COST-EFFECTIVENESS OF TOFACITINIB IN ACTIVE PSORIATIC ARTHRITIS AFTER CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS TREATMENT IN SPAIN

PSY16

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1 INTRODUCTION

- Currently, a broad range of therapeutic alternatives are available for treating Psoriatic Arthritis (PsA). After failure to conventional Disease-Modifying Antirheumatic Drugs (cDMARD), patients can switch to biological therapies (bDMARD), which include Tumor Necrosis Factor inhibitors (TNFi) and the new emerging treatments like interleukin (IL)-17A inhibitor secukinumab and IL-12/IL-23 inhibitor ustekinumab[1]; and to targeted synthetic DMARDs, like tofacitinib, a new oral Janus Kinase (JAK) inhibitor[2], and apremilast, a phosphodiesterase (PDE)-4 inhibitor[3].
- Thus, given the complex yet promising landscape of PsA treatments, economic evaluations are needed in order to assess their comparable efficiency.

2 OBJETIVE

To evaluate the cost-effectiveness of including **tofacitinib** for the treatment of PsA after failure or intolerance of csDMARD, in comparison to **TNFi biologic** treatments (bDMARD), from the Spanish National Health System (NHS) perspective.

3 METHODS

- A panel of experts defined two sets of therapeutic sequences consisting on six lines of treatment, where only first line was modified to compare **tofacitinib** *vs* **adalimumab** and **infliximab** (fig.1).

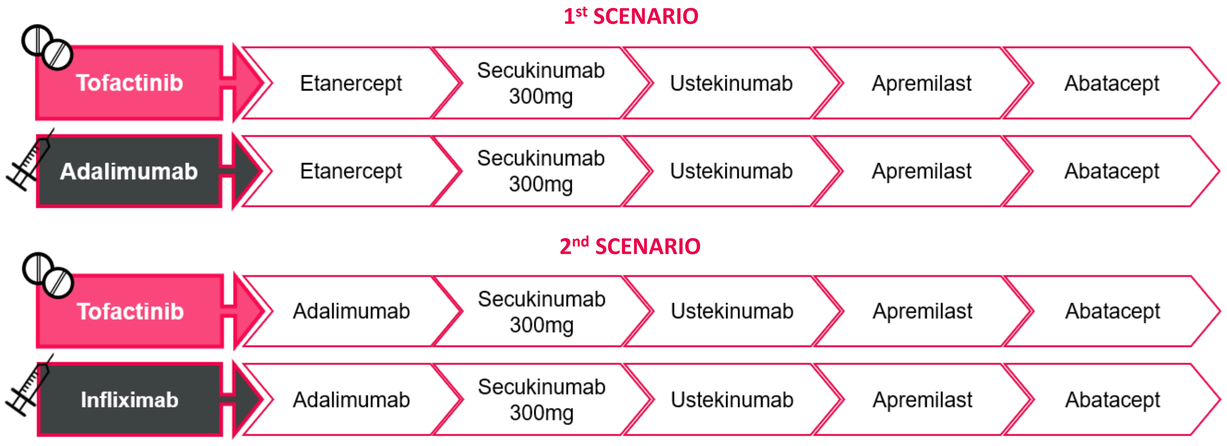

Figure 1: Treatment sequences compared in the model

- A combination of a decision-tree and a Markov model was developed, with cycles of 3 months and a lifetime horizon (fig.2).
- Patients lacking response were considered to switch to next treatment line after 6 months.
- Response was evaluted using 20% and 50% improvement in American College of Rheumatology criteria (ACR20 and ACR50, respectively) as efficacy measure.
- It is considered that 7% of responders will achieve remission[4] ›› in remission, 20% will discontinue treatment[5] ›› of those, 7% will have a new flare and restart treatment with the last therapy they were prescribed[6].

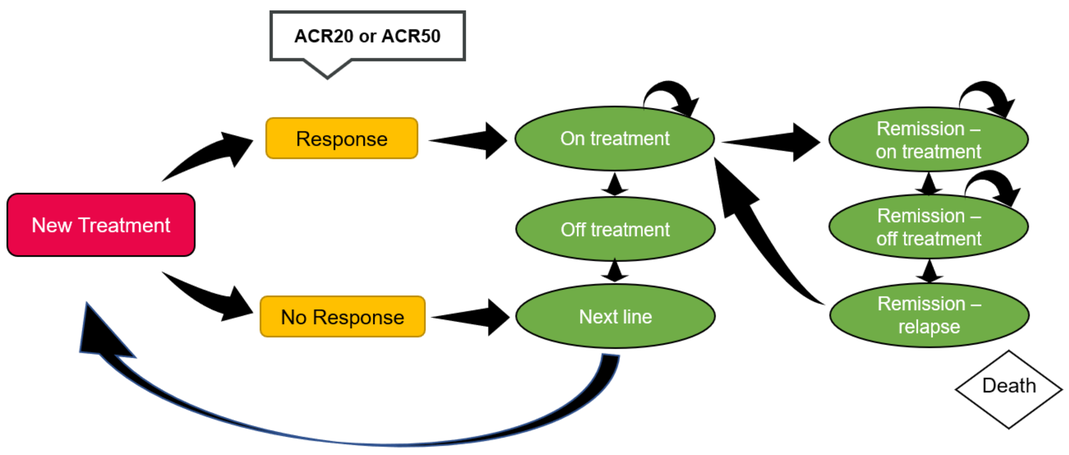

Figure 2: Structure of the model

- Patient profile was defined based on characteristics of patients included in tofacitinib's OPAL-BROADEN[7] clinical trial (table 1).
- Costs and utilities of adverse events (serious infections & cancer) were considered in the model. Probabilities were obtained from randomized clinical trials[7-14].
- Comparative efficacy data were inferred from a network meta-analysis[15] and utilities related to tratment response from a *post-hoc* analysis of tofacitinib's OPAL-BROADEN[7] clinical trial.

Table 1: Parameters used in the model

Parameter	Value
Baseline patient characteristics	
Mean age (years)	47.9[7]
Gender (% female)	53%[7]
Mean weight (Kg)	70*
Variables considered in the model	
Efficacy (ACR20;ACR50)	NMA[15]
Utilities (EQ-5D)	General population[16]; Treatment response[15]; SAE[17,18]
Mortality	Spanish general population[19] (according to age and sex)

**Asumption corresponding to the average Spanish population weihgt. ACR=American College of Rheumatology criteria; EQ-5D=Euroqol 5 Dimensions questionnaire; NMA=Network meta-analysis; SAE=Serious adverse events.*

4 METHODS Cont'

- Direct medical costs considered in the model were: drug acquisition, drug administration, monitoring, disease-related costs (medical visits, phototherapy) and adverse events (table 2). Local unitary costs (€, 2018) were applied.
- Acquisition costs were calculated based on public ex-factory prices[21] with mandatory deduction (7.5%)[22] or using reference price when available[23]. Doses per cycle (3 months) were estimated according to each specific SmPC[24].
- Costs and outcomes were discounted at 3%[25].
- Deterministic and probabilistic sensitivity analysis were conducted (€25,000/QALY threshold considered)[26].

Table 2: Costs used in the model

	Therapy	Unitary cost	Cost of drug induction per cycle (3 months)	Cost of drug maintenance per cycle (3 months)
Drug Costs[21-24]	Abatacept – 750mg	€309.71	€4,335.94	€2,818.36
	Adalimumab (BSM) – 80mg/40mg	€808.50	€2,829.74	€2,627.61
	Apremilast – 30mg	€758.50	€2,451.58	€2,465.13
	Etanercept – 50mg	€760.74	€2,472.73	€2,472.73
	Infliximab (BSM) – 5mg/kg	€439.75	€4,617.38	€2,501.08
	Secukinumab – 300mg	€1,057.38	€7,401.66	€3,172.14
	Tofacitinib – 5mg	**€762.20**	**€2,477.15**	**€2,477.15**
	Ustekinumab – 45mg	€2,541.31	€5,082.62	€2,753.09
Administration costs[20,24]	Abatacept – 750mg	€158.75	€793.75	€515.94
	Infliximab (BSM) – 5mg/kg	€259.76	€779.28	€422.11
Monitoring costs[20,*]	First year (cost per cycle):	€67.74	Second year (cost per cycle):	€32.33
SAE (cost per event)[20]	Serious infection:	€2,848.37	Cancer:	€6,407.95
Disease-related costs[27]	Patient with response to treatment (cost per cycle):	€66.91	Patient not responding to treatment (cost per cycle):	€200.73

**Same costs considered for all the pharmacological therapies included in the model. BSM=Biosimilar; SAE=Serious adverse events.*

5 RESULTS

- When comparing tofacitinib containing-sequence to adalimumab containing-sequence, tofacitinib was consistenly associated with less costs and comparable QALYs gain, both for ACR50 (tables 3 & 4) and ACR20 (table 4) .
- When compared to infliximab containing-sequence, tofacitinib was associated with less costs, specially when using ACR20. On the other hand, infliximab presents slightly more QALYs gain with ACR20 but comparable QALYs gain with ACR50.
- Interestingly, the probability of tofacitinib of being cost-effective increases when using a more restrictive efficacy measure (ACR50 *vs* ACR20).

Table 3: Base case results with ACR50 as efficacy measure

	1rst SCENARIO			2nd SCENARIO		
Sequence:	**Tofacitinib**	**Adalimumab**	**Incremental**	**Tofacitinib**	**Infliximab**	**Incremental**
Drug acquisition	€77,660.23	€80,244.99	-€2,584.76	€77,960.78	€87,869.38	-€9,908.60
Monitoring	€2,751.30	€2,742.43	€8.87	€2,750.93	€2,737.47	€13.46
Disease-related	€14,025.08	€13,917.80	€107.28	€14,025.05	€13,833.79	€191.26
SAE	€1,240.39	€811.53	€428.87	€1,285.61	€744.79	€540.82
Total costs	**€92,925.70**	**€94,974.31**	**-€2,048.61**	**€93,271.44**	**€102,447.95**	**-€9,176.51**
QALY	**15.02**	**15.06**	**-0.039**	**15.02**	**15.09**	**-0.071**
ICER	Tofacitinib containing sequence is less costly with similar effectiveness			Tofacitinib containing sequence is less costly with similar effectiveness		

ACR=American College of Rheumatology criteria; ICER=Incremental cost-effectiveness ratio; QALY=quality-adjusted life-years; SAE=Serious adverse events.

Table 4: Summary of base case results considering ACR20 and ACR50 efficacy measures

SEQUENCE COMPARISON:	TOFACITINIB VS ADALIMUMAB		TOFACITINIB VS INFLIXIMAB	
Efficacy measure	**ACR20**	**ACR50**	**ACR20**	**ACR50**
ΔTotal costs	-€2,036.56	-€2,048.61	-€21,217.92	-€9,176.51
ΔQALY	-0.059	-0.039	-0.393	-0.071
Probabilistic Sensitivity Analysis*	**64.2%**	**74.3%**	**99.6%**	**99.7%**

**Probability of tofacitinib-containing sequence of being cost-effective considering a €25,000/QALY willingness to pay threshold*
ACR=American College of Rheumatology criteria; QALY=quality-adjusted life-years; Δ=incremental.

6 CONCLUSIONS

Tofacitinib efficiency increases when using ACR50 instead of ACR20 as the efficacy outcome. When considering ACR50, tofacitinib is a cost-saving therapeutic option to treat PsA in bDMARD-naïve population in comparison to adalimumab and infliximab, with comparable QALYs gain and a probability of being cost-effective over 70%, from the Spanish NHS perspective.

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DISCLOSURE

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