ASCO ANNUAL MEETING 2026

RASolute 302

Daraxonrasib versus chemotherapy in previously treated metastatic pancreatic ductal adenocarcinoma. Phase 3, open-label, randomized.

TOTAL N	PRIMARY ENDPOINT	OS HAZARD RATIO	ORR
500	**OS & PFS**	**0.40**	**31.6%**
248 vs 252; 91.8% RAS G12	RAS G12 population	95% CI 0.30 to 0.53	vs 11.2%, overall pop.

Trial design

RASolute 302 was a phase 3, international, open-label, randomized trial conducted at 59 sites in six countries. Enrollment ran from October 16, 2024 to November 7, 2025. Patients were randomly assigned 1:1. Crossover to the other group was not permitted. An independent data monitoring committee oversaw safety.

Treatment arms

Daraxonrasib (n=248)

300 mg orally once daily. An oral RAS(ON) multiselective tri-complex inhibitor of the GTP-bound state of mutant and wild-type RAS. Treatment continued until disease progression, unacceptable toxicity, or consent withdrawal.

Investigator's choice chemotherapy (n=252)

One of four regimens, given per local prescribing practice: gemcitabine plus nab-paclitaxel; modified FOLFIRINOX; FOLFOX; or liposomal irinotecan plus fluorouracil and leucovorin.

Key eligibility

Age: at least 18 years

Disease: histologically or cytologically confirmed mPDAC with measurable disease per RECIST v1.1

Prior therapy: progression after one prior line of fluoropyrimidine- or gemcitabine-based therapy for metastatic disease (or progression less than 6 months after neoadjuvant/adjuvant therapy)

Performance status: ECOG 0 or 1

RAS status: documented tumor RAS mutational status by local testing (KRAS, NRAS, or HRAS at codon 12, 13, or 61, or no RAS mutation identified)

Key exclusions: known CNS metastases; prior RAS-targeted therapy

Stratification factors

ECOG performance status (0 vs 1)

Metastatic disease at initial diagnosis (yes vs no)

Liver metastases at baseline (yes vs no)

Tumor RAS mutational status (RAS G12D/V vs other RAS G12 vs RAS G13 or Q61 or no RAS mutation identified)

Endpoints

DUAL PRIMARY

Overall survival (OS) and progression-free survival (PFS) by blinded independent central review (BICR) per RECIST v1.1, in the RAS G12 population.

KEY SECONDARY

OS and PFS in the overall population; objective response rate (ORR) in the RAS G12 and overall populations; patient-reported time to deterioration (TTD) in pain and in global health status/quality of life, in both populations.

ADDITIONAL SECONDARY

Time to response and safety. Adverse events graded per NCI CTCAE v5.0.

The overall population included patients with RAS G12, G13, or Q61 mutations or with no RAS mutation identified. The RAS G12 population (459 patients, 91.8%) comprised those with RAS G12 mutations.

ANALYSIS TIMING

Data reported are from the first interim OS analysis (IA1), which was also the final PFS analysis, performed after enrollment completion and at least 166 deaths in the RAS G12 population. Data cutoff: February 10, 2026. Median follow-up: 8.5 months (range 3.2 to 15.9).

Overall survival

Population	Events, n (%)	Median OS, mo (95% CI)	HR (95% CI)	P value
RAS G12 · Daraxonrasib (n=228)	72 (32)	**13.2 (10.0–NE)**	**0.40 (0.30–0.54)**	P<0.001 5.9×10^{-10}
RAS G12 · Chemotherapy (n=231)	127 (55)	**6.6 (5.4–8.2)**		
Overall · Daraxonrasib (n=248)	79 (32)	**13.2 (10.0–NE)**	**0.40 (0.30–0.53)**	P<0.001 4.6×10^{-11}
Overall · Chemotherapy (n=252)	141 (56)	**6.7 (5.8–8.0)**		

NE = not estimable. HR by stratified Cox model.

53.2%
12-mo OS, daraxonrasib (overall pop.)

17.3%
12-mo OS, chemotherapy (overall pop.)

60%
Reduction in risk of death (both pops.)

RAS G12 12-month OS: 53.3% vs 18.7%.

Progression-free survival (BICR)

Population	Events, n (%)	Median PFS, mo (95% CI)	HR (95% CI)	P value
RAS G12 · Daraxonrasib (n=228)	112 (49)	**7.3 (6.3–8.1)**	**0.45 (0.34–0.59)**	P<0.001 3.2×10^{-9}
RAS G12 · Chemotherapy (n=231)	121 (52)	**3.5 (2.9–3.8)**		
Overall · Daraxonrasib (n=248)	127 (51)	**7.2 (5.7–7.5)**	**0.49 (0.38–0.64)**	P<0.001 5.2×10^{-8}
Overall · Chemotherapy (n=252)	130 (52)	**3.6 (2.9–4.2)**		

6-month PFS (RAS G12): 58.7% vs 31.7%. 6-month PFS (overall): 56.0% vs 32.9%.

Objective response (confirmed, BICR)

RAS G12 population

33.2%
Daraxonrasib
(n=237)
95% CI 27.0–39.9

11.8%
Chemotherapy
(n=221)
95% CI 7.8–16.8

Overall population

31.6%
Daraxonrasib
(n=248)
95% CI 25.8–38.0

11.2%
Chemotherapy
(n=252)
95% CI 7.5–15.9

Both comparisons P<0.0001. Median time to response was 1.9 months in both groups. ORR denominators are patients with measurable disease at baseline per BICR (RAS G12: daraxonrasib 237, chemotherapy 221; overall: 248 and 252). Duration of response and tumor-shrinkage (waterfall) data were not reported in the available sources.

Overall survival subgroups (overall population)

Hazard ratios and 95% CIs by **unstratified** Cox model. The unstratified "Overall" HR is 0.42 (0.32 to 0.55); the headline stratified HR is 0.40 (0.30 to 0.53). Events shown as daraxonrasib / chemotherapy. Point size is not scaled here; n's appear on every row.

Subgroup	Events (D/C)	HR (favors ← daraxonrasib | chemotherapy →)	HR (95% CI)
Overall	79/248 / 141/252		**0.42 (0.32–0.55)**
Age, years			
<65	37/114 / 68/121		**0.41 (0.27–0.61)**
≥65	42/134 / 73/131		**0.43 (0.29–0.63)**
Sex			
Male	45/131 / 77/144		**0.50 (0.35–0.73)**
Female	34/117 / 64/108		**0.33 (0.22–0.51)**
ECOG PS			
0	33/129 / 51/118		**0.48 (0.31–0.75)**
1	46/119 / 90/134		**0.38 (0.27–0.55)**
Tumor RAS mutational status			
RAS G12D/V	59/197 / 110/197		**0.38 (0.28–0.53)**

Other RAS G12	13/31 / 17/34		**0.70 (0.34–1.44)**
RAS G13/Q61 or none	7/20 / 14/21		**0.37 (0.15–0.93)**
Metastatic disease at diagnosis			
Yes	51/154 / 94/154		**0.38 (0.27–0.54)**
No	28/94 / 47/98		**0.49 (0.31–0.78)**
Prior 5-FU-based regimen			
Yes	62/181 / 103/186		**0.46 (0.34–0.64)**
No	17/67 / 38/66		**0.31 (0.17–0.55)**
Prior gemcitabine-based regimen			
Yes	31/110 / 61/114		**0.39 (0.25–0.61)**
No	48/138 / 80/138		**0.44 (0.30–0.63)**
Prior pancreatectomy			
Yes	21/83 / 40/92		**0.47 (0.27–0.79)**
No	58/165 / 101/160		**0.38 (0.28–0.53)**
Liver metastases at baseline			
Yes	68/174 / 113/176		**0.43 (0.32–0.58)**
No	11/74 / 28/76		**0.31 (0.15–0.63)**
Peritoneal metastases at baseline			
Yes	28/76 / 48/83		**0.44 (0.28–0.71)**
No	51/172 / 93/169		**0.41 (0.29–0.57)**
CA19-9 at baseline			
≥40 U/mL	70/211 / 121/195		**0.37 (0.28–0.50)**
<40 U/mL	9/36 / 19/56		**0.67 (0.30–1.49)**

Patient-reported time to deterioration (overall population)

Measure	Daraxonrasib, mo	Chemotherapy, mo	HR (95% CI)	P value
Pain (EORTC QLQ-PAN26)	**9.2**	**3.8**	0.51 (0.37–0.71)	P<0.001
Global health status / QoL (QLQ-C30)	**5.7**	**2.6**	0.60 (0.46–0.79)	P<0.001

RAS G12 pain medians were 9.0 vs 3.7 months; GHS/QoL 5.6 vs 2.4 months.

NOTE ON ATTRIBUTION

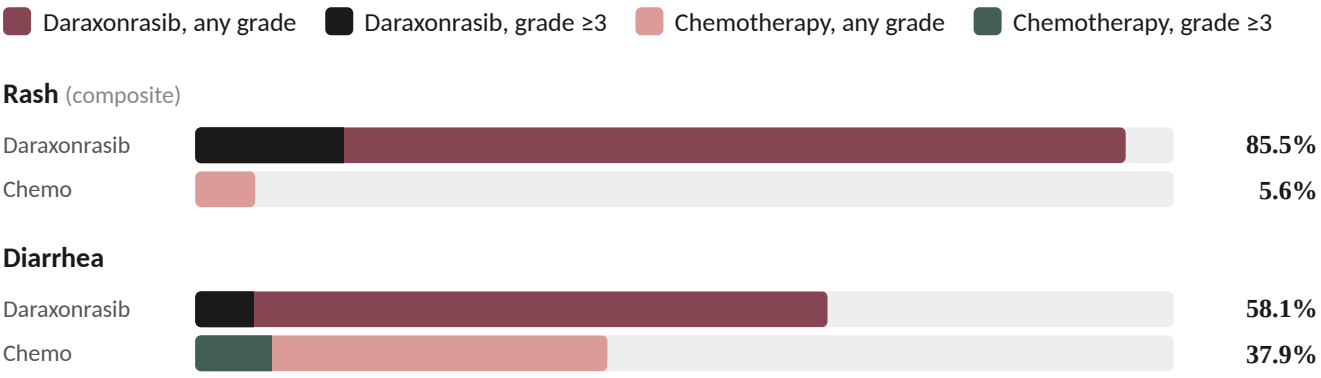
The overview table below reports **treatment-related** adverse events (TRAEs) except the first two rows, which are all-cause treatment-emergent (TEAE). The bar chart reports TRAEs.

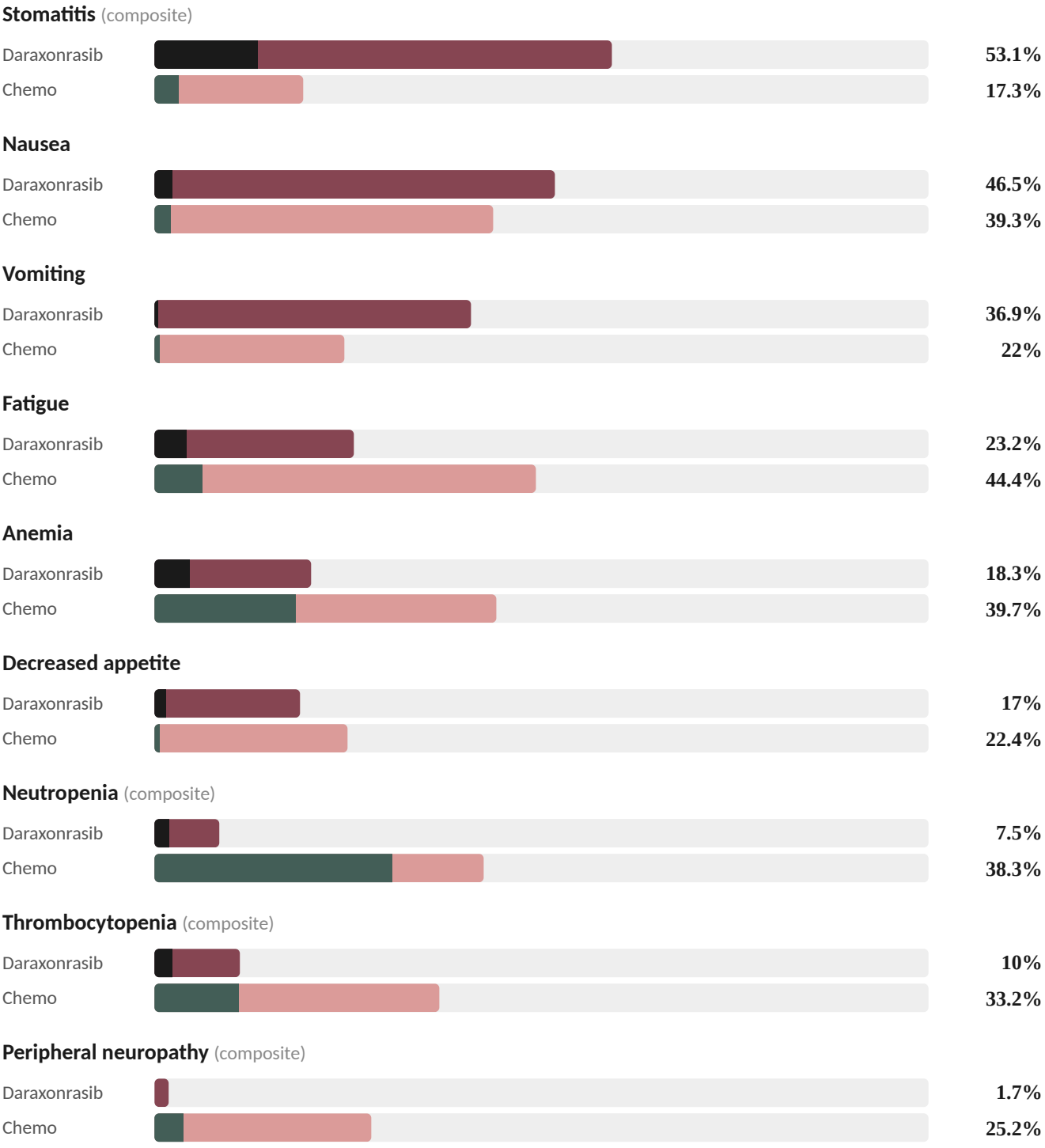
Safety overview

Event	Daraxonrasib (n=241)	Chemotherapy (n=214)
Median time on treatment, mo	**6.2**	**1.5–3.2***
Any TEAE (all-cause), n (%)	241 (100)	209 (97.7)
Grade ≥3 TEAE (all-cause), n (%)	149 (61.8)	149 (69.6)
Any TRAE, n (%)	236 (97.9)	200 (93.5)
Grade ≥3 TRAE, n (%)	105 (43.6)	123 (57.5)
Serious TRAE, n (%)	26 (10.8)	40 (18.7)
TRAE leading to dose reduction, n (%)	87 (36.1)	123 (57.5)
TRAE leading to dose interruption, n (%)	135 (56.0)	118 (55.1)
TRAE leading to discontinuation, n (%)	3 (1.2)	24 (11.2)
Grade 5 (fatal) TRAE, n (%)	1 (0.4)	0

*Chemotherapy median time on treatment is reported as a range across the four component regimens. One daraxonrasib patient died of treatment-related pneumonitis (the single grade 5 TRAE). Median dose intensity: 93.1% daraxonrasib vs 65.3 to 95.0% across chemotherapy regimens.

Treatment-related adverse events (any grade) in ≥20% of either arm





Any-grade incidence with grade ≥3 in parentheses. Threshold: any-grade incidence at least 20% in either arm. Grade ≥3 bars overlay the any-grade bar. Several terms are grouped composites (for example, rash, stomatitis, neutropenia, thrombocytopenia, and peripheral neuropathy).

Most common events by arm

Daraxonrasib (TRAE, any grade)

Rash 85.5%, diarrhea 58.1%, stomatitis 53.1%, nausea 46.5%, vomiting 36.9%. Mostly low-grade dermatologic and gastrointestinal events; grade ≥3 rash 13.7% and stomatitis 12.0% were the only grade ≥3 TRAEs at 10% or higher. No grade 4 TRAEs except as noted; one grade 5.

Chemotherapy (TRAE, any grade)

Fatigue 44.4%, anemia 39.7%, nausea 39.3%, neutropenia 38.3%, diarrhea 37.9%, thrombocytopenia 33.2%, peripheral neuropathy 25.2%. Grade ≥3 TRAEs at 10% or higher: neutropenia 27.6% and anemia 16.4%.

Primary sources

Journal article. O'Reilly EM, Wainberg ZA, Hendifar AE, et al. Daraxonrasib or chemotherapy in previously treated metastatic pancreatic cancer. N Engl J Med. Published online May 31, 2026. DOI: 10.1056/NEJMoa2605555.

Conference presentation. Wolpin BM, et al. Daraxonrasib, a RAS(ON) multiselective inhibitor versus chemotherapy in previously treated mPDAC: primary and final analysis from the phase 3 RASolute 302 study. Presented at the ASCO Annual Meeting 2026, Chicago.

Trial registration. ClinicalTrials.gov identifier `NCT06625320`. Sponsor: Revolution Medicines.

Abbreviations

AE — adverse event

ALT — alanine aminotransferase

AST — aspartate aminotransferase

BICR — blinded independent central review

CI — confidence interval

CNS — central nervous system

CR — complete response

CTCAE — Common Terminology Criteria for Adverse Events

DoR — duration of response

ECOG PS — Eastern Cooperative Oncology Group performance status

EORTC QLQ-C30 — EORTC Core Quality of Life Questionnaire

EORTC QLQ-PAN26 — EORTC pancreatic cancer module

FOLFOX — leucovorin, fluorouracil, oxaliplatin

GHS — global health status

GnP — gemcitabine plus nab-paclitaxel

GTP — guanosine triphosphate

HR — hazard ratio

mFOLFIRINOX — modified fluorouracil, irinotecan, leucovorin, oxaliplatin

mPDAC — metastatic pancreatic ductal adenocarcinoma

Nal-IRI — nanoliposomal irinotecan

NE — not estimable

ORR — objective response rate

OS — overall survival

PFS — progression-free survival

PO QD — orally once daily

PR — partial response

PRO — patient-reported outcome

QoL — quality of life

RECIST — Response Evaluation Criteria in Solid Tumors

TEAE — treatment-emergent adverse event

TRAE — treatment-related adverse event

TTD — time to deterioration

Cancer Communicator QuickView. Data reference tool compiled from the published NEJM article and the ASCO 2026 presentation for RASolute 302 (NCT06625320). Data cutoff February 10, 2026. Funded by Revolution Medicines. This summary is for educational purposes and is not medical advice.