Management Costs of Grade 3/4 Adverse Events Associated With Emerging and Existing Systemic Therapies for Metastatic Colorectal Cancer With at Least Two Prior Lines of Therapy in Italy, Portugal, Spain, and the United States

EE670

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Question

What are the management costs by country of grade 3/4 AEs related to fruquintinib, regorafenib, T/T, and T/T + bev for mCRC previously treated with oxaliplatin- and irinotecan-based chemotherapy?

Study design

Grade 3/4 AEs occurring in ≥5% of patients per trial

- **Fruquintinib** FRESCO / FRESCO-2*
- **Regorafenib** CORRECT
- **T/T** RECOURSE / SUNLIGHT*
- **T/T + bev** SUNLIGHT

AE management costs were based on DRG codes from:

- **Ministry of Health database** Italy, Portugal, and Spain
- **Healthcare Cost and Utilization Project** and **Fiscal Year 2023 Medicare Acute Inpatient Prospective Payment System Fee Schedule** USA

AE cost per patient

Cost per event was multiplied by each AE rate for every treatment

Costs inflated to 2023

*Aggregated using weighted average of both trials.

Key take aways

Fruquintinib demonstrates the lowest AE-related cost burden in the US, Italy, Portugal, and Spain compared with regorafenib, T/T, and T/T + bev for mCRC previously treated with oxaliplatin- and irinotecan-based chemotherapy

Results

Figure 1A: AE management costs per patient while on treatment in Italy, Portugal, and Spain

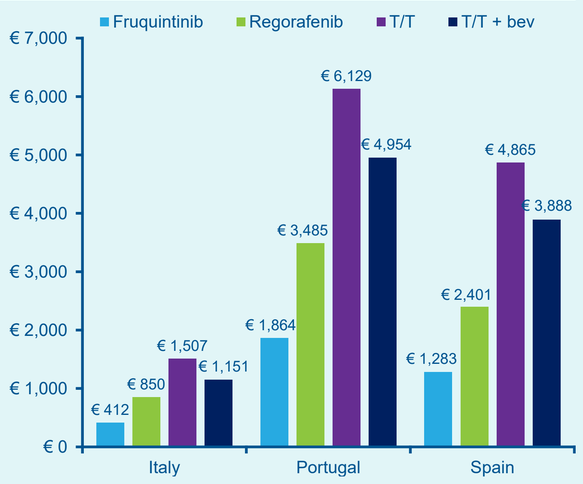
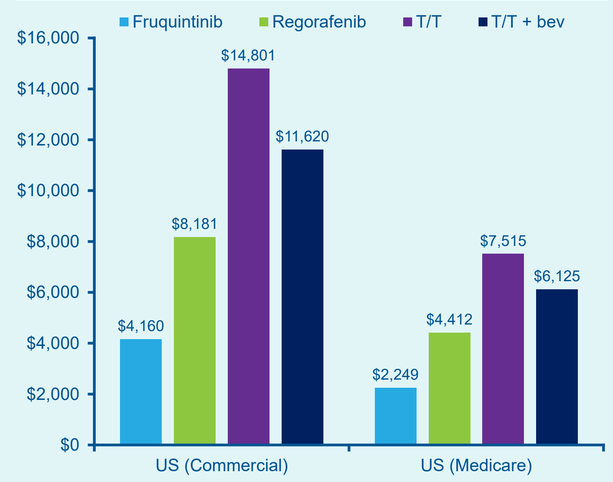


Figure 1B: AE management costs per patient while on treatment in the US



Background

- Colorectal cancer (CRC) is the third-most common cancer type globally and has the second-highest mortality rate of all cancer types[1]
- Between ~20% and ~30% of patients present with metastatic CRC (mCRC) at diagnosis, and up to half of patients with localized CRC eventually develop metastases[2-8]
- Systemic therapies such as fruquintinib, regorafenib, and trifluridine/tipiracil (T/T) have demonstrated survival benefits versus best supportive care (BSC) in patients with mCRC previously treated with oxaliplatin- and irinotecan-based chemotherapy, and T/T + bevacizumab (T/T + bev) has demonstrated survival benefit versus T/T in this population[9-13]
- Despite the available efficacy data, there is limited evidence on the relative safety profiles of these therapies and the adverse event (AE)-related cost burden

Objective

- This study estimates and compares the costs of grade 3/4 AEs related to fruquintinib, regorafenib, T/T, and T/T + bev for mCRC previously treated with oxaliplatin- and irinotecan-based chemotherapy from the national healthcare system perspectives in Italy, Portugal, Spain and from both Commercial and Medicare payer perspectives in the United States (US)

Methods

- Grade 3/4 AEs occurring in ≥5% of patients for any treatment in an individual trial were identified from the publications of the following Phase III randomized clinical trials: FRESCO[11] and FRESCO-2[12] (fruquintinib), CORRECT[9] (regorafenib), RECOURSE[10] and SUNLIGHT[13] (T/T), and SUNLIGHT (T/T + bev)[13]
- AE rates used in the cost analysis for fruquintinib and for T/T were aggregated using the weighted average of number of patients for each AE from FRESCO and FRESCO-2 for fruquintinib and from RECOURSE and SUNLIGHT for T/T
- AE management costs were based on inpatient management diagnosis-related group (DRG) codes (**Table 1**)
  - For Italy,[14] Portugal,[15] and Spain[16] costs were from their respective Ministry of Health public databases
  - For the US, Healthcare Cost and Utilization Project data[17] (Commercial perspective) and the Fiscal Year 2023 Medicare Acute Inpatient Prospective Payment System Fee Schedule[18] were used. Inpatient management Clinical Classifications Software Refined (CCSR) codes and DRG codes were used for the AE management costs from the Commercial and Medicare perspectives, respectively (**Table 1**)
- For all countries, an oncologist visit cost was used for laboratory abnormalities
- All costs were inflated to 2023
- The cost per event was multiplied by each AE rate for every treatment to derive the respective management cost per patient while receiving therapy
- The median treatment duration for each treatment was: fruquintinib 3.68 and 3.06 months in FRESCO[11] and FRESCO-2[12], respectively; regorafenib 1.70 months in CORRECT[9]; T/T 1.54 and 2.10 months in RECOURSE[10] and SUNLIGHT[13], respectively; and T/T + bev 5.00 months in SUNLIGHT[13]

Table 1. AE management costs (per event) by country

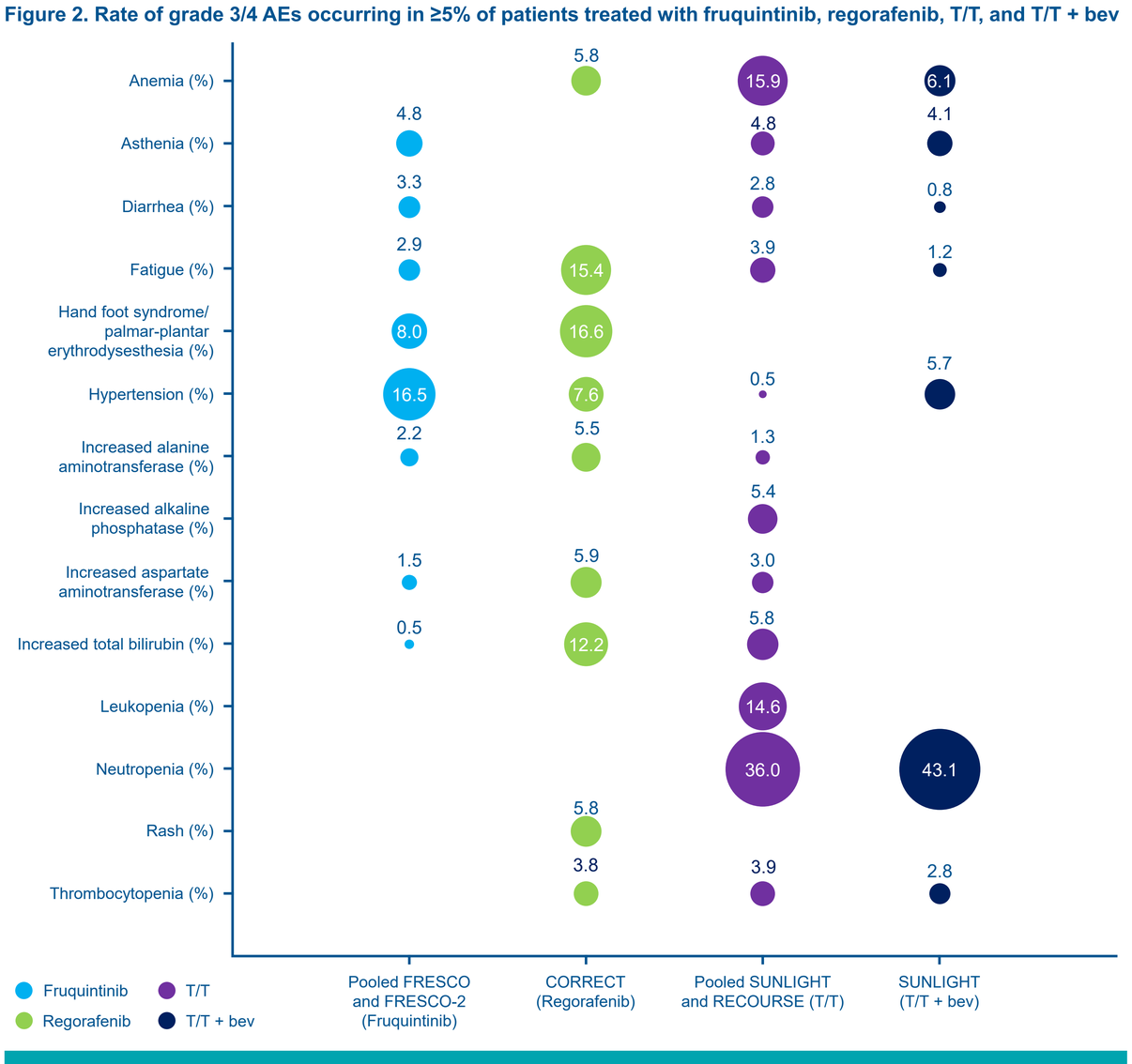
	Italy[14]*		Portugal[15]		Spain[16]†		US			
							Medicare[18]		*Commercial[17]*	
	DRG Code	Mean Cost	DRG Code	Mean Cost	DRG Code	Mean Cost	DRG Code	Mean Cost	CCSR Code	Mean Cost
Hypertension	134	€1,037	199	€5,247	199	€3,700	304-305	$6,000.46	CIR008	$9,925.65
Asthenia	464	€1,883	663	€4,898	861	€3,655	947-948	$6,109.69	SYM007	$14,586.58
Hand foot syndrome/palmar-plantar erythrodysesthesia	284	€784	811	€5,930	385	€3,557	606-607	$7,231.39	SKN002	$13,658.63
Neutropenia	399	€1,836	660	€8,856	660	€7,019	808-810	$10,779.63	BLD007	$20,350.23
Leukopenia	399	€1,836	660	€8,856	660	€7,019	814-816	$9,135.48	BLD007	$20,350.23
Anemia	395	€1,806	663	€4,898	663	€4,344	811-812	$7,571.50	BLD003	$14,587.64
Thrombocytopenia	397	€2,960	661	€8,722	661	€5,975	813	$10,735.85	BLD006	$19,497.50
Increased total bilirubin	206	€14	N/A	€118	283	€63	441-443	$128.43	END016	$221.00
Increased alkaline phosphatase	464	€14	N/A	€118	861	€63	947-948	$128.43	SYM017	$221.00
Fatigue‡	464	€1,883	663	€4,898	861	€3,655	947-948	$6,109.69	SYM007	$14,586.58
Rash	284	€784	811	€5,930	385	€3,557	606-607	$7,231.39	SYM014	$8,829.28
Increased alanine aminotransferase	464	€14	N/A	€118	861	€63	947-948	$128.43	SYM017	$221.00
Increased aspartate aminotransferase	464	€14	N/A	€118	861	€63	947-948	$128.43	SYM017	$221.00
Diarrhea	183	€1,033	249	€4,391	249	€3,241	391-392	$6,319.82	SYM006	$9,286.89

*Costs for 2013 have been inflated to 2023 costs using inflation factor of 1.0773. †Costs for 2021 have been inflated to 2023 costs using inflation factor of 1.0159.
‡The management cost associated with Fatigue was assumed to be the same as Asthenia for Italy, Spain, and the US. Note: DRG codes vary by country due to differences in the systems/versions used as well as country-specific adaptations.
N/A, not applicable.

Results

- Grade 3/4 AEs occurring in ≥5% for any treatment included: anemia, asthenia, diarrhea, fatigue, hand foot syndrome/palmar-plantar erythrodysesthesia, hypertension, leukopenia, neutropenia, rash, thrombocytopenia, and laboratory abnormalities (increased alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, and total bilirubin)
- Rates of grade 3/4 AEs that occurred in ≥5% of patients treated with fruquintinib (aggregated FRESCO and FRESCO-2), regorafenib (CORRECT), T/T (aggregated RECOURSE and SUNLIGHT), or T/T + bev (SUNLIGHT) are presented in **Figure 2**
- AE management costs per patient in the European countries (**Figure 1A, Summary Panel**) were consistently lowest with fruquintinib (€412 to €1,864) and highest with T/T treatment (€1,507 to €6,129)
- AE management costs per patient in the US were also lowest with fruquintinib ($2,249 to $4,160) and highest with T/T treatment ($7,515 to $14,801) from the Commercial and Medicare perspectives (**Figure 1B, Summary Panel**)
- Management of hematologic AEs were the main cost driver for the higher AE management costs and were highest with T/T and T/T + bev compared to the other treatments

Figure 2. Rate of grade 3/4 AEs occurring in ≥5% of patients treated with fruquintinib, regorafenib, T/T, and T/T + bev



Limitations

- These analyses were based on AE rates reported in randomized clinical trials, which may differ from rates and/or number of events per patient that may occur in real clinical practice

Conclusions

- Fruquintinib demonstrates lower costs associated with the management of grade 3/4 AEs versus regorafenib, T/T and T/T + bev in the treatment of mCRC previously treated with oxaliplatin- and irinotecan-based chemotherapy in the US, Italy, Portugal, and Spain
- The observed AE management cost benefits for fruquintinib are driven by lower rates of grade 3/4 AEs compared with regorafenib, T/T, and T/T + bev
- The cost of managing grade 3/4 hematologic AEs was a key driver. These events were most frequently reported with T/T and T/T + bev

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