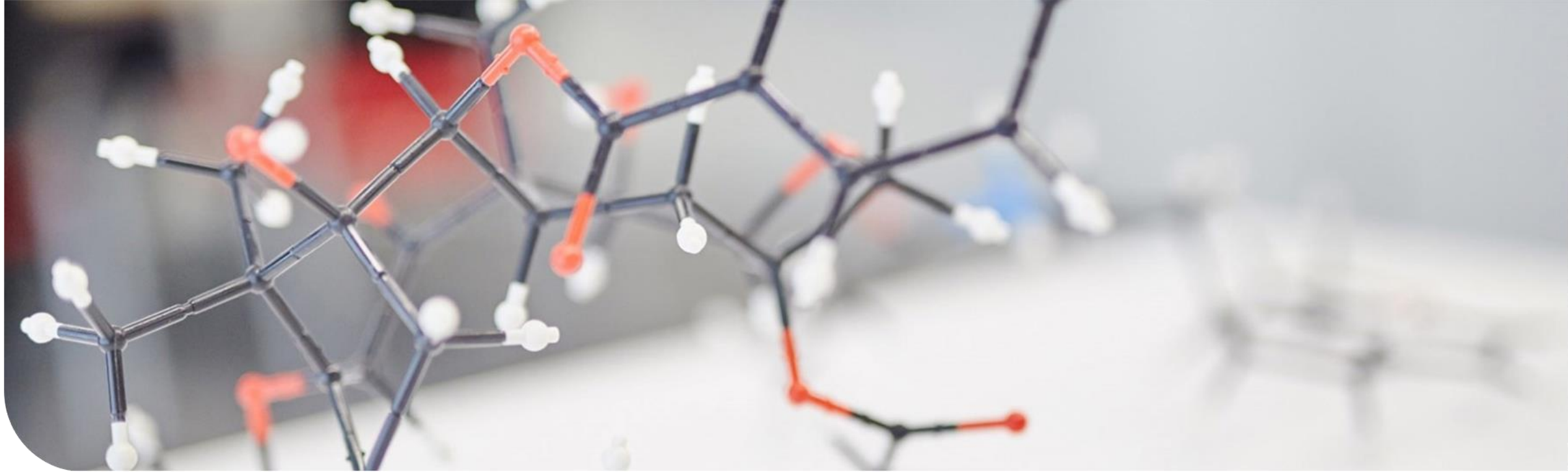

Fruquintinib 2025
Post-Congress Reactive Deck

Aug 2025
VV-MEDMAT-124939 / Germany
Global/US Medical

ONCOLOGY

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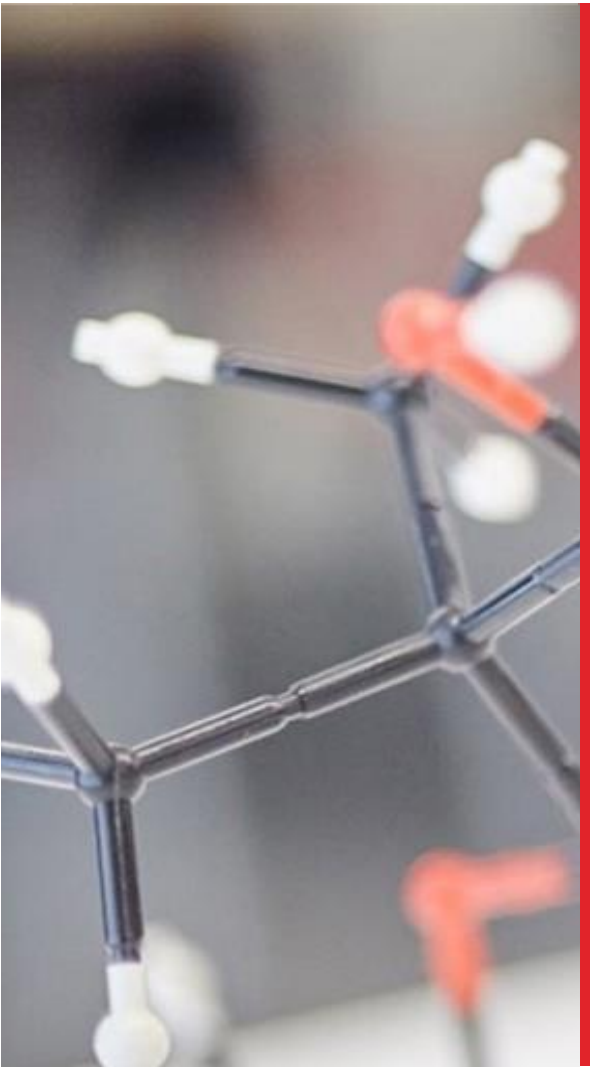

Click for additional fruquintinib data

*HUTCHMED investigator-initiated research (IIR). Takeda has no current involvement with any IIR studies with fruquintinib in China; all publications were developed independent of Takeda.
See slide notes for abbreviations

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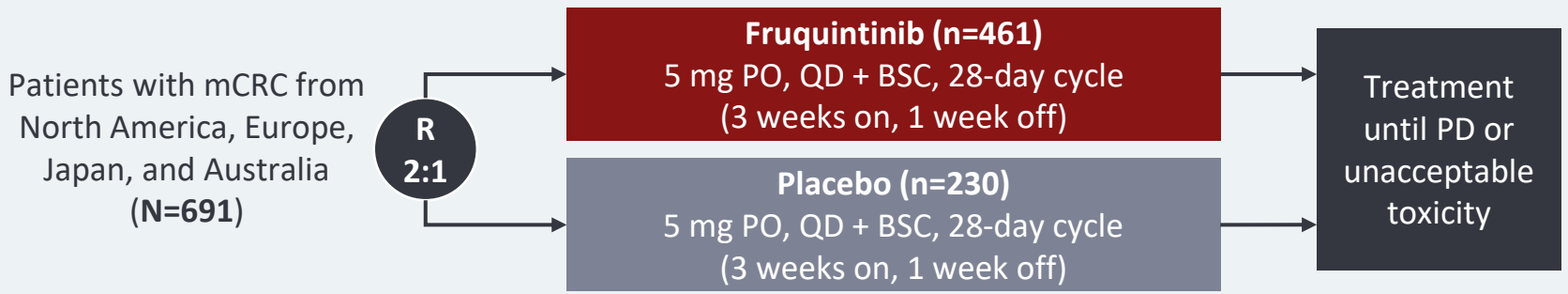
General FRESCO-2 and mCRC background

FRESCO-2 (NCT04322539) study design[1]:



Primary endpoint: OS

Key secondary endpoint: PFS

Other secondary endpoints: DCR, DOR, HRQOL, ORR, safety

Fruquintinib and FRESCO-2:

Fruquintinib is a selective oral inhibitor of all three VEGFRs (VEGFR-1, -2, and -3) that is approved in the US,[2] the EU,[3] the UK,[4] and Japan[5] for previously treated mCRC, regardless of biomarker status

FRESCO-2 was a global, double-blind, Phase 3 study conducted at 124 hospitals and cancer centers across 14 countries[1]

Eligible patients had received all standard treatments including fluoropyrimidine, oxaliplatin, and irinotecan chemotherapy; anti-VEGF therapy; anti-EGFR therapy (if *RAS* wild type); and had prior exposure to TAS-102 and/or regorafenib[1]

The FRESCO-2 study met its primary endpoint, demonstrating significantly improved OS with fruquintinib + BSC vs placebo + BSC[1]

Fruquintinib was well tolerated in FRESCO-2 with a safety profile consistent with the previously established monotherapy profile. In FRESCO-2, 20% of patients in the fruquintinib arm vs 21% of patients in the placebo arm discontinued treatment due to AEs[1]

mCRC:

Up to 70% of patients with CRC will experience metastatic disease, either at diagnosis or over the course of their treatment[6,7]

The prognosis for patients with mCRC is poor, with a 5-year relative survival rate of approximately 14%[8]

Later-line treatment options for mCRC are limited[9]

AE, adverse event; BSC, best supportive care; DCR, disease control rate; DOR, duration of response; EGFR, epidermal growth factor receptor; HRQOL, health-related quality of life; (m)CRC, (metastatic) colorectal cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, orally; QD, once daily; R, randomization; VEGF(R), vascular endothelial growth factor (receptor)

1. Dasari A, et al. Lancet 2023;402:41-53; 2. Fruzaqla (fruquintinib) Prescribing Information. Takeda Pharmaceuticals America, Inc. Feb 2025; 3. Fruzaqla (fruquintinib) Summary of Product Characteristics. Takeda Pharmaceuticals International AG Ireland. Nov 2024; 4. Fruzaqla (fruquintinib) MHRA Public Assessment Report. Takeda UK Ltd. Oct 2024; 5. Takeda Press Release. 2024. Available at: https://www.takeda.com/newsroom/newsreleases/2024/takeda-receives-approval-for-fruzaqla-in-japan-for-the-treatment-of-unresectable-advanced-or-recurrent-colorectal-cancer (accessed Aug 2025); 6. Vatandoust S, et al. World J Gastroenterol 2015;21:11767-76; 7. Van Cutsem E, et al. Ann Oncol 2009;20(Suppl. 4):61-3; 8. IARC. Available at: https://gco.iarc.fr/survival/survmark/visualizations/viz7/?groupby=%22country%22&period=%225%22&cancer=%22COLORECTAL%22&country=%22Australia%22&gender=%220%22&stage=%22SEER%22&age_group=%2215-99%22&show_ci=%22%22 (accessed Aug 2025); 9. Xue W-H, et al. Front Oncol 2023;13:1165040

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Company-sponsored research

1 ESMO GI 2025
Poster 32P

A novel, non-invasive imaging biomarker, quantitative vessel tortuosity (QVT), captures the antiangiogenic effect of fruquintinib in metastatic colorectal cancer using standard of care CT scans

Sara Lonardi,[1] Ozlem Yardibi,[2] Arvind Dasari,[3] Lucy F. Chen,[2] Varsha Sundaresan,[2] Anant Madabhushi,[4] Jayant Narang[2]

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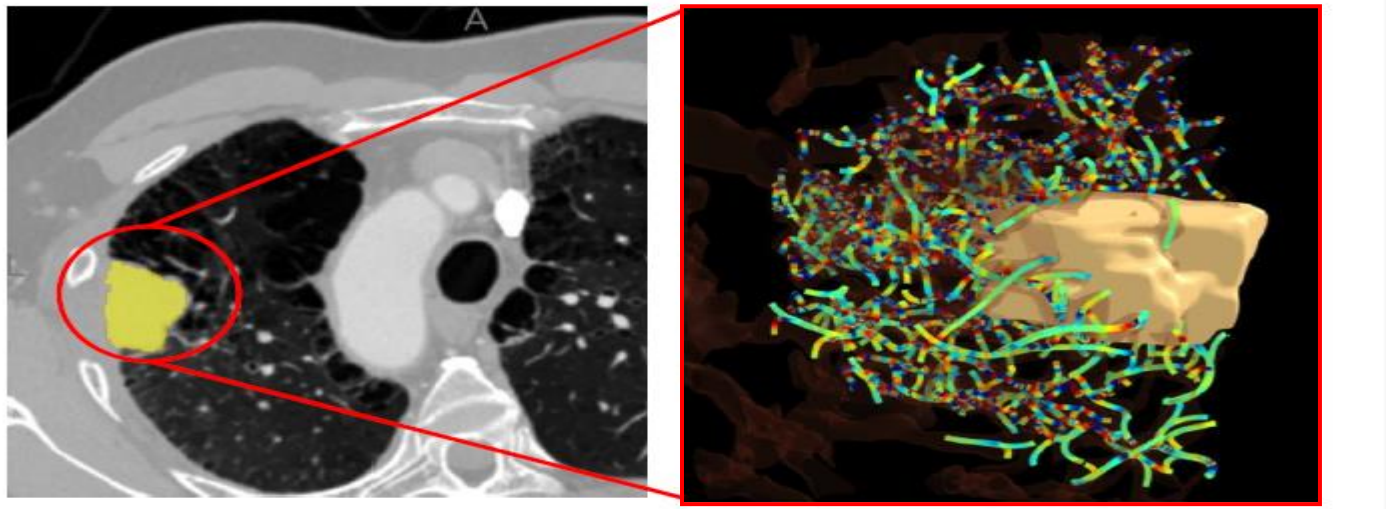
Background and objective

- **Traditional imaging methods** do not effectively capture the dynamic changes occurring within the tumor vasculature to accurately evaluate antiangiogenic mechanisms; some methods are **invasive** (eg, angiogram or biopsy) or require **specialized imaging procedures** (eg, contrast-enhanced perfusion CT or MRI scans)[1,2]
- The radiomic vascular features library, including **QVT,** provides a **novel approach to assess** the complex structure and twistedness of **blood vessels surrounding tumors,** using **standard CT scans**[1]
- **QVT** is an **imaging biomarker** that consists of a comprehensive suite of metrics that quantify vascular characteristics, including, but not limited to, **tortuosity, curvature, branching patterns, and volumetric measurements**[1,2]
- QVT includes hundreds of individual feature measurements, **engineered to capture biological variations** in vascular structures[1,2]

QVT visualization showing the curvature and twistedness of blood vessels



OBJECTIVE:

Demonstrate the antiangiogenic MOA of fruquintinib with vascular radiomics, and compare any potential changes to the QVT radiomic features in tumor-associated vasculature with fruquintinib vs placebo treatment[2]

- CT scans of metastatic lung lesions from patients in the FRESCO-2 trial were analyzed for QVT features to quantify peritumoral vascularity, and longitudinal changes in QVT features from baseline to C3D1 (ΔQVT) assessed to evaluate treatment-induced vascular changes[2]

(Δ)QVT, (delta) quantitative vessel tortuosity; C3D1, Cycle 3, Day 1; CT, computed tomography; MOA, mechanism of action; MRI, magnetic resonance imaging

1. Alilou M, et al. Sci Rep 2018;8:15290; 2. Lonardi S, et al. ESMO GI 2025 [poster #32P]

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Methods

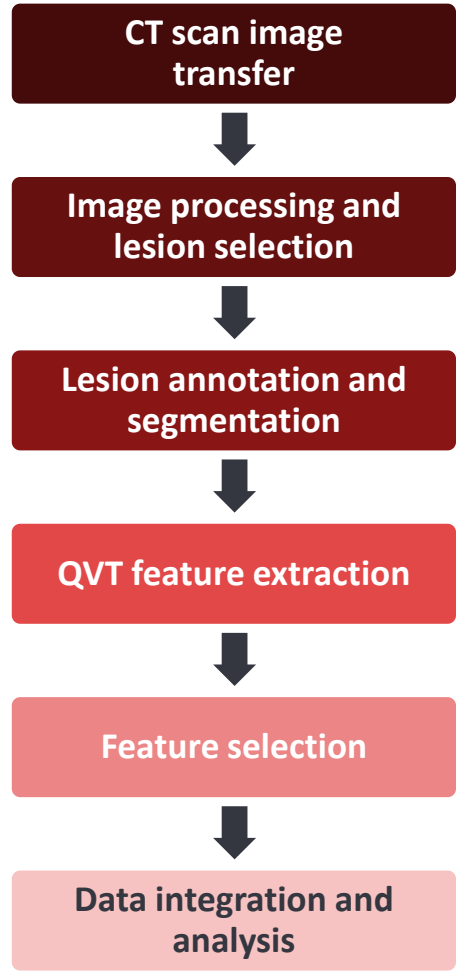
- Retrospective analysis conducted using CT scan images from 221 patients enrolled in the FRESCO-2 trial
- Metastatic lung lesions were annotated in 3D on CT scans taken at screening (baseline) and C3D1
  - Lung metastases were chosen for the primary objective due to both their frequency and clinical importance in mCRC*

	FRUQUINTINIB ARM	PLACEBO ARM
Number of lesions analyzed total, n	422	167
Number of patients with lesions analyzed, n	162	59

- Annotations were performed using manual segmentation of metastatic lung lesions using a cloud-based annotation platform
  - Final annotations were reviewed and approved by a practicing senior radiologist
  - Up to five lesions were manually annotated per scan, and the annotators selected lesions that were visible and measurable on both the baseline and first on-treatment scans (C3D1) for consistent tracking of treatment effect

- For each lesion, 909 QVT features were extracted to quantify the peritumoral vascularity
- To evaluate treatment-induced vascular changes, the longitudinal change in QVT features (ΔQVT) was calculated as the % change in features from baseline to C3D1
- A prespecified subpanel of 21 QVT features, selected by the model, was compared between fruquintinib vs placebo arms using the Mann-Whitney U test, with false discovery rate correction
  - Lesion-level ΔQVT features were also summarized per patient

Flow diagram demonstrating the analysis workflow



*Primary colorectal lesions were not analyzed due to the high rate of resection prior to screening in the patient population enrolled in the study, which yielded insufficient data quantity for analysis
(Δ)QVT, (delta) quantitative vessel tortuosity; C3D1, Cycle 3, Day 1; CT, computed tomography; mCRC, metastatic colorectal cancer
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Fruquintinib-induced vascular normalization

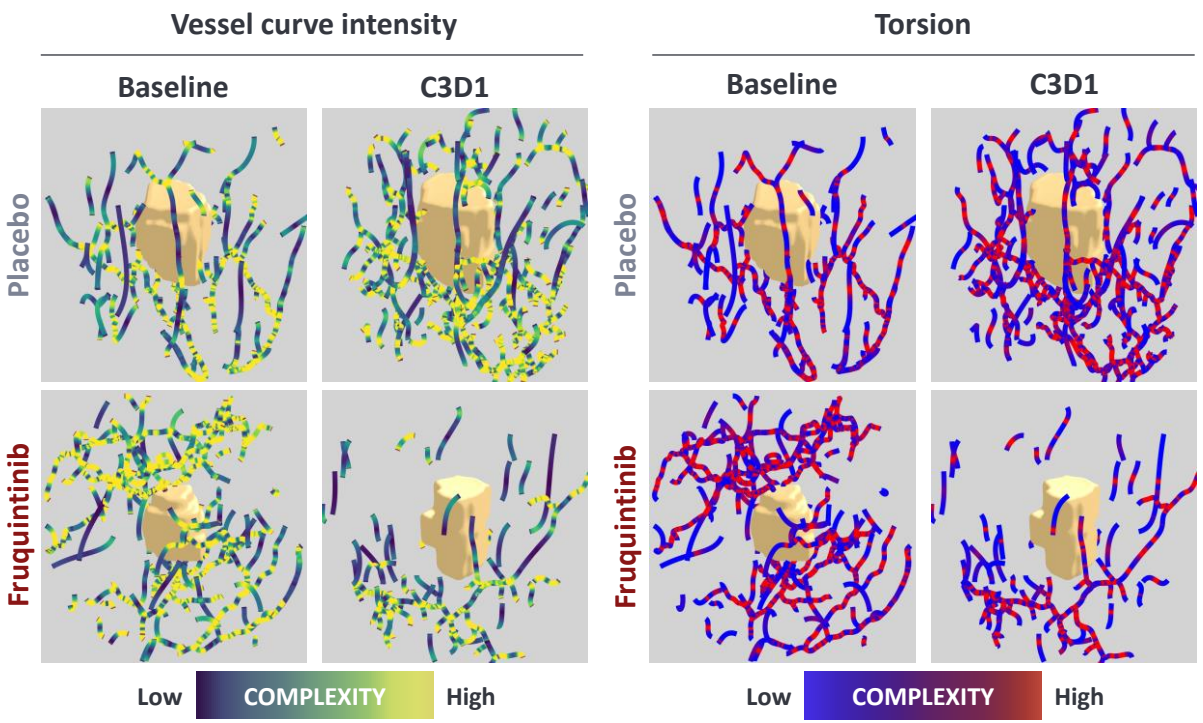
Fruquintinib-induced vascular normalization was observed across all ΔQVT feature groups, reinforcing the antiangiogenic effect of fruquintinib

Patient-level QVT change in lung lesions at C3D1 (fruquintinib vs placebo)*

QVT FEATURE GROUP	% CHANGE IN QVT FEATURE	FRUQUINTINIB	PLACEBO	P-VALUE
Curvature	Vessel curve intensity (mean)	↓	↑	0.02095
	Vessel curve intensity (SD)	↓	↑	0.01939
Abnormal branching	Branch length (mean)	↓	↑	0.04677
	Branch length (SD)	↓	↑	0.01939
	Number of branches	↓	↑	0.01460
Torsion	Torsion (mean)	↓	↑	0.01939
	Length-to-distance ratio	↓	↑	0.00991
Vessel inflection points	Number of inflection points	↓	↑	0.00606
Radius	Vessel radius (mean)	↓	↑	0.01282
	Vessel radius (SD)	↓	↑	0.01939
Vessel volume	Vessel volume	↓	↑	0.00606

Of the 21 pre-selected QVT features, 11 showed a statistically significant difference in ΔQVT with **fruquintinib** vs **placebo**†

Tumor visualization of change in vessel curve intensity and torsion



Fruquintinib demonstrated a clear normalizing effect on tumor-associated vasculature in lung metastases at C3D1

*A reduction (↓) represents the normalization of a feature; †All 11 of these features fell into six interpretable categories: vessel radius, volume, branching, branch length, curvature, and torsion
(Δ)QVT, (delta) quantitative vessel tortuosity; C3D1, Cycle 3, Day 1; SD, standard deviation
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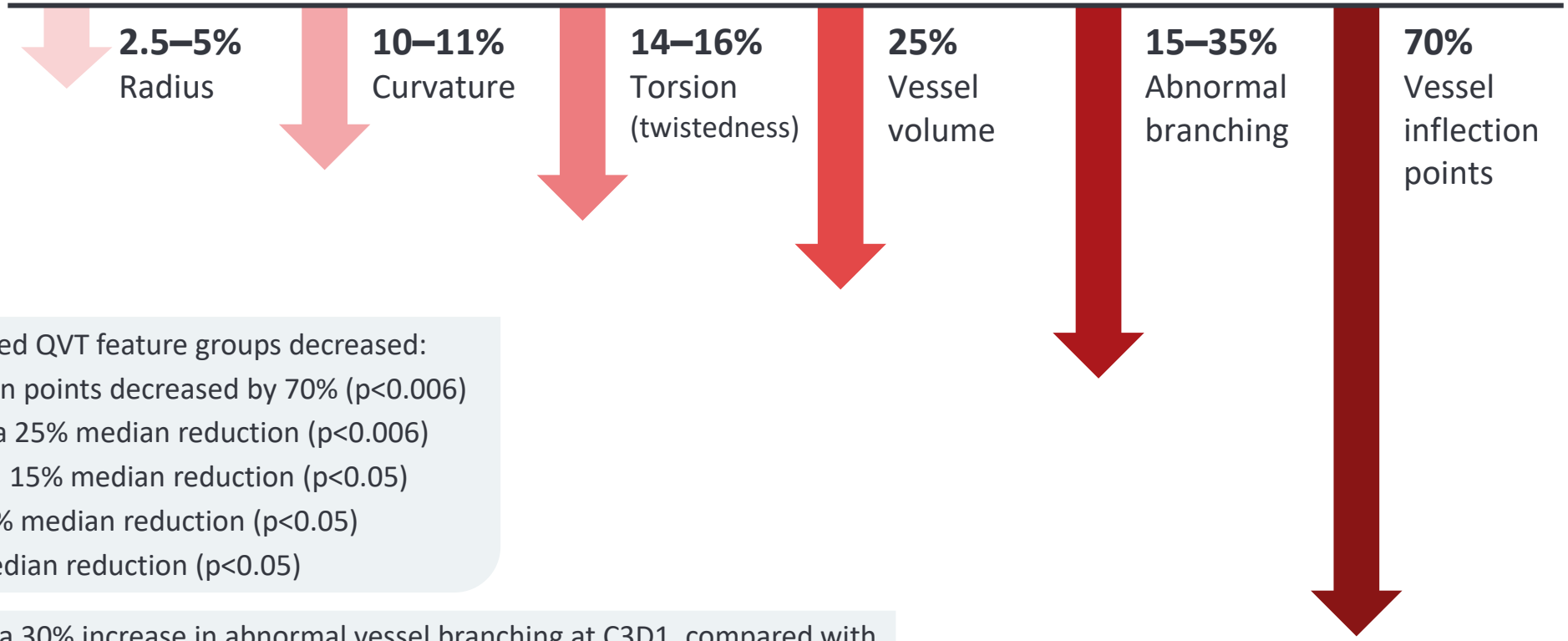
Change in QVT feature groups

Vascular improvement was detected early in treatment: significant changes in QVT features from baseline with fruquintinib were observed during the first assessment, demonstrating the early antiangiogenic action of fruquintinib

Reductions in select QVT feature group medians for lung lesions following treatment with fruquintinib from baseline to C3D1



- In the **fruquintinib arm**, all selected QVT feature groups decreased:
  - The number of vessel inflection points decreased by 70% ($p<0.006$)
  - Vessel volume demonstrated a 25% median reduction ($p<0.006$)
  - Vessel torsion demonstrated a 15% median reduction ($p<0.05$)
  - Curvature demonstrated a 10% median reduction ($p<0.05$)
  - Radius demonstrated a 5% median reduction ($p<0.05$)

- In contrast, the **placebo arm** had a 30% increase in abnormal vessel branching at C3D1, compared with baseline ($p<0.05$)

C3D1, Cycle 3, Day 1; QVT, quantitative vessel tortuosity

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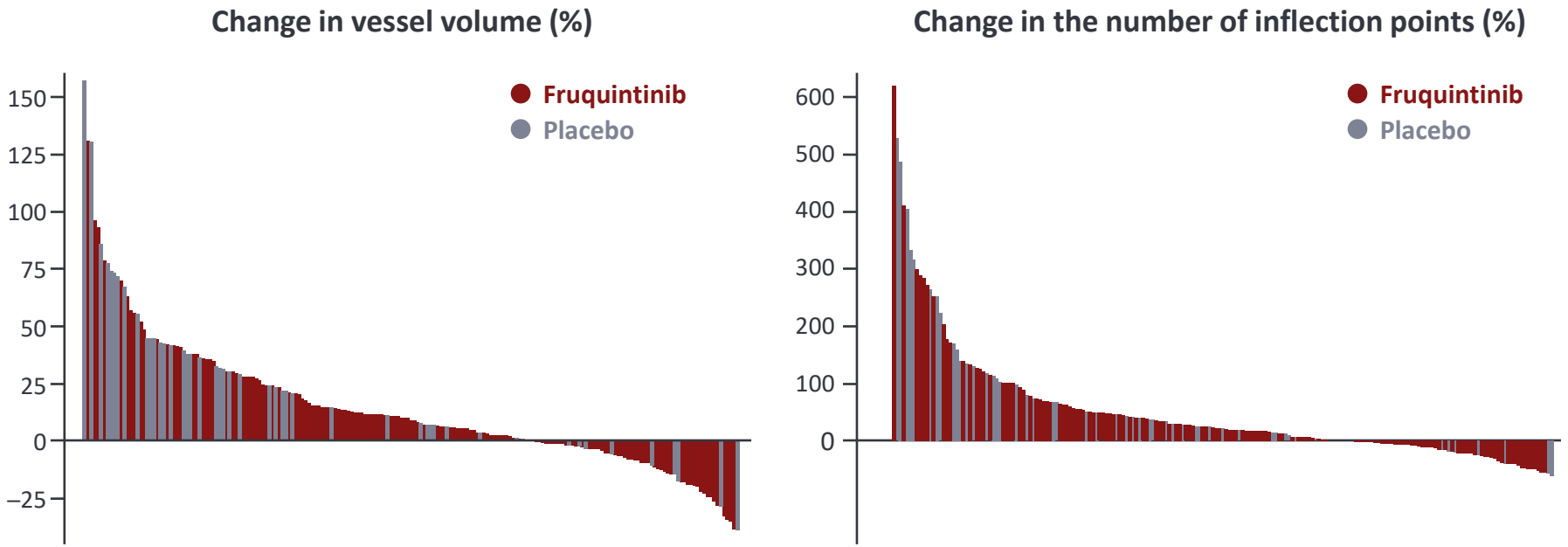
Patient-level changes in QVT feature groups

Fruquintinib-treated patients experienced a reduction in vasculature, while placebo-treated patients had increased vasculature, providing evidence of the fruquintinib MOA

- Visualization of treatment-induced vascular normalization in lung lesions: % change in QVT features from baseline to C3D1 for each patient
  - Patient-level granularity demonstrates the extent of fruquintinib-induced vessel normalization
  - Patients in the **fruquintinib arm** are more prevalent on the right side of the plots (**decrease** in % change), while patients in the **placebo arm** are more prevalent on the left side of the plots (**increase** in % change)

Patient-level changes from baseline to C3D1 in the two most significant QVT features for lung lesions: vessel volume and number of inflection points*



*Positive changes (left side of each plot) indicate an increase in the complexity of tumor-associated vasculature, while negative changes (right side of each plot) indicate a reduction or normalization of the vasculature

C3D1, Cycle 3, Day 1; MOA, mechanism of action; QVT, quantitative vessel tortuosity

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Authors' conclusions

This study demonstrates the utility of QVT, a non-invasive, novel, radiomic-based biomarker, in detecting the VEGFR inhibitory mechanism of action of fruquintinib

The observed differences in ΔQVT radiomic features with fruquintinib vs placebo quantify the ability of fruquintinib to prevent the formation of a twisted, heterogeneous vasculature, as shown by a significant reduction in multiple QVT features within 8 weeks of treatment

- **Significant changes in QVT features between patients in the fruquintinib and placebo arms were observed during the first assessment, demonstrating the rapid antiangiogenic benefit of fruquintinib**

These findings establish the value of QVT as a direct measure for fruquintinib-induced antiangiogenic activity, and support the use of this method as a potential tool to assess treatment effect based on the mechanism of action

Future analyses are planned to include liver lesions and a predictive model of OS

(Δ)QVT, (delta) quantitative vessel tortuosity; OS, overall survival; VEGFR, vascular endothelial growth factor receptor

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2

ESMO GI 2025

Poster 37P

Efficacy and safety of fruquintinib vs placebo by metastatic site in metastatic colorectal cancer: A FRESCO-2 subgroup analysis

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[1]Hospital Universitario 12 de Octubre, Imas12, UCM, Madrid, Spain; [2]The MD Anderson Cancer Center, Houston, TX, USA; [3]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [4]Vall d'Hebron Barcelona Hospital Campus, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [5]National Cancer Center Hospital East, Kashiwa, Chiba Japan; [6]AK Altona, Hamburg, Germany; [7]Veneto Institute of Oncology IOV-IRCCS Padua, Padua, Italy; [8]Hospital G. U. Gregorio Marañón, IiSGM, Universidad Complutense, Madrid, Spain; [9]Poitiers University Hospital, Poitiers, France; [10]Austin Hospital, Heidelberg, VIC, Australia; [11]HUTCHMED International Inc., Florham Park, NJ, USA; [12]Takeda Development Center Americas, Inc. (TDCA), Cambridge, MA, USA; [13]University of Pisa, Pisa, Italy

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Background and objective

- Metastases can occur at multiple sites in patients with CRC[1]
- The most common site of metastasis is the liver, and up to 50% of patients with CRC develop liver metastases over the course of their disease[1]
- Metastases in the lung, bone, and peritoneum are also clinically relevant, and can to a degree affect the prognosis of mCRC[2-4]

OS by baseline liver metastases (FRESCO-2 subgroup analysis)[5,*]

	MEDIAN OS, MONTHS		HR	P-VALUE
	FRUQ + BSC	PBO + BSC		
With baseline liver metastases ± other metastases	6.4	3.7	0.58	<0.001
Without baseline liver metastases	12.1	8.4	0.77	0.102

OBJECTIVE:

Evaluate the efficacy and safety of fruquintinib vs placebo according to the presence of baseline metastases at clinically relevant sites associated with prognosis of CRC[5]

- Metastatic sites[†]:
  - Liver metastases only
  - Lung metastases only
  - Bone metastases ± metastases at other sites
  - Peritoneal metastases ± metastases at other sites

*Data presented at ESMO 2024 – see Fruquintinib 2024 Post-Congress Reactive Deck for additional information; [†]These sites of metastases were selected due to their clinical relevance in mCRC; other sites (eg, brain metastases) were considered but not included in this analysis due to sample size and/or clinical relevance

BSC, best supportive care; FRUQ, fruquintinib; HR, hazard ratio; (m)CRC, metastatic colorectal cancer; OS, overall survival; PBO, placebo

1. Martin J, et al. WJCO 2020;11:761-808; 2. Wang J, et al. Cancer Med 2020;9:361-73; 3. Dell'Aquila E, et al. ESMO Open 2022;7:100606; 4. Franko J, et al. Lancet Oncol 2016;17:1709-19; 5. Garcia-Carbonero R, et al. ESMO GI 2025 [poster #37P]

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Baseline characteristics by baseline metastatic site

CHARACTERISTIC		LIVER METS ONLY		LUNG METS ONLY		BONE ± OTHER METS		PERITONEAL ± OTHER METS	
		FRUQ + BSC (n=19; 4.1%)	PBO + BSC (n=10; 4.3%)	FRUQ + BSC (n=25; 5.4%)	PBO + BSC (n=16; 7.0%)	FRUQ + BSC (n=51; 11.1%)	PBO + BSC (n=27; 11.7%)	FRUQ + BSC (n=67; 14.5%)	PBO + BSC (n=38; 16.5%)
Age, years	Median (range)	62.0 (57–70)	65.5 (59–71)	69.0 (58–72)	64.5 (57–68)	63.0 (55–71)	65.0 (52–66)	64.0 (58–69)	64.5 (56–70)
Sex, n (%)	Male	10 (52.6)	7 (70.0)	10 (40.0)	9 (56.3)	34 (66.7)	19 (70.4)	39 (58.2)	22 (57.9)
ECOG PS, %	0 / 1	63.2 / 36.8	50.0 / 50.0	52.0 / 48.0	56.3 / 43.8	33.3 / 66.7	33.3 / 66.7	34.3 / 65.7	36.8 / 63.2
Site at first diagnosis, n (%)	Colon, left	9 (47.4)	5 (50.0)	10 (40.0)	5 (31.3)	28 (54.9)	6 (22.2)	25 (37.3)	19 (50.0)
	Colon, right	4 (21.1)	2 (20.0)	5 (20.0)	2 (12.5)	8 (15.7)	9 (33.3)	22 (32.8)	10 (26.3)
	Colon, unknown	1 (5.3)	1 (10.0)	0	2 (12.5)	2 (3.9)	0	3 (4.5)	2 (5.3)
	Rectum only	3 (15.8)	2 (20.0)	10 (40.0)	7 (43.8)	13 (25.5)	12 (44.4)	17 (25.4)	6 (15.8)
	Colon, left and right	2 (10.5)	0	0	0	0	0	0	1 (2.6)
Duration of metastatic disease, n (%)	≤18 months	6 (31.6)	1 (10.0)	2 (8.0)	0	3 (5.9)	2 (7.4)	5 (7.5)	4 (10.5)
	>18 months	13 (68.4)	9 (90.0)	23 (92.0)	16 (100)	48 (94.1)	25 (92.6)	62 (92.5)	34 (89.5)
Prior LOT,* n (%)	≤3	7 (36.8)	3 (30.0)	6 (24.0)	6 (37.5)	9 (17.6)	3 (11.1)	12 (17.9)	13 (34.2)
	>3	12 (63.2)	7 (70.0)	19 (76.0)	10 (62.5)	42 (82.4)	24 (88.9)	55 (82.1)	25 (65.8)
Mutation status, n (%)	*RAS* mutation+	14 (73.7)	6 (60.0)	20 (80.0)	13 (81.3)	29 (56.9)	15 (55.6)	47 (70.1)	21 (55.3)
	BRAF mutation+	0	0	1 (4.0)	1 (6.3)	1 (2.0)	3 (11.1)	1 (1.5)	2 (5.3)
MSI status, n (%)	MSI-H and/or dMMR	0	0	0	0	0	1 (3.7)	1 (1.5)	2 (5.3)
Prior treatment, n (%)	VEGF inhibitor	18 (94.7)	10 (100)	25 (100)	15 (93.8)	50 (98.0)	27 (100)	65 (97.0)	34 (89.5)
	EGFR inhibitor	5 (26.3)	4 (40.0)	6 (24.0)	3 (18.8)	22 (43.1)	13 (48.1)	21 (31.3)	18 (47.4)
	TAS-102	12 (63.2)	8 (80.0)	11 (44.0)	11 (68.8)	25 (49.0)	9 (33.3)	33 (49.3)	22 (57.9)
	Regorafenib	2 (10.5)	0	1 (4.0)	3 (18.8)	1 (2.0)	3 (11.1)	4 (6.0)	5 (13.2)
	TAS-102 and regorafenib	5 (26.3)	2 (20.0)	13 (52.0)	2 (12.5)	25 (49.0)	15 (55.6)	30 (44.8)	11 (28.9)

*For metastatic disease

BSC. Best supportive care; dMMR, deficient mismatch repair; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, endothelial growth factor receptor; FRUQ, fruquintinib; LOT, line of treatment; met, metastasis; MSI(-H), microsatellite instability(-high); PBO, placebo; VEGF, vascular endothelial growth factor

Garcia-Carbonero R, et al. ESMO GI 2025 [poster #37P]

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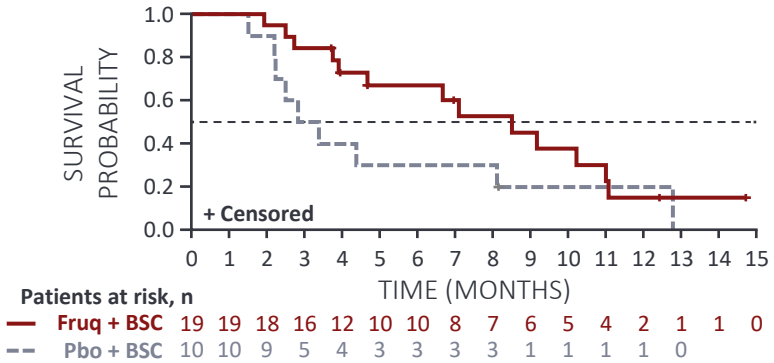
Overall survival by baseline metastatic site

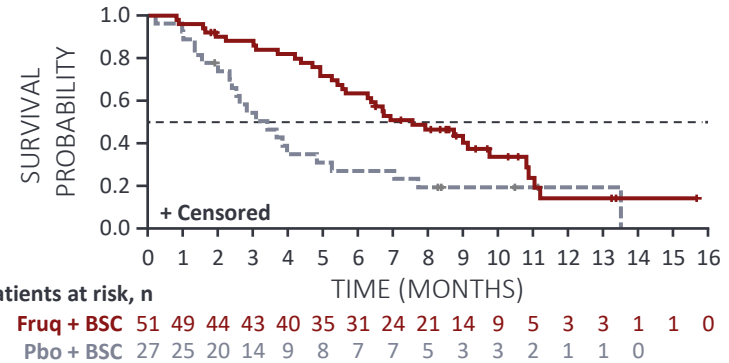
Median OS was longer with fruquintinib vs placebo in patients with liver metastases only, bone metastases, and peritoneal metastases*

OS in patients with liver mets only



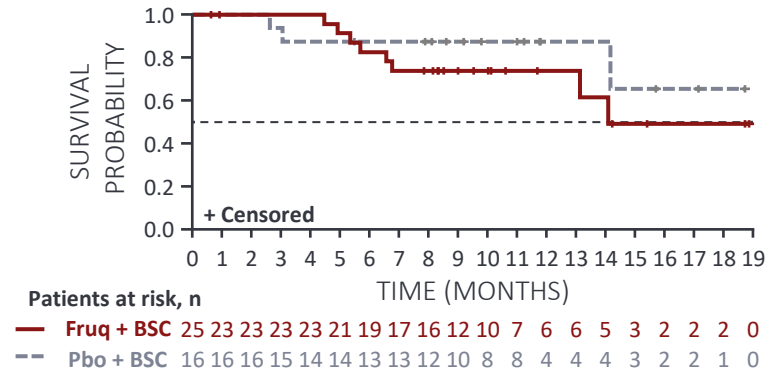
LIVER METS ONLY	FRUQ + BSC (n=19)	PBO + BSC (n=10)
Median OS, months	8.5	3.1
HR (95% CI) p-value	0.256 (0.079, 0.824) p=0.0760	

OS in patients with bone ± other mets



BONE ± OTHER METS	FRUQ + BSC (n=51)	PBO + BSC (n=27)
Median OS, months	7.6	3.4
HR (95% CI); p-value	0.399 (0.215, 0.741) p=0.0065	

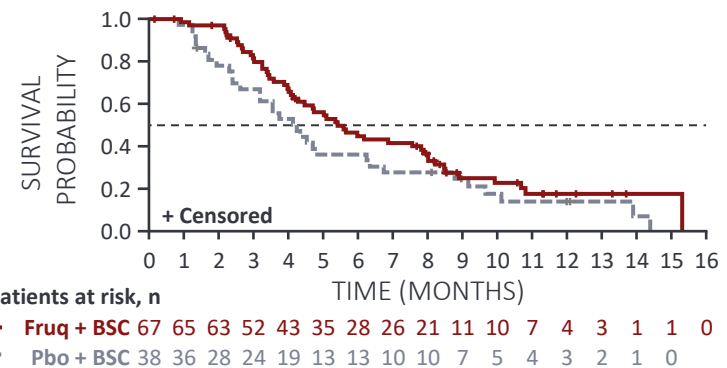
OS in patients with lung mets only



LUNG METS ONLY	FRUQ + BSC (n=25)	PBO + BSC (n=16)
Median OS, months	14.1	NE
HR (95% CI) p-value	0.998 (0.208, 4.792) p=0.9561	

13/16 patients with lung mets only in the placebo arm were censored (all 13 were alive at data cutoff); therefore, OS data were immature, and median OS was not evaluable

OS in patients with peritoneal ± other mets



PERITONEAL ± OTHER METS	FRUQ + BSC (n=67)	PBO + BSC (n=38)
Median OS, months	5.4	4.2
HR (95% CI); p-value	0.669 (0.395, 1.134) p=0.2453	

*OS evaluated by the Kaplan–Meier method with differences tested using the log-rank test; survival HRs were estimated using a Cox proportional hazards model. BSC, best supportive care; CI, confidence interval; FRUQ, fruquintinib; HR, hazard ratio; met, metastasis; NE, not evaluable; OS, overall survival; PBO, placebo

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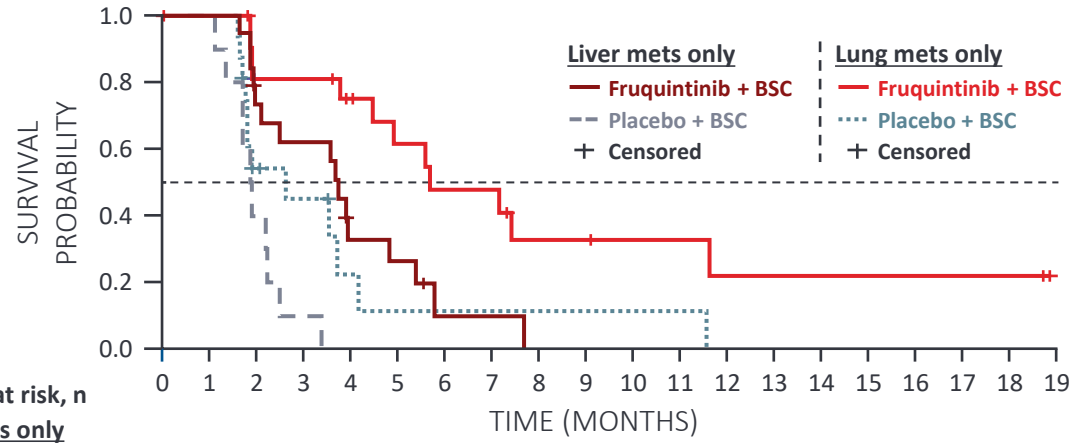
Progression-free survival by baseline metastatic site

Median PFS was longer with fruquintinib vs placebo regardless of baseline metastatic site(s)*

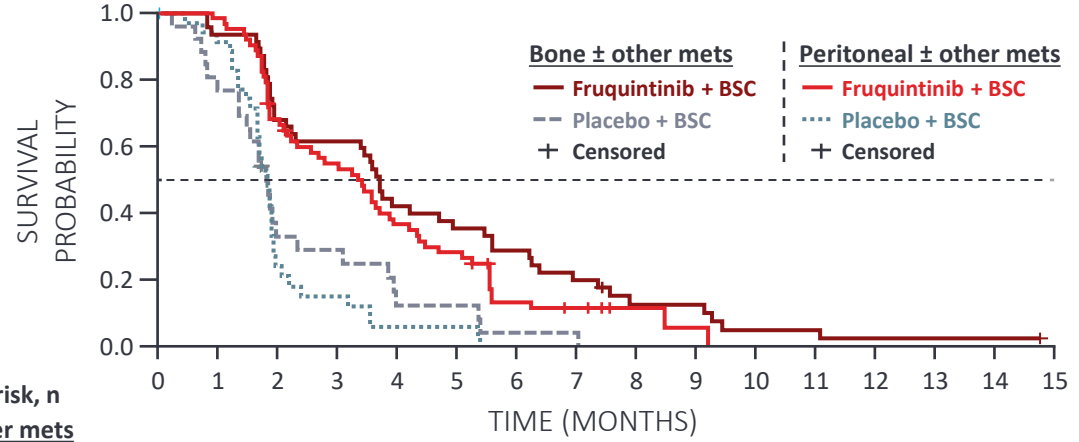
PFS in patients with liver or lung mets only



Patients at risk, n

Liver mets only																				
Fruquintinib + BSC	19	19	13	11	5	4	1	1	0											
Placebo + BSC	10	10	4	1	0															
Lung mets only																				
Fruquintinib + BSC	25	22	16	16	12	9	7	7	4	4	3	3	2	2	2	2	2	2	2	0
Placebo + BSC	16	16	7	5	2	1	1	1	1	1	1	1	0							

PFS in patients with bone or peritoneal mets ± mets at other sites



Patients at risk, n

Bone ± other mets																				
Fruquintinib + BSC	51	44	32	29	19	16	13	9	5	5	2	2	1	1	1	0				
Placebo + BSC	27	20	8	7	3	3	1	1	0											
Peritoneal ± other mets																				
Fruquintinib + BSC	67	62	42	33	22	17	7	5	2	1	0									
Placebo + BSC	38	32	8	5	2	2	0													

	LIVER METS ONLY		LUNG METS ONLY	
	FRUQ + BSC (n=19)	PBO + BSC (n=10)	FRUQ + BSC (n=25)	PBO + BSC (n=16)
Median PFS, months	3.7	1.9	5.7	2.6
HR (95% CI); p-value	0.157 (0.047, 0.526); p=0.0093		0.170 (0.056, 0.516); p=0.0063	

	BONE ± OTHER METS		PERITONEAL ± OTHER METS	
	FRUQ + BSC (n=51)	PBO + BSC (n=27)	FRUQ + BSC (n=67)	PBO + BSC (n=38)
Median PFS, months	3.7	1.8	3.4	1.8
HR (95% CI); p-value	0.354 (0.201, 0.621); p=0.0003		0.305 (0.180, 0.518); p=0.0002	

*PFS evaluated by the Kaplan–Meier method with differences tested using the log-rank test; survival HRs were estimated using a Cox proportional hazards model

BSC, best supportive care; CI, confidence interval; FRUQ, fruquintinib; HR, hazard ratio; met, metastasis; PBO, placebo; PFS, progression-free survival

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Tumor response rates by baseline metastatic site

n (%)	LIVER METS ONLY		LUNG METS ONLY		BONE ± OTHER METS		PERITONEAL ± OTHER METS	
	FRUQ + BSC (n=19)	PBO + BSC (n=10)	FRUQ + BSC (n=25)	PBO + BSC (n=16)	FRUQ + BSC (n=51)	PBO + BSC (n=27)	FRUQ + BSC (n=67)	PBO + BSC (n=38)
ORR	0	0	3 (12.0)	0	1 (2.0)	0	0	0
Best overall response								
CR	0	0	0	0	0	0	0	0
PR	0	0	3 (12.0)	0	1 (2.0)	0	0	0
SD	12 (63.2)	0	14 (56.0)	8 (50.0)	27 (52.9)	6 (22.2)	35 (52.2)	5 (13.2)
PD	5 (26.3)	6 (60.0)	4 (16.0)	7 (43.8)	12 (23.5)	12 (44.4)	20 (29.9)	22 (57.9)
NE	0	0	0	0	1 (2.0)	0	2 (3.0)	1 (2.6)
NA	2 (10.5)	4 (40.0)	4 (16.0)	1 (6.3)	10 (19.6)	9 (33.3)	10 (14.9)	10 (26.3)
DCR*	12 (63.2)	0	17 (68.0)	8 (50.0)	28 (54.9)	6 (22.2)	35 (52.2)	5 (13.2)
p-value†	0.001		0.255		0.006		<0.0001	

The DCR was improved with **fruquintinib** vs **placebo**, regardless of the site of baseline metastases

*For at least 7 weeks; †Two-sided p-value calculated using the Cochran–Mantel–Hanzel method

BSC, best suportive care; CR, complete response; DCR, disease control rate; FRUQ, fruquintinib; met, metastasis; NA, not applicable; NE, not evaluable; ORR, objective response rate; PBO, placebo; PD, progressive disease; PR, partial response; SD, stable disease

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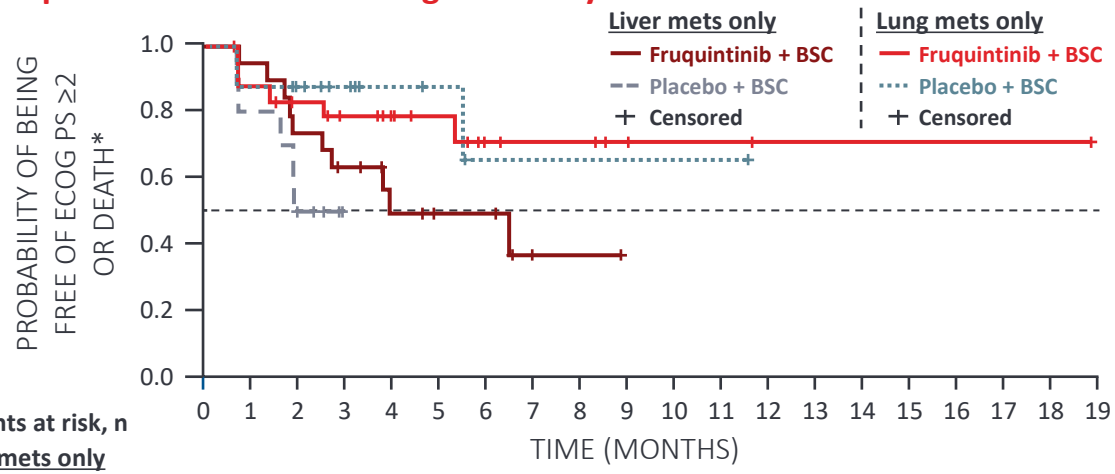
TTD to ECOG PS ≥2 or death by baseline metastatic site

ESMO GI 2025
Poster 37P

Median TTD to ECOG PS ≥2 or death was longer with fruquintinib vs placebo in patients with bone metastases and peritoneal metastases

TTD in patients with liver or lung mets only



Patients at risk, n

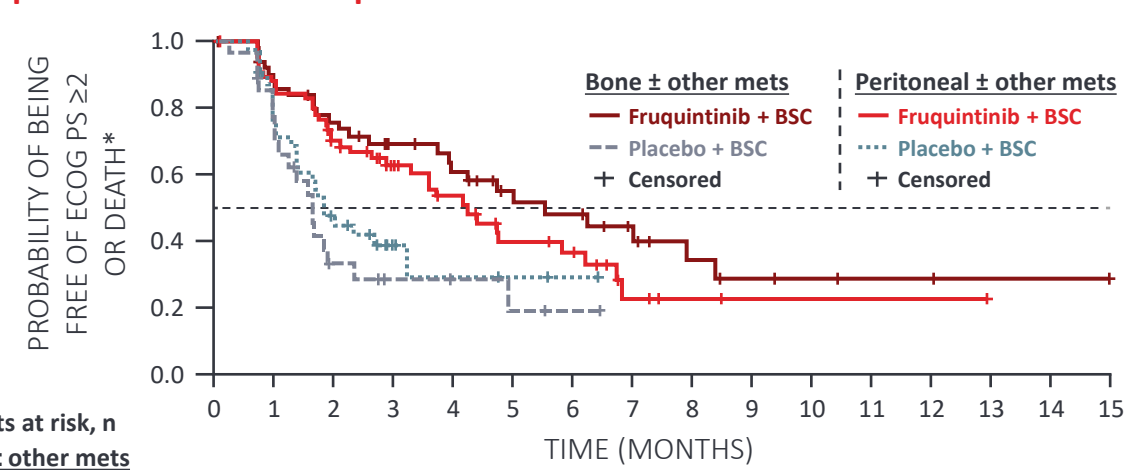
Liver mets only

Fruquintinib + BSC	19	18	14	11	7	5	5	1	1
Placebo + BSC	10	8	4	0					

Lung mets only

Fruquintinib + BSC	25	21	18	15	12	10	6	5	5	3	2	2	1	1	1	1	1	1	0
Placebo + BSC	16	14	12	5	6	4	1	1	1	1	1	1	0						

TTD in patients with bone or peritoneal mets ± mets at other sites



Patients at risk, n

Bone ± other mets

Fruquintinib + BSC	51	42	36	26	22	15	14	9	6	4	3	2	2	1	1	0
Placebo + BSC	27	18	7	4	3	2	1	0								

Peritoneal ± other mets

Fruquintinib + BSC	67	53	41	27	21	14	11	4	2	1	1	1	1
Placebo + BSC	38	27	17	4	3	2	1	0					

	LIVER METS ONLY		LUNG METS ONLY	
	FRUQ + BSC (n=19)	PBO + BSC (n=10)	FRUQ + BSC (n=25)	PBO + BSC (n=16)
Median TTD, months	3.9	NE	NE	NE
HR (95% CI); p-value	0.320 (0.071, 1.449); p=0.2889		1.040 (0.184, 5.887); p=0.8830	

	BONE ± OTHER METS		PERITONEAL ± OTHER METS	
	FRUQ + BSC (n=51)	PBO + BSC (n=27)	FRUQ + BSC (n=67)	PBO + BSC (n=38)
Median TTD, months	5.5	1.6	4.2	1.8
HR (95% CI); p-value	0.333 (0.166, 0.667); p=0.0015		0.464 (0.257, 0.838); p=0.0174	

*Within 37 days after last dose

BSC, best supportive care; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; HR, hazard ratio; met, metastasis; NE, not evaluable; PBO, placebo; TTD, time to deterioration

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Safety profile by baseline metastatic site*

In the fruquintinib arm, the incidence of Grade ≥3 TEAEs was numerically higher in the subgroups with bone or peritoneal mets ± mets at other sites, and lower in the subgroups with liver and lung mets only†

TEAE, n (%)	LIVER METS ONLY		LUNG METS ONLY		BONE ± OTHER METS		PERITONEAL ± OTHER METS	
	FRUQ + BSC (n=19)	PBO + BSC (n=10)	FRUQ + BSC (n=25)	PBO + BSC (n=16)	FRUQ + BSC (n=50)	PBO + BSC (n=27)	FRUQ + BSC (n=64)	PBO + BSC (n=39)
Any grade	18 (94.7)	9 (90.0)	24 (96.0)	12 (75.0)	50 (100)	24 (88.9)	64 (100)	36 (92.3)
Grade ≥3	10 (52.6)	4 (40.0)	14 (56.0)	5 (31.3)	32 (64.0)	19 (70.4)	45 (70.3)	19 (48.7)
Leading to dose reduction	4 (21.1)	0	11 (44.0)	0	8 (16.0)	1 (3.7)	11 (17.2)	2 (5.1)
Leading to dose interruption	9 (47.4)	4 (40.0)	14 (56.0)	3 (18.8)	19 (38.0)	10 (37.0)	29 (45.3)	12 (30.8)
Leading to discontinuation	4 (21.1)	1 (10.0)	6 (24.0)	3 (18.8)	9 (18.0)	8 (29.6)	14 (21.9)	8 (20.5)
Serious TEAE	4 (21.1)	4 (40.0)	6 (24.0)	3 (18.8)	20 (40.0)	15 (55.6)	31 (48.4)	16 (41.0)
Grade ≥3	4 (21.1)	4 (40.0)	6 (24.0)	3 (18.8)	20 (40.0)	15 (55.6)	31 (48.4)	15 (38.5)
Treatment-related	16 (84.2)	7 (70.0)	22 (88.0)	6 (37.5)	42 (84.0)	17 (63.0)	55 (85.9)	23 (59.0)
Grade ≥3	7 (36.8)	2 (20.0)	11 (44.0)	2 (12.5)	12 (24.0)	3 (11.1)	19 (29.7)	2 (5.1)
Leading to death	0	2 (20.0)	0	0	6 (12.0)	8 (29.6)	9 (14.1)	10 (25.6)
Most common Grade ≥3 TEAE‡								
Hypertension	3 (15.8)	0	3 (12.0)	0	5 (10.0)	0	8 (12.5)	0
Asthenia	2 (10.5)	0	1 (4.0)	0	4 (8.0)	2 (7.4)	2 (3.1)	3 (7.7)
PPE	2 (10.5)	0	5 (20.0)	0	2 (4.0)	0	1 (1.6)	0

The proportion of patients who **discontinued fruquintinib due to TEAEs** was **~20%** in each subgroup

*In the overall FRESCO-2 safety population, of five patients assigned to FRUQ, three did not receive FRUQ, and two received PBO instead; two patients assigned to PBO did not receive treatment; †Due to low patient numbers in some subgroups, these data should be interpreted with caution; ‡Occurring in ≥10% of patients who received FRUQ per subgroup

BSC, best supportive care; FRUQ, fruquintinib; met, metastasis; PBO, placebo; PPE, palmar–plantar erythrodysesthesia; TEAE, treatment-emergent adverse event

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Authors' conclusions

The site of metastasis in mCRC has previously been shown to be associated with survival outcome, with patients with lung metastases showing more favorable survival outcomes vs patients with liver, bone, or peritoneal metastases[1]

In this subgroup analysis, fruquintinib demonstrated improved outcomes vs placebo, regardless of the site of baseline metastases[2]

- Median OS was longer with fruquintinib vs placebo in patients with mCRC who had liver metastases only, bone metastases, or peritoneal metastases at baseline
- In addition, analyses of PFS and DCR indicated improved outcomes in patients with mCRC who had lung metastases only

There were small numerical differences in the incidence of Grade ≥3 TEAEs with fruquintinib between subgroups, likely due to patient numbers and differences in disease burden; however, the overall safety profile of fruquintinib was consistent with previous studies in patients with mCRC[2-4]

This was a *post hoc* analysis with low patient numbers per subgroup; therefore, definitive conclusions cannot be drawn[2]

The results of this analysis demonstrate the clinical benefit of fruquintinib in patients with mCRC, regardless of metastatic sites at baseline[2,*]

***Fruquintinib is not approved in all regions; in regions where it is not currently approved, there is no guarantee that it will receive regulatory approval**

DCR, disease control rate; mCRC, metastatic colorectal cancer; OS, overall survival; PFS, progression-free survival; TEAE, treatment-emergent adverse event

1. Prasanna T, et al. Acta Oncologica 2018;57:1438-44; 2. Garcia-Carbonero R, et al. ESMO GI 2025 [poster #37P]; 3. Li J, et al. JAMA 2018;319:2486-96; 4. Dasari A, et al. Lancet 2023;402:41-53

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3

ASCO GI 2025

Abstract 171

Overall survival with fruquintinib vs placebo after adjusting for subsequent anticancer therapy in patients with refractory metastatic colorectal cancer in the FRESCO-2 study

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Objective, methods, and most common subsequent ACT following fruquintinib or placebo

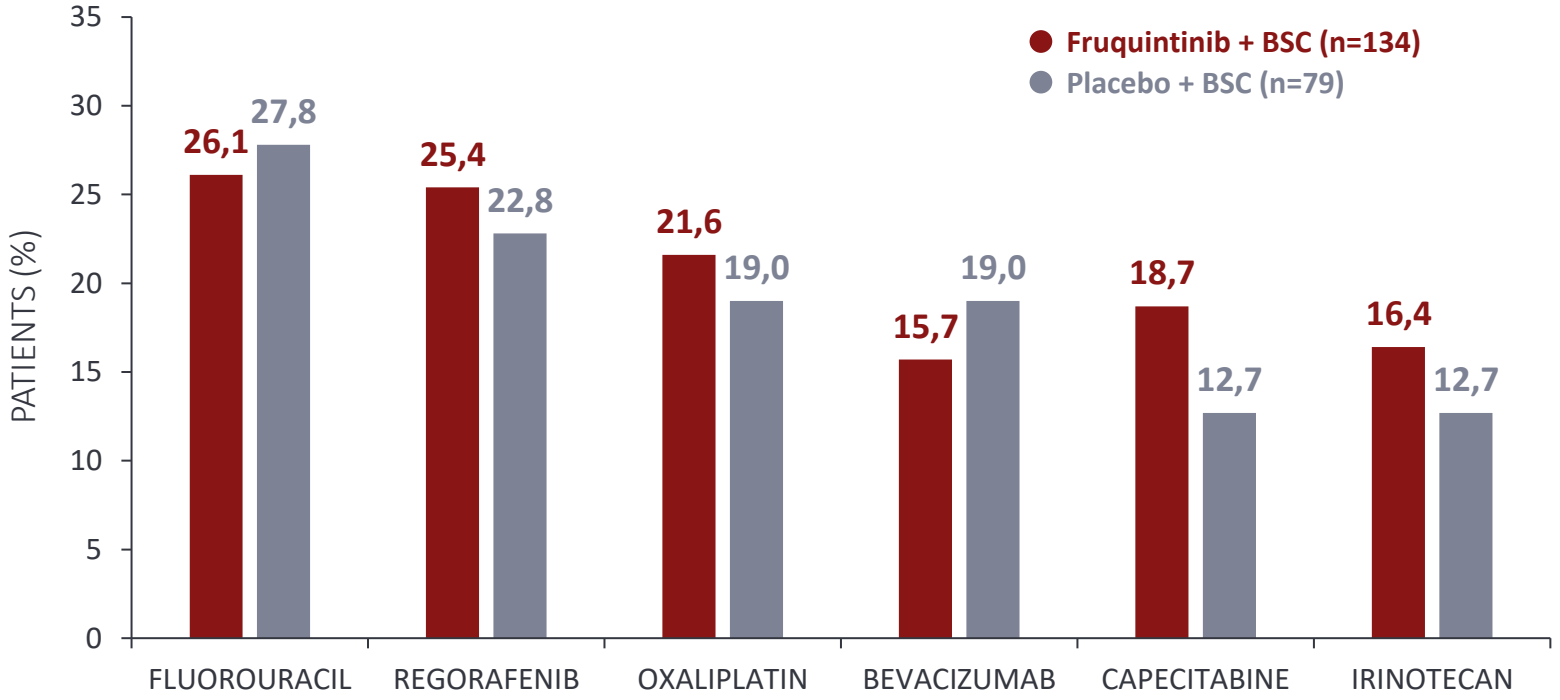
OBJECTIVE:

Assess the impact of subsequent ACT on OS in FRESCO-2 by excluding or censoring patients who received subsequent ACT, and determining the causal HR using IPCW and MSM approaches*

- **IPCWs** adjust observations by weighting them based on their probability of remaining uncensored, giving greater importance to uncensored patients
- **MSMs** assign weights to individuals according to the probability of both censoring and receiving subsequent ACT

Of the 456 and 230 patients who received fruquintinib and placebo in FRESCO-2, 134 (29.4%) and 79 (34.3%) received subsequent ACT, respectively

Most common† subsequent ACT during survival follow-up (safety population)‡,§



**Post hoc* analysis. Both IPCWs and MSMs use stabilized weights to mitigate the impact of extreme weights; †In ≥15% of patients in either arm; ‡Three patients randomized to receive fruquintinib did not receive treatment, and two patients received placebo instead; two patients randomized to placebo did not receive treatment; §The percentages for each treatment are calculated based on the total number of patients who received subsequent ACT in the fruquintinib and placebo arms

Note: data are only available on individual agents and not on their use in combination

ACT, anticancer therapy; BSC, best supportive care; HR, hazard ratio; IPCW, inverse probability censoring weight; MSM, marginal structural model; OS, overall survival

Lonardi S, et al. ASCO GI 2025 [poster #G9]; see the abstract

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Baseline characteristics (ITT population)

A lower proportion of patients* who received subsequent ACT had a baseline ECOG PS of 1 or liver metastases vs patients without subsequent ACT

Among patients who received subsequent ACT, a higher proportion* in the fruquintinib arm had a baseline ECOG PS of 1 or liver metastases than in the placebo arm

CHARACTERISTIC		PATIENTS WITH SUBSEQUENT ACT (n=213)		PATIENTS W/O SUBSEQUENT ACT (n=478)	
		FRUQ + BSC (n=135)	PBO + BSC (n=78)	FRUQ + BSC (n=326)	PBO + BSC (n=152)
Age, years	Median (range)	62.0 (36–81)	63.0 (30–79)	64.0 (25–82)	65.0 (35–86)
Male, %		51.1	55.1	54.0	63.8
Race, %	White / Asian / Black† / Other‡	79.3 / 10.4 / 3.7 / 6.7	87.2 / 9.0 / 1.3 / 2.6	79.8 / 8.9 / 2.5 / 8.9	81.6 / 7.2 / 3.9 / 7.2
ECOG PS, %	0 / 1	52.6 / 47.4	64.1 / 35.9	38.3 / 61.7	34.2 / 65.8
Time to first CRC diagnosis, months	Median (range)	43.7 (10.1–192.8)	48.1 (20.8–142.6)	48.0 (6.0–242.4)	50.2 (7.1–154.4)
Primary location at first diagnosis, %	Colon / rectum / both	58.5 / 28.1 / 13.3	62.8 / 23.1 / 14.1	61.3 / 32.2 / 6.4	57.9 / 34.2 / 7.9
Primary colon site at first diagnosis, %	Left / right / both	44.4 / 19.3 / 0	47.4 / 23.1 / 0	40.5 / 21.8 / 1.2	36.2 / 23.0 / 1.3
Duration of mCRC	Median (range), months	37.7 (10.1–192.8)	41.6 (14.6–117.0)	38.6 (6.0–128.0)	39.9 (7.1–147.1)
	≤18 / >18 months, %	8.9 / 91.1	2.6 / 97.4	7.7 / 92.3	7.2 / 92.8
Liver metastases, %		64.4	53.8	77.3	75.0
Mutation status, %	*RAS* wild type	40.0	34.6	35.6	38.2
	BRAF wild type	88.1	87.2	86.5	85.5
MSI status, %	MSS and/or pMMR	95.6	93.6	91.4	93.4
Number of prior LOTs for mCRC, %	≤3 / >3	29.6 / 70.4	29.5 / 70.5	26.1 / 73.9	27.0 / 73.0
Prior treatment, %	TAS-102 / regorafenib / both	57.0 / 10.4 / 32.6	59.0 / 10.3 / 30.8	50.0 / 8.0 / 42.0	49.3 / 6.6 / 44.1

*≥10% difference; †Or African American; ‡Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, Not Reported/Unknown, or Other as recorded on the demographics electronic case report form

ACT, anticancer therapy; BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; ITT, intent-to-treat; LOT, line of therapy; (m)CRC, (metastatic) colorectal cancer; MSI, microsatellite instability; MSS, microsatellite stable; PBO, placebo; pMMR, proficient mismatch repair; w/o, without

Lonardi S, et al. ASCO GI 2025 [poster #G9]; see the abstract

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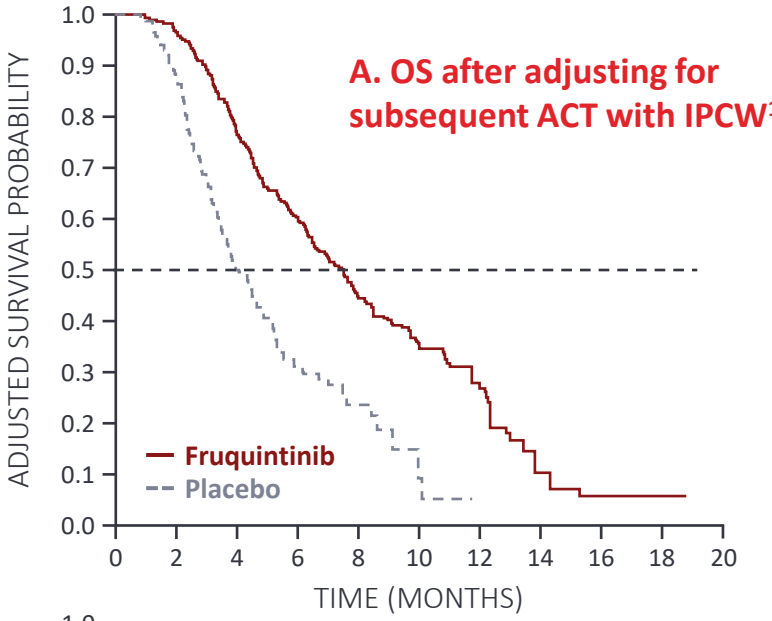
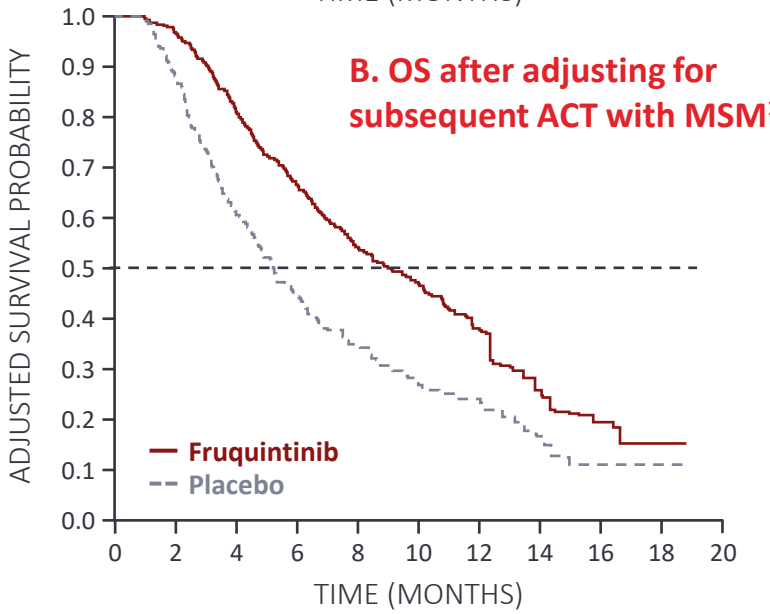
OS adjusted for subsequent ACT (ITT population)

The impact of subsequent ACT on OS in FRESCO-2[1]

	MEDIAN OS, MONTHS		HR (95% CI)	P-VALUE
	FRUQ + BSC	PBO + BSC		
ITT primary analysis[2]	7.4	4.8	0.66 (0.55, 0.80)	<0.001
Excluding ACT	5.7	3.2	0.45 (0.36, 0.57)	NA
Censoring ACT	7.2	4.4	0.49 (0.39, 0.61)	NA
Adjusting for ACT with IPCW (Fig. A)	7.6	4.3	0.425 (0.327, 0.552)	<0.0001
Adjusting for ACT with MSM (Fig. B)	9.1	5.3	0.479 (0.380, 0.604)	<0.0001

OS benefit with fruquintinib in the ITT population was improved when patients who had received subsequent ACT were excluded or censored, and after adjusting for subsequent ACT using IPCWs and MSMs[1]





ACT, anticancer therapy; BSC, best supportive care; CI, confidence interval; FRUQ, fruquintinib; HR, hazard ratio; IPCW, inverse probability of censoring weight; ITT, intent-to-treat; MSM, marginal structural model; NA, not applicable; OS, overall survival; PBO, placebo

1. Lonardi S, et al. ASCO GI 2025 [poster #G9]; see the abstract; 2. Dasari NA, et al. ESMO 2022 [oral #LBA25]

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Safety profile (safety population)*

Among patients who received subsequent ACT, 51.5% vs 19.0% had a Grade ≥3 TEAE and 13.4% vs 2.5% had a TEAE that led to discontinuation in the fruquintinib vs placebo arms, respectively

Among patients who did not receive subsequent ACT, 67.4% vs 66.9% had a Grade ≥3 TEAE and 23.3% vs 31.1% had a TEAE that led to discontinuation in the fruquintinib vs placebo arms, respectively

TEAE, n (%)	PATIENTS WITH SUBSEQUENT ACT (n=213)		PATIENTS WITHOUT SUBSEQUENT ACT (n=473)	
	FRUQ + BSC (n=134)	PBO + BSC (n=79)	FRUQ + BSC (n=322)	PBO + BSC (n=151)
Any TEAE	130 (97.0)	68 (86.1)	321 (99.7)	145 (96.0)
Grade ≥3	69 (51.5)	15 (19.0)	217 (67.4)	101 (66.9)
Treatment-related	120 (89.6)	46 (58.2)	275 (85.4)	84 (55.6)
Grade ≥3 treatment-related	52 (38.8)	6 (7.6)	112 (34.8)	20 (13.2)
Leading to dose reduction	35 (26.1)	4 (5.1)	75 (23.3)	5 (3.3)
Leading to dose interruption	58 (43.3)	11 (13.9)	155 (48.1)	50 (33.1)
Leading to discontinuation	18 (13.4)	2 (2.5)	75 (23.3)	47 (31.1)
Leading to death†	0	0	48 (14.9)	45 (29.8)

*Three patients randomized to receive fruquintinib did not receive treatment, and two patients received placebo instead; two patients randomized to placebo did not receive treatment;
†In FRESCO-2, there was one treatment-related death in each group (intestinal perforation in the fruquintinib group and cardiac arrest in the placebo group)

ACT, anticancer therapy; BSC, best supportive care; FRUQ, fruquintinib; PBO, placebo; TEAE, treatment-emergent adverse event

Lonardi S, et al. ASCO GI 2025 [poster #G9]; see the abstract

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Safety profile (safety population)*

Hypertension was the most common any-grade or Grade ≥3 TEAE among patients treated with fruquintinib + BSC who did and did not receive subsequent ACT

TEAE,† n (%)	PATIENTS WITH SUBSEQUENT ACT (n=213)				PATIENTS WITHOUT SUBSEQUENT ACT (n=473)			
	FRUQ + BSC (n=134)		PBO + BSC (n=79)		FRUQ + BSC (n=322)		PBO + BSC (n=151)	
	ANY GR	GR ≥3	ANY GR	GR ≥3	ANY GR	GR ≥3	ANY GR	GR ≥3
Hypertension	57 (42.5)	26 (19.4)	10 (12.7)	0	111 (34.5)	36 (11.2)	10 (6.6)	2 (1.3)
Asthenia	46 (34.3)	7 (5.2)	13 (16.5)	0	109 (33.9)	28 (8.7)	39 (25.8)	9 (6.0)
Diarrhea	41 (30.6)	5 (3.7)	7 (8.9)	0	69 (21.4)	11 (3.4)	17 (11.3)	0
PPE	30 (22.4)	10 (7.5)	2 (2.5)	0	58 (18.0)	19 (5.9)	4 (2.6)	0
Proteinuria	30 (22.4)	5 (3.7)	2 (2.5)	0	49 (15.2)	3 (0.9)	10 (6.6)	2 (1.3)
Decreased appetite	30 (22.4)	1 (0.7)	9 (11.4)	1 (1.3)	94 (29.2)	10 (3.1)	31 (20.5)	2 (1.3)
Nausea	26 (19.4)	1 (0.7)	16 (20.3)	1 (1.3)	53 (16.5)	2 (0.6)	26 (17.2)	1 (0.7)
Hypothyroidism	24 (17.9)	0	0	0	70 (21.7)	2 (0.6)	1 (0.7)	0
Fatigue	23 (17.2)	4 (3.0)	12 (15.2)	0	68 (21.1)	14 (4.3)	25 (16.6)	2 (1.3)

*Three patients randomized to receive fruquintinib did not receive treatment, and two patients received placebo instead; two patients randomized to placebo did not receive treatment;
†≥20% any-grade TEAE in either treatment arm in either subgroup

ACT, anticancer therapy; BSC, best supportive care; FRUQ, fruquintinib; Gr, Grade; PBO, placebo; PPE, palmar–plantar erythrodysesthesia; TEAE, treatment-emergent adverse event

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Authors' conclusions

- A slightly lower proportion of patients in the fruquintinib arm received subsequent ACT vs the placebo arm, which may have confounded OS outcomes in the primary analysis of the FRESCO-2 ITT population
- Consistent with the primary analysis, fruquintinib improved OS vs placebo after adjusting for the impact of subsequent ACT, with a greater magnitude of benefit with fruquintinib vs placebo (lower HRs) than in the primary analysis; these analyses are robust with consistent results reported using IPCW and MSM approaches
- Baseline characteristics were generally balanced between treatment arms and between patients who did and did not receive subsequent ACT; however, patients who received subsequent ACT were less likely to have had an ECOG PS of 1 and liver metastases at baseline than patients who did not receive subsequent ACT
- The overall safety profile of fruquintinib vs placebo was generally consistent with the ITT population except for a lower rate of Grade ≥3 TEAEs and TEAEs leading to discontinuation in patients who received subsequent ACT in both arms
- These findings support fruquintinib as an effective treatment option for patients with previously treated mCRC*

***Fruquintinib is not approved in all regions; in regions where it is not currently approved, there is no guarantee that it will receive regulatory approval**

ACT, anticancer therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IPCW, inverse probability of censoring weight; ITT, intent-to-treat; mCRC, metastatic colorectal cancer; MSM, marginal structural model; OS, overall survival; TEAE, treatment-emergent adverse event

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ASCO GI 2025

Abstract 142

Fruquintinib plus best supportive care for patients with metastatic colorectal cancer: characterization of patients who had an overall survival of ≥10 months in the FRESCO-2 study

Stefan Kasper,[1] Andrea Sartore-Bianchi,[2] Violaine Randrian,[3] Chiara Cremolini,[4] Dirk Arnold,[5] **Arvind Dasari**,[6] Cathy Eng,[7] Sara Lonardi,[8] Elena Elez,[9] Takayuki Yoshino,[10] Alberto F. Sobrero,[11] James C. Yao,[6] Howard S. Hochster,[12] Eric Van Cutsem,[13] David Tougeron,[3] Ziji Yu,[14] Qi Dong,[14] William R. Schelman,[15] François Ghiringhelli[16]

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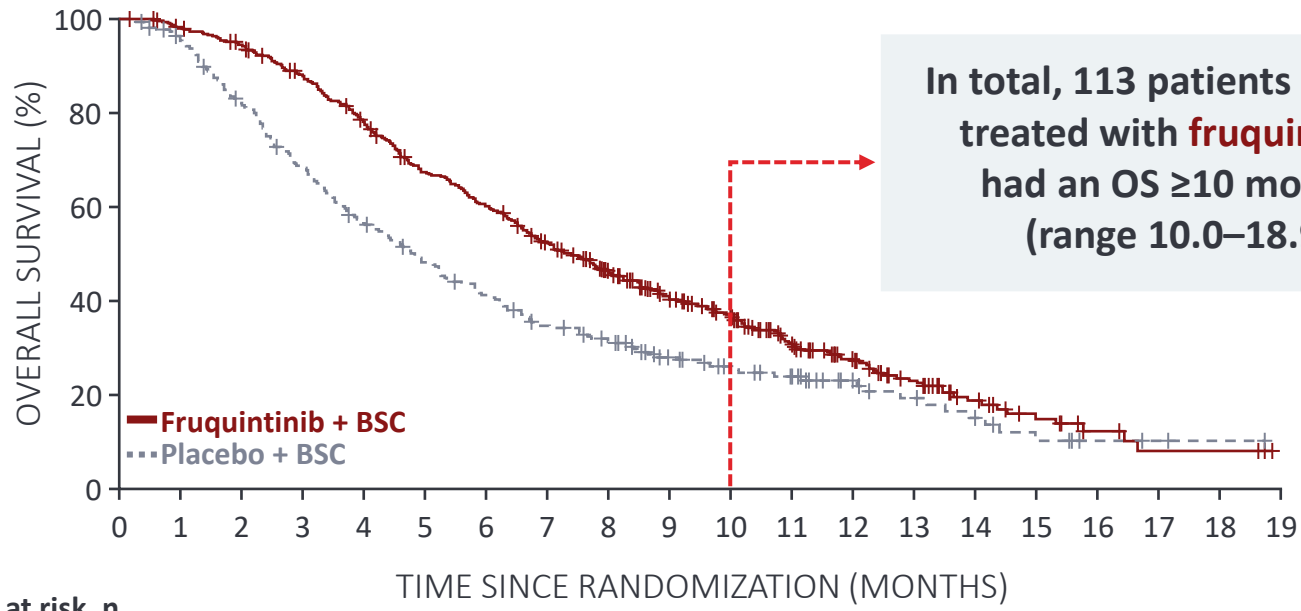
Objective, methods, and landmark survival analysis

OBJECTIVE:

Assess baseline characteristics and safety data from patients treated with fruquintinib + BSC in FRESCO-2 who gained an OS benefit of ≥10 months*

FRESCO-2 OS (ITT population)†



In total, 113 patients (24.5%) treated with fruquintinib had an OS ≥10 months (range 10.0–18.9)

Patients at risk, n

Fruquintinib	461	449	429	395	349	297	266	224	184	143	113	79	58	41	23	14	7	4	4	0
Placebo	230	216	184	153	125	105	89	73	63	45	37	31	20	15	10	6	3	2	1	0

RATE, % (95% CI)		FRUQ + BSC (n=461)	PBO + BSC (n=230)
OS	6-month	60.4 (55.9, 64.9)	41.5 (35.0, 48.0)
	9-month	41.1 (36.4, 45.8)	28.2 (22.1, 34.3)

RATE, % (95% CI)		FRUQ + BSC (n=461)	PBO + BSC (n=230)
PFS	6-month	23.8 (19.7, 28.0)	1.1 (0, 2.6)
	9-month	11.3 (8.1, 14.6)	0.5 (0, 1.6)

*Comparison of patient characteristics between the OS ≥10 months subgroup and the ITT population was descriptive only. The FRESCO-2 ITT population included all patients who were randomly assigned to a treatment group; the safety population included all patients who received at least one dose of fruquintinib or placebo; †The primary endpoint of OS was significantly improved with fruquintinib + BSC vs placebo + BSC (HR 0.66; 95% CI 0.55, 0.80; p<0.001). The key secondary endpoint of PFS was also significantly improved with fruquintinib + BSC vs placebo + BSC (HR 0.32; 95% CI 0.27, 0.39; p<0.001). HRs and 95% CIs between the two treatment arms were calculated from a stratified Cox proportional hazards model with the treatment group as the only covariate in the model

BSC, best supportive care; CI, confidence interval; FRUQ, fruquintinib; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PBO, placebo; PFS, progression-free survival

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Baseline characteristics and fruquintinib exposure in FRESCO-2

A higher proportion (>10% difference) of patients treated with fruquintinib + BSC with an OS ≥10 months had no liver metastases and an ECOG PS of 0 at baseline vs the ITT population

	CHARACTERISTIC		PATIENTS WITH OS ≥10 MONTHS (n=113)	ITT POPULATION (n=461)
BASELINE	Age, years	Mean (SD)	62.9 (10.4)	62.2 (10.4)
	Female, %		49.6	46.9
	Race, %	White / Asian / Black* / Other†	80.5 / 6.2 / 2.7 / 10.6	79.6 / 9.3 / 2.8 / 1.1
	ECOG PS, %	0 / 1	54.0 / 46.0	42.5 / 57.5
	Time since first CRC diagnosis, months	Median (range)	52.0 (10.1–242.4)	47.2 (6.0–242.4)
	Primary location at first diagnosis, %	Colon / rectum / both	51.3 / 35.4 / 13.3	60.5 / 31.0 / 8.5
	Primary colon site at first diagnosis, %	Left / right / both	42.5 / 15.9 / 0	41.6 / 21.0 / 0.9
	Duration of mCRC	Median (range), months	42.7 (10.1–121.0)	37.9 (6.0–192.8)
		≤18 / >18 months, %	5.3 / 94.7	8.0 / 92.0
	Liver metastases, %		58.4	73.5
	Number of prior LOTs for mCRC, %	≤3 / >3	26.5 / 73.5	27.1 / 72.9
	Prior treatment, %	TAS-102 / regorafenib / both	46.9 / 12.4 / 40.7	52.1 / 8.7 / 39.3
FRESCO-2	Duration of fruquintinib Tx, months	Median (range)	6.3 (0.7–19.1)	3.1 (0.3–19.1)
	Number of fruquintinib Tx cycles	Median (range)	7 (1–20)	3 (1–20)

Median **time since first CRC diagnosis** and median **duration of mCRC** was **~5 months longer for patients in the OS ≥10 months subgroup** vs the ITT population

*Or African American; †Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other as recorded on the demographics electronic case report form, and patients with multiple races selected

BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; LOT, line of therapy; (m)CRC, (metastatic) colorectal cancer; OS, overall survival; SD, standard deviation; Tx, treatment

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Safety profile

The proportion of patients who experienced a Grade ≥3 TEAE was similar between patients receiving fruquintinib + BSC with an OS ≥10 months and patients in the overall FRESCO-2 safety population

TEAE, n (%)	PATIENTS WITH OS ≥10 MONTHS (n=113)	SAFETY POPULATION* (n=456)
Any TEAE	112 (99.1)	451 (98.9)
Grade ≥3	70 (61.9)	286 (62.7)
Leading to dose reduction	45 (39.8)	110 (24.1)
Leading to dose interruption	63 (55.8)	213 (46.7)
Leading to treatment discontinuation	16 (14.2)	93 (20.4)
Leading to death	1 (0.9)	48 (10.5)
Treatment-related TEAEs	108 (95.6)	395 (86.6)
Grade ≥3	49 (43.4)	164 (36.0)
Leading to dose reduction	40 (35.4)	93 (20.4)
Leading to dose interruption	43 (38.1)	134 (29.4)
Leading to treatment discontinuation	13 (11.5)	45 (9.9)
Serious TEAEs	32 (28.3)	171 (37.5)
Grade ≥3	32 (28.3)	162 (35.5)
Treatment-emergent AESIs	107 (94.7)	368 (80.7)

A **higher proportion of patients in the OS ≥10 months subgroup** had a **TEAE leading to dose modification** vs the FRESCO-2 safety population (95.6% vs 70.8%, respectively), but a **lower proportion discontinued treatment due to TEAE**

A **higher proportion of patients in the OS ≥10 months subgroup** had a **treatment-emergent AESI** vs the FRESCO-2 safety population

*Five patients randomized to the fruquintinib arm did not receive fruquintinib treatment

AESI, adverse event of special interest; BSC, best supportive care; OS, overall survival; TEAE, treatment-emergent adverse event

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Authors' conclusions

This exploratory analysis showed that baseline characteristics were generally balanced between patients with an OS ≥10 months and patients in the ITT population

- **However, a higher proportion of patients receiving fruquintinib + BSC with an OS ≥10 months had an absence of liver metastases and an ECOG PS of 0 at baseline vs the ITT population**

As may be expected due to the longer overall duration of treatment, patients receiving fruquintinib + BSC with an OS ≥10 months required more dose modifications compared with those in the overall FRESCO-2 safety population

- **However, these patients were able to continue treatment for longer with fewer discontinuations due to TEAEs**

Fruquintinib is a novel treatment option* that demonstrates clinically meaningful and significantly improved survival compared with placebo, as evidenced by some patients gaining an OS benefit of ≥10 months

***Fruquintinib is not approved in all regions; in regions where it is not currently approved, there is no guarantee that it will receive regulatory approval**

BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; ITT, intent-to-treat; OS, overall survival; TEAE, treatment-emergent adverse event

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Investigator-initiated research

NCT05004831: Phase 2 study of fruquintinib + TAS-102 as 3L+ therapy in mCRC (1/2)*

ASCO GI 2025
Abstract 145 | Poster F6
(IIR)

Study design

Open-label, single-arm, multicenter, Phase 2 study (NCT05004831); study is ongoing

PATIENT ELIGIBILITY

- Metastatic or recurrent colorectal adenocarcinoma
- Aged 18–75 years
- ECOG PS 0 or 1
- ≥1 measurable lesion (RECIST v1.1)
- Failed ≥2 prior systemic treatments
- No prior anti-VEGFR treatment

→ **FRUQUINTINIB:**
4 mg QD, D1–21, Q4W
+
TAS-102
35 mg/m^2 BID, D1–5, D8–12, Q4W

→ **Until disease progression or unacceptable toxicity**

Primary endpoint: PFS

Secondary endpoints: ORR, DCR, OS, safety, tolerability

Baseline characteristics

CHARACTERISTIC		FRUQ + TAS-102 (N=50)
Age, years	Median (range)	60 (39–76)
Sex, n (%)	Male / Female	29 (58) / 21 (42)
Primary tumor site, n (%)	Left / Right colon	17 (34) / 9 (18)
	Rectum	24 (48)
RAS status, n (%)[†]	WT[‡]	16 (32)
	Mutant	21 (42)
Metastases, n (%)	≥2	38 (76)
Site of metastasis, n (%)	Lung	30 (60)
	Liver	29 (58)
	Peritoneal	9 (18)
Prior regimens	Median (range)	2 (1–4)
	3 / 4, n (%)	8 (16) / 2 (4)
Prior chemotherapy, n (%)	5-FU	50 (100)
	Irinotecan	45 (90)
	Oxaliplatin	46 (92)
	Raltitrexed	9 (18)
	S-1	1 (2)
Prior anti-VEGF / anti-EGFR, n (%)	Bevacizumab	44 (88)
	Cetuximab	13 (26)
	Both	10 (20)

Data cutoff: Sep 3, 2024; median follow-up: 17.6 months

*Earlier data cut (Jan 10, 2024; median follow-up: 15.5 months) presented at ASCO 2024 – see Fruquintinib 2024 Post-Congress Reactive Deck for additional information;
[†]Unknown in 12 (24%) patients; [‡]One patient was *RAS* WT and *BRAF* mutant

3L+, third- or later-line; BID, twice daily; D#, Day #; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; FRUQ, fruquintinib; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria In Solid Tumors; VEGF(R), vascular endothelial growth factor (receptor); WT, wild type

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NCT05004831: Phase 2 study of fruquintinib + TAS-102 as 3L+ therapy in mCRC (2/2)*

ASCO GI 2025
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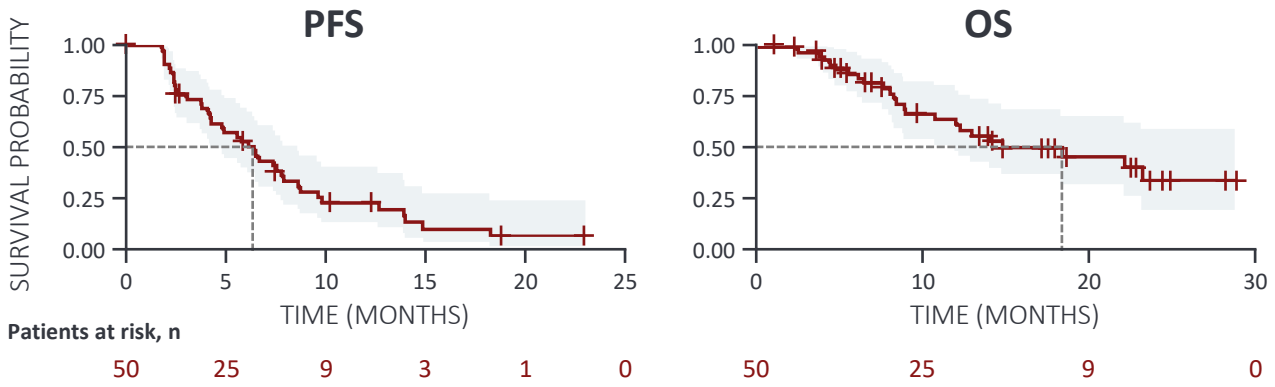
(IIR)

Efficacy results



SURVIVAL	FRUQ + TAS-102 (N=50)			
	MEDIAN (95% CI), MO	6-MO (95% CI), %	9-MO (95% CI), %	12-MO (95% CI), %
PFS	6.33 (4.20, 8.62)	53.0 (40.2, 70.0)	28.3 (17.4, 45.9)	23.1 (13.2, 40.5)
OS	18.4 (12.0, NA)	87.0 (77.8, 97.3)	66.9 (54.0, 82.9)	64.3 (51.1, 80.8)

PFS BASED ON METASTATIC SITE	n	MEDIAN PFS (95% CI), MO	P-VALUE
Liver metastasis	30	6.33 (4.13, 8.62)	0.54
Non-liver metastasis	20	6.46 (3.74, NA)	
Peritoneal metastasis	9	6.07 (3.74, NA)	0.95
Non-peritoneal metastasis	41	6.33 (4.20, 8.27)	

Safety results

TRAE, n (%)	FRUQ + TAS-102 (N=50)	
	ANY GRADE	GRADE 3/4
Neutrophil count decreased	40 (80)	27 (54)
WBC count decreased	35 (70)	13 (26)
Anemia	29 (58)	10 (20)
Proteinuria	25 (50)	2 (4)
Platelet count decreased	22 (44)	5 (10)
Lymphocyte count decreased	20 (40)	4 (8)
TSH increased	16 (32)	0
Hypoalbuminemia	15 (30)	1 (2)
Blood bilirubin increased	13 (26)	6 (12)
Hypertriglyceridemia	11 (22)	2 (4)
Loss of appetite	11 (22)	0
Cholesterol high	9 (18)	0
Elevated AST or ALT	7 (14)	0
Fatigue	7 (14)	0
Abdominal pain	6 (12)	0
Diarrhea	6 (12)	0
Vomiting	5 (10)	0
Headache	5 (10)	0
Hypertension	5 (10)	1 (2)
Nausea	5 (10)	0

Data cutoff: Sep 3, 2024; median follow-up: 17.6 months

*Earlier data cut (Jan 10, 2024; median follow-up: 15.5 months), including tumor response results presented at ASCO 2024 – see Fruquintinib 2024 Post-Congress Reactive Deck for additional information;

3L+, third- or later-line; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; FRUQ, fruquintinib; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; mo, months; NA, not applicable; OS, overall survival; PFS, progression-free survival; TRAE, treatment-related adverse event; TSH, thyroid-stimulating hormone; WBC, white blood cell

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NCT05634590: Phase 2 study of fruquintinib + FOLFIRI/mFOLFOX6 as 2L therapy in *RAS*-mutant mCRC (1/2)

ASCO GI 2025
Abstract 151 | Poster F12
(IIR)

Study design

Open-label, single-arm, multicenter, Phase 2 study (NCT05634590); study is ongoing

PATIENT ELIGIBILITY

- Unresectable locally advanced or metastatic CRC
- Aged ≥18 years
- ECOG PS 0 or 1
- ≥1 measurable lesion (RECIST v1.1)
- *RAS* mutation
- Failed 1L standard chemotherapy

→ **Fruquintinib:** 4 mg QD, PO, D1–21, Q4W + **FOLFIRI/mFOLFOX6* (ChT):** Q4W → **Until disease progression or intolerable toxicity**

Primary endpoint: PFS

Secondary endpoints: ORR, DCR, OS, safety

Baseline characteristics

CHARACTERISTIC		FRUQ + ChT (N=25)
Age, years	Median (range)	66 (35–73)
	<65, n (%)	12 (48)
	≥65, n (%)	13 (52)
Sex, n (%)	Male	11 (44)
	Female	14 (56)
ECOG PS, n (%)	0	8 (32)
	1	17 (68)
Primary tumor site, n (%)	Left	18 (72)
	Right	7 (28)
Metastatic sites, n (%)	1 or 2	18 (72)
	≥3	7 (28)
Liver metastases, n (%)	Yes	16 (64)
	No	9 (36)
Prior therapy, n (%)	Surgery	22 (88)
	Chemotherapy	25 (100)
	VEGF inhibitor	19 (76)

Data cutoff: Aug 30, 2024; median follow-up: not reported

*FOLFIRI: Irinotecan 180 mg/m^2 IV.gtt D1, D15; folinic acid 400 mg/m^2 D1, D15; 5-fluorouracil 400 mg/m^2 D1, D15, Q4W; mFOLFOX6: Oxaliplatin 85 mg/m^2 IV.gtt D1, D15; folinic acid 400 mg/m^2 D1, D15; 5-fluorouracil 400 mg/m^2 D1, D15, Q4W

1/2L, first-/second-line; ChT, chemotherapy; D#, Day #; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; FOLFIRI, folinic acid (leucovorin) + 5-fluorouracil + irinotecan; IIR, investigator-initiated research; IV.gtt, intravenous drip; (m)CRC, (metastatic) colorectal cancer; mFOLFOX6, modified regimen of folinic acid (leucovorin) + 5-fluorouracil + oxaliplatin; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria In Solid Tumors; VEGF, vascular endothelial growth factor

Xu Y, et al. ASCO GI 2025 [poster #F12]: see the abstract

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NCT05634590: Phase 2 study of fruquintinib + FOLFIRI/mFOLFOX6 as 2L therapy in *RAS*-mutant mCRC (2/2)

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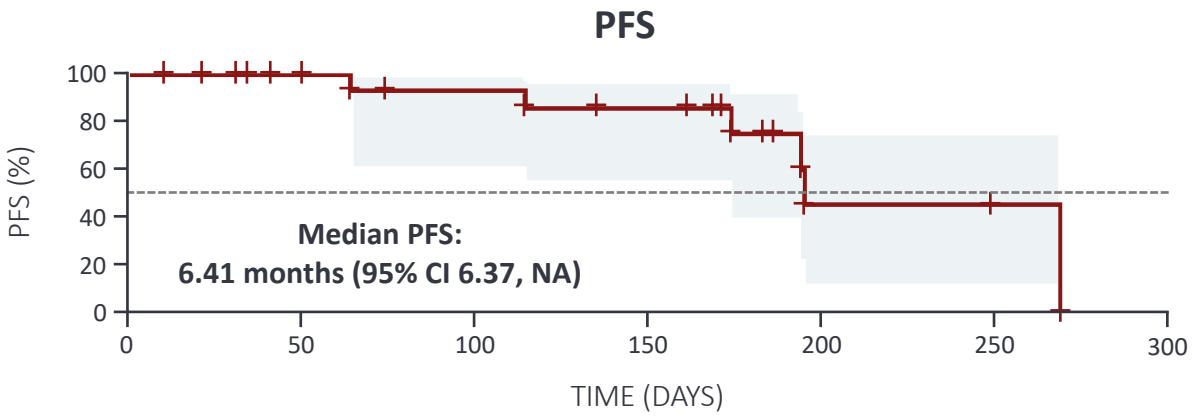
(IIR)

Efficacy results*



PFS BY PRESENCE OF LIVER METS	NO LIVER METS (n=7)	LIVER METS (n=7)
Median PFS, months	8.84	6.41
HR (95% CI); p-value	1.230 (0.2462, 6.148); p=0.7775	

TUMOR RESPONSE	ALL (n=14)	NO LIVER METS (n=7)	LIVER METS (n=7)
BOR, n (%)			
PR	5 (35.7)	3 (42.9)	2 (28.6)
SD	9 (64.3)	4 (57.1)	5 (71.4)
ORR, %	35.7	42.9	28.6
DCR, %	100	100	100

Safety results

TEAE, n (%)	FRUQ + ChT (n=22)	
	ANY GRADE	GRADE ≥3
Neutrophil count decreased	9 (40.9)	2 (9.1)
Hypoalbuminemia	9 (40.9)	0
Platelet count decreased	9 (40.9)	4 (18.2)
Hypertension	9 (40.9)	2 (9.1)
WBC count decreased	7 (31.8)	0
Hematuria	6 (27.3)	0
Fatigue	6 (27.3)	1 (4.5)
Oral mucositis	6 (27.3)	2 (9.1)
PPE	6 (27.3)	2 (9.1)
Diarrhea	6 (27.3)	1 (4.5)
AST increased	5 (22.7)	0
ALT increased	4 (18.2)	0
Bilirubin increased	4 (18.2)	0
Abdominal pain	4 (18.2)	0

Data cutoff: Aug 30, 2024; median follow-up: not reported. *Median OS was not reached

2L, second-line; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BOR, best overall response; ChT, chemotherapy; CI, confidence interval; DCR, disease control rate; FOLFIRI, folinic acid (leucovorin) + 5-fluorouracil + irinotecan; FRUQ, fruquintinib; HR, hazard ratio; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; mets, metastasis; mFOLFOX6, modified regimen of folinic acid (leucovorin) + 5-fluorouracil + oxaliplatin; NA, not applicable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PPE, palmar–plantar erythrodysesthesia; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event; WBC, white blood cell

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NCT05659290: Fruquintinib alternating with bevacizumab + capecitabine as maintenance after 1L therapy in mCRC (1/2)

ASCO GI 2025
Abstract 166 | Poster G4
(IIR)

Study design

Open-label, multicenter, Phase 2 study (NCT05659290); study is ongoing

PATIENT ELIGIBILITY

- Histologically confirmed mCRC
- Aged ≥18 years
- ECOG PS 0–2
- Previously received 1L bevacizumab combined with standard chemotherapy and achieved disease control (including CR, PR, and SD)

Part 1: Safety lead-in Phase 2a (N=20)

FRUQ: 5 mg QD, PO, D1–14, Q3W
Alternating
BEV: 7.5 mg/kg IV.gtt, D1, Q3W
+ CAPE: 850 mg/m^2 BID, PO, D1–14, Q3W

Part 2: Expansion Phase 2b (N=40)

R 1:1

FRUQ: RP2D, 3 mg
Alternating
BEV: 7.5 mg/kg IV.gtt, D1, Q3W
+ CAPE: 850 mg/m^2 BID, PO, D1–14, Q3W

BEV: 7.5 mg/kg IV, D1, Q3W
+
CAPE: 850 mg/m^2 BID, PO, D1–14, Q3W

Primary endpoints: RP2D, PFS

Secondary endpoints: ORR, DCR, OS, adverse events

Baseline characteristics

CHARACTERISTIC		FRUQ ALT WITH BEV + CAPE (N=20)
Age, years	Median (range)	59 (27–75)
	<65, n (%)	14 (70)
	≥65, n (%)	6 (30)
Sex, n (%)	Male	14 (70)
	Female	6 (30)
ECOG PS, n (%)	0	1 (5)
	1	19 (95)
Primary tumor site, n (%)	Left	14 (70)
	Right	6 (30)
Liver metastases, n (%)	Yes	11 (55)
Prior therapy, n (%)	Surgery	10 (50)
	VEGF inhibitor	20 (100)
Cycles of 1L therapy	Median (range)	8 (6–12)
PR in 1L (going into maintenance), n (%)		10 (50)

Data cutoff: Sep 5, 2024; median follow-up: not reported

1L, first-line; ALT, alternating; BEV, bevacizumab; BID, twice daily; CAPE, capecitabine; CR, complete response; D#, Day #; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; IIR, investigator-initiated research; IV.gtt, intravenous drip; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; PR, partial response; Q3W, every 3 weeks; QD, once daily; R, randomization; RP2D, recommended phase 2 dose; SD, stable disease; VEGF, vascular endothelial growth factor

Liao W, et al. ASCO GI 2025 [poster #G4]: see the abstract

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NCT05659290: Fruquintinib alternating with bevacizumab + capecitabine as maintenance after 1L therapy in mCRC (2/2)

ASCO GI 2025
Abstract 166 | Poster G4
(IIR)

Efficacy results

TUMOR RESPONSE	FRUQ ALTERNATING WITH BEV + CAPE (n=11)*
DCR, %	100

**PFS data were immature;
however, four patients had a median PFS that exceeded 8 months
(8.3, 8.6, 9.2, 13.4 months)**

**Following the safety lead-in,
the dose of fruquintinib was adjusted to 3 mg
for the Phase 2b dose expansion study**

Safety results

TEAE, n (%)	FRUQ ALTERNATING WITH BEV + CAPE (N=20)	
	ANY GRADE	GRADE ≥3
Proteinuria	12 (60)	1 (5)
Hypoalbuminemia	8 (40)	0
Hypertension	7 (35)	2 (10)
Hyperuricemia	6 (30)	0
Pain	6 (30)	0
Neutrophil count decreased	5 (25)	0
Fatigue	5 (25)	0
Platelet count decreased	5 (25)	1 (5)
PPE	4 (20)	0
Anemia	3 (15)	1 (5)
WBC count decreased	3 (15)	0
Hematochezia	3 (15)	0
AST increased	2 (10)	0
Bilirubin increased	2 (10)	0
Rash	2 (10)	0
Dysphonia	2 (10)	0
Oral mucositis	1 (5)	0
Urinary tract infection	1 (5)	0
Diarrhea	1 (5)	0
Appetite decreased	1 (5)	0
Musculoskeletal pain	1 (5)	0
Edema	1 (5)	1 (5)

Data cut off: Sep 5, 2024; median follow-up: not reported

*Among all patients, 11 had ≥1 tumor assessment

1L, first-line; AST, aspartate aminotransferase; BEV, bevacizumab; CAPE, capecitabine; DCR, disease control rate; FRUQ, fruquintinib; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; PFS, progression-free survival; PPE, palmar–plantar erythrodysesthesia; TEAE, treatment-emergent adverse event; WBC, white blood cell

Liao W, et al. ASCO GI 2025 [poster #G4]: see the abstract

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Multicohort study of treatment regimens for mCRC: Sequencing subgroup analysis between fruquintinib and regorafenib (1/2)

AACR 2025
Poster CT085
(IIR)

Study design

Open-label, multicohort study; study is ongoing

PATIENT ELIGIBILITY

- Aged ≥18 years
- Histologically confirmed mCRC
- ECOG PS 0 or 1
- Previously received ≥2 lines of standard chemotherapy

N=53

Fruquintinib → Regorafenib (F → R) n=35

Regorafenib → Fruquintinib (R → F) n=18

Primary endpoint: median OS

Secondary endpoints: median PFS and safety

Baseline characteristics

CHARACTERISTIC		OVERALL (N=53)	F → R (n=35)	R → F (n=18)	P
Age, years	Median (range)	58 (32–78)	56 (32–78)	60.5 (39–71)	0.985
	<65, n (%)	36 (68)	24 (69)	12 (67)	1.000
	≥65, n (%)	17 (32)	11 (31)	6 (33)	
Sex, n (%)	Female	17 (32)	11 (31)	6 (33)	1.000
	Male	36 (68)	24 (69)	12 (67)	
RAS status, n (%)	Mutation	20 (38)	13 (37)	7 (39)	1.000
	Wild type	33 (62)	22 (63)	11 (61)	
BRAF status, n (%)	Wild type	53 (100)	35 (100)	18 (100)	NA
Primary disease site, n (%)	Colon	24 (45)	13 (37)	11 (61)	0.171
	Rectum	29 (55)	22 (63)	7 (39)	
Lung metastasis, n (%)	No	23 (43)	16 (46)	7 (39)	0.855
	Yes	30 (57)	19 (54)	11 (61)	
Liver metastasis, n (%)	No	15 (28)	10 (29)	5 (28)	1.000
	Yes	38 (72)	25 (71)	13 (72)	
Metastatic sites, n (%)	Single	13 (25)	8 (23)	5 (28)	0.954
	Multiple	40 (75)	27 (77)	13 (72)	
Prior bevacizumab, n (%)	No	13 (25)	7 (20)	6 (33)	0.465
	Yes	40 (75)	28 (80)	12 (67)	
Received study drug (F or R) as part of combination therapy, n (%)		28 (53)	17 (49)	11 (61)	NA
Received first study drug (F or R) as 3L therapy, n (%)		49 (92)	34 (97)	15 (83)	NA

Data cutoff: Mar 1, 2025; median follow-up: not reported

3L, third-line; ECOG PS, Eastern Cooperative Oncology Group performance status; F, fruquintinib; F → R, sequential treatment with fruquintinib then regorafenib; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; NA, not applicable; OS, overall survival; PFS, progression-free survival; R, regorafenib; R → F, sequential treatment with regorafenib then fruquintinib

ALv W, et al. AACR 2025 [poster #CT085]: see the abstract

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Multicohort study of treatment regimens for mCRC: Sequencing subgroup analysis between fruquintinib and regorafenib (2/2)

AACR 2025
Poster CT085
(IIR)

Efficacy results

ALL PATIENTS	F → R (n=35)	R → F (n=18)
mOS, months	21.2	15.8
	p=0.587*	
mPFS, months	4.4†	3.7†
	p=0.14	
ORR, %	11.43	0
DCR, %	82.86	11.11

COMBINATION THERAPY SUBGROUP	F → R F COMBO (n=17)	R → F R COMBO (n=11)
mOS, months	23.6	12.3
	p=0.167*	
mPFS, months	7.3†	3.7†
	p=0.035	

3L-TREATMENT SUBGROUP	F → R FRUQ as 3L (n=34)	R → F REG as 3L (n=15)
mOS, months	21.2	17.7
	p=0.571*	

OS SUBGROUP ANALYSIS		F → R (n=35) EVENTS, n/N	F → R (n=35) mOS, MONTHS (95% CI)	R → F (n=18) EVENTS, n/N	R → F (n=18) mOS, MONTHS (95% CI)	FAVORS	HR‡ (95% CI)
All patients		**20/35**	**21.2 (11.7, NE)**	**13/18**	**15.8 (12.3, 24.9)**	F→R	**0.819 (0.407, 1.650)**
Age	<65	14/24	23.6 (10.7, NE)	9/12	13.4 (7.1, 24.9)	F→R	0.629 (0.268, 1.475)
	≥65	6/11	16.5 (5.0, NE)	4/6	20.2 (9.4, NE)	R→F	1.378 (0.343, 5.538)
Sex	Female	8/11	14.2 (8.0, NE)	4/6	20.2 (8.6, NE)	R→F	1.475 (0.442, 4.921)
	Male	12/24	26.3 (11.7, NE)	9/12	12.6 (7.1, 24.9)	F→R	0.620 (0.260, 1.479)
RAS status	Mutation	9/13	14.2 (8.3, 26.3)	6/7	12.9 (8.6, 19.1)	F→R	0.728 (0.251, 2.114)
	WT	11/22	23.6 (11.7, NE)	7/11	22.7 (7.1, NE)	F→R	0.905 (0.347, 2.359)
Primary site	Colon	8/13	21.2 (10.2, NE)	7/11	22.7 (8.6, NE)	R→F	1.072 (0.387, 2.970)
	Rectum	12/22	26.3 (10.7, NE)	6/7	12.9 (3.2, NE)	F→R	0.471 (0.169, 1.315)
Lung mets	No	10/16	13.3 (10.7, NE)	5/7	12.3 (7.1, NE)	R→F	1.015 (0.335, 3.082)
	Yes	10/19	26.3 (8.1, NE)	8/11	17.7 (9.4, NE)	F→R	0.649 (0.253, 1.661)
Liver mets	No	5/10	20.9 (10.6, NE)	3/5	22.7 (12.3, NE)	R→F	1.213 (0.267, 5.506)
	Yes	15/25	21.2 (10.7, NE)	10/13	13.9 (8.6, 24.9)	F→R	0.655 (0.290, 1.483)
Met sites	Single	4/8	10.7 (8.3, NE)	3/5	12.3 (8.6, NE)	F→R	0.964 (0.215, 4.330)
	Multiple	16/27	21.2 (11.7, NE)	10/13	17.7 (9.4, 24.9)	F→R	0.659 (0.295, 1.472)
Prior BEV	No	3/7	26.3 (10.7, NE)	5/6	18.3 (12.3, NE)	F→R	0.421 (0.099, 1.795)
	Yes	17/28	20.9 (10.7, NE)	8/12	15.0 (7.1, NE)	F→R	0.900 (0.387, 2.094)

No safety results were reported by the authors

Data cutoff: Mar 1, 2025; median follow-up: not reported

*Log-rank; †PFS analysis of fruquintinib vs regorafenib performed before sequential treatment; ‡HR of <1 favors F→R, HR of >1 favors R→F

3L, third-line; BEV, bevacizumab; CI, confidence interval; DCR, disease control rate; F/FRUQ, fruquintinib; F → R, sequential treatment with fruquintinib then regorafenib; HR, hazard ratio; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; met, metastasis; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/REG, regorafenib; R → F, sequential treatment with regorafenib then fruquintinib; WT, wild type

Lv W, et al. AACR 2025 [poster CT085]: see the abstract

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Additional fruquintinib data

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Additional fruquintinib data (1 of 4)

#	TITLE	CONGRESS	ABSTRACT	1ST AUTHOR	STUDY*	TRIAL ID	ADD'L INFO
Colorectal cancer (CRC)							
1	VEGFR-TKIs + PD-1 inhibitors as 3L+ treatment in patients with MSS mCRC: A retrospective study	ASCO GI 2025	Abs: 68 Poster: C5	X. Li	HM IIR	NA	NA
2	SCRT followed by fruquintinib + adebrelimab + CAPOX in the total neoadjuvant therapy of LARC: A multicenter, single-arm, open-label, Phase 2 study	ASCO GI 2025	Abs: 192 Poster: H4	Z. Lin	HM IIR	NCT06234007 (UNION TNT)	Earlier data at ASCO 24
3	Phase 1b/2 study of fruquintinib + 5-fluorouracil/leucovorin after progression on fruquintinib monotherapy in mCRC	ASCO GI 2025	Abs: 128 Poster: E14	W. Yang	NA	ChiCTR2000032640	Funding from Eli Lilly
4	Exploratory study of TAS-102 combined with intermittent administration of fruquintinib in the treatment of 3L mCRC	ASCO GI 2025	Abs: 174 Poster: G12	J. Niu	NA	ChiCTR2300078241	Not associated with TAK or HM
5	Meta-analysis of RCTs to evaluate the incidence of hemorrhage and VTE events in patients with GI cancers treated with fruquintinib	ASCO GI 2025	Abs: 118 Poster: E5	D. Jones	NA	NA	Not associated with TAK or HM
6	Meta-analysis of Phase 2/3 RCTs to determine the incidence of hypertension and proteinuria in patients with GI cancers treated with fruquintinib	ASCO GI 2025	Abs: 119 Poster: E6	R. Srinivasmurthy	NA	NA	Not associated with TAK or HM
7	Meta-analysis of Phase 2/3 RCTs to evaluate the incidence of HFSR/PPE in patients with GI cancers treated with fruquintinib	ASCO GI 2025	Abs: 117 Poster: E4	R. Nanda	NA	NA	Not associated with TAK or HM
8	Phase 1b/2 study of fruquintinib + capecitabine as maintenance therapy for *RAS/BRAF* wild-type mCRC after 1L treatment with cetuximab + chemotherapy	AACR 2025	Abs: CT222	K. Ou	HM IIR	NCT05016869	Poster
9	TKI + PD-1 blockade in TKI-responsive MSS/pMMR mCRC: Results of a multicenter Phase 2 trial	AACR 2025	Abs: 6002	J. Zhang	HM IIR	NCT04483219 (TRAP)	Poster
10	Efficacy and mechanism of radiotherapy + fruquintinib + tirelizumab in mCRC	AACR 2025	Abs: 1828	M. Zhang	HM IIR	NA	Poster
11	An observational/translational study to conduct real-world evidence and develop biomarkers of fruquintinib for patients with mCRC: FruBLOOM trial (JACCRO CC-19)	ASCO 2025	Abs: TPS3637 Poster: 304a	Y. Sunakawa	TAK IIR-JP	UMIN000056813	Trial in progress; no data presented
12	Final analysis of a multicenter, open-label, Phase 2 study evaluating the efficacy and safety of tislelizumab + fruquintinib in patients with selected solid tumors	ASCO 2025	Abs: 2604 Poster: 251	K-W. Lee	BeOne CS	NCT04716634	Similar to HALO
13	Safety of fruquintinib in young and late-elderly Chinese patients with CRC in real-world clinical practice: Age subgroup analysis of a fruquintinib Phase 4 study	ASCO 2025	Abs: e15512	Y. Wang	HM CS	NCT04005066	Epub only

Note: abstracts and trial IDs are hyperlinked

*Company associations are specified if known. Takeda has no current involvement with any HM IIR studies with fruquintinib in China and/or studies included here unless explicitly stated; those publications were developed independent of Takeda

#L(+), #- (or later-) line; AACR, American Association for Clinical Research; ASCO (GI), American Society of Clinical Oncology (Gastrointestinal Cancers); CAPOX, capecitabine + oxaliplatin; CS, company sponsored; GI, gastrointestinal; HFSR/PPE, hand–foot skin reaction/palmar–plantar erythrodysesthesia; HM, HUTCHMED; IIR, investigator-initiated research; JP, Japan; LARC, locally advanced rectal cancer; (m)CRC, (metastatic) colorectal cancer; MSS/pMMR, microsatellite stable/proficient mismatch repair; NA, not applicable; PD-1, programmed death receptor-1; RCT, randomized controlled trial; SCRT, short-course radiotherapy; TAK, Takeda; TKI, tyrosine kinase inhibitor; VEGFR, vascular endothelial growth factor receptor; VTE, venous thromboembolism

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Additional fruquintinib data (2 of 4)

#	TITLE	CONGRESS	ABSTRACT	1ST AUTHOR	STUDY*	TRIAL ID	ADD'L INFO
Colorectal cancer (CRC)							
14	Safety of fruquintinib monotherapy and combination therapy in Chinese patients with CRC in real-world clinical practice: A subgroup analysis from Phase 4 study	ASCO 2025	Abs: e15515	Z. Wang	HM CS	NCT04005066	Epub only
15	Real-world observational study of fruquintinib + irinotecan + capecitabine as 2L treatment in patients with advanced CRC	ASCO 2025	Abs: e15539	L. Xu	HM IIR	NCT06169202	Epub only
16	Evaluating the efficacy of fruquintinib vs regorafenib and trifluridine/tipiracil in treating advanced mCRC: A match-adjusted indirect comparison	ASCO 2025	Abs: e15550	S. Qin	HM IIR	NA	Epub only
17	Preliminary results of fruquintinib + FOLFIRI as 2L treatment for *RAS*-mutant mCRC: A prospective, single-center Phase 2 study	ASCO 2025	Abs: e15541	R. Jia	HM IIR	NCT05522738	Epub only
18	Disitamab vedotin + fruquintinib in patients with *HER2*-expressing or *HER2*-mutation/ amplified mCRC refractory to ≥2 standard regimens: A prospective, exploratory, single-arm study	ASCO 2025	Abs: e15562	F. Zhou	NA	NCT05661357	Epub only
19	A multicohort real-world study of treatment for mCRC: Overall efficacy analysis and subgroup analysis of previous bevacizumab use or not	ASCO 2025	Abs: e15530	W. Lv	HM IIR	NA	Epub only
20	Real-world experience of fruquintinib in patients with mCRC: A single-center retrospective study in the United States	ASCO 2025	Abs: e15613	N. Suleman	NA	NA	Epub only
21	Real-world evidence of fruquintinib efficacy after regorafenib and trifluridine–tipiracil in refractory mCRC	ASCO 2025	Abs: e23317	O. Abidoye	NA	NA	Epub only
22	Navigating 3L therapies: A comprehensive review of regorafenib vs fruquintinib with placebo comparator for mCRC—A systematic review and meta-analysis	ASCO 2025	Abs: e15514	A. Khan	NA	NA	Epub only
23	Overall survival based on sequencing of fruquintinib, regorafenib, and TAS-102 ± bevacizumab in treatment-refractory mCRC	ASCO 2025	Abs: e15527	J. Bauernfeind	NA	NA	Epub only
24	Cardiovascular toxicity of fruquintinib in patients with colorectal and other cancers: A systematic review and meta-analysis	ASCO 2025	Abs: e15520	O. Hamadi	NA	NA	Epub only
25	Toxicity profile of fruquintinib vs regorafenib in refractory mCRC	ASCO 2025	Abs: e15608	Y. Hamadneh	NA	NA	Epub only
26	Real-world data from fruquintinib in later-line metastatic colorectal cancer	ESMO GI 2025	Abs: 66P	F. Verdasca	NA	NA	Poster; not associated with TAK or HM

Note: abstracts and trial IDs are hyperlinked

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2L, second-line; 3L, third-line; ASCO, American Society of Clinical Oncology; CS, company sponsored; ESMO GI, European Society for Medical Oncology Gastrointestinal Cancers; FOLFIRI, folinic acid (leucovorin) + 5-fluorouracil + irinotecan; HM, HUTCHMED; IIR, investigator-initiated research; (m)CRC, (metastatic) colorectal cancer; NA, not applicable; PD-1, programmed cell death protein 1; TAK, Takeda

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Additional fruquintinib data (3 of 4)

#	TITLE	CONGRESS	ABSTRACT	1ST AUTHOR	STUDY*	TRIAL ID	ADD'L INFO
Gastric cancer/gastroesophageal junction cancer (GC/GEJC)							
1	PD-1 inhibitor (sintilimab) + fruquintinib + SOX as conversion therapy for initially unresectable GC/GEJC: Updated results from a single-arm, Phase 2 clinical trial	ASCO GI 2025	Abs: 406 Poster: D20	F. Ma	HM IIR	NCT05177068 HMPL-013-FLAG-G103	Earlier data at ASCO 24
2	Fruquintinib + sintilimab and SOX as conversion therapy for initially unresectable GC/GEJC: Updated response and surgical results from a single-arm, Phase 2 clinical trial	ASCO 2025	Abs: e16016	F. Ma	HM IIR	NCT05177068	Epub only; earlier data at ASCO GI 25
3	A Phase 2 study of fruquintinib + sintilimab as a 2L therapy for advanced GC/GEJC: Updated results	ASCO GI 2025	Abs: 407 Poster: D21	M. Jin	HM IIR	NCT05625737 HMPL-013-CC-GC003	Earlier data at ASCO GI 24
4	Updated results from the Phase 1b/2 study of fruquintinib + SOX + toripalimab in patients with advanced metastatic GC/GEJC	ASCO GI 2025	Abs: 423 Poster: E13	X. Meng	HM IIR	NCT05024812 HMPL-013-FLAG-G102	Earlier data at ASCO GI 24
5	Fruquintinib + PD-1 inhibitors + chemotherapy in the 1L treatment of *HER2*– advanced GC/GEJC: A single-arm, open-label Phase 2 study	ASCO GI 2025	Abs: 461 Poster: G2	C. Wang	HM IIR	NCT06158919 FDZL-FIX	First results for IIR
6	Updated results of fruquintinib + PD-1 inhibitors + chemotherapy in the 1L treatment of *HER2*– advanced GC/GEJC (FDZL-FIX): A single-arm, open-label Phase 2 study	ASCO 2025	Abs: 4046 Poster: 336	C. Wang	HM IIR	NCT06158919 FDZL-FIX	Earlier data at ASCO GI 25
7	Open-label, single-arm, single-center Phase 1b/2 clinical study of fruquintinib + trastuzumab + XELOX in the 1L treatment of *HER2*+ metastatic GC/GEJC	ASCO 2025	Abs: TPS4203 Poster: 492a	H. Lv	HM IIR	ChiCTR2300074767	Trial in progress; no data presented
8	Subgroup analysis of efficacy and safety of fruquintinib + paclitaxel vs paclitaxel in GEJC patients from FRUTIGA: A randomized Phase 3 clinical trial in 2L treatment of GC/GEJC	ASCO 2025	Abs: e16012	T. Liu	HM CS	NCT03223376 FRUTIGA	Epub only
9	The appropriate therapeutic sequence with angiogenesis inhibitor and chemotherapy in patients with advanced GC/GEJC: Exploratory analysis from the Phase 3 FRUTIGA study	ASCO 2025	Abs: e16011	J. Li	HM CS	NCT03223376 FRUTIGA	Epub only

Note: abstracts and trial IDs are hyperlinked

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1L, first-line; 2L, second-line; ASCO (GI), American Society of Clinical Oncology (Gastrointestinal Cancers); CS, company sponsored; GC/GEJC, gastric cancer/gastroesophageal junction cancer; HM, HUTCHMED; IIR, investigator-initiated research; NA, not applicable; PD-1, programmed cell death protein 1; SOX, S-1 + oxaliplatin; TAK, Takeda; XELOX, capecitabine + oxaliplatin

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Additional fruquintinib data (4 of 4)

#	TITLE	CONGRESS	ABSTRACT	1ST AUTHOR	STUDY*	TRIAL ID	ADD'L INFO
Esophageal squamous cell carcinoma (ESCC)							
1	Fruquintinib + camrelizumab + paclitaxel liposome and nedaplatin as 1L treatment for advanced ESCC: A single-arm, Phase 2 clinical trial	ASCO GI 2025	Abs: 445 Poster: F10	Y. Gu	HM IIR	NCT06010212 2022-013-CH11 IIT-ESCC	First results for IIR
2	Fruquintinib + camrelizumab + paclitaxel liposome and nedaplatin as 1L treatment for advanced ESCC: A single-arm, Phase 2 study	ASCO 2025	Abs: 4042 Poster: 332	Y. Gu	HM IIR	NCT06010212 2022-013-CH11 IIT-ESCC	Earlier data at ASCO GI 25
Endometrial cancer (EMC)							
1	Analysis of serous carcinoma subgroup in FRUSICA-1: Fruquintinib + sintilimab in treated advanced EMC patients with pMMR status	ASCO 2025	Abs: 5596 Poster: 494	X. Wu	HM CS	NCT03903705 FRUSICA-1	NA
2	The impact of prior neoadjuvant/adjuvant chemotherapy on fruquintinib + sintilimab outcomes in advanced EMC patients with pMMR status: A subgroup analysis of FRUSICA-1	ASCO 2025	Abs: 5611 Poster: 509	J. Wang	HM CS	NCT03903705 FRUSICA-1	NA
Sarcomas							
1	A Phase 2 study to evaluate the efficacy and safety of fruquintinib + envafolimab in patients with advanced or unresectable locally advanced osteosarcoma and soft tissue sarcoma	ASCO 2025	Abs: e23506	C. Zhou	HM IIR	NCT05941325	Epub only

Note: abstracts and trial IDs are hyperlinked

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1L, first-line; ASCO (GI), American Society of Clinical Oncology (Gastrointestinal Cancers); CS, company sponsored; EMC, endometrial cancer; ESCC, esophageal squamous cell carcinoma; HM, HUTCHMED; IIR, investigator-initiated research; NA, not applicable; pMMR, proficient mismatch repair

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