Disclosure of Interests: Iain McInnes Consultant of: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, AstraZeneca, Boehringer Ingelheim, Bristol Myers, Celgene, Janssen, Leo, Lilly, Novartis, Pfizer, and UCB, William Tillett Speakers bureau: AbbVie, Amgen, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, and UCB, Philip J Mease Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Grant/research support from: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers, Celgene, Galapagos, Genentech, Gilead, GlaxoSmithKline, Janssen, Leo, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Kurt de Vlam Speakers bureau: Celgene Eli Lilly, Galapagos, Novartis, and UCB, Consultant of: Celgene, Eli Lilly, Galapagos, Novartis, and UCB, Grant/research support from: Celgene and Galapagos, Louis Bessette Speakers bureau: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, and Sanofi, Consultant of: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, Gilead, Grant/research support from: Amgen, BMS, Janssen, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, Sanofi, and Gilead, Ralph Lippe Shareholder of: AbbVie, Employee of: AbbVie, Anna Manicchia Shareholder of: AbbVie, Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Dai Feng Shareholder of: AbbVie, Employee of: AbbVie, Koji Kato Shareholder of: AbbVie, Employee of: AbbVie, Andrew Ostor Consultant of: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, and Paradigm. DOI: 10.1136/annrheumdis-2021-eular.1633

POS1048

IN PHASE-3 TRIALS DISCOVER 1 & 2, GUSELKUMAB REDUCED FATIGUE OVER 52 WEEKS IN PATIENTS WITH PSORIATIC ARTHRITIS AND DEMONSTRATED INDEPENDENT TREATMENT EFFECTS ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20)

P. Rahman¹, P. Helliwell², A. Deodhar³, A. Kollmeier⁴, E. C. Hsia^{4,5}, B. Zhou⁶, X. Lin⁷, C. Han⁸, P. J. Mease⁹. ¹Memorial University of Newfoundland, Discipline of Medicine, Faculty of Medicine, St. Johns, Canada; ²University of Leeds, Clinical Rheumatology, Leeds, United Kingdom; ³Oregon Health & Science University, Division of Arthritis & Rheumatic Diseases, Oregon, United States of America; ⁴Janssen Research & Development, LJ IMMUNOLOGY, Spring House, United States of America; ⁵University of Pennsylvania School of Medicine, Division of Rheumatology, Philadelphia, United States of America; ⁶Janssen Research & Development, CLINICAL BIOSTATS PA, Spring House, United States of America; ⁷Janssen Research & Development, SMM-PA, Spring House, United States of America; ⁸Janssen Research & Development, STRATEGIC MKT ACCESS, Spring House, United States of America; ⁹Swedish Medical Center/Providence St Joseph Health and University of Washington School of Medicine, Department of Internal Medicine, Seattle, United States of America

Background: DISCOVER 1 & 2 are phase-3 trials of guselkumab (GUS, an IL-23 inhibitor) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (American College of Rheumatology 20% improvement criteria [ACR20]) and in other measures of arthritis and psoriasis at week (w) 24,^{1,2} and these improvements were maintained through 1 year of active treatment.^{3,4}

Objectives: To evaluate the effect of GUS on fatigue in DISCOVER 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.⁵

Methods: DISCOVER 1 & 2 enrolled patients with active PsA, despite non-biologic DMARDs or NSAIDs, who were biologic naïve except ~30% of patients in DISCOVER 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100 mg at w0, w4, then every (q) 8w; GUS 100 mg q4w; or matching PBO. At w24, PBO patients were switched to GUS q4w. Concomitant treatment with select non-biologic DMARDs, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO assessing fatigue and its impact on daily activities and function over the past 7 days, total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is considered clinically meaningful.⁵ The change from baseline in FACIT-Fatigue presented below is based on observed data. Mediation analysis⁶ was applied to the treatment effect of GUS on FACIT-Fatigue to estimate the natural direct and indirect effects, after adjusting for ACR20 response (Table 1).

Results: At baseline in DISCOVER 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating that patients with PsA experienced fatigue worse than the general population. At w24 in the DISCOVER trials, treatment with GUS led to significant improvements in FACIT-Fatigue scores compared with PBO, as early as w16 in DISCOVER 1 and w8 in DISCOVER 2. Improvements in fatigue were similar between GUS q4w and q8w

doses, and the improvements at w24 were maintained through w52 (Figure 1). After a switch to GUS q4w at w24, PBO patients achieved FACIT-Fatigue scores that were comparable to those of GUS patients (Figure 1). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue at w24 (P≤0.003). At w52, 61%-70% of both GUS and PBO to GUS groups reached this improvement. As evaluated by mediation analysis at w24, GUS had independent positive treatment effects on fatigue (12%-36% in the q8w GUS dosing group and 69%-70% in the q4w GUS group) after adjustment for ACR20 response (Table 1).

Conclusion: In 2 phase-3 trials, GUS treatment improved fatigue when compared to PBO during PBO-controlled periods and maintained improvements through 1 year of active treatment. Substantial proportions of those effects were independent of the effects on ACR20, especially for the q4w dosing group.

REFERENCES:

- [1] Deodhar et al. *Lancet* 2020;395:1115
- [2] Mease et al. *Lancet* 2020;395:1126
- [3] Ritchlin et al. *EULAR20*. SAT0397
- [4] McInnes et al. *EULAR20*. SAT0402
- [5] Cella et al. *J Patient-Reported Outcomes* 2019;3:30
- [6] Valeri et al. *Psychologic Meth* 2013;18:137

Table 1. Mediation Analysis: Guselkumab Has Direct Effects and Indirect Effects (Mediated through ACR20) on Fatigue in PsA

	Effect	GUS 100 mg q8w vs. PBO (95% CI)	GUS 100 mg q4w vs. PBO (95% CI)
DISCOVER-1	Total Effect	3.1 (1.0, 5.2)	3.8 (1.9, 5.4)
	% Direct Effect	(p<0.02) 11.7%	(p<0.02) 68.5%
	% Indirect effect mediated by ACR20	88.3%	31.5%
DISCOVER-2	Total Effect	4.0 (2.4, 5.5)	3.6 (2.1, 5.0)
	% Direct Effect	(p<0.02) 36.3%	(p<0.02) 69.7%
	% Indirect effect mediated by ACR20	63.7%	30.3%

ACR, American College of Rheumatology; CI, confidence interval; GUS, guselkumab; PBO, placebo; PsA, psoriatic arthritis; q4w, every 4 weeks; q8w, every 8 weeks

Disclosure of Interests: Proton Rahman Speakers bureau: Received speakers fees from Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, Pfizer, Grant/research support from: Received grant/research support from Janssen and Novartis, consultation fees from Abbott, AbbVie, Amgen, BMS, Celgene, Lilly, Janssen, Novartis, and Pfizer, Philip Helliwell Consultant of: Consultation fees paid to charity (AbbVie, Amgen, Pfizer, UCB) or himself (Celgene, Galapagos), Grant/research support from: Received grants/research support paid to charity (AbbVie, Janssen, Novartis), Atul Deodhar Speakers bureau: Received speakers fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant of: Received consultation fees from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myer Squibb (BMS), Eli Lilly, GSK, Janssen, Novartis, Pfizer, UCB, Grant/research support from: Received grant/research support from Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB, Consultant of: Received consultation fees from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB, Grant/research support from: Received grant/research support from Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB. DOI: 10.1136/annrheumdis-2021-eular.1686

POS1049

EFFECT OF FILGOTINIB ON PASDAS: DRIVERS OF LOW AND VERY LOW ACTIVITY UP TO WEEK 100

L. C. Coates¹, P. J. Mease^{2,3}, P. Helliwell⁴, F. Van den Bosch⁵, M. Trivedi⁶, M. Alani^{6,7}, F. O. Le Brun⁸, R. Besuyen⁹, L. Gheyle¹⁰, E. Gvozdenovic¹¹, D. D. Gladman¹². ¹University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom;

²Swedish Medical Center, Rheumatology Clinical Research Division, Seattle, United States of America; ³University of Washington, School of Medicine, Seattle, United States of America; ⁴University of Leeds, School of Medicine, Leeds, United Kingdom; ⁵Ghent University, VIB Center for Inflammation Research, Ghent, Belgium; ⁶Gilead Sciences, Inc., Clinical Research, Foster City, United States of America; ⁷University of Washington, Rheumatology Department, Seattle, United States of America; ⁸Galapagos GmbH, Biometrics, Basel, Switzerland; ⁹Galapagos BV, Clinical Research, Leiden, Netherlands; ¹⁰Galapagos NV, Clinical Research, Mechelen, Belgium; ¹¹Galapagos NV, Biometrics, Mechelen, Belgium; ¹²Schroeder Arthritis Institute, Krembil Research Institute, University Health Network, Toronto, Canada

Background: EQUATOR (NCT03101670) was a Phase 2, double-blind, randomised placebo (PBO)- controlled trial of the preferential Janus kinase 1 inhibitor filgotinib (FIL) for the treatment of psoriatic arthritis (PsA); EQUATOR2 (NCT03320876) is the open-label extension (OLE).

Objectives: This post-hoc analysis assessed the effect of FIL on individual Psoriatic Arthritis Disease Activity Score (PASDAS) components; and the association between PASDAS disease activity (DA) levels and DA levels achieved for each PASDAS component and patient-reported outcomes (PROs) up to OLE Week 100.

Methods: In EQUATOR, patients with active moderate-to-severe PsA were randomised 1:1 to oral FIL 200mg or PBO once daily (QD) for 16 wks.¹ At Wk 16, patients could continue into the 304-wk OLE, in which all patients received FIL 200mg QD. The proportions of patients with PASDAS of very low DA (VLDA; ≤ 1.9), LDA (>1.9 – <3.2), moderate DA (MoDA; ≥ 3.2 – <5.4), and high DA (HDA; ≥ 5.4) at core Wk 16 and OLE Wk 52 and 100 were assessed. The proportion with improved PASDAS status vs baseline (BL) at OLE Wk 52 and 100 was calculated. Percent change from BL in PASDAS components and PROs were assessed at core Wk 16 and OLE Wk 52 and 100 by PASDAS status (VLDA, LDA, other). Multivariate logistic regression analyses performed cross-sectionally identified PASDAS components and PROs associated with not achieving VLDA or LDA at core Wk 16 and OLE Wk 52 and 100; all analyses were observed cases.

Results: At OLE Wk 52, LDA and VLDA were achieved by 27.5% and 16.8% of randomised patients, respectively (44.3% combined). At OLE Wk 100, LDA and VLDA were achieved by 26.0% and 17.6% of patients (43.6% combined; Figure 1). Of patients with HDA at BL, 69% improved to MoDA/LDA/VLDA, <4% remained in HDA and 27% did not reach Wk 100; of those in MoDA at BL, 63% improved to VLDA/LDA, 11% remained stable, <4% worsened and 22% did not reach Wk 100. Patient Global Assessment of Disease Activity (PtGDA), Short Form-36 physical component scale (SF-36 PCS), Functional Assessment of Chronic Illness Therapy, and Health Assessment Questionnaire Disability Index were found to be important components/PRO measures in achieving VLDA vs LDA (Table 1). Logistic regression indicated that factors associated with not achieving LDA at Wk 52 were PtGDA (odds ratio [OR]: 1.20, 95% confidence interval [CI]: 1.07–1.35), physician GDA (PhGDA; OR: 1.58, 95% CI: 1.18–2.12), and SF-36 PCS (OR: 0.79, 95% CI: 0.67–0.95); PtGDA was associated with not achieving VLDA (OR: 1.30, 95% CI: 1.15–1.47).

Conclusion: The proportion of patients achieving PASDAS VLDA or LDA increased over time and remained stable between OLE Wk 52 and 100. Important factors in determining whether VLDA/LDA was met were PtGDA, PhGDA, and SF-36 PCS, although the low patient numbers is a limitation.

REFERENCES:

[1] Mease P, et al. *Lancet*. 2018;392:2367–77

Figure. Proportion of patients with VLDA, LDA, MoDA, and HDA at baseline, Core Week 16, OLE Week 52, and OLE Week 100

Proportions are based on the all randomised population
*Patients are presented according to original treatment in the core study. During the OLE all patients received filgotinib
*Missing includes patients who did not reach the timepoint or had a missing assessment
HDA, high disease activity; LDA, low disease activity; MoDA, moderate disease activity; OLE, open-label extension; VLDA, very low disease activity

Table 1. Mean % change from baseline in PASDAS components and PROs (observed cases)

	Core Wk 16 (FIL + PBO groups combined) n=122			OLE Wk 52 n=110			OLE Wk 100 n=97		
	VLDA	LDA	Others	VLDA	LDA	Others	VLDA	LDA	Others
	n=8	n=22	n=92	n=22	n=36	n=52	(24%)	n=34	n=40
	(7%)	(18%)	(75%)	(20%)	(33%)	(47%)	(35%)	(41%)	
PhGDA	–93	–75	–44	–94	–82	–56	–96	–84	–54
PtGDA	–87	–69	–13	–86	–58	–24	–90	–57	–13
Tender joint count 68	–94	–80	–42	–99	–84	–64	–98	–87	–61
Swollen joint count 66	–99	–80	–64	–99	–96	–78	–99	–94	–80
LEI	–100	–86	–32	–96	–100	–78	–100	–99	–78
Dactylitis	–100	–100	–73	–100	–100	–97	–100	–100	–98
C-reactive protein	–66	–22	17	138*	–32	–25	–12	–13	24
SF-36 PCS	53	26	11	33	23	9	47	23	16
FACIT	119	50	32	97	51	34	99	46	36
HAQ-DI	–84	–68	–18	–85	–51	–18	–88	–45	–19
PASI	–84	–66	–29	–54	–59	–56	–49	–76	–42

Components or PRO measures in bold are those for which numerical differences between VLDA and LDA are greatest across timepoints*Due to outlier (3784)FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area Severity Index; PhGDA, Physician Global Assessment of Disease Activity; PtGDA, Patient Global Assessment of Disease Activity; SF-36 PCS, Short Form-36 physical component summary; (V)LDA, (very) low disease activity

Acknowledgements: EQUATOR and EQUATOR2 were sponsored by Galapagos NV Mechelen, Belgium) and co-funded by Galapagos NV and Gilead Sciences, Inc (Foster City, CA, USA). Benjamin Pett and his team, employees of Galapagos, provided assistance with statistical analyses. Medical writing/editorial support was provided by Debbie Sherwood, BSc, CMPP (Aspire Scientific, Bollington, UK), and was funded by Galapagos NV.

Disclosure of interests: Laura C Coates Speakers bureau: AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Gilead, Janssen, Medac, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Novartis, and Pfizer, Philip J Mease Speakers bureau: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant of: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galapagos, Gilead Sciences, GlaxoSmithKline, Janssen, Novartis, Pfizer, SUN, and UCB, Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead Sciences, Janssen, Novartis, Pfizer, SUN, and UCB, Philip Helliwell Paid instructor for: Janssen, Novartis, and Pfizer, Consultant of: Eli Lilly, Filip van den Bosch Consultant of: AbbVie, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, and UCB, Grant/research support from: AbbVie, Merck, and UCB, Mona Trivedi Shareholder of: Gilead Sciences, Amgen, Employee of: Gilead Sciences, Muhsen Alani Shareholder of: Gilead Sciences, Employee of: Gilead Sciences, Franck Olivier Le Brun Shareholder of: Galapagos, Employee of: Galapagos, Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, Lien Gheyle Shareholder of: Galapagos, Employee of: Galapagos, Emilia Gvozdenovic Employee of: Galapagos, Dafna D Gladman Consultant of: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, and UCB., Grant/research support from: AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB. DOI: 10.1136/annrheumdis-2021-eular.1721

POS1050 SECUKINUMAB LEADS TO IMPROVEMENT ACROSS PSORIATIC ARTHRITIS MANIFESTATIONS OVER 2 YEARS REGARDLESS OF PREVIOUS EXPOSURE TO A TNF INHIBITOR: A POST HOC ANALYSIS OF FUTURE 5

A. M. Orbai¹, M. E. Husni², D. D. Gladman^{3,4,5}, B. Parikh⁶, X. Meng⁷, C. Gailliez⁸, P. J. Mease^{9,10}. ¹Johns Hopkins University School of Medicine, Division of Rheumatology, Baltimore, United States of America; ²Cleveland Clinic, Rheumatologic and Immunologic Disease, Cleveland, United States of America; ³Krembil Research Institute, Division of Rheumatology, Toronto, Canada; ⁴Toronto Western Hospital, Division of Rheumatology, Toronto, Canada; ⁵University of Toronto, Division of Rheumatology, Toronto, Canada; ⁶Novartis Pharmaceuticals Corporation, Rheumatology, East Hanover, United States of America; ⁷Novartis Pharmaceuticals Corporation, Biostatistics, East Hanover, United States of America; ⁸Novartis Pharma AG, Rheumatology, Basel, Switzerland; ⁹Swedish Medical Center/Providence St. Joseph Health, Rheumatology, Seattle, United States of America; ¹⁰University of Washington, Rheumatology, Seattle, United States of America