Background: Randomized controlled trials (RCTs) in psoriatic arthritis (PsA) have traditionally enrolled a homogenous subgroup of patients with more polyarticular disease, and the outcome measure used in PsA RCTs (ACR20) may not be ideal to measure differences between two active therapies nor capture change in patients with lower joint counts.

Objectives: 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 (TICO³A) trial to inform simulation of two hypothetical head-to-head trials comparing MTX to TNFi with 100 patients per arm. Within TICO³A, 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, used typical enrollment criteria (≥3 tender joint count (TJC) and ≥3 swollen joint count (SJC)) and 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 ≥3 TJC or not ≥3 SJC) were 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 across simulations was 1.0, IQR 0.84-1.17 (the RR in the SEAM trial at 24 wks was 1.04). Trials using PASDAS, cDAPSA, and RAPID3 outperformed ACR20.

Conclusion: 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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Figure 1. Risk Ratios (TNFi vs MTX) by Outcome Across 1000 Simulations

Figure 2. Risk Differences (TNFi – MTX) by Outcome Across 1000 Simulations

Table 1. Observed characteristics at drug initiation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Severe (n=148)</th>
<th>Not Severe (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX (n=127)</td>
<td>TNFi (n=21)</td>
<td>SMD MTX (n=02)</td>
</tr>
<tr>
<td>TICO³A Arm (no. (%)</td>
<td>Standard Care</td>
<td>57 (45%)</td>
</tr>
<tr>
<td></td>
<td>Intensive Management</td>
<td>70 (55%)</td>
</tr>
<tr>
<td></td>
<td>Female (no. (%)</td>
<td>65 (51%)</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>

Severe = ≥3 tender and ≥3 swollen joints
Not severe = <3 tender or <3 swollen joints

Abbreviations: SMD = standardized mean difference, TJC=tender joint count, SJC=swollen joint count
worsening. The mean change in each measure by patient-reported response (improved, stayed the same, or worsened) are shown in Figures 1A & B. In general, the mean score increased from ‘improved to ‘worsened’ as expected (with the exception of PROMIS PH which declines given a different direction of scoring). The MCII for each measure was as follows: RAPID3 -1.8 (-4.1 to 0.5), Patient Global -0.6 (-1.6 to 0.4), Physician Global -1 (-1.9 to -0.1), cDAPSA -5.7 (-9.8 to -1.7), and PROMIS PH 1.9 (-2.1 to 5.8). Correlation for each measure with the global assessment of response were: RAPID3 0.48, Patient Global 0.37, Physician Global 0.39, cDAPSA 0.51, and PROMIS PH 0.39.

Figure 1 A. Distribution of change (median, IQR) in RAPID3, Physician Global, Patient Global, PROMIS10a physical therapy by patient reported response.

Conclusion: This is the first study to test thresholds of meaning for these particular measures in PsA. The MCII values are relatively low for all outcome measures. This may be related to the relatively low disease activity at baseline but is consistent with patients seen in clinical practice initiating therapy.2

References:

Figure 2 B. Distribution of change (median, IQR) in clinical DAPSA by patient reported response.

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SAT0435 SECUKINUMAB EFFICACY IN PSA PATIENTS IS DEPENDENT ON PATIENTS’ BODY MASS INDEX

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis burdened by a series of metabolic comorbidities. Among them, obesity is very common in PsA, with a prevalence of 27%, as confirmed by a recent Spanish work (1). Obesity in PsA has been associated with higher disease activity and a worse effectiveness of biologic treatment in PsA. This has been certainly proven for anti-TNF-α as demonstrated by different studies reporting, in obese patients, a reduced treatment response and adherence. In particular, results coming from DAN-BIO and ICE-BIO registries, (2) point out that obesity is a risk factor for anti-TNF withdrawal due to poor response. Although a recent multi-centric, retrospective study in Spain has shown that obese subjects with psoriasis have a poor therapeutic response to secukinumab, (3) no data are currently available for secukinumab in PsA obese patients.

Objectives: Our studies focused on the relationship between BMI and clinical response to secukinumab in PsA.

Methods: We, retrospectively, analysed clinical data of 100 patients with PsA (57% female, median age 53 (49.2-55 years)) satisfying CASP AR criteria (4) for PsA, afferent to our clinic, who were treated with secukinumab. Patients were divided into 2 groups based on BMI (BMI<25 normal weight and BMI≥25 overweight/obese).

Results: In the normal weight group 75% were female, median age was 50.5 (41.5-64.6), median BMI was 22 (20.2-23.3) and median DAPSA was 19.19 (15.6-24.2). The features of the overweight/obese patients were similar to the normal weight group (48% were female, median age 54 (50-59), median BMI 29 (27.4-30.1) and median DAPSA 21.2 (19-24.4). Clinical response to therapy, evaluated as the achievement of low disease activity or remission according to DAPSA, was recorded 6 months after starting treatment. After 6 months of treatment, the variation of the DAPSA was inversely related to BMI: overweight/obese patients had in fact a better response to secukinumab compared to normal weight patients. By using a correlation coefficient (SPSS), to analyze the degree of association between BMI and DAPSA, we observed that BMI and DAPSA are inversely related in our PsA patients (p=0.05). Interestingly, analysis of serum levels of IL-17 in 20 obese patients compared to 20 non-obese patients, showed significantly higher serum levels of IL-17 in the former (Figure 1), indicating IL-17 as a key cytokine driving inflammation in PsA obese patients.

Conclusion: These are the first data about clinical response to secukinumab in obese PsA patients. Our results support the relevance of IL-17 in driving systemic inflammation in obese PsA patients, also providing evidence that obese patients may have a better response to secukinumab compared to non-obese patients. Interestingly, this effect was not

References:

Disclosure of Interests: Ilenia Pantano: None declared, DANIELA IACONO Speakers bureau: PFIZER, BRISTOL MAYERS SQUIBB, SANOFI, ENNIO GIULIO FAVALLI: None declared, GIUSEPPE SCALISE: None declared, Luisa Costa: None declared, Francesco Caso: None declared, Giuliana Gugino Grant/research support from: Pfizer, Celgene, Speakers bureau: Celgene, Sanofi, Pfizer, Raffaele Scarpa: None declared, francesco ciccia Grant/research support from: pfizer, novartis, lilly, abbvie, Speakers bureau: pfizer, novartis, lilly, abbvie
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