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# FRESCO-2: A global phase III multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer

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## Background

Effective treatment options are limited for patients (pts) with refractory metastatic colorectal cancer (mCRC). Fruquintinib (F), a highly selective, potent, oral tyrosine kinase inhibitor of VEGFR-1, -2, and -3, was approved in China in the 3L+ mCRC setting based on results from the FRESCO trial (NCT02314819). FRESCO-2 (NCT04322539) evaluated F in more heavily pre-treated pts reflecting current global practices.

## Methods

FRESCO-2 was a randomized, double-blind, placebo (P)-controlled, phase 3 MRCT conducted in the US, Europe, Japan & Australia, comparing F + best supportive care (BSC) with P + BSC. F or P was given 5 mg PO, QD, 3 wks on, 1 wk off, in 28-d cycles. Key criteria: Prior chemotherapy, anti-VEGF therapy, and, if *RAS* wild type (WT), anti-EGFR therapy; if BRAFV600E mutant (MT) or MSI-H, ≥1 targeted regimen; & prior exposure to trifluridine/tipiracil (T) and/or regorafenib (R). Pts were randomized 2:1 to F + BSC or P + BSC and stratified by: prior therapy T, R or both; *RAS* status (WT, MT) & duration of metastatic disease (≤18, >18 months [m]). The primary endpoint was overall survival (OS). Key secondary endpoints were progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR) & safety. Final analysis was after 480 OS events.

## Results

From 2Sep2020 to 14Dec2021, 691 pts were randomized; F:461 vs P:230. Baseline characteristics were balanced. F significantly improved OS (median: 7.4 m vs 4.8 m P; HR=0.66; [95% CI: 0.55, 0.80]; p<0.001) & PFS (median: 3.7 m vs 1.8 m P; HR=0.32; [95% CI: 0.27, 0.39]; p<0.001). The median duration of follow-up was 11.3 m F vs 11.2 m P. Subsequent anti-cancer therapies were 29.4% F vs 34.3% P. DCR was 55.5% F vs 16.1% P & ORR was 1.5% F vs 0% P. Grade ≥3 adverse events were 62.7% F vs 50.4% P; those occurring in ≥5% on F were hypertension (13.6% vs 0.9% P), asthenia (7.7% vs 3.9% P) & hand-foot syndrome (6.4% vs 0% P).

## Conclusions

F had a significant and clinically meaningful improvement in OS in pts with refractory mCRC. F was well tolerated, with a safety profile consistent with the established profile for F monotherapy. FRESCO-2 results are consistent with FRESCO and should support a new treatment option in refractory mCRC.

## Clinical trial identification

NCT04322539.


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