PUBLICATION SNAPSHOT

DARAXONRASIB FOR PREVIOUSLY TREATED *RAS*-MUTANT NSCLC

Arbour KC, et al. N Engl J Med 2026; 395:882-93

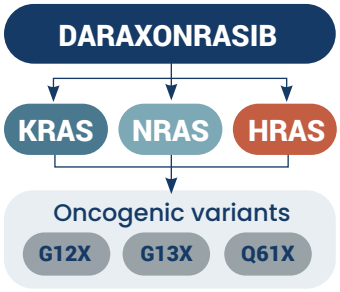
The unmet need

~ 30% of NSCLC harbours RAS mutations, spanning *KRAS, NRAS &* *HRAS* and multiple mutation subtypes

Targeted therapies are largely limited to *KRAS* G12C, leaving substantial unmet need for patients with non-G12C *RAS* mutations

Following progression on platinum-based chemo-immunotherapy, docetaxel remains a standard option, but outcomes are limited

A pan-*RAS* approach



Daraxonrasib (RMC-6236): oral, *RAS*(ON) multi-selective inhibitor

Designed to target multiple *RAS* proteins, including *KRAS, NRAS* and *HRAS*, and oncogenic variants including G12, G13 and Q61

Study design *(RMC-6236-001)*

Phase 1/2, open-label, single arm, dose-escalation expansion study; NSCLC subgroup reported

136 patients with previously treated, advanced *RAS*-mutant NSCLC

Prior platinum-based chemotherapy + anti-PD-(L)1 therapy; no prior *RAS*-targeted therapy

Daraxonrasib 10–400 mg once daily in 21-day cycles. Doses ≤300 mg included in analyses

Safety profile

Overall population (≤300 mg dose n=136):

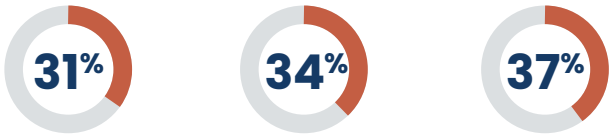
99% any-grade TRAEs
30% grade ≥3 TRAEs

160–220 mg dose range (n=59):

25% grade ≥3 TRAEs, mainly rash, diarrhea & vomiting
No grade 4/5 TRAEs

Antitumour activity by dose

ORR (Investigator-assessed, RECIST v1.1)



≤120 mg (n=26)	160–220 mg (n=59)	300 mg (n=51)

Docetaxel-naïve subgroup (160–220 mg) [n=38]

Prior platinum-CT + anti–PD-(L)1; no prior docetaxel

42% ORR
8.3 months mPFS
16.0 months mOS

- Responses observed across multiple *RAS* alterations
- Similar outcomes between patients with any *RAS* mutation vs *RAS* G12 mutations

Future development

200 mg once daily selected for further development

RASolve 301 (NCT06881784): phase 3 study, daraxonrasib vs docetaxel in previously treated *RAS*-mutant NSCLC

Clinical Takeaways

1. *RAS*-mutant NSCLC is heterogeneous: comprehensive biomarker testing is important
2. Non-G12C *RAS*-mutant NSCLC remains a major unmet need given limited targeted treatment options
3. Daraxonrasib provides a pan-*RAS* approach, with Phase 1/2 data supporting further evaluation at 200 mg once daily in RASolve 301

AE, adverse event; CT, chemotherapy; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed death (ligand)1; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumours (version 1.1); TRAE, treatment-related adverse events

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