SAT0401

SWOLLEN JOINTS ARE ASSOCIATED WITH ULTRASOUND POWER DOPPLER SYNOVITIS, WHEREAS TENDER JOINTS IN THE ABSENCE OF SWELLING ARE NOT: AN ANALYSIS OF AGREEMENT AND CORRELATION IN VERY EARLY DMARD NAÏVE PSORIATIC ARTHRITIS

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Background: Ultrasound (US) is an imaging adjunct to clinical joint examination adding sensitivity and objectivity to the assessment of inflammation. Previous studies in PsA have shown disparity between ultrasound and clinical findings with significant subclinical joint inflammation. A clinical challenge in PsA is to interpret tender joints (TJ) that are not swollen (SJ). As US is not widely used, alignment of clinical with US assessment is needed to determine its future role.

Objectives: To determine how joint clinical examination relates to US findings in very early DMARD naïve PsA.

Methods: Newly diagnosed DMARD naïve PsA patients, fulfilling CASPAR criteria, were recruited into the Leeds Spondyloarthritis Register for Research and Observation (SpARRO), a prospective observational cohort study. US examination of 48 joints per patient was conducted by trained ultra-sonographers, blinded to clinical details with semi-quantitative scoring (0-3) for gray scale (GS) and power Doppler (PD). TJ and SJ counts were independently recorded. Cross-sectional baseline analysis was performed. The prevalence-adjusted and bias-adjusted kappa (PABAK) was calculated to determine agreements between clinical and US parameters. Spearman's rank correlation coefficient was calculated to identify permutations of TJ/SJ correlating with GS ≥ 2 , PD ≥ 1 or both.

Results: A total 5927 joints were scanned in 155 PsA patients. The mean age was 44.4 years, (SD 12.8), median disease duration 5.1 weeks (0.4-13.1); median TJC=7 (3-14) and SJC=2 (1-7). Oligoarthritis was present in 63.9% (99/155). US GS ≥ 2 was frequently detected in the feet at MTPs1-4 (37.4- 53.6 %) and wrists (26.5- 33.6%). PD was most prevalent at wrists (17.5%) and MTP1 (12.6%) but observed less in other joints. Erosions were less frequent, the commonest site being MTP5 (17/310, 5.4%).

Overall, SJ demonstrated high agreement ($p < 0.001$) with US synovitis (GS ≥ 2 and/or PD ≥ 1). High agreement was equivalent between combined GS ≥ 2 and PD ≥ 1 compared with PD ≥ 1 alone ($p < 0.001$) indicating it was predominantly driven by PD. Agreement with TJ and SJ was consistently lower yet still significant ($p < 0.001$). Combinations of TJ/SJ were explored with US synovitis (table 1). Correlation was significant for T+ S+ and PD ≥ 1 at wrists, MCP1-5, PIP2-5, MCP3-4 ($p < 0.001$); DIP2 ($p < 0.05$), knees and ankles ($p < 0.01$) but weaker correlation in MTP3,4. In contrast, poor correlation was observed in the T+ S- group for most joints.

Table 1. Agreement between TJ or SJ with GS ≥ 2 & PD ≥ 1 and correlations for tender with/ without swollen combinations for right sided hand/feet joints.

Joint (Right)	Tender		Swollen		T+ S-	T+ S+
	A (%)	PABAK	A (%)	PABAK	r	r
Wrist	75.5	0.51*	89.1	0.78*	-0.09	0.35*
MCP1	84.1	0.68*	87.5	0.75*	0.09	0.44*
MCP2	77.7	0.55*	83.1	0.66*	0.08	0.35*
MCP3	79.1	0.58*	84.5	0.69*	0.005	0.50*
MCP4	78.4	0.57*	86.4	0.72*	0.07	0.22†
MCP5	87.8	0.76*	95.6	0.91*	-0.03	0.49*
MTP1	69.8	0.40*	83.9	0.68*	-0.03	-
MTP2	79.1	0.58*	90.5	0.81*	0.06	0.11
MTP3	77.0	0.54*	88.5	0.77*	0.05	0.22†
MTP4	77.7	0.55*	87.2	0.74*	-0.002	0.23†
MTP5	79.9	0.60*	89.9	0.80*	0.15	0.09

T+= tender, S+ =swollen, S- = not swollen, A=agreement (%), r =coefficient, † $p < 0.05$, ‡ $p < 0.01$, * $p < 0.001$.

Conclusion: Swollen joints demonstrate higher agreement with US synovitis (PD ≥ 1 alone or GS ≥ 2 & PD ≥ 1 combined) than tender joints in early PsA. In addition, joints that are tender but not swollen have poor correlation with US synovitis at the individual joint level indicating that swelling is a better clinical discriminator of active synovitis, and factors other than synovial inflammation may drive tenderness in very early, DMARD naïve PsA. These results suggest re-appraisal of clinical joint counts is needed to refine treatment decision making in early PsA.

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SAT0402

EFFICACY AND SAFETY OF GUSELKUMAB, A MONOCLONAL ANTIBODY SPECIFIC TO THE P19-SUBUNIT OF INTERLEUKIN-23, THROUGH WEEK 52 OF A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY CONDUCTED IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat psoriasis. Through Week24 (W24) of the Ph3, double-blind, placebo (PBO)-controlled trial in biologic-naïve pts with active PsA (DISCOVER-2), GUS every 4 or 8 weeks (Q4W or Q8W) demonstrated efficacy for joint & skin symptoms and inhibition of structural damage progression (Q4W), and was well tolerated.

Objectives: Assess GUS efficacy and safety through W52.

Methods: Biologic-naïve adults with active PsA (≥ 5 swollen+ ≥ 5 tender joints; CRP ≥ 0.6 mg/dL) were randomized (1:1:1) to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W; or PBO. At W24, PBO pts crossed over to GUS 100mg Q4W (PBO X Q4W). ACR response rates at W52, based on nonresponder imputation (NRI) for missing data and as observed in pts who continued study agent at W24, are shown. Observed data for additional endpoints, including PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52 (or at d/c) and scored in a new Read Campaign, are shown.

Results: 712/739 (96.3%) randomized & treated pts continued study agent at W24; 689/739 (93.2%) completed Wk52. NRI ACR20 response rates continued to increase after W24, and at W52 were 70.6% for GUS Q4W and 74.6% for GUS Q8W (Fig 1A). Similar response patterns were observed for the more stringent ACR50/70 criteria (Fig 1C,E). Observed ACR (Fig. 1B,D,F), IGA, PASI & MDA/VLDA responses; dactylitis & enthesitis resolution; and mean improvements in HAQ-DI and SF-36 PCS/MCS scores were also sustained through W52 in pts receiving Q4W & Q8W; W52 data for PBO X Q4W pts were generally consistent with other GUS-treated pts (Fig 1, Table 1). Changes in vdH-S scores were

Table 1. Observed Efficacy¹

	GUS	Q4W	GUS	Q8W	PBO X	GUS Q4W
	W24	W52	W24	W52	(W0-24)	(W24-52)
Data are % unless otherwise stated	W24	W52	W24	W52	W24	W52
Dactylitis at W0, n	116	111	107	105	95	93
Resolution	68.1	81.1	60.7	81.9	41.1	78.5
Enthesitis at W0, n	165	160	151	148	172	168
Resolution	45.5	60.0	57.6	65.5	32.6	67.3
$\geq 3\%$ BSA psoriasis, IGA ≥ 2 at W0, n	176	173	172	170	176	172
IGA 0/1 + ≥ 2 -grade decrease	71.0	84.4	72.1	77.1	19.9	84.3
PASI75	81.8	91.9	80.8	88.8	23.3	88.4
PASI90	63.6	81.5	70.3	77.1	10.2	76.7
PASI100	46.6	61.3	46.5	54.7	2.8	55.2
HAQ-DI, n	234	229	238	234	237	230
Mean change	-0.4	-0.5	-0.4	-0.5	-0.2	-0.4
SF-36 scores, n (mean change)	234	229	238	234	237	230
Physical Component - PCS	7.2	9.0	7.8	9.5	3.8	8.1
Mental Component - MCS	4.1	4.1	4.5	4.5	2.2	4.3
MDA/VLDA, n	234	228	238	234	238	231
MDA	19.7	36.8	26.5	32.9	6.3	31.6
VLDA	5.1	12.2 ²	4.6 ³	17.1	1.3	6.9

¹Randomized pts still on study agent at W24; ²N=229; ³N=237

similar for W24-52 (0.62) and W0-24 (0.46) for Q4W; less radiographic progression occurred from W24-52 v W0-24 for Q8W (0.23 v 0.73) & PBO X Q4W (0.25 v 1.00). In 731 GUS-treated pts, 4.2% had SAEs; 1.2% had serious infections; no pt died; and no pt had IBD, opportunistic infections or active TB, or anaphylactic or serum sickness-like reactions.

Conclusion: In biologic-naïve pts with active PsA, GUS elicited sustained improvements in joint & skin symptoms; inhibition of radiographic progression & improvements in physical function, quality of life & composite indices through W52. GUS safety in PsA was similar at W24¹ & W52 and consistent with GUS safety in psoriasis.

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Fig 1. NRI and Observed ACR20 (A & B), ACR50 (C & D), and ACR70 (E & F) responses through W52
(Note: patients randomized to PBO crossed over to GUS Q4W at W24)

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SAT0403

EFFICACY AND SAFETY OF 108 WEEKS' BIMEKIZUMAB TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS: INTERIM RESULTS FROM A PHASE 2 OPEN-LABEL EXTENSION STUDY

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Background: Bimekizumab (BKZ), a monoclonal antibody that selectively neutralises IL-17A and IL-17F, has shown clinical improvements in skin and joint outcomes over 48 weeks (wks) in patients (pts) with active psoriatic arthritis (PsA).¹ **Objectives:** To report 2-year interim results from a phase 2b dose-ranging study (BE ACTIVE; NCT02969525) and open-label extension (OLE; NCT03347110) of BKZ in pts with PsA.

Methods: Design of the dose-ranging study is described elsewhere.¹ Pts who completed 48 wks' BKZ treatment without meeting withdrawal criteria were eligible for OLE entry. All OLE pts received BKZ 160 mg Q4W, irrespective of prior dosing regimen.

Data are presented from dose-ranging study baseline (BL) to OLE Wk 60 (Wk 108 total). Efficacy outcomes are reported for the full analysis set (FAS): pts who received ≥1 dose BKZ (specifically those randomised to 160 mg, 160 mg with 320 mg loading dose [LD], or 320 mg at BL), with BL efficacy measurements to allow subsequent determination of ACR50. Outcomes include ACR20/50/70, body surface area (BSA) 0%, minimal disease activity (MDA), and enthesitis/dactylitis resolution. Rates of treatment-emergent adverse events (TEAEs) are reported for the Safety Set (SS; pts who received ≥1 dose BKZ in the dose-ranging study).

Results: BL mean (SD) tender/swollen joint counts were 21.7 (15.7) and 11.2 (8.4). 80 (65.0%) pts had BSA ≥3% and dactylitis/enthesitis were present in 41 (33.3%) and 68 (55.3%) pts. Over 108 wks' BKZ treatment, improvements were observed in skin/joint outcomes: ACR50 (66.7%), BSA 0% (75.4%), MDA (65.6%), and resolution of dactylitis (65.9%) and enthesitis (77.9%) (Table). Serious TEAEs occurred in 9.3% pts (Table); no deaths or major adverse cardiac events were reported. Oral candidiasis occurred in 16 (7.8%) pts (no serious cases).

Conclusion: BKZ leads to long-term efficacy for skin/joint manifestations of PsA, with >50% pts achieving high thresholds of disease control (ACR50, BSA 0%, MDA) after 108 wks' treatment. The safety profile reflects previous observations.¹

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