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Darolutamide efficacy, quality of life, and safety outcomes by age subgroup: ARANOTE post hoc analyses

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Background

In patients (pts) with metastatic hormone-sensitive prostate cancer (mHSPC), darolutamide (DARO) + ADT significantly improved radiological progression-free survival (rPFS) vs placebo (PBO) + ADT (HR 0.54, 95% CI 0.41–0.71; P<0.0001) in the phase 3 ARANOTE trial (NCT04736199), with a favourable safety profile. ARANOTE included pts with a wide range of ages (43–93 years); we assessed outcomes in subgroups based on age.

Methods

Pts were randomized 2:1 to DARO 600 mg orally twice daily or PBO, both with ADT. rPFS, time to deterioration (TTD) in Functional Assessment of Cancer Therapy–Prostate (FACT-P) total score, time to metastatic castration resistant prostate cancer (mCRPC), prostate-specific antigen (PSA) outcomes, and treatment-emergent adverse events (TEAEs) were assessed post hoc by age <65 y, 65–74 y, and ≥75 y.

Results

The median age of the 669 enrolled pts was 70 y, with 27% aged <65 y, 43% aged 65–74 y, and 29% aged ≥75 y (including 4% ≥85 y). Baseline characteristics were generally similar in all age subgroups. The significant rPFS benefit of DARO over PBO in the overall population was consistently achieved across all age subgroups (Table): in pts <65 y, DARO showed 56% reduction in risk of rPFS and 5.6 mo longer TTD in FACT-P total score vs PBO. All other endpoints strongly favored DARO. Older age groups benefited similarly from DARO. More than 60% of all pts independent of age subgroup reached undetectable PSA (PSA <0.2 ng/mL). The incidence and severity of TEAEs increased slightly with age, as expected, but with similar frequencies between DARO and PBO within each age subgroup. Discontinuation rates due to TEAEs were 5–7% in DARO age subgroups vs 5–11% in PBO age subgroups.Table: 2459P

ARANOTE efficacy and quality of life outcomes by age

Time to event		Median, mo		HR (95% CI)	
		Darolutamide	Placebo		
rPFS	Overall	NE	25.0	0.54 (0.41–0.71)	
<65 y	NE	14.2	0.44 (0.27–0.71)		
65–74 y	NE	NE	0.64 (0.42–0.98)		
≥75 y	NE	25.1	0.51 (0.31–0.84)		
TTD in FACT-P total score	Overall	16.6	11.6	0.76 (0.61–0.94)	
<65 y	16.8	11.2	0.70 (0.47–1.05)		
65–74 y	17.1	12.0	0.76 (0.55–1.05)		
≥75 y	16.3	12.1	0.81 (0.55–1.19)		
mCRPC	Overall	NE	13.8	0.40 (0.32–0.51)	
<65 y	NE	11.1	0.37 (0.24–0.55)		
65–74 y	NE	16.8	0.43 (0.30–0.61)		
≥75 y	NE	16.9	0.40 (0.25–0.64)		
PSA progression	Overall	NE	16.8	0.31 (0.23–0.41)	
<65 y	NE	12.9	0.28 (0.17–0.46)		

Time to event	Median, mo		HR (95% CI)
	Darolutamide	Placebo	
65–74 y	NE	16.8	0.31 (0.20–0.48)
≥75 y	NE	20.1	0.33 (0.19–0.58)

NE, not estimable.

Conclusions

In all age groups, DARO consistently showed high efficacy, positive impact on HRQoL, and minimal burden of TEAEs.

Clinical trial identification

NCT04736199.

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