Factors influencing choice of rituximab versus an alternative TNF inhibitor following TNF inhibitor failure in patients with rheumatoid arthritis: Sub-analysis of a global, observational comparative effectiveness study

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ABSTRACT

Background: SWITCH-RA is a global, observational study evaluating the effectiveness of switching to an alternative TNFi or rituximab (RTX) following failure of a prior TNFi. This analysis considered the reasons for discontinuation of initial TNFi therapy and factors that drive choice of RTX versus alternative TNFi as subsequent therapy.

Methods: RETRIEVE is the name of the SWITCH-RA discontinuation and rationale for selection of alternative TNFi therapy study. The association between various factors and choice of RTX or alternative TNFi was assessed using logistic regression analysis with a stepwise method for variable selection.

Results: A total of 1117 enrolled patients (mean age 55.6 years, mean disease duration 8.3 years) were analyzed. Reasons for discontinuing initial TNFi were lack of efficacy (44.0%), intolerance (16.0%), other (18.0%) and treatment intolerance (4.0%) as alternative TNFi. Factors associated with selection of RTX or alternative TNFi are shown in Figure 2.

Conclusions: Lack of efficacy is the most frequent reason for discontinuation of an initial TNFi. Factors associated with selection of RTX versus alternative TNFi were primarily associated with treatment characteristics related to the safety profile (ie lymphoma risk, low infection risk), and long good tolerability after infusion and frequency of administration. Factors most clearly associated with selection of RTX were generally associated with treatment characteristics related to safety and efficacy as well as frequency of administration.

INTRODUCTION

• Patients with rheumatoid arthritis (RA) may discontinue therapy with a tumour necrosis factor inhibitor (TNFi) for a number of reasons. Around 35% of patients treated with ≥1 prior TNFi cease therapy for primary inefficacy, and more patients lose responsiveness over time (secondary inefficacy) or discontinue treatment due to adverse events.1

• Options available to patients with an inadequate response or intolerance to TNFi include treatment with an alternative TNFi and switching to a biologic therapy with a different mode of action.

• The factors associated with the selection of subsequent therapy, both from the physician and patient perspective, have not been evaluated in depth.

• SWITCH-RA is a prospective, multicenter, global, observational study whose primary objective is to compare the effectiveness of an alternative TNFi with rituximab (RTX) following an inadequate response to a first TNFi in patients with RA treated in real-world clinical practice.

OBJECTIVE

• To assess the reasons for discontinuation of initial TNFi therapy and factors that drive physicians to choose RTX versus alternative TNFi as subsequent therapy.

METHODS

Study design and patient population

• Eligible patients were ≥18 years old and starting RTX or an alternative TNFi as second biologic.

• Enrollment up to 4 weeks after commencing the second biologic.

• Patients receiving a second biologic therapy within an RA clinical trial were excluded.

• No additional visits or laboratory tests were required outside of routine clinical practice.

Primary/secondary inefficacy of initial TNFi was assessed by independent investigators.

Data collected at baseline

• Demographic and clinical variables were collected at time of switching to a new biologic therapy.

• Reasons for discontinuation of the first TNFi.

• Physicians’ rationale for selecting the subsequent TNFi.

• Multivariate association between the treatment groups (RTX and TNFi) and the factors potentially related to selection of second biologic therapy were evaluated using a logistic regression model with the dependent variable being the type of second biologic (RTX or alternative TNFi), with each factor added as a binary independent variable.

• Independent variables were categorized as:
  • Medical rationale
  • Characteristics of the new treatment
  • Patient characteristics

• Using a stepwise regression approach, only those factors that were significantly associated (ie 95% confidence intervals surrounding the odds ratio both ≥1 or <1) with the choice of RTX over an alternative TNFi were included in the final analysis.

RESULTS

Patients

• A total of 1111 patients were enrolled from 11 countries (Table 1).

• Overall, 604 (54.4%) received RTX and 507 (46.6%) an alternative TNFi as subsequent therapy.

• Factors most clearly associated with selection of RTX were generally related to the physician’s appreciation of treatment characteristics:
  • Safety profile: No lymphoma risk
  • Low infection risk
  • Long-term tolerance after infusion
  • Treatment profile: Compatible treatment with patient’s professional life

Table 2. Patient baseline demographics and clinical characteristics.

<table>
<thead>
<tr>
<th>Country</th>
<th>n (%): RTX (n=604)</th>
<th>n (%): Alternative TNFi (n=507)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>104 (17.2)</td>
<td>80 (15.8)</td>
</tr>
<tr>
<td>China/Russia</td>
<td>221 (36.6)</td>
<td>200 (39.4)</td>
</tr>
<tr>
<td>France</td>
<td>209 (34.6)</td>
<td>224 (44.3)</td>
</tr>
<tr>
<td>Greece</td>
<td>67 (11.1)</td>
<td>72 (14.2)</td>
</tr>
<tr>
<td>Spain</td>
<td>31 (5.1)</td>
<td>39 (7.7)</td>
</tr>
<tr>
<td>Spain/Portugal</td>
<td>17 (2.8)</td>
<td>20 (4.0)</td>
</tr>
<tr>
<td>Spain/Greece</td>
<td>38 (6.3)</td>
<td>43 (8.5)</td>
</tr>
<tr>
<td>Portugal</td>
<td>103 (17.1)</td>
<td>70 (13.8)</td>
</tr>
<tr>
<td>Other Europe</td>
<td>105 (17.4)</td>
<td>92 (18.1)</td>
</tr>
<tr>
<td>Other Countries</td>
<td>145 (23.9)</td>
<td>122 (24.0)</td>
</tr>
</tbody>
</table>

• Most patients discontinued due to inefficacy (74%), and of these:
  • Primary inefficacy (40.8%)
  • Secondary inefficacy (33.2%)
  • Primary inefficacy (40.8%) and secondary inefficacy (33.2%)

• Reasons for discontinuation of initial TNFi are shown in Figure 1.

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• Factors associated with selection of rituximab versus an alternative TNFi

• Figure 2 illustrates the main factors associated with selection of RTX or an alternative TNFi.

CONCLUSIONS

• Factors most clearly associated with selection of RTX were generally related to the physician’s appreciation of treatment characteristics:
  • Safety profile: No lymphoma risk
  • Low infection risk
  • Long-term tolerance after infusion
  • Treatment profile: Compatible treatment with professional life

• Factors associated with selection of RTX over an alternative TNFi tended to be associated with the physician’s appreciation of treatment characteristics related to the long-term safety profile and low frequency of administration.

• Factors associated with selection of an alternative TNFi were related to:
  • Administration profile: Route of administration
  • Availability
  • Patient characteristics: Treatment compatibility with professional life

Table 3. Reasons for discontinuation of initial TNFi.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Incedence (n=827)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inefficacy</td>
<td>74%</td>
</tr>
<tr>
<td>Primary inefficacy</td>
<td>40.8%</td>
</tr>
<tr>
<td>Secondary inefficacy</td>
<td>33.2%</td>
</tr>
<tr>
<td>Primary + secondary inefficacy</td>
<td>40.8% + 33.2%</td>
</tr>
</tbody>
</table>

• Most patients discontinued due to inefficacy (74%), and of these:
  • Primary inefficacy (40.8%)
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REFERENCES