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## Cost-effectiveness assessment of biologic strategies for rheumatoid arthritis in Portugal

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Objectivos (Objectives): Chronic conditions like rheumatoid arthritis (RA) often require the use of different therapeutic options used in a sequential manner in case of an insufficient response to the previous agent. In absence of clinical trials comparing various sequences of biologic agents, simulation models can assess successive strategies to provide relevant information on optimal treatment sequences and their cost-effectiveness. Using the perspective of the public payer in Portugal, to assess the cost-effectiveness of different biologic treatment strategies based on achieving a low disease activity state (LDAS) in moderate to severe RA.

Metodologia (Methodology): Advanced simulation models were developed to assess the cost-effectiveness of different biologic sequential strategies composed of 3 biologic agents with decision to switch at 6-months intervals in case of an insufficient response to the previous agent: Sequence 1: etanercept-abatacept-adalimumab; Sequence 2: etanerceptrituximab- adalimumab; Sequence 3: etanercept-adalimumab-abatacept; Sequence 4: etanercept-adalimumabinfliximab. LDAS (DAS28  $\leq$  3.2) was selected as a clinically meaningful effectiveness endpoint and was derived from published clinical trials and long-term extension studies. Effectiveness was expressed in expected number of days in LDAS for each sequence over 2 years. Portuguese RA direct medical costs were derived from resource utilization assessed in 713 RA patients from the National Data Bank for Rheumatic Diseases-Portugal (NDB), where patients completed detailed self-report questionnaires at 6-month intervals. Biologic drug costs were estimated based on recommended dosing. Cost-effectiveness was reported as cost per day in LDAS. Monte-Carlo simulations generated mean values and standard deviations of costs, effectiveness and mean cost-effectiveness over 2 years. Significance tests were performed to confirm potential differences.

Resultados (Results): Sequence 1 including abatacept after an insufficient response to 1 anti-TNF agent was significantly more efficacious over 2 years (102 days in LDAS) compared to Sequence 2 including rituximab as second biologic agent (82 days in LDAS). Mean cost-effectiveness ratios also showed significantly lower overall medical costs per day in LDAS with Sequence 1 (311  $\in$ ) versus Sequence 2 (375 $\in$ ). Sequence 3 including abatacept after an insufficient response to 2 anti-TNF agents was more efficacious over 2 years (64 days in LDAS) compared to Sequence 4 composed of anti-TNF agents only (32 days in LDAS). Mean cost-effectiveness ratios also showed significantly lower overall medical costs per day in LDAS with Sequence 3 (526 $\in$ ) versus Sequence 4 (880 $\in$ ).

Conclusões (Conclusions): Advanced simulation models allow comparison of complex strategies such as the use of sequential biologic treatments in RA. The results of this innovative model suggest that the sequence using abatacept after an insufficient response to 1 anti-TNF agent appears more efficacious and cost-effective compared to a similar biologic sequence using rituximab. In case of use after an insufficient response to 2 anti-TNF agents, abatacept appears more efficacious and cost-effective than using a 3rd anti-TNF agent



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