A Matching-Adjusted Indirect Comparison of the Efficacy of Bimekizumab and Secukinumab at 52 Weeks for the Treatment of Psoriatic Arthritis

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Objectives

To assess the 52-week comparative efficacy of bimekizumab (BKZ) 160 mg every 4 weeks (G4W) vs secukinumab (SEC) 150 or 300 mg G4W in patients with psoriatic arthritis (PsA) who are either biologic disease-modifying anti-rheumatic drug-naïve (bio-naïve) or tumour necrosis factor inhibitor-experienced (TNFi-ex).

Background

• Bimekizumab (BKZ), a monoclonal IgG2 antibody that selectively inhibits interleukin (IL)-17A in addition to IL-17A, has shown efficacy and tolerability in phase 3 trials in patients with active PsA for 52 weeks in two Phase 3 trials: BE OPTIMAL (NCT03395203) and BE COMMUNITY (NCT02963764). Secukinumab (SEC), an IL-17A inhibitor, has also demonstrated efficacy and safety in patients with PsA for 52 weeks in the FUTURE 2 (NCT02563349) phase 3 trial.

• Due to the absence of direct comparison trials or control arms to compare the efficacy of BKZ and SEC in PsA, a matching-adjusted indirect comparison (MAC) was conducted to evaluate the relative efficacy of BKZ 160 mg G4W compared to SEC 150 or 300 mg G4W at 52 weeks in bio-naïve and TNFi-experienced patients with PsA.

Methods

• Relevant trials were identified as part of a systematic literature review. Specifically, FUTURE 2 randomized controlled trial for SEC was identified as most relevant for this MAC analysis as it was the pivotal trial used for RHT and HTA assessment in Europe.

• The MAC method was followed in accordance with Signorovitch et al. in the National Institute for Health and Care Excellence Decision Support Unit Technical Support Document 18 NICE DSU TSU.

• Figure 3 shows how individual patient data (IPD) from BKZ trials were matched to SEC trials.

• To adjust for cross-trial differences, patients from the BKZ trials were reweighted to match the baseline characteristics (Table 1) of the SEC trial patients; weights were determined using a logistic regression model on sex, age, methotrexate use, Health Assessment Questionnaire-Disability Index score, percentage with previous infecting rheumatoid arthritis, body surface area, swolen and tender joint counts, and disease duration. The adjustment variables were selected based on expert consensus (S=5).

• Reanalysis of the BKZ 52-week outcomes for American College of Rheumatology (ACR) 20/50/70 and minimal disease activity (MDA) criteria in the non-responder imputation (NRI) were compared to SEC outcomes via non-placebo-adjusted comparisons and were reported as odds ratios (ORs). The likelihood of outcome (e.g., greater or worse) was determined by the exclusion level 1 from the 95% CIs. All analyses were conducted with R version 3.6.2 using the program provided in the NICE DSU TSU 18.

Results

• In bio-naïve patients, the matching effective sample size (ESS) for BKZ was 236 (55% of original sample size (OSS)) for the comparison to both SEC 150 and 300 mg Figure 2 A/B and Figure 3 A/B.

• BKZ had a greater likelihood of achieving ACR70 response at 52 weeks compared to SEC 150 mg and SEC 300 mg.

• In TNFi-ex patients, the matching ESS for BKZ was 146 (55% of OSS) for comparison to both SEC 150 mg and SEC 300 mg Figure 2 C/D and Figure 3 C/D.

• BKZ had a greater likelihood of response than SEC 150 mg for ACR20, ACR50, ACR70, and MDA outcomes at 52 weeks.

• BKZ had a greater likelihood of achieving ACR50 and MDA outcomes at 52 weeks compared to SEC 300 mg.

• The MAC-adjusted ORs did not differ greatly from the unadjusted ORs for any outcome.

Conclusions

Using MAC methodology, bio-naïve patients treated with BKZ had a higher probability of achieving ACR70 response at 52 weeks compared to patients who received SEC 150 mg and 300 mg.

TNFi-ex patients treated with BKZ had a higher probability of achieving at ACR response levels compared to those who received SEC 150 mg, and a higher probability of achieving ACR50 and MDA responses compared to those who received SEC 300 mg at 52 weeks. These findings align with a recently published NMA where BKZ showed improvements over SEC in terms of efficacy for most joint outcomes at 16 to 24 weeks.

Figure 1

Summary of MAC method

- MACs use IPD from trials of one treatment to match baseline aggregative statistics reported from trials of another treatment.

- By using an approach similar to propensity score weighting, treatment outcomes can be compared across balanced trial populations after matching.

Figure 2

Matching-adjusted odds ratio comparison of BKZ vs SEC at Week 52 (NRI)

- Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BE OPTIMAL</th>
<th>BE COMPLETE</th>
<th>SEC FUTURE 2 150 mg</th>
<th>SEC FUTURE 2 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean DQI unless stated</td>
<td>15 (IQR: 8-23)</td>
<td>13 (IQR: 8-22)</td>
<td>13 (IQR: 7-21)</td>
<td>14 (IQR: 7-22)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57 (IQR: 47-66)</td>
<td>56 (IQR: 47-65)</td>
<td>52 (IQR: 43-62)</td>
<td>52 (IQR: 43-62)</td>
</tr>
<tr>
<td>Male</td>
<td>56%</td>
<td>56%</td>
<td>53%</td>
<td>53%</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>6.0 (IQR: 3.7-9.9)</td>
<td>6.0 (IQR: 3.8-9.6)</td>
<td>6.0 (IQR: 3.5-9.9)</td>
<td>6.0 (IQR: 3.5-9.9)</td>
</tr>
<tr>
<td>T2DM</td>
<td>9%</td>
<td>9%</td>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>SEC (66 patients)</td>
<td>9.0 (IQR: 6.2-14.9)</td>
<td>11.0 (IQR: 9.1-14.9)</td>
<td>9.1 (IQR: 7.3-14.9)</td>
<td>11.0 (IQR: 9.1-14.9)</td>
</tr>
<tr>
<td>T2DM (66 patients)</td>
<td>16.0 (IQR: 11.4-21.4)</td>
<td>20.3 (IQR: 17.4-24.7)</td>
<td>18.4 (IQR: 13.5-25.6)</td>
<td>23.5 (IQR: 20.1-37.1)</td>
</tr>
<tr>
<td>T2DM OR (95% CI)</td>
<td>1.92 (1.39-2.64)</td>
<td>0.68 (0.49-0.97)</td>
<td>0.73 (0.50-1.09)</td>
<td>1.03 (0.76-1.40)</td>
</tr>
</tbody>
</table>

Notes: *For the T2DM baseline characteristics were assumed to be similar among Group 1 and Group 2 in the MAC analysis of patients randomized to receive SEC, SEC 150 mg, or SEC 300 mg.

Figure 3

Matching-adjusted response rates of BKZ vs SEC in patients with active PsA at Week 52 (NRI)

A) Bio-n patients

- BKZ vs SEC 150 mg

<table>
<thead>
<tr>
<th>Response rate</th>
<th>BKZ 160 mg (182 patients)</th>
<th>SEC 150 mg (193 patients)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% response</td>
<td>71.3% (95.0% CI)</td>
<td>52.2% (95.0% CI)</td>
<td>1.51 (1.03-2.21)</td>
</tr>
</tbody>
</table>

B) Bio-n patients

- BKZ vs SEC 300 mg

<table>
<thead>
<tr>
<th>Response rate</th>
<th>BKZ 160 mg (182 patients)</th>
<th>SEC 300 mg (193 patients)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% response</td>
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<td>52.2% (95.0% CI)</td>
<td>1.51 (1.03-2.21)</td>
</tr>
</tbody>
</table>

C) TNFi-ex patients

- BKZ vs SEC 150 mg

<table>
<thead>
<tr>
<th>Response rate</th>
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<th>SEC 150 mg (193 patients)</th>
<th>OR (95% CI)</th>
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D) TNFi-ex patients

- BKZ vs SEC 300 mg

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<thead>
<tr>
<th>Response rate</th>
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