DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB WAS ASSOCIATED WITH IMPROVEMENTS IN PATIENT-REPORTED AND QUALITY-OF-LIFE OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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Background: Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease primarily affecting the sacroiliac joints and spine, causing pain, stiffness and loss of mobility and function. These manifestations can severely impair patients’ quality of life (QoL).1 Dual neutralisation of IL-17 in addition to IL-17A has been shown to reduce inflammation to a greater extent than inhibition of IL-17A alone in disease–relevant cell models.2 Results previously reported from this Phase 2b study (NCT02963506) demonstrated that, during the 12-week double-blind treatment period, bimekizumab provided substantial clinical improvements in disease outcome measures, including Assessment of SpondyloArthritis International Society 40% (ASAS40), in patients with active AS.3

Objectives: To assess the impact of bimekizumab on patient-reported and QoL outcomes at Week 12 in patients with active AS.

Methods: In this 48-week Phase 2b study (double blind to Week 12 then dose blind to Week 48), 303 patients with active AS (Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Disease Activity Index [BASDAI] >4; spine pain >0 [0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 1:1:1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo Q4W for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and exploratory endpoints included: BASDAI >50% improvement in BASDAI (BASDAI 50). Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient’s Global Assessment of Disease Activity (PGA) at Week 12. Safety was also assessed.

Results: Overall, 297 (98.0%) patients completed the 12-week double-blind period. Baseline scores on patient-reported and QoL outcomes were similar across treatment groups (Table). At Week 12, BASDAI 50 was achieved by 23.7% (0.6%), ASQoL (-2.3 to -4.6 vs -1.3) and PGADA (-1.9 to -3.3 vs -1.0). The overall incidence of treatment-emergent adverse events was 89/243 (36.6%) for bimekizumab-treated patients versus 23/60 (38.3%) for placebo; the majority were of mild or moderate intensity. No unexpected safety findings were observed.

Conclusion: Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and QoL outcomes including pain, fatigue and tenderness in patients with active AS after 12 weeks of treatment. No new safety findings were observed versus previous studies of bimekizumab.4,5


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METAKIMAB REDUCES THE DISEASE ACTIVITY OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS OF ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17A antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA) and psoriasis.1-3

Objectives: The abstract presents 16-week data from ongoing ASTERA study (NCT03447704) in pts with active r-axSpA and/or psoriasis.

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled study. 228 adult pts with r-axSpA active (BASDAI ≥ 4) despite the standard NSAIDs, were randomly assigned (1:1) to receive 120 mg NTK or PBO SC at Week (Wk) 0, 1.2 and then q2w through Wk 16. After Wk 16 all pts will start to receive NTK up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.
Axial spondyloarthritis (axSpA) is associated with important extra-articular manifestations (EAMS), most notably acute anterior uveitis (AAU), inflammatory bowel disease (IBD) and psoriasis, which may influence the choice of biologic agent used to treat axSpA.

**Background:** Axial spondyloarthritis (axSpA) is associated with important extra-articular manifestations (EAMS), most notably acute anterior uveitis (AAU), inflammatory bowel disease (IBD) and psoriasis, which may influence the choice of biologic agent used to treat axSpA.

**Methods:** First-line biologic data was available for 441 patients, comprising of 284 (64.4%) adalimumab (ADA), 109 (24.7%) etanercept (ETA) and 48 (10.9%) certolizumab (CZP). Pre-treatment EAMS in the entire cohort were 568 cases of AAU, 247 IBD and 264 psoriasis. Prior diagnosis of AAU was associated with a choice of ADA over the other TNFi (ETA and CZP) [OR=3.13, 95% CI: 1.78 – 5.52]. Conversely, a diagnosis of AAU was associated with less preference for ETA (OR=0.16, 95% CI: 0.07 – 0.37) compared with ADA and CZP.

The choice of a particular TNFi was not associated with HLA-B27, age, gender, axSpA disease duration, BASDAI or BASFI scores. When IBD and psoriasis, and interactions with AAU, were considered in multivariable models (Table), a diagnosis of either AAU or IBD was associated with more preference of ADA versus other TNFi. In contrast, a diagnosis of either AAU or IBD was associated with significantly less preference of ETA over other TNFi. The preference of CZP was not associated with presence any pre-treatment extra-articular manifestations.

**Conclusion:** EAMS appear to play an important role in the choice of TNFi in axSpA. Patients with previous AAU and IBD are more likely to be prescribed ADA vs. ETA and CZP [OR=3.13, 95% CI: 1.78 – 5.52]. Conversely, a diagnosis of AAU was associated with less preference for ETA (OR=0.16, 95% CI: 0.07 – 0.37) compared with ADA and CZP.

The choice of a particular TNFi was not associated with HLA-B27, age, gender, axSpA disease duration, BASDAI or BASFI scores. When IBD and psoriasis, and interactions with AAU, were considered in multivariable models (Table), a diagnosis of either AAU or IBD was associated with more preference of ADA versus other TNFi. In contrast, diagnosis of either AAU or IBD was associated with significantly less preference of ETA over other TNFi. The preference of CZP was not associated with presence any pre-treatment extra-articular manifestations.

**Table 1. Safety data**

<table>
<thead>
<tr>
<th>% of patients with</th>
<th>NTK (n = 114)</th>
<th>PBO (n = 114)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE/SAE</td>
<td>33.3% (38)</td>
<td>25.4% (29)</td>
<td>0.245</td>
</tr>
<tr>
<td>TRAE</td>
<td>17.5% (20)</td>
<td>14.0% (16)</td>
<td>0.586</td>
</tr>
<tr>
<td>SAE</td>
<td>0.9% (1)</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>Grade 3-4 AE</td>
<td>2.6% (3)</td>
<td>3.5% (4)</td>
<td>1.0</td>
</tr>
<tr>
<td>Grade 3-4 TRAE</td>
<td>1.8% (2)</td>
<td>1.8% (2)</td>
<td>1.0</td>
</tr>
<tr>
<td>Local reactions</td>
<td>1.8% (2)</td>
<td>0.9% (1)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

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**REFERENCES:**