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Efficiency of treatment sequences containing Tofacitinib for Rheumatoid Arthritis in Spain

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BACKGROUND

- The availability of oral janus kinase inhibitors (JAK), as tofacitinib, has extended the treatment pathways for management of patients with rheumatoid arthritis (RA).[1]
- Tofacitinib is an oral JAK inhibitor approved for patients with moderate to severe RA who have not adequately responded or are intolerant to one or several conventional synthetic disease-modifying antirheumatic drugs (csDMARDs); as well as for its use in monotherapy in case of intolerance to methotrexate (MTX) or when treatment with MTX proves inadequate.[2]

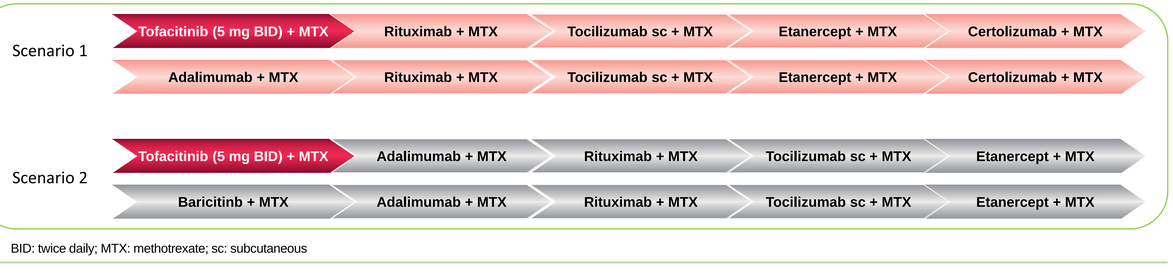
OBJECTIVE

- To assess the cost-effectiveness of treatment sequences initiated with tofacitinib as second-line treatment compared to treatment sequences containing standard biological-therapies in patients with moderate to severe RA after failure of csDMARDs, who did not achieve an adequate response or who are intolerant to said therapy, from the perspective of the Spanish National Health System.

METHODS

- A patient-level microsimulation model was used to compare the lifetime cost and quality-adjusted life-years (QALY) for treatment sequences initiating with tofacitinib (5 mg twice daily) followed by biological therapies versus sequences of biological treatments excluding tofacitinib. The sequences were selected by a panel of experts based on clinical practice in Spain. Concomitant treatment with MTX was considered along all the therapies in the treatment sequences.[3] (Figure 1).
- Model parameters included age, weight, initial Health Assessment Questionnaire (HAQ) score and clinical response to short and long treatment. Serious adverse event (SAE) information derived from literature.[4]

Figure 1. Treatment sequences



BID: twice daily; MTX: methotrexate; sc: subcutaneous

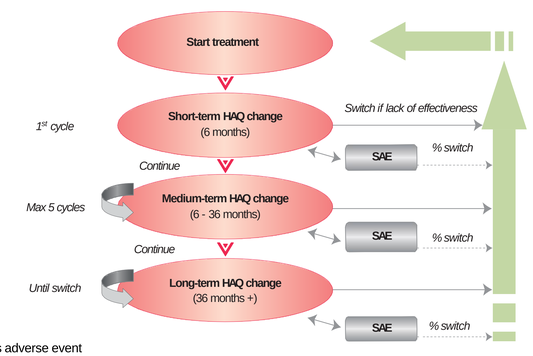
- Profile of each individual patient of the total cohort assessed was defined based on characteristics of RA patients from a national registry[5,6], to assign age, weight, duration of RA and starting HAQ value. (Table 1)
- HAQ score change for each 6-month cycle reflected the efficacy of therapies which were established for 3 intervals: short-term (initial 6-month period), medium-term (6-36 months) and long-term (>36 months from treatment initiation) [7]. (Figure 2)
- Source for efficacy inputs were mixed-treatment comparison (for first 6 months)[8] and long-term extension trials (for later periods).

Table 1. Baseline patients characteristics

Parameter	Value
Initial HAQ score	1.45[6]
Age: mean (SD) (years)	47.7 (16.3)[5]
Gender (% males)	39.6%[5]
Weight: mean (kg)	72.02 (>45 years)[9]
RA duration at beginning of simulation (years)	6.2 [95%CI: 2.2-12.8][5]

HAQ: Health Assessment Questionnaire; SD: standard deviation; RA: rheumatoid arthritis; CI: confidence interval

Figure 2. Model structure



HAQ: Health Assessment Questionnaire; SAE: serious adverse event

METHODS

- Health-related quality of life was directly associated with patient HAQ score. Utilities were derived by mapping HAQ to EQ-5D and HUI-3 scores obtained from a Spanish patient data-set.[10]
- Occurrence of related SAE (represented as serious infections) was applied in each cycle, with the consequent decrement (0.157 for a 4-week period)[10] of the utility.
- Disease progression[13] and SAE management (€5,871.08).[13]
- Total cost (€, 2018) estimation included:
  - Acquisition cost which were calculated based on public ex-factory prices[12] with mandatory deduction applied or reference price, following Summary of product characteristics (SmPC) for each drug. (Table 2)
  - Administration cost associated to parenteral drugs: €252.42 (hospital day required for intravenous infusion)[14] and €27.10 (for education related to subcutaneous drugs)[14], disease progression and SAE management costs.
- Probabilistic sensitivy analyses (PSA) were also performed.
- A 3% annual discount rate was applied to costs and outcomes.[15]

Table 2. Pharmaceutical costs

Therapy	Number of administrations per 6-month period		Unitary cost (ex factory Price) [11]	Drug cost per 6-month cycle (in combination with MTX)
	Initial 6-month period	Subsecuent 6-month period		
Adalimumab- 40 mg	13	13	€404.25**	€5,255.37
Baricitinib- 4 mg	182	182	€31.08	€5,672.24
Certolizumab- 200 mg	13	13	€438.45	€5,699.99
Etanercept- 50 mg	26	26	€169.07*	€4,395.96
Rituximab- 500 mg	1.33	1.33	€970.65**	€1,294.34
Tocilizumab- 162 mg	26	26	€225.98	€5,875.62
Tofacitinib- 5 mg	365	365	€13.61	€4,968.05
Methotrexate- 2.5 mg	26	26	€0.05	-

* Reference price; ** Lowest biosimilar price

RESULTS

- The base case results showed that sequences initiating with tofacitinib provided greater outcomes than the correspondent sequences excluding tofacitinib. (Table 3)
- In scenario 1, the sequence initiating with tofacitinib provided 13.99 QALYs versus 13.92 QALYs for sequence initiating with adalimumab. In scenario 2, the sequence initiating with tofacitinib provided 13.75 QALYs versus 13.62 QALYs for sequence initiating with baricitinib.
- Tofacitinib containing sequences provided lower total costs than the alternative sequences (-€5,783 and -€13,975 for the pairwise comparisons previolusly described). Consequently, tofacitinib containing sequences resulted in dominant treatment options due to lower incremental costs and better health outcomes.
- On the PSA, sequences initiating with tofacitinib resulted in a cost-effective therapeutic option in 64.0% (scenario 1) and 56.9% (scenario 2) of the 1,000 Monte Carlo iterations performed, because incremental cost-effectiveness ratio fell below a €25,000/QALY gained willingness to pay threshold.

Table 3. Results

	Scenario 1			Scenario 2		
	Tofacitinib-containing sequence	Comparator sequence	Incremental vs comparator sequence	Tofacitinib-containing sequence	Comparator sequence	Incremental vs comparator sequence
QALY	13.991	13.924	0.067	13.753	13.620	0.133
Total cost	€224,143	€229,926	-€5,783	€225,851	€239,826	-€13,975
Drug acquisition	€164,786	€164,802	-€16	€173,644	€187,969	-€14,326
Administration	€27,928	€30,861	-€2,933	€19,689	€18,609	€1,080
Disease management	€28,116	€28,513	-€397	€29,570	€30,526	-€955
SAE management	€3,313	€5,750	-€2,437	€2,948	€2,722	€226
ICER	Tofacitinib-containing sequence dominates (less costly, more effective)			Tofacitinib-containing sequence dominates (less costly, more effective)		

QALY: quality-adjusted life-years; SAE: serious adverse event; ICER: incremental cost-effectiveness ratio

CONCLUSION

These results suggest that the inclusion of tofacitinib (5 mg BID) in combination with MTX in a treatment sequence with antirheumatic drugs resulted in a dominant strategy (more effective and less costly) versus alternative sequences in the treatment of moderate to severe RA patients after csDMARDs failure, for the Spanish NHS.

REFERENCES

[1] Aletaha D, et al. JAMA 2018;320(13):1360-72.
[2] Xeljanz® SmPC. www.ema.europa.eu/ema/.
[3] Claxton L, et al. Curr Med Res Opin. 2018;34(11):1991-2000.
[4] Strand V, et al. Arthritis Res Ther. 2015;17:362. .
[5] Biobadaser. https://biobadaser.ser.es/docs/informe_2014.pdf.
[6] Cárdenas M, et al. Rheumatol Int. 2016;36(2):231-41.
[7] Bansback N, et al Pharmacoeconomics. 2008;26(5):395-408.
[8] Vieira MC, et al. Clin Ther. 2016;38(12):2628-41.
[9] Statistics National Institute. www.ine.es.
[10] Carreño A, et al. Value Health. 2011;14(1):192-200.
[11] Oppong R, et al. Eur J Health Econ. 2013;14(2):197-209.
[12] BOT Plus. www.portalfarma.com
[13] Lajas C, et al. Arthritis Rheum. 2003;49(1):64-70.
[14] eSalud. Oblikue consulting. www.oblikue.com
[15] López-Bastida J, et al. Eur J Health Econ. 2010;11(5):513-20.
[16] Vallejo-Torres L, et al. Health Econ. 2018;27(4):746-61.

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