

COST-EFFECTIVENESS OF TOFACITINIB FOR THE TREATMENT OF MODERATE-TO-SEVERE ULCERATIVE COLITIS AFTER CONVENTIONAL THERAPY 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.
- Thus, given the broad 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 treating patients with moderate-to-severe ulcerative colitis (UC) after conventional therapy (anti-inflammatory and immunosuppressant) failure or intolerance, from the Spanish National Health System (NHS) perspective.

3 METHODS

- A panel of experts defined three sets of therapeutic sequences consisting on two lines of treatment, where only first line was modified to compare **tofacitinib vs adalimumab, infliximab and vedolizumab** (fig.1).
- A markov model was developed with cycles of **8 weeks** and a lifetime horizon (fig.2). For the model 2 different treatment periods were considered: **induction** and **maintenance**.
- 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%⁴, with the possibility of post-surgery complications.

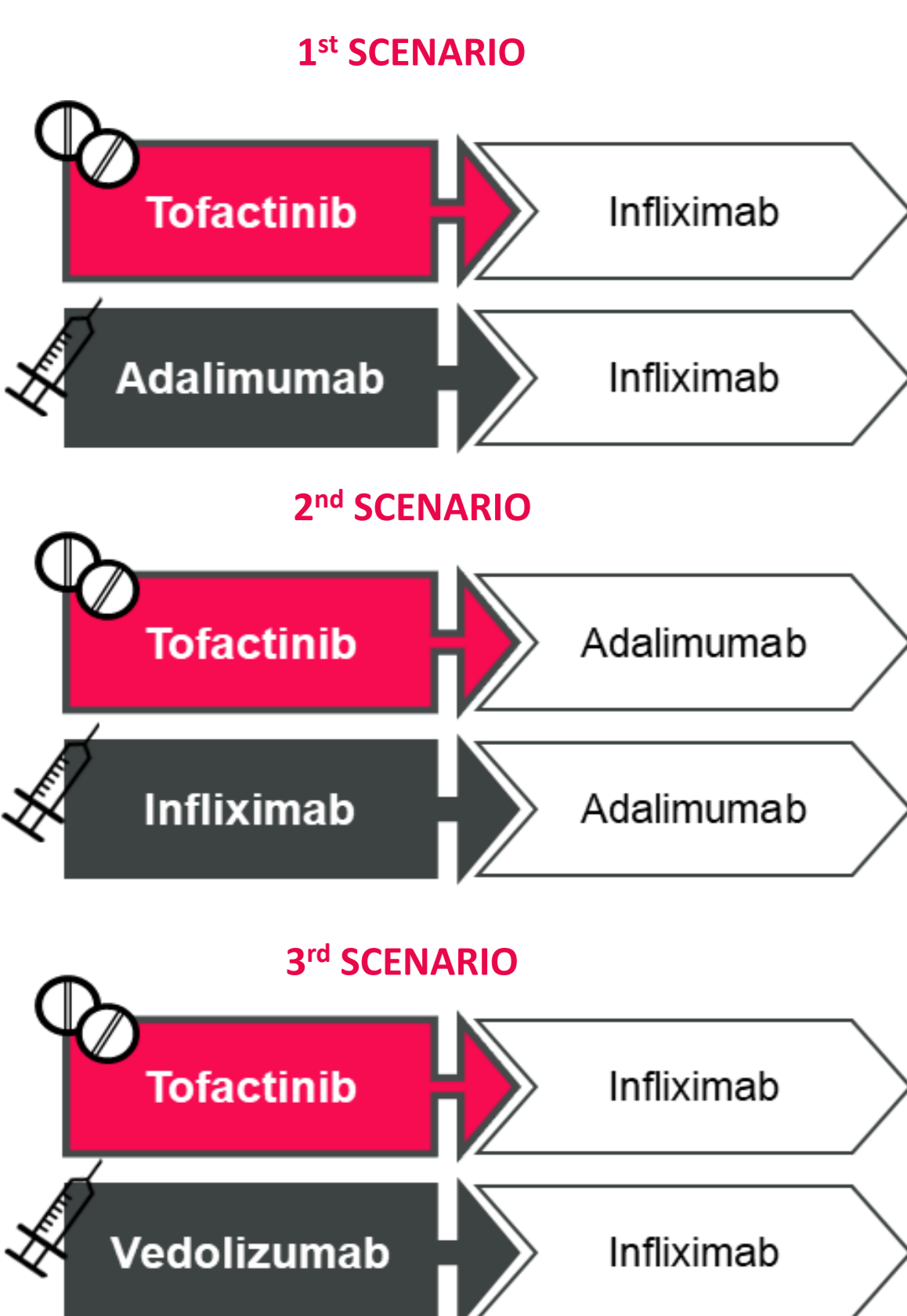


Figure 1: Treatment sequences compared in the model

- Patient profile was defined based on characteristics of patients included in tofacitinib's OCTAVE induction 1 & 2 clinical trials⁵ (table 1).
- Comparative efficacy data were inferred from a network meta-analysis⁷, where specific analyses for induction and maintenance periods were considered.
- Utilities were obtained from literature^{8,9}.
- 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 ⁵
Gender (% male)	59.2% ⁵
Mean weight (Kg)	71.93 ⁶
Variables considered in the model	
Efficacy (Mayo)	NMA ⁷
	Remission: 0.87 ⁸
	Response: 0.76 ⁸
Utilities (EQ-5D)	Active UC: 0.41 ⁸
	Remission after surgery: 0.68 ⁹
Mortality	Spanish general population ⁶
Mortality after surgery	1.18% (mean incidence) ¹⁰

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

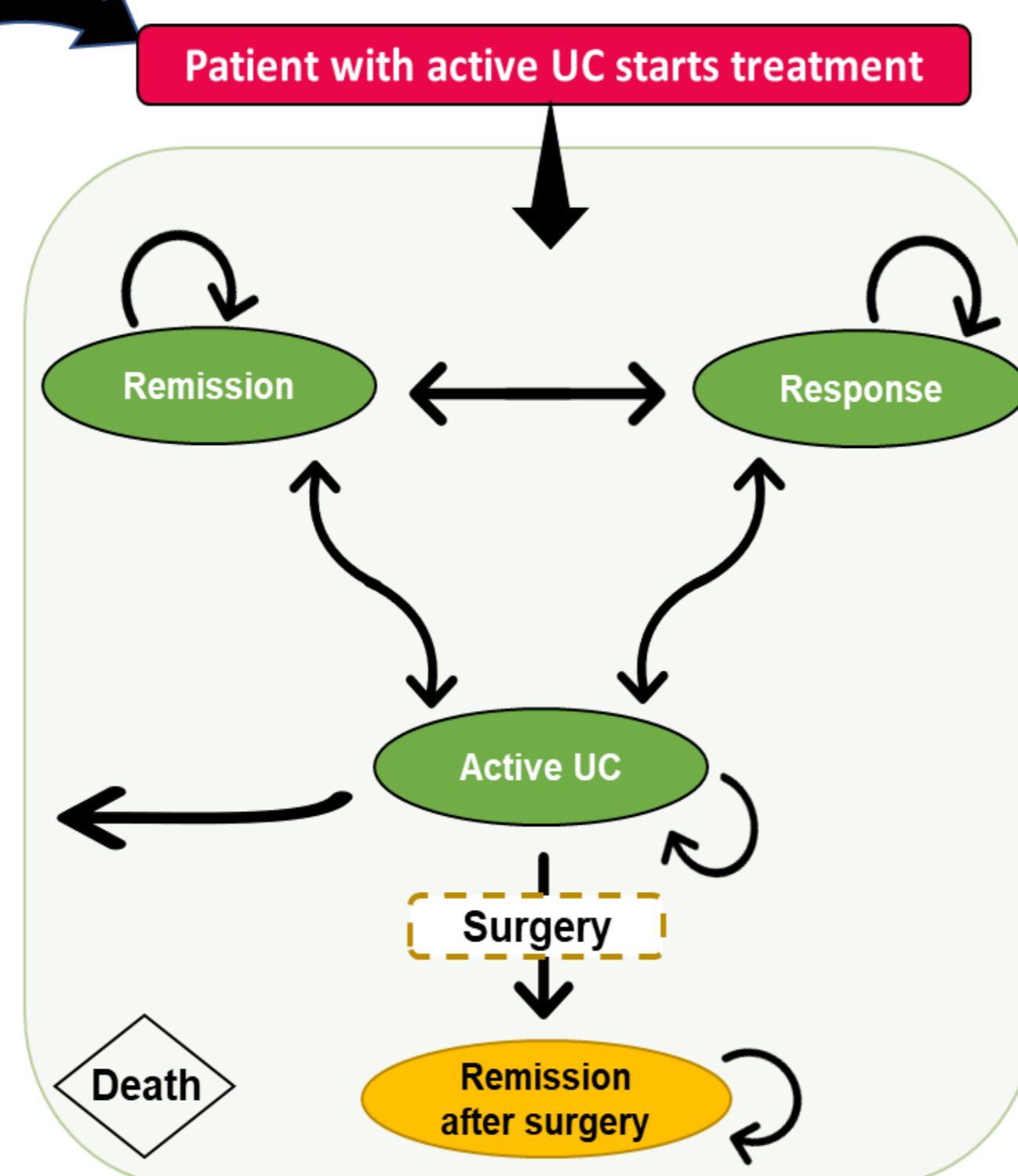


Figure 2: Structure of the model

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 (table 2 & 3). Local unitary costs (€, 2019) were applied^{11,12}.
- Acquisition costs were calculated based on public ex-factory prices¹⁴ with mandatory deduction (7.5%)¹⁵ or using reference price when available¹⁶. Dosis per cycle (8 weeks) were estimated with each specific SmPC¹⁷.
- Costs and outcomes were discounted at 3%¹⁸.
- Probabilistic sensitivity analysis were conducted (€25,000/QALY threshold considered)¹⁹.

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	€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 ^{14,17}	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	€3,048.80
	Vedolizumab	56 tablets 10mg	€1,524.40	€1,524.40
Administration costs ¹²	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 comparing tofacitinib containing-sequence to infliximab and vedolizumab containing-sequences, **tofacitinib was consistently associated with less costs** and comparable QALYs gain (tables 4 & 5).
- Despite a small QALY difference, tofacitinib containing-sequence was dominant vs vedolizumab containing-sequences.
- In comparison to adalimumab containing-sequence, tofacitinib containing-sequence was cost-effective with an ICER of €7,143.82/QALY (table 4).
- The probability of tofacitinib containing-sequence of being **cost-effective is above 60%** when compared to **adalimumab and infliximab, and above 80% in comparison to vedolizumab**.

Table 4: Base case results

Sequence:	1 st SCENARIO			2 nd SCENARIO			3 rd SCENARIO		
	Tofacitinib	Adalimumab	Δ	Tofacitinib	Infliximab	Δ	Tofacitinib	Vedolizumab	Δ
Drug acquisition (€)	35,635.81	31,421.29	4,214.52	29,001.25	31,371.24	-2,369.99	35,635.81	57,250.42	-2,614.61
Drug administration (€)	3,374.21	3,615.78	-241.58	177.12	3,714.29	-3,537.17	3,374.21	5,312.54	-1,938.33
Disease-related costs (€)	141,323.18	143,741.50	-2,418.32	144,519.06	143,717.37	801.69	141,323.18	141,328.32	-5.14
SAE related costs (€)	1,251.26	1,420.66	-169.40	661.88	1,426.86	-764.98	1,251.26	1,508.76	-257.49
Total costs (€)	181,584.46	180,199.23	1,385.23	174,359.31	180,229.76	-5,870.45	181,584.46	205,400.03	-23,815.58
QALY	11.94	11.75	0.194	11.69	11.75	-0.066	11.9439	11.9437	0.00014
ICER	€7,143.82/QALY			Tofacitinib containing sequence is less costly with less effectiveness			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	€1,385.23	-€5,870.45	-€23,815.58
ΔQALY	0.194	-0.066	0.00014
Probabilistic Sensitivity Analysis*	62.20%	65.90%	82.50%

*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 and from the Spanish NHS perspective, for treating moderately-to-severely UC biologic-naïve patients after conventional therapy failure or intolerance, QALY production appears to be equal for all three comparisons. Tofacitinib resulted the most cost-saving therapy in comparison to infliximab and vedolizumab, being also cost-effective when compared to adalimumab.

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DISCLOSURE

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