COST-EFFECTIVENESS OF TOFACITINIB FOR THE TREATMENT OF MODERATE-TO-SEVERE ULCERATIVE COLITIS AFTER CONVENTIONAL THERAPY IN SPAIN

PGI17

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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].
- 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 developped 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.

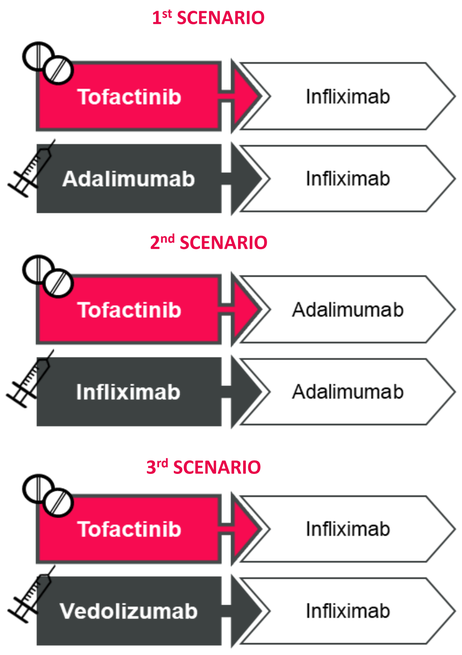

Figure 1: Treatment sequences compared in the model

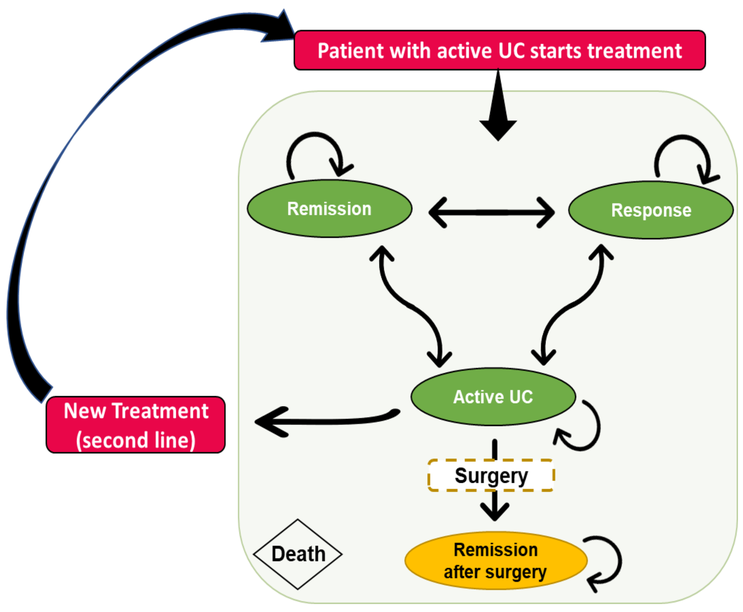

Figure 2: Structure of the model

- Patient profile was defined based on characteristics of patients included in tofacitinib's OCTAVE induction 1 & 2 clinical trials[5] (table 1).
- Comparative efficacy data were inferred from a network meta-analysis[7], 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]
Utilities (EQ-5D)	Remission: 0.87[8] Response: 0.76[8] 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.

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 prices[14] with mandatory deduction (7.5%)[15] or using reference price when available[16]. Dosis per cycle (8 weeks) were estimated with each specific SmPC[17].
- 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
Costs of health states (cost per cycle)[12,13]	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)[11,12]	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	€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[12]	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 comparing tofacitinib containing-sequence to infliximab and vedolizumab containing-sequences, **tofacitinib was consistenly associated with less costs** and comparable QALYs gain (tables 4 & 5).
- Despite a small QALY difference, tofacitinib containing-sequence was dominant vs vedolizumab containaning-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

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