week 12, and week 24. RNA from these samples was extracted and sequenced on the Illumina HiSeq 2500 platform following globin RNA depletion. Correlations between baseline gene expression and disease measurements were performed using Spearman's rank partial correlation to account for covariates. Differentially expressed genes (DEGs) were identified using voom-limma. Biological pathway analyses were performed on v6.1 of the Molecular Signature Database using single sample gene set enrichment analysis (GSEA) with the focus on immune signaling pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG). A false-discovery rate of 5% was applied for all analyses.

Results: Differential gene expression analyses comparing baseline samples with after-treatment samples revealed rapid onset of transcriptional changes in FIL-treated pts, most notably for the two FIL 200mg arms. Fewer DEGs were observed at all timepoints in PBO+MTX treated patients with a peak number at week 24, an observation consistent with the clinical response kinetics of MTX.[4] Up to 3x as many significant DEGs were observed in the FIL 200mg+MTX arm compared to the FIL 100mg+MTX arm, a finding consistent with the superior clinical efficacy of the FIL 200mg dosage. As with other FIL clinical trial RNA-seq studies and consistent with the selective MoA of FIL, JAK-STAT pathway-induced genes SOCS2 and CISH were significantly downregulated across FIL treatment arms and timepoints, but not for PBO+MTX. RA disease activity-associated genes[2-3] FAM20A and METTL7B were significantly reduced at all timepoints in FIL-treated pts, but only at week 24 in PBO+MTX pts. While no significant changes in KEGG immune signaling pathways were observed in the PBO+MTX arm, a dose-dependent effect on pathway modulation was observed in the FIL arms, including reductions in JAK-STAT, toll-like receptor, chemokine, and RIG-I like receptor signaling.

Conclusion: More rapid and sustained changes of transcriptional activity in the whole blood transcriptional profile of RA pts after FIL treatment were found compared to PBO+MTX. Dose-dependent changes were observed in FIL-treated pts, most notably in the KEGG JAK-STAT signaling pathway. These observations confirm an inhibition of JAK-STAT signaling by FIL and are consistent with the observed clinical efficacy of FIL in these pts.

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SAT0156

EFFECTIVE OF BARICITINIB ON RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE AT 48 WEEKS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD MULTICENTER CLINICAL DATA

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Background: Baricitinib (bari) is an oral Janus kinase 1 (JAK1)/JAK2 selective inhibitor that has demonstrated good efficacy in patients with rheumatoid arthritis (RA) and adequate response to conventional synthetic (cs) DMARDs in some clinical trials [1,2]. We report the efficacy and safety of bari within 24 weeks in real-world clinical data at EULAR2019.

Objectives: To evaluate the radiographic progression of structural joint damage at 48 weeks in Japanese patients with RA in real-world multicenter clinical data.

Methods: We included 53 Japanese patients with RA who showed an inadequate response to csDMARDs or biologic (b) DMARDs. Patients were scheduled to receive a once-daily dose of 4 or 2 mg/day bari as monotherapy or in combination with other csDMARDs. We divided the patients into two groups: those treated with 2 mg/day of bari (2mg-group; n = 27) and those treated with 4 mg/day of bari (4-mg group; n = 26) throughout the observation period. Patients were allowed to decrease their predonisolone and csDMARDs combined with bari treatment if their disease activity improved. First, we evaluated changes in CDAI and HAQ-DI after 48 weeks. Second, we evaluated the change in the van der Heijdge modified total sharp score (ΔmTSS), erosion score (ΔERN), and joint space narrowing score (ΔJSN). In addition, we assessed predictors for suppression of joint destruction at 48 weeks after bari treatment.

Results: The baseline characteristics of the patients were as summarized in Table 1. There were no significant differences in any items. CDAI scores significantly improved 4 weeks after the treatment. This tendency continued until the final evaluation (Table 2). At 48 weeks, remission and low disease activity rates were 37.0% and 74.1% in the 2-mg group and 38.4% and 76.9% in the 4-mg group, respectively. Structural remission (mTSS ≤ 0.5) was noted in 21 patients (80.8%) and 21 patients (77.8%) in 4-mg group and 2-mg group, respectively (Figure). Mean scores (ΔmTSS, ΔERN, and ΔJSN) of all patients in the 2-mg group and 4-mg groups were (0.26, 0.15, and 0.11), (0.30, 0.17, and 0.13) and (0.23, 0.13, and 0.10), respectively (Figure). There were no significant differences in ΔmTSS scores between the two groups. A matrix metalloproteinase-3 score within the standard value at 12 weeks after the treatment was associated with a predictor for suppression of joint destruction at 48 weeks (logistic regression analysis; odds ratio = 11.6, 95% confidence interval: 1.5–112.4, P = 0.020).

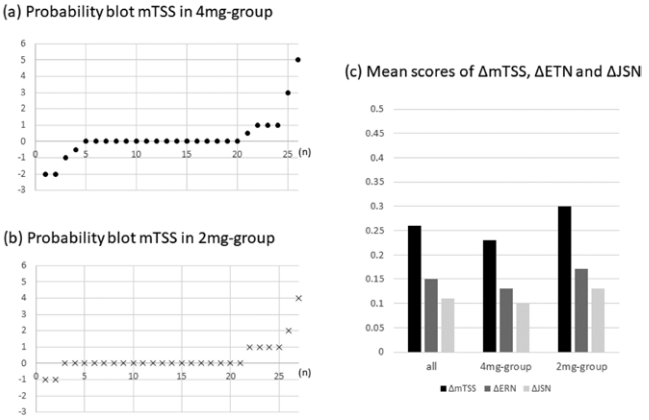
Table 1. Characteristics of patients at baricitinib initiation

	2mg-group (n=27)	4mg-group (n=26)	p-value
Age (years)	69.1 (12.0)	65.6 (10.3)	0.20
Gender, female, n (%)	19 (73.1)	23 (85.2)	0.28
Disease duration (years),	9.7 (10.4)	5.7 (7.4)	0.23
Prior use of biologics, (0/1/2/3)	(18/6/2/1)	(18/2/5/1)	------
MTX (mg/week),	4.5 (3.7)	6.5 (4.29)	0.08
PSL (mg/day)	1.0 (1.9)	1.2 (1.8)	0.49
RF, U/ml	254 (372)	134 (222)	0.21
ACPA, U/m	152 (176)	133 (301)	0.45
MMP-3	196 (220)	215 (221)	0.43

Table 2. Serial change of clinical assessment

2mg-group	Baseline	4 week	12 week	24 week	48 week
CDAI	22.5 (9.2)	7.4 (7.7)	6.7 (6.9)	6.9 (6.8)	6.9 (6.8)
HAQ-DI	0.88 (0.51)	0.45 (0.47)	0.53 (0.58)	0.56 (0.56)	0.56 (0.56)
MMP-3	196 (221)	98.9 (62.2)	115 (164)	106 (78)	106 (78)
4mg-group	Baseline	4 week	12 week	24 week	48 week
CDAI	24.4 (9.7)	9.4 (5.7)	8.6 (6.3)	6.7 (8.6)	6.8 (8.6)
HAQ-DI	1.01 (0.51)	0.58 (0.48)	0.54 (0.60)	0.45 (0.49)	0.44 (0.45)
MMP-3	216 (222)	99 (62)	101 (123)	89 (72)	95 (81)

Figure



Conclusion: The data showed that bari has a favorable effect on the radiographic progression of structural joint damage regardless of its dose in a real-world clinical setting. In consideration of the risk/benefit balance, we suggest that the dose of bari could be reduced in patients with favorable disease activity.

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SAT0157 NINTEDANIB DOSE ADJUSTMENTS AND ADVERSE EVENTS IN PATIENTS WITH PROGRESSIVE AUTOIMMUNE DISEASE-RELATED INTERSTITIAL LUNG DISEASES IN THE INBUILD TRIAL

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Background: In the INBUILD trial in patients with progressive fibrosing ILDs, the adverse event (AE) profile of nintedanib was characterised predominantly by gastrointestinal AEs. Dose adjustments were used to manage AEs.
Objectives: Assess AEs and dose adjustments in patients with autoimmune disease-related ILDs in the INBUILD trial.
Methods: Patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis were randomised to nintedanib 150 mg bid or placebo. Dose reductions to 100 mg bid and treatment interruptions were permitted to manage AEs. AEs over 52 weeks of treatment (or 28 days after last trial drug intake for patients who discontinued drug before week 52) were assessed in patients who received ≥1 dose of trial drug.
Results: Of 663 patients in the INBUILD trial, 170 (82 nintedanib, 88 placebo) had autoimmune disease-related ILDs (89 RA-ILD, 39 SSc-ILD, 19 MCTD-ILD, 23 other autoimmune ILDs). In the nintedanib and placebo groups of patients with autoimmune disease-related ILDs, respectively, over 52 weeks, the proportions of patients with ≥1 dose reduction were 28.0% and 3.4%, with ≥1 treatment interruption were 31.7% and 10.2%, and with ≥1 dose reduction and/or treatment interruption were 40.2% and 12.5% (Table). Dose intensity (amount of drug administered divided by amount that would have been received had 150 mg bid been administered over 52 weeks or until permanent treatment discontinuation) was >90% in 80.5% of patients in the nintedanib group and 95.5% in the placebo group. AEs led to permanent treatment discontinuation in 17.1% and 10.2% of patients treated with nintedanib and placebo, respectively. Diarrhoea was the most common AE, reported in 63.4% and 27.3% of patients in the nintedanib and placebo groups, respectively. Diarrhoea AEs led to dose reduction, treatment interruption and permanent treatment discontinuation in 7.3%, 9.8% and 4.9% of patients in the nintedanib group, compared with 0%, 1.1% and 1.1% of patients in the placebo group, respectively. Of the nintedanib-treated patients who experienced ≥1 diarrhoea AE, 80.8% experienced 1 or 2 events and 76.9% experienced events that were mild at worst (Common Terminology Criteria for Adverse Events [CTCAE] grade 1).
Conclusion: In the INBUILD trial, management of AEs via dose adjustments enabled most patients with autoimmune disease-related ILDs to remain on treatment for 52 weeks. Diarrhoea was the AE that most commonly led to dose adjustment.

Table

	Nintedanib (n=82)	Placebo (n=88)
Patients with ≥1 dose reduction or treatment interruption	33 (40.2)	11 (12.5)
Patients with ≥1 dose reduction	23 (28.0)	3 (3.4)
Total number of dose reductions	25	3
Patients with ≥1 dose re-escalation after dose reduction	5 (6.1)	2 (2.3)
Patients with ≥1 treatment interruption	26 (31.7)	9 (10.2)
Total number of treatment interruptions	32	11
Total duration of treatment interruptions, days, mean (SD)	20.1 (15.1)	19.3 (20.7)

Data are n (%) of patients unless otherwise indicated.

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SAT0158 EFFICACY AND SAFETY OF FILGOTINIB IN METHOTREXATE-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: FINCH 3 52-WEEK RESULTS

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Background: Filgotinib (FIL) is a potent, selective JAK 1 inhibitor. FINCH 3 assessed FIL efficacy and safety in methotrexate (MTX)-naïve patients (pts) with rheumatoid arthritis (RA); week (W)24 primary outcome results were previously presented.[1]
Objectives: To report FINCH 3 (NCT02886728) results through W52.
Methods: This global, phase 3, double-blind, active-controlled study randomised MTX-naïve pts with moderately to severely active RA 2:1:1:2 to oral FIL 200 mg once daily + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg monotherapy (mono) + placebo (PBO), or PBO + MTX up to W52. Comparisons at W52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities.
Results: Of 1249 treated pts, 975 received study drug through W52. FIL efficacy was sustained up to W52. Treatment with FIL + MTX or FIL mono increased proportions of pts achieving ACR20/50/70 and clinical disease remission by DAS28(CRP) <2.6 (FIL 200 mg + MTX, 53%; FIL mono, 46%), CDAI, SDAI, and Boolean criteria; improved HAQ-DI; and halted radiographic progression vs MTX alone (Table 1 and **Figure**). Safety was consistent with W24 data (Table 2).

Table 1. Efficacy outcomes at week 52

	FIL 200 mg + MTX (n = 416)	FIL 100 mg + MTX (n = 207)	FIL 200 mg (n = 210)	MTX (n = 416)
ACR20, %	75.0***	73.4**	74.8***	61.8
ACR50, %	62.3***	59.4**	61.4**	48.3
ACR70, %	47.8***	40.1*	45.2***	29.8
mTSS[a]	0.21***	0.27*	0.23**	0.74
HAQ-DI[b]	−1.00***	−0.97	−0.95*	−0.88

[a]Least-squares mean change from baseline.
[b]Mean change from baseline.
*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.
FIL, filgotinib; mTSS, van der Heijde modified total Sharp score; MTX, methotrexate.