drug exposure. DAS28-CRP might however not capture the full disease spectrum in PsA. Trials using PsA specific endpoints are needed to investigate tapering in a prospective and randomized manner.

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Table 1. Baseline characteristics of PsA patients

Characteristic	PsA (N=152)
Female, n (%)	60(39%)
Age in years at inclusion, mean (SD)	52(11)
Disease duration at inclusion, years, median	9(3-14)
(IQR)	
Rheumatoid factor negative, n (%)*	132 (87%)
Anti-CCP negative, n (%)**	136 (89%)
Erosions on radiographic imaging, n (%)	34(22%)
Number of previous bDMARD, n (%)	
-0	102(67%)
-1	39(26%)
-2 or 3	11(7%)
Number of previous csDMARD, n (%)	
-0	21(14%)
-1	50(33%)
-≥ 2	81(53%)
Current bDMARD use, n (%)	
-Adalimumab	49(32%)
-Etanercept	81(53%)
-Golimumab	3(2%)
-Infliximab	19(13%)
Current csDMARD use, n (%)	
-None	71(46%)
-Methotrexate	65(43%)
-Leflunomide	12(8%)
-Hydroxychloroquine	1(1%)
-Sulfasalazine	3 (2%)
Duration of current bDMARD use at inclusion, years, median (IQR)	3(1-5)
Duration of follow-up, months, median (IQR)	43(28-58)

*Available for 144 of 152 patients** Available for 145 of 152 patients

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POS0194

ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB OR ADALIMUMAB: A POST HOC ANALYSIS OF EXCEED

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Background: Enthesitis is a key musculoskeletal manifestation of psoriatic arthritis (PsA). EULAR guidelines recommend biologics for patients with enthesitis and an inadequate response to or intolerance of nonsteroidal anti-inflammatory drugs, although no guidance on specific biologics is offered. In the EXCEED head-to-head, double-blind study (NCT02745080), secukinumab (SEC) and adalimumab (ADA) showed a similar efficacy in joints and in resolution of enthesitis at Week 52 for patients with PsA,¹ although a detailed analysis of enthesitis was not conducted.

Objectives: To explore detailed enthesitis treatment response, including temporal and additional enthesitis assessment data, in patients with PsA treated with SEC or ADA over 52 weeks.

Methods: In this post hoc analysis, patient data from EXCEED were grouped by presence or absence of baseline enthesitis based on the Leeds Enthesitis Index (LEI) and the Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). Baseline characteristics of these groups were summarized. Median time to resolution of LEI/SPARCC enthesitis score in patients receiving SEC or ADA was assessed using Kaplan-Meier analysis. Efficacy was further assessed among the enthesitis subset by LEI and SPARCC change from baseline, resolution of enthesitis (LEI/SPARCC) at Weeks 24 and 52, and resolution of enthesitis at Week 52 by baseline enthesitis severity. Relapse of enthesitis after a first resolution was evaluated at Weeks 24 and 52. Missing data were imputed by nonresponder imputation.

Results: Baseline demographics were well balanced in the LEI/SPARCC enthesitis subsets, although a higher proportion of all patients with enthesitis were women vs those with no enthesitis (LEI: 54.6% vs 40.5%; SPARCC: 53.2% vs 36.2%). Patients with baseline enthesitis had higher disease activity vs patients without enthesitis (LEI/SPARCC enthesitis vs no LEI/SPARCC enthesitis: tender joint count of 78 joints [22.8/22.1 vs 15.8/13.8], Health Assessment Questionnaire-Disability Index [1.3/1.3 vs 1.1/1.1], and mean Psoriasis Area and Severity Index [6.4/6.1 vs 5.1/5.3]). Median time to resolution of LEI and SPARCC enthesitis was similar between patients receiving either SEC or ADA (Table 1). Both treatment groups experienced a similar mean change from baseline in LEI and SPARCC enthesitis counts and a similar resolution of LEI and SPARCC at Weeks 24 and 52 (Table 1). Achievement of enthesitis resolution was similar between treatment groups irrespective of disease severity (Figure 1). The proportion of patients who experienced relapse after achieving resolution was low across both treatments (Table 1).

Conclusion: In EXCEED, patients with baseline enthesitis presented with higher disease burden, consistent with the FUTURE trials.² SEC and ADA showed similar kinetics of response and efficacy on enthesitis, irrespective of baseline enthesitis severity.

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Table 1. Clinical Improvements Among Patients With Baseline LEI or SPARCC Enthesitis Treated with Secukinumab or Adalimumab (nonresponder imputation)

Outcomes ^a	Secukinumab		Adalimumab	
	300 mg		40 mg	
	LEI	SPARCC	LEI	SPARCC
	(n=234)	(n=301)	(n=264)	(n=331)
Baseline enthesitis count, mean (SD)	2.6 (1.5)	5.0 (3.8)	2.8 (1.6)	5.4 (4.0)
Median time to enthesitis resolution, days (95% CI)	85 (57–113)	113 (85–169)	85 (57–86)	88 (85–114)
Enthesitis count, mean improvement from baseline (SD)				
Week 24	-1.6 (1.6)	-3.3 (3.5)	-1.6 (1.6)	-3.1 (3.5)
Week 52	-1.8 (1.6)	-3.6 (3.2)	-2.1 (1.7)	-3.9 (3.8)
Resolution of enthesitis, n (%)				
Week 24	116 (49.6)	138 (45.8)	115 (43.6)	144 (43.5)
Week 52	142 (60.7)	160 (53.2)	146 (55.3)	170 (51.4)
Enthesitis relapse, n/M (%)				
Week 24	37/210 (17.6)	38/274 (13.9)	49/232 (21.1)	47/293 (16.0)
Week 52	40/208 (19.2)	56/267 (21.0)	32/208 (15.4)	41/263 (15.6)

LEI, Leeds Enthesitis Index; M, number of evaluable patients; SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index. ^a Based on respective enthesitis measures.

Figure. Proportion of Patients Achieving Resolution of Enthesitis at Week 52 by Baseline (A) LEI and (B) SPARCC Enthesitis Severity^a

LEI, Leeds Enthesitis Index; SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index.

^a Error bars represent 95% confidence intervals.

Figure 1.

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POS0195

GUSELKUMAB TREATMENT MODULATES CORE PSORIATIC ARTHRITIS GENE EXPRESSION IN TWO PHASE 3 CLINICAL TRIALS (DISCOVER-1 AND -2)

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Background: Guselkumab (GUS), an interleukin-23 p19-subunit monoclonal antibody, demonstrated efficacy compared with placebo (PBO) in reducing signs and symptoms of psoriatic arthritis (PsA) in the phase 3 DISCOVER-1 & 2 studies.^{1,2}

Objectives: To evaluate gene expression in the blood of PsA patients (pts) in the DISCOVER-1 & -2 studies and the impact of GUS on the expression of these genes.

Methods: Pts were treated with GUS 100mg every 4 weeks (Q4W); GUS 100mg at W0, W4, then Q8W; or matching PBO. Whole transcriptome profiling by RNA-sequencing was performed using the Novaseq platform on blood samples obtained from a subset of 673 pts with PsA at baseline across the 2 DISCOVER studies, as well as from 21 demographically (age, sex, and ethnicity) matched healthy controls procured independently of the clinical program. A subgroup (N=227) also had serial blood samples (W0/W4/W24) evaluated; the subgroup pts were selected based on having baseline characteristics (demographics, disease activity, medication use) representative of the overall cross-study PsA population. Significance of differentially expressed genes (DEGs) between PsA and healthy controls was defined by a false discovery rate (FDR) <0.05 based on a log-linear model using edgeR. Top genes were defined by significance and |logFC| >1. For cell type analysis, genes that changed with GUS treatment were tested for enrichment using Cibersort. Gene enrichment scores were calculated using Gene Set Variation Analysis (GSVA).

Results: To define disease genes, we compared genes at baseline in pts with active PsA vs. healthy control whole blood transcriptomes and detected 355 upregulated and 314 downregulated (top genes shown in Table 1), defined here as core disease genes. Upregulated genes were largely related to neutrophils, monocytes, macrophages, and extracellular matrix, whereas downregulated genes were related to T cells. The upregulated disease genes were significantly decreased and the downregulated disease genes were significantly increased by GUS treatment vs. PBO at W4 and W24 (Fig 1). Upon stratification by Psoriasis Area and Severity Index 75% response and American College of Rheumatology 20% response, changes in core disease gene expression from W0 were statistically significant among responders, but not in non-responders, at W4 and W24 (data not shown). We then performed the second differential expression analysis comparing baseline to W4 and W24 for both PBO and GUS treatment arms to define genes that change with treatment arm over time. At W4 and W24 we

found many DEGs from baseline with GUS treatment and none with PBO. These included genes related to B-, T-, NK-, and plasma cells (increased by GUS) and neutrophils, monocytes, eosinophils, and macrophages (decreased by GUS), suggestive of a partial normalization of immune cell composition in whole blood. **Conclusion:** Using whole transcriptome profiling, we detected DEGs in blood samples obtained from PsA pts vs. healthy controls, suggesting a dysregulation of immune cell profiles in PsA. The majority of these disease-associated genes were modulated by GUS, with directionality toward a normalization of whole blood transcriptomic signatures.

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Table 1. Top DEGs derived from PsA vs. healthy whole blood transcriptomes.

Upregulated in PsA				Downregulated in PsA			
Gene	logFC	logCPM	FDR	Gene	logFC	logCPM	FDR
ADGRG7	5.92	-0.90	0.02101	AK8	-1.36	-1.06	1.61E-07
ADAMTS2	4.06	0.82	0.006466	FTCD	-1.48	-1.74	1.67E-05
PGF	3.21	-0.68	0.006466	GPR15	-1.54	1.81	1.67E-05
PCSK9	3.21	-2.96	0.023872	CHRM3	-1.54	-2.62	9.6E-08
OLAH	2.76	0.75	0.004539	RFPL4AL1	-1.69	-3.34	0.009738
MAOA	2.55	-0.26	0.005463	SPACA3	-1.85	-3.23	0.000216
SLC2A14	2.30	0.59	0.022594	VANGL2	-1.95	-1.79	9.6E-08
MMP1	2.25	-1.16	0.004745	RFPL4A	-2.04	-1.28	0.004539
DAAM2	2.12	4.31	0.024628	GLYATL2	-2.77	-2.78	1.93E-15
				BCAR1	-3.13	-2.58	6.24E-26

Bold indicates positive change. CPM = counts per million.

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Figure. Change from baseline in median GSVA scores for upregulated and downregulated genes in PsA for GUS and PBO treatment arms from DISCOVER-1 and 2.

*, **, *** p < 0.05, 0.01, 0.001, respectively. Wilcoxon test performed between GUS (Q4W, dashed line; Q8W, solid line) and PBO.

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POS0196

UPADACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS REFRACTORY TO BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: 56-WEEK DATA FROM THE PHASE 3 SELECT-PSA 2 STUDY

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