Adalimumab biosimilar in rheumatoid arthritis: a total-evidence assessment to evaluate equivalence with the originator based on network meta-analysis

Sirs,

In pre-approval trials of biosimilars, fewer patients are evaluated as compared with originators. For this reason, some physicians are reluctant to employ biosimilars in clinical practice and prefer originators (1). An original approach to strengthen the evidence concerning the biosimilarity of a drug, has recently been described (2-4). According to this method, a network meta-analysis is carried out, that includes not only the equivalence study comparing the biosimilar with the originator, but also the randomised studies comparing the originator with the previous standard of care (SOC). We retrospectively applied this approach to the approval of adalimumab biosimilar (ABP501) for the treatment of active rheumatoid arthritis (RA) in combination with methotrexate in patients not responsive to methotrexate monotherapy. In particular, we compared adalimumab biosimilar ABP501 with Humira (originator).

The clinical data about ABP501 were extracted from the randomised trial by Matsutomo et al. (5), while the meta-analysis published by Hazlewood et al. (6) provided the data on both Humira and SOC, i.e. methotrexate monotherapy (6). The end-point was the response at 24–26 weeks in terms of ACR50 according to the American College of Rheumatology. Our network meta-analysis was based on the Bayesian method proposed by NICE (7). Odds ratio (OR) for all pairwise comparisons was the output of the analysis along with the ranking histogram and 95% credible intervals (CrIs). Since no significant heterogeneity was found in the clinical trials, the Bayesian statistics was run with a fixed-effect model.

The data of ACR50 response from the 6 randomised trials selected by Matsutomo et al. are shown in Table I. Our network meta-analysis estimated an OR of 1.15 (95%CrI: 0.76–1.66) for the comparison of biosimilar vs. originator, 0.41 (95%CrI: 0.34–0.49) for SOC vs. originator, and 0.35 (95%CrI: 0.23–0.56) for SOC vs. biosimilar. In terms of effectiveness, ABP501 ranked: first in 76% of Bayesian simulations; second in 24%, third in 0%; the originator: first, 24%, second, 76%, third, 0%; SOC always ranked third. The number of evaluated patients was increased by this approach from 521 (trial of Matsutomo et al. (5) to 2,044 (network meta-analysis).

Table I. Data of ACR50 response at 24–26 weeks reported in the randomised trials included in our network meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Adalimumab biosimilar (ABP501)</th>
<th>Adalimumab originator</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matsumoto et al. (2015)</td>
<td>194/260</td>
<td>189/261</td>
<td>–</td>
</tr>
<tr>
<td>Kim et al. (2007)</td>
<td>–</td>
<td>40/65</td>
<td>9/62</td>
</tr>
<tr>
<td>HOPEFUL-I study (2014)</td>
<td>–</td>
<td>129/171</td>
<td>92/163</td>
</tr>
<tr>
<td>OPTIMA trial (2013)</td>
<td>–</td>
<td>207/466</td>
<td>112/460</td>
</tr>
<tr>
<td>Overall crude rate</td>
<td>194/260 (74.6%)</td>
<td>780/1296 (60.2%)</td>
<td>318/1009 (31.5%)</td>
</tr>
</tbody>
</table>

SOC: standard of care.

The complete references for the trials shown in this table are reported in the Supplementary material.

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References