Budget impact analysis of introducing fruquintinib for the treatment of previously treated metastatic colorectal cancer in the United States from the payer perspective

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Background

- Colorectal cancer (CRC) is a leading cause of cancer morbidity and death in the United States (US), and resulted in approximately 153,000 incident cases and 52,000 deaths in 2023[1]
- In the US, the five-year relative survival of CRC is 65%, which reflects a wide survival disparity between localized (91.1%) and distantly metastasized disease (15.7%).[2] Patients with refractory metastatic CRC (mCRC) have limited treatment options due to lack of tumor response and/or resistance to systemic therapies[3]
- Fruquintinib, a selective small-molecule tyrosine kinase inhibitor of all three vascular endothelial growth factor receptors (VEGFRs -1, -2, and -3) was approved by the US Food and Drug Administration (FDA) on November 8, 2023, for the treatment of adult patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if *RAS* wild-type and medically appropriate, an anti-EGFR therapy[4]

Objectives

- This study quantified the budgetary impact of the introduction of fruquintinib to the US payer health plan (commercial and Medicare) for the treatment of adult patients with mCRC in the above-mentioned target population

Methods

Model Overview

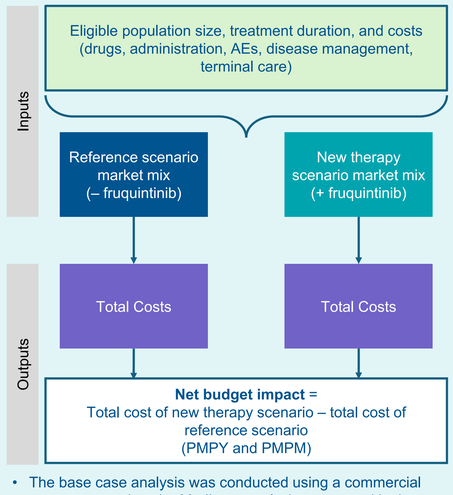
- A budget impact model (BIM) was developed to compare a reference scenario reflecting the current therapy market mix without fruquintinib and a new therapy market mix scenario with fruquintinib (**Figure 1, Summary Panel**)
- The model includes three health states: a progression-free state in which patients could be on or off their initial treatment, a post-progression state in which patients could be on or off subsequent treatment, and death. At the end of each four-week model cycle, patients remained in the existing health state, or disease progression or death occurred
- The target population was consistent with the US label for fruquintinib
- The number of newly eligible patients was informed by epidemiological data of the target population (**Table 2**), and the BIM allocates patients to their assigned treatments each year based on market share data
- In the base case, the market shares in the new scenario were estimated by assuming a proportional displacement of shares of the existing treatments based on the uptake rate of fruquintinib
- Clinical inputs were sourced from data from the clinical trials included in the US FDA Prescribing Information for each treatment to inform the proportion of patients remaining alive or progression-free over the time horizon (**Table 2**). In the base case, time on treatment, progression-free survival (PFS), and overall survival (OS) for fruquintinib were based on Kaplan–Meier curves from the individual patient-level data from FRESCO with exponential extrapolation, as the patient population enrolled in FRESCO most closely resembles that of the expected treatment population in the US based on the FDA indication
- The treatment costs of the initial and subsequent treatment were accrued based on the treatment duration. Upon non-fatal progression, patients received subsequent treatments depending on their initial treatment
- Adverse event (AE) management costs for newly eligible patients starting initial treatments were applied as one-off costs. Terminal care costs were also accrued as a one-off cost associated with the time of death

Question

What is the budgetary impact of introducing fruquintinib to the US payer health plan (commercial and Medicare) for treatment of adult patients with mCRC previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and if *RAS* wild-type and medically appropriate, an anti-EGFR therapy?

Study design

Figure 1. Budget impact model



- The base case analysis was conducted using a commercial payer perspective; the Medicare analysis was tested in the scenario analysis

Results

Table 1. Budget impact of fruquintinib over 5 years (commercial, base case) in the eligible treatment population: N=194

Cost parameter	Reference scenario, $	New therapy scenario, $	Cost difference, $
Drug acquisition	13,486,031	16,076,595	2,590,565
Drug administration	380,279	285,210	-95,070
AE management	2,386,315	1,984,403	-401,912
Disease management	120,058,179	122,159,014	2,100,836
Subsequent treatment	2,966,128	2,858,069	-108,059
Terminal care	3,851,530	3,842,545	-8,986
TOTAL	**143,128,463**	**147,205,836**	**4,077,373**

Key takeaways

- **The overall budget impact of fruquintinib in the US commercial population is low ($0.07 PMPM over a 5-year period)**
- **In the Medicare population, the budget impact was slightly greater ($0.17 PMPM over a 5-year period) due to a higher number of patients with CRC eligible for fruquintinib**

Table 2. Epidemiologic, clinical, and cost* inputs

Parameter	Base-case estimate	Source
Epidemiologic inputs		
Incident patients with CRC, per 100,000 in commercial/Medicare health plan	50.6†/ 122.1‡	NCI SEER 2023,[5] US Census Bureau 2021,[6] CMS 2023,[7] NCI SEER[2]
Percentage mCRC (including progressors from early stages)	61.50§	Ciardiello et al. 2022,[8] NCI SEER[2]
Percentage first-line drug-treated patients with mCRC	77.24¶	Hess et al. 2019[9]
Percentage second-line drug-treated patients with mCRC	31.32**	Neuberger et al. 2023[10]
Percentage target population	51.48††	
Median treatment duration, months‡‡		
Fruquintinib	3.70	FRESCO trial data[11]
Regorafenib	1.70	CORRECT; Grothey et al. 2013[12]
Trifluridine/tipiracil	1.54	RECOURSE; Mayer et al. 2015[13]
Trifluridine/tipiracil with bevacizumab	5.00	SUNLIGHT; Prager et al. 2023[14]
Drug acquisition cost per 4-week cycle (without adjustment for RDI)		
Fruquintinib	$25,200	Merative Micromedex® RED BOOK®[15] (assumed same for commercial and Medicare perspective) RDI, source: 92%, Li et al. 2018[16]
Regorafenib	$21,628	Merative Micromedex® RED BOOK®[15] (assumed same for commercial and Medicare perspective) RDI, source: 78.9%, Grothey et al. 2013[12]
Trifluridine/tipiracil	$15,802	Merative Micromedex® RED BOOK®[15] (assumed same for commercial and Medicare perspective) RDI, source: 89%, Mayer et al. 2015[13]
Trifluridine/tipiracil with bevacizumab, commercial/Medicare perspective	$20,325/$20,314	Merative Micromedex® RED BOOK®[15] / CMS ASP Pricing File[17] RDI, source: trifluridine/tipiracil: 88.3%, Prager et al. 2023[14] RDI, source: bevacizumab: 87.6%, Prager et al. 2023[14]
Drug administration cost per administration		
IV treatments, commercial/Medicare perspective	$471/$132	PMIC Medical Fees Directory 2023,[18] CMS Physician Fee Schedule 2023[19]
BSC	$0	Assumption§§
Total one-off AE management costs, by treatment, commercial/Medicare perspective		
Fruquintinib	$4,015/$2,308	Calculated¶¶
Regorafenib	$8,181/$4,412	
Trifluridine/tipiracil	$17,110/$8,630	
Trifluridine/tipiracil with bevacizumab	$11,620/$6,125	
BSC	$227/$137	
Disease management cost per 4-week cycle (assumed same for commercial and Medicare perspective)		
Progression-free	$49,925[a]	Neuberger et al. 2023[10]
Post-progression	$59,910[b]	Neuberger et al. 2023,[10] Reyes et al. 2019[20]
Terminal care, one-off costs		
Commercial/Medicare perspective	$22,060/$10,761	Claxton et al. 2020[21] MedPAC Chapter 10: Hospice services (March 2023 Report)[22]

*Costs are expressed as 2023 US dollars; as necessary, costs were inflated to 2023 based on Bureau of Labor Statistics inflation data.[23]
†Calculated as a weighted average based on 2021 US age and sex contribution and SEER age-adjusted incidence rates.[5,6]
‡Calculated as a weighted average based on 2022 Medicare age distribution and SEER age-adjusted incidence.[2,7]
§Calculated from percentage of patients with mCRC at diagnosis (23%) plus the percentage of progressors from earlier stages (38.5% [based on the percentage of patients without metastases at diagnosis (77%) × the percentage of patients with localized CRC who develop metastases (50%)]).[2,8]
¶Calculated from patients treated with anti-cancer therapy divided by the total patients in the Flatiron mCRC cohort.[9]
**Calculated from patients with mCRC who progressed to second-line treatment among those who received first-line treatment.[10]
††Calculated from patients with mCRC who progressed to third- or fourth-line treatment among those who received second-line treatment.[10]
‡‡In the base case, treatment duration for fruquintinib was based on Kaplan-Meier data through month 19 followed by an exponential fit; treatment duration for regorafenib, trifluridine/tipiracil, and trifluridine/tipiracil with bevacizumab was an exponential function based on median treatment duration. For subsequent treatments, treatment duration was estimated based on median treatment duration.
§§Costs for BSC treatment were assumed to be captured in disease management costs.
¶¶Calculated by multiplying the cost per AE[24] by the percentage of patients experiencing each AE and totaling them for each treatment.
[a]Calculated from the per patient per month costs for inpatient, emergency department visit, outpatient, and pharmacy of patients with mCRC receiving third line and fourth-line or later therapies reported in Neuberger et al. 2023.[10] These costs were converted to costs per four-week cycle.
[b]Calculated from pre-progression costs based on Neuberger et al. 2023[10] multiplied by 1.2 based on an estimate of the increase in costs following progression based on Reyes et al. 2019.[20]
AE, adverse event; ASP, average sales price; BSC, best supportive care; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; IV, intravenous; mCRC, metastatic CRC; MedPac, Medicare payment advisory commission; NCI, National Cancer Institute; PMIC, Practice Management Information Corporation; RDI, relative dose intensity; SEER, Surveillance, Epidemiology, and End Results; US, United States.

Results

- In the base case, over a five-year time horizon, the model estimated 194 people to be eligible to receive treatment for mCRC in a commercial health plan of one million members (**Table 3**)
- The total five-year incremental budget impact across the reference and new scenario was $4,077,373 (**Table 4**). Expressed in per member cost, the five-year budget impact of fruquintinib was estimated to be $0.07 per member per month (PMPM) and $0.82 per member per year (PMPY). The total annual budget impact of fruquintinib increased from $627,630 in year 1 to $874,120 in year 3, after which it stayed stable through year 5 (**Table 4**)
- Over the entire time horizon of the model, the incremental costs for drug acquisition and disease management in the new scenario (with fruquintinib) were the key drivers of the budget impact. These costs were partially offset by the savings due to treatment administration, AE management, subsequent therapy, and terminal care (**Table 1, Summary Panel**). The increase in disease management costs in the new market mix scenario reflects that the addition of fruquintinib contributes to patients having prolonged PFS and OS compared with patients in the reference market mix scenario without fruquintinib
- Scenario analyses and one-way sensitivity analyses showed that the budget impact PMPM after the introduction of fruquintinib was found to be low in all scenarios, ranging from $0.05 to $0.10. In the scenario where the Medicare perspective was adopted, the budget impact PMPM was $0.17 and PMPY was $2.10. This was greater than the base case, due to a higher number of patients with CRC eligible for fruquintinib in the Medicare program
- All eligible patients in the US could be treated with an incremental budget of approximately $296 million per year. The annual incremental budget was estimated as the product of PMPY cost and the number of eligible Americans under commercial/Medicare (65.6 million Medicare members – assumed inclusion of 25.4% of all 258.3 million US adults, with the remaining assumed to be Commercial plan members). This is well below the threshold for prescription drugs ($735–$777 million) proposed by the Institute for Clinical and Economic Review (ICER) for 2023–2024[25,26]

Table 3. Number of eligible patients in each scenario: commercial US payer perspective

Patients, n	Reference market mix scenario with fruquintinib		New market mix scenario with fruquintinib	
	Annual number (Year 1–5)*	Total†	Annual number (Year 1–5)*	Total†
Fruquintinib	0	0	10	48
Regorafenib	13	65	10	48
Trifluridine/tipiracil	13	65	10	48
Trifluridine/tipiracil with bevacizumab	13	65	10	48
Total number of patients*	**39**	**194**	**39**	**194**

*It was assumed that in the reference scenario, the market shares were evenly distributed among the relevant comparators for the target population. Additionally, the market shares in the reference and new market mix scenarios were assumed to be constant over time due to a lack of alternative available data.
†Numbers may not sum due to rounding.

Table 4. Incremental costs (new therapy scenario – reference scenario) in the eligible treatment population: N=194

Budget impact outcome, $	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Incremental total cost	627,630	821,160	874,120	879,390	875,073	4,077,373
Incremental total cost per treated member of the beneficiary population per month	1,348	1,764	1,878	1,889	1,880	1,752
Incremental total cost per member of the beneficiary population per month	0.05	0.07	0.07	0.07	0.07	0.07

Conclusions

- Introducing fruquintinib for its approved indication has a limited budget impact from the US payer perspective that is well below the proposed threshold from ICER

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Disclosures

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