TPS4230 Poster Session

Trial in progress: RASolute 302—A phase 3, multicenter, global, open-label, randomized study of daraxonrasib (RMC-6236), a RAS(ON) multi-selective inhibitor, versus standard of care chemotherapy in patients with previously treated metastatic pancreatic ductal adenocarcinoma (PDAC).

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Background: Patients with previously treated metastatic PDAC have significant need for treatments with improved efficacy and tolerability. RAS is an oncogenic driver in > 90% of patients with PDAC. Daraxonrasib (RMC-6236) is an oral, RAS(ON) multi-selective, tri-complex inhibitor of GTP-bound mutant and wild-type RAS. In the ongoing Phase 1 monotherapy trial (NCT05379985), daraxonrasib exhibited a manageable safety profile with primarily low-grade rash and GI toxicities, and encouraging ORR, PFS and OS in a broad population of previously treated patients with RAS mutant metastatic PDAC (J Clin Oncol 43, 2025 [suppl 4; abstr 722]). The significant unmet need for alternative treatment options, along with the preliminary clinical data of daraxonrasib monotherapy, support its evaluation in the ongoing Phase 3 clinical trial, RASolute 302, in patients with previously treated metastatic PDAC. **Methods:** RASolute 302 is a global, multicenter, open-label, randomized study (NCT06625320) designed to evaluate daraxonrasib outcomes compared to investigator's choice of standard of care chemotherapy as a 2L treatment in patients with metastatic PDAC. Eligibility includes patients ≥18 years old, ECOG performance status 0 or 1, disease progression on 1 prior line of either a 5-fluorouracil or gemcitabine-based regimen in the metastatic setting, and documented RAS mutation status (mutant or wild-type). Eligible RAS mutations are defined as nonsynonymous mutations in KRAS, NRAS, or HRAS at codons 12, 13, or 61 (G12, G13, or Q61). Patients with tumors that are RAS wild-type and received appropriate approved targeted therapy for actionable mutations are also eligible. A 1:1 randomization of approximately 460 patients will receive daraxonrasib 300 mg daily or investigator's choice of chemotherapy (gemcitabine/nab-paclitaxel, mFOLFIRINOX, nal-IRI/5-FU/LV, or FOLFOX) until unacceptable toxicity or disease progression. For patients randomized to daraxonrasib, recommended prophylactic measures for rash include oral antibiotics and topical corticosteroids. Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) tumor assessments will be performed every 8 weeks until disease progression, withdrawal of consent, lost to follow up, or death, whichever occurs first. Dual primary endpoints are progression-free survival (PFS) as assessed by blinded independent central review and overall survival (OS) in the RAS G12X-mutant population. Key secondary endpoints include PFS, OS, objective response and quality of life measures in the all-patient population with tumors carrying RAS mutations (G12X, G13X or Q61X) or RAS wild-type. Enrollment for the trial commenced in October 2024. Clinical trial information: NCT06625320. Research Sponsor: Revolution Medicines, Inc.