Cost-Effectiveness analysis of tofacitinib for the treatment of active ankylosing spondylitis in Greece.

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Introduction

- Ankylosing Spondylitis (AS), is a chronic, progressive, inflammatory, multidimensional, musculoskeletal disease primarily involving the axial skeleton [(1)].
- Similarly, to other chronic diseases, AS is associated with increased morbidity and mortality, significantly affecting productivity and overall quality of life (QoL) [(2-4)].
- Despite the progress in AS treatments, there is an unmet clinical need in terms of achieving and maintaining treatment goals in real world settings. Taking into consideration this unmet need, new Janus Kinase (JAK) inhibitors have exhibited promising results for the treatment of AS in a number of phase III trials[(5-6)].
- More recently, tofacitinib citrate, an oral JAKi with functional selectivity for cytokine receptors associated with JAK1 and/or JAK3 has been approved by European Medicines Agency (EMA) for adult patients with AS who have responded inadequately to conventional therapy.
- Two clinical trials (phase 3 A3921120 [NCT03502616][(7)] and phase 2 A3921119 [NCT01786668])[(8)] demonstrated the efficacy and safety of tofacitinib compared with conventional care (CC).
- The A3921120 study[(7)] met its primary endpoint, showing that the percentage of patients achieving an ASAS20 response at week 16 was significantly greater with tofacitinib (56.4%) vs placebo (29.4%) (p<0.0001). In addition, the percentage of ASAS40 response was significantly greater with tofacitinib (40.6%) vs placebo (12.5%) (p<0.0001), a key secondary endpoint of the study.

Objective

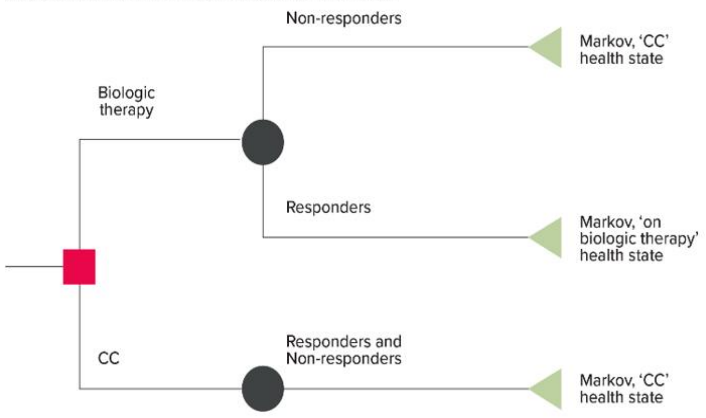
The aim of the present study was to evaluate the cost-effectiveness of tofacitinib compared to currently marketed biologic treatment in patients with active AS who have are inadequate responders to conventional therapy in Greece.

Methods(1/2)

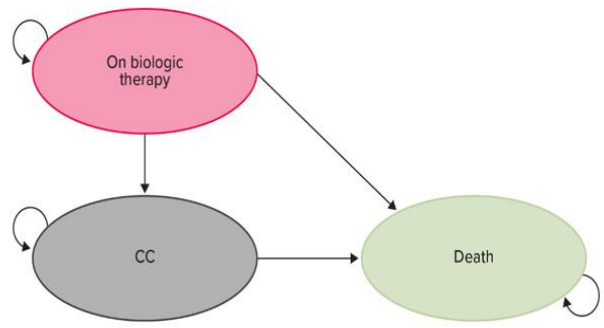
- A previously published[(9)] cohort modeling approach combining a decision tree model in the first 16 weeks and a 3-state Markov model for the remainder of modeled time horizon, with a cycle length of 16 weeks was locally adapted from a Greek public payer perspective (Figure 1).

Figure 1: Model structure

A. Decision tree in the first 16 weeks of the model



B. Markov model beyond the first 16 weeks



- The target population was adult patients with active AS based on the modified New York Criteria for AS despite NSAID therapy or adult patients who were intolerant to NSAIDs, including both biologic disease-modifying anti-rheumatic drugs (bDMARD-naïve) and bDMARD/ tumor necrosis factor-alfa inhibitors (TNFi)-IR populations.
- The definition of the target population was in line with that of the intention-to-treat (ITT) population of the phase 3 A3921120 clinical trial for tofacitinib (including a mix of bDMARD-naïve [approximately 77%] and bDMARD/TNFi-IR [23%] populations)
- The economic model considered two distinct subpopulations of patients with active AS: 1. bDMARD-naïve patients and 2. bDMARD/TNFi-IR patients.
- The relevant comparators to tofacitinib in the bDMARD-naïve and bDMARD/TNFi-IR populations were reflective of local clinical practice, taking into consideration the availability of clinical data to allow robust economic evaluation.

Methods (2/2)

- More specifically, for the bDMARD - naïve population, the comparator was adalimumab, while for bDMARD/TNFi-IR population, the comparator was secukinumab.
- These comparisons were chosen on the grounds that adalimumab and secukinumab are highly effective and widely tested therapies in routine clinical practice, representing the most marketed biological therapies for the treatment of AS in Greece (standard practice).
- Clinical data and utility values were extracted from published studies. In the absence of head-to-head clinical trials of tofacitinib compared to adalimumab and secukinumab, a network meta-analysis (NMA) was conducted to examine the relative treatment effect on response rates for the comparators using the CC (placebo) arm as the reference treatment arm.
- Direct medical costs related to drug acquisition as well as administration, monitoring, disease management and management of adverse events were considered in the analysis. All costs were expressed or inflated to 2022 euros (Table 1).
- Model extrapolated outcomes included quality-adjusted life years (QALYs), costs as well as incremental cost-effectiveness ratios (ICERs).
- Probabilistic sensitivity analysis (PSA) and deterministic one-way sensitivity analysis (OWSA) were performed.
- Although there is no official willingness-to-pay (WTP) threshold for Greece, a WTP threshold of € 60,000 per QALY[(10)] was used in the current analysis which equals to three times multiplied by the GDP per capita as sourced from the official website of International Monetary Fund.

Table 1 :Unit cost considered in the model

Cost description		
Drug acquisition costs per cycle		
	Cycle 1*	**Cycle 2+**
Tofacitinib (5MG/Tab BT x 56 tabs)	€2,105	€2,105
Adalimumab (40MG/0,4 ML PF.SYR BTx1)	€2,011	€2,011
Secukinumab (PF.SYR 150MG/ML BTx1)	€2,936	€1,515
	Unit cost	**Source**
Disease management costs	€ 1,749	NICE[(9)] &Tzanetakos et al[(11)].
Adverse event costs		
Tuberculosis (TB)	€1,800	DRG issued by the Greek Ministry of Health
Other serious infections	€1,195	

Tab: tablets PFS: Per prefilled syringe, DRG: Diagnosis Related Groups *Drug price bulletin issued by the Greek Ministry of Health

Results (1/2)

- In the bDMARD-naive population, the analysis indicated that over a lifetime horizon that total cost per patient for tofacitinib and adalimumab was estimated to be €149,500 and €147,096 respectively (Table 2).
- With respect to effectiveness in terms of QALY, tofacitinib was found to be associated with 10.730 QALYs, while the QALY for adalimumab was 10.672. The incremental analysis of tofacitinib versus adalimumab resulted in an ICER of €41,378 per QALY gained (Table 2).
- The analysis in bDMARD- TNFi-IR population showed, that over a lifetime horizon tofacitinib was associated with 0.13 increment in QALYs compared with secukinumab, at an additional cost of €5,614. The corresponding ICER of tofacitinib compared to secukinumab was €42,784 per QALY gained (Table 2).

Table 2 : Cost-effectiveness analysis base-case results

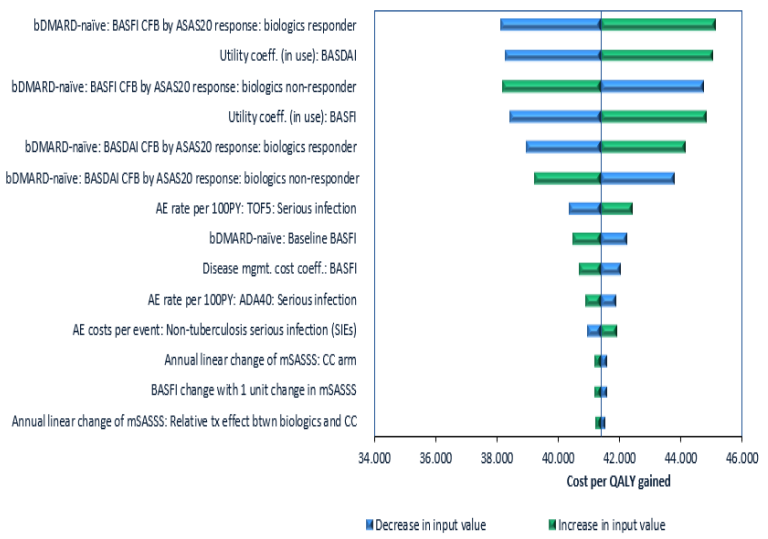
Technology	Total costs[a]	Total QALYs	ICER per QALY gained
bDMARD -naive population			
Tofacitinib	€149,500	10.730	-
Adalimumab	€147,096	10.672	**€41,378**
bDMARD/TNFi-IR population			
Tofacitinib	€151,371	9.780	-
Secukinumab	€145,757	9.649	**€42,784**

Notes: [a] Total costs include drug acquisition, monitoring, adverse event, and disease management costs. Abbreviations: ICER, Incremental cost- effectiveness ratio; QALY, Quality Adjusted Life Year, bDMARD, biologic disease-modifying antirheumatic drug; TNFi, tumor necrosis factor-alfa inhibitor

Results (2/2)

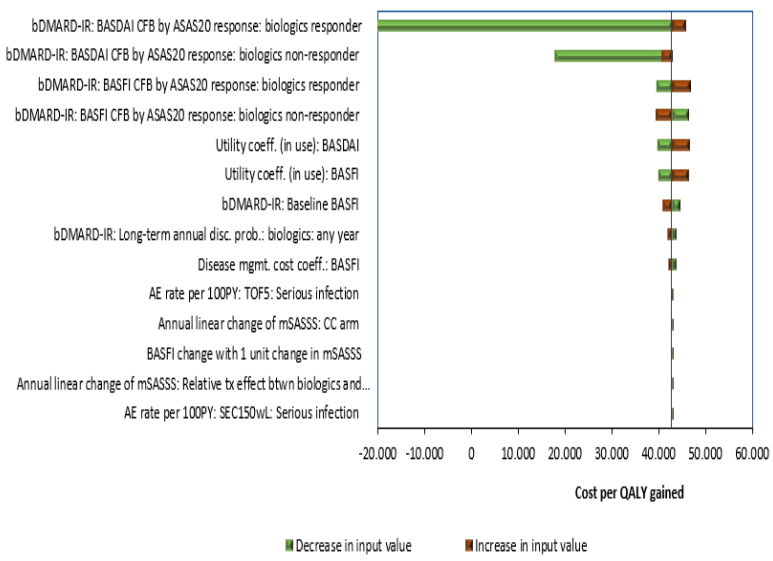
- In the bDMARD-naive population, the results of OWSA for the comparison of tofacitinib versus (vs) adalimumab indicated that, the most influential parameters on the model results were the response-dependent Bath Ankylosing Spondylitis Disease Activity Index (BASFI) and the coefficient for BASFI score in the utility equation (Figure 2).

Figure 2: One-way sensitivity analysis results of tofacitinib vs adalimumab, bDMARD-naïve population



- While in in bDMARD- TNFi-IR population, the results of OWSA for the comparison of tofacitinib vs secukinumab reported that, the response-dependent Bath Ankylosing Spondylitis Disease Activity Index and BASFI CFB by ASAS20 were the parameters with the greatest effects on the base case results (Figure 3).

Figure 3: One-way sensitivity analysis results of tofacitinib vs secukinumab, bDMARD/TNFi-IR population



- Worthy of note is that tofacitinib maintained its cost-effective profile in both populations, when the model time horizon was set at 10, 20, 30 and 40 years as well as in all tested sensitivity analyses, exhibiting ICERs below the WTP threshold of €60,000 per QALY gained.
- PSA indicated that the total costs of each intervention and QALY yielded were comparable to the base-cases analyses. The ICER on PSA was €46,167 of tofacitinib compared to adalimumab in bDMARD -naive population, and €51,651 of tofacitinib compared to secukinumab in bDMARD/TNFi-IR population. The results of PSA confirmed the robustness of base case results in both populations.

Conclusion

The results of the analysis suggest that tofacitinib was estimated to be a cost-effective therapy versus adalimumab and secukinumab in the treatment of active AS in Greece for both biologic-naive and biologic-experienced patients. Important to note is that these favourable results for tofacitinib were found against adalimumab and secukinumab, the most marketed biological therapies for the treatment of AS in Greece

Acknowledgements

Funding was provided by Pfizer Hellas Hellas SA.

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