

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



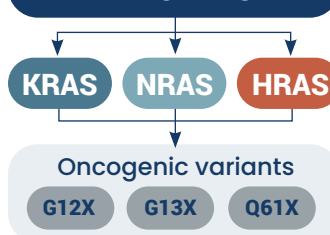
Targeted therapies are largely limited to *KRAS* G12C, leaving substantial unmet need for patients with non-G12C RAS mutations



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

A pan-RAS approach

DARAXONRASIB



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

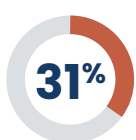
30% grade ≥3 TRAEs

160–220 mg dose range (n=59):

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

Antitumour activity by dose

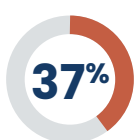
ORR (Investigator-assessed, RECIST v1.1)



≤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

