**Introduction**

Rheumatoid Arthritis (RA) is a chronic, progressive, autoimmune disease characterized by joint inflammation. RA is responsible for high morbidity rates that, in the long term, significantly interfere with the patients’ quality of life. RA significantly affects patients' physical functioning and ability to work requiring greater use of health care and causing significant economic impact to society 1, 2.

The initial therapeutic approach for RA consists of using classic Disease Modifying Anti-Rheumatic Drugs (DMARDs) such as methotrexate, leflunomide, sulfasalazine and hydroxychloroquine. After Inadequate Response (IR) to these drugs patients may change to a biological agent (DMARDO).

Toxicilumab (TCZ) is a monoclonal antibody with an innovative mechanism of action that has shown to reduce significantly RA signs and symptoms thus presenting as an important therapeutic alternative for RA patients.

This study intends to evaluate the cost-effectiveness and cost-utility of treatment with therapeutic sequences initialized with tocilizumab (RoActemra®) versus similar therapeutic sequences commonly used in clinical practice initialized with an anti-TNF for the treatment of moderate to severe RA patients with inadequate response to previous DMARD therapy (DMARD-IR) in Portugal.

**Methodology**

A cost-utility and a cost-effectiveness analysis were carried out by the Portuguese National Health Service (NHS) and societal perspectives. A Markov model, population-based, considering an hypothetical cohort of 10,000 patients diagnosed with moderate / severe RA and DMARD-IR was used. Projection of costs, Life Years Gained (LYG) and Quality-Adjusted Life Year (QALYs) until the end of life was performed.

Figure 1 – Schematic representation of the model

The analysis compares DMARD-IR patient outcomes in three different scenario (Table 1): a treatment sequence initialized with tocilizumab followed by a TNF inhibitor, rituximab, abatacept and supportive care versus the same sequence initialized with a TNF inhibitor. Patients switched from one treatment to the following according to the ACR response rates for biologic treatments obtained from a mixed treatment comparison analysis 4.

Table 1 – Therapeutic alternatives considered in the analysis for each of the three scenarios

<table>
<thead>
<tr>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st treatment</td>
<td>Tocilizumab</td>
<td>Tocilizumab</td>
</tr>
<tr>
<td>2nd treatment</td>
<td>Adalimumab</td>
<td>Etanercept</td>
</tr>
<tr>
<td>3rd treatment</td>
<td>Etanercept</td>
<td>Etanercept</td>
</tr>
<tr>
<td>4th treatment</td>
<td>Abatacept</td>
<td>Abatacept</td>
</tr>
<tr>
<td>Supportive care</td>
<td>60% MTX; 10% Leflunomide; 20% MTX+Leflunomide; 5% MTX+Cyclosporine</td>
<td>5% MTX+Hydroxychloroquine</td>
</tr>
</tbody>
</table>

**Results**

**Deterministic Sensitivity Analysis**

One-way deterministic sensitivity analyses were performed with variables identified having greater potential to bias namely:

- Biological drugs cost (±15%);
- Discount rate (0%);
- Rituximab dosage (re-treatment 6/6 months or 12/12 months);
- Patient weight (pooled population data from phase III clinical trials: 72.8 kg);
- Monitoring associated with tocilizumab and abatacept (12 appointments/year);
- Unadjusted response rate.

The sequences initialized with tocilizumab remained dominant in the sensitivity analyses for all the tested parameters, except when all biological drugs - except tocilizumab – costs were reduced by 15% and when patients weight was 72.8 kg.

**Probabilistic Sensitivity Analysis (PSA)**

The probabilistic sensitivity analysis (10,000 patients, 2,000 samples) carried out demonstrated the robustness of the results:

- Scenario 1 - The sequence initialized with tocilizumab was cost-effective under the threshold of €30,000/QALY in 98.5% and a dominant alternative in 72.0% of the samples.
- Scenario 2 - The sequence initialized with tocilizumab was cost-effective under the threshold of €30,000/QALY in 93.0% and a dominant alternative in 96.0% of the samples.
- Scenario 3 - The sequence initialized with tocilizumab was cost-effective under the threshold of €30,000/QALY in 95.0% and a dominant alternative in 69.0% of the samples.

**Conclusions**

- The model consistently predicts that treatment initialized with tocilizumab in DMARD-IR patients with moderate to severe RA is a dominant alternative compared to similar treatment sequences initialized with a TNF-inhibitor in Portugal.
- Tocilizumab therefore allows important gains in health and significant cost savings for society.

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**References**