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SAT0433 TRIAL SIMULATION TO INFORM ENROLLMENT CRITERIA AND OUTCOME MEASURES FOR PRAGMATIC TRIALS IN PSA

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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 (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.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.

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 across simulations was 1.0, IQR 0.84-1.17 (the RR in the SEAM trial at 24 wks was 1.20, 95%CI:1.05-1.35). In the "full cohort", the median RR was 1.0, IQR 0.81-1.04. Trials using PASDAS, cDAPSA, and RAPID3 were more likely to differentiate between TNFi and MTX in the severe cohort (figure) but in the full cohort the results favored MTX.

Table 1. Observed characteristics at drug initiation

	Severe (n=148)			Not Severe (n=75)		
	MTX (n=127)	TNFi (n=21)	SMD	MTX (n=52)	TNFi (n=23)	SMD
TICOPA Arm (no. (%))						
Standard Care	57 (45%)	4 (19%)	0.58	28 (54%)	3 (13%)	0.96
Intensive Management	70 (55%)	17 (81%)		24 (46%)	20 (87%)	
Female (no. (%))	65 (51%)	11 (52%)	0.02	22 (42%)	12 (52%)	0.20
TJC (mean (SD))	17.8 (15.3)	19.1 (17.3)	0.08	3.5 (4.6)	16.4 (19.1)	0.93
SJC (mean (SD))	9.2 (7.4)	10.2 (12.1)	0.10	2.4 (3.4)	2.2 (2.4)	0.05

Severe = ≥ 3 tender and ≥ 3 swollen joints

Not-severe = < 3 tender or < 3 swollen joints

*Pseudo-baseline characteristics were at the time of drug initiation. In cases where the patient started a TNFi between visits, these were the values at the previous visit.

Abbreviations: SMD = standardized mean difference, TJC=tender joint count, SJC=swollen joint count

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

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SAT0434 MINIMAL CLINICALLY IMPORTANT DIFFERENCE IN OUTCOME MEASURES FOR USE IN CLINICAL CARE AND PRAGMATIC TRIALS IN PSA

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Background: While several outcome measures have been studied for use in clinical studies of psoriatic arthritis, little is known about thresholds of meaning such as minimal clinically important improvement (MCII).

Objectives: To investigate the distribution of scores for candidate outcome measures for pragmatic trials in PsA and to calculate the MCII for each outcome measure.

Methods: We performed a longitudinal cohort study within the Psoriatic Arthritis Research Consortium (PARC), a multi-center study based in the US. Patients completed validated PROs (patient reported outcomes) and rheumatologists completed skin, joint, enthesitis and dactylitis scores at therapy initiation and follow up 12-16 weeks later. In addition, patients completed a global assessment of response at the follow up visit, categorizing their status as improved, stayed the same, or worsened and then rated the importance of the change on a scale from 0-7.¹ We then calculated and plotted the change in each of the following measures: Routine Assessment of Patient Index Data (RAPID3), clinical Disease Activity of Psoriatic Arthritis (cDAPSA), Patient Reported Outcome Measure Information System (PROMIS) Global Health short form (10a) physical health (PH) subscore, patient pain assessment, patient global assessment (0-10 NRS), and physician global assessments (0-10 NRS) of the joints and overall. We calculated the MCII as the mean change in score (with 95% confidence interval) among patients who reported improvement and rated the level of improvement as "almost none/hardly at all" or "a little important." Additionally, we calculated Spearman's correlation coefficients between the measures and the global assessment of response.

Results: Among 148 unique patients, 233 therapy change visits were eligible for analysis. The average age was 52.5 years, 52% were female and mean BMI was 29.6. Baseline RAPID3 was 11.1 (SD 6), cDAPSA 17.9 (SD 13.9), PROMIS PH 42 (SD 8), patient global 4.2 (SD 2.5), TJC 5.9 (SD 7.5), and SJC 2.9 (SD 4.5). TNFi comprised 61% of drug initiations, 21% were IL17i and the remainder were other biologics and oral systemic therapies. At follow up, 63 (27%) patients rated themselves as improved whereas 103 (44%) stayed the same and 67 (29%) reported

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

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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 CASPAR 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 $\geq$ 25 overweight/obese).

Results: In the normal weight group 75% were female, median age was 50.5 (41-54.6), 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

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