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 relapses[1]. UC is known to be a costly disease with great impact on patient's quality of life and productivity[2].
- Current treatments for moderately-to-severily 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 option[1].
- According to the American College of Gastroenterology clinical guidelines[4]: 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

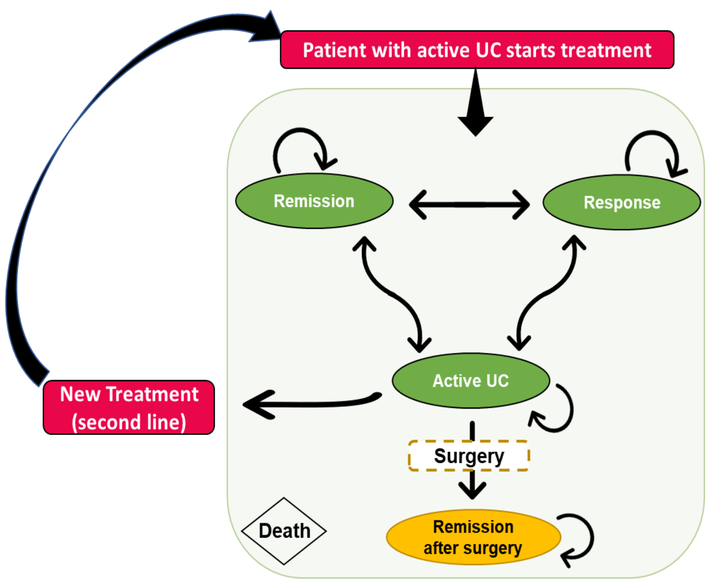

Figure 2: Structure of the model

- 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 trials[6] (table 1).
- Comparative efficacy data were inferred from a network meta-analysis[8], 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]
Utilities (EQ-5D)	Remission: 0.87[9] Response: 0.76[9] 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 prices[15] with mandatory deduction (7,5%)[16] or using reference price when available[17]. Dosis per cycle (8 weeks) were estimated with each specific SmPC[18].
- 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
Costs of health states (cost per cycle)[13,14]	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
SAE (cost per event)[12,13]	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	€1,616.99
	Infliximab - BSM	1 vial 100mg	€402.21	€4,339.64	€1,446.55
	Tofacitinib	56 tablets 5mg	€762.20	€3,048.80	€1,524.40
		56 tablets 10mg	€1,524.40		
	Vedolizumab	1 vial 300mg	€3,206.05	€9,618.15	€3,206.05
Administration costs[13]	Adalimumab - BSM	SC	-	€121.84	€10.97
	Infliximab - BSM	IV	-	€787.86	€262.62
	Vedolizumab	IV	-	€481.47	€160.49

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 efficacy[8] 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

	1st SCENARIO			2nd SCENARIO			3rd SCENARIO		
Comparison:	**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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