

Value-Based Assessment of Trifluridine/Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer

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J. Henrique¹, P. Amorim¹, A. António¹, M. Silva², J. Rocha², J. Félix², S. Yahiaoui³
¹Servier Portugal, ²Exigo Consultores, Lisboa, Portugal, ³Servier International, Suresnes, France

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OBJECTIVES

- Metastatic Colorectal Cancer (mCRC) is associated with poor prognosis and 5-Year relative survival under 20%.
- Trifluridine/tipiracil plus bevacizumab is recommended by ESMO, NCCN and ASCO clinical guidelines for third line refractory mCRC.
- We performed a value-based assessment of trifluridine/tipiracil plus bevacizumab in mCRC measuring both clinically meaningful outcomes for patients (OS, QoL, treatment mortality, treatment interruption, and grade 3/4 AEs) and economic implications for public payers.

METHODS

- A long-term semi-Markov partitioned survival model (initially developed by DeltaHat) was adapted to evaluate the cost-effectiveness of trifluridine/tipiracil plus bevacizumab relative to trifluridine/tipiracil alone.
- Efficacy, safety and health state utility values from the SUNLIGHT trial (NCT04737187, [1]) contributed to life years (LY) and quality-adjusted life-years (QALYs) estimation. Health state utility values were mapped from the EQ-5D-5L assessed at SUNLIGHT RCT using the Portuguese tariffs set in Ferreira et al [2].
- Variable informing modelling cohort characteristics, health state utilities and adverse events frequency are presented in table 1.

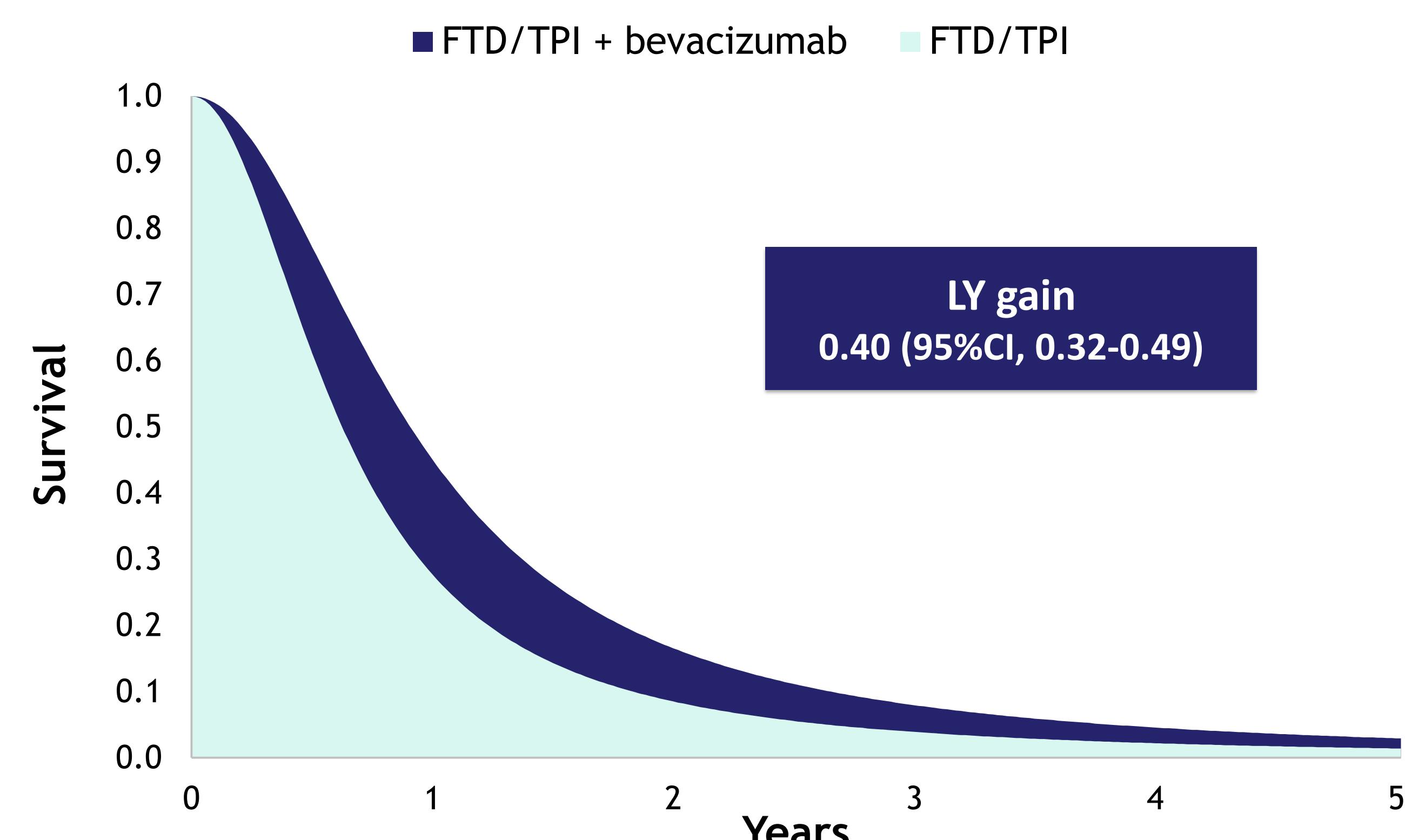
Table 1. Model variables

Parameters	FTD-TPI plus Bevacizumab	FTD-TPI	Data source
Cohort characteristics			
Age (mean)	61.7 Yrs		
Females (%)	48.0%		SUNLIGHT RCT [1]
BSA (m ²)	1.82		
Weight (Kg)	74		
Utilities			
Progression-free	0.867	0.834	SUNLIGHT RCT [1]
Progression	0.809	0.777	and Ferreira et al [2]
Adverse events (Grade 3 or 4)			
Neutropenia	43.1%	32.1%	
Anaemia	6.1%	11.0%	
Hypertension	5.7%	1.2%	
Neutrophil count decreased	8.9%	5.3%	

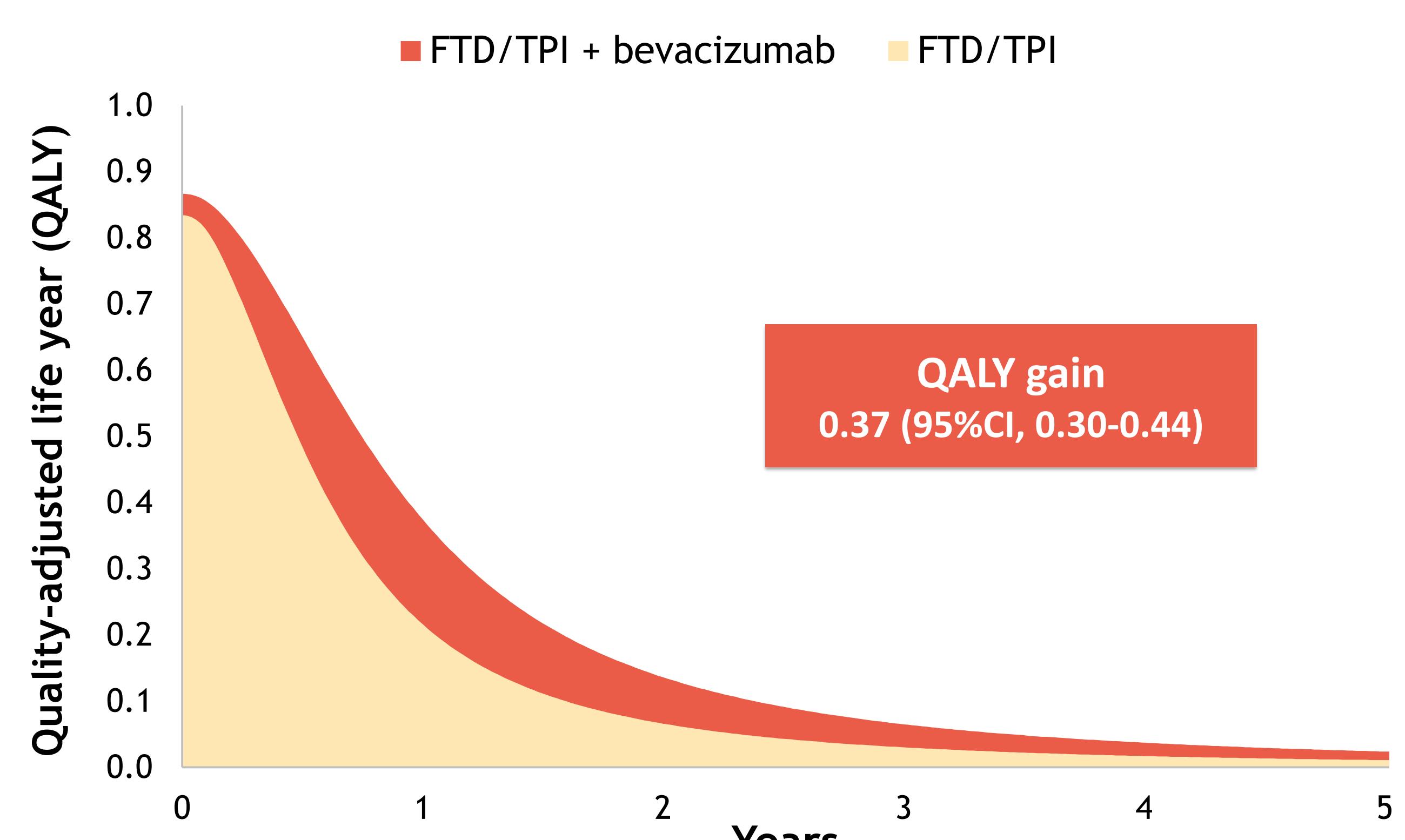
- Adverse events disutilities were from Sullivan et al [3]: Neutropenia or neutrophil count decreased (-0.090); Anaemia (-0.021); Hypertension (-0.025).
- Only direct medical costs related to medicines, adverse events, health resource use, subsequent treatments and terminal care were considered.
- The basket of subsequent treatment medicines was derived from SUNLIGHT RCT, by treatment arm which included: capecitabine, fluorouracil, folinic acid plus oxaliplatin (FOLFOX), bevacizumab plus FOLFOX, fluorouracil, folinic acid plus irinotecan (FOLFIRI), FTD/TPI, capecitabine, capecitabine plus oxaliplatin, and bevacizumab plus capecitabine.
- Health resource utilization costs: Medical oncologist visit (€118); GP visit (€77.5); nurse specialist visit (€16); home care visit (€42); CT scan (€84.5).
- Adverse events costs: Neutropenia or neutrophil count decreased (€3,405); Anaemia (€3,405); Hypertension (€3,789).
- End-of-life cost (€4,150).
- Modelling robustness was checked with Monte-Carlo probabilistic sensitivity analyses assuming 5% significance level. We adopt the public NHS perspective.
- The economic model used a 15-year time horizon.

RESULTS

- Use of trifluridine/tipiracil plus bevacizumab as third-line treatment for mCRC resulted in mean overall survival of 1.35LY (95%CI, 1.29-1.42) and incremental benefit of 0.40LY (95%CI, 0.32-0.49) over monotherapy with trifluridine/tipiracil (Figure 1).



- QALYs were substantially improved with trifluridine/tipiracil plus bevacizumab 1.12QALY vs 0.75QALY (difference 0.37QALY: 95%CI, 0.30-0.44) (Figure 2).
- These outcomes were considered of major therapeutic added value by the Portuguese HTA body.



- On average, total costs were 56.3% (95%CI, 52.3%-59.7%) higher with trifluridine/tipiracil plus bevacizumab and were mainly driven by longer treatment duration (5.0 vs. 2.5 months).
- The mean incremental cost-effectiveness ratio (undiscounted) of trifluridine/tipiracil plus bevacizumab (biosimilar: 94.5% of market share) was €24,012/QALY, with 96.7% probability of being cost-effective below €30,000/QALY threshold.

CONCLUSION

- Trifluridine/tipiracil plus bevacizumab as third-line treatment for metastatic colorectal cancer improves life expectancy and quality of life while providing good value for money from the Portuguese public payers' perspective.

[1]. Prager GW, Taib J, Fakih M, Ciardiello F, Van Cutsem E, Elez E, Cruz FM, Wyrwicz L, Stroyakovskiy D, Pápai Z, Poureau PG, Liposits G, Cremolini C, Bondarenko I, Modest DP, Benhadji KA, Amella N, Leger C, Vidot L, Tabernero J; SUNLIGHT Investigators. Trifluridine-Tipiracil and Bevacizumab in Refractory Metastatic Colorectal Cancer. *N Engl J Med*. 2023 May 4;388(18):1657-1667.

[2]. Ferreira PL, Antunes P, Ferreira LN, Pereira LN, Ramos-Goñi JM. A hybrid modelling approach for eliciting health state preferences: the Portuguese EQ-5D-5L value set. *Qual Life Res*. 2019 Dec;28(12):3163-3175.

[3]. Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. *Med Decis Making*. 2006 Jul-Aug;26(4):410-20.