OP0224

FILGOTINIB TREATMENT LEADS TO RAPID AND SUSTAINED REDUCTIONS IN INFLAMMATORY BIOMARKERS IN PATIENTS WITH MODERATE TO SEVERE PSORIATIC ARTHRITIS

D. D. Gladman[1], W. Jiang[2], A. Hertz[2], V. Malkov[2], O. K. Yoon[2], M. Trivedi[2], M. Alani[2,3], L. Vestergaard[2], R. Besuyen[4], R. Galien[5], A. M. Mirza[2], V. Chandran[1]. *[1]University of Toronto and Krembil Research Institute, Toronto Western Hospital, Toronto, Canada; [2]Gilead Sciences Inc., Foster City, United States of America; [3]University of Washington, Seattle, United States of America; [4]Galapagos BV, Leiden, Netherlands; [5]Galapagos SASU, Romainville, France*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease characterized by musculoskeletal and cutaneous inflammation. In the recent EQUATOR study (NCT03101670), patients (pts) with active PsA receiving the oral, selective Janus kinase 1 (JAK1) inhibitor filgotinib (FIL) had significant and sustained improvements versus placebo (PBO) in clinical signs and symptoms. We present here updated results of the EULAR 2019 presentation of EQUATOR on circulating biomarkers in PsA.
Objectives: To evaluate the impact of FIL on the levels of circulating proinflammatory cytokines and chemokines, adhesion molecules, and markers of matrix remodeling in EQUATOR pts with active PsA.
Methods: EQUATOR was a 16-week, double-blind, multicenter, Phase 2 study in pts with active PsA. Pts were randomized 1:1 to FIL 200 mg (n=65) or PBO (n=66) once daily. Serum samples (FIL n=60 and PBO n=61) were collected at baseline (BL) and at Weeks 1, 4, and 16. The association of BL biomarkers with PsA disease characteristics was analyzed by Spearman's rank-order correlation. Biomarker changes from BL were assessed in time-paired serum samples using multiplex and high sensitivity ELISA-based assays. Analytes were grouped by hierarchical clustering; treatment effect on a biomarker was defined as a difference in change from BL between pts receiving FIL versus PBO. Improvements in PsA clinical signs and symptoms were determined by assessing changes from BL in a number of clinical disease activity scores including psoriatic arthritis disease activity score (PASDAS), psoriasis area and severity index (PASI) and disease activity index for psoriatic arthritis (DAPSA) scores.
Results: BL levels of numerous biomarkers were associated ($p<0.05$) with clinical measures of PsA. Several clusters of biomarkers were identified based on the rate and magnitude of FIL treatment response. Cluster 1 included biomarkers with substantial reductions from BL with FIL by week 1, such as the acute phase proteins CRP and SAA (>50%), and the inflammatory mediators IL-6, CXCL10, and IL-23 (>25%). Cluster 2 included biomarkers of cell adhesion (ICAM-1, VCAM1) with a 5%–15% reduction from BL with FIL by week 1. Cluster 3 included biomarkers of matrix remodeling (MMP1, SC1M) with a delayed >25% reduction from BL with FIL that was significant by Week 4. Finally, Cluster 4 included biomarkers with a modest (5%–10%) increase from BL with FIL (Eotaxin, IL-15, and adiponectin). Spearman rank correlation analyses showed that at BL, many biomarkers were positively associated with disease scores, and tended to segregate between psoriasis weighted scores such as PASI and arthritis weighted scores such as DAPSA. The observed decrease in proinflammatory cytokines were associated with on-treatment improvements from BL in disease score for pts receiving FIL.
Conclusion: Compared with PBO, FIL significantly decreased BL levels of circulating biomarkers associated with PsA disease activity, including proinflammatory cytokines and chemokines, adhesion molecules, and markers of matrix remodeling. The observed decreases in circulating proinflammatory cytokines and biomarkers of both bone pathobiology and psoriatic disease suggest that FIL improves PsA clinical signs and symptoms at a molecular level. These findings are consistent with reduced disease activity in pts with PsA and suggest that FIL treatment leads to a rapid and sustained reduction of inflammation in PsA.
Acknowledgments: This study was funded by Gilead Sciences, Inc. Editorial support was provided by Fishawack Communications Inc and funded by Gilead Sciences, Inc.
Disclosure of Interests: Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Wendy Jiang Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Angie Hertz Shareholder of: Gilead Sciences Inc, Employee of: Gilead Sciences Inc, Vlad Malkov Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Oh Kyu Yoon Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Mona Trivedi Shareholder of: Amgen and Gilead Sciences, Employee of: Gilead Sciences, Muhsen Alani Employee of: Gilead Sciences, Lene Vestergaard Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Robin Besuyen Shareholder of: Galapagos, Employee of: Galapagos, René Galien Shareholder of: Galapagos, Employee of: Galapagos, Amer M. Mirza Shareholder of: Gilead Sciences Inc., Employee of: Gilead Sciences Inc., Vinod Chandran Grant/research support from: Abbvie, Celgene, Consultant of: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lily, Janssen, Novartis, Pfizer, UCB, Employee of: Spouse employed by Eli Lily
DOI: 10.1136/annrheumdis-2020-eular.4927

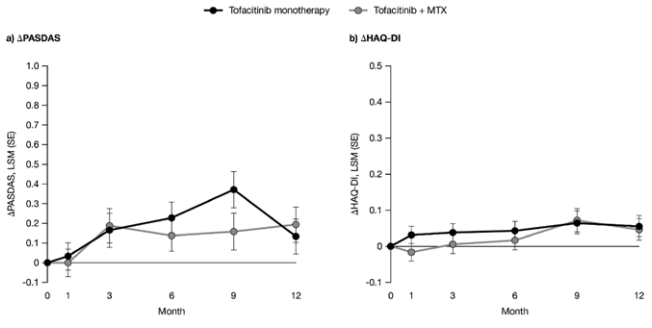
OP0225

TOFACITINIB AS MONOTHERAPY FOLLOWING METHOTREXATE WITHDRAWAL IN PATIENTS WITH PSORIATIC ARTHRITIS PREVIOUSLY TREATED WITH OPEN-LABEL TOFACITINIB + METHOTREXATE: A RANDOMISED, PLACEBO-CONTROLLED SUBSTUDY OF OPAL BALANCE

P. Nash[1], L. C. Coates[2], P. J. Mease[3], A. Kivitz[4], D. D. Gladman[5], F. Behrens[6], J. C. C. Wei[7], D. Fleishaker[8], J. Wu[9], C. Wang[8], A. B. Romero[10], L. Fallon[11], M. A. Hsu[8], K. Kanik[8]. *[1]Griffith University, Brisbane, Australia; [2]University of Oxford, Oxford, United Kingdom; [3]Swedish Medical Center and University of Washington, Seattle, United States of America; [4]Altoona Center for Clinical Research, Duncansville, United States of America; [5]University of Toronto, Toronto, Canada; [6]Goethe University, Frankfurt, Germany; [7]Chung Shan Medical University Hospital, Taichung, Taiwan, Republic of China; [8]Pfizer Inc, Groton, United States of America; [8]Pfizer Inc, Groton, United States of America; [10]Pfizer Inc, Barcelona, Spain; [11]Pfizer Inc, Montreal, Canada*

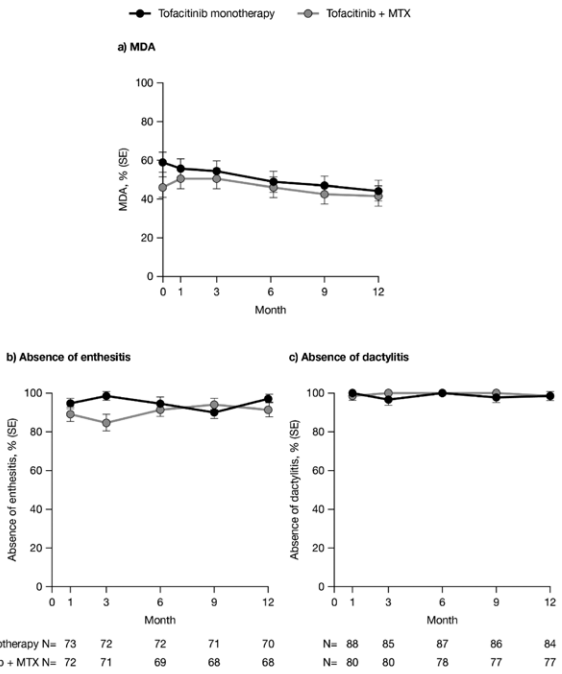
Background: Tofacitinib is an oral JAK inhibitor for the treatment of psoriatic arthritis (PsA).
Objectives: To assess tofacitinib 5 mg BID as monotherapy after methotrexate (MTX) withdrawal vs with continued background MTX in patients (pts) with PsA.
Methods: OPAL Balance (NCT01976364) was an open-label (OL) long-term extension (LTE) study of tofacitinib in pts with PsA who participated in Phase (P)3 studies (OPAL Broaden, NCT01877668; OPAL Beyond, NCT01882439). Pts who completed ≥24 months' tofacitinib treatment in the LTE (stable 5 mg BID for ≥3 months) and were receiving oral MTX (7.5–20 mg/week; stable for ≥4 weeks) entered the multicentre, 12-month, double-blind, MTX withdrawal substudy. Pts remained on OL tofacitinib 5 mg BID and were randomised 1:1 to receive placebo (tofacitinib monotherapy, ie, blinded MTX withdrawal) or MTX (tofacitinib + MTX; same stable doses). Primary endpoints were changes from substudy baseline (Δ) in PASDAS and HAQ-DI at Month (M)6. Secondary efficacy endpoints were assessed at all time points. Safety was assessed throughout the substudy.
Results: Of 180 pts randomised, 179 were treated (tofacitinib monotherapy n=90; tofacitinib + MTX n=89). Pt characteristics were similar between treatment arms. At M6, least squares mean (LSM) (standard error [SE]) ΔPASDAS was 0.229 (0.079) for tofacitinib monotherapy and 0.138 (0.081) for tofacitinib + MTX, and LSM (SE) ΔHAQ-DI was 0.043 (0.027) and 0.017 (0.028), respectively (Figure 1); no clinically meaningful differences were observed. Efficacy and pt-reported outcomes were generally similar between treatment arms at M6 and M12 (data not shown). Rates of pts achieving minimal disease activity, and maintaining an absence of enthesitis and dactylitis, were sustained to M12 in both treatment arms (Figure 2). Adverse event rates (Table) and laboratory parameters were comparable between treatment arms, but liver enzyme elevations were more common with tofacitinib + MTX.
Conclusion: No clinically meaningful differences in efficacy and safety were observed in PsA pts who received OL tofacitinib 5 mg BID as monotherapy after MTX withdrawal vs with continued MTX. Safety was consistent with previous P3 studies. The substudy was an estimation study and not powered for hypothesis testing.

Figure 1. LSM (SE) a) ΔPASDAS[a] and b) ΔHAQ-DI[a] up to Month 12 of the MTX withdrawal substudy



[a]Primary endpoints at Month 6
Results were based on a repeated measures model with the fixed effects of treatment, visit, treatment by visit interaction, and baseline value, without imputation for missing values; a common unstructured covariance matrix was used. The numbers of patients included in the repeated measures model from tofacitinib monotherapy and tofacitinib + MTX arms were 90 and 89, respectively, for both PASDAS and HAQ-DI. For each endpoint at each time point, the 95% CI of the LSM difference between the tofacitinib monotherapy and tofacitinib + MTX arms included 0
Δ, change from substudy baseline; CI, confidence interval; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least squares mean; MTX, methotrexate; PASDAS, Psoriatic Arthritis Disease Activity Score; SE, standard error

Figure 2. Proportion (SE) of patients achieving a) MDA,[a] and maintaining absence of b) enthesitis[b] and c) dactylitis,[c] up to Month 12 of the MTX withdrawal substudy



[a]Missing response=non-response. The numbers of patients included in this analysis were 90 and 89 for tofacitinib monotherapy and tofacitinib + MTX, respectively; [b]In patients with LEI=0 at baseline, no imputation; [c]In patients with DSS=0 at baseline, no imputation DSS, Dactylitis Severity Score; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; MTX, methotrexate; SE, standard error

Table. Safety outcomes to Month 12

Pts with events, n (%) AEs of special interest	Tofacitinib monotherapy N=90	Tofacitinib + MTX N=89
AE	43 (47.8)	41 (46.1)
Serious AE	4 (4.4)	3 (3.4)
Discontinuations due to AE	3 (3.3)	4 (4.5)
Death	0	0
Herpes zoster (serious/non-serious)	1 (1.1)	2 (2.2)
Serious infection	0	2 (2.2)
Opportunistic infection[a]	0	1 (1.1)
Malignancy (excl. NMSC)[a]	1 (1.1)	1 (1.1)
NMSC[a]	0	0
Major adverse cardiovascular event[a]	0	0
Venous thromboembolism[c]	0	0
Arterial thromboembolism[c]	1 (1.1)	0
Gastrointestinal perforation[a]	0	0
Interstitial lung disease[b]	0	0
Laboratory parameters[d]		
ALT ≥3×ULN	0	5 (5.6)
ALT (IU/L), mean (SE)	-2.7 (1.6)	2.5 (1.3)
AST ≥3×ULN	0	3 (3.4)
AST (IU/L), mean (SE)	-1.5 (1.2)	1.7 (0.8)

Reviewed by independent [a]external/[b]internal adjudication committee
[c]Per Standardised MedDRA Query terms
[d]Without regard to baseline abnormality
ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by Christina Viegelmann of CMC Connect and funded by Pfizer Inc.
Disclosure of Interests: Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, MSD, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Laura C Coates: None declared, Philip J Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – grant/research support, Consultant of: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical, UCB – consultant, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Eli Lilly, Genentech, Janssen, Pfizer, UCB – speakers bureau, Alan Kivitz Shareholder of: AbbVie, Amgen, Gilead, GSK, Pfizer Inc, Sanofi, Consultant of: AbbVie, Boehringer Ingelheim,,Flexion, Genzyme, Gilead, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi, SUN Pharma Advanced Research, UCB, Paid instructor for: Celgene, Genzyme, Horizon, Merck, Novartis, Pfizer, Regeneron, Sanofi, Speakers bureau: AbbVie, Celgene, Flexion, Genzyme, Horizon, Merck, Novartis, Pfizer Inc, Regeneron, Sanofi, Dafna D Gladman Grant/research support from: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – grant/research support, Consultant of: AbbVie, Amgen Inc., BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB – consultant, Frank Behrens Grant/research support from: Pfizer, Janssen, Chugai, Celgene, Lilly and Roche, Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche and Chugai, James Cheng-Chung Wei Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Consultant of: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, Eisai, Janssen, Novartis, Pfizer Inc, Sanofi-Aventis, UCB Pharma, Dona Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Joseph Wu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Cunshan Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Ana Belen Romero Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lara Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Ming-Ann Hsu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Keith Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
DOI: 10.1136/annrheumdis-2020-eular.529

OP0226 NETAKIMAB DECREASES DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM A RANDOMIZED DOUBLE-BLIND PHASE 3 CLINICAL TRIAL (PATERA)

T. Korotaeva[1], I. Gaydukova[2], V. Mazurov[2], A. Samtsov[3], V. Khayrutdinov[3], A. Bakulev[4], M. Kokhan[5], A. Kundzer[6], N. Soroka[7], E. Dokukina[8], A. Eremeeva[8].
[1]Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; [2]Mechnikov North-Western State Medical University, St-Petersburg, Russian Federation; [3]Kirov Military Medical Academy, St-Petersburg, Russian Federation; [4]Razumovsky Saratov State Medical University, Saratov, Russian Federation; [5]Ural Research Institute of Dermatovenereology and Immunopathology, Ekaterinburg, Russian Federation; [6]Healthcare Institution Municipal Clinical Hospital No. 1, Minsk, Belarus; [7]Scientific and Practical Center of Surgery, Transplantology and Hematology, Minsk, Belarus; [8]JSC BIOCAD, St-Petersburg, Russian Federation

Background: Netakimab (NTK) is a humanized anti-interleukin 17A antibody approved for the treatment of moderate-to-severe plaque psoriasis.
Objectives: To determine the efficacy and safety of NTK in patients (pts) with active psoriatic arthritis (PsA), based on 24-week (Wk) data from an ongoing phase 3 study (NCT03598751, PATERA).
Methods: 194 eligible adult pts with PsA (CASPAR, 2006) with inadequate response to csDMARD or one TNFi, were randomized (1:1) to receive NTK 120 mg or placebo (PBO) subcutaneously at Wk 0, 1, 2, 4, 6, 8, 10, 14, 18, 22. 84 pts from PBO arm who did not meet ACR20 (20% improvement of the American College of Rheumatology criteria) by Wk 16 were switched to NTK 120 mg. The primary endpoint was ACR20 at Wk 24. DAPSA (Disease Activity Index for Psoriatic Arthritis), the proportion of pts achieved ACR50/70, minimal disease activity (MDA) (≥5/7 MDA criteria) and Psoriatic arthritis response criteria (PsARC) were also analyzed.
Results: Baseline demographics and disease characteristics were similar across treatment arms (Table 1). 80 (82.47%) pts in NTK arm and 9 (9.28%) in the PBO arm achieved ACR20 at Wk 24 (p<0.0001). A significantly greater percentage of NTK-treated pts had ACR50/70, PsARC response, MDA at Wk 24 (Figure 1). By Wk 24 DAPSA significantly improved for NTK vs PBO. DAPSA remission was achieved by 36.08% and 13.40% in NTK and PBO arms, respectively (p=0.003). NTK was well tolerated. The most frequent AEs (≥3%) were lymphopenia, neutropenia, hypercholesterolemia, ALT increased, upper respiratory tract infection, systolic blood pressure increased, hyperglycemia, hyperbilirubinemia. Most AEs were mild to moderate. Severe treatment-related AEs were observed in 1.03% vs 2.06% for NTK and PBO, respectively. No treatment-related SAEs were reported. No anti-drug antibodies were detected.

Table 1. Baseline demographics and disease severity characteristics

Arm	NTK (N=97)	PBO (N=97)
Age (years) *	44.0 (11.66)	43.1 (11.88)
Male, n (%)	52 (53.61)	50 (51.55)
PsA duration, mo*	63.1 (73.12)	68.2 (77.49)
DAS28-CRP*	4.62 (0.97)	4.41 (1.11)
DAPSA*	32.19 (12.23)	33.54 (15.98)
TJC (66/68) *	12.9 (9.97)	12.0 (9.88)
SJC (66/68) *	7.0 (4.93)	7.2 (7.18)
MTX at baseline	83 (85.6)	83 (85.6)
Previous PsA therapy		
Sulfasalazine, n (%)	9 (9.28)	11 (11.34)
Leflunomide, n (%)	4 (4.12)	8 (8.25)
Anti-TNFα, n (%)	22 (22.68)	17 (17.53)

* mean (standard deviation); Mo=months, PsA=psoriatic arthritis, SJC=swollen joint count, TJC=tender joint count, DAS28=Disease Activity Score, MTX=methotrexate, CRP=C-reactive protein, DAPSA=Disease activity index for psoriatic arthritis, TNF=tumor necrosis factor