Prostate-specific antigen outcomes of darolutamide and androgen deprivation therapy in patient subgroups by age, comorbidities, and concomitant medications: ARANOTE *post hoc* analyses

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Darolutamide demonstrated consistent efficacy in patients with mHSPC across all patient subgroups, including those who are older, have substantial comorbidities, or require greater use of concomitant medications

SUMMARY

- **What the study was about:** We tested whether darolutamide, a prostate cancer drug taken with hormone therapy, could lower PSA (a blood marker that rises when prostate cancer grows) in men with advanced prostate cancer, and whether it worked the same way in different types of patients
- **It worked in different patient types:** Darolutamide lowered PSA levels better than a placebo (a pill with no medicine inside) across all patient groups, wheth er patients were young or old, had other health conditions like diabetes or heart disease, or were taking many other medications at the same time
- **Cancer stayed under control longer:** Patients receiving darolutamide were more likely to reach very low PSA levels, and when PSA did start rising again, it took about 421 days on average, compared to only 256 days for patients receiving placebo
- **It was well-tolerated:** No new or unexpected safety problems were found, suggesting darolutamide is a reliable treatment option even for patients with complex health

Footnotes:

*Metastatic disease confirmed by conventional imaging as a positive ^{99m}Tc-phosphonate bone scan or soft tissue/visceral metastases on contrast-enhanced abdominal/pelvic/chest CT or MRI, assessed by central review.

†FACT-P comprises 39 questions on prostate cancer-related quality of life in the domains of social/family well-being, functional well-being, physical well-being, emotional well-being, and prostate cancer symptoms.

‡Prostate-specific antigen (PSA) progression with serum testosterone at castrate level <0.50 ng/mL, which is defined as a ≥25% increase above the nadir (lowest at or after baseline) and an increase in absolute value of ≥2 ng/mL above the nadir and at least 12 weeks from the random assignment date, which is confirmed by a second value three or more weeks later. All PSA values between the initial assessment meeting the PSA progression criteria and confirmation assessment must be ≥2 ng/mL and ≥25% increase above the nadir; serum testosterone at castrate level <0.50 ng/mL is requested at initial assessment.

§One of the 13 patients in the placebo group that reported PSA progression reached undetectable PSA only after PSA progression. This patient was not included in the time to PSA progression analyses.

¶Among patients who reported PSA ≥0.2 ng/mL at baseline.

Abbreviations:

ADT, androgen deprivation therapy; **BID**, twice daily; **comorbid**; comorbidities; **conmed**; concomitant medications; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **FACT-P**, Functional Assessment of Cancer Therapy–Prostate; **HR**, hazard ratio; **mCRPC**, metastatic castration-resistant prostate cancer; **mHSPC**, metastatic hormone-sensitive prostate cancer; **OS**, overall survival; **PSA**, prostate-specific antigen; **QoL**, quality of life; **rPFS**, radiological progression-free survival; **Y**, yes.

References:

1. Saad F, et al. J Clin Oncol 2024;42:4271–4281. **2.** Saad F, et al. Annals of Oncology 2025:36S1250. **3.** Saad F, et al. J Clin Oncol 2026;44:178.

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BACKGROUND

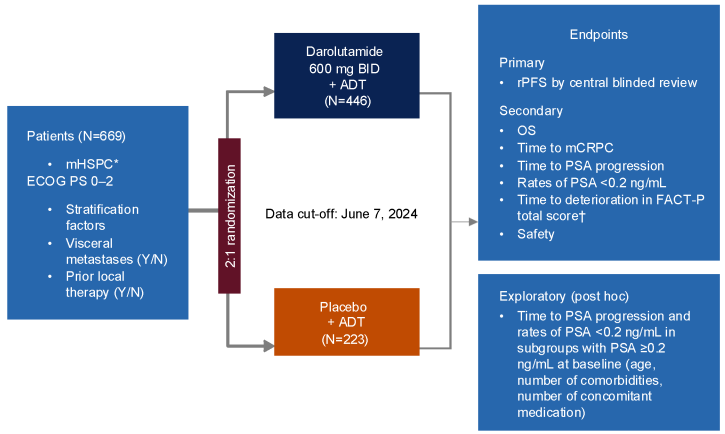
- Darolutamide + ADT significantly improved rPFS versus placebo + ADT (HR 0.54; 95% CI 0.41-0.71; P<0.0001) in the phase 3 ARANOTE trial, with a favorable safety profile, in patients with mHSPC'
  - In a post hoc analysis, efficacy (rPFS, time to mCRPC, and time to PSA progression), QoL, and safety outcomes with darolutamide + ADT were improved in patients with mHSPC versus placebo + ADT, regardless of age?
  - In another *post hoc* analysis, an rPFS benefit was previously seen across all patient subgroups with mHSPC, regardless of the number of comorbidities and concomitant medications reported at baseline with no new safety signals?

OBJECTIVE

- Here, we report the impact of age, comorbidities, and use of ongoing concomitant medications at baseline on PSA outcomes in patients treated with darolutamide + ADT or placebo + ADT

STUDY DESIGN

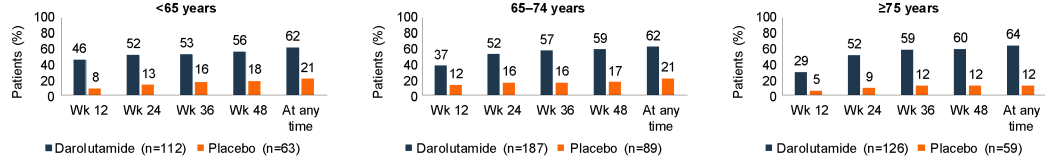
- ARANOTE (NCT04736199) is a global, randomized, double-blind, placebo-controlled, phase 3 study



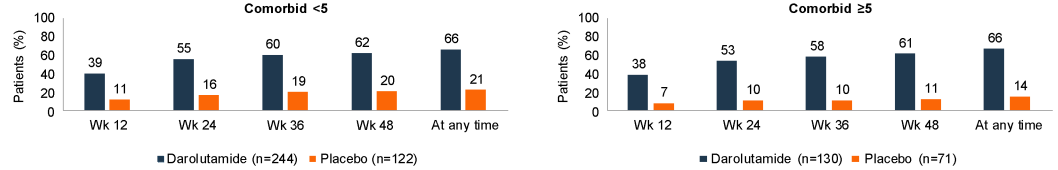
PSA RATES: CONCLUSIONS

- Rates of PSA <0.2 ng/mL were consistently higher with darolutamide versus placebo across all age, comorbid, and conmed subgroups
- Overall, among patients that reported a metabolic or cardiovascular comorbidity at baseline, rates of reaching PSA <0.2 ng/mL were similar with darolutamide, with slightly brewer palents with a caralovascular comorolany witnout comesponaing conmeas reacning PSA <0.2

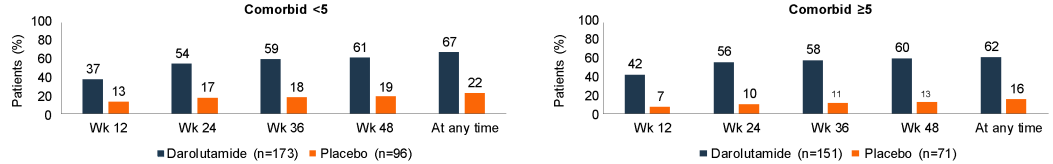
RATES OF REACHING PSA <0.2 NG/ML: AGE



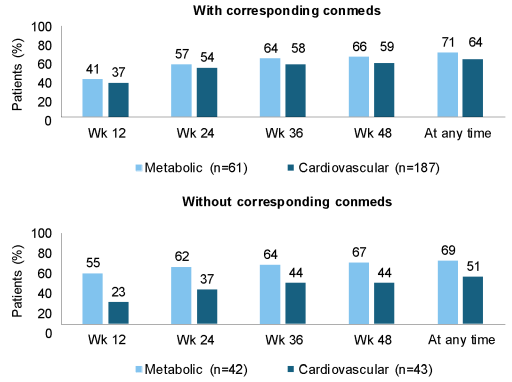
RATES OF REACHING PSA <0.2 NG/ML: COMORBIDITIES



RATES OF REACHING PSA <0.2 NG/ML: CONCOMITANT MEDICATIONS

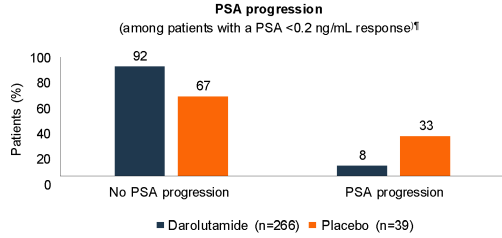


RATES OF REACHING PSA <0.2 NG/ML WITH DAROLUTAMIDE: METABOLIC OR CARDIOVASCULAR COMORBIDITY



PSA PROGRESSION: OVERALL

- Among patients who achieved PSA <0.2 ng/mL, fewer patients experienced PSA progression‡ with darolutamide versus placebo
- Time to PSA progression was longer with darolutamide versus placebo§:
  - Darolutamide: 421 days (range, 85–702)
  - Placebo: 256 days (range, 85–514)



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