**PROPORTIONS OF PATIENTS ACHIEVING A MINIMAL DISEASE ACTIVITY STATE UPON TREATMENT WITH TILDRAKIZUMAB IN A PSORIATIC ARTHRITIS PHASE 2B STUDY**

**P. Nash, M. E. Luggren, L. Espinoza, F. J. García Fructuoso, R. C. Chou, A. M. Mendelsohn, S. Rozzo, I. McInnes.**

**Background:** Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody approved in the US, EU, and Australia to treat moderate to severe plaque psoriasis. A randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study evaluating the efficacy and safety of TIL was recently completed (NCT02980692).

**Objectives:** To characterise and evaluate the rate of minimal disease activity (MDA) up to week (W)52 from the phase 2b study.

**Methods:** Patients (pts) ≥18 years old with active psoriatic arthritis (PsA) and ≥3 tender and ≥3 swollen joints were randomised 1:1:1:1:1 to receive TIL 200 mg every 4 weeks (Q4W) to W52, TIL 200 mg Q12W to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W to W24—TIL 200 mg Q12W to W52, or placebo (PBO) Q4W to W24—TIL 200 mg Q12W to W52. MDA was assessed throughout the study; an MDA response was achieved when 5 of 7 criteria were met. Safety was assessed throughout the study and included treatment-emergent adverse event (TEAE) monitoring.

**Results:** Of 500 pts screened, 391 were randomised and received ≥1 dose of study drug. At baseline (BL), mean age was 48.8 years, 55% were female, 97% were White, mean body mass index was 29.7 kg/m², and pts had PsA for a median (range) of 4.4 (0–42.8) years since diagnosis. Baseline disease characteristics related to MDA varied little between study arms (Table).

By W24, MDA state was achieved in significantly more pts receiving TIL vs PBO (24%–39% vs 7%; p<0.02 for all groups); the proportion further increased with continued TIL treatment to W52 (45%–64%), including pts who switched from PBO to TIL (47%) (Figure). Among the overall pt population from BL—W24/W25—W52, 50.4%/39.9% and 18.9%/11.9% experienced a TEAE and serious TEAE, respectively. From BL—W24, 1 serious infection (chronic tonsillitis) was reported for TIL 20 mg—200 mg Q12W arm. From W25—W52, there was 1 malignancy (TIL 20 mg Q12W). There were no reports of candidiasis, uveitis, inflammatory bowel disease, major adverse cardiac events, or deaths from BL—W24 or W25—W52.

**Conclusion:** TIL produced clinically meaningful improvement in pts with PsA, resulting in a large proportion of pts achieving MDA by W52, and was well tolerated through W52.

**References:**


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**Table. Baseline disease characteristics related to minimal disease activity**

<table>
<thead>
<tr>
<th></th>
<th>TIL 200 mg</th>
<th>TIL 100 mg</th>
<th>TIL 20 mg</th>
<th>PBO</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Q4W (n=78)</td>
<td>Q12W (n=77)</td>
<td>Q12W (n=77)</td>
<td>Q12W (n=78)</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>10.4</td>
<td>10.0</td>
<td>11.0</td>
<td>9.4</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>16.6</td>
<td>19.5</td>
<td>21.3</td>
<td>19.0</td>
</tr>
<tr>
<td>Patient GADA score</td>
<td>57.8</td>
<td>61.1</td>
<td>60.3</td>
<td>61.9</td>
</tr>
<tr>
<td>Patient pain</td>
<td>55.4</td>
<td>59.6</td>
<td>59.2</td>
<td>60.9</td>
</tr>
<tr>
<td>Enthesitis (LEI) score</td>
<td>1.9</td>
<td>1.5</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>PASI</td>
<td>7.6</td>
<td>6.2</td>
<td>8.8</td>
<td>6.6</td>
</tr>
<tr>
<td>HAQ-DI score</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Data are reported as mean.

*Total patients analysed (n) = 76, 79, 76, 78, respectively.
†Total patients analysed (n) = 75, 79, 75, 75, respectively.
1GADA, global assessment of disease activity; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 hours; Q12W, every 12 hours; TIL, tildrakizumab.
Background: Female sex has been associated with more severe disease and poorer treatment outcomes in PsA. These observations are often based on small populations or national cohorts registries.

Objectives: To investigate the effects of sex on disease characteristics and disease impact in PsA, using data of 929 consecutive patients (pts) from PsABio.

Methods: PsABio is a real-world, non-interventional European study in PsA pts treated with UST or TNFi based on their rheumatologist’s choice. Observed male and female baseline (BL) data were described and compared using 95% CI.

Results: Women in PsABio (n=512 [55%]) were numerically older than men (mean [SD]: 50.5 [12.7] / 48.7 [12.3] years, respectively). Women were more obese (BMI >30), % (95% CI): F: 35 (30, 39), M: 24 (20, 29), men more overweight (BMI >25–30): F: 31 (27, 36), M:51 (46, 57). Age at diagnosis, delay from first symptom to diagnosis, and disease duration were similar for both sexes.

Women entered PsABio more often on 3rd line treatment, whereas men started on 1st-line biologic treatment more often (F/M 1st line 47%/55%; 2nd line 34%/33%; 3rd line 20%/12%). Numerically, concomitant MTX was given more often to women vs men (32% vs 27%). At BL, 60% of women and 64% of men were on NSAIDs; 79% and 2.5% on antidepressant drugs. Women had significantly more comorbidities, with numerically more cardiovascular disease and anxiety/depression, and 3 times more IBD.

Women had significantly higher 68 tender joint counts (TJC): 13.0 vs 10.4, while 66 swollen joint counts were not significantly different: 5.8 vs 5.5. Axial or combined axial-peripheral disease was similarly frequent, in 29% of women and 26% of men (Figs. 1, 2).

Clinical Disease Activity index for Psoriatic Arthritis (cDAPSA) was higher in women (31.8 vs 27.3); pt-reported levels of pain, global disease activity (VAS scales) and higher TJC contributed to this. While enthesitis prevalence (based on Leeds Enthesitis Index) was comparable, men had significantly more frequent dactylitis, nail disease and worse skin psoriasis. At BL, 3.4% of women vs 7.1% of men, were in MDA.

Regarding physical functioning (HAQ-DI), impact of disease (PSAID-12) and quality of life (EQ5D-3L health state), women with PsA starting a biologic (b) DMARD, expressed significantly greater negative impact and more limitations due to their disease (Fig. 2).

Conclusion: In routine care, women with PsA starting a bDMARD presented with worse outcomes over a range of assessments compared with men (higher pt-reported pain and disease activity, TJC, and worse physical functioning and QoL), while men had worse dactylitis and psoriasis. Follow-up analysis will report whether the effects of biologic therapy are different in both sexes. The increased prevalence of associated features related to pain and impact on functioning and QoL may indicate the need for a more comprehensive treatment approach for women to avoid unnecessary and premature bDMARD stop or switch.

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We conducted a simulation study to determine how changing the inclusion criteria and the primary outcome measure would impact the outcome of a future RCT.

**Methods:** We used the Tight Control of PsA (TICOPA)\(^1\) trial to inform simulation of two hypothetical head-to-head trials comparing MTX to TNFi with 100 patients per arm. Within TICOPA, we identified MTX and TNFi new users; the visit at drug initiation became the hypothetical trial baseline visit, and the follow-up visit was 12 weeks later. These data informed prediction models to simulate enrolled patients. We utilized propensity score-adjusted outcome models to account for potential confounding by indication. Trial 1, modeled after the SEAM-PsA trial\(^2\), used typical enrollment criteria (≥3 tender joint count (TJC) and ≥3 swollen joint count (SJC))\(^2\); Trial 2 required ≥1 TJC/SJC.\(^3\) For each trial, five binary outcomes were simulated:

- ACR20, Disease Activity in PsA (DAPSA), clinical DAPSA (cDAPSA), Routine Assessment of Patient Index Data (RAPID3), and PsA Disease Activity Score (PASDAS), where low disease activity was the cutoff for continuous measures. Each hypothetical trial was simulated 1000 times, and the distribution of estimated effects was summarized using standard summary statistics and graphs.

**Results:** Among 188 patients in TICOPA, 179 patients initiated MTX, and 43 patients initiated TNFi within the first 36 weeks. Among these, 107 MTX initiators and 15 TNFi initiators had ≥3 TJC and ≥3 SJC at drug initiation. Baseline characteristics of those in the “severe” (≥3 TJC and ≥3 SJC) and not severe (not meeting ≥3 TJC and ≥3 SJC) are shown in Table 1. Among “severe” patients, the mean probability of achieving ACR20 across simulations was approximately 0.27 in both arms and the observed relative risk (RR) TNFi vs MTX severe cohort mean probability of achieving ACR20 across simulations was approximately 0.27 meeting ≥3 TJC and ≥3 SJC) are shown in Table 1. Among “severe” patients, the mean probability of achieving ACR20 across simulations was approximately 0.27 in both arms and the observed relative risk (RR) TNFi vs MTX severe cohort mean probability of achieving ACR20 across simulations was approximately 0.27 meeting ≥3 TJC and ≥3 SJC) are shown in Table 1. Among “severe” patients, the mean probability of achieving ACR20 across simulations was approximately 0.27 in both arms and the observed relative risk (RR) TNFi vs MTX severe cohort mean probability of achieving ACR20 across simulations was approximately 0.27 meeting ≥3 TJC and ≥3 SJC.\(^1\) For each trial, five binary outcomes were simulated:

- ACR20, Disease Activity in PsA (DAPSA), clinical DAPSA (cDAPSA), Routine Assessment of Patient Index Data (RAPID3), and PsA Disease Activity Score (PASDAS), where low disease activity was the cutoff for continuous measures. Each hypothetical trial was simulated 1000 times, and the distribution of estimated effects was summarized using standard summary statistics and graphs.

**Conclusions:** Including patients with lower joint counts in an RCT reduced the ability to detect change with therapy. Additionally, among the outcome measures used to detect a difference between two active therapies, PASDAS, cDAPSA, and RAPID3 outperformed ACR20.

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**Table 1. Observed characteristics at drug initiation**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Severe (n=148)</th>
<th>Not Severe (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX</td>
<td>MTN (n=127)</td>
<td>TICOPA (n=117)</td>
</tr>
<tr>
<td>Standard Care</td>
<td>57 (45%)</td>
<td>4 (19%)</td>
</tr>
<tr>
<td>Intensive Management</td>
<td>70 (55%)</td>
<td>17 (81%)</td>
</tr>
<tr>
<td>Female (no. (%))</td>
<td>65 (51%)</td>
<td>51 (52%)</td>
</tr>
<tr>
<td>TJC (mean (SD))</td>
<td>17.8 (15.3)</td>
<td>19.1 (17.3)</td>
</tr>
<tr>
<td>SJC (mean (SD))</td>
<td>9.2 (7.4)</td>
<td>10.2 (12.1)</td>
</tr>
</tbody>
</table>

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**References:**


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