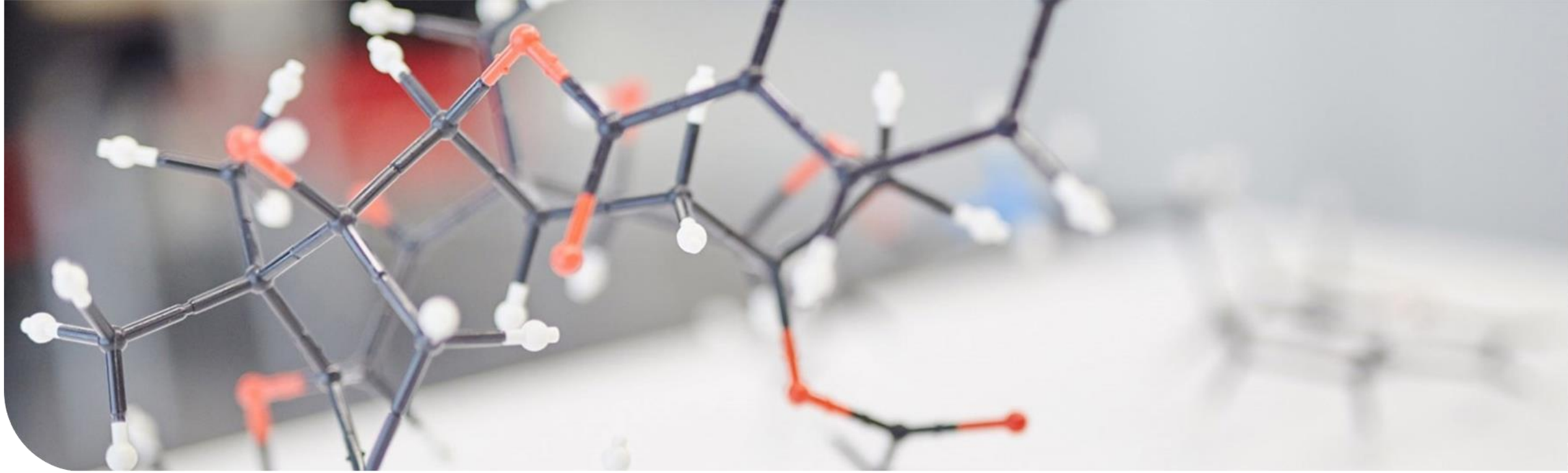


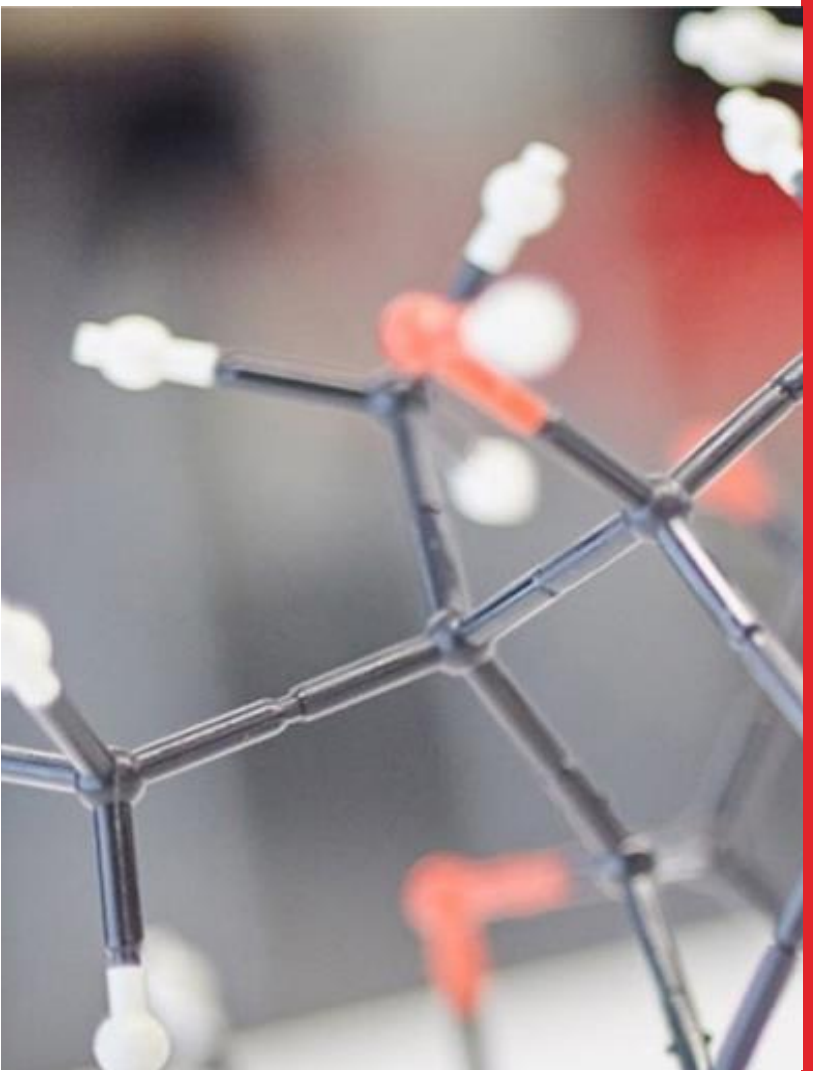
Fruquintinib 2024
Post-Congress Reactive Deck

February 2024

VV-MEDMAT-100929

ONCOLOGY

Contents



Company-sponsored research

1 Q-TWiST analysis of fruquintinib + BSC compared with placebo + BSC in mCRC: Results from the FRESCO-2 trial — ASCO GI 2024. Stintzing S, et al

Investigator-initiated research

2 Retrospective cohort study to evaluate fruquintinib plus PD-1 inhibitors vs TAS-102 plus bevacizumab in late-line mCRC* — ASCO GI 2024. Li R, et al

3 Initial efficacy evaluation of fruquintinib plus capecitabine vs capecitabine as maintenance treatment for mCRC* — ASCO GI 2024. Li W, et al

4 Preliminary efficacy and safety of fruquintinib as maintenance therapy after first-line treatment in mCRC (the FRONT study)* — ASCO GI 2024. Xu X, et al

5 Additional fruquintinib data — Click here

*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

BSC, best supportive care; mCRC, metastatic colorectal cancer; PD-1, programmed cell death protein 1; Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity

Company-sponsored research

ASCO GI 2024
Abstract 116

Quality-adjusted Time Without Symptoms of disease or Toxicity (Q-TWiST) analysis of fruquintinib + best supportive care (BSC) compared with placebo + BSC in metastatic colorectal cancer (mCRC): Results from the FRESCO-2 trial

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Introduction

Fruquintinib, a selective, oral inhibitor of all three VEGF receptors (VEGFR-1, -2, and -3),[1] was approved in China in 2018 as third- or later-line of therapy for mCRC, based on the results from the Phase 3 FRESCO study (NCT02314819)[2]

The global, Phase 3 FRESCO-2 study (NCT04322539) investigated the efficacy and safety of fruquintinib + BSC in a population that better reflected patient characteristics and current treatment practices outside of China[3]

- Patients enrolled in FRESCO-2 had received all standard cytotoxic and targeted therapies and had progressed on, or were intolerant to, TAS-102 or regorafenib, or both[3]
- Fruquintinib + BSC improved median OS by 2.6 months vs placebo + BSC (7.4 vs 4.8 months; HR 0.66; 95% CI 0.55, 0.80; p<0.001)[3]
- Fruquintinib + BSC demonstrated a manageable safety profile without negatively impacting QOL compared with the placebo arm[3,4]

Based on the results from FRESCO and FRESCO-2, fruquintinib was approved by the FDA for previously treated mCRC, regardless of biomarker status[3,5]

As mCRC and its treatment can adversely impact QOL, maintaining QOL is an important treatment goal in addition to improving survival outcomes, particularly as patients progress through lines of therapy

Q-TWiST measures the quality of patients' survival by assessing the proportion of survival time that is free of symptoms or toxicity; it can be used to inform clinical decision-making by integrating patient preferences with clinical data. It is a quality-adjusted life-year metric that can be used in oncology treatment assessment as a proxy for patient QOL that is typically assessed through patient-reported outcomes[1]

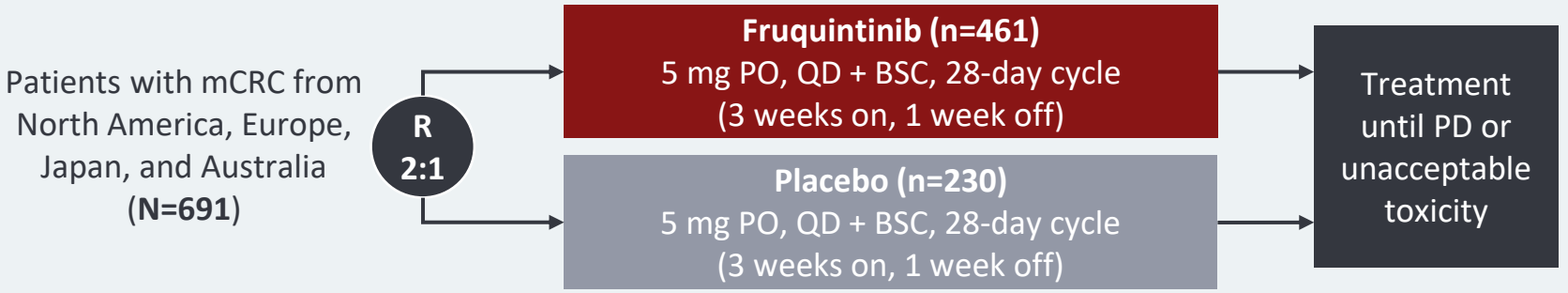
- Q-TWiST analysis of the FRESCO study demonstrated that fruquintinib + BSC provided a clinically meaningful quality-adjusted survival benefit vs placebo + BSC in Chinese patients[2]

BSC, best supportive care; CI, confidence interval; FDA, US Food and Drug Administration; HR, hazard ratio; mCRC, metastatic colorectal cancer; OS, overall survival; Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity; QOL, quality of life; VEGF(R), vascular endothelial growth factor (receptor)

1. Sun Q, et al. Cancer Biol Ther 2014;15:1635–45; 2. Li J, et al. JAMA 2018;319:2486–96; 3. Dasari N, et al. Lancet 2023;402:41–53;
4. Sobrero AF, et al. J Clin Oncol 2023;41(suppl 4):67; 5. FRUZAQLA™ (fruquintinib) USPI. Takeda Pharmaceuticals America, Inc. Nov 2023

Methods

The FRESCO-2 study design:



Primary endpoint: OS

Key secondary endpoint: PFS

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

***Post hoc* analysis:** Q-TWiST

Health state definitions:

TOX: Time spent with Grade 3 or 4 TEAEs after randomization and before disease progression (any day with multiple Grade 3 or 4 TEAEs was only counted once)*

TWiST: Time from randomization to disease progression without TOX

REL: Time from disease progression to death or censoring

The Q-TWiST analysis method:

Assuming a utility coefficient of 1 to account for 100% of the duration of TWiST (U_{TWiST}), and of 0.5 to account for 50% of the duration of TOX (U_{TOX}) and REL (U_{REL}), Q-TWiST was calculated as the utility-weighted sum of the mean durations of each health state:

- $\textbf{Q-TWiST} = (\textbf{TOX} \times U_{TOX}) + (\textbf{TWiST} \times U_{TWiST}) + (\textbf{REL} \times U_{REL})$

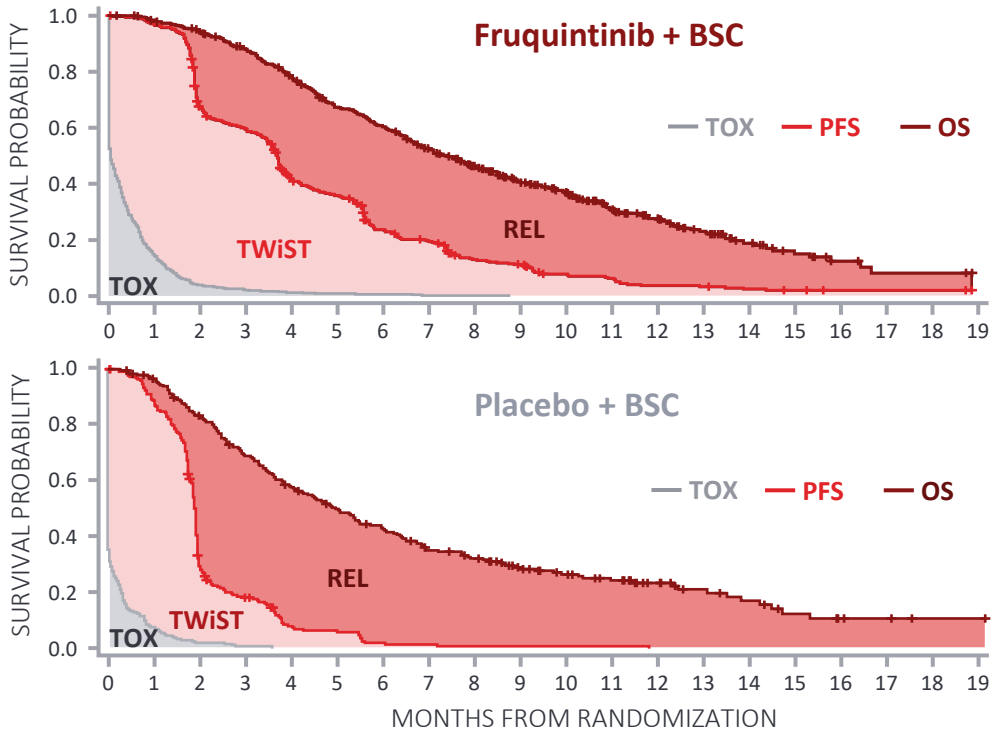
*A sensitivity analysis was conducted in which Q-TWiST was re-derived using any serious TEAE instead of Grade 3 or 4 TEAEs in the TOX state to ensure that the conclusion from the primary Q-TWiST analysis was robust in terms of toxicity

BSC, best supportive care; DCR, disease control rate; DOR, duration of response; HRQOL, health-related quality of life; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, orally; QD, once daily; Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity; R, randomization; TEAE, treatment-emergent adverse event

Stintzing S, et al. ASCO GI 2024 [poster #G20]: see the abstract

Results

Kaplan–Meier curves for OS, PFS, and toxicity[1]:



TOX: Area under the TOX curve

TWiST: Area between the PFS and TOX curves

REL: Area between the OS and PFS curves

Mean duration of health states[1]:

HEALTH STATE	MEAN DURATION,* MONTHS (95% CI)	
	FRUQUINTINIB + BSC (n=461)	PLACEBO + BSC (n=230)
Q-TWiST	6.25 (5.89, 6.61)	4.21 (3.81, 4.60)
Difference (95% CI),† p-value	**2.04 (1.51, 2.57), p<0.05**	
TOX	0.45 (0.37, 0.53)	0.21 (0.15, 0.28)
Difference (95% CI),† p-value	0.24 (0.13, 0.34), p<0.05	
TWiST	4.06 (3.75, 4.36)	1.92 (1.75, 2.10)
Difference (95% CI),† p-value	2.14 (1.78, 2.49), p<0.05	
REL	3.93 (3.55, 4.32)	4.36 (3.75, 4.96)
Difference (95% CI),† p-value	-0.43 (-1.15, 0.29), p≥0.05	

Q-TWiST was significantly improved with fruquintinib + BSC vs placebo + BSC, with a **relative improvement‡ of 31.4%** in favor of fruquintinib + BSC,[1,§] suggesting a 'clearly clinically important' difference[2]

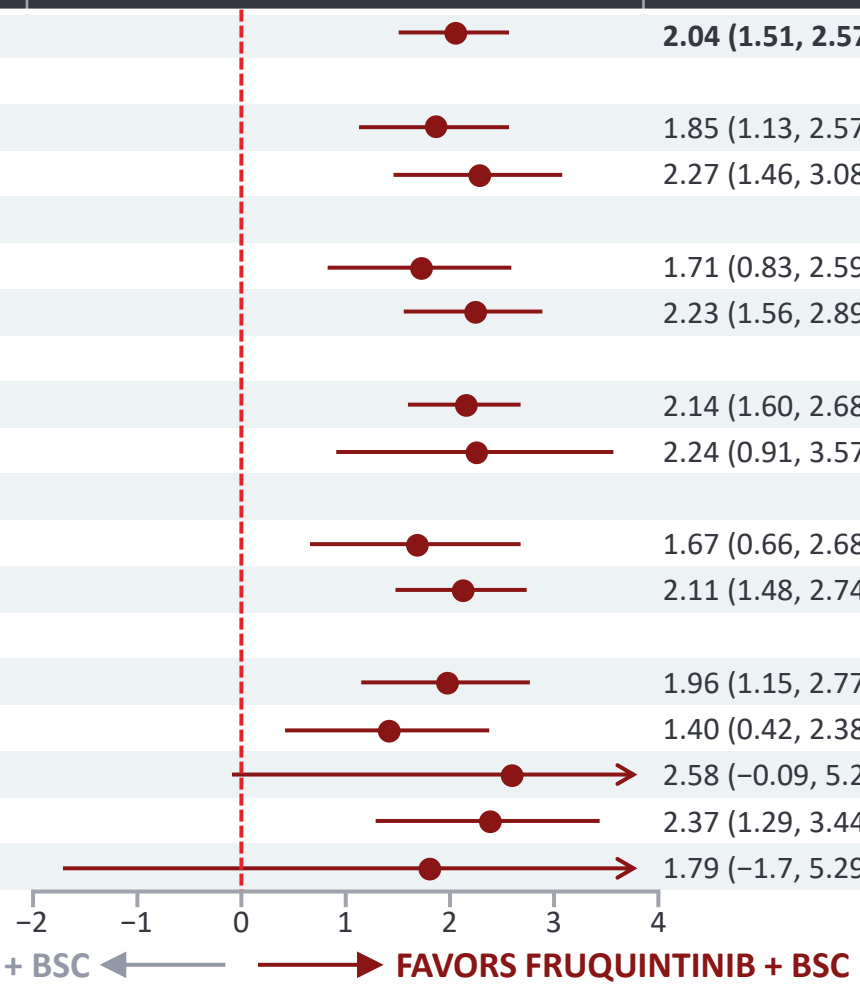
*The mean time spent in each health state was calculated using Kaplan-Meier analysis; †95% CIs for the differences between treatment arms were calculated using the non-parametric bootstrap method; ‡The relative improvement (%) of Q-TWiST for the fruquintinib + BSC group was calculated by dividing the Q-TWiST difference by the mean OS in the placebo + BSC group. **Relative Q-TWiST improvements of >10% imply a 'clinically important' difference; improvements of >15% suggest a 'clearly clinically important' difference[2]**; §Sensitivity analysis demonstrated the robustness of the primary analysis: Q-TWiST was 6.41 months for fruquintinib + BSC vs 4.26 months for placebo + BSC, leading to a mean Q-TWiST difference of 2.14 months (95% CI 1.61, 2.68; p<0.05) and a relative improvement of 33.0%

BSC, best supportive care; CI, confidence interval; OS, overall survival; PFS, progression-free survival, Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity

1. Stintzing S, et al. ASCO GI 2024 [poster #G20]: see the abstract; 2. Revicki D, et al. Qual Life Res 2006;15:411–23

Results: *Post hoc* subgroup analysis

SUBGROUP	PATIENTS, n (%)	MEAN DIFFERENCE (95% CI)	IMPROVEMENT (%)
Overall	**691 (100)**	**2.04 (1.51, 2.57)**	**31.43**
Age			
<65	366 (53.0)	1.85 (1.13, 2.57)	28.51
≥65	325 (47.0)	2.27 (1.46, 3.08)	34.98
Sex			
Female	306 (44.3)	1.71 (0.83, 2.59)	26.35
Male	385 (55.7)	2.23 (1.56, 2.89)	34.36
Liver metastases			
Yes	495 (71.6)	2.14 (1.60, 2.68)	32.97
No	196 (28.4)	2.24 (0.91, 3.57)	34.51
Prior LOT for metastatic disease			
≤3	189 (27.4)	1.67 (0.66, 2.68)	25.73
>3	502 (72.6)	2.11 (1.48, 2.74)	32.51
Primary site			
Colon left	284 (41.1)	1.96 (1.15, 2.77)	30.20
Colon right	150 (21.7)	1.40 (0.42, 2.38)	21.57
Colon unknown	38 (5.5)	2.58 (−0.09, 5.26)	39.75
Rectum only	213 (30.8)	2.37 (1.29, 3.44)	36.52
Colon left and right	6 (0.9)	1.79 (−1.7, 5.29)	27.58



Consistent Q-TWiST improvements were observed in all subgroups, except in patients whose primary tumor site was unknown or in those with both left- and right-sided tumors, due to very small number of patients in these subgroups

Note: This study was not powered to detect statistically significant differences between arms in subgroups

BSC, best supportive care; CI, confidence interval; LOT, line of therapy; Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity

Stintzing S, et al. ASCO GI 2024 [poster #G20]: see the abstract

Authors' conclusions

The Q-TWiST analysis can evaluate trade-offs between potential treatment toxicities and survival time, which is clinically important for treatment decision-making in later-line mCRC for patients whose QOL has been worsened by their disease and the prior therapies received

Fruquintinib + BSC demonstrated a clinically meaningful improvement in Q-TWiST vs placebo + BSC for patients in FRESCO-2

- There was a Q-TWiST improvement of 2.04 months with fruquintinib + BSC vs placebo + BSC (6.25 vs 4.21 months; 95% CI 1.51, 2.57; $p<0.05$)
- The improvement was robust, supported by the sensitivity analysis, and was mostly consistent across key subgroups

Post hoc Q-TWiST showed that fruquintinib delays disease progression and prolongs patient survival without substantially increasing toxicity, which is particularly notable considering the toxicity was evaluated against an inactive comparator (ie, placebo)

Fruquintinib has the potential to provide an improved survival benefit without negatively impacting QOL for patients with previously treated mCRC, who have limited treatment options

BSC, best supportive care; CI, confidence interval; mCRC, metastatic colorectal cancer; OS, overall survival; QOL, quality of life; Q-TWiST, Quality-adjusted Time Without Symptoms of disease or Toxicity

Stintzing S, et al. ASCO GI 2024 [poster #G20]: see the abstract

Investigator-initiated research

Retrospective cohort study to evaluate fruquintinib plus PD-1 inhibitors vs TAS-102 plus bevacizumab in late-line mCRC

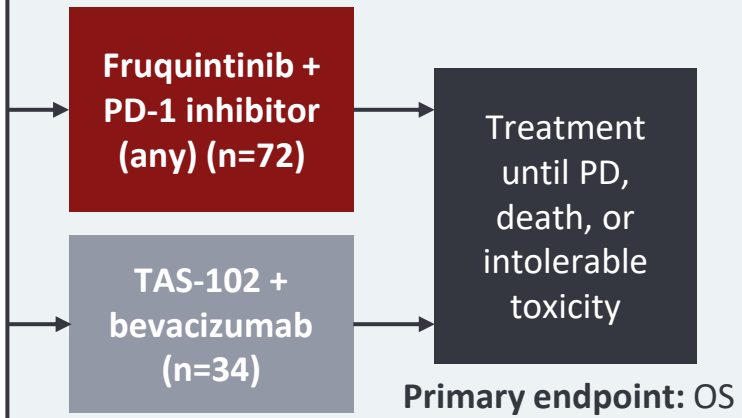
ASCO GI 2024
Abstract 95 (IIR)

Study design

Retrospective cohort study*

PATIENT ELIGIBILITY

- Confirmed mCRC
- ≥1 measurable lesion per RECIST v1.1
- ≥2 prior systemic treatments received
- Medication of fruquintinib + PD-1 inhibitor or TAS-102 + bevacizumab ≥8 weeks
- No crossover medication until cutoff date



- PS calculated to balance the baseline characteristics of the two cohorts
- Sample sizes matched with PSM and IPW
- Methods for OS hazard ratios calculations and adjustments: Multivariable Cox proportional-hazards model (with and without additional adjustment for PS†), IPW, and PSM

Baseline characteristics

CHARACTERISTIC, n (%)		BEFORE PSM		AFTER PSM	
		FRUQ + PD-1i (n=72)	TAS-102 + BEV (n=34)	FRUQ + PD-1i (n=49)	TAS-102 + BEV (n=29)
Sex	Male	42 (58.3)	18 (52.9)	29 (59.2)	18 (62.1)
Age, years	Median (range)	56.5 (35–76)	56.5 (37–71)	58 (38–76)	56 (37–71)
	≥65	11 (15.3)	7 (20.6)	7 (14.3)	5 (17.2)
ECOG PS	0	20 (27.8)	17 (50.0)	16 (32.7)	12 (41.4)
	1	51 (70.8)	17 (50.0)	32 (65.3)	17 (58.6)
	2	1 (1.4)	0	1 (2.0)	0
Primary lesion	Resected	56 (77.8)	32 (94.1)	45 (91.8)	27 (93.1)
Radiotherapy	Prior treatment	25 (34.7)	14 (41.2)	20 (40.8)	12 (41.4)
Target lesion	Right-sided	23 (31.9)	13 (38.2)	15 (30.6)	12 (41.4)
Metastases	Liver	51 (70.8)	23 (67.6)	36 (73.5)	18 (62.1)
	Lung	47 (65.3)	25 (73.5)	38 (77.6)	21 (72.4)
	Bone	11 (15.3)	7 (20.6)	8 (16.3)	5 (17.2)
Line	≥4	43 (59.7)	22 (64.7)	30 (61.2)	17 (58.6)

*106 patients enrolled from July 2019 to October 2022. Median follow-up: 14 months
†Multivariate Cox proportional-hazards model adjustments: Sex, age >65 years, ECOG PS, resection of primary lesion, prior radiotherapy, location of target lesions (left- or right-sided), metastasis (liver, lung, bone), and current line ≥3

BEV, bevacizumab; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; IIR, investigator-initiated research; IPW, inverse probability of treatment weighting; mCRC, metastatic colorectal cancer; OS, overall survival; PD, progressive disease; PD-1(i), programmed cell death protein 1 (inhibitor); PS(M), propensity score (matching); RECIST, Response Evaluation Criteria In Solid Tumors

Li R, et al. ASCO GI 2024 [poster #F18]: see the abstract

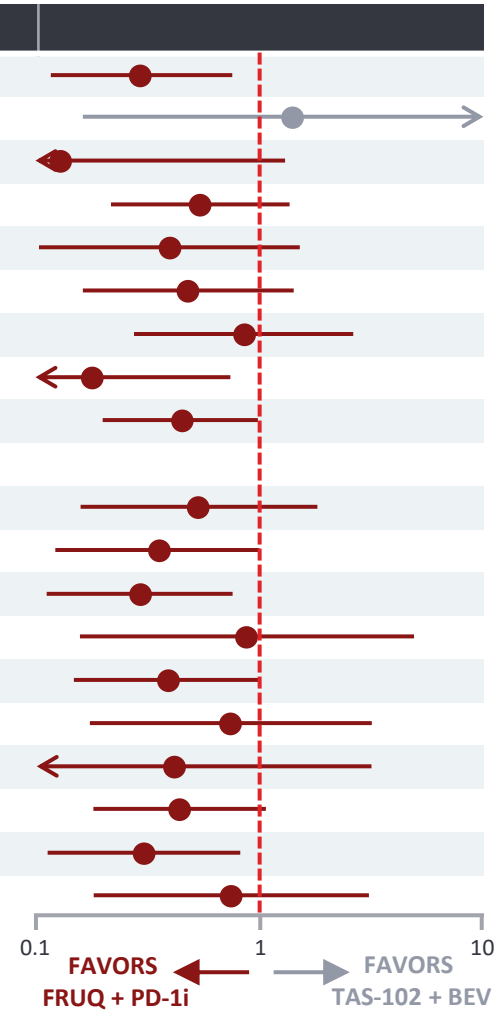
Retrospective cohort study to evaluate fruquintinib plus PD-1 inhibitors vs TAS-102 plus bevacizumab in late-line mCRC

Efficacy results[1,2]

EFFICACY	FRUQ + PD-1i (n=72)	TAS-102 + BEV (n=34)
Median OS, months (95% CI)	19.4 (17.9, NR)	11.6 (10.0, 17.2)
HR for OS (95% CI)		
Crude analysis	0.384 (0.192, 0.769); p=0.0052	
Multivariable analysis	0.323 (0.149, 0.704)	
With IPW	0.437 (0.200, 0.953)	
With PSM*	0.446 (0.201, 0.990)	
With additional adjustment for PS	0.339 (0.153, 0.748)	
DCR, %*	93.1	73.5
OR (95% CI)	4.824 (1.518, 17.030)	

Subgroup analysis (after PSM)[1]

TERM	SUBGROUP	N_{FP}	N_{TB}	HR (95% CI)
Sex	Male	29	18	0.296 (0.117, 0.753)
	Female	20	11	1.410 (0.162, 12.300)
Age ≥65	Yes	7	5	0.128 (0.013, 1.290)
	No	42	24	0.542 (0.217, 1.360)
ECOG PS	0	16	12	0.395 (0.104, 1.500)
	1	32	17	0.478 (0.162, 1.410)
Lesion location	Left	34	17	0.852 (0.278, 2.610)
	Right	15	12	0.177 (0.043, 0.736)
Resected primary lesion	Yes	45	27	0.448 (0.200, 1.000)
	No	4	2	
Prior radiotherapy	Yes	20	12	0.533 (0.157, 1.810)
	No	29	17	0.354 (0.122, 1.030)
Liver metastasis	Yes	36	18	0.291 (0.112, 0.756)
	No	13	11	0.877 (0.157, 4.890)
Lung metastasis	Yes	38	21	0.388 (0.148, 1.020)
	No	11	8	0.742 (0.175, 3.150)
Bone metastasis	Yes	8	5	0.417 (0.055, 3.150)
	No	41	24	0.439 (0.182, 1.050)
Current line ≥4	Yes	30	17	0.303 (0.113, 0.812)
	No	19	12	0.747 (0.182, 3.060)



*Analysis performed with PS-matched cohorts: FRUQ + PD-1i, n=49; TAS-102 + BEV, n=29[2]

BEV, bevacizumab; CI, confidence interval; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; HR, hazard ratio; IIR, investigator-initiated research; IPW, inverse probability of treatment weighting; mCRC, metastatic colorectal cancer; N_{FP}, number (FRUQ + PD-1i); NR, not reached; N_{TB}, number (TAS-102 + BEV); OR, odds ratio; OS, overall survival; PD-1(i), programmed cell death protein 1 (inhibitor); PS(M), propensity score matching

1. Li R, et al. ASCO GI 2024 [poster #F18]; 2. Li R, et al. ASCO GI 2024 [abstract #95]: see the abstract

Initial efficacy evaluation of fruquintinib plus capecitabine vs capecitabine as maintenance treatment for mCRC

ASCO GI 2024
Abstract 119 (IIR)

Study design

Randomized, controlled Phase Ib/II study (NCT05451719); study is ongoing

PATIENT ELIGIBILITY

- Histologically confirmed mCRC (stage IV)
- Aged ≥18 years
- ECOG PS 0–2
- Achieved disease control (CR/PR/SD) after ≥6 cycles of 1L standard chemotherapy and disease still unresectable

Part 1: Safety lead-in phase (N=6)

Fruquintinib:
4 mg, PO, QD, D1–21, Q4W
+
Capecitabine*

Part 2: Expansion phase (N=110)†

Fruquintinib:
RP2D, 3 mg
+
Capecitabine*

R 1:1

Capecitabine*

Randomization stratified by:
- *RAS* status (WT vs mutated)
- Primary tumor site (left vs right)

Primary endpoint: RP2D, PFS

Secondary endpoints: OS, ORR, DCR, AEs

Baseline characteristics

CHARACTERISTIC, n (%)		FRUQ + CAP (n=14)	CAP (n=12)
Sex	Male	10 (71.4)	8 (66.7)
Age, years	Median (range)	61.5 (39–78)	57.5 (32–75)
	<65	8 (57.1)	7 (58.3)
Primary tumor site	Left-sided	9 (64.3)	8 (66.7)
	Right-sided	5 (35.7)	4 (33.3)
***RAS* status**	Mutated	7 (50.0)	7 (58.3)
Metastases	Liver	6 (42.9)	7 (58.3)
Treatment history	Chemotherapy	14 (100.0)	12 (100.0)
	VEGF inhibitors	8 (57.1)	7 (58.3)
	EGFR inhibitors	5 (35.7)	3 (25.0)

Data cutoff: Sept 10, 2023

*Dosing: 850 mg/m² PO, BID, D1–7 and D15–21, Q4W, DLT in first cycle; †At data cutoff, 34 patients had been enrolled and 26 considered evaluable for efficacy

1L, first-line; AE, adverse event; BID, twice daily; CAP, capecitabine; CR, complete response; D#, Day #; DCR, disease control rate; DLT, dose-limiting toxicity; 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; PD, progressive disease; PFS, progression-free survival; PO, orally; PR, partial response; Q4W, every 4 weeks; QD, once daily; R, randomization; RP2D, recommended Phase 2 dose; SD, stable disease; VEGF, vascular endothelial growth factor; WT, wild type

Li W, et al. ASCO GI 2024 [poster #H4]: see the abstract

Initial efficacy evaluation of fruquintinib plus capecitabine vs capecitabine as maintenance treatment for mCRC

ASCO GI 2024
Abstract 119 (IIR)

Efficacy results

EFFICACY	FRUQ + CAP (n=14)	CAP (n=12)
Best overall response, n		
PR	3	0
SD	10	8
PD	1	4
ORR, %	21.4	0
DCR, %	92.9	66.7
Median PFS, months (95% CI)	9.1 (5.0, NR)	3.8 (2.3, 5.7)
HR (95% CI)	0.289 (0.083, 1.01); p=0.039	

Safety results

TEAE, n (%)	FRUQ + CAP (n=18)		CAP (n=16)	
	ANY GRADE	GRADE ≥3	ANY GRADE	GRADE ≥3
Hypertension	7 (38.9)	2 (11.1)	0	0
Voice alteration	6 (33.3)	1 (5.6)	0	0
Oral mucositis	4 (22.2)	1 (5.6)	1 (6.3)	1 (6.3)
Bilirubin increased	2 (11.1)	1 (5.6)	0	0
Acrodynia	3 (16.7)	1 (5.6)	2 (12.5)	1 (6.3)
Diarrhea	1 (5.6)	0	1 (6.3)	1 (6.3)

Most TEAEs were Grade 1–2 across both groups

Data cutoff: Sept 10, 2023

CAP, capecitabine; CI, confidence interval; DCR, disease control rate; FRUQ, fruquintinib; HR, hazard ratio; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; NR, not reached; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event

Li W, et al. ASCO GI 2024 [poster #H4]: see the abstract

Preliminary efficacy and safety of fruquintinib as maintenance therapy after first-line treatment in mCRC (the FRONT study)

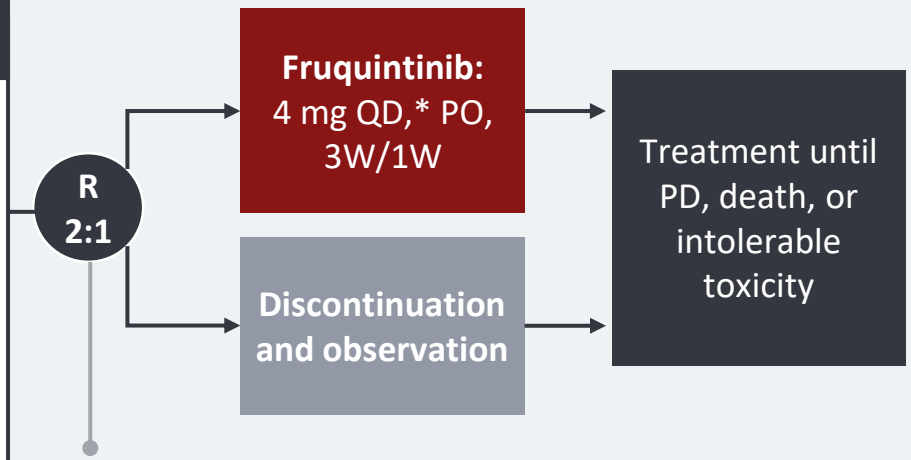
ASCO GI 2024
Abstract 126 (IIR)

Study design

Multicenter, randomized, open-label, controlled study (NCT04296019); study is ongoing

PATIENT ELIGIBILITY

- Histologically or cytologically confirmed mCRC
- Aged ≥18 years
- ECOG PS 0–1
- Achieving CR, PR, or SD after a 16–24-week standard 1L treatment



Primary endpoint: PFS

Secondary endpoints: OS, TEAEs

Baseline characteristics

CHARACTERISTIC, n (%)†		FRUQ (n=28)	OB (n=14)
Sex	Male	20 (71.4)	10 (71.4)
Age, years	Median (IQR)	61 (56–66)	66.5 (56–73)
	Range	44–73	36–81
Lesion	Right-sided	10 (35.7)	1 (7.1)
Primary lesion	Resected	16 (57.1)	13 (92.9)
***RAS* status**	Mutated	26 (92.9)	11 (78.6)
Metastases	Liver	17 (60.7)	7 (50.0)
	Lung	12 (42.9)	9 (64.3)
	Lymph node	12 (42.9)	7 (50.0)
BOR in 1L	PR	5 (17.9)	4 (28.6)
	SD	23 (82.1)	10 (71.4)

Data updated: Aug 22, 2023

*6 patients in fruquintinib group initiated at a lower dose (3 mg); †No *BRAF* mutations were detected; no CR reported at baseline

1L, first-line; 3W/1W, 3 weeks on, 1 week off; BOR, best overall response; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; FRUQ, fruquintinib; IIR, investigator-initiated research; IQR, interquartile range; mCRC, metastatic colorectal cancer; OB, observation; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PO, orally; PR, partial response; QD, once daily; R, randomization; SD, stable disease; TEAE, treatment-emergent adverse event

Xu X, et al. ASCO GI 2024 [poster #H11]: see the abstract

Preliminary efficacy and safety of fruquintinib as maintenance therapy after first-line treatment in mCRC (the FRONT study)

ASCO GI 2024
Abstract 126 (IIR)

Efficacy results

EFFICACY, n (%)	FULL ANALYSIS SET		
	FRUQ (n=25)	OB (n=13)	OR (95% CI)
Best overall response			
SD	22 (88.0)	7 (53.8)	6.29 (1.31, 36.7); p=0.0267
PD	3 (12.0)	6 (46.2)	
DCR	22 (88.0)	7 (53.8)	
	FRUQ (n=28)	OB (n=14)	p-value
mPFS (95% CI), months	5.26 (3.71, 19.12)	2.99 (1.91, 4.63)	0.0158

EFFICACY, n (%)	PER-PROTOCOL SET		
	FRUQ (n=19)	OB (n=13)	OR (95% CI)
Best overall response			
SD	17 (89.5)	7 (53.8)	7.29 (1.32, 58.9); p=0.0331
PD	2 (10.5)	6 (46.2)	
DCR	17 (89.5)	7 (53.8)	
	FRUQ (n=22)	OB (n=14)	p-value
mPFS (95% CI), months	6.51 (3.88, 19.12)	2.99 (1.91, 4.63)	0.0061

Safety results

FRUQUINTINIB ARM

- **Common any-Grade AEs:** Hypertension, hand-foot syndrome, fatigue, rash, oral mucositis, and proteinuria
- **Grade ≥3 AEs:** Hand-foot syndrome, hypertension, oral mucositis, and proteinuria

No new safety signals were observed

Data updated: Aug 22, 2023

AE, adverse event; CI, confidence interval; DCR, disease control rate; FRUQ, fruquintinib; IIR, investigator-initiated research; mCRC, metastatic colorectal cancer; mPFS, median progression-free survival; OB, observation; OR, odds ratio; PD, progressive disease; SD, stable disease

Xu X, et al. ASCO GI 2024 [poster #H11]: see the abstract

Additional fruquintinib data

Additional fruquintinib data: Investigator-initiated research*

COLORECTAL CANCER – Poster Presentation

- Fruquintinib with PD-1 inhibitors vs fruquintinib monotherapy in late-line mCRC: A retrospective cohort study based on propensity score matching. An T, et al. J Clin Oncol 2024;42(suppl 3; abstr 139)*

ESOPHAGEAL/GASTRIC CANCER – Poster Presentations

- A phase 2 study of fruquintinib in combination with S-1 for second-line treatment of esophageal squamous cell carcinoma after first-line immunotherapy failure. Li N, et al. J Clin Oncol 2024;42(suppl 3; abstr 323)*
  - Clinical Trial Registration Number: NCT05636150
- Efficacy and safety of fruquintinib with nab-paclitaxel in advanced G/GEJ cancer after exposure to immune checkpoint inhibitors: A single-center prospective clinical trial. Ma X , et al. J Clin Oncol 2024;42(suppl 3; abstr 327)*
  - Clinical Trial Registration Number: ChiCTR2200059976
- Fruquintinib combined with sintilimab as a second-line therapy for advanced gastric and gastroesophageal junction adenocarcinoma (GC/GEJC): A phase II, single-arm, prospective study. Jin M , et al. J Clin Oncol 2024;42(suppl 3; abstr 332)*
  - Clinical Trial Registration Number: NCT05625737
- A phase Ib/II study of fruquintinib in combination with SOX and toripalimab as first-line treatment for advanced metastatic gastric/gastroesophageal junction adenocarcinoma (GC/GEJC). Meng X , et al. J Clin Oncol 2024;42(suppl 3; abstr 335)*
  - Clinical Trial Registration Number: NCT05024812

HEPATOBILIARY CANCER– Poster Presentation

- Fruquintinib combined with sintilimab plus transarterial chemoembolization (TACE) for unresectable hepatocellular carcinoma: A single-arm Phase II study. Shao G, et al. J Clin Oncol 2024;42(suppl 3; abstr 499)*
  - Clinical Trial Registration Number: NCT05971199

*Takeda has no current involvement with any investigator-initiated studies with fruquintinib in China; all publications were developed independent of Takeda. Questions regarding any of the studies above should be directed to HUTCHMED Med Info or the respective authors

G(C), gastric (cancer); GEJ(C), gastroesophageal junction (cancer); mCRC, metastatic colorectal cancer; PD-1, programmed cell death protein 1; SOX, S1 + oxaliplatin