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DOI: 10.1136/annrheumdis-2021-eular.1066

POS0197

RESPONSIVENESS OF ULTRASOUND SYNOVITIS AND CLINICAL OUTCOMES IN PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB: DATA FROM THE ULTIMATE TRIAL

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Background: Power Doppler ultrasonography is a sensitive imaging tool to assess synovitis in psoriatic arthritis (PsA).^{1,2} ULTIMATE (NCT02662985) is the first large, randomised, double-blind placebo-controlled phase IIIb study in PsA, using ultrasound to evaluate early response to secukinumab on synovitis. The use of the standardised and reliable global EULAR-OMERACT composite ultrasound synovitis score at patient level (GLOESS) as the primary endpoint showed the early and significant benefit of secukinumab vs. placebo on synovitis at week 12.³

Objectives: To investigate the responsiveness and discriminative validity of GLOESS compared to clinical outcomes on joints at week 12 and report ultrasound and clinical efficacy data up to week 24.

Methods: This is a 52-week study with a 12-week double-blind, placebo-controlled period followed by 12-week open-label (OL) and 6-month OL extension. All placebo patients were switched to secukinumab (300 or 150 mg) at week 12.³ Discriminative validity of GLOESS was analysed post-hoc: within-group responsiveness was assessed by comparing its standardised response mean (SRM) to that of core set of ACR response in the initial secukinumab group over 12 and 24 weeks. Mean change from baseline up to week 12 of GLOESS was determined with mixed-effect model repeated measures analysis (MMRM) and from week 12-24 as observed. 24 week efficacy outcomes included ACR responses, HAQ-DI, PASI response and resolution of dactylitis. These outcomes were exploratory and reported either according to non-responder imputation (ACR response), or as observed (HAQ-DI, PASI response and resolution of dactylitis).

Results: Of 166 patients enrolled, a total of 155 patients (93%) completed 24 weeks of treatment (secukinumab, 79 patients 95%; placebo, 76 patients 92%). Mean change from baseline to week 24 in GLOESS was similar in the initial secukinumab and placebo-secukinumab groups. A continued improvement in GLOESS was observed in the secukinumab group, with catch-up improvement in the placebo group after switch to active therapy (Figure 1). Both SRM of GLOESS and ACR core components over 12 and 24 weeks were high (Table 1). Similar

clinical response rates were reported for clinical joint count, skin, dactylitis and function at week 24 in secukinumab and placebo switchers groups (Table 1).

Conclusion: These analyses highlight the responsiveness and high discriminative validity of GLOESS in PsA, resembling that of key clinical PsA manifestations and physical function.

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Table 1. Responsiveness of GLOESS - analysed by standardised response mean and efficacy outcomes at week 24

Standardised response mean (Initial secukinumab)	Efficacy of secukinumab				
	Week 0–12 (N = 83)	Week 0–24 (N = 83)	Responders (%)	Secukinumab week 0–24 (N = 83)	Placebo switchers week 12–24 (N = 83)
GLOESS	1.05	1.06	ACR20	87	74
Tender joint count	1.03	1.35	ACR50	64	49
Swollen joint count	0.91	1.18	ACR70	34	23
Patient global assessment of disease activity	1.37	1.55	HAQ-DI [†]	80	63
Physician global assessment of disease activity	1.59	2.39	PASI 75 [†]	72	59
Pain	1.32	1.53	PASI 90 [†]	62	45
HAQ-DI score	1.32	1.32	Resolution of dactylitis (LDI=0)	67	59

[†]HAQ-DI response is defined as an improvement of at least 0.35 score points compared to baseline (change ≤ -0.35).[†]N value for PASI response in secukinumab and placebo groups are 36 and 33, respectively. PASI response was calculated for patients with BSA ≥ 3 %. BSA, Body Surface Area; LDI, Leeds Dactylitis Index

Disclosure of Interests: Maarten Boers Consultant of: BMS, Novartis, Pfizer, GSK, Philip G Conaghan Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Consultant of: AbbVie, AstraZeneca, BMS, Eli Lilly, Galapagos, Gilead, Novartis and Pfizer, Georg Schett Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, Peter Mandl Speakers bureau: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Roche and UCB, Grant/research support from: AbbVie, BMS, Celgene, Janssen, Eli Lilly, MSD, Novartis, Roche and UCB, Esperanza Naredo Speakers bureau: AbbVie, Roche, BMS, Pfizer, UCB, Eli Lilly, Novartis, Janssen, and Celgene, Consultant of: AbbVie, Novartis and BMS, Grant/research support from: Eli Lilly, Filip van den Bosch Speakers bureau: AbbVie, Celgene, Janssen, Eli Lilly, Galapagos, Merck, Novartis, Pfizer, and UCB Pharma, Consultant of: AbbVie, Celgene, Janssen, Eli Lilly, Galapagos, Merck, Novartis, Pfizer, and UCB Pharma, Ruben Burgos-Vargas: None declared, Anne-Marie Duggan Employee of: Novartis, Punit Goyanka Employee of: Novartis, Corine Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, Maria-Antonietta D'Agostino Speakers bureau: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly, Consultant of: Sanofi, Novartis, BMS, Janssen, Celgene, Roche, AbbVie, UCB, and Eli Lilly

DOI: 10.1136/annrheumdis-2021-eular.1720

POS0198

EFFICACY AND SAFETY OF DEUCRAVACITINIB, AN ORAL, SELECTIVE TYROSINE KINASE 2 INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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*P < 0.05. Data presented as MMRM up to week 12. At week 12, mean difference (SE) = -3.16 (1.19), 95% CI = [-5.52, -0.83], P = 0.004. Data presented as observed from week 12 to 24. Open label period from week 12-24 (shaded area). No significant difference was observed in comparison of GLOESS score at week 24 between treatment groups as tested using t-test. At week 24, mean difference = 0.36, 95% CI = [-3.62, 3.74], P = 0.83.

ESLAR, European League Against Rheumatism; GLOESS, OMERACT ESUAR global synovitis score; LD, Leeds Dactylitis Index; MMRM, mixed effect model repeated measures; n, number of evaluable patients; OMERACT, Outcome Measures in Rheumatology

Figure 1. Mean change from baseline in GLOESS by treatment through Week 24

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Background: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling by key cytokines involved in psoriatic arthritis (PsA) and plaque psoriasis (PsO) pathogenesis. Deucravacitinib is a novel oral agent that selectively inhibits TYK2 via an allosteric mechanism by binding to the nonconserved regulatory domain of the kinase. A previous Phase 2 trial in PsO had demonstrated that deucravacitinib was efficacious and well tolerated, with no laboratory abnormalities observed.

Objectives: To evaluate the efficacy and safety of deucravacitinib in active PsA.

Methods: This is an ongoing, 1-year, randomized, double-blind, placebo (PBO)-controlled (initial 16 weeks), multiregional, Phase 2 trial (NCT03881059). Eligible patients had a PsA diagnosis for ≥ 6 months, met CASPAR criteria, and had active disease with ≥ 3 tender and ≥ 3 swollen joints, C-reactive protein ≥ 3 mg/L (ULN, 5 mg/L), and ≥ 1 psoriatic lesion (≥ 2 cm). Patients had failed or were intolerant to ≥ 1 nonsteroidal anti-inflammatory drug, corticosteroid, conventional synthetic disease-modifying antirheumatic drug (csDMARD), and/or 1 TNF inhibitor (TNFi; $\leq 30\%$). Patients were randomized 1:1:1 to deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. The primary endpoint was achievement of ACR 20 response at Week 16. Additional endpoints included the proportion of patients achieving ACR 50/70 response, Health Assessment Questionnaire-Disability Index (HAQ-DI) response (≥ 0.35 improvement from baseline), enthesitis resolution (Leeds Index score of 0), minimal disease activity, change from baseline in SF-36 physical component score (SF-36 PCS) and mental component score (SF-36 MCS), Psoriasis Area and Severity Index (PASI) 75 response, adverse events (AEs), and laboratory parameters.

Results: Of 203 patients randomized, 180 (89%) completed 16 weeks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and baseline disease characteristics were similar across groups. Mean age was 49.8 years, 51% of patients were female, median PsA duration was 4.5 years, 66% of patients used csDMARDs at baseline and throughout the study, and 15% had used a TNFi. This study met its primary endpoint, with deucravacitinib 6 mg and 12 mg QD demonstrating significantly higher ACR 20 responses versus PBO at Week 16 (Figure 1). Additional endpoints were also met with deucravacitinib versus PBO (Figure 1). Adjusted mean changes from baseline in SF-36 PCS and SF-36 MCS at Week 16, respectively, were significantly higher in the deucravacitinib 6 mg QD group (5.6 vs 2.3, $P=0.0062$; 3.6 vs 0.7, $P=0.0211$) and 12 mg QD group (5.8 vs 2.3, $P=0.0042$; 3.5 vs 0.7, $P=0.0263$) compared with PBO. PASI 75 responses were also significantly higher in the deucravacitinib groups ($P\leq 0.0136$ vs PBO). The most common AEs in the deucravacitinib 6 mg/12 mg/PBO groups, respectively, during the 16-week treatment period were nasopharyngitis (5.7%/17.9%/7.6%), sinusitis (0%/7.5%/0%), headache (7.1%/1.5%/4.5%), and rash (4.3%/6.0%/0%). No serious AEs, herpes zoster infections, opportunistic infections, or thrombotic events were reported in deucravacitinib-treated patients during this period. Additionally, no significant changes from baseline in hematologic parameters (lymphocytes, neutrophils, platelets, and hemoglobin) or serum lipids were observed with deucravacitinib treatment.

Conclusion: Deucravacitinib was efficacious versus PBO over 16 weeks in patients with active PsA. Treatment was generally well tolerated and the safety and laboratory parameter profile of deucravacitinib was consistent with that observed in an earlier Phase 2 PsO trial.

Acknowledgements: This study was sponsored by Bristol Myers Squibb. Professional medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Bristol Myers Squibb.

Figure. Response Endpoints at Week 16

Nominal P values for pairwise comparisons vs placebo. Response endpoints were evaluated using a Cochran-Mantel-Haenszel test with stratification factors (body weight and prior TNFi use), with nonresponder imputation for missing values. ACR, American College of Rheumatology; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; QD, once daily.

Disclosure of Interests: Philip J Mease Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN Pharma, UCB, Atul Deodhar Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Glaxo Smith & Kline, Janssen, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Eli Lilly, Glaxo Smith & Kline, Novartis, Pfizer, UCB, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma, Frank Behrens Consultant of: Pfizer, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche, Chugai, Bristol Myers Squibb, UCB Pharma, Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Roche, Alan Kivitz Shareholder of: Pfizer, Sanofi, GlaxoSmithKline, Gilead Sciences, Inc., Novartis, Paid Consultant: AbbVie, Boehringer Ingelheim, Flexion, Janssen, Pfizer, Sanofi, Regeneron, SUN Pharma Advanced Research, Gilead Sciences, Inc., Speakers bureau: Celgene, Merck, Lilly, Novartis, Pfizer, Sanofi, Genzyme, Flexion, AbbVie, Jonghyeon Kim Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Shalabh Singhal Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Miroslawa Nowak Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb, Subhashis Banerjee Shareholder of: Bristol Myers Squibb, Employee of: Bristol Myers Squibb

DOI: 10.1136/annrheumdis-2021-eular.2603

POS0199 TIME-SERIES ANALYSIS IN MODERATE TO SEVERE PLAQUE PSORIASIS UNDER DIFFERENT BIOLOGICS TREATMENTS

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Background: Moderate to Severe Plaque Psoriasis is an inflammatory skin disease that is associated with multiple comorbidities and substantially diminishes patients' quality of life. As one of the most significant therapeutic advancements in the field of dermatology, Biologics such as TNF inhibitors, IL-12/23 inhibitor, IL-17 inhibitors, and IL-23 inhibitors, have higher efficacy compared with oral medications or phototherapy¹. However, the previous studies did not focus on the simultaneous comparison of molecular changes in different classes of biologics. The identification of time-series genes (TSGs) could help to uncover the mechanisms underlying transcriptional regulation².

Objectives: In this study, we aimed to compare the differences in expression patterns and functions of time-series genes in Moderate to Severe Plaque Psoriasis under different biologics treatments.

Methods: The transcription profile of GSE117239 and GSE51440 were obtained from the Gene Expression Omnibus database (GEO). The GSE117239 included 19 samples treated with Etanercept (TNF inhibitors) and 16 samples treated with Ustekinumab (IL-12/23 inhibitor). The GSE51440 included 4 samples treated with Guselkumab (IL-23 inhibitors). Skin biopsy samples (LS: lesion, NL: non-lesion) were collected at baseline, weeks 1 and 12, respectively. After background adjustment and other pre-processing, differentially expressed genes (DEGs) were extracted from LS skin biopsy and untreated NL skin biopsy at different times after three different biologics treatments, respectively. The Short Time-series Expression Miner (STEM) software was used to cluster and compare average DEGs with coherent changes. Afterward, the different expression patterns of TSGs under the three treatment groups were compared. GO analysis and KEGG pathway enrichment analysis of TSGs were performed by Metascape.

Results: Different DEGs varied in LS skin compared with those of NL skin biopsy: 976 genes in Ustekinumab group, 996 genes in Etanercept group, and 601 genes in Guselkumab group (detailedly ($P < 0.05$ and $|\log FC| > 1$). Gene landscapes suggested the signatures of LS gradually changed during the treatment process, and gradually converge to NL signatures (Fig.1a, 2a,3a). Time-series genes in the three treatment groups had different expression patterns and functions. In the Ustekinumab group, a total of 448 TSGs in profile 3 showed a stable-stable-decreasing expression trend and significantly