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 200mg (n=85) or PBO (n=86) 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 adipoctin). 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 pathology 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.

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Figure 1. LSM (SE) and CI (U95%) for DAPSA-DI and JADAS-6 (CI) by Month 12 of the MTX withdrawal study.