Block active RAS. Test the benefit.

Daraxonrasib (RASONQUE) | Metastatic pancreatic adenocarcinoma

The clinical problem

RASolute 302 studied metastatic pancreatic cancer after progression on one systemic treatment line. A randomized comparison against physician-selected chemotherapy tested whether targeting active RAS could improve survival. [1,2]

The mechanism

Daraxonrasib binds cyclophilin A; the resulting complex engages active RAS and obstructs effector interactions. Preclinical studies connect this intervention to reduced growth signaling. The drawing explains the molecular sequence rather than depicting a measured patient response. [4; Figure 1]

From mechanism to a clinical claim

The phase 3 study showed improved survival and disease control in the overall population. The US approval in August 2026 covers previously treated adults and adults who are not candidates for multiagent systemic therapy; that label is broader than the randomized trial population. [1,3]

The molecular mechanism supports the rationale. The randomized trial quantifies benefit in a defined population; it does not imply equal benefit across every RAS genotype.

Continue the story

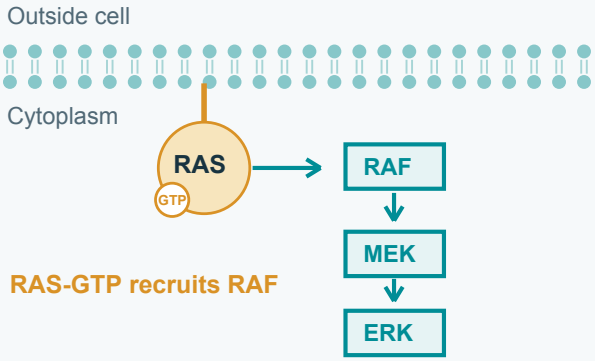
Watch the film and explore the mechanism

The animation explains biology. The following pages examine measured patient outcomes.

Figure 1. Daraxonrasib: blocking active RAS

Follow the mechanism from left to right, then down each row.

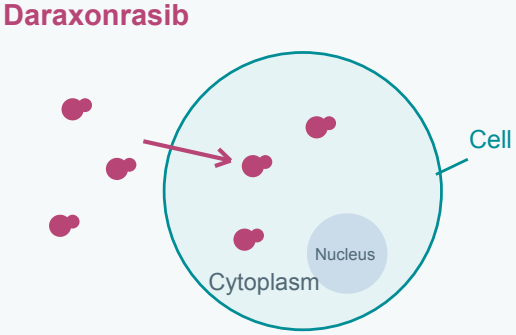
A Active RAS signaling



Active RAS drives growth signaling. [1]

RAF activates the MEK-ERK pathway.

B Intracellular access

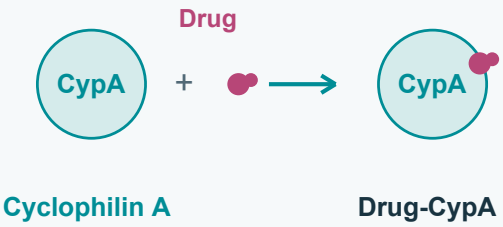


The small molecule reaches the cytosol. [1]

Its binding partners are inside the tumor cell.

C Cyclophilin A binding

Inside the tumor cell

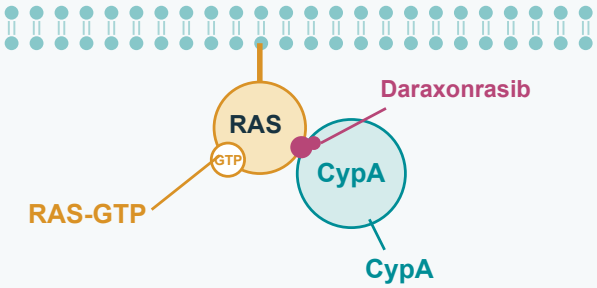


Daraxonrasib associates with CypA. [1,2]

This complex can engage active RAS.

D Tri-complex formation

Inner membrane surface

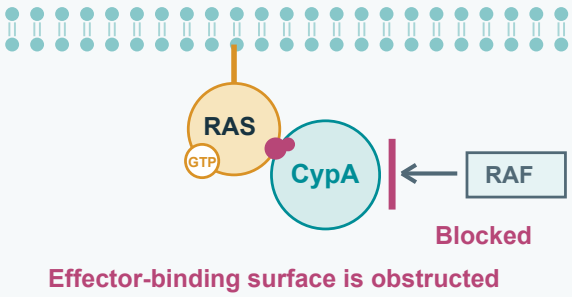


The drug bridges CypA and active RAS. [1,2]

The tri-complex forms at the inner membrane.

E Effector blockade

Inner membrane surface

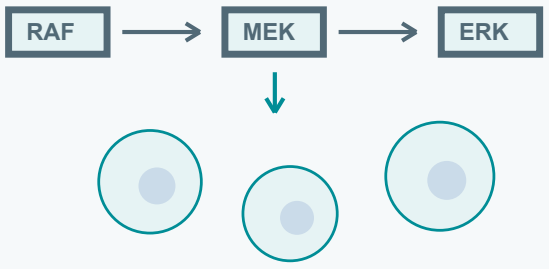


The tri-complex limits RAF access. [1,2]

Downstream MEK-ERK signaling falls.

F Cellular consequence

Lower growth signaling



Proliferation and survival can decrease. [1]

This does not imply uniform tumor-cell death.

[1] Jiang et al., Cancer Discovery (2024), doi:10.1158/2159-8290.CD-24-0027.
[2] Cregg et al., J Med Chem (2025); PDB 9BG6.

Schematic, not to scale. Mechanism does not predict an individual clinical response.

A randomized survival comparison.

RASolute 302 | Open-label phase 3 | Daraxonrasib n=248; physician-choice chemotherapy n=252. Overall randomized population. [1,2]

Overall population | 500 randomized [1,2]

Median overall survival	**13.2 vs 6.7 months** HR 0.40 (95% CI 0.30-0.53)
Median progression-free survival	**7.2 vs 3.6 months** BICR; HR 0.49 (95% CI 0.38-0.64)
Objective response rate	**30% vs 11%** 95% CI 25-36 vs 7-15; BICR

BICR: blinded independent central review. Each comparison had p<0.0001 in the label. Median survival is not a promised survival duration.

RAS G12 population | 459 patients [2]

Median overall survival	**13.2 vs 6.6 months** HR 0.40 (95% CI 0.30-0.54)
Median progression-free survival	**7.3 vs 3.5 months** BICR; HR 0.45 (95% CI 0.34-0.59)

The G12 population and overall population overlap. They are not independent replications or evidence of equal benefit in the small non-G12 group.

What the evidence means.

Benefit, uncertainty and safety belong in the same clinical story.

Who was studied

Eligible patients had progression after one prior regimen, measurable disease and ECOG performance status 0-1. Most had KRAS G12 mutations. Frailer patients and other molecular groups are not equally represented. [2]

What the comparison supports

Randomization supports a treatment-effect claim against the trial chemotherapy choices. Blinded radiologic review reduces assessment bias for PFS and response, while the trial itself was open-label. Overall survival measures death from any cause; tumor response measures something narrower. [1,2]

Read the risks alongside the benefit

The label highlights skin / soft-tissue toxicity, oral disorders, diarrhea, gastrointestinal perforation, ILD / pneumonitis and embryo-fetal toxicity. Serious adverse reactions occurred in 30% of the 241 daraxonrasib-treated patients; the treated safety denominator differs from the randomized efficacy denominator. [2]

Separate approval from extrapolation

The FDA approved use after at least one prior systemic therapy or when a patient is not a candidate for multiagent systemic therapy. The latter group was not the same population as the randomized second-line trial. An approved indication should not be presented as an identical subgroup result. [3]

What the molecular image cannot show

Preclinical inhibition and a tri-complex structure support the proposed mechanism. They do not measure delivery through a particular patient tumor or establish a uniform clinical response. Figure 1 is a pathway schematic; the film compresses biological time. [4]

Sources you can follow.

Numbered citations on pages 1, 3 and 4 refer to this list. Figure 1 retains its own source key.

[1] O'Reilly EM et al. Daraxonrasib or chemotherapy in previously treated metastatic pancreatic cancer. NEJM (2026).

DOI: 10.1056/NEJMoa2605555

Peer-reviewed RASolute 302 report, published 31 May 2026. Randomized efficacy and trial methods.

[2] RASONQUE US prescribing information, August 2026.

Revolution Medicines | US label

Regulatory source. Sections 5-6 and 14; efficacy Table 6 and distinct treated safety population.

[3] FDA approval of daraxonrasib, 26 August 2026.

FDA | Approval summary

Official indication and approval date, distinct from trial eligibility.

[4] Jiang J et al. Translational and therapeutic evaluation of RAS-GTP inhibition by RMC-6236. Cancer Discovery (2024).

DOI: 10.1158/2159-8290.CD-24-0027

Primary translational study supporting Figure 1. Preclinical findings are not randomized clinical outcomes.

[5] Cregg et al. Discovery of daraxonrasib (RMC-6236), a RAS(ON) tri-complex inhibitor. J Med Chem (2025).

DOI: 10.1021/acs.jmedchem.4c02314

Primary medicinal chemistry source used by Figure 1; experimental complex PDB 9BG6.

How this brief was prepared

Selected primary publications, prescribing information and clearly identified conference material were checked on 7 September 2026. Data are not pooled across trials or cutoffs. This is a focused evidence summary, not a systematic review, prescribing guide or health-economic analysis.