COST-UTILITY OF TOFACITINIB FOR THE TREATMENT OF SEVERE TO MODERATE RHEUMATOID ARTHRITIS IN PORTUGAL

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Objective

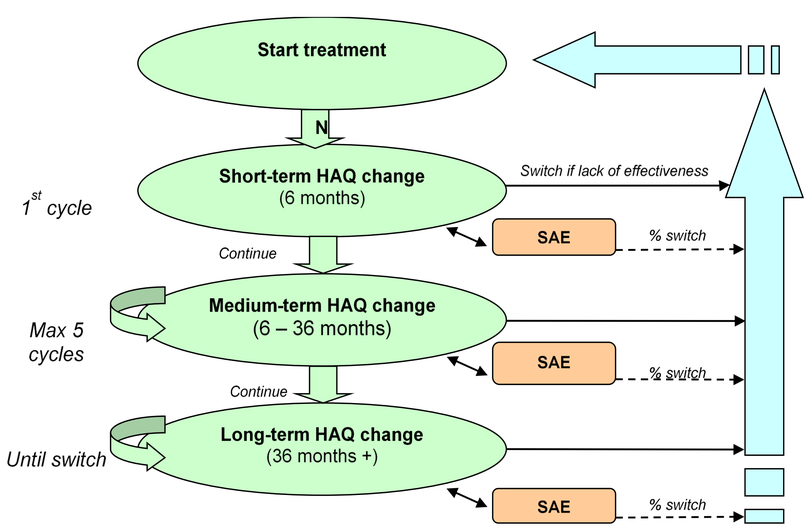
- This study aims to assess the cost-utility of tofacitinib compared to adalimumab, in combination with methotrexate (MTX), for the treatment of patients with moderate to severe rheumatoid arthritis (RA) who had inadequate response or are intolerant to previous therapy with disease-modifying anti-rheumatic drugs (DMARD-IR) in Portugal.

Methods

ECONOMIC MODEL

- A lifetime individual-patient simulation model was used to estimate costs, mortality, and quality of life based on patient's disease severity (as measured by Health Assessment Questionnaire [HAQ]).

Figure 1. Model structure.



- The model uses cycles of six months and captures a treatment sequence of up to six therapy lines. A societal perspective was considered. A lifetime horizon was assumed. Costs and consequences were discounted at 5%.

CLINICAL DATA

- Baseline characteristics and 6-months HAQ change were sourced from the tofacitinib clinical trial (ORAL Strategy)[1]. Initial responses of sequential treatments were based on a systematic review and network meta-analysis[2]. Medium-term response (6-36 months) was based on published literature[3]. After 36 months it was assumed that the HAQ level was maintained.

Table 1. Treatment effect – HAQ change.

	Initial effect	Medium-term effect	Long-term effect
Tofacitinib + MTX	- 0.62 (0.617)	- 0.016 (0.250)	0 (0.150)
Adalimumab + MTX	- 0.57 (0.596)	- 0.030 (0.250)	0 (0.150)

- Patients discontinue treatment if there is inadequate response to therapy at 6 months, loss of response or serious adverse events (AE). AE rate was obtained from a meta-analysis of tofacitinib studies. Only serious infections were considered in model.
- Portuguese all-cause mortality (INE, 2019) was adjusted for the increased mortality associated with RA through the following equation[4]

$$RA\ Mortality = All\text{-}cause\ mortality \times 1.33^{HAQ}$$

- Treatment sequence in clinical practice in Portugal was based on experts´ opinion.

Table 2. Treatment sequence.

2nd line	Tofacitinib + MTX	Adalimumab + MTX
3rd line	Adalimumab + MTX	Etanercept + MTX
4th line	Etanercept + MTX	Tocilizumab + MTX
5th line	Tocilizumab + MTX	Rituximab + MTX
6th line	Rituximab + MTX	Abatacept + MTX

UTILITIES

- Utility values by HAQ were estimated by a regression using data from the tofacitinib trials

$$Utility = 0.7793 - 0.2529\ HAQ - 0.038\ HAQ^2 + 0.0013\ age + 0.0010\ AR\ duration + 0.0310\ female$$

- Disutility due to AE was considered in the model.

COSTS

- Direct and indirect costs were considered. Resource consumption by HAQ level was based on an expert panel of five rheumatologists and on National 2015 DRG microdata. Costs were redistributed by HAQ based on a published study[5]. Transportation was considered for patient travel to hospital.
- Indirect costs considered productivity loss from early retirement. The probability of early retirement due to rheumatic diseases was based on a Portuguese study[6] and a risk of unemployment per HAQ was considered.
- Unit costs were based on national legislation (Portaria nº 207/2017 and Despacho nº 7702-A/2012) and official drug cost database (Infomed, ACSS Catalog, accessed in june 2019).
- In base-case scenario, the cost of adalimumab was based on Humira® cost. Other brand costs were tested in sensitivity analyses.

Results

Base case results

- Compared to the adalimumab treatment sequence, the tofacitinib sequence was associated to average savings of € 15.881 per patient, and to an incremental 0.07 QALY. Cost differences were due mainly to the acquisition of drugs (Figure 2).

Figure 2. Base case results.

Tofacitinib increases QALY by 0.07

↑ 0.02 LY
14.18 *vs*. 14.17

↑ 0.07 QALY
8.87 *vs*. 8.79

Tofacitinib is associated with lifetime costs savings of 15,881€

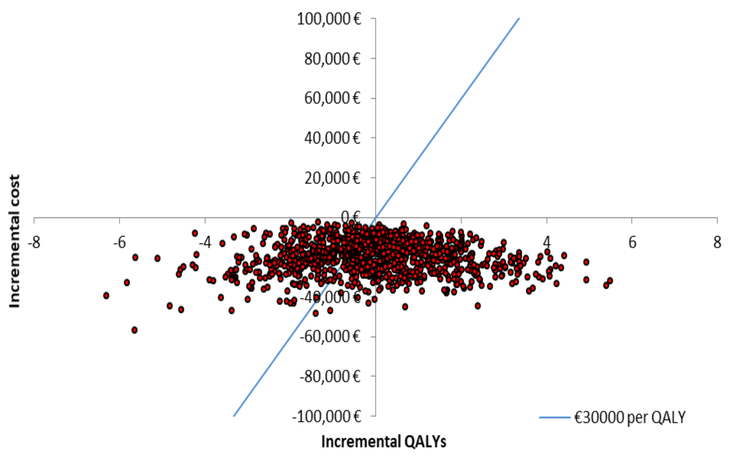
	Tofacitinib + MTX	Adalimumab + MTX	Incremental
LY	14.18	14.17	0.02
QALY	8.87	8.79	0.07
Drug costs	93,523€	108,306€	-14,783€
Administration costs	686€	1.423€	-807€
Healthcare resource costs	22,245€	22,381€	-136€
Adverse events costs	1,262€	1,379€	-117€
Indirect costs	9,228	9,266€	-38
Total costs	126,944€	142,825€	-15,881€

Tofacitinib is a dominant strategy.

Sensitivity analyses

- Using different adalimumab brand costs conducted to a variation in incremental costs that ranged between -15% and 41%. Even though, tofacitinib sequence maintained as a dominant strategy.
- Probabilistic sensitivity analysis was conducted (1,000 simulations), showing that the main uncertainty was located around clinical results (Figure 3).

Figure 3. Cost-effectiveness plane.



Conclusions

- Tofacitinib treatment sequence in RA is a less expensive and more effective option than adalimumab treatment sequence. Therefore it can be considered a dominant treatment strategy in the Portuguese setting.

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References

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