Conclusion: The 0-4 SQ grade was not equivalent to that of the 0-3 SQ grade used PD scoring and it increased the variance in the majority of SQ grades. This study does show that the PD pixel algorithm has a stronger linear correlation when compared to the SQ grading, suggesting a more accurate method at interpreting treatment response, as the intervals between grades are more equal. Therefore, built in algorithms to detect PD signal in US machines are the future for drug monitoring in inflammatory arthritis.

REFERENCES:

[1] D'Agostino et al. RMD 2017.

Figure 1. A) Definitions of US PD scoring scale 0-3 using the OMERACT grading system and a revised 0-4 score. B) Comparison between SQ 0-3 and 0-4 PD score, with the mean and standard deviation and 95% confidence intervals of PD signal/synovial area ratio. C) Scoring system found by K-means clustering algorithm showing the optimum ratio boundaries and the mean standard deviation and 95% confidence intervals of the ratio in each quantitative grade 0-3.

A Synovitis grade	Power Doppler OMERACT score	Power Doppler revised score
Grade 0 (normal)	No Doppler signal	No Doppler signal
Grade 1 (minimal)	Up to three single Doppler spots OR up to one confluent spot and two single spots OR up to two confluent spots	1-2 Doppler spots OR up to one confluent spot
Grade 2 (mild)	>Grade 1 but ≤50% Doppler signals in the total greyscale background	More than 2 Doppler spots or scattered single spots or <25% Doppler signals in the total greyscale background
Grade 3 (moderate)	>Grade 2 (>50% of the total greyscale background)	25-50% Doppler signals in the total greyscale background
Grade 4 (severe)		>50% of the total greyscale background

B SQ PD Grade	0	1	2	3	4
3-Score					
Mean	0.02%	4.14%	16.02%	40.8%	
SD	0.09%	3.71%	8.14%	11.74%	
95% CI Upper	0.20%	11.56%	32.30%	64.28%	
95% CI Lower	-0.16%	-3.28%	-0.26%	17.32%	
4-Score					
Mean	0.02%	3.92%	15.82%	38.72%	54.25%
SD	0.09%	3.69%	8.19%	9.01%	14.63%
95% CI Upper	0.20%	11.30%	32.20%	56.74%	83.51%
95% CI Lower	-0.16%	-3.46%	-0.56%	20.70%	24.99%

C K-means Grade	0	1	2	3
Ratio Boundaries	[0,5.30]	[5.30,15.97]	[15.97,32.79]	[32.79,100]
Mean	0.7%	9.9%	22.03%	43.55%
SD	1.33%	3.10%	4.38%	9.47%
95% CI Upper	-1.96%	3.70%	13.27%	24.61%
95% CI Lower	3.36%	16.10%	30.79%	62.49%

Figure 2. A) US images demonstrating the spread in PD signal/synovial area ratio with the same SQ PD grade 3 score. B) Comparison between SQ 0-3 and 0-4 PD grading, illustrating the spread of the PD signal/synovial area percentage ratio in each SQ grade category. C) Density graph using K-means statistical test demonstrating how the spread between the individual grades can be minimised compared to the 3 score PD signal/synovial area ratio in Figure 2B.

- [2] Terslev et al. RMD 2017.
- [3] Terslev et al. Rheum 2012.
- [4] Dougados et al. ARD 2010.
- [5] Ammitzboll-Danielsen et al. Rheum 2016.
- [6] Schmidt et al. Rheum 2015.

Disclosure of Interests: Nirupam Purkayastha: None declared, Samiha Ismail: None declared, Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Costantino Pitzalis Grant/research support from: Celgene, Stephen Kelly: None declared

DOI: 10.1136/annrheumdis-2019-eular.1527

Late breaking abstract session

LB0003

EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS NAÏVE TO METHOTREXATE THERAPY: FINCH3 PRIMARY OUTCOME RESULTS

Rene Westhovens¹, William Rigby², Désirée van der Heijde³, Daniel Ching⁴, Beatrix Bartok⁵, Franziska Matzki⁵, Zhaoyu Yin⁵, Ying Guo⁵, Chantal Tasset⁶, John Sundy⁷, Neelufar Mozaffarian⁷, Osvaldo Messina^{7,8}, Robert B.M. Landewe⁹, Tatsuya Atsumi¹⁰, Gerd Rüdiger Burmester¹¹. ¹University Hospitals, Leuven, Belgium; ²Dartmouth College, Lebanon, United States of America; ³Leiden University Medical Center, Leiden, Netherlands; ⁴Timaru Hospital, Timaru, New Zealand; ⁵Gilead Sciences, Inc., Foster City, United States of America; ⁶Galapagos NV, Mechelen, Belgium; ⁷Cosme Argerich Hospital, Buenos Aires, Argentina; ⁸IRO Medical Center, Buenos Aires, Argentina; ⁹Amsterdam University Medical Center, Amsterdam, Netherlands; ¹⁰Hokkaido University, Sapporo, Japan; ¹¹Charité-University Medicine Berlin, Berlin, Germany

Background: Filgotinib (FIL), an orally administered, potent, selective inhibitor of Janus kinase 1 (JAK1), has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA).

Objectives: To compare efficacy and safety of FIL with and without methotrexate (MTX) in patients with RA who were naïve to MTX therapy.

Methods: This phase 3, double-blind, active-controlled study randomized patients with moderately to severely active RA (2:1:1:2) to FIL 200mg daily + MTX weekly (up to 20mg), FIL 100mg + MTX, FIL 200mg (+placebo [PBO]), or MTX (+PBO) for up to 52 weeks; results through week 24 are presented. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 24; additional assessments included ACR50 and ACR70 responses; DAS28-CRP score ≤3.2 and <2.6, and changes in van der Heijde mTSS, HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events (AEs). Logistic regression adjusting for stratification factors with nonresponder imputation was used for treatment comparisons for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints.

Results: Of 1,252 randomized patients, 1,249 received study drug (416 FIL 200mg+MTX; 207 FIL 100mg+MTX; 210 FIL 200mg monotherapy; 416 MTX monotherapy) and were analyzed; 1,130 completed week 24. Most (76.9%) were female; mean time since RA diagnosis was 2.2 years (median 0.4 years); mean (standard deviation [SD]) DAS28-CRP was 5.7 (1.0); and 35.9% were using oral steroids at baseline. At week 24, significantly more patients in the FIL 200mg +MTX (81.0%; $P<0.001$) and FIL 100mg+MTX (80.2%; $P<0.05$) arms achieved an ACR20 response compared to MTX monotherapy (71.4%) (Table 1). Compared to MTX monotherapy, more patients receiving FIL with or without MTX achieved

Table 1. Efficacy Outcomes at Week 24*

	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
ACR20, %	81.0***	80.2*	78.1	71.4
ACR50, %	61.5***	57.0**	58.1***	45.7
ACR70, %	43.8***	40.1***	40.0***	26.0
DAS28-CRP ≤ 3.2, %	68.8***	62.8***	60.0***	46.2
DAS28-CRP < 2.6, %	54.1***	42.5***	42.4***	29.1
mTSS, mean change from BL	0.20	0.22	-0.04**	0.52
HAQ-DI, mean change from BL	-0.94***	-0.90**	-0.89**	-0.79
SF-36 PCS, mean change from BL	12.3***	11.1**	10.4	9.7
FACIT-Fatigue, mean change from BL	10.6	11.4	10.2	10.1

*All patients who were randomized and received at least 1 dose of study drug were included in efficacy analyses. ** $P<0.05$ vs MTX monotherapy; *** $P<0.01$ vs MTX monotherapy; **** $P<0.001$ vs MTX monotherapy. *Comparison not adjusted for multiplicity. ACR20/50/70, 20%/50%/70% improvement in American College of Rheumatology criteria; BL, baseline; DAS28-CRP, Disease Activity Score based in 28 joints with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire Disability Index; mTSS, modified total Sharp score; MTX, methotrexate; PBO, placebo; SF-36 PCS, Short-Form 36 Physical Component Summary.

Table 2. Safety Events of Interest through Week 24

	FIL 200 mg + MTX (N = 416)	FIL 100 mg + MTX (N = 207)	FIL 200 mg Monotherapy (N = 210)	MTX Monotherapy (N = 416)
Patients with event, n (%)				
Serious AEs	17 (4.1)	5 (2.4)	10 (4.8)	12 (2.9)
Serious infections	4 (1.0)	2 (1.0)	3 (1.4)	4 (1.0)
Herpes zoster	2 (0.5)	1 (0.5)	1 (0.5)	2 (0.5)
Adjudicated MACEs	2 (0.5)	0	1 (0.5)	2 (0.5)
Venous thrombotic events	0	0	0	1 (0.2)
Malignancies	0	0	0	1 (0.2)
Deaths	1 (0.2) ^a	0	0	0

^aCause of death was lupus myocarditis.
AE, adverse event; MACE, major adverse cardiovascular event

ACR50 and ACR70 responses, DAS28-CRP <2.6 and ≤3.2, and reported improvements in SF-36 PCS (Table 1). The onset of activity was rapid, with significantly more patients achieving ACR50 and DAS28-CRP <2.6 with FIL than MTX at week 2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Conclusion: The JAK1 inhibitor FIL in combination with MTX led to significant improvements in RA signs and symptoms, physical function, and patient-reported outcomes compared to MTX alone and was well tolerated in patients with early active RA naïve to MTX. Clinically meaningful response to FIL occurred as early as 2 weeks after treatment initiation.

Disclosure of Interests: Rene Westhovens Grant/research support from: Celltrion, Galapagos/Gilead, Consultant for: Celltrion, Galapagos-Gilead, William Rigby Consultant for: Gilead, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Daniel Ching Speakers bureau: AbbVie, Beatrix Bartok Shareholder of: Gilead, Employee of: Gilead, Franziska Matzkies Shareholder of: Gilead, Employee of: Gilead, Zhaoyu Yin Shareholder of: Gilead, Employee of: Gilead, Ying Guo Shareholder of: Gilead, Employee of: Gilead, Chantal Tasset Shareholder of: Warrants from Galapagos, Employee of: Galapagos, John Sundry Shareholder of: Gilead Sciences, Inc., Employee of: Gilead Sciences, Inc., Neelufar Mozaffarian Shareholder of: Gilead, Employee of: Gilead (former employee), Osvaldo Messina Consultant for: Consultant for Eli Lilly, Amgen, Pfizer, and Americas Health Foundation., Robert B.M. Landewé: None declared, Tatsuya Atsumi Grant/research support from: Astellas Pharma Inc., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co. Ltd., Otsuka Pharmaceutical Co., Ltd. and Pfizer Inc. Alexion Inc., Bayer Yakuhin, Ltd./Otsuka Pharmaceutical Co., Ltd. Chugai Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Eisai Co., Ltd., Bristol-Myers Squibb Co., Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma Co., Asahi Kasei Pharma Co., Consultant for: ONO PHARMACEUTICAL CO., LTD Sanofi K.K. Daiichi Sankyo Co., Ltd. Pfizer Inc., Speakers bureau: Mitsubishi Tanabe Pharma Co., Chugai Pharmaceutical Co., Ltd., Astellas Pharma Inc., Takeda Pharmaceutical Co., Ltd., Pfizer Inc., Daiichi Sankyo Co. Ltd., Bristol-Myers Squibb Co., Eli Lilly Japan K.K., Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme

DOI: 10.1136/annrheumdis-2019-eular.8678

LB0004

METHOTREXATE WITHDRAWAL IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVE LOW DISEASE ACTIVITY WITH TOFACITINIB MODIFIED-RELEASE 11 MG ONCE DAILY + METHOTREXATE: A RANDOMISED NON-INFERIORITY PHASE 3B/4 STUDY

Stanley B. Cohen¹, Janet Pope², Boulos Haraoui³, Fedra Irazoque-Palazuelos⁴, Mariusz Korkosz⁵, Annette Diehl⁶, Jose Luis Rivas⁷, Tatjana Lukic⁸, Shixue Liu⁹, Lori Stocker⁶, Noriko Iikuni⁸, Edward Keystone¹⁰. ¹Metroplex Clinical Research Center, Dallas, TX, United States of America; ²Western University, London, ON, Canada; ³Institut de Rhumatologie de Montréal, Montréal, QC, Canada; ⁴Centro de Investigación y Tratamiento Reumatológico, México City, Mexico; ⁵Jagiellonian University Medical College, Kraków, Poland; ⁶Pfizer Inc, Collegeville, PA, United States of America; ⁷Pfizer SLU, Madrid, Spain; ⁸Pfizer Inc, New York, NY, United States of America; ⁹Pfizer Inc, Shanghai, China; ¹⁰University of Toronto, Toronto, ON, Canada

Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). The impact of methotrexate (MTX) withdrawal in patients (pts) with RA who achieve low disease activity (LDA) or remission following treatment with tofacitinib in combination with MTX is unclear.

Objectives: To compare the efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (QD) with and without MTX in pts with RA who have achieved LDA with tofacitinib and MTX.

Methods: ORAL Shift (NCT02831855) was a global Phase 3b/4 study in pts aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label (OL) tofacitinib MR 11 mg QD with MTX (tofacitinib + MTX) for 24 weeks. Pts achieving LDA (CDAI ≤10) at Week (W)24 entered the 24-week double-blind (DB) MTX withdrawal phase and were randomised 1:1 to receive tofacitinib MR 11 mg QD with placebo (tofacitinib monotherapy; ie underwent blinded MTX withdrawal) or continue tofacitinib + MTX. The primary endpoint was least squares mean change from W24 to W48 (Δ; DB phase) in DAS28 4(ESR). Non inferiority of tofacitinib monotherapy vs tofacitinib + MTX was declared if the upper bound of the 95% two-sided confidence interval (CI) for the difference in ΔDAS28-4(CRP) between arms was <0.6. Secondary endpoints included ΔDAS28-4(CRP), ΔSDAI, ΔCDAI, ΔHAQ-DI; rates of ACR20/50/70 response, HAQ-DI response, DAS28-4(ESR)- and CDAI-defined LDA and remission, and ACR-EULAR Boolean-defined¹ remission (W48); and safety (OL and DB phases).

Results: Of 694 pts in the OL phase, 530 achieved CDAI-defined LDA at W24 and were treated in the DB phase (tofacitinib monotherapy: n=264; tofacitinib + MTX: n=266). Demographics and pt characteristics at OL-phase baseline were similar between treatment arms. The difference (95% CI) between arms in ΔDAS28 4(ESR) (primary endpoint) was 0.30 (0.12, 0.48; Table 1) at W48, demonstrating that tofacitinib monotherapy was non-inferior to tofacitinib + MTX. Consistent with the primary endpoint, ΔDAS28-4(CRP)/SDAI/CDAI were greater for tofacitinib monotherapy vs tofacitinib + MTX, but these differences were not clinically meaningful; ACR/HAQ-DI response and LDA rates were generally similar between arms (Table). Remission rates were also similar between arms and generally did not change after MTX withdrawal. In the DB phase, rates of AEs, serious AEs, discontinuations due to AEs and AEs of special interest were generally comparable between arms (Table 1).

Table. Efficacy and safety outcomes during the double-blind MTX withdrawal phase (W24 [randomisation] to W48)

	Tofacitinib MR 11 mg QD monotherapy N=264 ^a	Tofacitinib MR 11 mg QD + MTX N=266 ^a
Efficacy		
Change from W24 to W48, least squares mean (95% CI)		
DAS28-4(ESR) (primary endpoint)	0.33 (0.20, 0.46)	0.03 (-0.10, 0.16)
Least squares mean (95% CI) difference, tofacitinib monotherapy minus tofacitinib + MTX		0.30 (0.12, 0.48) ^b
DAS28-4(CRP)	0.29 (0.16, 0.41)	0.01 (-0.11, 0.13)
SDAI	3.16 (2.18, 4.15)	0.94 (-0.03, 1.91)
CDAI	2.57 (2.05, 3.00)	0.84 (-0.09, 1.76)
HAQ-DI	0.01 (-0.04, 0.07)	-0.00 (-0.06, 0.05)
Response, n (%)		
W24		W48
ACR20 ^c	250 (94.7)	193 (73.1)
ACR50 ^c	203 (76.9)	146 (55.3)
ACR70 ^c	122 (46.2)	100 (37.9)
HAQ-DI ^d	200 (75.8)	181 (68.6)
LDA, n (%)		
W24		W48
DAS28-4(ESR) ≤3.2	134 (50.8)	119 (45.1)
CDAI ≤10 ^e	262 (99.2)	262 (98.5)
Remission, n (%)		
W24		W48
DAS28-4(ESR) <2.6	80 (30.3)	63 (23.9)
CDAI ≤2.8	72 (27.3)	75 (28.4)
ACR-EULAR Boolean ¹	62 (23.5)	59 (22.4)
Safety		
W24		W48
AEs, n (%)	107 (40.5)	109 (41.0)
SAEs, n (%)	10 (3.8)	5 (1.9)
Discontinuations due to AEs, n (%)	5 (1.9)	5 (1.9)
Deaths, n (%)	0	2 (0.8)
Most common (≥2%) AEs by MedDRA PT, n (%)		
W24		W48
Arthralgia	7 (2.7)	2 (0.8)
ALT increased	5 (1.9)	10 (3.8)
AST increased	5 (1.9)	6 (2.3)
Nasopharyngitis	5 (1.9)	7 (2.6)
URI	4 (1.5)	6 (2.3)
Bronchitis	3 (1.1)	7 (2.6)
AEs of special interest, n (%)		
W24		W48
Serious infections	2 (0.8)	2 (0.8)
Herpes zoster ^f	2 (0.8)	3 (1.1)
Malignancies excluding NMCS ^g	1 (0.4)	0
NMCS ^g	1 (0.4)	1 (0.4)
MACEs ^h	0	1 (0.4) ⁱ

^aEfficacy data are from the full analysis set (all patients who received at least one dose of tofacitinib + MTX during the open-label phase, and were randomised and received at least one dose of tofacitinib + MTX or tofacitinib monotherapy in the double-blind phase). Continuous endpoint results are from a mixed-effect model of repeated measures. Binary data are calculated using non-responder imputation. The number of patients who completed each efficacy outcome measure (n) may be less than the overall N. The safety analysis set during the double-blind phase is the same as that for efficacy. ^bNon-inferiority criteria were met; upper bound of 95% CI was <0.6. ^c20/50/70% improvement in tender and swollen joint counts and 20/50/70% improvement in three of the four other criteria (PGA, PGA, HAQ-DI, ESR). ^dHAQ-DI decrease of ≥0.22, relative to open-label phase baseline. ^eHAQ-DI decrease of ≥0.22, relative to open-label phase baseline. ^fDue to protocol deviations, some patients who had not received LDA at W24 (randomisation) were randomised and received study treatment; they were therefore included in the analysis. ^gAll herpes zoster events reported involved one or two adjacent dermatomes and were non-serious. ^hAdjudicated events. ⁱOccurred >28 days after the last dose of the study treatment.

ACR, American College of Rheumatology; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CDAI, Clinical Disease Activity Index; CI, confidence interval; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; HAQ-DI, Health Assessment Questionnaire Disability Index; LDA, low disease activity; MACE, major adverse cardiovascular event; MedDRA, Medical Dictionary for Regulatory Activities; MR, modified-release; MTX, methotrexate; NMCS, non-melanoma skin cancer; PGA, Physician Global Assessment; PT, preferred term; PGA, Patient Global Assessment; QD, once daily; SAE, serious adverse event; SDAI, Simplified Disease Activity Index; URI, upper respiratory tract infection; VAS, visual analogue scale; W, Week.

Conclusion: Pts receiving tofacitinib MR 11 mg QD + MTX who achieve LDA may withdraw MTX up to W48 without significant worsening of disease activity. Pts in remission tend to remain in remission after MTX withdrawal. Safety appeared consistent with the known profile of tofacitinib.

REFERENCE

[1] Felson DT *et al*. *Arthritis Rheum* 2011;63:573-586

Acknowledgement: Study sponsored by Pfizer Inc. Medical writing support was provided by C Viegelmann of CMC Connect and funded by Pfizer Inc.

Disclosure of Interests: Stanley B. Cohen Grant/research support from: AbbVie, Eli Lilly, Genentech, Gilead, Pfizer Inc, Consultant for: AbbVie, Eli Lilly, Genentech, Gilead, Pfizer Inc, Janet Pope Grant/research support from: Bristol-Myers Squibb, Roche, Seattle Genetics, UCB, Consultant for: AbbVie, Actelion, Amgen, Bayer, Bristol-Myers Squibb, Lilly, Merck, Novartis, Pfizer Inc, Roche, Sandoz, Sanofi, UCB, Boulos Haraoui Grant/research support from: AbbVie, Pfizer Inc, Consultant for: AbbVie, Amgen, Eli Lilly, Merck, Pfizer Inc, UCB, Fedra Irazoque-Palazuelos Consultant for: Bristol-Myers Squibb, Janssen, Pfizer Inc, Roche, UCB, Mariusz Korkosz Consultant for: AbbVie, Lilly, MSD, Novartis, Roche, UCB, Annette Diehl Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Jose Luis Rivas

Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Tatjana Lukic Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Shixue Liu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Lori Stockert Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Noriko Ikuni Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Edward Keystone Grant/research support from: AbbVie, Amgen, Lilly Pharmaceuticals, Pfizer Inc, PuraPharm, Sanofi-Aventis, Consultant for: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Celltrion, Crescendo Bioscience, F. Hoffman-La Roche, Genentech, Gilead, Janssen, Lilly Pharmaceuticals, Merck, Pfizer Inc, Sandoz, Sanofi-Genzyme, Samsung Bioepis, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb Canada, F. Hoffman-La Roche, Janssen, Merck, Pfizer Inc, Sanofi-Genzyme, UCB
DOI: 10.1136/annrheumdis-2019-eular.8657

LB0005

MULTICENTRE, RANDOMISED, OPEN-LABEL, ASSESSOR-BLINDED, PARALLEL-GROUP HEAD-TO-HEAD COMPARISON OF THE EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADALIMUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS NAIVE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS: 24-WEEK RESULTS

Philip J. Mease¹, Josef S. Smolen², Frank Behrens³, Peter Nash⁴, Soyi Liu Leage⁵, Li Lingnan⁵, Hasan Tahir⁶, Melinda Gooderham⁷, Eswar Krishnan⁵, Paul Emery⁵, Sreekumar Pillai⁵, Philip Helliwell⁸. ¹Swedish Medical Center & University of Washington, Seattle, United States of America; ²Medical University of Vienna, Vienna, Austria; ³Goethe University, Frankfurt, Germany; ⁴University of Queensland, Brisbane, Australia; ⁵Eli Lilly, Indianapolis, United States of America; ⁶Barts Health, London, United Kingdom; ⁷Skin Centre for Dermatology, Peterborough, Canada; ⁸NIHR BRC LTH & LIRRM, University of Leeds, United Kingdom

Background: There have been few head-to-head clinical trials comparing different biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients (pts) with psoriatic arthritis (PsA).
Objectives: To report 24-week (wk) results of a study directly comparing efficacy and safety of ixekizumab (IXE), an IL-17A inhibitor, and adalimumab (ADA), a TNF inhibitor, in bDMARD-naïve pts with PsA.
Methods: The study (NCT03151551; SPIRIT-H2H) included pts with active PsA (≥3 TJC + ≥3SJC) and plaque psoriasis (BSA ≥3%) who were bDMARD naïve and inadequate responders to csDMARD therapy. Patients were randomised (1:1) to IXE or ADA for 52 wks (on-label dosing based on presence/absence of moderate to severe psoriasis). The primary objective was superiority of IXE vs ADA measured by the proportion of pts achieving both ACR50 and PASI100 responses at wk 24. Key secondary objectives versus ADA at wk 24 were (1) non-inferiority of IXE for ACR50 (noninferiority margin -12%) and (2) superiority of IXE for PASI100. Additional PsA, skin, composite treat-to-target (T2T: MDA, DAPSA 4), PASDAS remission and patient-reported outcomes, and safety were assessed. Nine pts had PASI=0 and BSA≥3% (a medical inconsistency) at baseline; these pts were considered PASI100 responders if PASI=0 and BSA=0 at wk 24. Categorical variables were evaluated using logistic regression analyses with NRI in the ITT population. Continuous variables were analysed using mixed models for repeated measure analysis.
Results: 566 pts were randomised (283 to IXE and 283 to ADA). Baseline demographics and disease characteristics were generally well balanced between groups (Table 1). All primary and key secondary efficacy endpoints at wk 24 were met (Figure). The proportion of pts achieving both ACR50 and PASI100 was significantly greater for IXE than ADA (36% vs 28%; p<0.05). IXE was non-inferior to ADA for ACR50 response and superior for PASI100 response (Figure). While improvements from baseline were achieved with both treatments, significantly better results were seen with IXE vs ADA for skin and composite T2T outcomes, enthesitis resolution (Figure 1), and skin-related quality of life (Table 2). No unexpected safety signals were observed.

Table 1. Patient baseline demographics/characteristics

	IXE (N=283)	ADA (N=283)
Age, years	47.5 (12.0)	48.3 (12.3)
Male, n (%)	162 (57)	150 (53)
PsA duration since diagnosis, years	6.6 (7.4)	5.9 (6.4)
Concomitant csDMARD use, n (%)	193 (68)	199 (70)
TJC	19.1 (12.7)	21.3 (15.4)
SJC	10.1 (7.5)	10.7 (8.1)
PASI	7.9 (8.7)	7.7 (7.3)

Data are mean (SD), unless stated otherwise

Figure

Pts were stratified by conventional synthetic DMARD use and presence of moderate to severe psoriasis.
*There were 193 IXE- and 171 ADA-treated pts with SPARCC enthesitis index scores >2 at baseline; these patients were evaluated at wk 24. *There were 62 IXE- and 58 ADA-treated pts with LDI scores >0 at baseline; these patients were evaluated at wk 24. ADA, adalimumab 40 mg q2w then 40 mg every 2 wk from wk 1 for pts with moderate to severe psoriasis or 40 mg q2w then 40 mg every 2 wk for pts without moderate to severe psoriasis; IXE, ixekizumab 160 mg q2w then 80 mg every 2 wk to wk 12 and every 4 wk thereafter for pts with moderate to severe psoriasis or 160 mg q2w then 80 mg every 4 wk for pts without moderate to severe psoriasis; ACR, American College of Rheumatology criteria; PASI, Psoriasis Area Severity Index score; MDA, minimal disease activity - PsA; DAPSA, Disease Activity for Psoriatic Arthritis; PASDAS VLDL, Psoriatic Arthritis Disease Activity Score very low disease activity; SPARCC, Spondyloarthritis Research Consortium of Canada; LDI, Leeds Dactylitis Instrument; *p < .05, **p < .01 IXE vs ADA

Table 2. Patient reported outcomes

	IXE (N=283)		ADA (N=283)	
	Baseline	LS mean change at wk 24	Baseline	LS mean change at wk 24
HAQ-DI	1.20	-0.63	1.27	-0.56
SF-36 PCS	36.80	9.96	36.12	8.82
SF-36 MCS	45.40	4.47	44.85	3.93
Dermatology Life Quality Index	9.77	-7.81*	9.82	-6.48
Fatigue Severity Numeric Rating Scale	5.87	-2.66	6.46	-2.53

LS, least square; *p<.001 vs ADA

Conclusion: In bDMARD naïve pts with active PsA and skin disease, IXE showed superior efficacy to ADA based on simultaneous achievement of ACR50 and PASI100 responses at wk 24. Greater improvements with IXE vs ADA were also attained in individual PsA domains and composite T2T outcomes.
Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB., Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB., Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB., Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Frank Behrens Grant/research support from: AbbVie, Pfizer, Roche, Chugai, Prophylis, Bioline, Novartis, Consultant for: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Speakers bureau: Ad board: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, MSD, Celgene, Gilead, Soyi Liu Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Li Lingnan Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Hasan Tahir Grant/research support from: Novartis, Eli Lilly, Speakers bureau: AbbVie, Janssen, Eli Lilly, and Novartis, Melinda Gooderham Grant/research support from: AbbVie Inc., Actelion Pharmaceuticals, Akros Pharma Inc., AMGEN Inc., Arcutis Pharmaceuticals Inc., Boehringer Ingelheim International GmbH, Bristol-Myers Squibb, Celgene Corporation, Dermira Inc., Eli Lilly and Company, Galderma SA, Glenmark, Janssen Inc., LEO Pharma, MedImmune, Merck and Co., Novartis Pharmaceuticals, Pfizer Inc., Regeneron Pharmaceuticals Inc., Roche Laboratories, Sanofi Genzyme, UCB, Valeant Pharmaceuticals Inc., Consultant for: Akros Pharma Inc., AMGEN Inc., Boehringer Ingelheim International GmbH, Celgene Corporation, Eli Lilly and Company, Galderma SA, Glenmark, Janssen Inc., LEO Pharma, Novartis Pharmaceuticals, Pfizer Inc., Regeneron Pharmaceuticals Inc., Sanofi Genzyme, Valeant Pharmaceuticals Inc., Eswar Krishnan Shareholder of: Eli Lilly and