Fruquintinib (Colorectal)

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

Index

Indication

3rd line or later treatment of metastatic colorectal cancer (mCRC) when previous treatment has included:

- fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, with or without an anti-VEGF therapy
- an anti-EGFR therapy if RAS wildtype, unless this was not suitable
- bevacizumab and trifluridine and tipiracil, unless this was not suitable

ECOG PS 0-1

(NICE TA 1079)

Response Rates

FRESCO-2 trial of fruquintinib vs placebo (n=461 vs 230).

- Median OS 7.4m vs 4.8m.
- Median PFS improvement of 1.9m (3.7m vs 1.8m respectively).
- Previous FRESCO trial showed median OS improvement of 2.7m.

Treatment related mortality

Treatment-related death 0.2%. Treatment related grade ≥3 events in 36% patients.

Regimen details

Day	Drug	Dose	Route
1-21 (followed by a 7 day break)	Fruquintinib	5mg OD	PO

Cycle frequency
28 days
Fruquintinib should be taken for 21 days followed by a 7 day break.

Number of cycles
Until disease progression or unacceptable toxicity

Pre-medication
Nil

Supportive medication
Emollient e.g. Epimax cream PRN
Urea 10% cream
Loperamide PRN
Antiemetics as per local policy e.g. metoclopramide 10mg TDS PRN

Emetogenicity
This regimen has minimal emetic potential – refer to local policy

Administration
Swallow capsules whole, with or without food. If a dose is missed by less than 12 hours, it should be taken, and the next dose should be taken as scheduled. If a dose is missed by more than 12 hours, it should be skipped, and the next dose should be taken as scheduled.
If vomiting occurs after taking a dose, the dose should not be repeated on the same day, but treatment should be restarted the following day.

Extravasation
N/A

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)	14 days
LFT	14 days
Thyroid function	14 days
Blood pressure	Adequately controlled prior to starting
Urine dipstick (to assess for proteinuria)	Baseline

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours (+ day 15 of cycle 1 only)
U&E (including creatinine)	96 hours (+ day 15 of cycle 1 only)
LFT	96 hours (+ day 15 of cycle 1 only)
Blood pressure	Weekly for first cycle, monthly thereafter
Urine dipstick for proteinuria	Monthly
Thyroid function	3 monthly

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Investigation	Limit
Neutrophils	> 1.0 x 10^9/L
Platelets	> 75 x 10^9/L
Creatinine Clearance	> 15mL/min
Bilirubin	< 1.5 x ULN
ALT	< 3 x ULN
Urine dipstick	1+ on dipstick, < 2g/24 hours on urinalysis
Blood pressure	< 140/90mmHg

Dose modifications

Starting dose	5mg OD
First dose reduction	4mg OD
Second dose reduction	3mg OD
Fruquintinib should be stopped permanently in patients unable to tolerate 3mg OD	

Haematological toxicity

If neutrophils < 1.0 x 10^9/L withhold treatment until recovery to ≥ 1.0 x 10^9/L then restart at next lower dose level.

If platelets drop to 50 - 74 x 10^9/L withhold treatment until recovery to ≥ 75 x 10^9/L. If recovery within 7 days, restart at same dose level. If recovery > 7 days restart at one level dose reduction.
If platelets drop to < 50 x 10^9/L withhold treatment until recovery to ≥ 75 x 10^9/L and restart at next lower dose level.

Renal impairment

No dosage adjustment required

Hepatic impairment

No dose adjustment is required for mild or moderate hepatic impairment. Fruquintinib has not been studied in severe hepatic impairment and treatment is not recommended.

Other toxicities

Toxicity	Definition	Action/Dose adjustment
Hypertension (most likely to occur in first 2 weeks of treatment)	Grade 3 Systolic BP ≥ 160 mm Hg; Diastolic BP ≥ 100 mm Hg	Withhold if persists despite initiation or modification of antihypertensive treatment. If recovers to Grade 1 or baseline – restart treatment at next lower dose level. If hypertension occurs at 3mg OD stop treatment permanently.
	Grade 4 (life-threatening)	Permanently discontinue
Haemorrhagic event	Grade 2	Withhold until bleed recovers to grade 1 or baseline then restart treatment at the next lower dose level. If Grade 2 haemorrhage still occurs at 3mg OD then stop treatment permanently.
	Grade 3 or more	Stop treatment permanently
Proteinuria	Urine dipstick 2+ protein	Continue treatment but arrange a 24hr urine protein within 1 week.
	Urine dipstick 3+ protein	Withhold fruquintinib and arrange 24hr urine protein.
	24 hr urinalysis: ≥ 2g/24 hours	Withhold until proteinuria fully resolves or recovers to <1g/24 hours (grade 1), then restart treatment at the next lower dose level. If proteinuria ≥ 2g/24 hours still occurs with 3mg OD then stop treatment permanently.
	Nephrotic Syndrome	Stop treatment permanently.

Toxicity	Definition	Action/Dose adjustment
LFT Abnormalities	ALT/AST > 3 x ULN if baseline was normal, or > 3 x baseline if this was abnormal; **OR** Bilirubin > 1.5 x ULN if baseline was normal or > 1.5 x baseline if baseline was abnormal	Withhold until LFT abnormality recovers to Gr 1 or baseline. Resume at reduced dose level. If Gr 2 or 3 LFT abnormality still occurs with 3mg OD then stop treatment permanently.
	ALT/AST > 3x ULN with concurrent bilirubin > 2 x ULN (in absence of other cause)	Stop treatment permanently
	ALT/AST > 20 x ULN if baseline was normal, or > 20 x baseline if this was abnormal; OR bilirubin > 10 x ULN or > 10 x baseline if baseline was abnormal	Stop treatment permanently
Palmar-plantar erythrodysestheia (PPE)	Grade 2	Supportive treatment. Withhold until recovers to Grade 1 or baseline then restart at the same dose level.
	Grade 3	Supportive treatment. Withhold until recovers to Grade 1 or baseline. Then restart at the next lower dose level. If Grade 3 PPE despite dose reduction to 3mg OD then stop treatment permanently.
Other Adverse Reactions	Grade 3	Withhold until the reaction recovers to Grade 1 or baseline. Resume at reduced dose level. If Grade 3 toxicity still occurs at 3mg OD then stop treatment permanently.
	Grade 4	Stop treatment permanently. Consider resuming at reduced dose level if the toxicity recovers to Grade 1 or baseline and potential benefit outweighs the risks.
Infection	Grade 3 or 4	Withhold fruquintinib for Grade 3 or 4 infections or worsening infection of any grade. Fruquintinib should be restarted at the same dose once the infection resolves.

Delayed wound healing

Delayed wound healing has been reported in 0.1% of patients receiving fruquintinib. Patients are recommended to withhold fruquintinib prior to surgery. No specific timelines are given by the manufacturer but based on half life holding treatment for 2 weeks prior to surgery is recommended. Fruquintinib should be resumed after surgery as clinically indicated when there is evidence of adequate wound healing.

Side Effects

Toxicity		FRESCO		FRESCO-2	
		Any grade (%)	G3 or 4 (%)	Any grade (%)	G3 or 4 (%)
Haematological	Thrombocytopenia	13.3	2.5	NA	NA
Non-Haematological	Hypertension	55.4	21.2	37	14
	Palmar-plantar erythrodysesthesia	49.3	10.8	19	6
	Proteinuria	42.1	3.2	17	2
	Dysphonia	36.0	0	16	0
	Asthenia	NA	NA	34	8
	TSH elevated	24.8	0	NA	NA
	AST elevated	23.0	0.4	11	0
	Infection	NA	NA	21	7
	Bilirubin elevated	20.1	1.4	NA	NA
	Diarrhoea	20.1	2.9	24	4
	Abdominal pain	NA	NA	18	3
	ALT elevated	18.0	0.7	10	3
	Nausea	NA	NA	17	1
	Constipation	NA	NA	17	<1
	Stomatitis	16.9	0.4	15	2
	Decreased appetite	16.2	1.1	27	2
	Hypothyroidism	15.5	0	21	<1
	Haemorrhage	NA	NA	14	2
	Vomiting	NA	NA	14	2
	Fatigue	11.9	1.1	20	4
	Weight loss	11.2	1.1	12	1
	Arthralgia	NA	NA	11	1
	Back pain	NA	NA	10	1
	GI perforation	NA	NA	4	2

Specific drug related side effects:

Common (>10%)	Uncommon (1-10%)	Rare (<1%)
Thrombocytopenia	Pneumonia/URTI	Posterior reversible encephalopathy
Hypothyroidism	Leukopenia/neutropenia	Pancreatitis
Hypertension	Hypokalaemia	
Dysphonia	Epistaxis	
Diarrhoea/stomatitis	Throat pain	
Fatigue/asthenia	GI haemorrhage	
ALT and bilirubin increased	GI perforation	
PPE	Pancreatic enzyme increase	
Musculoskeletal discomfort/arthralgia	Oral pain	
Proteinura	Rash	
	Mucosal inflammation	

Additional information

Women of childbearing potential and male patients with female partners of childbearing potential should be advised to use effective barrier contraception during treatment and for at least 2 weeks following the last dose of fruquintinib. 'if conception occurs during treatment, there is potential for harm to the foetus. Patients should not breast feed whilst on treatment as there is no data on if fruquintinib or its metabolites are present in breast milk.

It is recommended to avoid starting treatment with fruquintinib in patients with a history of thromboembolic events (including deep vein thrombosis and pulmonary embolism) within the past 6 months or if they have a history of stroke and/or transient ischemic attack within the last 12 months. If arterial thrombosis is suspected, fruquintinib should be discontinued immediately.

Significant drug interactions – for full details consult product literature/ reference texts

Strong and moderate CYP3A inducers (e.g. apalutamide, enzalutamide, rifampicin, carbamazepine, phenytoin, and St. John's wort, phenobarbital, primidone): concomitant use should be avoided.
P-gp and BCRP substrates (e.g. dabigatran, digoxin, rosuvastatin) Fruquintinib may increase or decrease exposure, if co-administered with substrates with a narrow therapeutic range, monitor closely.
Anticoagulants: Monitor haematologic and coagulation profiles more frequently in patients treated with anticoagulants or other concomitant medicinal products that increase the risk of bleeding.

References

- National Institute for Health and Care Excellence (TA1079) accessed 7 November 2025 via www.nice.org.uk
- Summary of Product Characteristics Fruquintinib (Takeda) accessed 7 November 2025 via www.medicines.org.uk
- Li, J. et al. Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer. The FRESCO Randomized Clinical Trial. JAMA 2018;319(24):2486-2496.
- Dasari A. et al. Fruquintinib versus placebo in patients with refractory metastatic colorectal cancer (FRESCO-2): an international, multicentre, randomised, double-blind, phase 3 study. Lancet 2025; 402(10395):41-53

Version	Issue date	Review date	Revision	Written/Checked/Authorised
1	Nov 2025	Nov 2028	New protocol	Written: Dr K Bond (Oncology SpR, UHBW NHS Trust), Dr T Strawson-Smith (Consultant Oncologist, UHBW NHS Trust), Dr H Brooks (Consultant Oncologist, UHBW NHS Trust). Checked: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance) Authorised: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)