Figure 1. Relative risk of developing cancer between rituximab and csDMARDs. (A) any cancer; (B) all cancer types excluding NMSC; (C) solid tumors; (D) hematological cancer; (E) NMSC; or (F) melanoma. csDMARDs: conventional synthetic disease-modifying antirheumatic drugs. NMSC: non-melanoma skin cancer.

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FRI0113

THE BASELINE SOLUBLE GP130 IS ASSOCIATED WITH THE RESPONSE OF RHEUMATOID ARTHRITIS PATIENTS TO SARILUMAB

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Background: IL-6 contributes significantly to the chronic inflammatory process of rheumatoid arthritis (RA). Sarilumab (SRL), a human anti-human IL-6 receptor alpha monoclonal antibody that blocks the signaling originated by the IL-6/IL-6R complex like tocilizumab, is an effective treatment. However, predictors of the response to sarilumab are still required.

Objectives: We aimed to combine IL-6, soluble IL-6R (sIL-6R) and gp130 (sgp130) levels to identify groups of sarilumab responses.

Methods: This research is a retrospective study. A total of 32 RA patients with SRL therapy in our department from February 1 in 2018 to December 31 in 2019 were included. Serum and clinical data from 32 RA patients were collected before treatment and until the last visit. Follow-up period was up to one year after starting SRL treatment. Serum were tested for IL-6 (Human IL-6 Quantikine ELISA Kit, R&D systems), sIL-6R (Human soluble IL-6R alpha Quantikine ELISA Kit, R&D systems) and sgp130 (Human soluble gp130 Quantikine ELISA Kit, R&D systems), using specific ELISAs according to the manufacturer's instructions. Hierarchical cluster analysis (JMP14.3.0) was used to establish the relationship between IL-6, sIL-6R and sgp130. We evaluated the efficacy of SRL treatment on the last visit using European League Against Rheumatism (EULAR) response criteria in the groups of patients. The other statistical analyses were performed with EZR 1.41, and p Values less than 0.05 were considered significant.

Results: The median age of patients was 70.5 (IQR: 66.5-74.3) years and the median of disease duration was 7.3 (1.7-15.3) years. Nine (28.1%) patients were biologic and Jakinibs naive. The median follow-up periods were 24 (12-26) weeks. The baseline DAS28 was median 4.39 (3.77 - 5.43), and CDAI was 21.1 (11.7-29.5). When comparing responders and non-responders, there were no significant differences in any of the baseline parameters and cytokines. Four statistical significant clusters of RA patients (i.e., Group1, Group2, Group3 and tocilizumab use group before SRL) were defined by serum concentrations of IL-6, sIL-6R and sgp130 at baseline. The levels of IL-6 expressed as median in Group1 patients were 25.6 (14.4-72.2) pg/ml, in Group2 5.9 (3.3-11.3) pg/ml, and in Group3 70.2 (45.4-86.1) pg/ml ($p < 0.002$, significant difference only between Group2 and Group3). The levels of sIL-6R expressed as median in Group1 patients were 38.7 (34.7-45.1) ng/ml, in Group2 35.1 (24.8-41.9) ng/ml, and in Group3 35.7 (34.2-39.8) ng/ml ($p = 0.5477$). The levels of sgp130 expressed as median in Group1 patients were 272.6 (263.0-277.2) ng/ml, in Group2 223.1 (221.0-228.0) ng/ml, and in Group3 204.6 (192.0-207.6) ng/ml ($p < 0.00003$, significant difference between the three groups respectively). There were no significant differences in any of the baseline clinical features and laboratory findings between the three groups. Out of the 8 patients in Group1 had a good or moderate response to SRL. Conversely, the percentage of patients with no response to SRL was higher in Group3 than in Group1 and Group2.

Conclusion: RA patients could be easily stratified prior to the therapeutic intervention with sgp130 related to the IL-6 signal regulation. Group1 patients, who had the best response to SRL, had the highest level of sgp130.

Table 1. Comparison of baseline serum IL-6, sIL-6R and sgp130 of each groups of patients

	TCZ use before SRL	Group 1	Group 2	Group 3	P value
	n=3	N=9	N=8	N=9	
IL-6, pg/mL	69.8, 592.6	Median 25.6 [IQR] [14.4-72.2]	5.9 [3.3-11.3]	70.2 [45.4-86.1]	<0.002 c
sIL-6R, ng/mL	390.5, 481.7	Median 38.7 [IQR] [34.7-45.1]	35.1 [24.8-41.9]	35.7 [34.2-39.8]	0.547
sgp130, ng/mL	205.6, 239.8	Median 273 [IQR] [263-277]	223 [221-228]	205 [192-208]	<0.001 abc

*a, b and c mean that statically significant difference between subgroups as a: group1 vs. 2, b: group 1 vs. 3, c: group 2 vs. 3.

Figure 1. Patients from each group categorized as good, moderate, and no response after sarilumab treatment according to the EULAR criteria

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FRI0114

EFFICACY OF LEVILIMAB, NOVEL MONOCLONAL ANTI-IL-6 RECEPTOR ANTIBODY, IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1-YEAR RESULTS OF PHASE 2 AURORA STUDY

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Background: Previously, 12-week results of phase 2 clinical study of levilimab (LVL) in patients with active rheumatoid arthritis (RA) have been reported¹. The study has met the primary endpoint at W12 confirming that treatment with LVL 162 mg SC + methotrexate (MTX) either QW or Q2W is superior to MTX alone in patients with RA and inadequate response to methotrexate (MTX-IR). Here we report 1-year efficacy and safety data in QW and Q2W arm of the study.

Objectives: This study was aimed to assess the efficacy and safety of 2 dosing regimens of LVL in active MTX-IR RA subjects.

Methods: This multicenter double-blind placebo-controlled study (NCT03455842) enrolled 105 MTX-IR subjects with active RA (ACR2010). The study design is outlined on Figure 1. Secondary endpoints for the open-label period included ACR20/50/70, LDA, remission rates, and DAS28-CRP(4), among others. The safety was evaluated up to W56.

Figure 1. Study design

Results: At W12 ACR20 was reached by 77.1% and 57.1% of subjects of QW and Q2W arms respectively. Within open-label (OLE) period further increase in clinical response degree was observed up to W52, more pronounced in ACR50 and even more in ACR70 / RA LDA and Remission rates (Table 1). Figure 1 summarizes the dynamic of DAS28-CRP(4) change throughout the study. QW regimen showed better efficacy results.

Table 1. Efficacy results (full analysis set), n (%).

	QW + MTX (n = 35)	Q2W + MTX (n = 35)	p-value
ACR20 W12	27 (77.1)	20 (57.1)	0.07
W52	32 (91.4)	25 (71.4)	0.03
ACR50 W12	18 (51.4)	11 (31.4)	0.09
W52	26 (74.3)	23 (65.7)	0.43
ACR70 W12	10 (28.6)	7 (20.0)	0.40
W52	23 (65.7)	16 (45.7)	0.09
LDA (DAS28 <3.2) W12	20 (57.1)	10 (28.6)	0.02
W52	29 (82.9)	24 (68.6)	0.16
EULAR Remission W24	4 (11.4)	2 (5.7)	0.67
W52	10 (28.6)	10 (28.6)	1.00

Table 2 shows the main safety endpoints for the entire study (W0 – W56). The most common treatment related AEs (registered >5% of subjects) were laboratory abnormalities (neutrophil count decrease, ALT / AST increase, blood cholesterol/triglycerides increased). SAE occurred within the blinded study period were reported previously¹. During OLE, starting from W12, four new serious AE (SAEs) were reported: 3 in LVL QW arm: haemorrhage (gr.3, unrelated), vaginal cyst (gr.3, unrelated) and keratitis (gr.2, unrelated); 1 in LVL Q2W arm: myocardial ischemia with cardiovascular insufficiency (gr.5, unrelated).

Table 2. Safety results (full analysis set, W0 – W56), n (%).

	QW + MTX (n = 35)	Q2W + MTX (n = 35)
Any TEAEs/SAEs	34 (97.1)	29 (82.9)
Any SAEs	4 (11.4)	2 (5.7)
Any gr. 3-4 AEs	16 (45.7)	12 (34.3)
Gr. 3-4 neutropenia	4 (11.4)	5 (14.3)
AEs of special interest (ALT / AST high; Leucopenia / Neutropenia; Infections; Cholesterol/triglycerides high)	28 (80.0)	26 (74.3)
Treatment discontinuation due to AE	0	4 (11.3)
Deaths	0	2 (5.7) (unrelated)

Conclusion: Within 1 year of treatment LVL + MTX showed sustained efficacy, with continuous clinical improvement in MTX-IR subjects with active RA. The safety profile of LVL was consistent with other IL6R inhibitors. LVL QW regimen was shown to be safe with better efficacy in terms of time and magnitude and was selected for phase 3 confirmatory clinical study.

References:

[1] <http://dx.doi.org/10.1136/annrheumdis-2019-eular.7220>

Figure 2. Absolute DAS-28-CRP(4) change (median ± IQR, full analysis set)

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Rheumatoid arthritis - non biologic treatment and small molecules

FRI0115

FILGOTINIB PROVIDED RAPID AND SUSTAINED IMPROVEMENTS IN FUNCTIONAL STATUS, PAIN, AND HEALTH-RELATED QUALITY OF LIFE, AND REDUCED FATIGUE OVER TIME IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE METHOTREXATE-NAÏVE: RESULTS FROM THE FINCH 3 STUDY

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Background: In the FINCH 3 study, filgotinib (FIL)—a potent, selective, oral small molecule Janus kinase 1 inhibitor¹—in combination with methotrexate (MTX), demonstrated significant improvements in the signs and symptoms of rheumatoid arthritis (RA) vs MTX alone in patients (pts) who were MTX-naïve.² For pts with RA, rapid control of pain and fatigue along with maintenance of physical function and health-related quality of life (HRQoL) are important outcomes of their care.³ Thus, patient-reported outcomes (PROs) can provide physicians with evidence to guide treatment decisions beyond the guideline-recommended treatment targets of reducing immune inflammation to prevent joint damage, physical disability, and mortality.⁴

Objectives: To evaluate the rate and magnitude of change in PROs assessing functional status, pain, HRQoL, and fatigue from FINCH 3.

Methods: In the FINCH 3 study (NCT02886728), pts with active RA who were MTX-naïve received FIL 200mg daily + MTX, FIL 100mg + MTX, FIL 200mg (+ placebo [PBO]), or MTX (+ PBO) for up to 52 weeks. PROs were recorded prospectively and included HAQ-DI (functional status) and VAS pain scale (day 1, week [W]2, W4, W8, W12, W16, W20, W24, W30, W36, W44, W52), SF-36 (HRQoL), and FACIT-Fatigue (day 1, W4, W12, W24, W36, W52). The least squares mean of the change from baseline (CFB) at each time point up to W52 and p values (each FIL arm vs MTX) were analysed using a mixed-effects model for repeated measures. For HAQ-DI, the proportion of pts who achieved the minimum clinically important difference (MCID; reduction ≥0.22) between each FIL arm and MTX was analysed using logistic regression analysis. P values for the comparisons of PROs were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200mg + MTX and FIL 100mg + MTX vs MTX.

Results: Of the 1249 pts randomised and treated (FIL 200mg + MTX, n = 416; FIL 100mg + MTX, n = 207; FIL 200mg, n = 210; MTX, n = 416), 1025 (82.1%) completed the study. Compared with MTX alone, a nominally significantly greater CFB in functional status and pain from W2 to W24 was observed in all FIL arms; the benefit was sustained from W30 to W52 (Fig 1). By W2, a nominally significantly greater proportion of pts achieved the HAQ-DI MCID or greater (≥0.22) in all FIL arms (FIL 200mg + MTX: 61.9%, p <0.001; FIL 100mg + MTX: 58.5%, p <0.001; FIL 200mg: 53.9%, p = 0.004) compared with MTX (42.2%). By W8, ≥72% of pts in all FIL arms vs 63% of pts in the MTX arm achieved the HAQ-DI MCID; a numerically greater proportion of pts in FIL arms vs MTX achieved HAQ-DI MCID through W52. SF-36 physical component summary and FACIT-Fatigue scores were nominally significantly improved with FIL treatment vs MTX alone at various time points (Fig 2A, B). Improvements in SF-36 mental component summary scores were nominally significant for pts in all FIL arms vs MTX alone as early as W4, and the CFB reached at W12 for FIL arms was generally sustained up to W52 (Fig 2A).

Figure 1. Change in HAQ-DI and VAS pain scale at each visit

*p <0.001, †p <0.01, ‡p <0.05 for LS mean of the difference between FIL arm vs MTX. P values were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200mg + MTX and FIL 100mg + MTX vs MTX. CFB, change from baseline; FIL, filgotinib; LS, least squares; MTX, methotrexate; SE, standard error; VAS, visual analog scale.