modifying antirheumatic drugs (DMARDs). Primary endpoints were adverse events (AEs) and confirmed laboratory safety data. Secondary endpoints included clinical efficacy measures (American College of Rheumatology [ACR] 20/50/70 response rates, Disease Activity Score using 28 joint counts and erythrocyte sedimentation rate [DAS28-4(ESR)], Health Assessment Questionnaire-Disability Index [HAQ-DI] and clinical disease activity index [CDAI]). Safety data were included up to Month 105 and efficacy data up to Month 90 (n≤100 at Month 96).

Results: A total of 4967 patients were treated (mean [max] duration: 1215 [3182] days). Total tofacitinib exposure was 16,711 patient-years; 77.4% of patients maintained their initial dose. In total, 2370 patients (47.7%) discontinued (AEs: 1131 [22.8%]; insufficient clinical response: 175 [3.5%]). The most common AE classes were infections and infestations (68.9%) and musculoskeletal/connective tissue disorders (39.0%). The most common AEs were nasopharyngitis (18.7%), upper respiratory tract infection (17.2%), bronchitis and urinary tract infection (12.2% each). Serious AEs occurred in 28.6% of patients and serious infection events (SIEs) in 8.8% of patients. Malignancies, excluding non-melanoma skin cancer, were reported in 3.0% of patients. Incidence rates (IR; patients with events per 100 patient-years) for AEs of interest (with 95% confidence intervals [CIs]) and laboratory observations are provided in Table 1. IRs for SIEs and malignancies through Month 105 did not increase compared with reported data through Month 96.1 No new safety risks were identified. Clinical responses were sustained from Month 1 to Month 90 (Table 2).

Table 1. Safety outcomes and laboratory observations in LTE studies (up to 105 months) of tofacitinib in patients with RA

	Tofacitinib (5 and 10 mg BID) ± background DMARDs N=4967
Incidence rates (patients with events per 100 patient-years) for AEs of interest (95% CI)	
SAEs	9.5 (9.0, 10.0)
SIEs	2.6 (2.4, 2.9)
Malignancies (excluding NMSC)	0.9 (0.8, 1.0)
Confirmed laboratory abnormalities, n (%)	
Haemoglobin ≤7 g/dL or decrease in haemoglobin of ≥3 g/dL from BL	97 (2.0)
Neutrophil <0.5 x 10^3/mm^3	0 (0.0)
Lymphocyte <0.5 x 10^3/mm^3	64 (1.3)
ALT ≥3 x ULN	292 (5.9)
AST ≥3 x ULN	167 (3.4)
Increase in serum creatinine of ≥50% from BL	147 (3.0)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BL, baseline; CI, confidence interval; DMARDs, disease-modifying antirheumatic drugs; LTE, long-term extension; NMSC, non-melanoma skin cancer; RA, rheumatoid arthritis; SAEs, serious adverse events; SIEs, serious infection events; ULN, upper limit of normal.

Table 2. Clinical outcomes in LTE studies (up to 90 months) of tofacitinib in patients with RA

	Tofacitinib (5 and 10 mg BID) ± background DMARDs		
	BL	Month 1	Month 90
		N=4907	N=171
ACR20 response rates, %	–	73.0	83.0
ACR50 response rates, %	–	49.2	56.1
ACR70 response rates, %	–	28.9	32.7
	N=4782	N=4776	N=168
DAS28-4(ESR), mean (SE)	6.29 (0.01)	3.75 (0.02)	3.38 (0.09)
	N=4924	N=4880	N=170
HAQ-DI, mean (SE)	1.42 (0.01)	0.82 (0.01)	0.76 (0.05)
		N=4802	N=169
CDAI, mean change from BL (SE)	–	-24.0 (0.20)	-28.5 (1.02)

ACR, American College of Rheumatology criteria; BID, twice daily; BL, baseline; CDAI, clinical disease activity index; DAS28-4(ESR), Disease Activity Score using 28 joint counts and erythrocyte sedimentation rate; DMARDs, disease-modifying antirheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; LTE, long-term extension; RA, rheumatoid arthritis; SE, standard error.

Conclusions: In patients with RA who remained in the LTE studies, tofacitinib (5 or 10 mg BID) with or without background DMARDs was associated with consistent safety through Month 105 and sustained clinical efficacy through Month 90.

References:

[1] Wollenhaupt J et al. Arthritis Rheumatol 2015; 67 (suppl 10): Abstract 1645.

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THU0198 COMPARISON OF EFFICACY BETWEEN COMBINATION THERAPY WITH IGURATIMOD AND SULFASALAZINE WITH METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS

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Background: Iguratimod (IGU) is a small-molecule disease-modifying antirheumatic drug (DMARD) that has been shown to suppress inflammation via the inhibition of nuclear factor-kappa B activation in vitro. The efficacy of combination therapy with IGU and methotrexate (MTX) has been demonstrated in comparison with that of placebo in rheumatoid arthritis (RA). However, its efficacy in comparison with other DMARDs such as sulfasalazine (SSZ) has not been elucidated.

Objectives: To clarify the efficacy of combination therapy with IGU in comparison with that of SSZ with MTX in typical clinical practice.

Methods: We analyzed data from 16,825 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2011 to March 2015 (1). In this study, we compared the two groups who received IGU or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, and IGU or SSZ the year prior to the study period, and those whose regimens were changed to other DMARDs such as tacrolimus and bucillamine. Baseline characteristics were compared using the *t* test, Wilcoxon test, or chi-square test. Fisher analysis was conducted for both outcomes. The predicted probability of IGU treatment was calculated by fitting a logistic regression model using all clinically relevant variables as presented in Table 1. Moreover, to reduce the effect of treatment-selection bias and potential confounding in this observational study, we performed rigorous adjustment for significant differences in the baseline characteristics of patients with propensity-score matching using the following algorithm: 1:1 optimal match with a ±0.15 caliper and no replacement. We used the standardized difference to measure covariate balance, whereby a standardized mean difference of >0.1 represents meaningful imbalance. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of IGU or SSZ therapy.

Results: The group that received IGU in addition to MTX included 66 patients; the other group that received SSZ in addition to MTX included 163 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics. Sixty-five patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 77.2% (44/57 patients) and 71.7% (38/53 patients; P=0.52) in the IGU and SSZ groups, respectively.

Table 1. Patients' Characteristics in Full and Propensity Score-Matched Cohorts according to Initiation of Iguratimod or Sulfasalazine

Characteristic	Full Cohort			Propensity Score-Matched Cohort		
	IGU (n = 66)	SSZ (n = 163)	SMD	IGU (n = 65)	SSZ (n = 65)	SMD
Sex, male (%)	32 (19.6)	11 (16.7)	0.077	13 (20.0)	11 (16.9)	0.079
Age per decade (mean [SD])	5.57 (1.44)	5.70 (1.15)	0.097	5.78 (1.36)	5.66 (3.24)	0.099
MTX (mg/week) (mean [SD])	9.38 (3.38)	9.34 (3.28)	0.01	9.26 (3.51)	9.42 (3.24)	0.048
PSL (mg/day) (mean [SD])	1.72 (2.53)	1.71 (2.53)	0.002	1.51 (2.32)	1.74 (2.54)	0.093
SJC 66 (mean [SD])	2.38 (3.57)	3.03 (3.68)	0.207	3.15 (4.10)	2.97 (3.67)	0.047
TJC 68 (mean [SD])	2.70 (4.61)	2.85 (4.52)	0.033	2.57 (4.91)	2.86 (4.55)	0.062

IGU: iguratimod; MTX: methotrexate; PSL: prednisolone; SD: standard deviation; SJC: swollen joint count; SMD: standardized mean difference; SSZ: sulfasalazine; TJC: tender joint count

Conclusions: Combination therapy with IGU or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity. Further studies are needed.

References:

[1] Matsui T, Kuga Y, Kaneko A, et al. Disease Activity Score 28 (DAS28) using C-reactive protein underestimates disease activity and overestimates EULAR response criteria compared with DAS28 using erythrocyte sedimentation rate in a large observational cohort of rheumatoid arthritis patients in Japan. Ann Rheum Dis. 2007;66(9):1221–6.

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