FARNESYL TRANSFERASE PROGRAM REVIEW – CLINICAL UPDATE FROM ESMO 2025

Our goal is to develop transformative therapies to extend and improve the lives of patients with cancer

October 18, 2025

FORWARD-LOOKING STATEMENTS

This presentation contains forward-looking statements. Such statements include, but are not limited to, statements regarding our research, preclinical and clinical development activities, plans and projected timelines for ziftomenib, darlifarnib (KO-2806) and tipifarnib, development plans and timelines for our menin inhibitor candidate in diabetes, expectations regarding the combinability of our product candidates with other therapies, expectations regarding the therapeutic and commercial potential of our product candidates, anticipated significant near-term milestones, market opportunities and expectations regarding our collaboration with Kyowa Kirin. The words "believe," "may," "should," "will," "estimate," "promise," "plan", "continue," "anticipate," "intend," "expect," "potential" and similar expressions (including the negative thereof) are intended to identify forward-looking statements. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: our preclinical studies and clinical trials may not be successful; the U.S. Food and Drug Administration (FDA) may not agree with our interpretation of the data from clinical trials of our product candidates; we may decide, or the FDA may require us, to conduct additional clinical trials or to modify our ongoing clinical trials; we may experience delays in the commencement, enrollment, completion or analysis of clinical testing for our product candidates, or in the reporting of data from such clinical testing, or significant issues regarding the adequacy of our clinical trial designs or the execution of our clinical trials may arise, which could result in increased costs and delays, or limit our ability to obtain regulatory approval; our product candidates may not receive regulatory approval or be successfully commercialized; unexpected adverse side effects or inadequate therapeutic efficacy of our product candidates could delay or prevent regulatory approval or commercialization; we may not be able to obtain additional financing; and our collaboration with Kyowa Kirin may not be successful. Additional risks and uncertainties may emerge from time to time, and it is not possible for Kura's management to predict all risk factors and uncertainties.

All forward-looking statements contained in this presentation speak only as of the date on which they were made. Other risks and uncertainties affecting us are described more fully in our filings with the Securities and Exchange Commission. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

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TODAY'S AGENDA

Review of Clinical Data Presented at ESMO 2025

Darlifarnib Monotherapy in Advanced *HRAS*m Solid Tumors
Phase 1a Data for KO-2806 Monotherapy in *HRAS*m Solid Tumor Patients

FTI and TKI Combinations in RCC
Phase 1a Data for KO-2806 and Cabozantinib Combination in RCC Patients

FTI and PI3Kα Inhibitor Combinations in HNSCC
Phase 1a Data for Tipifarnib and Alpelisib Combination in *HRAS*m HNSCC Patients

Q&A Session

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KURA IS ADVANCING A ROBUST PIPELINE OF THERAPEUTIC PRODUCT CANDIDATES

Ziftomenib: Potentially Best-in-Class Menin Inhibitor for AML

Relapsed/refractory (R/R) and frontline acute myeloid leukemia (AML) U.S. market opportunity could exceed $7B per year

NDA in R/R NPM1-m AML under FDA Priority Review with PDUFA target date of 30-Nov-2025; registration-enabling trials in 1L AML underway

Kyowa Kirin collaboration funds expansive AML development program

Farnesyl Transferase Inhibitors (FTIs) in Large Solid Tumor Indications

FTIs may overcome innate and adaptive resistance to PI3Kα inhibitors, KRAS inhibitors and tyrosine kinase inhibitors (TKIs) in certain indications

Target indications include renal cell carcinomas, HNSCC, lung, colorectal, breast, endometrial and NETs

Presentations of clinical data at ESMO Congress in October 2025

Additional Therapeutic Opportunities for Menin Inhibitors

Ziftomenib + imatinib currently in Phase 1 dose escalation in gastrointestinal stromal tumors (GIST); additional potential $1B opportunity

Next-generation menin inhibitor candidate nominated for IND-enabling studies for diabetes; development plans and timelines to be shared in future update

RATIONALE FOR FTIs: OVERCOMING RESISTANCE TO TARGETED THERAPIES

Combination therapy using FTIs has potential to address drug resistance and provide deeper and more durable anti-tumor activity

THERE IS A NEED TO IMPROVE STANDARDS OF CARE FOR PATIENTS TREATED WITH TARGETED THERAPIES

Despite impressive progress with small molecule targeted therapies, resistance limits the potential of many agents

- Targeted therapies are often effective but insufficient as monotherapies
- Combinations (*e.g.*, KRAS/EGFR inhibitors in CRC) have demonstrated enhanced response
- No established mechanism to resensitize tumors to innate and adaptive resistance after exposure to targeted therapy

There is a significant need to identify combination therapeutics that address mechanisms of innate and adaptive resistance

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There is a significant need to identify combination therapeutics that address mechanisms of innate and adaptive resistance

Kura Oncology is pioneering FTIs to enhance the therapeutic potential of targeted therapies

- mTOR is a clinically validated target, and FTIs reduce mTOR activation by blocking RHEB farnesylation
- RHEB/mTOR inhibition is relevant to anti-VEGF TKIs, KRAS inhibitors and PI3Kα inhibitors

Simultaneous inhibition of RHEB/mTOR using FTIs has potential to address resistance and provide deeper and more durable anti-tumor activity

KO-2806

Class-leading FTI drug candidate aims to address innate and adaptive resistance to various classes of targeted therapies

DARLIFARNIB (KO-2806) REPRESENTS A CLASS LEADING FTI

Darlifarnib

Next Gen FTI optimized for combination drug development. Preclinical data demonstrates improvements over prior FTIs :

Enhanced potency and selectivity

Manageable tolerability and combinability (with adagrasib, cabozantinib, and other agents) in long-term *in vivo* studies

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Pharmacokinetic and metabolic profiles support projected efficacious dose of **<< 1200 mg QD**

Excellent drug-like properties

Extended IP protection as an NCE

DARLIFARNIB MONOTHERAPY IN ADVANCED *HRAS*-MUTANT SOLID TUMORS

Glenn J. Hanna, M.D.

981P

BERLIN 2025 ESMO congress

A phase 1 study of the next-generation farnesyltransferase inhibitor (FTI) KO-2806 as monotherapy in advanced solid tumors

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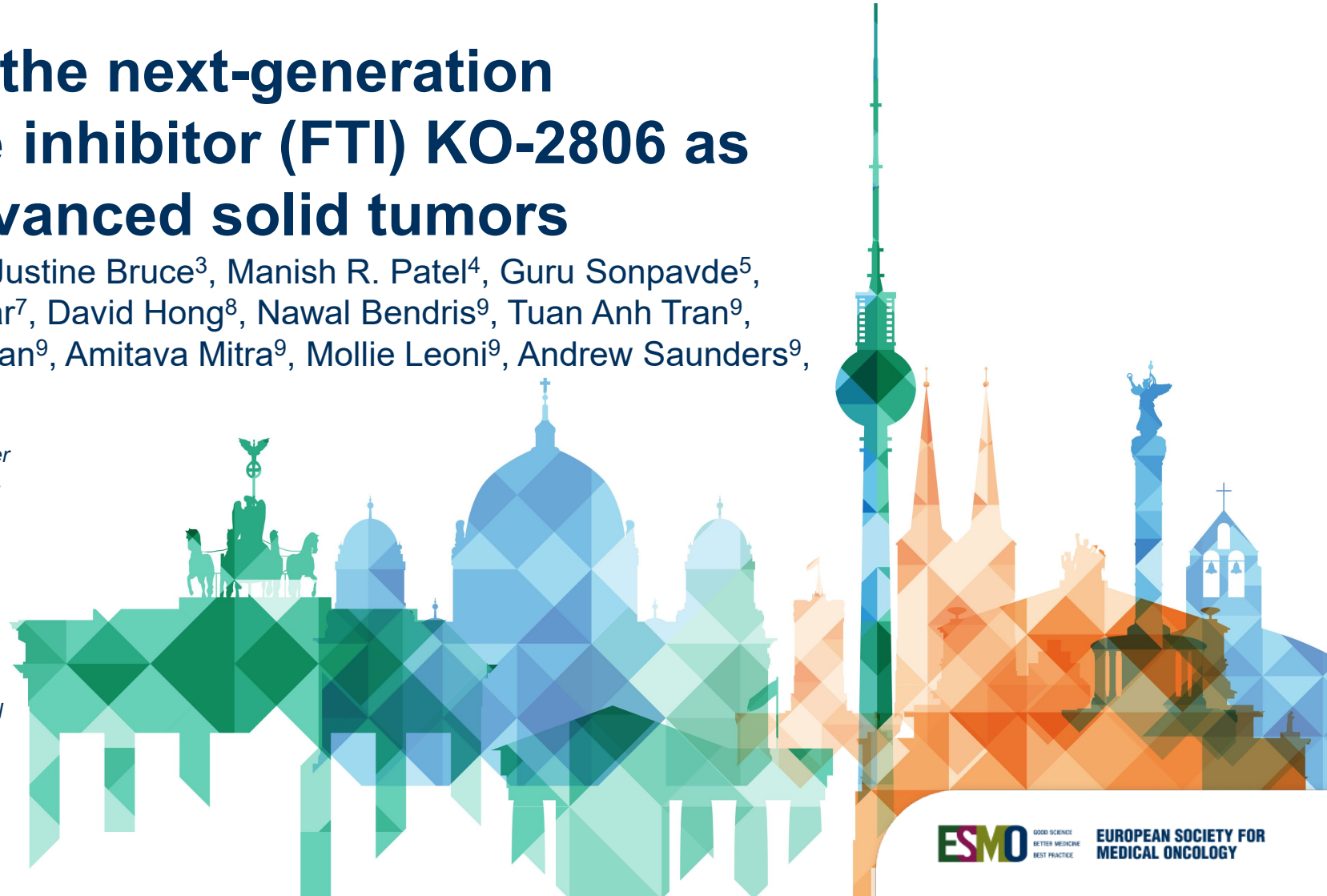

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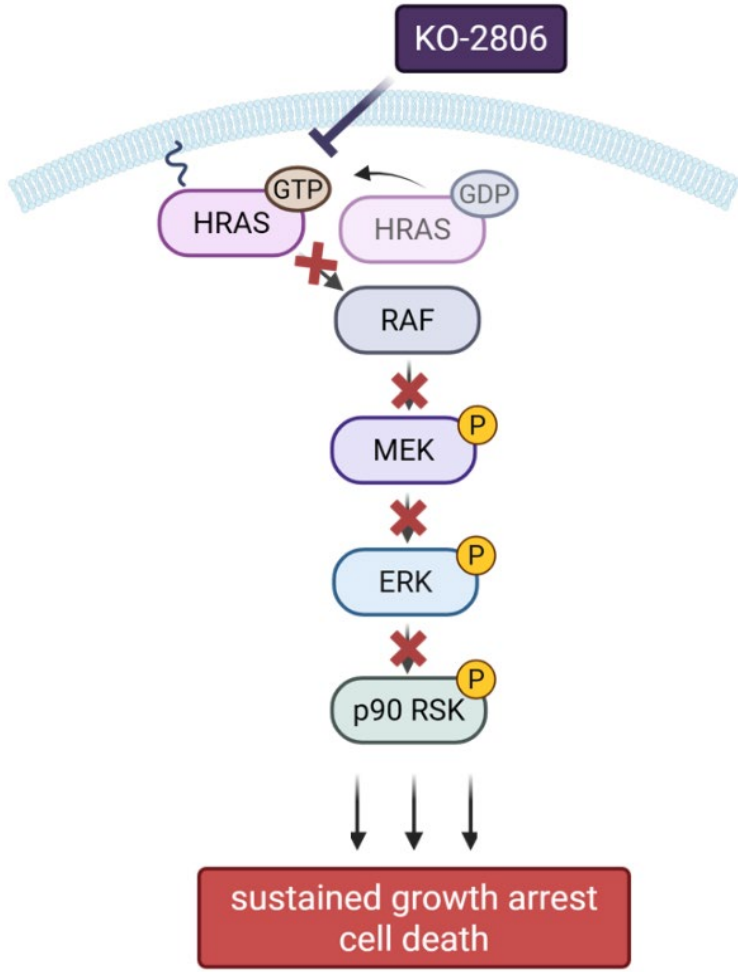
KO-2806 MECHANISM OF ACTION FOR MONOTHERAPY IN *HRAS*-MUTANT SOLID TUMORS

- **Farnesylation** anchors proteins to cell membranes to facilitate signaling complexes critical for cellular function[1]
- **Key signaling proteins** require farnesylation for localization and activity in oncogenic pathways[2-4]
- **HRAS and RHEB** depend solely on farnesylation for function, whereas NRAS and KRAS can use geranylgeranylation[2-4]
- ***HRAS*-mutant** tumors are sensitive to FTIs, with tipifarnib having demonstrated encouraging clinical activity in patients with *HRAS*-m tumors[5,6]
- **KO-2806 (darlifarnib)**, a next-generation FTI, offers enhanced potency and optimized pharmacokinetic (PK) properties, potentially improving therapeutic outcomes[7-9]

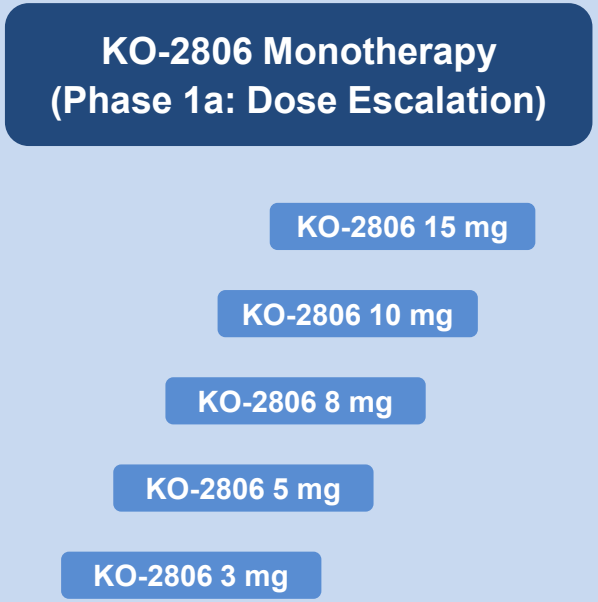


1. Mijimolle N et al. *Cancer* Cell 2005;7:313-24; 2. Whyte DB et al. *J Biol Chem* 1997;272:14459-64; 3. McGeady P et al. *J Biol Chem* 1995;270:26347-51; 4. Castro AF et al. *J Biol Chem* 2003;278:32493-6; 5. Ho AL et al. *J Clin Oncol* 2021;39:1856-64; 6. Ho AL et al. *Ann Oncol* 2023;34(suppl_2):S1286-7. 7. 7. Gatchalian J et al. Poster (abstract #34634) presented at the 36th EORTC-NCI-AACR Symposium, October 11–15, 2023, Boston, MA, USA; 8. Patel HV et al. Poster (abstract #34968) presented at the 36th EORTC-NCI-AACR Symposium, October 11–15, 2023, Boston MA, USA; 9. Smith A et al. Poster (abstract #34971) presented at the 36th EORTC-NCI-AACR Symposium, October 11–15, 2023, Boston MA, USA.

FIT-001 MONOTHERAPY STUDY DESIGN

FIT-001 is an ongoing first-in-human, multicenter, open-label, phase 1a/b trial of KO-2806 alone and in combination in patients with advanced solid tumors

- KO-2806 monotherapy portion conducted in patients with *RAS*-altered solid tumors
  - Any solid tumor: *HRAS*-mutation/-amplification
  - HNSCC: HRAS overexpression
  - NSCLC/CRC: *KRAS*/*NRAS*/*HRAS*-mutation/-amplification
- KO-2806 was orally administered once daily on days 1-7 and 15-21 in 28-day cycles (data cutoff date 15 Aug 2025)



Monotherapy activity anticipated in *HRAS* mutant patients only

BASELINE CHARACTERISTICS AND DEMOGRAPHICS

	KO-2806 3 mg (n=3)	KO-2806 5 mg (n=5)	KO-2806 8 mg (n=12)	KO-2806 10 mg (n=10)	KO-2806 15 mg (n=1)
Median age, years (range)	63 (61–74)	61 (53–75)	57 (36–70)	54 (47–76)	77 (77-77)
Male, n (%)	1 (33)	3 (60)	8 (67)	9 (90)	1 (100)
Race, n (%)					
White	3 (100)	5 (100)	8 (67)	8 (80)	1 (100)
Other	0	0	2 (17)	1 (10)	0
Asian	0	0	2 (17)	0	0
Black or African American	0	0	0	1 (10)	0
Ethnicity, n (%)					
Hispanic or Latino	0	0	2 (17)	1 (10)	0
Not Hispanic or Latino	3 (100)	5 (100)	10 (83)	8 (80)	1 (100)
Not reported	0	0	0	1 (10)	0
Primary tumor type, n (%)					
Pancreas	1 (33)	3 (60)	1 (8)	3 (30)	0
Rectum	1 (33)	1 (20)	2 (17)	2 (20)	0
Colon	0	0	1 (8)	4 (40)	0
Head and neck[a]	1 (33)	1 (20)	2 (17)	0	1 (100)
Other	0	0	4 (33)	0	0
Salivary gland[a]	0	0	1 (8)	1 (10)	0
Thyroid gland[a]	0	0	1 (8)	0	0
Karnofsky Performance Status, n (%)					
50-70	0	0	1 (8)	0	0
80-100	3 (100)	5 (100)	11 (92)	10 (100)	1 (100)
Prior therapy lines[b], n (%)					
1	0	2 (40)	3 (25)	0	0
2	2 (67)	0	2 (17)	5 (50)	1 (100)
≥3	1 (33)	2 (40)	7 (58)	5 (50)	0
***HRAS* alteration, n (%)**	1 (33)	2 (40)	8 (67)	1 (10)	1 (100)

[a] *HRAS*-m-driven tumors. [b] Prior therapy lines in the advanced/metastatic setting.

KO-2806 DEMONSTRATES ENCOURAGING SAFETY AND TOLERABILITY PROFILE

	Candidate RP2D Doses			*Maximum Tolerated Dose*	
Treatment Emergent Adverse Events n (%)	**KO-2806 3 mg (n=3)**	**KO-2806 5 mg (n=5)**	**KO-2806 8 mg (n=12)**	**KO-2806 10 mg (n=10)**	**KO-2806 15 mg (n=1)**
Any-Grade TEAEs (≥25% of all patients)	3 (100)	5 (100)	11 (92)	9 (90)	1 (100)
Neutropenia	2 (67)	2 (40)	5 (42)	7 (70	1 (100)
Anemia	3 (100)	3 (60)	7 (58)	1 (10)	1 (100)
Nausea	1 (33)	1 (20)	5 (42)	4 (40)	0
Thrombocytopenia	0	0	5 (42)	4 (40)	1 (100)
Fatigue	0	3 (60)	1 (8)	3 (30)	1 (100)
Grade ≥3 TEAEs (≥5% of all patients)	3 (100)	1 (20)	8 (67)	6 (60)	1 (100)
Neutropenia	0	0	4 (33)	6 (60)	1 (100)
Anemia	1 (33)	0	3 (25)	1 (10)	1 (100)
Thrombocytopenia	0	0	1 (8)	2 (20)	1 (100)
Leukopenia	0	0	1 (8)	1 (10)	1 (100)
Ascites	1 (33)	1 (20)	0	0	0
Hypokalemia	0	0	2 (17)	0	0

ENCOURAGING KO-2806 MONOTHERAPY CLINICAL ACTIVITY IN PATIENTS WITH *HRAS*-MUTANT SOLID TUMORS

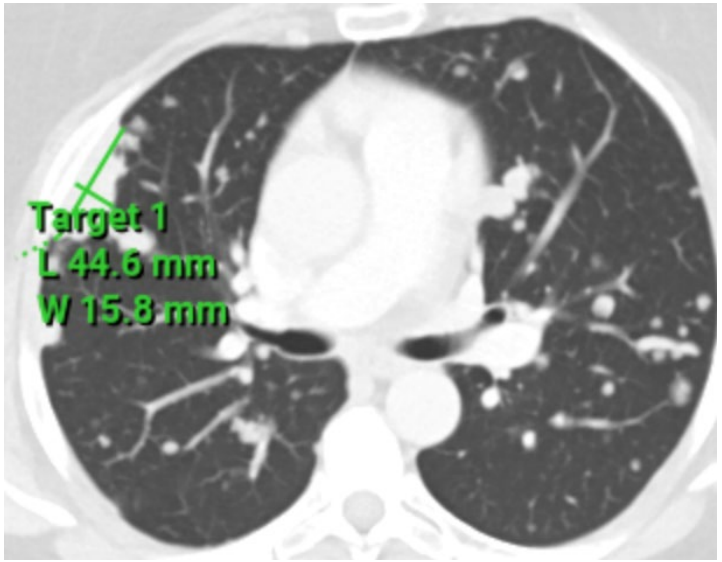
Subset of response-evaluable[a] patients with *HRAS*-m tumors who had antitumor activity[b]

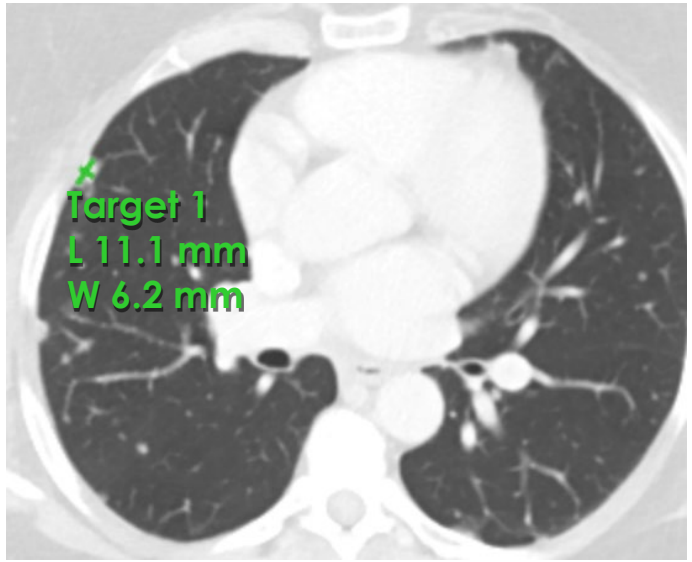
Dose	Indication	*HRAS*-m	BOR	Max. Tumor Shrinkage, %	Time on Treatment
3 mg[c]	Salivary[d]	Q61R	SD	0	21 mo[e]
5 mg	Salivary[d]	Q61R	PR	63	20 mo[f]
	Salivary	Q61R	SD	18	4 mo
8 mg	SCC (HN)[d]	G13V	PR	61	3 mo
	SCC (vulva)[d]	K117N	PR[g]	56	2 mo
	Medullary thyroid	G13R	SD	0	6 mo
10 mg	Salivary	Q61R	SD	25%	11 mo

[a] Response-evaluable patients had ≥1 post baseline scan. [b] 8 of 13 patients with HRAS-m tumors were response-evaluable; 1 patient did not have clinical benefit with KO-2806 monotherapy. [c] Dose was increased to KO-2806 5 mg at week 20. [d] On study treatment as of 15 Aug 2025. [e] Patient progressed 13.9 months after treatment initiation; as of 18 Jun 2025, patient remains on study treatment (time from cycle 1 day 1 to most recent scan: 19.4 months). [f] Durable response. [g] Unconfirmed PR as of data cutoff.

BOR, best overall response; HN, head and neck; PFS, progression-free survival; PR, partial response; SD, stable disease.

DEEP AND DURABLE RESPONSE IN A PATIENT WITH *HRAS*-MUTANT SALIVARY GLAND CARCINOMA





Baseline
Nov 2023

cPR, TL SoD -62.8%
from Baseline

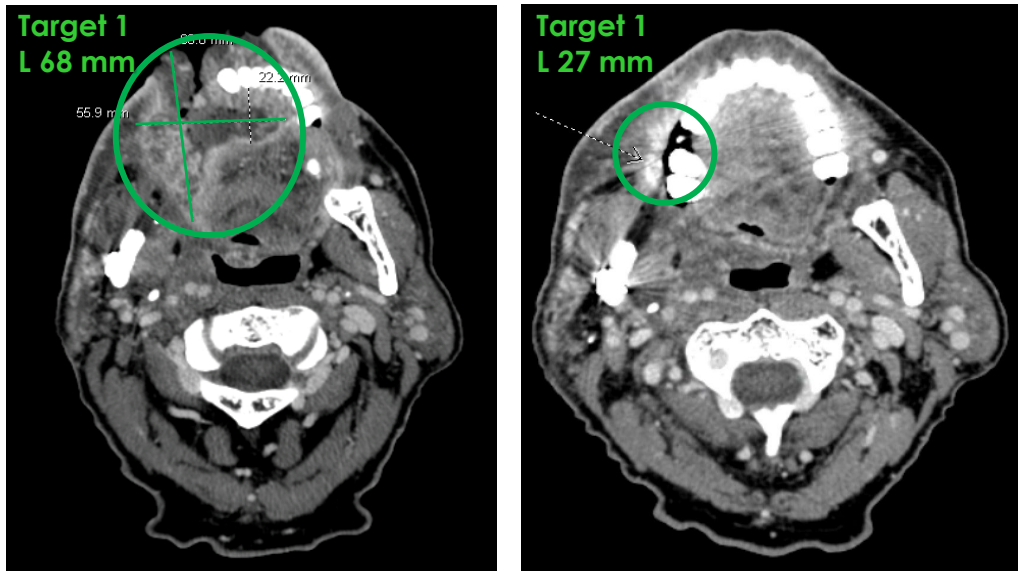
Week 80
Jul 2025

PATIENT BACKGROUND

- 60-year-old female patient with stage IVC salivary gland carcinoma
  - HRAS Q61R, VAF 16%
  - PD-L1 TPS 1%
- Prior therapies:
  - Left total parotidectomy (Aug 2014), radiotherapy (Nov 2014), right lung VATS and wedge resection (Feb 2021)
- Initiated KO-2806 5 mg in Dec 2023
- **Response: Confirmed PR (62.8% tumor shrinkage vs baseline)**
- As of data cutoff, patient remained on treatment at week 80

cPR, confirmed partial response; PD-L1 TPS, programmed death ligand-1 tumor proportion score; PR, partial response; SOD, sum of diameters; TL, target lesion; VAF, variant allele frequency; VATS, video-assisted thoracic surgery.

EARLY AND DEEP RESPONSE IN 4L PATIENT WITH ADVANCED *HRAS*-MUTANT HNSCC



PATIENT BACKGROUND

- 70-year-old male patient with stage IVA HNSCC
  - HRAS G13V, VAF 61%[a]
  - PD-L1 CPS 60%[a]
- Prior therapies:
  - MM + MRND (Oct 2022)
  - Adjuvant radiotherapy (Jan to Feb 2023)
  - 1L CP + P then P (Sep 2023 to Jul 2024)
  - 2L CP + P (Sep to Dec 2024)
  - 3L cetuximab + ficlatuzumab (Feb 2025 to Apr 2025)
- Initiated KO-2806 8 mg treatment in May 2025
- **Response: Confirmed PR (60% tumor shrinkage at week 8 vs baseline)**
- As of data cutoff, patient remained on treatment

[a] Sample collected Jan 2024, sequenced Jul 2024; patient received 3 treatment lines from time of biopsy to KO-2806 treatment initiation.

CP, carboplatin + paclitaxel; cPR, confirmed partial response; HNSCC, head and neck squamous cell carcinoma; MM, marginal mandibulectomy; MRND, modified radical neck dissection; P, pembrolizumab; PD-L1 CPS, programmed death ligand-1 combined positive score; PR, partial response; SoD, sum of diameters; VAF, variant allele frequency; TL, target lesion.

CONCLUSIONS FROM KO-2806 MONOTHERAPY

KO-2806 demonstrates manageable safety and tolerability profile supporting QD dosing every other week

Encouraging monotherapy antitumor activity was observed at multiple doses in advanced *HRAS*-m solid tumors, evidencing on-target activity and a broad therapeutic window

These data support further evaluation of KO-2806 in combination with targeted therapies

KO-2806 is currently being evaluated in combination with cabozantinib (RCC) and adagrasib (KRAS G12C-mutant NSCLC, CRC, or PDAC) in the FIT-001 study (NCT06026410)

KO-2806 (darlifarnib) is optimized for use as a QD oral agent in combination with various targeted therapeutics

1. Ho AL et al. *J Clin Oncol* 2021;39:1856-1864; 2. Hanna GJ et al. *Cancer* 2020;126:3972-3981.

DARLIFARNIB + CABOZANTINIB COMBINATION IN RENAL CELL CARCINOMA

Mollie Leoni, M.D., Chief Medical Officer

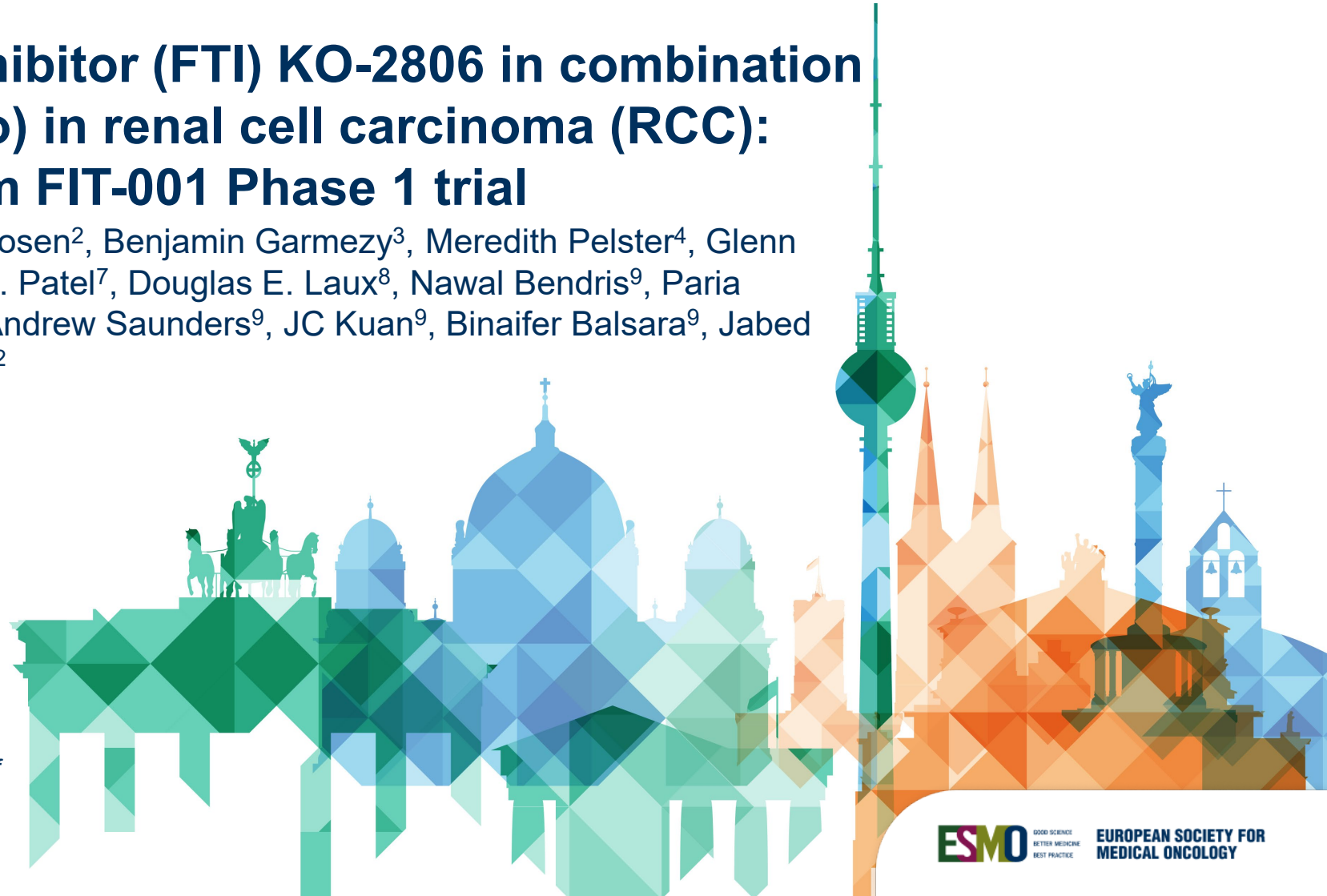
2604P

BERLIN 2025 ESMO congress

Farnesyltransferase inhibitor (FTI) KO-2806 in combination with cabozantinib (cabo) in renal cell carcinoma (RCC): Preliminary results from FIT-001 Phase 1 trial

Adanma Ayanambakkam[1], Lee S. Rosen[2], Benjamin Garmezy[3], Meredith Pelster[4], Glenn J. Hanna[5], Jacob Thomas[6], Manish R. Patel[7], Douglas E. Laux[8], Nawal Bendris[9], Paria Mahboub Johnson[9], Stephen Dale[9], Andrew Saunders[9], JC Kuan[9], Binaifer Balsara[9], Jabed Seraj[9], Mollie Leoni[9], Adam E. Singer[2]

[1]Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [2]Division of Hematology-Oncology, University of California Los Angeles Medical Center, Los Angeles, CA, USA; [3]Genitourinary Cancer Research, Sarah Cannon Research Institute, Nashville, TN, USA; [4]Gastrointestinal Cancer Research, Sarah Cannon Research Institute, Nashville, TN, USA; [5]Center for Head and Neck Oncology, Dana-Farber Cancer Institute, Boston, MA, USA; [6]Division of Medical Oncology, Department of Medicine, University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [7]Florida Cancer Specialists, Sarah Cannon Research Institute, Sarasota, FL, USA; [8]Division of Hematology, Oncology and Blood & Marrow Transplantation, University of Iowa Hospitals and Clinics, Iowa City, IA, USA; [9]Kura Oncology, Inc., San Diego, CA, USA



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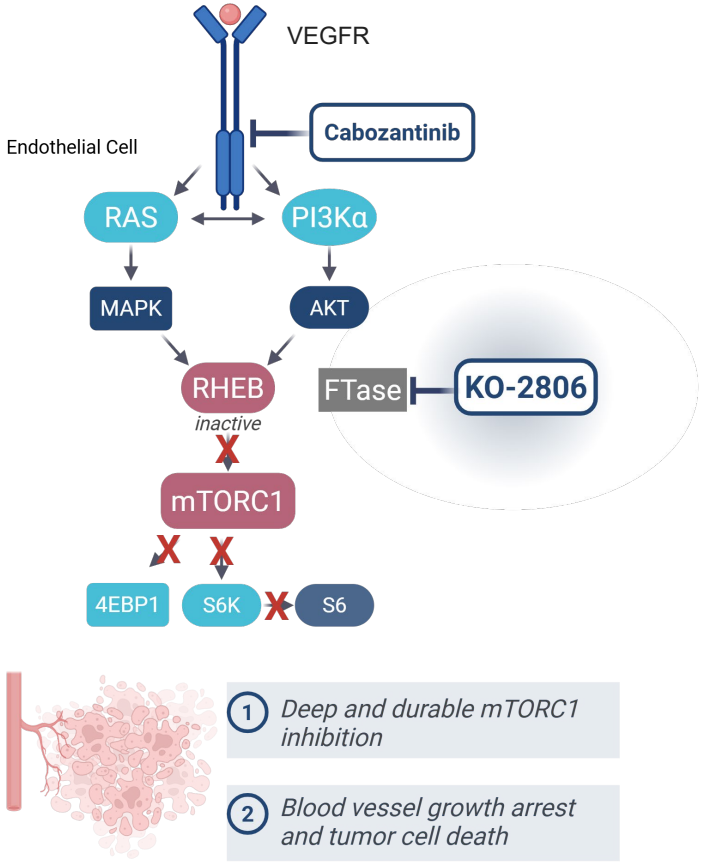
KO-2806 MECHANISM OF ACTION IN RENAL CELL CARCINOMA

- **Overactive mTOR pathway** signaling drives cell growth, proliferation and survival in RCC tumors and is associated with poor prognosis[1-3]
- **Rapalogs** are FDA approved in RCC but have seen limited use due to tolerability issues[4-6]
- **Cabozantinib** offers clinical benefit (2L: ORR 28%, SD 60%[7]); however, reduced activity with subsequent TKIs underscores the need to optimize VEGFR-targeted therapies[8,9]
- **KO-2806 inhibits farnesylation of RHEB**, essential to activation of mTORC1, and spares mTORC2 and associated toxicities[10-11]
- **KO-2806 enhances cabozantinib's antiangiogenic activity** in both endothelial cells and pericytes in RCC xenografts[11]

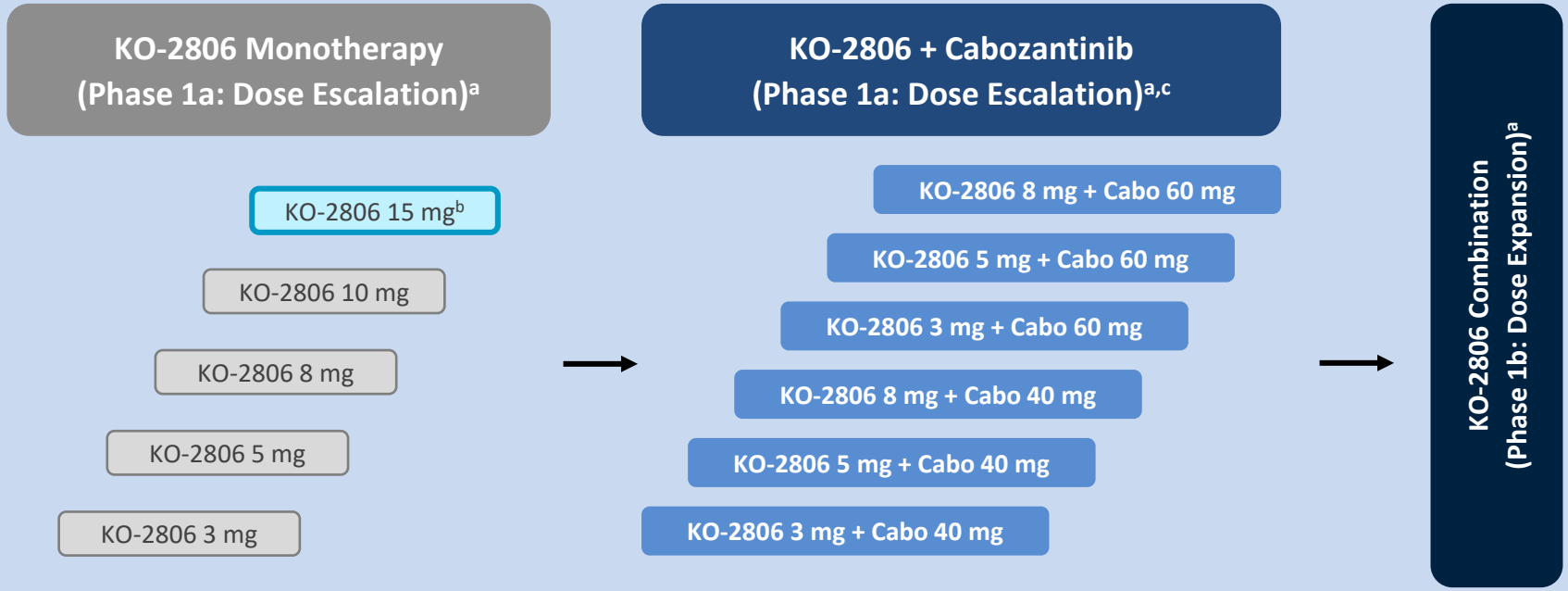


1. Grabiner BC et al. Cancer Discov 2014;4:554–63; 2. Ghosh AP et al. Oncotarget 2015;6:17895–910; 3. Cancer Genome Atlas Research Network. Nature 2013;499:43–9; 4. Hudes G et al. N Engl J Med 2007;356:2271–81; 5. Molina AM et al. Cancer 2012;118:1868–76; 6. White DA et al. Am J Respir Crit Care Med 2010;182:396-403; 7. Tannir et al. JAMA Oncology 2022;8:1411–1418; 8. Choueiri TK et al. N Engl J Med 2015;373:1814–1823; 9. Sharma R et al. J Exp Clin Cancer Res 2021;40:186; 10. Patel HV et al. bioRxiv 2024;12.20.629824; 11. Gasendo G et al. Oral presentation (abstract #6370) presented at the AACR Annual Meeting, April 25–30, 2025, Chicago, IL, USA.

FIT-001 KO-2806 MONOTHERAPY AND CABOZANTINIB COMBINATION STUDY DESIGNS

FIT-001 is an ongoing first-in-human, multicenter, open-label, phase 1a/b dose-escalation/-expansion study of KO-2806 alone and in combination in patients with advanced solid tumors

- **KO-2806 + cabozantinib combination for patients with ccRCC or non-ccRCC**
- KO-2806 3, 5, or 8 mg was administered QD orally Days 1-7 and 15-21 plus continuous cabozantinib 40 mg or 60 mg QD in 28-day cycles (data cutoff date 15 Aug 2025)



[a] Each individual patient will receive one of the planned DLs of KO-2806. [b] Non-tolerated DL. [c]KO-2806 + adagrasib combination for patients with KRAS G12C-mutated NSCLC, CRC, or PDAC is also being assessed.
cc, clear cell; CRC, colorectal cancer; DL, dose level; IO, immune checkpoint inhibition; NSCLC, non-small cell lung cancer; PDAC, pancreatic ductal adenocarcinoma; PS, performance status; QD, once daily; RCC, renal cell carcinoma.

BASELINE CHARACTERISTICS AND DEMOGRAPHICS

	Cabozantinib 40 mg			Cabozantinib 60 mg		
	KO-2806 3 mg (n=9)	KO-2806 5 mg (n=12)	KO-2806 8 mg (n=12)	KO-2806 3 mg (n=2)	KO-2806 5 mg (n=12)	KO-2806 8 mg (n=9)
Median age, years (range)	58 (47–83)	67 (50–80)	59 (39–80)	76 (73–79)	68 (42–76)	72 (61–78)
Male, n (%)	5 (56)	10 (83)	9 (75)	1 (50)	10 (83)	9 (100)
Race, n (%)						
White	7 (78)	6 (50)	6 (50)	1 (50)	9 (75)	9 (100)
Non-White[a]	2 (22)	6 (50)	6 (50)	1 (50)	3 (25)	0
RCC type, n (%)						
Clear cell	7 (78)	8 (67)	9 (75)	1 (50)	11 (92)	9 (100)
Non-clear cell[b]	2 (22)	4 (33)	3 (25)	1 (50)	1 (8)	0
Karnofsky PS, n (%)[c]						
50-70	0	1 (8)	0	0	0	0
80-100	9 (100)	11 (92)	11 (92)	1 (50)	12 (100)	9 (100)
Prior therapy lines, n (%)						
1	4 (44)	3 (25)	4 (33)	0	9 (75)	7 (78)
2	2 (22)	4 (33)	2 (17)	1 (50)	2 (17)	2 (22)
≥3	3 (33)	5 (42)	4 (33)	1 (50)	1 (8)	0
Prior therapy type(s), n (%)[d]						
IO	4 (44)	7 (58)	6 (50)	0	10 (83)	5 (55.5)
IO + TKI combination[e]	7 (78)	7 (58)	6 (50)	2 (100)	3 (25)	3 (33)
Cabozantinib	7 (78)	8 (67)	5 (42)	1 (50)	0	0
Other[f]	0	7 (58)	4 (33)	0	2 (17)	0

[a] Includes Black or African American, Asian, American Indian or Alaska Native, Other, and Multiple; [b] Including papillary (n=4), chromophobe (n=3), sarcomatoid (n=2) and unknown tumor type (n=2). [c] Karnofsky PS was missing for 2 patients. [d] Patients may have received multiple prior therapies. [e] Including cabozantinib. [f] Patients received HIF2a inhibitors or experimental therapies.
IO, immunotherapy; PS, performance status; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor.

ENCOURAGING SAFETY AND TOLERABILITY PROFILE OF KO-2806 + CABOZANTINIB COMBINATION

n (%)	Cabozantinib 40 mg			Cabozantinib 60 mg		
	KO-2806 3 mg (n=9)	KO-2806 5 mg (n=12)	KO-2806 8 mg (n=12)	KO-2806 3 mg (n=2)	KO-2806 5 mg (n=12)	KO-2806 8 mg (n=9)
Any-Grade TEAEs (≥25% of all patients)	**9 (100)**	**12 (100)**	**11 (92)**	**1 (50)**	**12 (100)**	**8 (89)**
Diarrhea	5 (56)	5 (42)	4 (33)	1 (50)	9 (75)	2 (22)
Neutropenia	1 (11)	5 (42)	6 (50)	0	6 (50)	5 (56)
Fatigue	2 (22)	2 (17)	7 (58)	0	6 (50)	3 (33)
Stomatitis	3 (33)	4 (33)	4 (33)	1 (50)	4 (33)	3 (33)
Nausea	3 (33)	4 (33)	3 (25)	0	6 (50)	2 (22)
Decreased appetite	3 (33)	4 (33)	3 (25)	0	5 (42)	2 (22)
Grade ≥3 TEAEs (≥5% of all patients)	**6 (67)**	**11 (92)**	**6 (50)**	**0**	**7 (58)**	**5 (56)**
Neutropenia	0	5 (42)	6 (50)	0	2 (17)	3 (33)
Anemia	2 (22)	1 (8)	3 (25)	0	0	1 (11)
Fatigue	0	1 (8)	1 (8)	0	1 (8)	1 (11)
Thrombocytopenia	0	1 (8)	2 (17)	0	0	0
Diarrhea	0	1 (8)	1 (8)	0	1 (8)	0
Embolism	0	1 (8)	0	0	2 (17)	0

ENCOURAGING CLINICAL ACTIVITY OF KO-2806 AND CABOZANTINIB IN RESPONSE-EVALUABLE[a] RCC PATIENTS

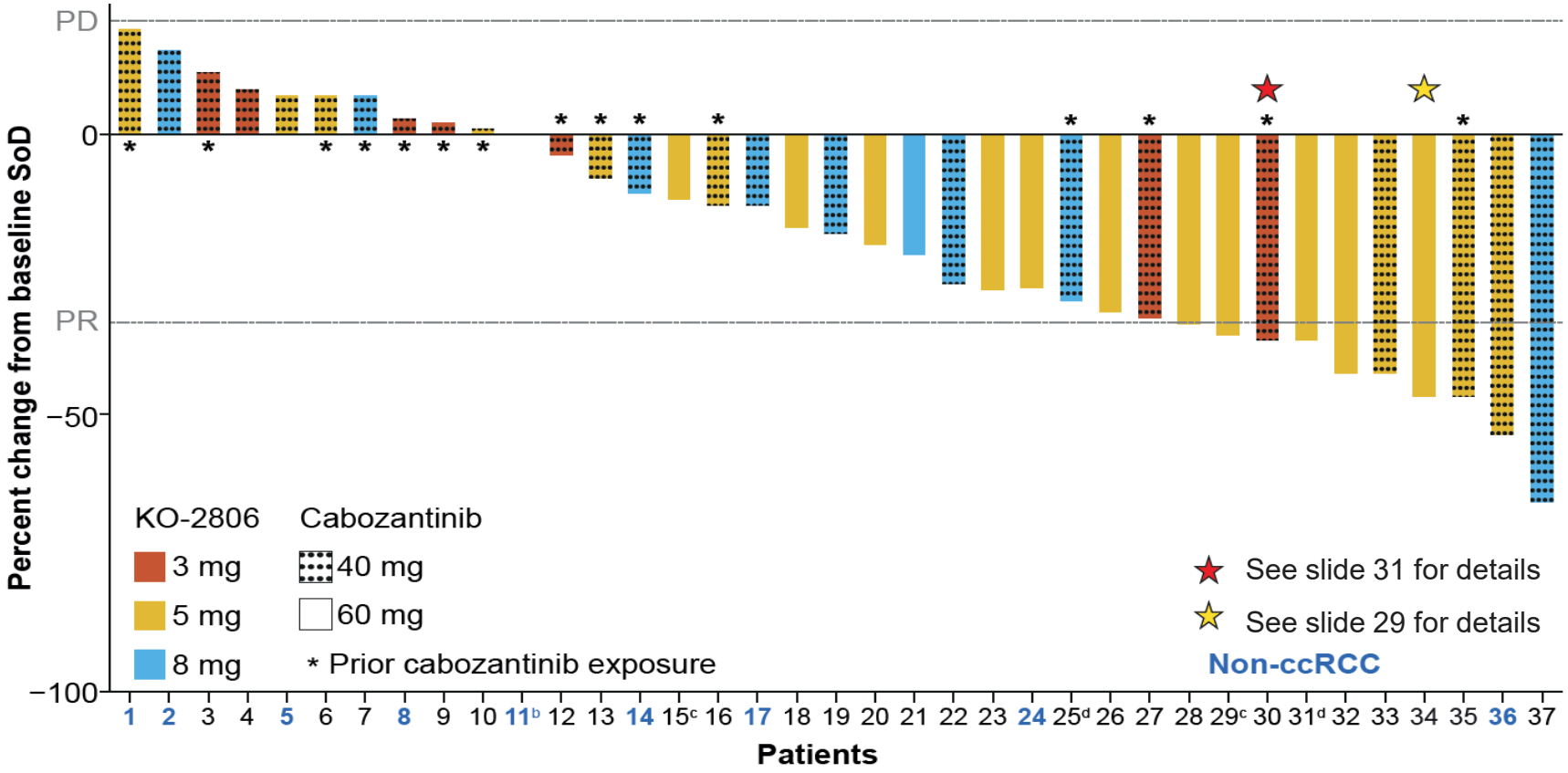
	Cabozantinib 40 mg			Cabozantinib 60 mg[b]
	KO-2806 3 mg (n=6)	KO-2806 5 mg (n=6)	KO-2806 8 mg (n=6)	KO-2806 5 mg (n=10)
ORR (CR+PR)				
ccRCC n (%)	2 (33)	2 (33)	2 (33)[c]	5 (50)[d]
95% CI	4.3–77.7	4.3–77.7	4.3–77.7	18.7–81.3
ccRCC with prior cabozantinib, n/N (%)	2/6 (33)	1/6 (17)	1/2 (50)[e]	NA
95% CI	4.3-77.7	0.4-64.1	1.3-98.7	NA
PR, n (%)	2 (33)	2 (33)	2 (33)[c]	5 (50)[d]
SD, n (%)	3 (50)	4 (67)	4 (67)	3 (30)
DCR (CR+PR+SD) n (%)	5 (83)	6 (100)	6 (100)[c]	8 (80)[d]
95% CI	35.9–99.6	54.1–100	54.1–100	44.4–97.5

[a] Response-evaluable patients had ≥1 post baseline scan. [b] As of the Aug 15, 2025 data cutoff, enrollment in KO-2806 3 mg + cabozantinib 60 mg is ongoing, and response data for KO-2806 8 mg + cabozantinib 60 mg are not yet mature. [c] Including n=1 confirmed PR, n=1 unconfirmed PR. [d] Including n=4 confirmed PR, n=1 unconfirmed PR. [e] n = 1 unconfirmed PR.

CI, confidence interval; CR, complete response; DCR, disease control rate; NA, not applicable; ORR, objective response rate; PR, partial response; SD, stable disease.

ENCOURAGING CLINICAL ACTIVITY OF KO-2806 AND CABOZANTINIB IN RESPONSE-EVALUABLE[a] RCC PATIENTS

Best overall response in all response-evaluable[a] patients across dose levels

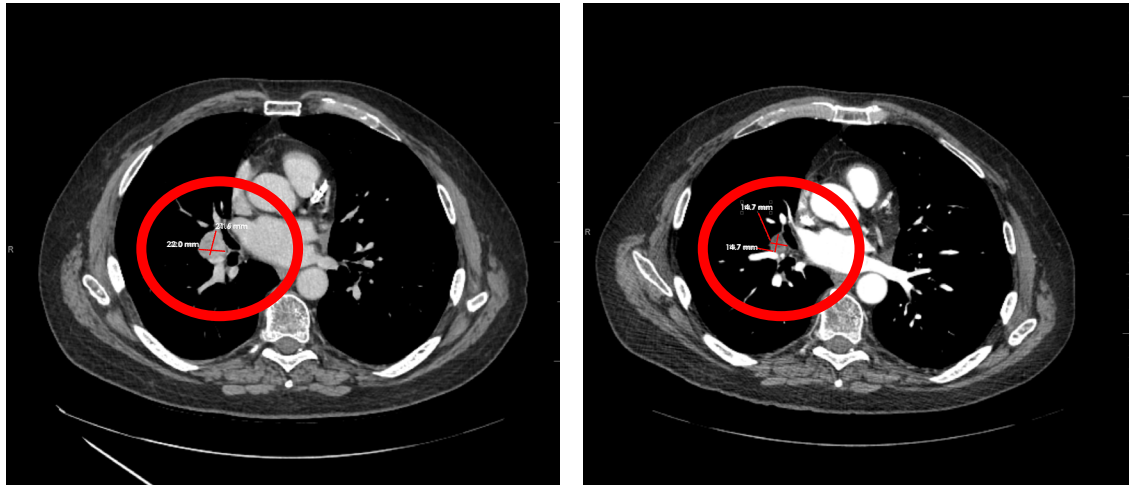


[a] Response-evaluable patients had ≥ 1 post-baseline scan. [b] Patient received KO-2806 3 mg + cabozantinib 40 mg. [c] Patient had BOR of PD due to new lesion. [d] Unconfirmed PR.

BOR, best overall response; ccRCC, clear cell renal cell carcinoma; PD, progressive disease; PR, partial response; SoD, sum of diameters.

DEEP RESPONSE IN PATIENT TREATED WITH KO-2806 AND CABOZANTINIB

Scans From A Responder Treated With KO-2806 5 mg + Cabo 60 mg



Screening → Week 16

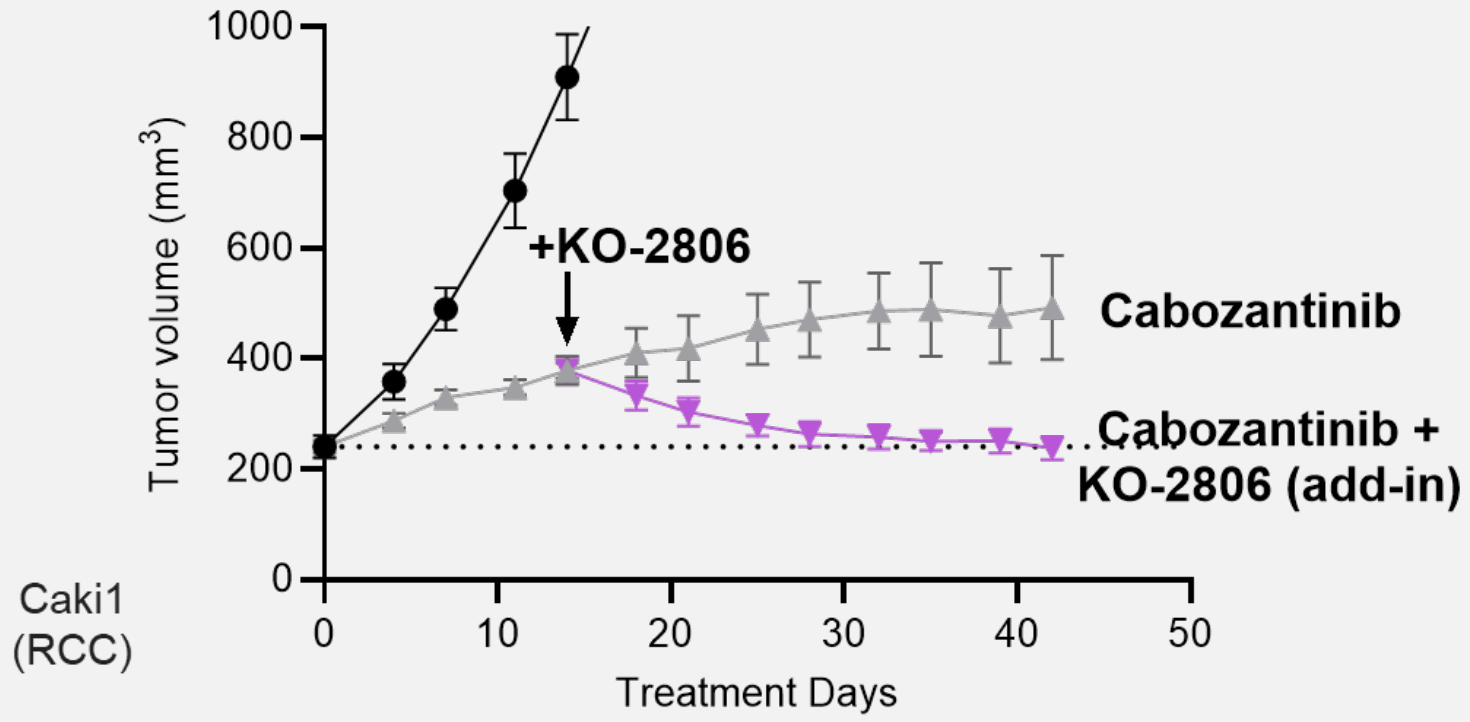
PATIENT BACKGROUND

- 61-year-old male with ccRCC
- Prior therapy:
  - Pembrolizumab as adjuvant therapy (nodal metastasis after two months of treatment)
- At study start:
  - Stage IV (right hilar lymph node)
- **Response: PR (38% reduction at week 8; 44% reduction at week 16)**
- As of data cutoff, patient remained on treatment

ccRCC, clear cell renal cell carcinoma; PR, partial response; SD, stable disease; W, week.

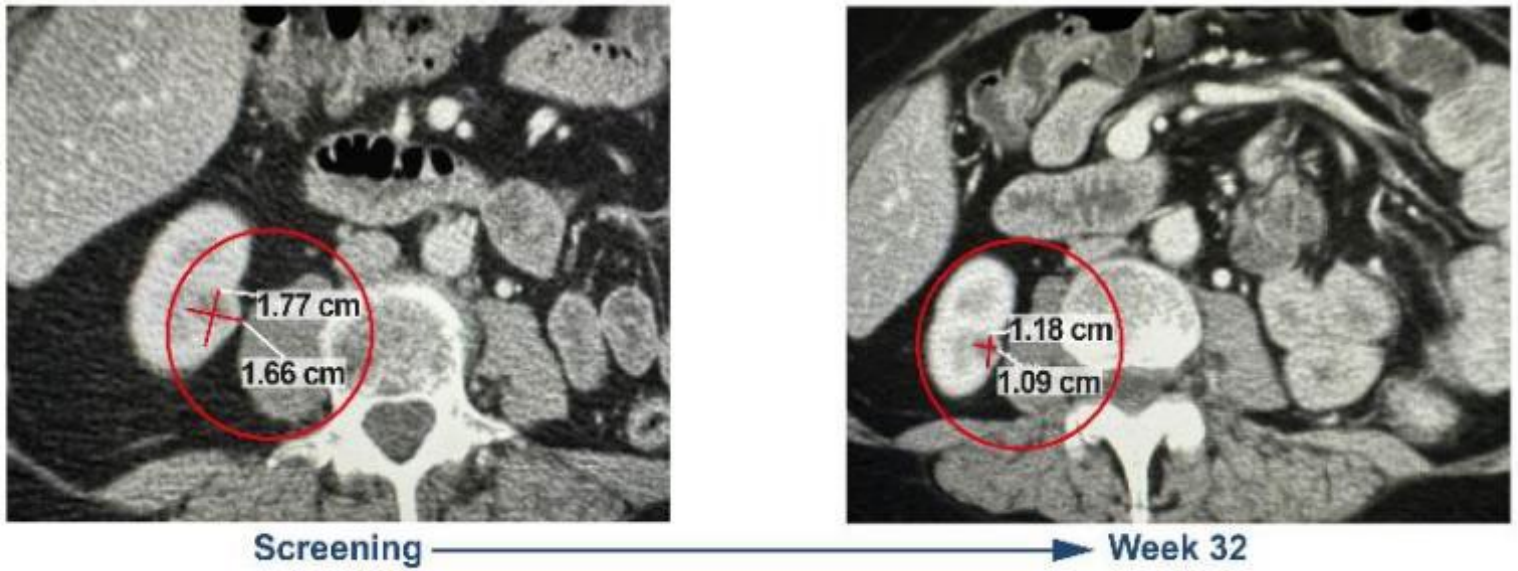
RCC XENOGRAFTS PROGRESSING ON ANTI-VEGFR TKIS RESPOND TO KO-2806 + CABOZANTINIB COMBINATION

Combination induces regressions in tumors previously exposed to cabozantinib



- KO-2806 enhances activity of cabo and other TKIs across their full activity range in ccRCC models
- Enhancement of antiangiogenic TKI activity by FTI-mediated RHEB/mTOR inhibition is effective in tumors progressing on first- or second-line TKI monotherapy

ACTIVITY IN PATIENT WITH PRIOR CABO EXPOSURE SUGGESTS BENEFIT OF KO-2806 + CABO COMBINATION



PATIENT BACKGROUND

- 53-year-old female patient with ccRCC diagnosed in 2021
- Prior therapy:
  - 1L: Ipilimumab + nivolumab (BOR: SD)
  - 2L: Nivolumab + **cabozantinib** (BOR: SD)
- At study start:
  - Stage IV; Initiated study treatment Oct 2024
- Dosage:
  - KO-2806 3 mg + cabo 40 mg
- **Response:**
  - **Confirmed PR, which was durable through week 40 (33% and 37% reductions at weeks 8 and 16)**
- As of data cutoff, patient remained on treatment

CONCLUSIONS FROM KO-2806 + CABOZANTINIB COMBINATION IN RCC PATIENTS

KO-2806 + cabozantinib demonstrated a manageable safety profile across dose levels assessed

Antitumor activity of KO-2806 + cabozantinib combination was observed across all doses in RCC (potentially exceeding the activity of cabozantinib alone), including among patients with prior cabozantinib exposure

- ORR: 33%–50% in ccRCC (with prior cabozantinib: 17%–50%)
- DCR: 80%–100% in ccRCC

Activity of the KO-2806 + cabozantinib combination supports the hypothesis that KO-2806 enhances antiangiogenic activity of cabozantinib

Data support dose optimization of KO-2806 and cabozantinib as well as further investigation of KO-2806 combinations in RCC

FTI AND PI3Kα INHIBITOR COMBINATIONS IN HNSCC

Glenn J. Hanna, M.D.

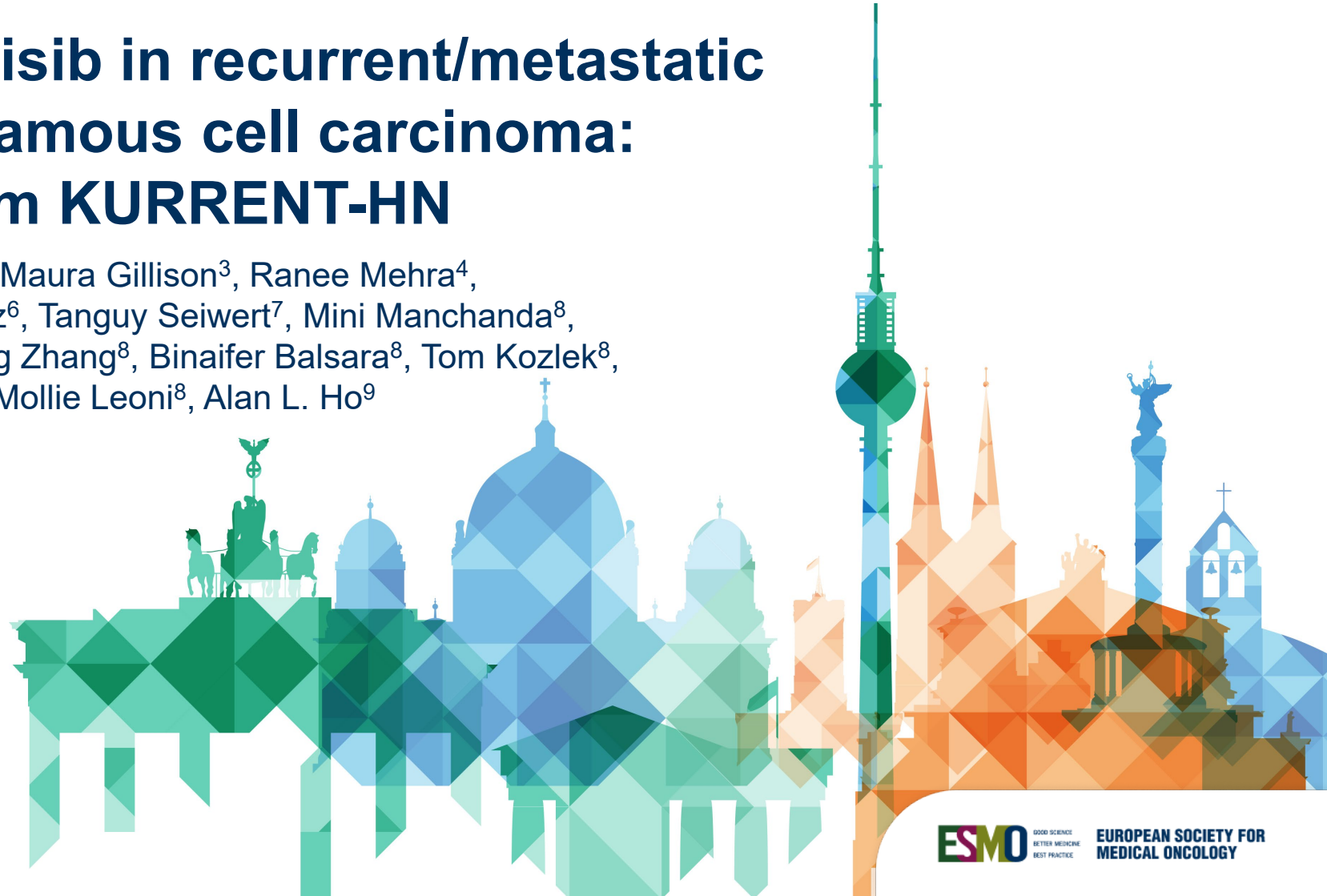
1349P

BERLIN 2025 ESMO congress

Tipifarnib and alpelisib in recurrent/metastatic head and neck squamous cell carcinoma: Phase 1 results from KURRENT-HN

Glenn J. Hanna[1], Douglas Adkins[2], Maura Gillison[3], Ranee Mehra[4], Justine Yang Bruce[5], Cesar A. Perez[6], Tanguy Seiwert[7], Mini Manchanda[8], Harris S. Soifer[8], Jeanne Britt[8], Zijing Zhang[8], Binaifer Balsara[8], Tom Kozlek[8], Stephen Dale[8], Andrew Saunders[8], Mollie Leoni[8], Alan L. Ho[9]

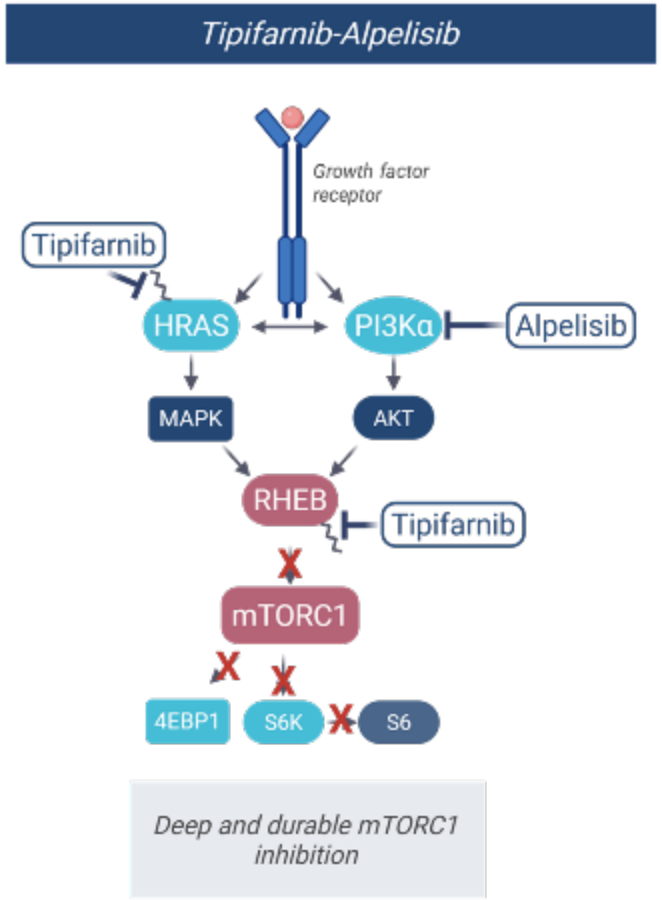
[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]Marlene and Stewart Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, MD, USA; [5]University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [6]Sarah Cannon Research Institute at Florida Cancer Specialists, Orlando, FL, USA; [7]Johns Hopkins Hospital, Baltimore, MD, USA; [8]Kura Oncology, Inc., San Diego, CA, USA; [9]Memorial Sloan Kettering Cancer Center, New York, NY, USA



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

FTI MECHANISM OF ACTION IN COMBINATION WITH ALPELISIB IN *PIK3CA*-MUTANT SOLID TUMORS

- Alpelisib shows modest clinical activity as monotherapy in *PIK3CA*-altered (mutated or amplified) head and neck cancers (ORR: 0%; best response: SD)[1], highlighting a need for combination strategies to counter pathway reactivation
- Tipifarnib, a potent first-generation FTI, is unlikely to provide clinical benefit as monotherapy in *PIK3CA*-altered head and neck cancers
- RHEB (Ras homolog enriched in brain), an obligately farnesylated GTP-binding protein, is essential for downstream signaling activation[2]
- Preclinical data suggest FTIs may suppress MAPK and mTOR feedback reactivation by inhibiting RHEB, supporting their use in combination

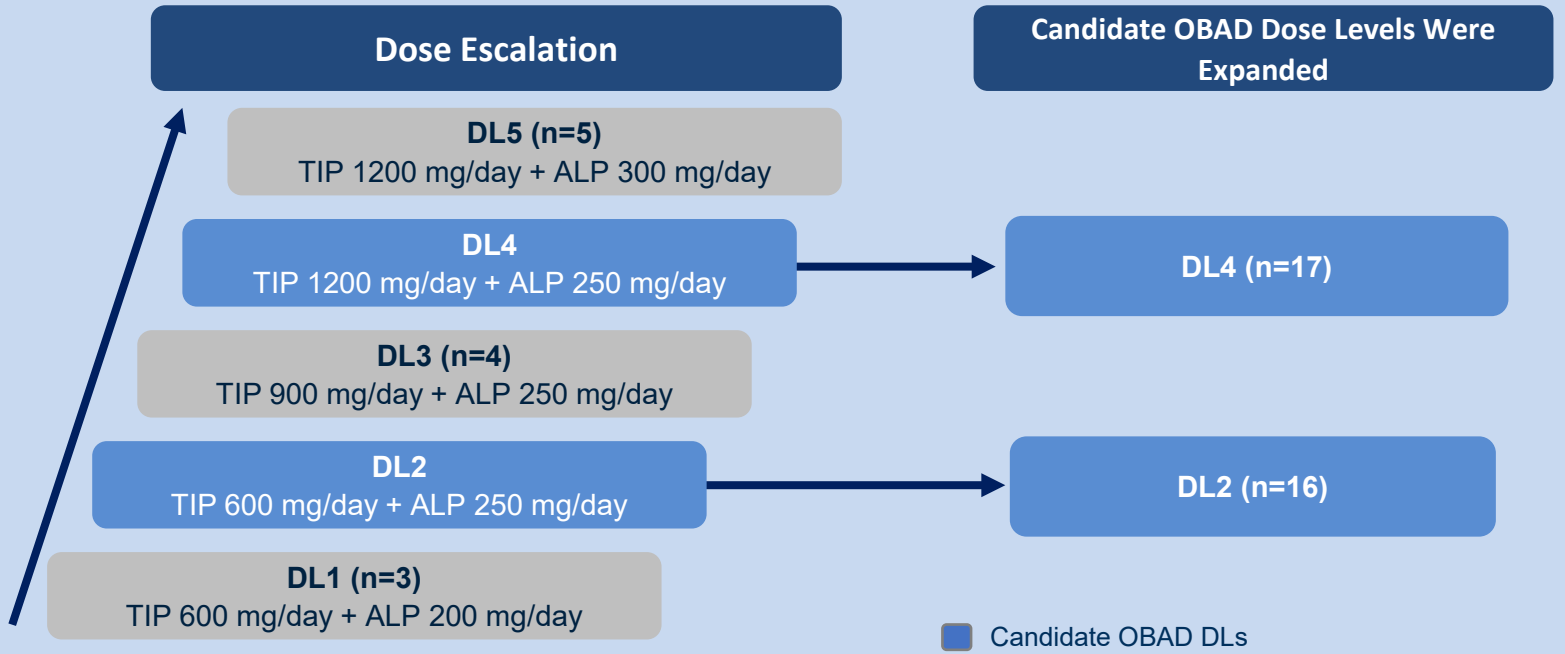


1. Juric D, et al. *J Clin Oncol* 2018;36:1291–9. 2. Smith et al. *Cancer Res* 2023;83:3252–3263

KURRENT-HN STUDY DESIGN

KURRENT-HN is a Phase 1 dose escalation study of tipifarnib in combination with alpelisib in patients with *PIK3CA*-altered R/M HNSCC

- Patients received tipifarnib on Days 1–7 and 15–21 and alpelisib daily in 28-day cycles
- Bayesian logistic regression modeling (BLRM) was used to characterize safety, tolerability, and clinical activity of the combination with the goal of identifying the optimal biologically active dose (OBAD)
- Additional patients were enrolled in the candidate OBAD cohorts



BASELINE CHARACTERISTICS AND DEMOGRAPHICS

	DL1 TIP 600 mg/day + ALP 200 mg/day (n=3)	DL2 TIP 600 mg/day + ALP 250 mg/day (n=16)	DL3 TIP 900 mg/day + ALP 250 mg/day (n=4)	DL4 TIP 1200 mg/day + ALP 250 mg/day (n=17)	DL5 TIP 1200 mg/day + ALP 300 mg/day (n=5)
Age, median (range), y	57 (37–65)	60 (36–76)	60 (54–67)	58 (41–75)	61 (49–62)
Male, n (%)	2 (67)	15 (94)	3 (75)	15 (88)	5 (100)
ECOG performance status, n (%)					
0	3 (100)	9 (56)	2 (50)	8 (47)	2 (40)
1	0	7 (44)	2 (50)	9 (53)	3 (60)
HPV positive, n (%)	2 (67)	13 (81)	2 (50)	12 (71)	4 (80)
***PIK3CA*-mutated, n (%)**	3 (100)	14 (88)	1 (25)	16 (94)	5 (100)
***PIK3CA*-amplified[a], n (%)**	1 (33)	2 (13)	2 (50)	3 (18)	0
Primary tumor site, n (%)					
Pharynx	1 (33)	12 (75)	2 (50)	11 (65)	3 (60)
Oral cavity	0	1 (6)	2 (50)	3 (18)	1 (20)
Nasopharyngeal	0	1 (6)	0	1 (6)	0
Larynx	0	1 (6)	0	0	1 (20)
Sinonasal	0	0	0	1 (6)	0
Other/unknown	2 (67)	1 (6)	0	1 (6)	0
Prior therapies, median (range)	1 (1-2)	2 (1-5)	4 (2-4)	2 (1-12)	2 (1–2)
Prior immunotherapy, n (%)	3 (100)	15 (94)	4 (100)	16 (94)	5 (100)
Immunotherapy as immediate prior line of therapy	3 (100)	11 (69)	1 (25)	11 (65)	4 (80)

[a] Defined as *PIK3CA* gene copy number ≥6 determined by local or central NGS. [b] Other includes salivary gland, left posterior hypopharynx, and squamous cell carcinoma of maxillary sinus (n=1 each); 1 patient had an unknown tumor site. ALP, alpelisib; DL, dose level; ECOG, Eastern Cooperative Oncology Group; HPV, human papillomavirus; TIP, tipifarnib

ENCOURAGING SAFETY AND TOLERABILITY PROFILE OF TIPIFARNIB + ALPELISIB COMBINATION

n (%)	DL2 TIP 600 mg/day + ALP 250 mg/day (n=16)	DL4 TIP 1200 mg/day + ALP 250 mg/day (n=17)	DL5 TIP 1200 mg/day + ALP 300 mg/day (n=5)
Grade ≥3 TRAEs (≥5% of all patients)			
Tipifarnib	6 (38)	12 (71)	1 (20)
Fatigue	2 (13)	1 (6)	0
Nausea	1 (6)	1 (6)	1 (20)
Neutrophil count decreased	0	7 (41)	0
Anemia	0	3 (18)	0
Alpelisib	10 (63)	11 (65)	2 (40)
Hyperglycemia	4 (25)	4 (24)	0
Rash maculo-papular	3 (19)	1 (6)	1 (20)
Fatigue	2 (13)	1 (6)	0
Lipase increased	2 (13)	0	0
Lymphocyte count decreased	1 (6)	4 (24)	0
Nausea	1 (6)	1 (6)	1 (20)
Stomatitis	1 (6)	0	1 (20)
Neutrophil count decreased	0	6 (35)	0

ALP, alpelisib; DL, dose level; TIP, tipifarnib, TRAE, treatment-related adverse event

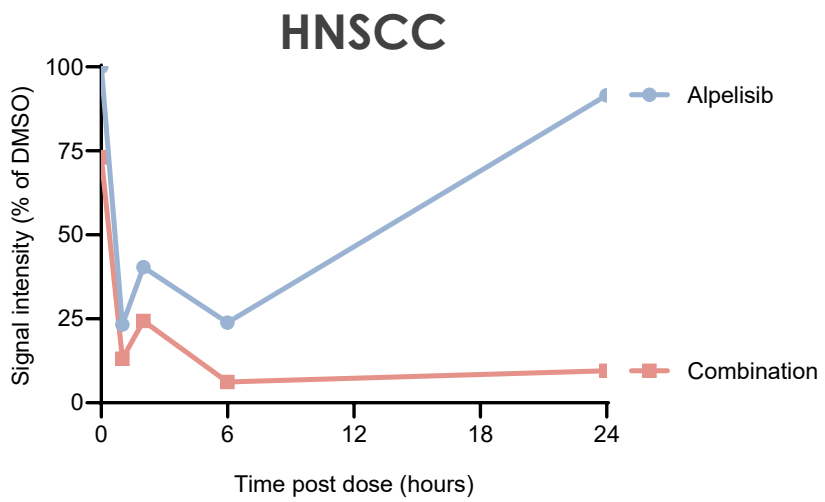
ENCOURAGING ACTIVITY OF TIPIFARNIB AND ALPELISIB IN EVALUABLE PATIENTS[a] WITH *PIK3CA* ALTERATIONS

	DL2 TIP 600 mg/day + ALP 250 mg/day (n=12)	DL4 TIP 1200 mg/day + ALP 250 mg/day (n=15)	DL5 TIP 1200 mg/day + ALP 300 mg/day (n=4)
Objective response rate (CR + PR)			
n (%)	2 (17) [b]	7 (47) [c]	1 (25)
95% CI	2.1–48.4	21.3–73.4	0.6–80.6
CR, n (%)	0	1 (7)	0
PR, n (%)[d]	2 (17) [b]	6 (40) [c]	1 (25)
SD, n (%)	6 (50)	4 (27)	0
Disease control rate (CR + PR + SD), n (%)	8 (67) [b]	11 (73) [c]	1 (25)
Clinical benefit rate (CR + PR + SD for ≥12 weeks)			
n (%)	7 (58) [b]	9 (60) [c]	1 (25)
95% CI	27.6–84.8	32.3–83.7	0.6–80.6
Duration of objective response, median (95% CI), months	17.9 (NE–NE)	5.5 (5.1–NE)	19.5 (NE–NE)

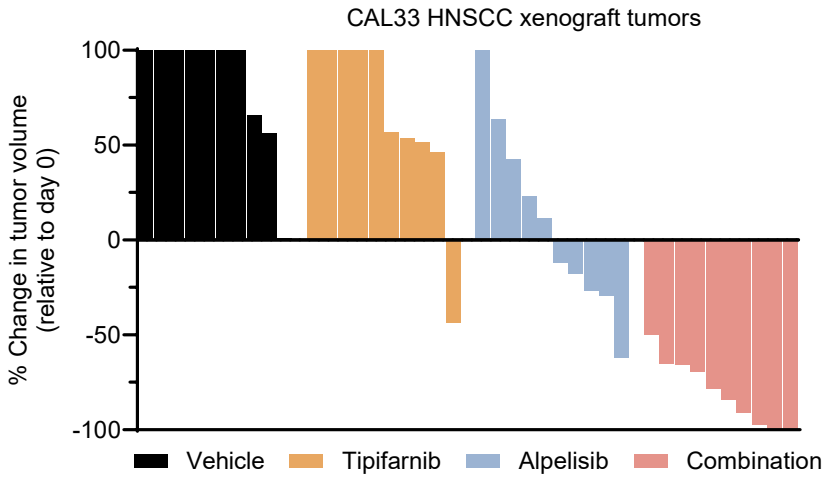
- **ORR was 47% with DL4** (tipifarnib 1200 mg/day + alpelisib 250 mg/day)
- In a prior study of patients with *PIK3CA*-altered head and neck cancer treated with **alpelisib alone, ORR was 0% (BOR: SD)**[1]

[a] Evaluable patients had ≥1 post baseline scan. [b] Includes confirmed (n = 1) and unconfirmed (n = 1) PR. [c] Includes confirmed (n = 3) and unconfirmed (n = 3) PR.
[d] Includes confirmed (n = 5) and unconfirmed (n = 4) PR; reasons for unconfirmed include disease progression (n=2), withdrawn consent, and cardiac event (n = 1 each).
1. Juric et al. *J Clin Oncol* 2018;36(13):1291-9.
ALP, alpelisib; CI, confidence interval; CR, complete response; DL, dose level; NE, not estimable; PR, partial response; SD, stable disease; TIP, tipifarnib

TIPIFARNIB ENHANCES THE ACTIVITY OF ALPELISIB IN PRECLINICAL MODELS OF PIK3CA-MUTANT HNSCC

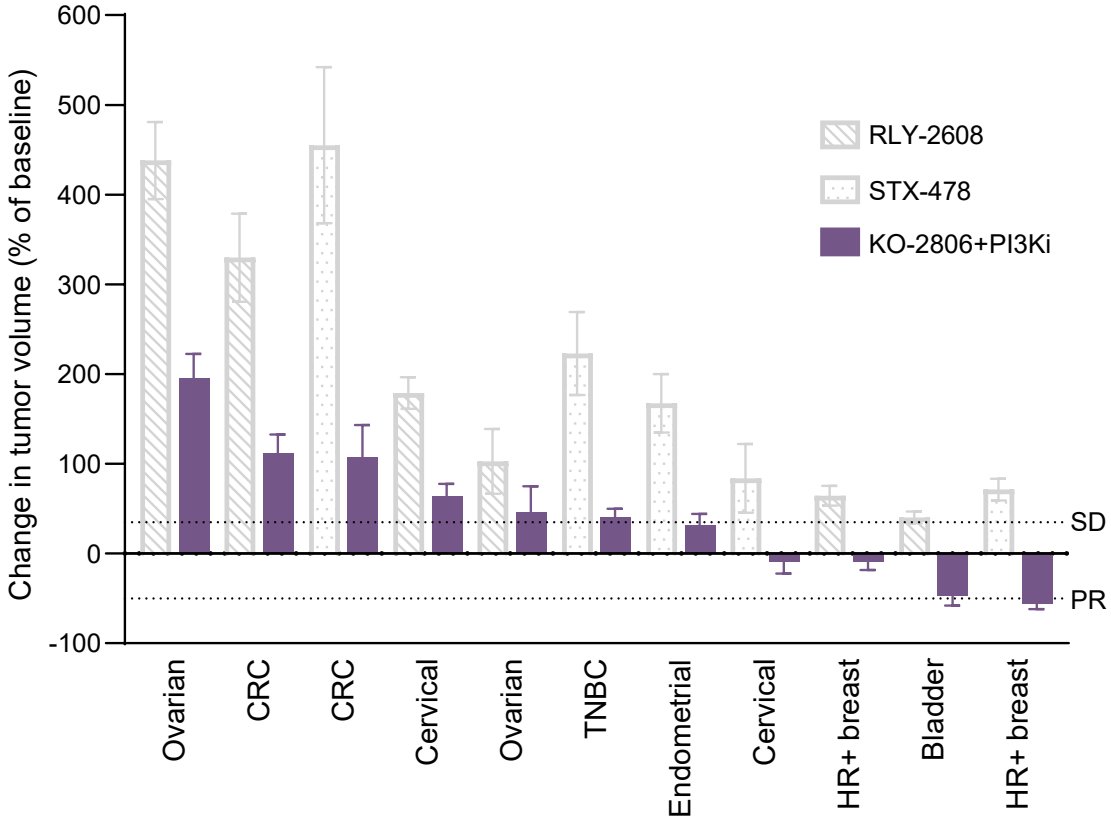


Tipifarnib inhibits mTOR signaling rebound observed with alpelisib alone

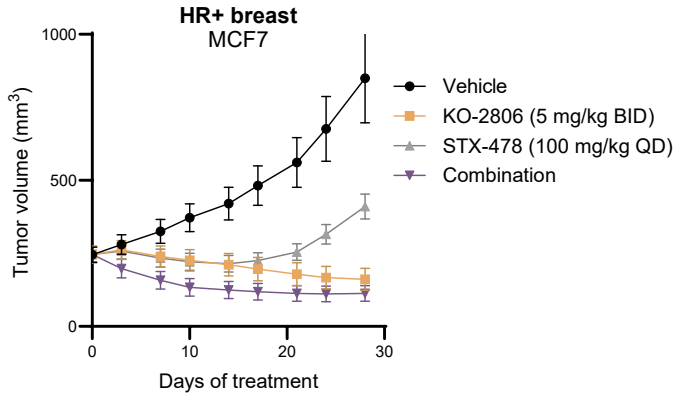


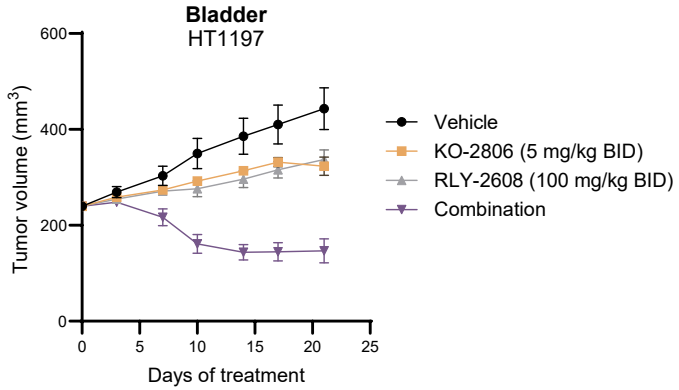
Combination of tipifarnib and alpelisib results in deep regression in a PIK3CA-mutant HNSCC CDX model

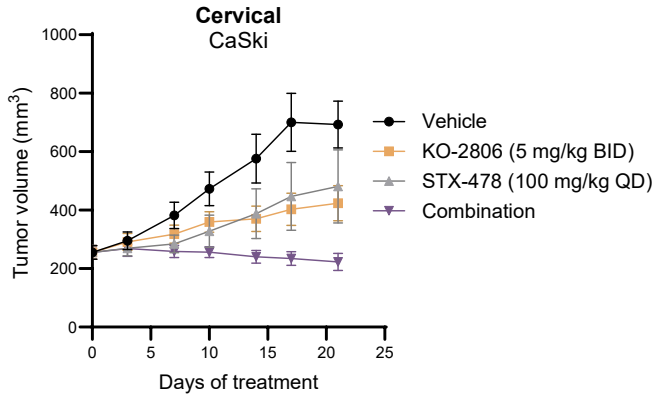
KO-2806 ENHANCES ANTI-TUMOR ACTIVITY OF PI3Kα INHIBITORS ACROSS DIFFERENT INDICATIONS



Addition of KO-2806 consistently enhances the activity of both mutant-selective PI3Kα inhibitors in preclinical models

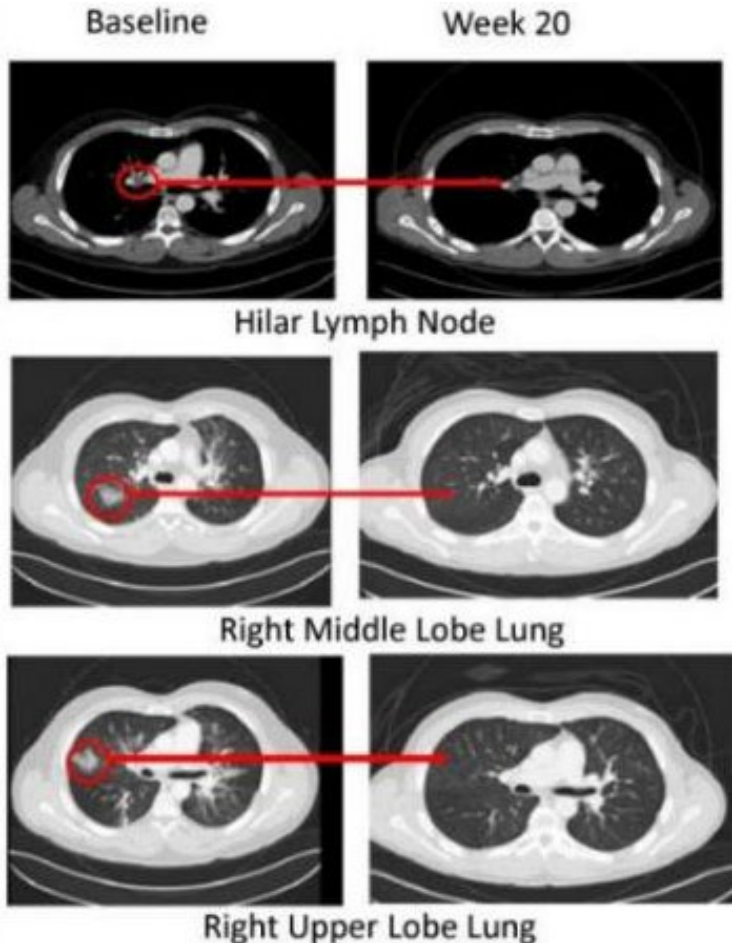






DEEP RESPONSE IN PATIENT TREATED WITH TIPIFARNIB AND ALPELISIB

Scans from a responder treated with tipifarnib 600 mg + alpelisib 250 mg

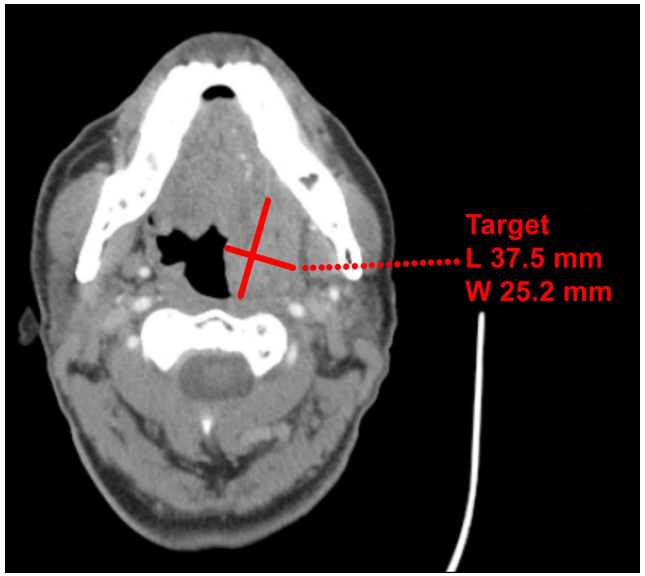


PATIENT BACKGROUND

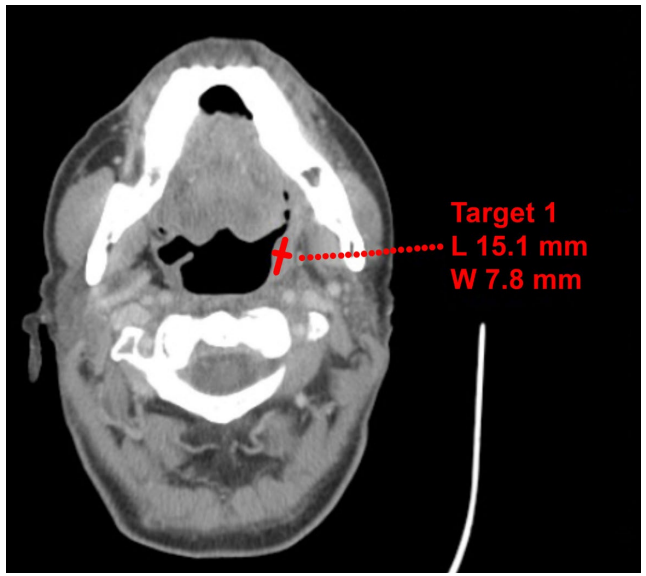
- 36-year-old HPV-positive nonsmoker male diagnosed with squamous cell carcinoma of the tonsil (oropharynx)
- Prior therapy: 1L Cemiplimab + ISA101b; BOR: SD
- At study start: Stage IV (lung metastasis) with *PIK3CA* R88Q mutation
- **Response: PR (81% reduction at week 4)**
- Patient deceased (pneumonia) Jan 2024
- Key considerations:
  - Durable response lasted 18 months
  - Patient progressed radiologically but continued to have clinical treatment

DEEP RESPONSE IN PATIENT TREATED WITH TIPIFARNIB AND ALPELISIB

Scans from a responder treated with tipifarnib 1200 mg + alpelisib 250 mg



27 Dec 2023
Baseline
Neck left – tongue base



06 Feb 2024
Week 4 post-C1D1
Neck left – tongue base

PATIENT BACKGROUND

- 75-year-old male presented with *PIK3CA*-mutated HNSCC of the oral cavity (T3N0M0)
- Prior lines of therapy:
  - 1L: Cisplatin; BOR: SD
  - 2L: Pembrolizumab; BOR: SD
- **Response at week 4**
  - **Overall response per RECIST: PR (shrinkage 56%)**

CONCLUSIONS FROM TIPIFARNIB + ALPELISIB COMBINATION IN *PIK3CA* MUTANT HNSCC PATIENTS

The combination of tipifarnib and alpelisib was well tolerated with a manageable safety profile

Robust anti-tumor activity was observed in heavily pretreated patients with R/M HNSCC, a population where alpelisib monotherapy provides only modest clinical benefit (ORR: 0%; BOR: SD) and single-agent tipifarnib is not expected to provide clinical benefit

An ORR of 47% was observed at a dose of tipifarnib 1200 mg/day + alpelisib 250 mg/day, demonstrating improved clinical activity versus other doses assessed

These data support targeting RHEB to address innate/adaptive resistance to PI3Kα inhibitors

Data support use of FTIs to target RHEB/mTORC1 pathway activation and potentially improve clinical activity of PI3Kα inhibitors

NEXT STEPS

NEXT STEPS FOR DEVELOPMENT OF DARLIFARNIB AND CLINICAL UPDATES IN 2026

Next Steps Planned for the Darlifarnib (KO-2806) program

- Complete dose escalation for KO-2806 + cabozantinib combo
- Conduct Phase 1b for KO-2806 + cabozantinib combo to determine optimal biologically active dose (OBAD)
- Complete dose escalation for KO-2806 + adagrasib in KRAS G12C-mutated NSCLC, CRC and PDAC
- Develop data generation options for darlifarnib + PI3Kα inhibitor combinations in solid tumors

Additional Clinical Data Anticipated in 2026

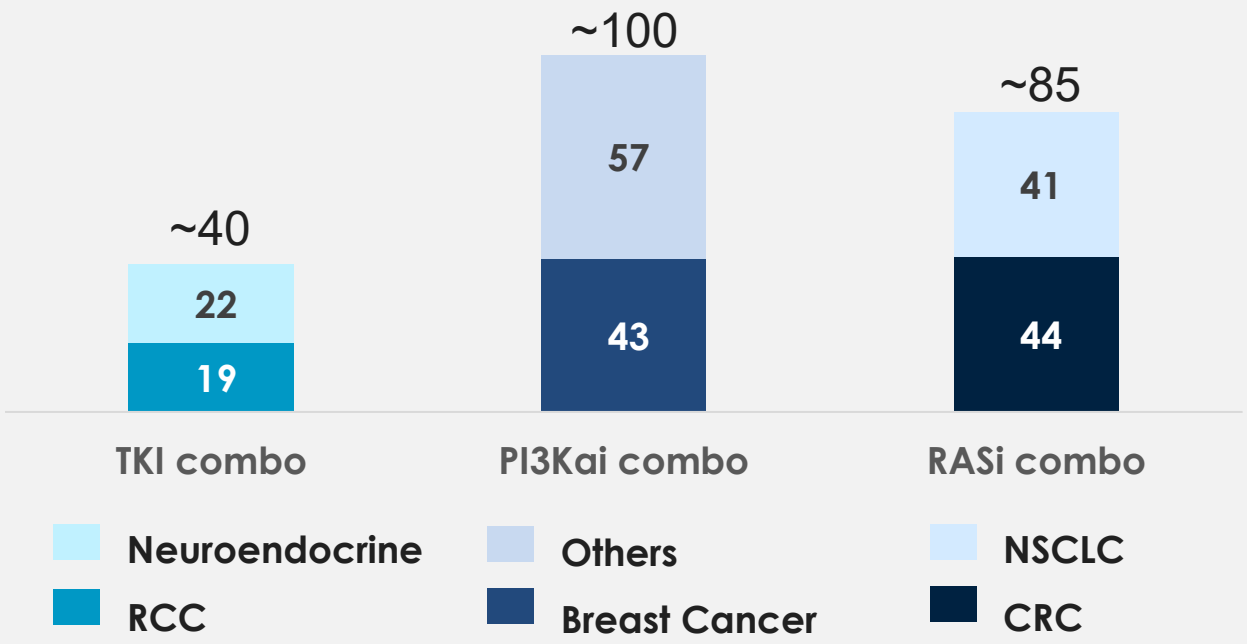
- Updated data on dose escalation for KO-2806 + cabozantinib combo
- Preliminary clinical data for KO-2806 + adagrasib

OPPORTUNITY

Clinical Activity in Combination Drives a Large Potential Addressable Market Opportunity

LARGE POTENTIAL OPPORTUNITY IN KO-2806 WITH > 200K ANNUAL INCIDENT PATIENTS IN THE U.S.

Annual US Incidence, 2025
thousands of patients



OPPORTUNITY AREAS

VEGFR TKI

- Potential to combine with cabozantinib and other TKIs in RCC and potentially in NET
- Potential to combine with TKI and I/O in 1L RCC

KRAS and PI3Kα

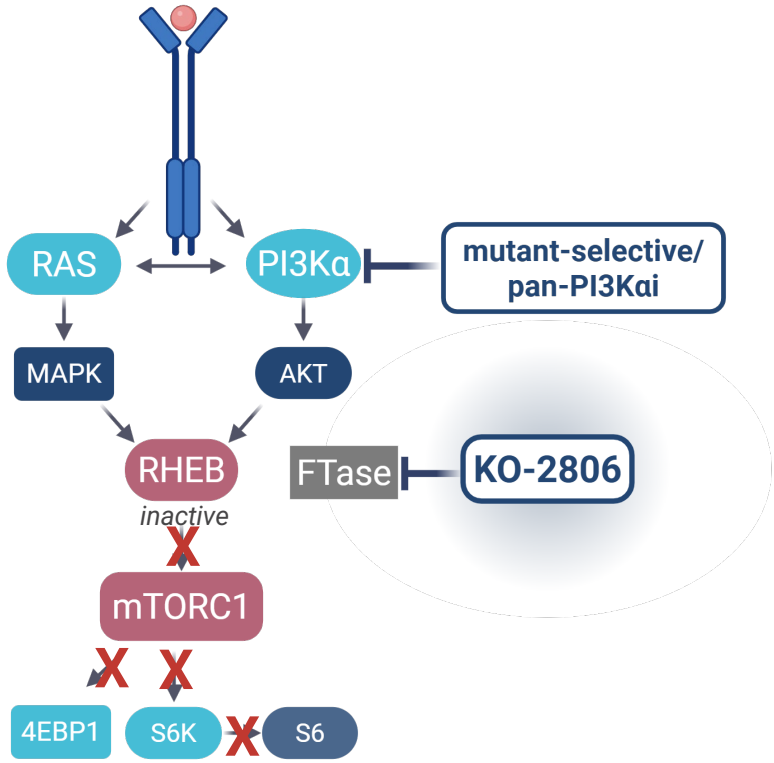
- Potential to combine with multiple agents in KRAS- and PI3Kα-driven cancers across major solid tumors
- Potential for synergistic efficacy, lifecycle management and multi-drug revenues

QUESTIONS & ANSWERS

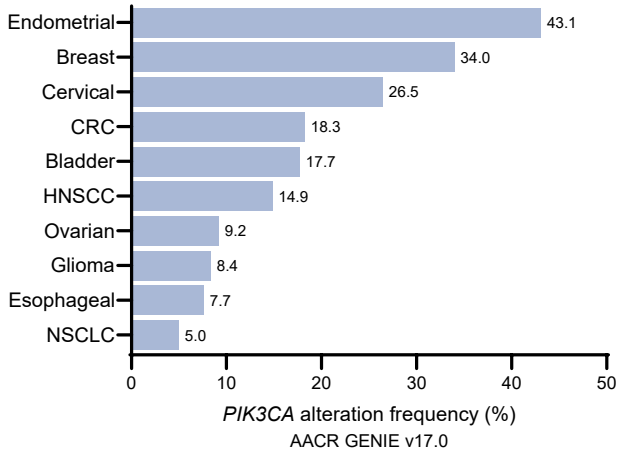
THANK YOU

Our goal is to develop transformative therapies to extend and improve the lives of patients with cancer

FTIs ENHANCE PRECLINICAL ACTIVITY OF PI3Kα INHIBITORS ACROSS TUMOR TYPES BY INHIBITING THE mTORC1 NODE



Deep and durable mTORC1 inhibition



- *PIK3CA* is one of the **most commonly mutated genes** in solid cancers
- Feedback reactivation of PI3K–mTOR signaling limits benefit of PI3K inhibitors, **necessitating development of rational combination strategies**
- FTIs blunt mTORC1 effects by blocking farnesylation of RHEB, leading to more effective reduction of mTOR signaling, while sparing mTORC2