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:

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Late breaking abstract session

LB0003 EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS NAÏVE TO METHOTREXATE THERAPY: FINCHS PRIMARY OUTCOME RESULTS
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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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ACR20, %</th>
<th>ACR50, %</th>
<th>ACR70, %</th>
<th>DAS28-CRP ≤3.2, %</th>
<th>DAS28-CRP ≤2.6, %</th>
<th>mTSS, mean change from BL</th>
<th>HAQ-DI, mean change from BL</th>
<th>SF-36 PCS, mean change from BL</th>
<th>FACIT-Fatigue, mean change from BL</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIL 200 mg</td>
<td>81.0**</td>
<td>57.0**</td>
<td>45.7**</td>
<td>60.4**</td>
<td>44.0**</td>
<td>0.20</td>
<td>-0.94**</td>
<td>11.1**</td>
<td>10.2</td>
</tr>
<tr>
<td>FIL 100 mg</td>
<td>80.2**</td>
<td>51.8**</td>
<td>26.0</td>
<td>60.0**</td>
<td>42.4**</td>
<td>0.22</td>
<td>-0.96**</td>
<td>11.1**</td>
<td>10.2</td>
</tr>
<tr>
<td>MTX monotherapy</td>
<td>71.4</td>
<td>45.7**</td>
<td>26.0</td>
<td>60.0**</td>
<td>42.4**</td>
<td>0.20</td>
<td>-0.94**</td>
<td>11.1**</td>
<td>10.2</td>
</tr>
</tbody>
</table>

**P<0.01 vs MTX monotherapy; *P<0.05 vs MTX monotherapy; *P<0.01 vs MTX monotherapy; Comparison not adapted for multiplicity.

ACR20/50/70, 28-joint ACR20/50/70 improvement in American College of Rheumatology criteria. BL, baseline; DAS28-CRP, Disease Activity Score based on 28 joints with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; HAQ-DI, health assessment questionnaire Disability Index; MDS, multidimensional health score; MTX, methotrexate; PBO, placebo; SF-39 PCS, Short Form 36 Physical Component Summary.

All patients were randomized and received at least 1 dose of study drug; drug were included in efficacy analyses. *P<0.05 vs MTX monotherapy; **P<0.01 vs MTX monotherapy; ***P<0.001 vs MTX monotherapy; *P<0.01 vs MTX monotherapy. No comparison not adapted for multiplicity.
ACR50 and ACR70 responses, DSAS2-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 DSAS2-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 Westhoven 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, Gen, Gail, 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, Franceska Matzkie Shareholder of: Gilead, Employee of: Gilead, ZhaoYu Yin Shareholder of: Gilead, Employee of: Gilead, Ying Guo Shareholder of: Gilead, Employee of: Gilead, Daniel Ching Speakers bureau: AbbVie, Beatrix Bartok Shareholder of: Gilead, Employee of: Gilead. 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.


**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 generally similar between treatment arms. The difference (95% CI) between arms in ΔDAS28 4(CRP) (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).

**METHODS**

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

**Objective:** To compare the efficacy and safety of tofacitinib modified-release (MR) 11 mg once daily (OD) 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 OD 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 DSAS2 4(CRP). Non inferiority of tofacitinib monotherapy vs tofacitinib + MTX was declared if the difference in ΔDAS2 4(CRP) between arms was <0.6. Secondary endpoints included ΔDAS2 4(CRP), ΔSDAI, ΔCDAI, ΔHAQ-DI; rates of ACR20/50/70 response, HAQ-DI response, DSAS2 4(CRP)- and CDAI-defined LDA and remission, and ACR-EULAR Boolean-defined 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 generally similar between treatment arms. The difference (95% CI) between arms in ΔDAS28 4(CRP) (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).


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**References**


**MULTICENTRE, RANDOMISED, OPEN-LABEL, ASSESSOR-BLINDED, PARALLEL-GROUP HEAD-TO-HEAD COMPARISON OF THE EFFICACY AND SAFETY OF IXEKIZUMAB VERSUS ADAлимум 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, Philip J. Mease1, Josef S. Smolen 2, Frank Behrens3, Peter Nash4, Soyi Liu Leage5.

**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-naive pts with psoriatic arthritis (PsA).

**Methods:** The study (NCT03151551; SPIRIT-H2H) included pts with active PsA (≥3 TJC ≥3SJC) and plaque psoriasis (BSA ≥3%) who were bDMARD naive and inadequate responders to csDMARD therapy. Patients were randomised (1:1) to IXE or ADA for 24 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 (non-inferiority margin -12%) and (2) superiority of IXE for PASI100. Additional PsA, skin, composite treat-to-target (T2T: MDA, DAPSA 4), PASI90 responder, and patient-reported outcomes, and safety were assessed. Nine pts had PASI=0 and BSA=0 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, enthesis resolution (Figure 1), and skin-related quality of life (Table 2). No unexpected safety signals were observed.

**Conclusion:** In bDMARD naive 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.