

Conclusions: Pain is a frequent and relentless suffering during the long-term course of rheumatoid arthritis. In this study, 34% of the patients had unacceptable pain 15 years after diagnosis indicating unsatisfactory treatment. Unacceptable pain also occurred in patients in remission indicating that pain in RA is multifactorial. Therefore, the cause of pain should be identified and treatment initiated accordingly.

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SAT0117 RETENTION RATES OF ADALIMUMAB, ETANERCEPT, AND INFlixIMAB AS 1ST- OR 2ND-LINE BIOTHERAPY FOR RHEUMATOID ARTHRITIS PATIENTS IN DAILY PRACTICE IN AUVERGNE

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Background: The use of anti-tumor necrosis factor-alpha agents, or anti-TNFs, has greatly improved the treatment of rheumatoid arthritis (RA). The first three anti-TNFs available to us (infliximab, adalimumab, and etanercept) are the most widely used in treating RA. Their efficacy and safety, demonstrated in extensive randomized and controlled trials (RCTs), were not shown to vary significantly when compared indirectly based on randomized studies. Nevertheless, the randomized studies were of short duration and included a selected population that differed from patients treated in daily practice.

Objectives: To compare, in real-life conditions, the retention rates of the initial anti-TNF treatment (etanercept [ETN], adalimumab [ADA], and infliximab [IFX]) initiated as first-line biotherapy for rheumatoid arthritis (RA) and to evaluate, in case of failure, the switch to another anti-TNF or a non-anti-TNF biological.

Methods: Monocentric retrospective cohort including all patients with RA starting a first anti-TNF between 2001 and 2015.

Results: Among the 346 patients analyzed, 201 received ETN, 82 ADA, and 63 IFX. The first anti-TNF was interrupted in 151 cases. The retention rates were 82.8%, 67.6%, 46.5%, 28.1%, and 22.5% at 1, 2, 5, 10, and 15 years, respectively, with a median retention duration of 52.8 [18.9–136.2] months (ETN: 59.3 [19.1–NA], ADA: 79.9 [19.3–136.2], and IFX: 37.2 [17.5–134.5], $p=0.49$). The predictive factors of discontinuation were active RA (DAS28-CRP HR: 1.22 [1.03–1.45]), inflammatory syndrome (ESR HR: 1.01 [1.0–1.02]; CRP HR: 1.00 [1.00–1.01]), absence of MTX treatment (HR: 0.60 [0.43–0.83]), and corticosteroid use (HR: 1.91 [1.31–2.78]). The patients who switched to another anti-TNF treatment had an inferior retention than those who switched to a non-anti-TNF treatment (HR: 0.39 [0.17–0.87], $p=0.02$). $p=0.02$.

Conclusions: In real life, there was no difference in retention among the three anti-TNF agents, and 25% of patients continued them at 15 years. After failure of an anti-TNF, the switch to a non-anti-TNF biotherapy showed better retention.

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SAT0118 SAFETY AND EFFICACY OF ALTERNATE-DAY CORTICOSTEROIDS AS ADJUNCTIVE THERAPY IN RHEUMATOID ARTHRITIS

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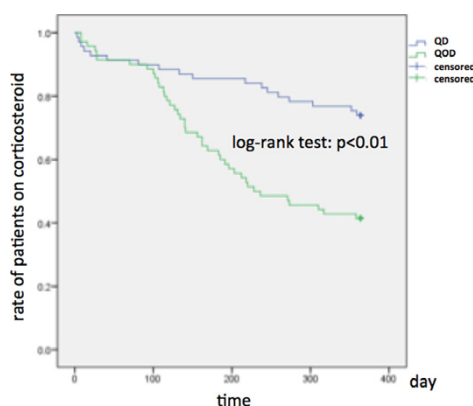
Background: Corticosteroids are often used for treating rheumatoid arthritis. However, minimizing adverse events while maximizing efficacy remains challenging. An alternate-day corticosteroid dose is known to decrease adverse events.

Objectives: To investigate the safety and efficacy of an alternate-day corticosteroid dose for treating rheumatoid arthritis.

Methods: We have conducted a retrospective cohort study among patients over 18-year-old who started oral corticosteroids (prednisolone and methylprednisolone) as treatment of rheumatoid arthritis from 2005 to 2014 at St. Luke's International Hospital, a tertiary-level community teaching hospital in Tokyo, Japan. Patients were included if they met the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for rheumatoid arthritis, and had positive anti-cyclic citrullinated peptide antibody. They were excluded for a history of corticosteroid use for other diseases, or if they were lost to follow-up within 1 year after starting corticosteroids. We divided patients into a daily corticosteroid group (QD) and an alternate-day corticosteroid group (QOD). Patients who received both daily and alternate-day corticosteroids were assigned to the daily group. We investigated the percentage of patients without any infection within 1 year after starting corticosteroids. We have conducted multivariate logistic regression model analysis to calculate adjusted odds ratio for QD/QOD to the outcome. We also investigated the mean decrease in

C-reactive protein (CRP) at 1 month as a marker of short-term effectiveness, and the percentage of patients free from corticosteroid at one year, using student's t-test.

Results: In total, 139 patients were analysed (69 in the QD group, 70 in the QOD group). The maximum dose of corticosteroid in one year was not significantly different in two groups (11.4 ± 7.7 mg/day VS 10.1 ± 5.3 mg/day; $P=0.267$), and the mean daily dose of corticosteroid in one year was significantly higher in the QD group (6.1 ± 4.4 mg/day vs 3.9 ± 1.7 mg/day; $P<0.01$). The percentage of patients without any infection was 49.2% in QD group, and 75.7% in QOD group. Univariate analysis showed QD group is significantly associated with higher incidence of infection ($P=0.001$). After multivariate analysis adjusted with age, gender, initial CRP value, mean daily dose of corticosteroid in one year, use of biologic DMARDs, and duration of rheumatoid arthritis, the odds ratio of QD for any infection in 1 year was 3.9 (95% confidence interval [CI], 1.7–8.8; $P=0.001$). The mean decrease of CRP at 1 month was 1.5 mg/dl in QD group, and 1.1 mg/dl in QOD group ($P=0.435$). The percentage of patients free from corticosteroids at one year was 26.1% in QD group, and 58.6% in QOD group ($P<0.01$). Kaplan-Meier plot showed that QD group patients are more difficult to become free from corticosteroid (log-rank test: $p<0.01$).



Conclusions: Alternate-day corticosteroid dose has a lower adverse event rate and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis.

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SAT0119 PREGNANCY OUTCOMES IN WOMEN WITH AND WITHOUT RHEUMATOID ARTHRITIS

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Background: Prior studies have suggested higher rates of preterm birth in pregnancies to women with rheumatoid arthritis.

Objectives: We sought to identify differences in the pregnancy outcomes of women with and without RA, and pregnancies that occurred prior to and following RA diagnosis.

Methods: A cross-sectional survey was completed by 75 women with RA age-matched to 75 women without RA. Information collected about each prior pregnancy included: pregnancy outcome (spontaneous abortion, stillbirth, elective termination, ectopic pregnancy, or live birth); the timing of delivery; infant anomalies; methotrexate exposure in pregnancy; and whether the pregnancy was planned. Simple statistics were used to compare pregnancy outcomes between women with and without RA and pregnancies prior to and following RA diagnosis.

Results: The majority of women with RA (83%) and controls (64%) were white, and 11% of women with RA and 28% of controls were African American. About half of controls and 31% of women with RA had education beyond college. The average age at the time of the survey was 32 years (SD: 5) in both RA patients and controls, and the average age at RA diagnosis was 23 years (SD: 10). There were 76 pregnancies in 40 women with RA and 99 pregnancies in 33 healthy controls (see table). The overall rates of live birth, spontaneous abortion, and ectopic pregnancies were similar between groups; there were no stillbirths. The rate of elective termination was significantly different, with 9% of RA and 30% of control pregnancies terminated ($p=0.005$). The large majority of the terminations in women with RA occurred prior to diagnosis. The higher frequency of unplanned pregnancy among the controls (38% unplanned RA vs 67% unplanned controls, $p=0.0002$) likely contributed to this higher termination rate. Of unplanned pregnancies, 45% were terminated in controls, 33% in pre-RA pregnancies, and 9% in post-RA pregnancies. No planned pregnancies were terminated. Three pregnancies in women with RA were exposed to methotrexate (2 unplanned, 1 planned) resulting in 2 spontaneous abortions and 1 live birth, born at term without any reported abnormalities.

The rates of preterm birth and infant abnormalities did not differ significantly between those with and without RA, though among women with RA, all preterm births and infant abnormalities occurred after RA diagnosis. Each of the RA preterm births was delivered between 31–34 weeks gestation. Preeclampsia

was more common in women with RA, but did not differ significantly between pregnancies prior to and after RA diagnosis.

A total of 41% of the post-RA pregnancies had an adverse pregnancy outcome (miscarriage, preterm delivery, or infant abnormality), compared to 13% of pre-RA pregnancies ($p=0.01$) and 20% of control pregnancies ($p=0.01$).

	Pregnancies in Healthy Controls	Pregnancies in women with RA	Pregnancies prior to RA	Pregnancies after RA
Number of Pregnancies	99	76	32	44
Live Births	53 (54%)	51 (67%)	20 (63%)	31 (70%)
Spontaneous Abortion	13 (13%)	15 (20%)	4 (13%)	11 (25%)
Ectopic Pregnancies	3 (3%)	3 (4%)	2 (6%)	1 (2%)
Elective Termination	30 (30%)	7 (9%)†	6 (19%)	1 (2%)
Preterm Birth	6/53 (11%)	5/51 (10%)	0	5/31 (16%)
Preeclampsia	1/53 (2%)	9/51 (18%)†	5/20 (25%)	4/31 (13%)
C-section	14/52 (27%)	15/51 (29%)	7/20 (35%)	8/31 (26%)
Abnormal Infant	3/54 (6%)*	3/51 (6%)	0	3/31 (10%)
Adverse Pregnancy Outcome	20 (20%)	22 (29%)	4 (13%)	18 (41%)‡

*one twin pregnancy in controls

† $p<0.05$, controls vs. RA pregnancies

‡ $p<0.05$, pre- vs. post-RA pregnancies

Conclusions: Women with RA, overall, had similar rates of miscarriage, stillbirth, and ectopic pregnancy compared to healthy women, but pregnancies that occurred after RA diagnosis had higher rates of these adverse outcomes. More pregnancies in women with RA were planned, leading to a lower rate of elective termination.

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SAT0120 EVALUATION OF THE RISK OF OVERALL MALIGNANCY AND MALIGNANT LYMPHOMA WITH METHOTREXATE AND BIOLOGICAL AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE IORRA COHORT DURING A 14-YEAR OBSERVATION PERIOD

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Background: While dramatic progress has been made in this decade with treatments for rheumatoid arthritis (RA), such as methotrexate (MTX) and biological agents, concern about the safety, including the occurrence of malignancy, of these highly effective drugs still exists in daily clinical practice. There has not been an evident association between the use of biological agents and the occurrence of malignancy in most reports from clinical trials¹ and observational studies², although MTX use might be associated with the development of malignant lymphoma, called MTX-associated lymphoproliferative disorder³, in patients with RA. In an analysis of risk factors for overall and site-specific malignancies in Japanese patients with RA, higher disease activity was identified to be a risk factor for overall malignancies (hazard ratio [HR] 1.10, 95% CI 1.02–1.19), suggesting that tight control of RA disease activity would reduce the occurrence of malignancies in patients with RA⁴. However, the risk of malignancies with RA treatments including MTX and biological agents was not assessed in that analysis.

Objectives: We investigated the association between the occurrence of malignancies (overall and malignant lymphoma) and drug use (MTX and biological agents) in a large observational cohort of Japanese patients with RA over a long-term period.

Methods: Among Japanese patients with RA enrolled in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort from April 2000 to September 2013, data for all malignancies were extracted from patients' self-reports and confirmed by medical records. Data for malignancies occurring in patients who dropped out of the IORRA study during the subsequent three months were also collected from medical information from affiliated hospitals. We analysed whether MTX and biological agents were risk factors for overall malignancy and malignant lymphoma using a marginal structural Cox proportional hazards model⁵ adjusted for age, gender, smoking history, body mass index, RA disease duration, rheumatoid factor positivity and disease activity (28-joint disease activity score).

Results: Among 11,106 Japanese patients with RA representing 68,483 person-years, 507 overall malignancies, including 68 malignant lymphomas, were confirmed. Neither MTX nor biological agent use was a significant risk factor for overall malignancy, with an HR (95% CI) of 1.18 (0.77–1.81) and 1.01 (0.65–1.57), respectively, or for malignant lymphoma, with an HR (95% CI) of 1.17 (0.55–2.48) and 1.26 (0.43–3.64), respectively.

Conclusions: The use of MTX and biological agents was not significantly associated with the occurrence of overall malignancy or malignant lymphoma during long-term longitudinal observation of Japanese patients with RA.

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Disclosure of Interest: N. Sugimoto Speakers bureau: Takeda Pharmaceutical and Bristol Myers Squibb., E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., E. Inoue: None declared, M. Kawano: None declared, M. Ochiai: None declared, Y. Shimizu: None declared, R. Yamaguchi: None declared, K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.

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SAT0121 COMORBIDITIES AND DISEASE ACTIVITY ARE RELEVANT FOR FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS

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Background: Health status in rheumatoid arthritis (RA), as measured by Health Assessment Questionnaire - Disability Index (HAQ-DI), has been established as a relevant quantitative measure to assess and monitor the disease (1). Current RA therapy has shown improvement in patient-reported outcomes, but more data on specific factors influencing health status are needed (2).

Objectives: To assess the relationship between functional disability and clinical factors in patients with RA, using the HAQ score.

Methods: Cross-sectional study in patients with RA according to the ACR classification criteria from three Brazilian University Hospitals. Demographic and comprehensive clinical data, including components of metabolic profile were collected. Blood pressure, weight and height were determined in the assessment visit and recent laboratory data were assessed from medical records. Disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28) and functional disability was assessed by the HAQ-DI, considering an index >0.5 as disability. All analyses were performed using Stata for MAC 12.0 software. Variables that achieved a p -value <0.3 in the univariate analysis were considered as candidates to take part of a multivariate binomial logistic model, and in this model, variables were considered as statistically significant at the 0.05 significance level (3).

Results: 453 patients were included, 380 (83.9%) women, mean age 55.7 (± 12) years, 356 (79.1%) Caucasian, and mean disease duration of 13.3 (± 9) years. Methotrexate were used by 73.5% of the sample. Mean DAS28 was 3.9 (± 1.4), mean HAQ score was 1.11 (± 0.77), and 23.9% of the patients had HAQ score >0.5. Dyslipidemia, diabetes mellitus (DM), high blood pressure (HBP) and family history of premature cardiovascular disease occurred in 28.6%, 12.8%, 51% and 21.4% of the patients, respectively. Mean body mass index (BMI) was 27.1 (± 4.9) kg/m². In multivariate analysis age, DAS28, tobacco use, and diabetes mellitus were independently associated with HAQ >0.5 (TABLE 1).

Table 1. Association between clinical parameters, disease activity, and functional disability (HAQ >0.5)

Parameters	OR (IC95%)	p
Age	1.01 (1.01;1.03)	<0.001
DAS28	2.74 (1.69;4.45)	<0.001
Tobacco use	1.37 (1.06;1.77)	0.016
Diabetes Mellitus	1.83 (1.82;1.83)	<0.001

DAS28 – disease activity score in 28 joints; BMI – body mass index; OR – odds ratio.

Conclusions: Our results depicted that distinct factors could reflect in the functional status response in RA patients. This is relevant since it may influence the clinically important difference when evaluating the HAQ response in populations with diverse cultural features and different comorbidities prevalence.