

BIOSIMILARS' IMPACT ON THE RHEUMATOID ARTHRITIS TREATMENT: A COST-EFFECTIVENESS MODEL FROM SPANISH NATIONAL HEALTHCARE SYSTEM PERSPECTIVE

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ES2204216280

INTRODUCTION

Rheumatoid arthritis (RA) is a highly debilitating chronic disease posing significant financial burden to the Spanish National Healthcare System (SNS). RA treatment is largely based on Disease-Modifying Anti-Rheumatic Drugs (bDMARDs), which might be, in turn, grouped by Mechanism Of Action (MoA) in biologics, conventional and targeted synthetic (bDMARDs, csDMARDs and tsDMARDs, respectively). Anti-tumor necrosis factor (anti-TNFb) biosimilars, such as those of adalimumab (bADA), etanercept (bETN) and infliximab (bINF), have arguably brought a change to RA's clinical practice by means of significant reduction in therapy drug acquisition costs^{2,3}, whilst certainly paving the way to broaden access to highly effective therapies.

OBJECTIVES

- We aimed to assess the incremental cost-effectiveness ratio (ICER) of different treatment sequences made of anti-TNF biosimilars, bDMARDs, and tsDMARDs – all compared to csDMARDs -, following an initial loss or insufficient of response (IR) to the latter.
- Additionally, considering a standard Willingness to Pay (WTP) threshold €20,000 per Quality Adjusted Life Year (QALY) gained, for the same treatment structure, to calculate the Net Monetary Benefit (NMB) per patient, as $NMB = \Delta QALY * WTP - \Delta Costs$, taking the least costly strategy for the SNS as reference.

MATERIALS AND METHODS

- A Targeted Literature Review, (TLR) reported following the "Preferred Reported Items for Systematic Reviews and Meta-Analyses" (PRISMA) was performed (Figure 1).
- TLR returned 68 Randomised Controlled Trials (RCTs) either with placebo or active control as comparator arm.
- To account for Treatment Effect Modifiers (Clinical Outcomes), we sourced or derived either the Simplified Disease Activity Index (SDAI) or the EULAR (European League Against Anti-Rheumatoid Diseases) response, according to previously reported algorithms^{4,5}
- Drug acquisition costs were sourced from public tenders database (commercial)⁶, on top of that, we also took into account medical direct and indirect costs (Treatment Administration, Laboratory and procedures, Hospitalisations, Specialist Visits, etc...)
- QALYs were derived from different Health States, by converting reported Health Assessment Quality-Disease Index (HAQ-DI) into EuroQoL 5 Dimensions (EQ-5D) scores⁷
- Finally, a cohort-based Markov model simulating the RA treatment course in Spain over 5 and 10 years was erected. Transitions between different treatments, were derived from the Spanish BIOBADASER registry⁸ reported Kaplan-Meier survival curves by MoA. (Figure 2).
- We compared four different treatment strategies (Figure 3), from early biosimilar introduction (strategy #1), including delayed starting (following MTX failure), and another one with a choice of tsDMARD followed by bDMARD. Treatment line changes either by non response (as per SDAI or EULAR response criteria) or any Adverse Effect leading to withdrawal.
- Both Costs and QALYs were discounted at a 3% yearly rate.
- Both One Way and Probabilistic Sensitivity Analyses (OWSA, PSA) were performed to reassure the findings' robustness.

Figure 1.

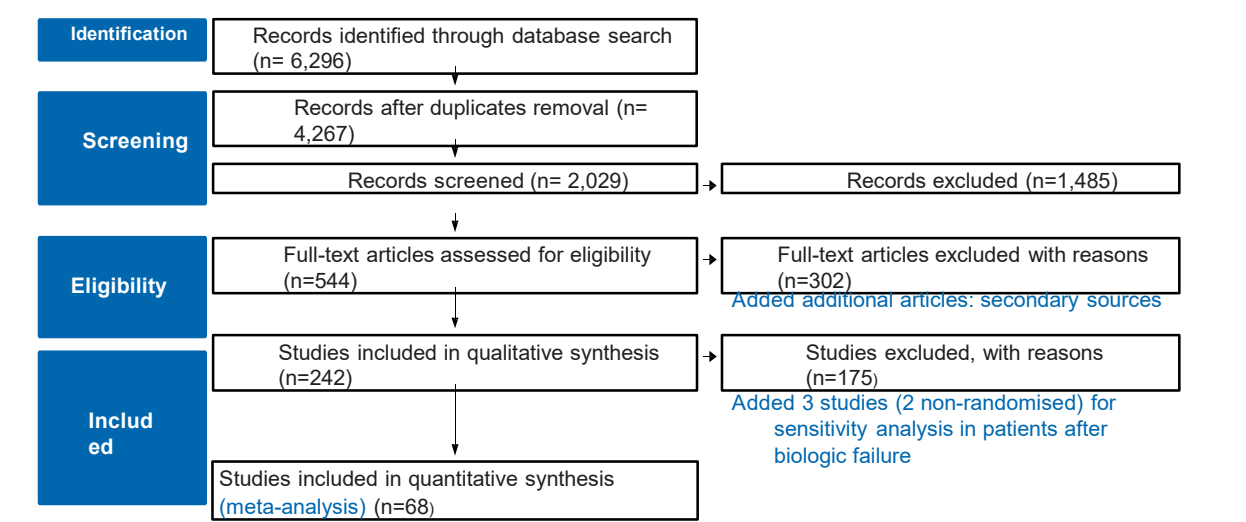
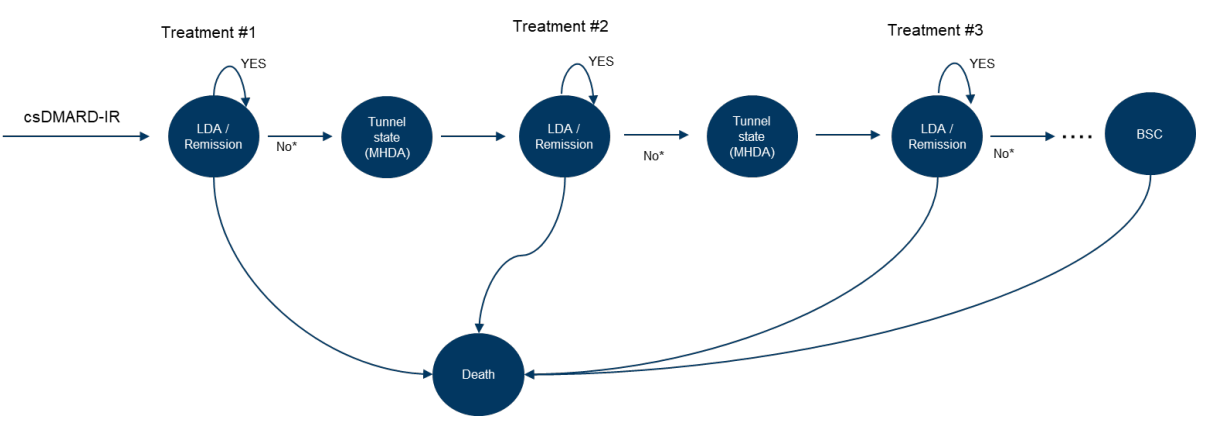


Figure 2.



LDA= Low Disease Activity, MHDA= Moderate & High Disease Activity; BSC= Best Supportive Care, IR= Insufficient Response
 ** Withdraw may be caused either by Adverse Effects, Loss or Insufficient Response to a particular treatment

RESULTS

- When compared to initial csDMARDs, treatment sequences made followed by early bADA were dominant; with bADA followed by bETN turning out the most cost-effective alternative. From the payers' perspective in a 5 years' time horizon we found a NMB of €6,022 (95%CI: €5,888 - €6,781) and in a 10-year horizon yielded €10,256 (95%CI: €9,438 - €11,001), using SDAI as response criteria. **Table 1.**
- Sequencing in any order biosimilars and tsDMARDs, led to more costly but more effective outcomes; in a 5 years' time horizon, bADA followed by upadacitinib (UPA) provided a NMB of €2,255 (95%CI: €1,987 - €2,604); whilst UPA followed by bADA returned €1,460 (95%CI: €1,187 - €1,781) (EULAR response criteria as clinical response). **Table 2.**

Table 1.

TREATMENT SEQUENCE	COSTS	QALYs	ICER	NMB	RANKING
csDMARDs->bADA->UPA->bETN	€ 64.500	4,50	REFERENCE	REFERENCE	REFERENCE
bADA->bETN->UPA->bINF	€ 55.192	4,55	dominant	10.256 €	1
UPA->bADA->BAR->bETN	€ 64.677	4,60	1.777 €	1.820 €	8
bADA->bETN->BAR->TOF	€ 61.288	4,52	dominant	3.711 €	3
bETN->TOF->bADA->BAR	€ 62.561	4,53	dominant	2.451 €	6
TOF->bETN->BAR->bADA	€ 62.293	4,52	dominant	2.536 €	5
bETN->bADA->BAR->TOF	€ 61.377	4,52	dominant	3.572 €	4
bADA->UPA->bETN->BAR	€ 59.654	4,56	dominant	6.046 €	2
UPA->bADA->TOF->bINF	€ 64.164	4,60	dominant	2.435 €	7

QALY= Quality Adjusted Life Year; ICER= Incremental cost-effectiveness ratio; NMB=Net Monetary Benefit; dominant= less costly and more effective treatment.csDMARDs= conventional DMARDs, bETN=etanercept biosimilar, bADA= adalimumab biosimilar, TOF= tofacitinib, BAR=baricitinib, UPA=upadacitinib, bINF= infliximab biosimilar

CONCLUSIONS

- Previous studies have assessed the savings following the introduction of biosimilars^{2,3}, mainly concerning monoclonal antibodies as anti-TNF⁹. The results obtained by our cost-effective model analysis clearly indicate that, in moderate-to-severe RA, early biosimilar treatment is the most cost-effective choice for SNS.

Figure 3.

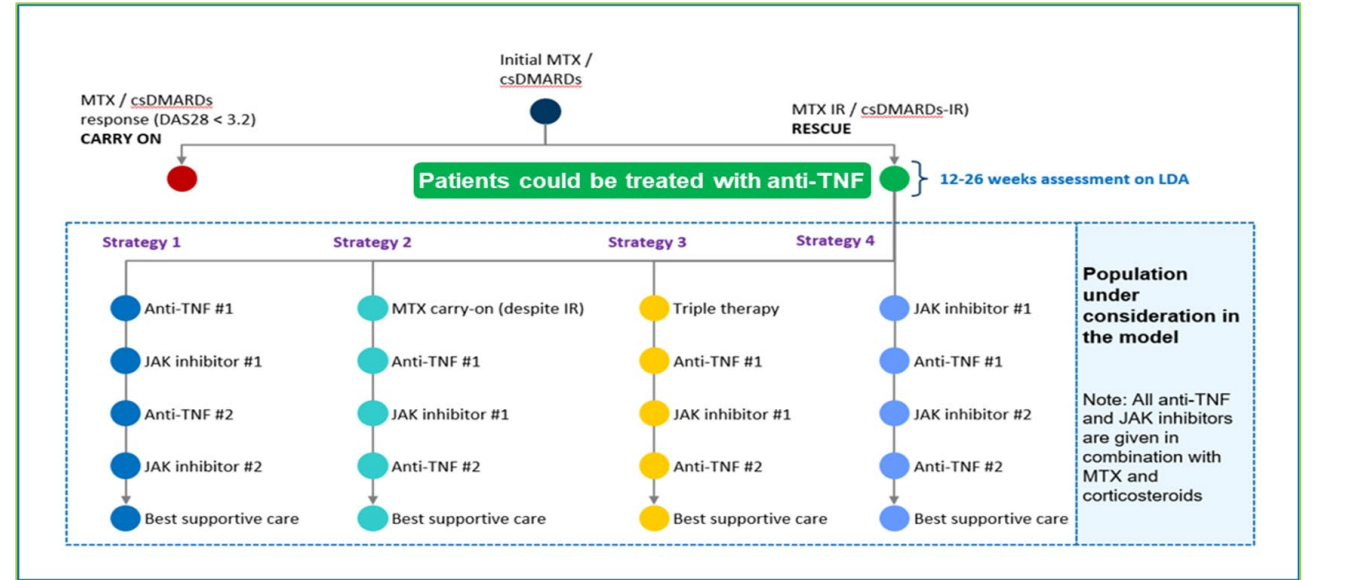


Table 2.

TREATMENT SEQUENCE	COSTS	QALYs	ICER	NMB	RANKING
csDMARDs->bADA->bETN->UPA	€ 43.989	2,85	REFERENCE	REFERENCE	REFERENCE
UPA->bADA->TOF->bINF	€ 45.214	2,99	9.128,15 €	1.460 €	2
bADA->UPA->BAR->bINF	€ 43.692	2,95	dominant	2.255 €	1

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