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Daraxonrasib, a RAS(ON) multi-selective inhibitor vs chemotherapy in previously treated metastatic pancreatic adenocarcinoma (mPDAC): Additional subgroup analyses from the ph3 RASolute 302 study

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Background

Multiagent systemic chemo offers limited benefit in mPDAC. Aberrant RAS(ON) signaling drives PDAC; >90% of cases harbor mutant (mut) RAS, and RAS WT PDAC remains dependent on RAS pathway signaling. Daraxonrasib is an oral, RAS(ON) multi-selective, tri-complex inhibitor of active, GTP-bound mut and WT RAS. Daraxonrasib significantly improved OS and PFS vs SOC chemo in pts with previously treated mPDAC overall (with or without an identified tumor RAS mut; mOS 13.2 vs 6.7 mo; HR, 0.40; mPFS 7.2 vs 3.6 mo; HR, 0.49) and in pts with RAS G12 mut mPDAC (OS HR, 0.40; PFS HR, 0.45) with manageable safety in the RASolute 302 primary analysis (NCT06625320). We report additional subgroup analyses from RASolute 302.

Methods

Pts with previously treated mPDAC were randomized 1:1 to daraxonrasib 300 mg PO QD or investigator’s choice of SOC chemo (GnP, mFOLFIRINOX, NaI-IRI+5-FU/LV, or FOLFOX). Dual primary endpoints (EPs) were OS and PFS in the RAS G12 mut population; key secondary EPs included OS and PFS in the overall population. Additional analyses evaluated OS in clinically relevant subgroups by locally determined tumor RAS mut status, preselected chemo regimen, and disease setting of prior treatment.

Results

At data cutoff (10 Feb 2026), median follow-up was 8.5 mo (range, 3.2-15.9). OS benefit with daraxonrasib vs chemo was observed across all RAS mut subgroups (Table). Daraxonrasib showed a consistent OS treatment effect across preselected chemo subgroups (HRs, 0.32-0.46). OS data by disease setting of prior treatment will also be presented. Table: LBA82

OS in subgroups			
	n (%)		OS HR (95% CI)
	Daraxonrasib n=248	Chemo n=252	
Tumor RAS mut status			
G12D	95 (38)	121 (48)	0.49 (0.33-0.74)
G12V	102 (41)	76 (30)	0.32 (0.19-0.54)
G12R	30 (12)	31 (12)	0.61 (0.29-1.30)
RAS Q61	11 (4)	11 (4)	0.37 (0.09-1.44)
No RAS mut identified	9 (4)	7 (3)	0.43 (0.09-1.98)

Conclusions

Daraxonrasib demonstrated OS benefit vs chemo across clinically relevant subgroups including pts with or without an identified tumor RAS mut. Directionally consistent OS benefit across these subgroups further reinforces the potential for daraxonrasib to be a new SOC for eligible pts with mPDAC.

Clinical trial identification

NCT06625320.

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Legal entity responsible for the study

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Disclosure

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