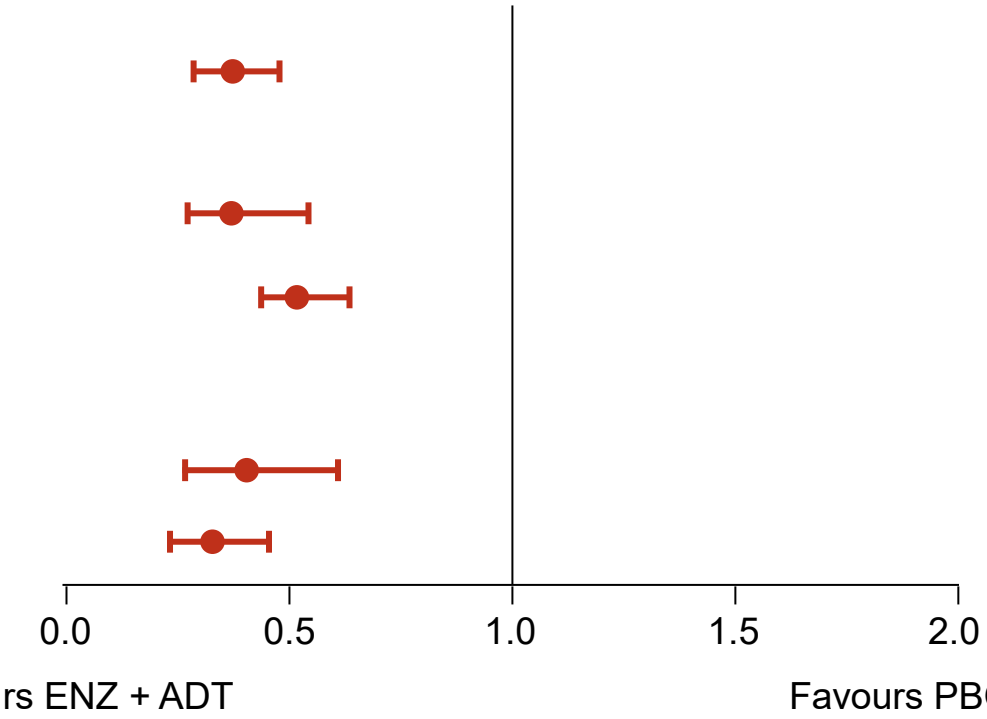


Figure adapted from Stenzl A, et al. 2019[2]
*Stratified by disease volume as defined by CHAARTED criteria; †Stratified by disease risk as defined by the LATITUDE criteria.
ADT, androgen deprivation therapy; CI, confidence interval; E, event; ENZ, enzalutamide; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; PBO, placebo; rPFS, radiographic progression-free survival.
1. Armstrong AJ, et al. *J Clin Oncol* 2019;37:2974–2986; 2. Stenzl A, et al. Presented at ESMO, 27 September–1 October 2019, Barcelona, Spain. Poster 853P.
MAT-NL-XTD-2025-00032 | July 2025

Genitourinary Masterclass

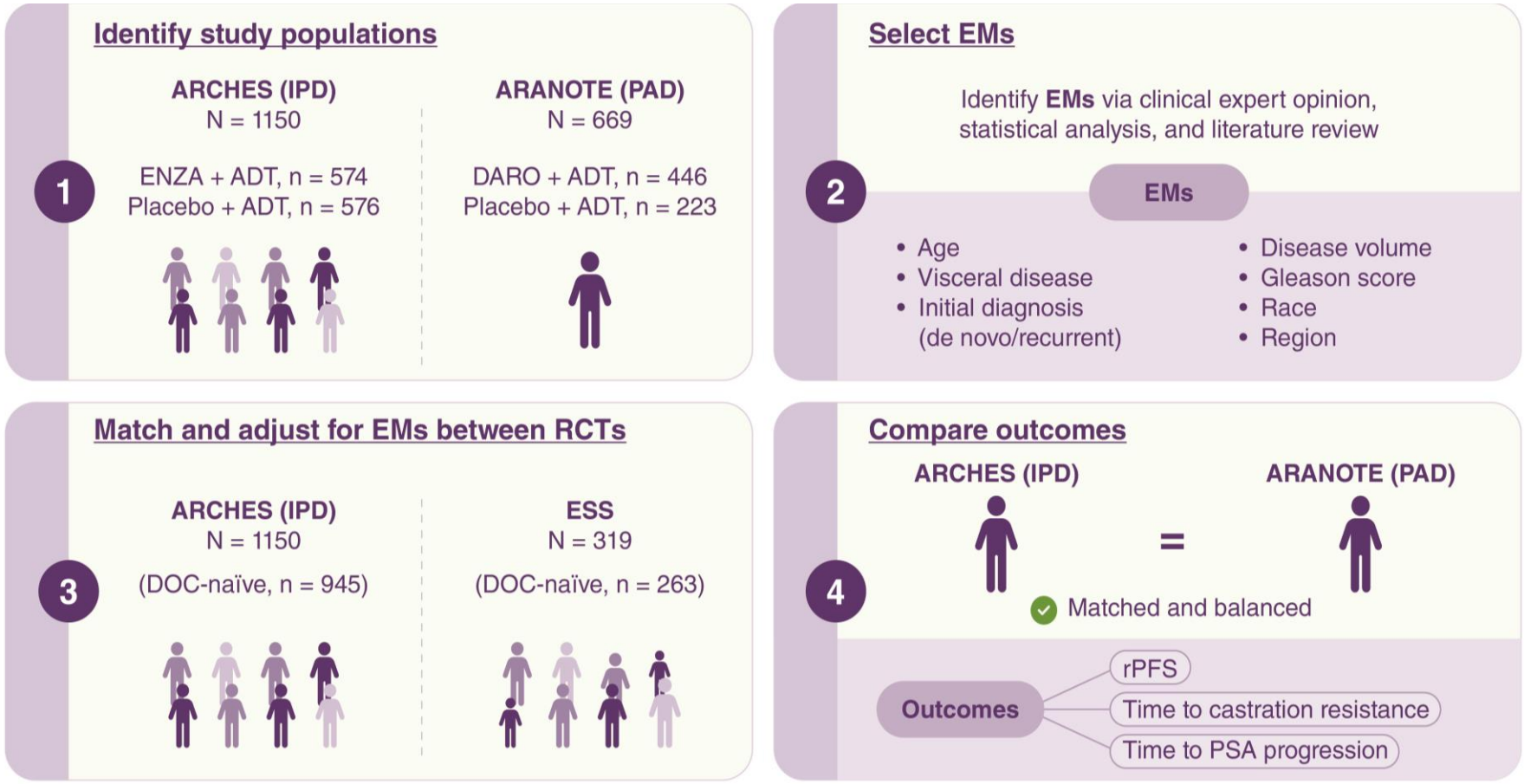
Matching-adjusted indirect comparison between enzalutamide and darolutamide doublet therapy for metastatic hormone-sensitive prostate cancer

Arun Azad, Bhavik J Pandya, Hemant Singh Bhadauria, Arijit Ganguli, Vagia Daki, Georgios Kantidakis, and Andrew Armstrong

Presented at EAU 2025 March 21–25, 2025, in Madrid, Spain

RCC, renal cell carcinoma.

Methods: MAIC analysis



- **Objective:** In the absence of direct head-to-head RCTs, the aim of this analysis was to assess the comparative efficacy of ENZA + ADT vs DARO + ADT in the treatment of patients with mHSPC using the MAIC methodology
- Assessment of heterogeneity between the ARCHES and ARANOTE study designs and populations revealed differences in sample size, geography and length of follow-up, as well as baseline disease characteristics and demographics
- The adjustment for the multiple EMs yielded an estimated ESS of 319 for the total population and 263 for the DOC-naïve population; in both cases, the ESS was sufficient to ensure reliable estimates

No comparative safety analysis was conducted as part of this MAIC, therefore, comparative safety conclusions cannot be drawn.
ADT, androgen-deprivation therapy; DARO, darolutamide; DOC, docetaxel; EM, effect modifier; ENZA, enzalutamide; ESS, effective sample size; IPD, individual patient data; MAIC, matching-adjusted indirect comparison; PAD, published aggregate data; PSA, prostate-specific antigen; RCT, randomised controlled trial; rPFS, radiographic progression-free survival.
Azad A, et al. Presented at EAU 2025 21–24, March 2025, Madrid, Spain. Poster P181.
MAT-NL-XTD-2025-00032 | July 2025

Results: Imbalances in baseline disease and demographic characteristics between the ARCHES and ARANOTE RCTs

Assessment of heterogeneity between the ARCHES and ARANOTE study designs and populations revealed differences in baseline disease characteristics and demographics

Study	Population	Median Age, (Range)	Race White, n (%)	Race Asian, n (%)	Race Black or African American, n (%)	Region North America, n (%)	Region Europe and RoW, n (%)[a]	Region Latin America, n (%)	Region Asia, n (%)	Region Other, n (%)
ARCHES	ENZA + ADT, n = 574	70 (46–92)	466 (81.2)	75 (13.1)	8 (1.4)	86 (15.0)	341 (59.4)	32 (5.6)	104 (18.1)	11 (1.9)
	Placebo + ADT, n = 576	70 (42–92)	460 (79.9)	80 (13.9)	8 (1.4)	77 (13.4)	344 (59.7)	30 (5.2)	113 (19.6)	12 (2.1)
ARANOTE	DARO + ADT, n = 446	70 (43–93)	251 (56.3)	144 (32.3)	41 (9.2)	0 (0.0)	186 (41.7)	119 (26.7)	141 (31.6)	0 (0.0)
	Placebo + ADT, n = 223	70 (45–91)	125 (56.1)	65 (29.1)	24 (10.8)	0 (0.0)	88 (39.5)	72 (32.3)	63 (28.3)	0 (0.0)

Study	Population	ECOG PS 0, n (%)	ECOG PS 1, n (%)	Any prior use of DOC, n (%)	Visceral disease present, n (%)	Any prior use of ADT, n (%)	Median PSA (Range), ng/mL	Gleason score ≥8, n (%)
ARCHES	ENZA + ADT, n = 574	448 (78.0)	125 (21.8)	103 (17.9)	64 (11.1)	534 (93.2)	5.4 (0.0–4,823.5)	386 (67.2)
	Placebo + ADT, n = 576	443 (76.9)	133 (23.1)	102 (17.7)	64 (11.1)	514 (89.2)	5.1 (0.0–19,000.0)	373 (64.8)
ARANOTE	DARO + ADT, n = 446	235 (52.7)	199 (44.6)	0 (0.0)	53 (11.9)	446 (100)	21.4 (0.02–15,915.0)	311 (69.7)
	Placebo + ADT, n = 223	98 (43.9)	117 (52.5)	0 (0.0)	27 (12.1)	223 (100)	21.2 (0.02–8,533.0)	146 (65.5)

ADT, androgen-deprivation therapy; DARO, darolutamide; DOC, docetaxel; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ENZA, enzalutamide; PSA, prostate-specific antigen; RCT, randomised controlled trial; RoW, rest of world.

Azad A, et al. Presented at EAU 2025 21–24, March 2025, Madrid, Spain. Poster P181.

Guideline recommendations

EAU guideline recommendations[1]	Strength
Do not offer AR antagonist monotherapy to patients with M1 disease	Strong
Do not offer ADT monotherapy to patients whose first presentation is M1 disease if they have no contraindications for combination therapy and have sufficient life expectancy to benefit from combination therapy (≥1 year) and are willing to accept the increased risk of side effects	Strong

PSA after 7 months after start of ADT	Median survival on ADT monotherapy
<0.2 ng/ml	75 months
0.2–≤0.4 ng/ml	44 months
>0.4 ng/ml	13 months

[2]

Table (top) adapted from Cornford P, et al., 2025;[1] Table (bottom) adapted from Hussain M, et al., 2006.[2]
ADT, androgen deprivation therapy; AR, androgen receptor; M1, metastatic; PSA, prostate-specific antigen.
1. Cornford P, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2025_2025-03-24-120144_rinw.pdf. Last accessed: June 2025; 2. Hussain, M., et al. *J Clin Oncol* 2006.24:3984.

Summary[1]

- Reducing disease progression is often the primary consideration of treatment
- 1L treatment in HSPC is the most impactful and important choice
- Greater PSA declines and lower PSA concentrations in patients with mHSPC:
  - Are strongly associated with improved long-term clinical outcomes after 3 and 6 months of treatment
  - Are more commonly observed with enzalutamide + ADT vs. placebo + ADT
- ADT + ARPI is the backbone of SOC treatment for mHSPC
- The choice of ARPI should be determined based on patient and disease-related characteristics
- There are contradictions with data that show radiographic disease progression independent of PSA level[2]
- MAIC is a methodology increasingly used to compare active treatments in the absence of a head-to-head trial.
- Specific situations may require the addition of a third treatment to SOC (RT or DOC)
- Sequential use of ARPIs is not recommended in guidelines (EAU 2025)[4]

1L, first-line; ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; DOC, docetaxel; (m)HSPC, (metastatic) hormone-sensitive prostate cancer; MAIC, matching-adjusted indirect comparison; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; SOC, standard of care; RT, radiotherapy.

1. Author's conclusions; 2. Armstrong AJ, et al. Poster presented at ASCO 2022, 3–7 June 2022, Chicago, IL, USA:5072; 3. Azad A, et al. Presented at EAU 2025 21–24, March 2025, Madrid, Spain. Poster P181; 4. Cornford P, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2025_2025-03-24-120144_rinw.pdf. Last accessed: June 2025.

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astellas

Please refer to the EMA SmPC for XTANDI™ (enzalutamide) via the following link: https://www.ema.europa.eu/en/documents/product-information/xtandi-epar-product-information_en.pdf

Scan/click here for the XTANDI™ UK prescribing information

Scan/click here for the XTANDI™ NL SmPC

XTANDI™ is subject to medicinal prescription.
Astellas Pharma B.V., Sylviusweg 62, 2333 BE Leiden, The Netherlands.
EMA, European Medicines Agency; SmPC, Summary of Product Characteristics.
MAT-NL-XTD-2025-00032 | July 2025