Yearly progression of mTSS (n = 116)

To investigate prognostic factor for CRRP, clinical data in baseline, 6, 12 months between ten patients with CRRP and 82 patients with structural remission were compared. As shown in Table 1, longer disease duration, more SJC ($P < 0.05$), High CRP level ($P < 0.005$) were prognostic for CRRP in IGU treated patients.

Conclusion: Iguratimod suppressed not only clinical activities but also joint destruction in RA patients resistant to csDMARDs therapy.

Table 1. Prognostic factor for CRRP

	$\Delta mTSS > 3$ (n=10)	$\Delta mTSS \leq 0.5$ (n=82)	P value
Age(yrs)	63.2(12.2)	63.8(11.3)	N.S
Sex(F)	8(80%)	59(72%)	N.S
Disease duration (M)	152.2(28.9)	89.1(88.1)	0.0427*
MTX dose (mg/w)	5.4(1.5)	6.2(4.7)	N.S
PSL dose(mg/d)	2.8(3.2)	2.2(2.2)	N.S
ACPA(U/ml)	210.8(97.5)	212.5(311.3)	N.S
RF(IU/ml)	183.9(137.8)	164.0(285.4)	N.S
MMP3(ng/ml)	183.2(42.5)	165.3(213.1)	N.S
DAS28-ESR	4.6(1.2)	4.3(1.1)	N.S
DAS28-ESR(6M)	3.9(0.4)	3.6(1.2)	N.S
DAS28-ESR(12M)	4.2(1.3)	3.6(1.2)	0.1812
CDAI	17.4(9.5)	16.2(8.5)	N.S
CDAI(6M)	14.3(6.2)	11.5(7.7)	N.S
CDAI(12M)	12.9(7.3)	11.0(9.2)	N.S
mHAQ	0.7(0.6)	0.5(0.6)	N.S
mHAQ(6M)	0.5(0.4)	0.4(0.5)	N.S
mHAQ(12M)	0.4(0.3)	0.4(0.6)	N.S
CRP(mg/dl)	11.6(28.0)	1.5(2.5)	0.0014*
ESR(mm/hr)	44.0(25.6)	30.2(22.5)	0.0743
TJC	2.7(1.7)	4.4(4.7)	N.S
SJC	6.3(4.6)	4.2(2.9)	0.0480*
patient VAS	43.5(8.0)	39.2(25.3)	N.S
mTSS	78.1(87.4)	37.1(67.2)	0.0826
mTSS/y	6.6(5.2)	8.5(13.9)	N.S

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SAT0147

EFFICACY AND SAFETY OF IGURATIMOD AS FIRST-LINE DISEASE-MODIFYING ANTIRHEUMATIC DRUG THERAPY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Although methotrexate is the anchor drug, it took some days to check contraindications, such as interstitial pneumonia, hepatitis B virus infection, and latent tuberculosis infection. Therefore, we sometimes start rheumatoid arthritis (RA) treatment with other disease-modifying antirheumatic drug (DMARD) in daily clinical setting. Iguratimod (IGU) is a newly developed DMARD approved in Japan in September 2012, and the efficacy of IGU for DMARD naïve patients has not been thoroughly evaluated.

Objectives: The aim of this prospective single-center study was to demonstrate the efficacy and safety of IGU when used as a first-line daily DMARD for patients with RA in a clinical setting.

Methods: Enrolled patients included those diagnosed with RA according to the 2010 American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria who took IGU as a first-line DMARD at Niigata Rheumatic Center between April 2016 and December 2018 (IGU group). There were no constraints regarding the addition or withdrawal of other DMARDs. Details of the patients' background, clinical parameters, and laboratory findings were obtained, including C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), matrix metalloproteinase-3 (MMP-3), rheumatoid factor (RF), Disease Activity Score for 28-joint counts based on the erythrocyte sedimentation rate (DAS28-4[ESR]), Clinical Disease Activity Index (CDAI), and Health Assessment Questionnaire Disability Index (HAQ-DI). The efficacy of IGU was evaluated at week 24. The IGU group's data were then compared with 64 patients who took salazosulfapyridine or bucillamine as first-line DMARD in our hospital (other DMARD group). The data were expressed as median values. Comparisons between the parameters were performed using nonparametric method.

Results: Forty-three patients (15 males, 28 females) received IGU as a first-line DMARD for RA. The age was 69.0 years and the duration of disease was 2.0 months. Twenty patients received prednisolone (PSL) concomitantly at a median dose of 5.0 mg/day. At 24 weeks medications were utilized in patients as follows: IGU in 36 (83.7%), methotrexate in 18 (41.2%), PSL in 17 (39.5%), BUC in 10 (23.2%), and biological DMARD in 7 (15.2%) patients. Although 7 patients discontinued taking IGU due to liver enzyme elevation (n=4), nausea (n=1), creatinine elevation (n=1), and skin rash (n=1) during the 24-week period, serious adverse events requiring hospitalization were not observed. Clinical parameters that improved from baseline after 24 weeks of treatment included: ESR from 42.0 mm/h to 16.0 mm/h with $p < 0.001$; CRP from 0.70 mg/dL to 0.10 mg/dL with $p < 0.001$; MMP-3 from 136 ng/mL to 91.5 ng/mL with a p value of 0.11; RF went from 18.0 IU/mL to 8.00 IU/mL with $p < 0.001$; DAS28(4)-ESR dropped from 5.13 to 2.73 with $p < 0.001$; CDAI dropped from 20.0 to 5.00 with $p < 0.001$, and HAQ-DI decreased from 0.55 to 0.00 with $p < 0.001$. Patients who achieved a good or moderate response based on EULAR response at 24 weeks, included 90.7% in the IGU group versus 70.5% in the other DMARD group (Fisher's exact test, $p=0.046$). The retention rate of the IGU group was 81.4%, roughly equivalent to the 81.2% retention rate in the other DMARD group (Log-rank test, $p=0.733$).

Conclusion: Our study indicates IGU is safe and effective for DMARD naïve RA patients. Starting treatment with IGU might be a new and effective strategy for RA patients without previous use of a DMARD.

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SAT0148

TAPERING OF CONVENTIONAL SYNTHETIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN SUSTAINED RHEUMATOID ARTHRITIS REMISSION: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Sustained remission is the goal of rheumatoid arthritis (RA) care, and more patients reach and maintain this state on conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) with treat-to-target strategies. The knowledge about whether csDMARDs can be tapered in RA remission is limited.

Objectives: The primary objective of the study was to assess the effect of tapering of csDMARDs on the risk of flares in RA patients in sustained clinical remission.

Methods: In the open, phase 4, non-inferiority ARCTIC REWIND trial, RA patients in clinical remission for ≥ 12 months on stable csDMARD therapy were randomised to continued stable csDMARD or half dose csDMARD. Patients had to be in DAS remission at inclusion with no swollen joints (of 44). The primary endpoint was the proportion of patients with a disease flare during 12 months (defined as a combination of DAS >1.6 , change in DAS >0.6 and ≥ 2 swollen joints, or the physician and patient agreed that a clinically significant flare had occurred). Patients attended visits every 4 months, with extra visits in case of flares. The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. Mixed effect logistic regression was used to test the inferiority null-hypothesis in the per-protocol population. Radiographs at 0 and 12 months were scored by van der Heijde Sharp score (average score of two readers, progression: ≥ 1 unit change/year). Clinicaltrials.gov NCT01881308.

Results: We enrolled 160 patients, 155 received the allocated treatment strategy. Baseline characteristics were overall well balanced (Table). 78% of patients in the stable csDMARD arm and 84% in the half-dose csDMARD arm used methotrexate monotherapy. In the primary analysis, we observed flares in 6% of patients on stable csDMARD, compared to 25% in the half-dose csDMARD arm, giving a risk difference (95% CI) of 18.3% (7.2% to 29.3%, Fig 1). Non-inferiority could not be claimed, with the results showing superiority of the stable arm over the half-dose arm (Fig 1). Similar results were found in methotrexate monotherapy users. In the stable arm, 2/5 (40%) escalated DMARD medication following the flares, compared to 18/19 (95%) in the tapering arm. No progression of radiographic joint damage was observed in 79.5% of patients on stable DMARDs and 62.7% of those tapering, difference (95% CI) -17.7% (-33.0%, -2.3%, Fig 2E). At 12 months, 92% of patients in the stable and 85% of patients in the tapered arm were in DAS remission (Fig 2C). The frequency of adverse events was 75 in the stable arm and 53 in the tapered arm, with serious adverse events in 2 (2.6%) of patients in the stable and 4 (5.1%, including two serious infections) patients in the tapered arm.

Conclusion: In RA patients in sustained remission on csDMARDs, continued csDMARD therapy with stable dosage led to significantly fewer disease activity flares and less frequent radiographic joint damage progression than tapered csDMARD treatment.

Table. Baseline values; mean (SD), n (%) or median (IQR)

	Stable, n=78	Tapering, n=78
Age, yrs	55 (12)	56 (12)
Female	50 (64%)	54 (69%)
ACPA+	57 (73%)	63 (81%)
Symptom dur., yrs	3.7 (1.8)	3.4 (1.4)
DAS	0.8 (0.4)	0.8 (0.3)
CRP mg/L	2 (1, 3)	2.0 (1, 3)
MTX monotherapy	61 (78%)	65 (84%)

Figure 1: Non-inferiority plot of stable vs half-dose csDMARD treatment in per protocol set, full analysis set and in patients treated by methotrexate monotherapy.
The broken vertical line represents the non-inferiority margin.

Figure 2: Secondary endpoints

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SAT0149

EXPOSURE-RESPONSE RELATIONSHIPS FOR EFFICACY AND SAFETY OF FILGOTINIB AND ITS METABOLITE GS-829845 IN SUBJECTS WITH RHEUMATOID ARTHRITIS BASED ON PHASE 2 AND PHASE 3 STUDIES

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