

COST-EFFECTIVENESS OF TOFACITINIB FOR THE TREATMENT OF MODERATE-TO-SEVERE ACTIVE ULCERATIVE COLITIS AFTER BIOLOGICAL FAILURE OR INTOLERANCE IN SPAIN

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1 INTRODUCTION

- Ulcerative colitis (UC) is a chronic inflammatory disease which main symptoms are abdominal pain, bloody diarrhoea and alternated periods of remission and relapses¹. UC is known to be a costly disease with great impact on patient's quality of life and productivity².
- Current treatments for moderately-to-severely UC include conventional therapy (such as steroids or thiopurines), immunosuppressant, biological drugs and the more recent oral small molecules such as tofacitinib, a Janus Kinase inhibitor^{1,3}. Surgery is considered the last option¹.
- According to the American College of Gastroenterology clinical guidelines⁴: patients who are primary nonresponders to an anti-TNF should be evaluated and considered for alternative mechanisms of disease control (e.g., in a different class of therapy) rather than cycling to another drug within the anti-TNF class.
- Thus, given the promising spectrum of new emerging therapeutic options, economic evaluations are needed in order to help healthcare systems making informed decisions.

2 OBJETIVE

To evaluate the cost-effectiveness of using tofacitinib for the treatment of moderate-to-severe active ulcerative colitis after failure or intolerance to a first line of biologic treatment, from the Spanish National Health System (NHS) perspective.

3 METHODS

- A panel of experts defined three different scenarios to compare **tofacitinib** vs **adalimumab**, **infliximab** and **vedolizumab** treatments after failure/intolerance to a biologic drug (fig.1).
- A markov model was developped with cycles of **8 weeks** and a lifetime horizon (fig.2).
- Two different treatment periods were considered: **induction** and **maintenance**.



Figure 1: Comparisons made in the model

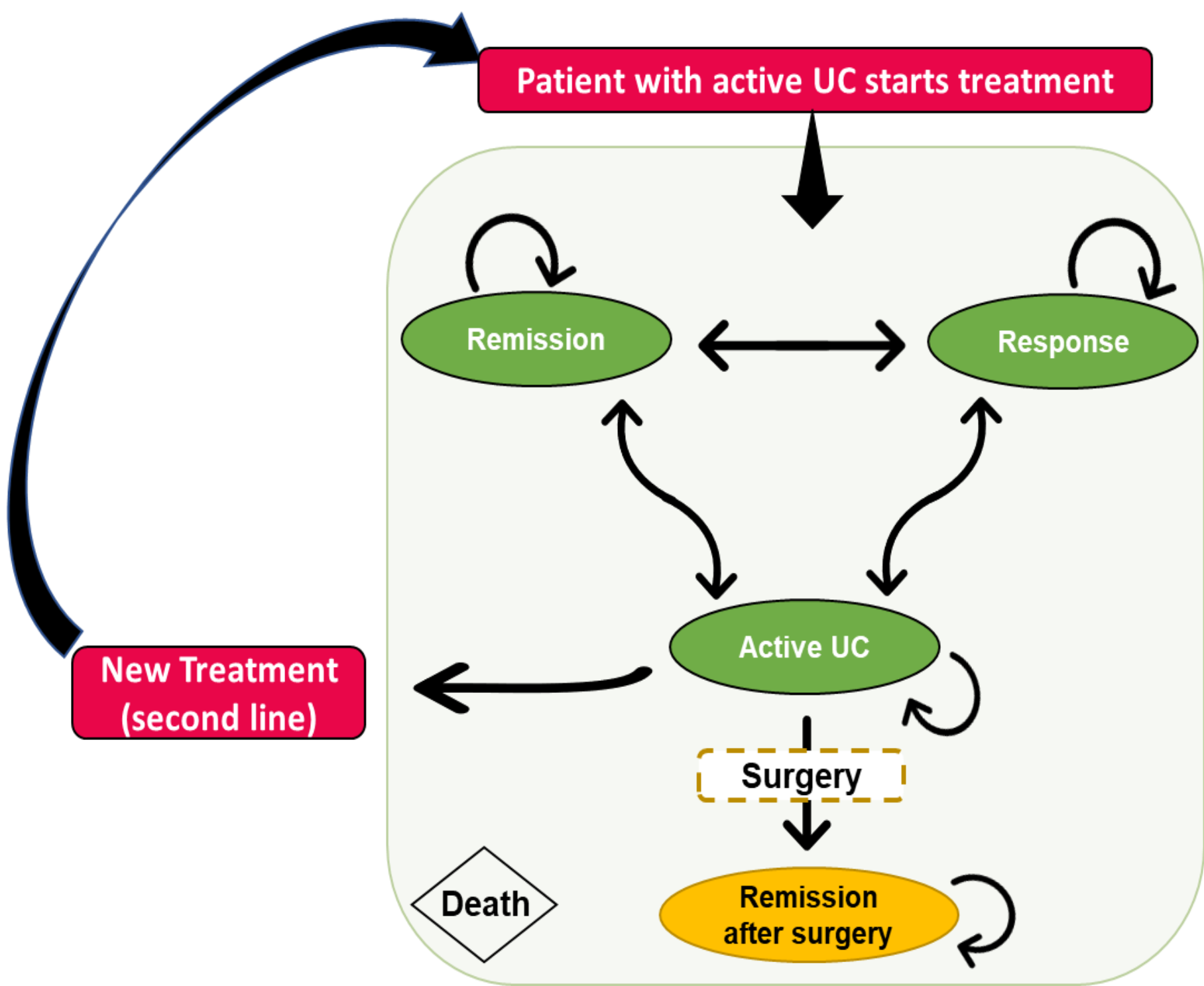


Figure 2: Structure of the model

- A hypothetical cohort of 1,000 patients can shift through 5 different health states, defined according to the Mayo's scale score as (fig.2):
 - Remission** (Mayo score = 0-2; and all subscores ≤1)
 - Response** (decrease in baseline Mayo score of ≥3 and at least a 30%; with a decrease in rectal bleeding subscore of ≥1 point or a value of 0-1)
 - Moderate-to-severe active UC** (Mayo score ≥ 6)
 - Remission after surgery**
 - Death**
- Patients can change to second line treatment: **1)** if they remain with active UC after induction; or **2)** if there is a loss of response under maintenance treatment (patients shift to active UC state again).
- The model considered an annual rate for surgery of 1,44%⁵, with the possibility of post-surgery complications.
- Patient profile was defined based on characteristics of patients included in tofacitinib's OCTAVE induction 1 & 2 clinical trials⁶ (table 1).
- Comparative efficacy data were inferred from a network meta-analysis⁸, where specific analyses for induction and maintenance periods were considered.
- Utilities were obtained from literature^{9,10}.
- Serious adverse events were included: serious infections – upper respiratory tract infections – tuberculosis – malignancies – herpes zoster – acute reaction after infusion – infusion site reactions.

Table 1: Parameters used in the model

Parameter	Value
Baseline patient characteristics	
Mean age (years)	41.2 ⁶
Gender (% male)	59.2% ⁶
Mean weight (Kg)	71.93 ⁷
Variables considered in the model	
Efficacy (Mayo)	NMA ⁸
	Remission: 0.87 ⁹
	Response: 0.76 ⁹
Utilities (EQ-5D)	Active UC: 0.41 ⁹
	Remission after surgery: 0.68 ¹⁰
Mortality	Spanish general population ⁷
Mortality after surgery	1.18% (mean incidence) ¹¹

EQ-5D=Euroqol 5 Dimensions questionnaire; NMA=Network meta-analysis.

4 METHODS Cont'

- Direct medical costs considered in the model were: drug acquisition, drug administration, disease-related costs according to health-state and adverse events^{12,13} (table 2 & 3). Local unitary costs (€, 2019) were applied.
- Acquisition costs were calculated based on public ex-factory prices¹⁵ with mandatory deduction (7,5%)¹⁶ or using reference price when available¹⁷. Dosis per cycle (8 weeks) were estimated with each specific SmPC¹⁸.
- Costs and outcomes were discounted at 3%¹⁹.
- Probabilistic sensitivity analysis were conducted (€25,000/QALY threshold considered)²⁰.

Table 2: Costs used in the model

Parameter	Costs
Active UC	€1,149.84
Remission	€199.53
Response	€426.08
Cost of surgery (procedure)	€26,918.56
Remission after surgery	0-2 years €426.90
	> 2 years €194.38
Serious infection	€5,293.57
Upper respiratory tract infection	€3,737.70
Tuberculosis	€7,682.64
Malignancies	€9,842.51
Herpes zoster	€4,450.39
Infusion related acute AE	€3,462.45
Site infusion reaction	€3,193.77

AE=Adverse events; UC=Ulcerative colitis; SAE=Serious adverse events.

Table 3: Costs used in the model

Therapy	Characteristics	Unitary cost	Cost per induction cycle	Cost per maintenance cycle
Drug costs ^{15,18}	Adalimumab - BSM	2 syringe 40mg	€808.50	€3,233.99
	Infliximab - BSM	1 vial 100mg	€402.21	€4,339.64
	Tofacitinib	56 tablets 5mg	€762.20	
		56 tablets 10mg	€1,524.40	€3,048.80
	Vedolizumab	1 vial 300mg	€3,206.05	€9,618.15
Administration costs ¹³	Adalimumab - BSM	SC	-	€121.84
	Infliximab - BSM	IV	-	€787.86
	Vedolizumab	IV	-	€481.47

BSM=Biosimilar; IV=Intravenous; SAE=Serious adverse events; SC=Subcutaneous

5 RESULTS

- When compared to **infliximab** and **vedolizumab**, **tofacitinib is a dominant treatment option** and generates cost savings (tables 4 & 5).
- When compared to adalimumab, tofacitinib generates small QALY gain with slight incremental costs (table 4) ►► **adalimumab had a lower comparative efficacy⁸ thus increasing treatment discontinuation and thereby reducing acquisition costs.**
- The probability of **tofacitinib of being cost effective was above 70%** in comparison to **infliximab** and **vedolizumab** (table 5).

Table 4: Base case results

Comparison:	1st SCENARIO			2nd SCENARIO			3rd SCENARIO		
	Tofacitinib	Adalimumab	Δ	Tofacitinib	Infliximab	Δ	Tofacitinib	Vedolizumab	Δ
Drug acquisition (€)	8,351.09	5,996.89	2,354.2	8,351.09	8,577.87	-226.78	8,351.09	18,123.27	-9,772.18
Drug administration (€)	0.00	140.58	-140.58	0.00	1,557.31	-1,557.31	0.00	907.22	-907.22
Disease-related costs (€)	152,294.67	153,392.60	-1,097.93	152,294.67	152,634.56	-339.90	152,294.67	152,796.87	-502.20
SAE related costs (€)	261.92	415.92	-154.00	261.92	1,028.84	-766.92	261.92	517.87	-255.95
Total costs (€)	160,907.67	159,945.99	961.68	160,907.67	163,798.58	-2,890.91	160,907.67	172,345.23	-11,437.56
QALY	11.06	10.97	0.091	11.06	11.03	0.028	11.06	11.02	0.042
ICER	€10,567.21/QALY			Tofacitinib is Dominant			Tofacitinib is Dominant		

ICER=Incremental cost-effectiveness ratio; QALY=Quality-adjusted life-years; SAE=Serious adverse events; Δ=Incremental.

Table 5: Summary of base case results

SEQUENCE COMPARISON:	TOFACITINIB VS ADALIMUMAB	TOFACITINIB VS INFlixIMAB	TOFACITINIB VS VEDOLIZUMAB
ΔTotal costs	€961.68	-€2,890.91	-€11,437.56
ΔQALY	0.091	0.028	0.042
Probabilistic Sensitivity Analysis*	59.7%	74.2%	90.6%

*Probability of tofacitinib-containing sequence of being cost-effective considering a €25,000/QALY willingness to pay threshold. QALY=Quality-adjusted life-years; Δ=Incremental.

6 CONCLUSIONS

According to our results, after failure or intolerance to biologic therapy, tofacitinib is a cost-saving therapy for the treatment of moderate-to-severe UC patients with similar QALY gains vs infliximab and vedolizumab; besides being a cost-effective alternative when compared to adalimumab.

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DISCLOSURE

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