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Preliminary Safety, Pharmacokinetics, and Efficacy of ERAS-0015: Results From the AURORAS-1 First-in-human Trial

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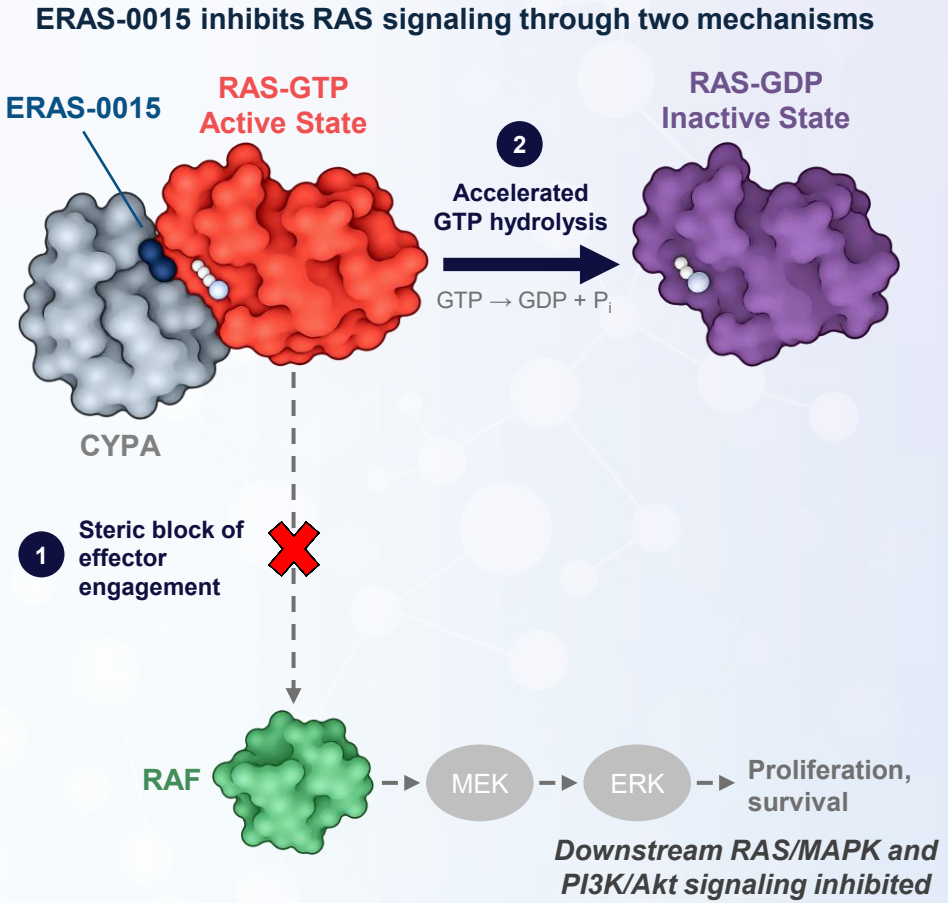
Introduction

- RAS GTPases are key to the RAS/MAPK pathway, and are pivotal in tumor cell proliferation and survival[1-3]
- Oncogenic mutations that shift RAS from a GDP- to GTP-bound (RAS-On) state lead to prolonged pathway activation and tumorigenesis; in addition, wild-type RAS also actively contributes to oncogenic signaling[4,5]
- ERAS-0015 is a next-generation, pan-RAS molecular glue[6] designed to achieve differentiated efficacy, tolerability, and combinability relative to other RAS-targeting molecules
- ERAS-0015 binds cyclophilin A, ultimately forming a ternary complex with RAS-On, which sterically blocks effector engagement and enhances GTP hydrolysis[6]
- **Here we report the first-in-human results from AURORAS-1 (NCT06983743), an ongoing open-label, phase 1 study evaluating safety, pharmacokinetics, and preliminary efficacy of ERAS-0015 in patients with advanced solid tumors with RAS alterations**



CYPA, cyclophilin A; GDP, guanosine diphosphate; GTP, guanosine triphosphate.

1. Prajapati V, et al. *RSC Med Chem.* 2025;16:1923–1940; 2. Bonni A, et al. *Science.* 1999;286:1358–1362; 3. Drosten M, et al. *Embo J.* 2010;29:1091–1104; 4. Prior IA, et al. *Cancer Res.* 2020;80:2969–2974; 5. Sealover NE, et al. *Sci Signal.* 2025;18:eadx5186; 6. Lew E, et al. *Cancer Res.* 2025;85:390.

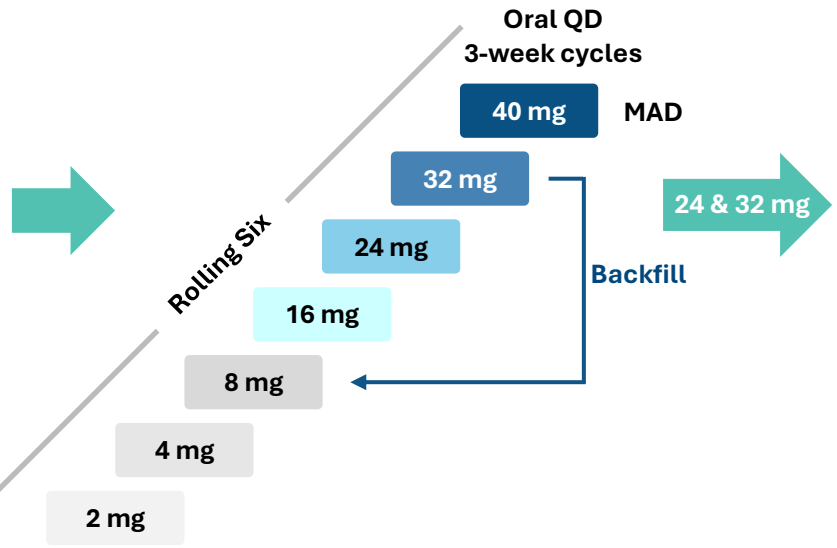
AURORAS-1: Study Design and Patient Disposition

ERAS-0015 Monotherapy in Solid Tumors

Key Eligibility Criteria

- Adults with locally advanced or metastatic:
  - PDAC
  - NSCLC with KRAS G12X/G13X
  - GI tumors with KRAS G12X/G13X
- ECOG PS 0–1
- Measurable disease
- Stable brain metastases

Part 1: Dose Escalation[a]



Part 1: Expansion

- PDAC
- NSCLC
- Other solid tumors

Patient Disposition

Patients treated (N=148)[b]

Discontinued treatment (n=56 [37.8%])

37 (25.0%)	PD
5 (3.4%)	AE
4 (2.7%)	Consent withdrawal
4 (2.7%)	Death
6 (4.1%)	Other

On treatment (n=92 [62.2%])

Monotherapy until progression or unacceptable toxicity

Primary Endpoints

- DLTs
- PK parameters
- Safety assessments

Secondary Endpoints

- ORR
- DOR
- DCR
- PFS
- TTR
- OS

Median Time on Study

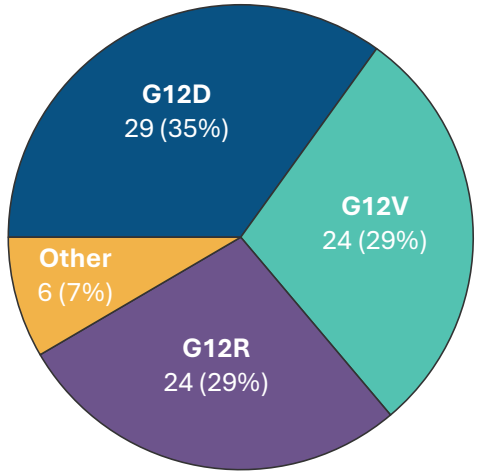
- 16–32 mg: 3.5 months

Disposition data cutoff date: September 1, 2026. [a]Intrapatient dose escalation was allowed. [b]Safety analysis set includes all patients who were exposed to study drug at least once in part 1 dose escalation and part 1 expansion cohorts; among the 148 patients, 4 patients with PDAC received ERAS-0015 in the first-line setting and 1 patient with NSCLC had received prior KRAS G12C inhibitor therapy. AE, adverse event; DCR, disease control rate; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GI, gastrointestinal; MAD, maximum administered dose; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PDAC, pancreatic ductal adenocarcinoma; PFS, progression-free survival; PK, pharmacokinetic; QD, once daily; TTR, time to response.

AURORAS-1: Demographics and Baseline Disease Characteristics

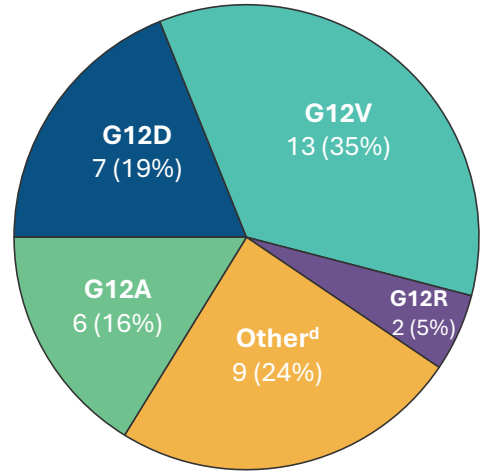
	Total (N=148)
Age, median (range), years	65.0 (36–88)
Female, n (%)	62 (41.9)
ECOG PS 1, n (%)	109 (73.6)
Tumor type, n (%)	
PDAC	87 (58.8)
NSCLC	38 (25.7)
BTC	13 (8.8)
Other	10 (6.8)
	PDAC (N=83)[a]
Sites of metastatic disease – liver/lung, n (%)	61 (73.5)/31 (37.3)
Prior systemic therapy[c]	
Regimen containing gemcitabine/5-FU, n (%)	63 (75.9)/77 (92.8)
Median (range) number of prior lines	2.0 (1–8)
1/2/≥3 prior lines of systemic therapy, %	26.5/42.2/31.3
	NSCLC (N=37)[b]
Smoking status, n (%)	
Never/former	10 (27.0) / 24 (64.9)
Current	3 (8.1)
Sites of metastatic disease – brain, n (%)	10 (27.0)
Prior systemic therapy[c]	
ICI/platinum-based chemotherapy, n (%)	35 (94.6)/36 (97.3)
Median (range) number of prior lines	2.0 (0–6)
0/1/2/≥3 prior lines of systemic therapy, %	2.7/40.5/27.0/29.7

Patients With PDAC (N=83)
KRAS Mutation Type



- 64% of patients had G12D/V mutations
- Enriched for G12R mutations (29%)

Patients With NSCLC (N=37)
KRAS Mutation Type

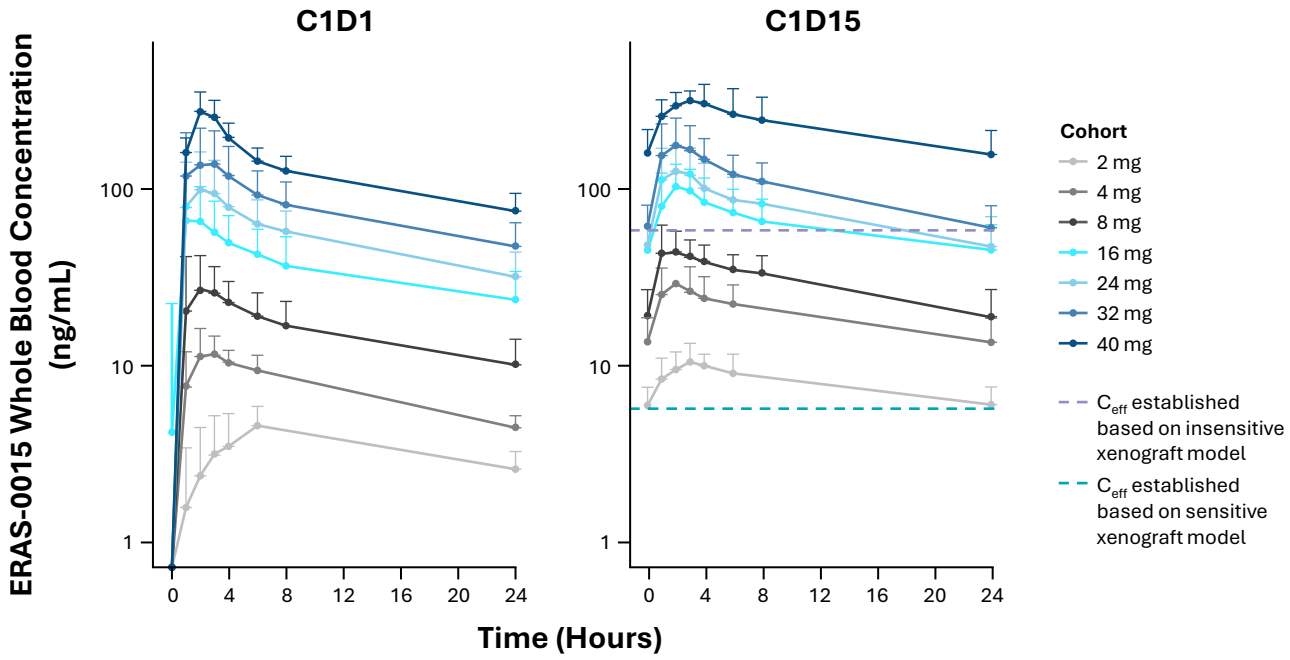


- 54% of patients had G12D/V mutations

Data cutoff date: September 1, 2026.
[a]4 patients with PDAC who received ERAS-0015 in the first-line setting were not included; [b]1 patient with NSCLC who had received prior KRAS G12C inhibitor therapy was not included; [c]No patients had received prior RAS inhibitor therapy; [d]Includes a patient with G12D and G12V double mutations.
5-FU, 5-fluorouracil; BTC, biliary tract cancer; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; PDAC, pancreatic ductal adenocarcinoma.

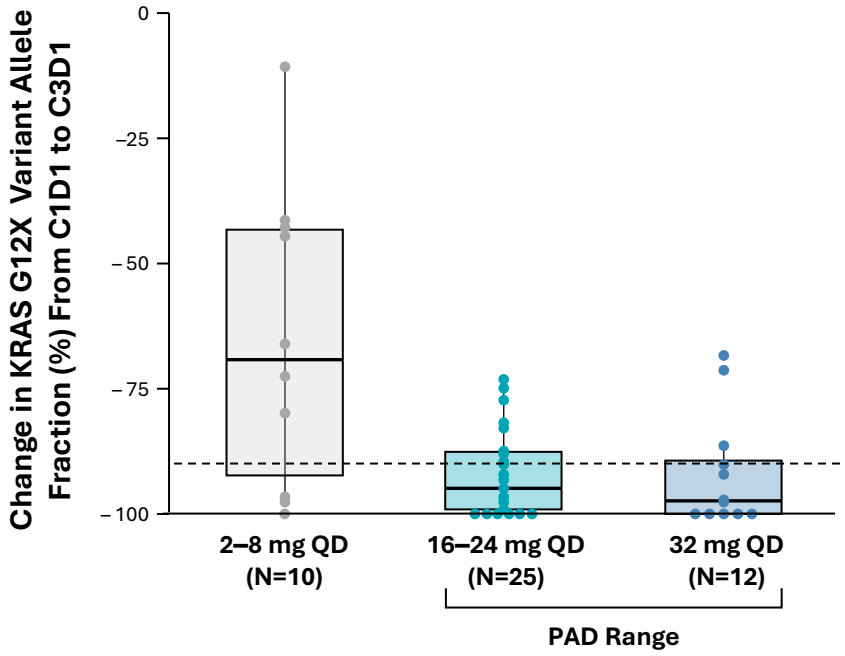
AURORAS-1: ERAS-0015 Exhibited Linear PK and Robust Reduction of KRAS G12X ctDNA

Mean PK Profiles



Linear PK; PAD range: 16–32 mg QD; RDEs: 24 and 32 mg QD

Change in Solid Tumor ctDNA KRAS G12X VAF from C1D1 to C3D1



At 32 mg QD, 75% achieved ≥90% reduction in KRAS G12X VAF

Data cutoff date: PK data as of September 18, 2026; data points in the figures are presented as mean ± standard deviation; ctDNA data as of October 2, 2026; data points in the figures are presented as median ± IQR/range. C, cycle; C_{eff}, effect-site concentration; ctDNA, circulating tumor deoxyribonucleic acid; D, day; IQR, interquartile range; PAD, pharmacologically active dose; PK, pharmacokinetics; QD, once daily; RDE, recommended dose for expansion; VAF, variant allele fraction.

AURORAS-1: ERAS-0015 Was Safe and Generally Well Tolerated Across Pharmacologically Active Dose Range

TRAEs in Patients Receiving ERAS-0015 16–32 mg (N=122)						
TRAEs in ≥10% of patients, n (%)	**Grade 1**	**Grade 2**	**Grade 3[a]**	**Grade 4**	**Grade 5**	**All Grades**
Rash[b]	61 (50.0)	34 (27.9)	4 (3.3)	0	0	99 (81.1)
Diarrhea	30 (24.6)	8 (6.6)	1 (0.8)	0	0	39 (32.0)
Nausea	22 (18.0)	7 (5.7)	0	0	0	29 (23.8)
Stomatitis/mucositis	15 (12.3)	8 (6.6)	3 (2.5)	0	0	26 (21.3)
TRAEs leading to dose interruptions, n (%)						15 (12.3)
TRAEs leading to dose reductions, n (%)						13 (10.7)
TRAEs leading to dose discontinuations, n (%)						2 (1.6)
Treatment Exposure: ERAS-0015 16–32 mg (N=122)						
Duration of exposure, median (range), weeks						14.4 (0.7–47.0)
Relative dose intensity, median (range), %[c]						100.0 (42.6–133.9)

- **No observed dose-limiting toxicities; maximum tolerated dose was not reached**
- **No prophylaxis recommended per protocol**

Data cutoff date: September 1, 2026. Safety set included all patients who received at least one dose of ERAS-0015. [a]One Grade 3 TRAE of pneumonitis progressed to Grade 5 after withdrawal of supportive care per patient decision. [b]Rash events are identified using the following preferred terms: rash pustular, rash papular, rash maculo-papular, rash macular, rash, erythema, and dermatitis acneiform (uncoded terms rash acneiform and rash are also included). [c]N=119. QD, once daily; TRAE, treatment-related adverse event.

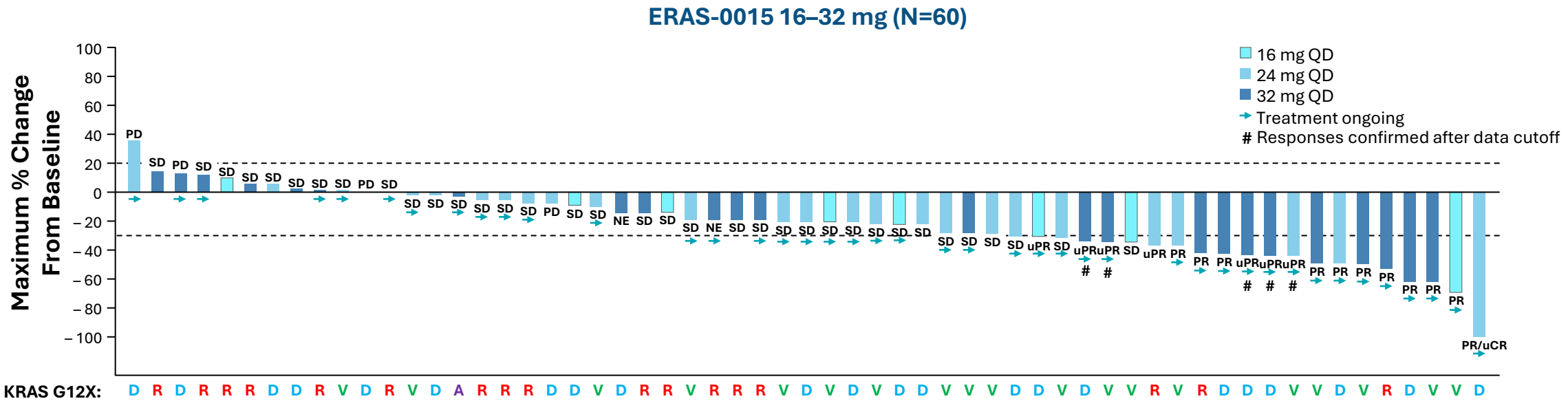
AURORAS-1: ERAS-0015 Safety at 32 mg Was Similar to 16–32 mg Dose

TRAEs in Patients Receiving ERAS-0015 at PAD of 16–32 mg and at 32 mg		
TRAEs in ≥10% of patients (16-32 mg), n (%)	**16–32 mg QD (N=122)**	**32 mg QD (N=54)**
Rash[a]	99 (81.1)	43 (79.6)
Diarrhea	39 (32.0)	19 (35.2)
Nausea	29 (23.8)	12 (22.2)
Stomatitis/mucositis	26 (21.3)	14 (25.9)
TRAEs leading to dose interruptions, n (%)	15 (12.3)	7 (13.0)
TRAEs leading to dose reductions, n (%)	13 (10.7)	9 (16.7)
TRAEs leading to dose discontinuations, n (%)	2 (1.6)	0

- **No prophylaxis recommended per protocol**

Data cutoff date: September 1, 2026. Safety set included all patients who received at least one dose of ERAS-0015. [a]Rash events are identified using the following preferred terms: rash pustular, rash papular, rash maculo-papular, rash macular, rash, erythema, and dermatitis acneiform (uncoded terms rash acneiform and rash are also included). PAD, pharmacologically active dose; QD, once daily; TRAE, treatment-related adverse event.

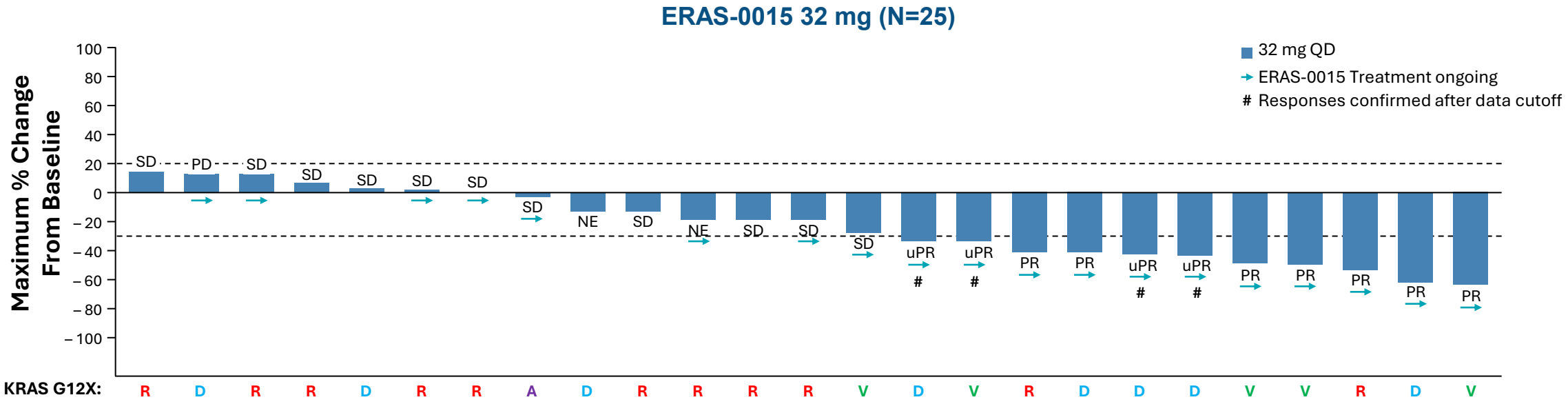
AURORAS-1: Tumor Reduction and Response in 2L+ KRAS G12X PDAC at 16–32 mg QD



Population	2L+	
ERAS-0015 Dose	16-24 mg[a] (N=35)	32 mg[a] (N=25)
ORR[b]	14.3%	44.0%
DCR	88.6%	88.0%

Data cutoff date: September 1, 2026. Efficacy evaluable population included all patients who received first dose of ERAS-0015 at least 8 weeks prior to the data cutoff. One patient is not included in the waterfall plot because no post-baseline tumor assessment was available [a]24 mg: one of two unconfirmed responses were confirmed after data cutoff; 32 mg: all four unconfirmed responses were confirmed after data cutoff. [b]All responses were confirmed. DCR, disease control rate; 2L, second line; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; PDAC, pancreatic ductal adenocarcinoma; QD, once daily; SD, stable disease; uCR, unconfirmed complete response; uORR, unconfirmed objective response rate; uPR, unconfirmed PR.

AURORAS-1: Tumor Reduction and Response in 2L+ KRAS G12X PDAC at 32 mg QD



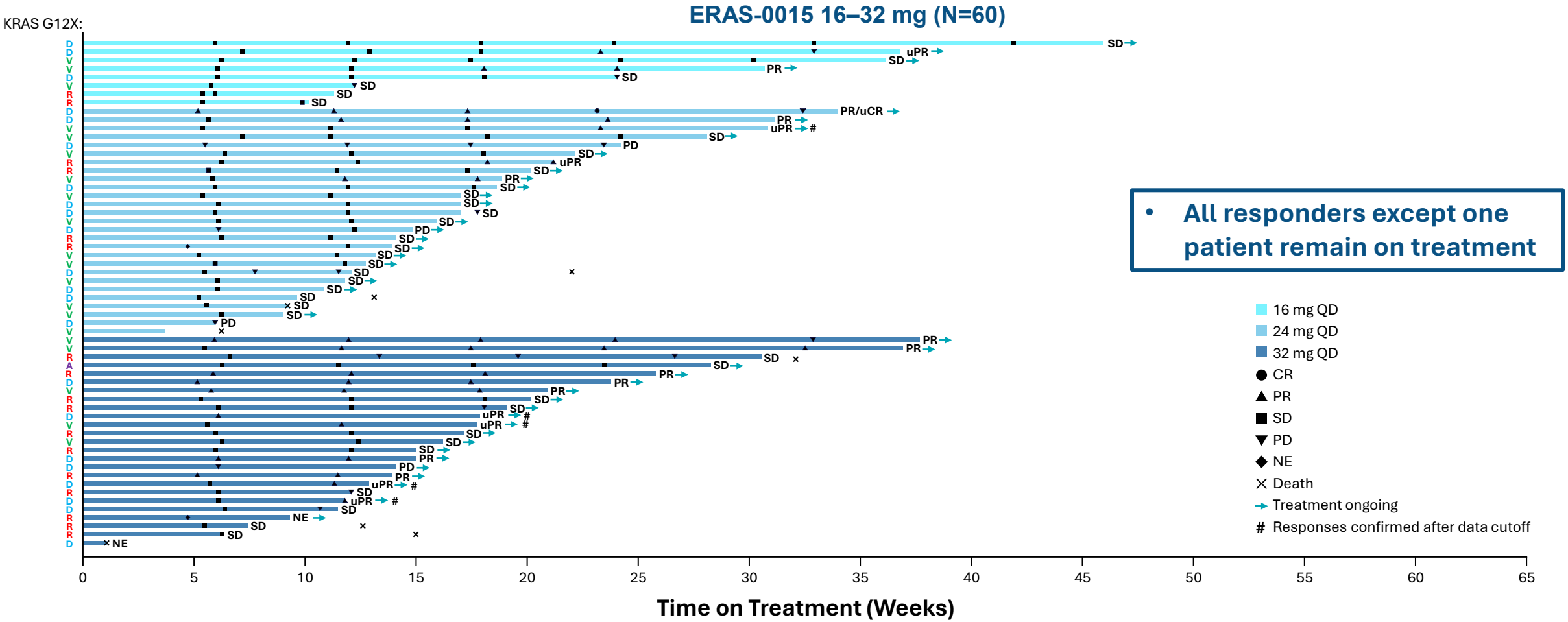
ERAS-0015, 2L+	
32 mg QD	KRAS G12X (N=25)
ORR[a]	44.0%
DCR	88.0%

Among patients treated with 32 mg QD ERAS-0015
- **16% were 2L**
- **84% were 3L+**

Population	2L+ ORR by KRAS G12X mutations			
ERAS-0015, 32 mg	KRAS G12D (N=8)	KRAS G12V (N=5)	KRAS G12R (N=11)	KRAS G12D or G12V (N=13)
ORR[a]	62.5%	80.0%	18.2%	69.2%
DCR	75.0%	100.0%	90.9%	84.6%

Data cutoff date: September 1, 2026. Efficacy evaluable population included all patients who received first dose of ERAS-0015 at least 8 weeks prior to the data cutoff; [a]All responses were confirmed. For 32 mg, all four unconfirmed responses were confirmed after data cutoff. DCR, disease control rate; 2L, second line; 3L, third line; NE, not evaluable; ORR, objective response rate; PD, progressive disease; PR, partial response; PDAC, pancreatic ductal adenocarcinoma; QD, once daily; SD, stable disease; uPR, unconfirmed PR.

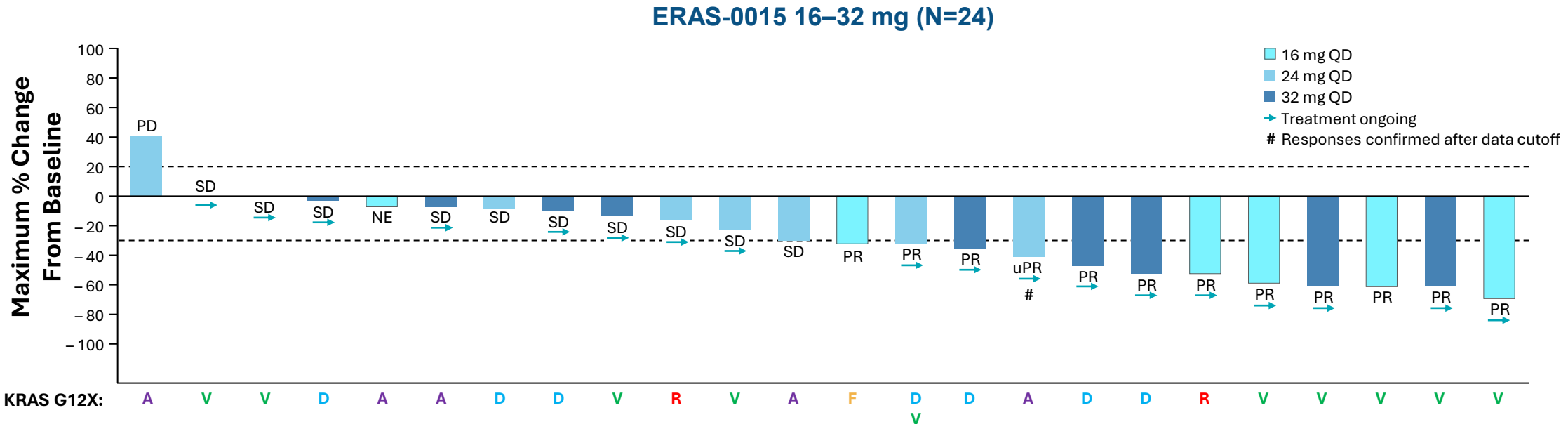
AURORAS-1: Duration of Treatment in 2L+ KRAS G12X PDAC



- All responders except one patient remain on treatment

Data cutoff date: September 1, 2026. CR, complete response; NE, not evaluable; PD, progressive disease; PDAC, pancreatic ductal adenocarcinoma; PR, partial response; QD, once daily; SD, stable disease; uCR, unconfirmed CR; uPR, unconfirmed PR.

AURORAS-1: Tumor Reduction and Response in 2L+ KRAS G12X NSCLC at 16-32 mg QD

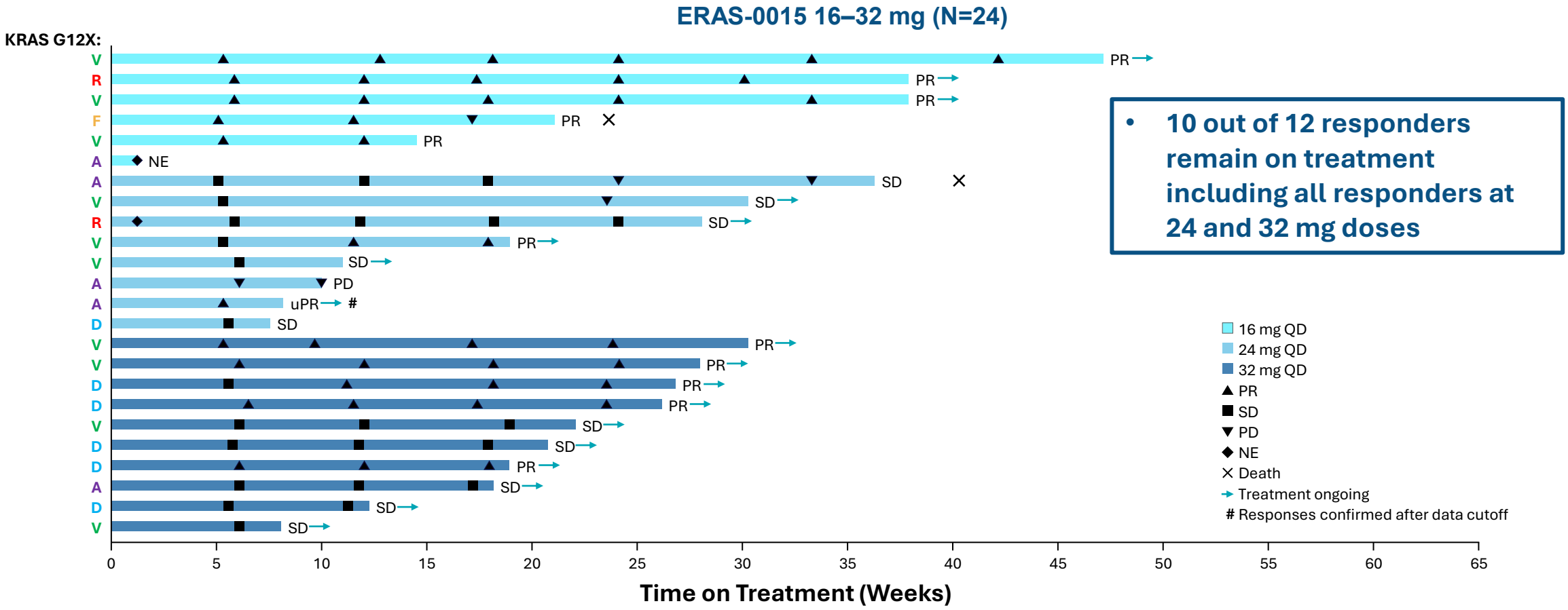


Population	2L+		ICI/ platinum and no taxane monotherapy (ERAS-0015 2L or 3L)	
ERAS-0015 Dose	32 mg (N=10)	16–32 mg (N=24)	32 mg (N=5)	16–32 mg (N=12)
ORR[a]	50.0%	50.0%	60.0%	58.3%
DCR	100.0%	91.7%	100.0%	91.7%

Population	2L+ ORR by KRAS G12X mutation	
ERAS-0015 32 mg	KRAS G12D (N=5)	KRAS G12V (N=4)
ORR[a]	60.0%	50.0%
DCR	100.0%	100.0%

Data cutoff date: September 1, 2026. Efficacy evaluable population included all patients who received first dose of ERAS-0015 at least 8 weeks prior to the data cutoff. [a]All responses were confirmed; one 24 mg response was confirmed after data cutoff. uDCR, disease control rate. ICI, immune checkpoint inhibitor; 2L, second line; 3L, second line; NE, not evaluable; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease.

AURORAS-1: Duration of Treatment in 2L+ KRAS G12X NSCLC

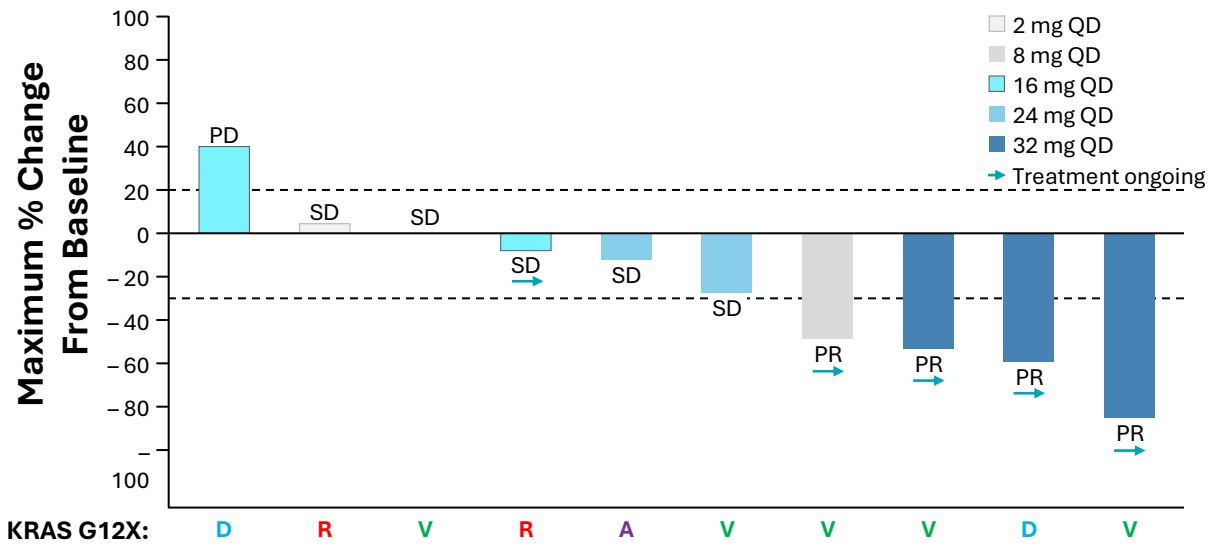


- **10 out of 12 responders remain on treatment including all responders at 24 and 32 mg doses**

Data cutoff date: September 1, 2026. NE, not evaluable; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed PR.

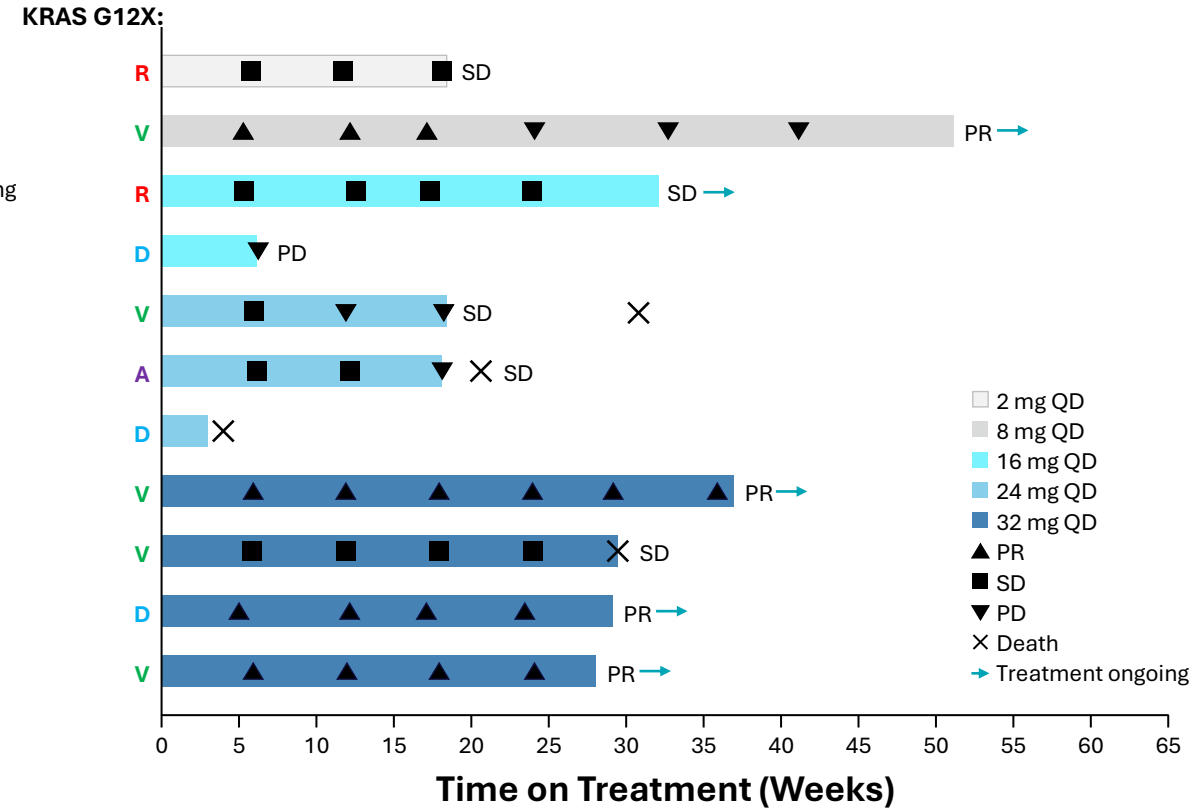
AURORAS-1: Tumor Reduction, Response, and Duration of Treatment in KRAS G12X BTC

ERAS-0015 2–32 mg (N=11)



Response in BTC[b]		
ERAS-0015 Dose	32 mg (N=4)	8–32 mg (N=10)
ORR[c]	75.0%	40.0%

ERAS-0015 2–32 mg (N=11)[a]



Data cutoff date: September 1, 2026. [a]Efficacy evaluable population included all patients who received first dose of ERAS-0015 at least 8 weeks prior to the data cutoff. One patient is not displayed in the waterfall plot because no post-baseline tumor assessment was available; [b]1 patient was treated in 1L and declined standard of care therapy; remainder of the patients were treated in 2L+, [c]All responses were confirmed. BTC, biliary tract cancer; 1L, first line; 2L, second line; ORR, objective response rate; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease.

Conclusions: AURORAS-1 Phase 1

- ERAS-0015 exhibited linear PK across the dose range
- Preliminary safety data from AURORAS-1 suggest ERAS-0015 was safe and generally well tolerated
  - ERAS-0015 was safe and generally well tolerated at pharmacologically active doses of 16–32 mg and at 32 mg with no observed dose-limiting toxicities and 100% median relative dose intensity; maximum tolerated dose was not reached
- ERAS-0015 showed promising early clinical activity in PDAC, NSCLC, and BTC
  - At 32 mg:
    - ORR of 44% in KRAS G12X 2L+ PDAC despite heavy pretreatment (84% in 3L+) and high frequency of G12R mutations (44% of pts had G12R); ORR of 69% in KRAS G12D or G12V 2L+ PDAC
    - ORR of 60% in KRAS G12X NSCLC post ICI and platinum-based chemotherapy
    - ORR of 75% in KRAS G12X BTC
- Phase 1 AURORAS-1 (NCT06983743) study is currently ongoing and enrolling patients with RAS alterations across multiple solid tumor types in ERAS-0015 monotherapy and combination cohorts

Clinical data cutoff date: September 1, 2026; PK data cutoff date: September 18, 2026; ctDNA data cutoff date: October 2, 2026. BTC, biliary tract cancer; ICI, immune checkpoint inhibitor; 2L, second line; 3L, second line; NSCLC, non-small cell lung cancer; ORR, objective response rate; PDAC, pancreatic ductal adenocarcinoma; PK, pharmacokinetic.

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