EFFICACY AND SAFETY OF DAROLUTAMIDE PLUS ANDROGEN-DEPRIVATION THERAPY IN PATIENTS WITH METASTATIC HORMONE-SENSITIVE PROSTATE CANCER FROM THE PHASE 3 ARANOTE TRIAL

Zachary Klaassen, MD[1], presenting on behalf of Neal D. Shore, MD[2], Bertrand Tombal, MD, PhD[3], Maha Hussain, MD[4], Fred Saad, MD[5], Karim Fizazi, MD, PhD[6], Cora N. Sternberg, MD[7], E. David Crawford, MD[8], Todd Fralich, MD[9], Rui Li, MS[9], Matthew R. Smith, MD, PhD[10]

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DAROLUTAMIDE

INTRODUCTION

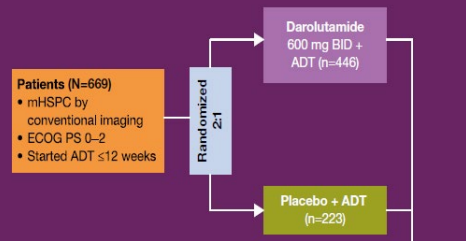
In the Phase 3 ARASENS study, darolutamide + androgen deprivation therapy (ADT) + docetaxel significantly improved overall survival (OS) versus placebo + ADT + docetaxel in patients with metastatic hormone-sensitive prostate cancer (mHSPC)[1]

OBJECTIVE

ARANOTE was designed to evaluate treatment without docetaxel (darolutamide + ADT versus ADT alone) to provide a new treatment option for mHSPC

METHODS

Global, randomized, double-blind, placebo-controlled, Phase 3 study



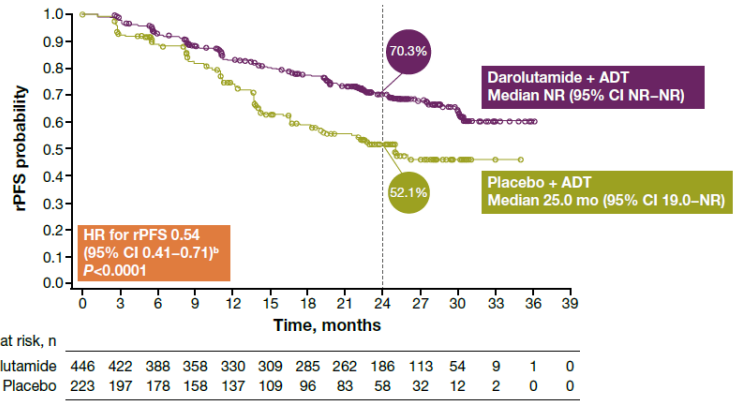
Data-cut off: June 7, 2024
Primary endpoint: rPFS by central blind review

Secondary endpoints: OS, time to initiation of subsequent anticancer therapy, time to mCRPC, time to PSA progression, rates of undetectable PSA (<0.2 ng/mL), time to pain progression (BPI-SF), and safety

ADT, androgen deprivation therapy; BID, twice-a-day; BPI-SF, Brief Pain Inventory (Short Form); ECOG PS, Eastern Cooperative Oncology Group Performance Status; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiologic progression-free survival.

Risk of radiologic progression or death reduced by 46% with darolutamide versus placebo

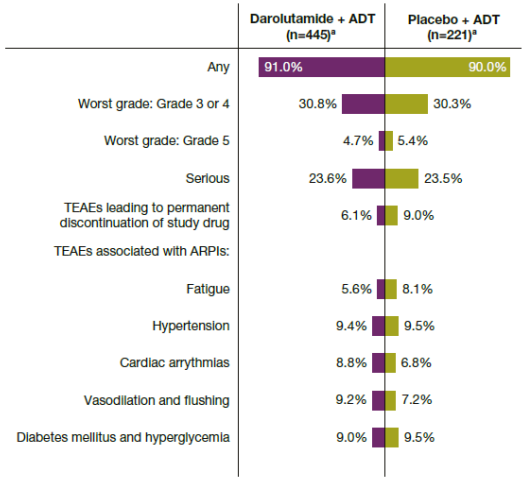
Primary endpoint: rPFS[a]



Patients at risk, n														
Darolutamide	446	422	388	358	330	309	285	262	186	113	54	9	1	0
Placebo	223	197	178	158	137	109	96	83	58	32	12	2	0	0

[a]Primary analysis occurred after 222 events (darolutamide 128; placebo 94). [b]HR and 95% CI were calculated using the Cox model stratified on visceral metastases (y/n) and prior therapy (y/n).
ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; NR, not reached; rPFS, radiologic progression-free survival.

Incidence of treatment-emergent adverse events was similar between groups

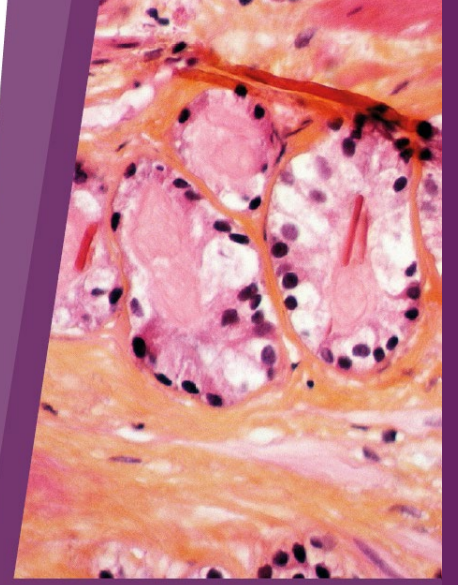


[a]Two patients who were randomized to the placebo group but received darolutamide are analyzed in the darolutamide group for the safety analysis.
ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; TEAE, treatment-emergent adverse event.

Darolutamide showed a benefit across all secondary endpoints

	Overall survival	Time to mCRPC	Time to PSA progression	Time to subsequent systemic therapy	Time to pain progression
Median, months (n/N; %)					
Darolutamide + ADT	NR (103/446; 23.1%)	NR (154/446; 34.5%)	NR (93/446; 20.9%)	NR (68/446; 15.2%)	NR (124/446; 27.8%)
versus	versus	versus	versus	versus	versus
Placebo + ADT	NR (60/223; 26.9%)	13.8 (143/223; 64.1%)	16.8 (108/223; 48.4%)	NR (74/223; 33.2%)	29.9 (79/223; 35.4%)
Stratified HR (95% CI)	0.81 (0.59–1.12)	0.40 (0.32–0.51)	0.31 (0.23–0.41)	0.40 (0.29–0.56)	0.72 (0.54–0.96)

[a]At the time of primary analysis, OS data are immature.
ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; NR, not reached; OS, overall survival; PSA, prostate-specific antigen.



CONCLUSIONS

- Darolutamide + ADT significantly improved rPFS in patients with mHSPC
- Darolutamide showed a benefit across all secondary endpoints with a favorable safety profile
- Darolutamide + ADT without docetaxel should become an additional standard of care for mHSPC

SCAN ME FOR MORE INFO

Medical writing services were provided by Kennedy Shaw, MSc, of Adelphi Communications Ltd (Bollington, UK), funded by Bayer, in accordance with Good Publication Practice 2022 guidelines.

Reference: 1. Smith MR, et al. N Engl J Med 2022;386:1132–42.

Poster presented at the 89th Annual Meeting of the Southeastern Section of the AUA, Grand Hyatt Nashville, Tennessee, March 12–15, 2025.

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Supplementary material

Zachary Klaassen, MD[1], presenting on behalf of Neal D. Shore, MD[2], Bertrand Tombal, MD, PhD[3], Maha Hussain, MD[4], Fred Saad, MD[5], Karim Fizazi, MD, PhD[6], Cora N. Sternberg, MD[7], E. David Crawford, MD[8], Todd Fralich, MD[9], Rui Li, MS[9], Matthew R. Smith, MD, PhD[10]

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Baseline demographics and disease characteristics

	Darolutamide + ADT (n=446)	Placebo + ADT (n=223)
Age, median (range), years	70 (43–93)	70 (45–91)
Race		
White	251 (56.3)	125 (56.1)
Asian	144 (32.3)	65 (29.1)
Black	41 (9.2)	24 (10.8)
Other	10 (2.2)	9 (4.0)
Region		
Asia	141 (31.6)	63 (28.3)
Latin America	119 (26.7)	72 (32.3)
Europe and Rest of World	186 (41.7)	88 (39.5)
ECOG PS		
0	235 (52.7)	98 (43.9)
1–2	211 (47.3)	125 (56.1)
Gleason score ≥8 at initial diagnosis	311 (69.7)	146 (65.6)
Serum PSA, median (range), ng/mL	21.4 (0.02–15,915)	21.2 (0.02–8,533)
Metastases at initial diagnosis		
Yes (de novo)	317 (71.1)	168 (75.3)
No (recurrent)	100 (22.4)	45 (20.2)
Disease volume[a]		
High	315 (70.6)	157 (70.4)
Low	131 (29.4)	66 (29.6)
Visceral metastases		
Yes	53 (11.9)	27 (12.1)
No	393 (88.1)	196 (87.9)
Prior local therapy		
Yes	80 (17.9)	40 (17.9)
No	366 (82.1)	183 (82.1)

Data are presented as n (%) unless otherwise stated.

[a]Disease volume defined by CHAARTED criteria: presence of visceral metastases and/or ≥4 bone metastases with ≥1 beyond vertebral bodies and pelvis (Sweeney CJ, et al. N Engl J Med 2015;373:737–746).

ADT, androgen deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PSA, prostate-specific antigen.

Saad F *et al*. *J Clin Oncol* 2024; 42(36): 4271–4281.

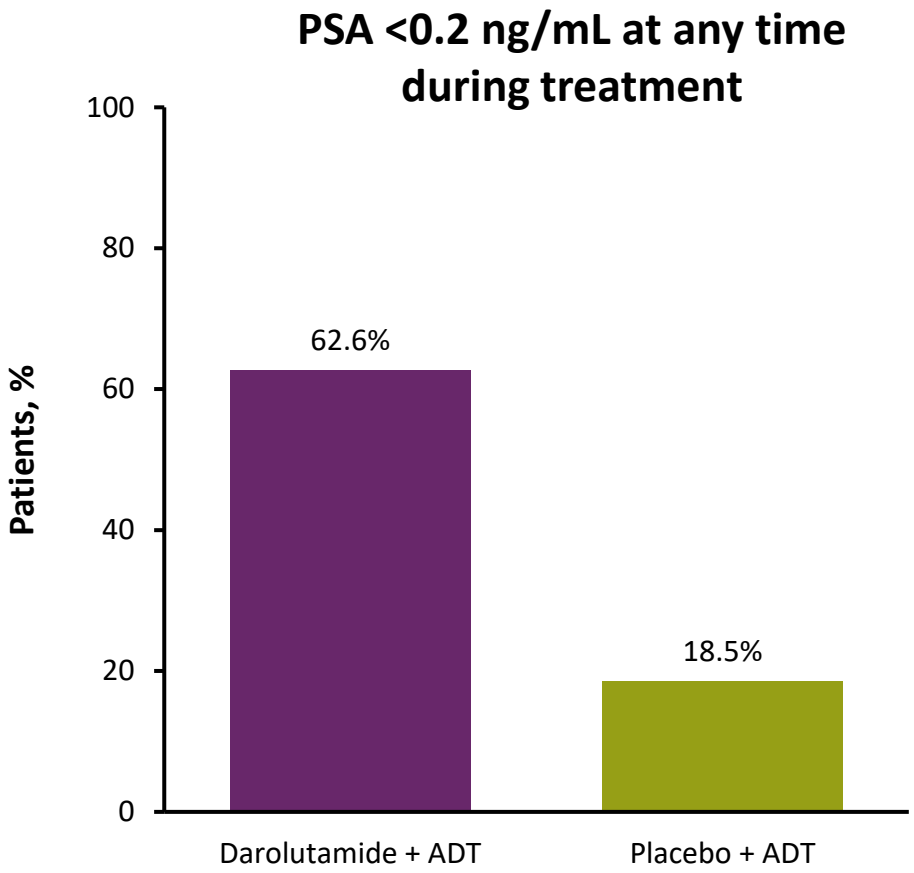
rPFS subgroup analysis and safety

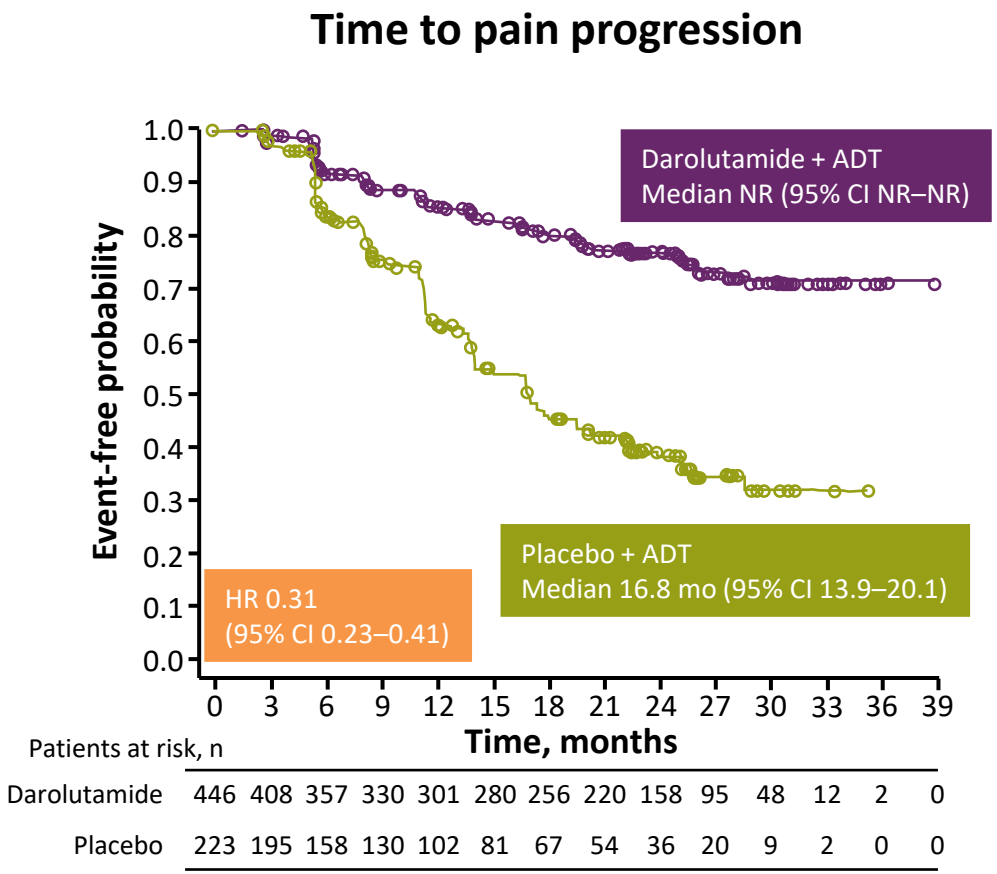
- The benefit of darolutamide on rPFS was consistent across prespecified patient subgroups, including:
  - Patients with high- and low-volume mHSPC (HR, 0.60; 95% CI, 0.44–0.80 and HR, 0.30; 95% CI, 0.15–0.60, respectively)
  - Patients with baseline PSA values < median and ≥ median (HR, 0.55; 95% CI, 0.37–0.81 and HR, 0.55; 95% CI, 0.38–0.80, respectively)
  - Patients with baseline ECOG PS 0 and ≥1 (HR, 0.55; 95% CI, 0.37–0.83 and HR, 0.56; 95% CI, 0.39–0.79, respectively)
  - Patients with baseline Gleason score <8 and ≥8 (HR, 0.46; 95% CI, 0.28–0.75 and HR, 0.58; 95% CI, 0.42–0.81, respectively)

- TEAEs associated with ARPIs were generally similar between treatment groups

HR and 95% CI were calculated from univariate analysis using unstratified Cox regression.
ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; rPFS, radiologic progression-free survival.
Saad F *et al*. *J Clin Oncol* 2024; 42(36): 4271–4281.

Darolutamide showed a higher rate of PSA <0.2 ng/mL and delayed time to PSA progression





Conclusions

- Darolutamide + ADT significantly improved rPFS in patients with mHSPC
- Darolutamide showed a benefit across all secondary endpoints
- Darolutamide had a favorable safety profile
- **Darolutamide + ADT without docetaxel should become an additional standard of care for mHSPC**

- For further information, please see the published article: https://pmc.ncbi.nlm.nih.gov/articles/PMC11654448/

Saad F *et al*. *J Clin Oncol* 2024; 42(36): 4271–4281.