Economic Evaluation of Adalimumab Biosimilars and JAK Inhibitors for the Treatment of Moderate-to-Severe Rheumatoid Arthritis

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Objectives

To determine the cost-effectiveness of adalimumab biosimilars, which are anti-tumour necrosis factor (TNF) biologics, and current licensed Janus kinase (JAK) inhibitors for the treatment of moderate-to-severe rheumatoid arthritis (RA).

Methods

A treatment sequence age-dependent Markov model was developed to compare the cost-effectiveness of subcutaneous adalimumab versus oral JAK inhibitors (upadacitinib, filgotinib, tofacitinib and baricitinib) (Figure 1). The model followed a hypothetical cohort of patients through health states, defined by American College of Rheumatology (ACR) response. The modelled cohort were patients with moderate-to-severe RA who are methotrexate-monotherapy inadequate responders and are eligible for anti-TNFs or JAK inhibitors. Patients received a total of two separate treatments, including adalimumab or a JAK inhibitor and best supportive care (BSC), which was always the last option in a sequence.

The time on each intervention is separated into two distinct phases: induction and maintenance. All treatments were assumed to have an induction period which was used to establish whether patients had responded to the treatment. Patients entered the model and received the first treatment in the sequence. At the end of the first cycle, patients were assigned to one of the four health states, dependent on their ACR response probability.

The probabilities for reaching ACR20/50/70 responses for each of the treatments were generated through a Bayesian network meta-analysis using a multinomial model with a probit link function based on outcomes from FINCH 1[1], SELECT-COMPARE[2], ORAL Standard[3], RA-BEAM[4] and RA-BUILD[5] studies. Both fixed and random effects models were assessed. The network meta-analysis was conducted in STAN (https://mc-stan.org/) following the methodology specified in NICE TSD 2. The model was fit using 4 Monte Carlo Markov chains, with 10,000 iterations for each chain, a burn-in of 5,000 iterations and no thinning. Non-informative distributions were used for the priors for treatment effects, study-specific intercepts and heterogeneity.

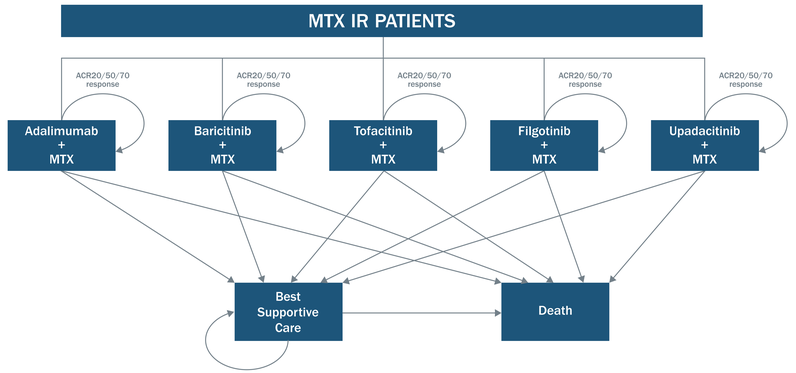
Patients achieving responses of ACR20 or greater remained on treatment and moved into the maintenance period. Conversely, patients not achieving at least ACR20 at Week 24 were deemed to have had an inadequate response to treatment and were moved to BSC for the lifetime model time horizon. Patients were also moved to BSC in the event of treatment discontinuation due to other reasons than lack of efficacy. These discontinuation probabilities were obtained from the above mentioned randomised clinical trials.

Utilities were calculated from ACR response following a 2-step approach. ACR responses were associated with health assessment questionnaire (HAQ) scores based on available literature[6] and HAQ scores were mapped to quality-adjusted life years (QALY's) using an average of several mapping validated equations.[7]

Unit costs were taken from publicly available databases with adalimumab discounting based on current market dynamics.

Uncertainty was assessed through probabilistic (5000 Monte Carlo Simulations) and deterministic sensitivity analysis (+/–20% for each model parameter).

Figure 1. Schematic representation of the model structure.



ACR, American College of Rheumatology response; IR, inadequate responder; MTX, methotrexate.

Results

- Incremental QALYs per patient were calculated to be 0.14 (tofacitinib), 0.09 (baricitinib), 0.07 (filgotinib) and 0.04 (upadacitinib).
- Incremental costs per patient within the JAK inhibitor arms at list price and with a 30% discount were determined for Belgium, Germany, Spain and the United Kingdom (Table 1).

Table 1. Incremental costs per patient at either JAK inhibitor list price or 30% discount

	Belgium		Germany		Spain		UK	
Country	0%	30%	0%	30%	0%	30%	0%	30%
Baricitinib	€24,556	€13,295	€15,376	€4,219	€29,715	€8,561	£32,848	£21,634
Tofacitinib	€5,797	€165	–€4,437	–€9,613	€10,947	€5,243	£13,603	£8,166
Filgotinib	€19,355	€9,654	€16,172	€4,810	–*	–*	£31,901	£20,970
Upadacitinib	€16,612	€7,732	€11,994	€1,884	€24,404	€14,834	£27,495	£17,883

*price of filgotinib not available at time of preparation

Assessment of the incremental cost-effectiveness ratios (ICERs) for the adalimumab biosimilars were dominant in all scenarios except for tofacitinib in Germany (Figure 2 and 3).

Scenarios and Sensitivity Analysis

The Deterministic Sensitivity Analysis showed the model results were most influenced by discontinuation rates and ACR response probabilities. Discontinuation rates were obtained from registered randomised clinical trials. Expert elicitations or real-world data could help to decrease uncertainty around this model parameter.

The Probabilistic Sensitivity Analysis yielded results similar to the base case which suggests a high confidence in the base-case results.

The results of this cost-effectiveness analysis suggest adalimumab biosimilars could be a cost-effective treatment option for patients with moderate-to-severe RA in Belgium, Germany, Spain and the United Kingdom.

Figure 2. Incremental cost-effectiveness ratio (ICER) with 0% JAK inhibitor discounting.

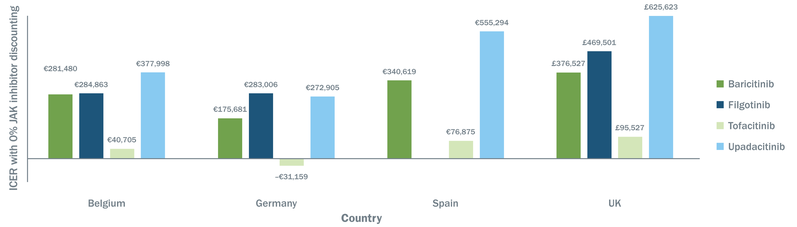
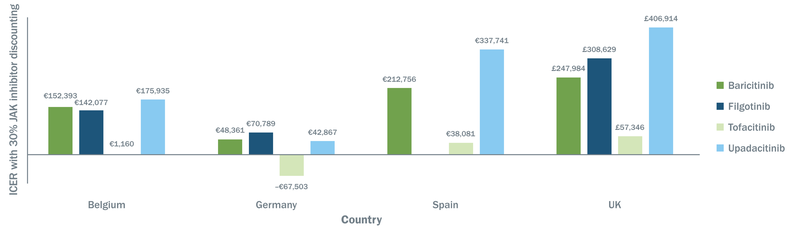


Figure 3. Incremental cost-effectiveness ratio (ICER) with 30% JAK inhibitor discounting.



Conclusions

Adalimumab biosimilars continue to be a cost-effective option in the treatment of moderate-to-severe RA. The uptake and use of adalimumab biosimilars continue to increase the affordability and therefore possible access to treatments for patients suffering from this chronic long-term condition.

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Disclosures of interest I Rickard, T Lessing, M Furrer and S Keady are employees of Biogen, and hold stock in Biogen.
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