Cost-effectiveness analysis of regorafenib versus FTD-TPI + bevacizumab in patients with metastatic colorectal cancer from the perspective of the Brazilian supplementary health system

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Background & Objectives

Metastatic colorectal cancer (mCRC) is one of the leading causes of cancer mortality in Brazil.[1] With rising healthcare costs and the increasing burden of cancer treatment, economic evaluations are critical to guide resource allocation. In this context, the following study evaluates the cost-effectiveness of regorafenib compared to trifluridine-tipiracil (FTD-TPI) + bevacizumab (beva) in this patient population.

The objective of this analyses was to assess the cost-effectiveness of regorafenib versus FTD-TPI + bevacizumab in mCRC patients, from the perspective of the Brazilian supplementary health system, aiming to provide evidence on the most cost-efficient option to inform policy decisions and enhance the sustainability of cancer care in the Brazilian supplementary health system.

Methods

A partitioned survival model with a 10-year time horizon was developed, with three health states: pre-progression, post-progression, and death.

Outcomes analyzed included life years (LY) and quality-adjusted life years (QALY).

Probabilistic sensitivity analyses (PSA) and deterministic sensitivity analyses (DSA) were conducted to assess uncertainties.

Model inputs

Data from the prospective observational OSERO study (Chida A et al. 2024)[2], which provided progression-free survival (PFS) and overall survival (OS) data for regorafenib and FTD-TPI + bevacizumab, were used to extrapolate survival curves.

The proportion of patients in each health state was estimated by extrapolating the Kaplan-Meier curves of OS and PFS using R version 4.4.1.

The treatment duration was considered up to disease progression, based on the PFS curves of regorafenib and FTD-TPI + bevacizumab.

Utility data were derived from the pooled analysis submitted to NICE in the appraisal of FTD-TPI + bevacizumab (TA1008).[3]

Costs included medications based on the manufacturing list price, with taxes applied equally to all drugs and used the lowest-priced option available for bevacizumab. Additionally, costs for adverse event management and disease monitoring were derived from the economic model of FTD-TPI submitted to the Brazilian supplementary health agency.[4]

Table 1. Manufacturing list price including 18% ICMS taxes

Drug	Package presentation	Price*
Regorafenib	84 tablets, 40mg	BRL 20,066.54
Trifluridine-tipiracil	60 tablets, 20mg + 8.19mg	BRL 17,856.26
Bevacizumab**	4ml solution containing 25 mg/ml	BRL 657.40

Source: manufacturing list price with 18% tax of November/2025, CMED; Label references considered: Regorafenib (Stivarga®); Trifluridine-tipiracil (Lonsurf®); Bevacizumab (Mvasi®; similar)
*Regorafenib and bevacizumab are exempt from taxes under CMED agreement 162/94; for the purpose of analysis, taxes were applied equally to all treatments in the base-case analysis.[5]
**To calculate the cycle cost with bevacizumab, a cost without wastage was considered, taking into account a patient with an average weight of 66.85kg, same weight used in the ANS submission.
ICMS (Tax on the Circulation of Goods and Services / *imposto sobre Circulação de Mercadorias e Serviços)*

Results

Figure 1. Costs per cycle within health states

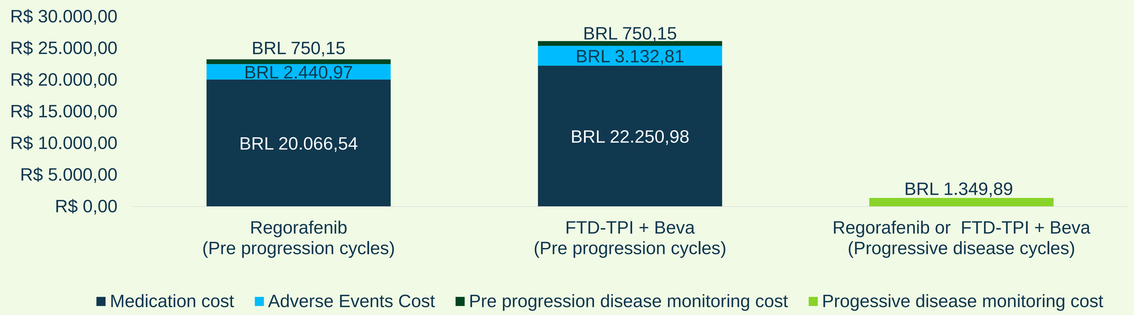
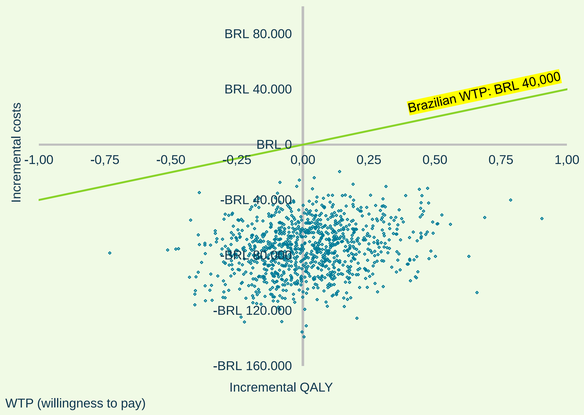


Table 2. Cost-effectiveness results

Treatment	Total cost (BRL)	LYG	QALY	Δ Cost	Δ LYG	Δ QALY
Regorafenib	67,921.58	1.033	0.719	-	-	-
FTD-TPI + Beva	142,064.33	0.983	0.702	-74,142.75	0.050	0.016
Regorafenib vs	**ICER/LYG**	**ICER/QALY**	**Conclusion**			
FTD-TPI + Beva	-1,478,154	-4,556,326	**Regorafenib dominant**			

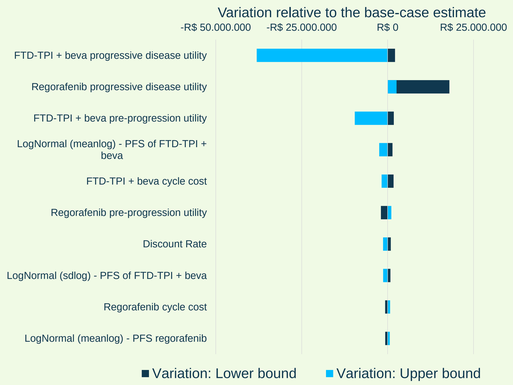
FTD-TPI (trifluridine tipiracil); Beva (bevacizumab); LYG (Life Years Gained); QALY (Quality Adjusted Life Years); ICER (Incremental Cost-Effectiveness Ratio)

Figure 2. Probabilistic sensitivity analysis



WTP (willingness to pay)

Figure 3. One-way sensitivity analysis



Regorafenib had a total cost of BRL 67,921.57 and generated 0.719 QALY, while the combination of FTD-TPI + bevacizumab had a total cost of BRL 142,064.33 and produced 0.702 QALY. **Regorafenib was the dominant treatment** compared to FTD-TPI + bevacizumab, with a negative incremental cost of BRL -4,556,326.82 and an incremental benefit of 0.016 QALY, **indicating that regorafenib offers more QALYs with less costs.**

Sensitivity analyses showed that the utility values for PFS were the most sensitive parameters in the model. The PSA showed that **all iterations were less costly for regorafenib**, though the effectiveness varied. Additionally, **52% of the iterations demonstrated regorafenib as dominant** preference over FTD/TPI + bevacizumab. Considering a willingness to pay (WTP) threshold of one reference value established by the Brazilian Ministry of Health, **100% of the iterations were cost-effective for the regorafenib treatment.**

Conclusions

Regorafenib demonstrated to be a dominant alternative to FTD-TPI plus bevacizumab for patients with mCRC in Brazil.

Additionally, **several factors may influence the outcomes** of this cost-effectiveness analysis, such as the **baseline characteristics** of the population, the potential benefits of the **ReDOS regimen**, and **tax exemptions**, which apply to regorafenib and bevavizumab but not to FTD-TPI as seen in the CMED agreement 162/94.[5-7]

References

1. INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA SILVA (INCA). Estimativa 2023: Incidência de Câncer no Brasil. Rio de Janeiro: INCA, 2022. 160 p. ISBN 978-65-88517-10-9 (Online)
2. Chida, A., et al. Prospective observational study investigating the impact of treatment sequence using regorafenib and FTD/TPI for metastatic colorectal cancer on overall survival (OSERO Study). Poster presentation at ASCO Gastrointestinal Cancers Symposium 2024.
3. National Institute for Health and Care Excellence (NICE). Trifluridine–tipiracil with bevacizumab for treating metastatic colorectal cancer after 2 systemic treatments. Technology appraisal guidance TA1008, published 25 September 2024. Available at: https://www.nice.org.uk/guidance/ta1008.
4. AGÊNCIA NACIONAL DE SAÚDE SUPLEMENTAR (ANS). Consulta Pública nº 94. Documentos de apoio da UAT 09: Trifluridina + Cloridrato de Tipiracila para Câncer Colorretal Metastático. Disponível em: https://www.gov.br/ans/pt-br/acesso-a-informacao/participacao-da-sociedade/consultas-publicas/consultas-publicas-encerradas/consulta-publica-cp-no-94-tem-como-objetivo-receber-contribuicoes-para-a-revisao-lista-cobertura-planos-saude
5. CONSELHO NACIONAL DE POLÍTICA FAZENDÁRIA (CONFAZ). ICMS Agreement No. 162, December 7, 1994. Authorizes States and the Federal District to grant ICMS exemption on operations with cancer treatment medications. Published in the Official Federal Gazette on December 14, 1994. Available at: https://www.confaz.fazenda.gov.br/legislacao/convenios/1994/CV162_94
6. Kim RD, et al. Real-world study of metastatic colorectal cancer patients with long-term response to regorafenib in the USA: An updated analysis. Poster presentation at ESMO Gastrointestinal Cancers 2024; Poster 82P
7. Bekaii-Saab et al. Regorafenib dose-optimisation in patients with refractory metastatic colorectal cancer (ReDOS): a randomised, multicentre, open-label, phase 2 study. Lancet Oncol. 2019 Aug;20(8):1070-1082. doi: 10.1016/S1470-2045(19)30272-4. Epub 2019 Jun 28. PMID: 31262657; PMCID: PMC9187307.

Contact the author for more detailed information about the data/results