Methods: The "Institute of Rheumatology, Rheumatoid Arthritis (IORRA)" is a single-center prospective observational cohort study established at our institute in 2000. Data (physicians' and patients' disease assessments, laboratory data, and many other patient information) were collected from approximately 5,000 RA patients biannually. More than 99% of RA patients treated at our institute were enrolled in this cohort, and >98% of patients answered and mailed their questionnaires back to us every time. Among the RA patients who were registered in the IORRA cohort study from 2011 through 2015, 603 patients fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Boolean-based definition of remission in RA, at least once and used only MTX as disease-modifying antirheumatic drugs (DMARDs) including biological DMARDs for 5 years. Relationships between MTX dosages and gender, disease duration, height, body weight, body mass index, body surface area, serum creatinine (SCr), estimated glomerular filtration rate (eGFR), creatinine clearance (by Cockcroft-Gault Equation), rheumatoid factor, and anti-cyclic citrullinated peptide antibody when remission was first reached by each patient were analyzed by univariate analyses using Pearson correlation coefficient and Welch's *t* test. Subsequently, a multiple regression analysis was performed.

Results: Univariate analyses detected several candidate clinical variables associated with MTX monotherapy dosages in RA patients who achieved remission: height, body weight, body surface area, SCr, eGFR, and CCR ($p = 0.004, 0.050, 0.241, <0.001, <0.001$, and <0.001 , respectively). Subsequently, a multiple regression model developed a best-fit model with the following variables: age, height, body weight, and SCr (standardized partial regression coefficient = $-0.20, 0.10, 0.07$, and -0.22 , respectively), while its adjusted coefficient of determination was 0.114.

Conclusions: There were significant relationships between MTX monotherapy dosages and age, height, body weight, and renal function in RA patients who achieved remission. However, the low coefficient of determination indicated the model accounted for limited variability with the specified variables.

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THU0205 EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON MULTIBIOMARKER DISEASE ACTIVITY SCORES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE

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Background: Filgotinib (GLPG0634, GS-6034) is an oral selective JAK1 inhibitor that has been evaluated in a 24-week phase 2B study (DARWIN 1) on the background of methotrexate (MTX) treatment in active rheumatoid arthritis (RA) patients who were MTX inadequate responders¹.

Objectives: To evaluate the effect of filgotinib compared to placebo on a multi-biomarker disease activity (MBDA) score that measures 12 disease-related biomarkers of inflammation and joint injury in RA patients taking background MTX.

Methods: Serum samples of RA patients who were on a stable dose of MTX and received either placebo (PBO) or filgotinib 100mg or 200mg once daily (QD), were tested for MBDA components (Crescendo Biosciences, CA, US) at baseline, week 4 and week 12. Median % change from baseline for MBDA score and individual components are reported for week 4 and week 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups vs. PBO.

Results: Baseline MBDA scores and component values (median; interquartile range) were similar in PBO (55; 45–64), 100mg QD (58; 42–66), and 200mg QD (59; 50–67.5) treatment groups. Filgotinib treated patients had reductions in the MBDA score from baseline at both the 100mg and 200mg QD dose levels, but not in the PBO group. At both weeks 4 and 12, these reductions in the filgotinib treated groups were significantly different from the PBO group. Most of the individual components contributed to the decrease in MBDA score, but the largest reductions were observed for serum amyloid A (SAA), C-reactive protein (CRP), and IL-6, and the biomarkers of joint-damage, matrix metalloproteinase 3 (MMP3), MMP1, vascular endothelial growth factor (VEGF), and YKL40 (human cartilage glycoprotein 39). There was an increase in leptin and no change in epidermal growth factor (EGF) concentrations.

Table 1. Median percent change from baseline of MBDA score and component concentrations

	Week 4			Week 12		
	PBO (N=62)	Filgotinib 100mg QD (N=63)	Filgotinib 200mg QD (N=68)	PBO (N=65)	Filgotinib 100mg QD (N=62)	Filgotinib par 200mg QD (N=68)
MBDA SCORE	-1	-20***	-24***	-5	-19***	-24***
CRP	15	-57***	-71***	-8	-66***	-78***
EGF	14	-18 ^{NS}	-8 ^{NS}	0	-10 ^{NS}	0 ^{NS}
IL-6	-15	-34**	-60***	-20	-41***	-63***
LEPTIN	0	8 ^{NS}	18 ^{NS}	6	14 ^{NS}	23*
MMP-1	10	-16***	-24***	-6	-18***	-26***
MMP-3	0	-24**	-33***	-9	-25***	-43***
RESISTIN	1	-12**	-22***	-1	-15*	-16***
SAA	8	-45***	-65***	7	-49***	-67***
TNF-RI	0	-11***	-26***	0	-11***	-15***
VCAM-1	5	-10***	-15***	0	-8**	-16***
VEGF	3	-16***	-25***	-2	-16***	-26***
YKL-40	2	-12*	-32***	-7	-17 ^{NS}	-33***

p-values comparing % changes between filgotinib and PBO groups NS, $p > 0.05$; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Conclusions: RA patients treated with filgotinib in combination with MTX had significant reductions in the MBDA score that was driven by key RA biomarkers encompassing both inflammation and joint injury. These findings are consistent with the filgotinib efficacy observed in RA patients over 12 weeks.

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THU0206 THE JAK1-SELECTIVE INHIBITOR FILGOTINIB REDUCES MULTIPLE MARKERS OF INFLAMMATION LINKED TO VARIOUS PATHOLOGIC CELL TYPES AND PROCESSES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: JAK1, 2, 3 and TYK2 are cytoplasmic tyrosine kinases that mediate intracellular signaling of many cytokines and growth factors. Filgotinib (GLPG0634, GS-6034) is a JAK inhibitor with high selectivity for JAK1 over other JAK family members. Filgotinib has a favorable safety and efficacy profile in two Phase 2B studies in active rheumatoid arthritis (RA) patients who were methotrexate (MTX) inadequate responders.

Objectives: To assess the effect of filgotinib on a background of MTX treatment on markers of inflammation in RA patients.

Methods: Serum samples from RA patients who were on a stable dose of MTX and received either placebo (PBO), filgotinib 100mg or 200mg once daily (QD), were collected at baseline, week 4 and week 12 and analyzed for 35 soluble serum biomarkers by validated single-plex or multiplex immunoassays. Median % changes from baseline for biomarkers are reported. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.

Results: Filgotinib treatment induced a dose-dependent and significant decrease