Table 1. Outcomes at 12 months among patients with RA who initiated the first biologic

	Moderate-RA (n=264)	Severe-RA (n=219)	P-Value
Remission, n (%)	111 (50)	45 (23)	<0.0001
Low disease activity, n (%)	151 (59)	74 (35)	<0.0001
Change in DAS from baseline ≥ 1.2 , n (%)	168 (66)	164 (78)	0.0049
HAQ-DI change >0.22 , n (%)	98 (53)	83 (52)	0.7974
Change in DAS28 from baseline, mean (SD)	-1.4 (1.3)	-2.2 (1.5)	<0.0001
Change in HAQ-DI from baseline, mean (SD)	-0.29 (0.57)	-0.30 (0.66)	<0.0001
Change in fatigue from baseline, mean (SD)	-0.98 (3.2)	-1.11 (3.2)	<0.0001
Change in sleep from baseline, mean (SD)	-0.85 (3.6)	-1.05 (3.9)	0.0004

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POS0450

INCIDENCE RATES OF DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE

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Background: A definition of difficult-to-treat rheumatoid arthritis (D2T RA) was recently proposed by the European League Against Rheumatism (EULAR) [1]. However, information on the incidence rates of D2T RA in real-world clinical practice is lacking.

Objectives: The aim of this retrospective cross-sectional study was to evaluate the incidence rates of D2T RA in clinical practice in Japan.

Methods: Data from the Toyohashi RA database (TRAD) was used. The TRAD is a collection of single-center retrospective data. Patients with RA who fulfilled the following three requirements were included in this study: (1) had been treated with >1 biological or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD); (2) >1 year had passed since b/tsDMARD treatment was initiated; and (3) regularly visited our institute at the time of investigation. The number of targeted patients was 363. The criteria of D2T RA used in this study were modified from the EULAR definition for simplification of the investigation as follows: (a) ≥ 2 b/tsDMARDs with different mechanisms of action had been administered; (b) at least moderate disease activity (DAS28-ESR > 3.2 or clinical disease activity index [CDAI] > 10) at the time of investigation; and (c) 7.5-mg/day of prednisolone (PSL) or more was administered at the time of investigation. In this study, D2T RA was defined as criteria (a) + (b) or (a) + (c) or (a) + (b) + (c). The 363 patients were categorized into four groups as follows: group A, D2T RA; group B, patients with RA who had been treated with ≥ 2 b/tsDMARDs and did not fulfill the D2T RA definition; group C, RA patients who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., two kinds of tumor necrosis factor inhibitors) and fulfilled either or both criteria (b) and (c); and group D, patients with RA who had been treated with one kind of b/tsDMARD with the same mechanism of action (e.g., a tumor necrosis factor inhibitors or two interleukin 6 inhibitors) and did not fulfill either or both criteria (b) and (c). The incidence rates of D2T RA were calculated, and the patients' characteristics at the time of initiation of the b/tsDMARD treatment were compared between the groups.

Results: The number of patients in groups A, B, C, and D were 34, 53, 94, and 182, respectively. Of all the patients included in this study, 9.4% were categorized into group A, those with D2T RA, and 39.1% were treated with ≥ 2 b/tsDMARDs and categorized into group A (Fig 1). The patients' characteristics were as follows (group A/B/C/D): mean age (57.1/54.3/61.4/56.2 years), RA duration (10.0/6.7/13.8/8.2 years), %Steinbrocker stage III+IV (%; 84.0/60.0/77.3/54.3), %Steinbrocker class 3+4 (%; 68.0/33.3/43.4/23.0), methotrexate (MTX) concomitant rate (%; 79.4/92.5/74.5/91.8), PSL concomitant rate (%; 91.2/52.8/55.3/43.4), DAS28-ESR score (5.5/5.0/5.5/4.7), and CDAI score (12.3/13.7/22.7/16.9). There were statistically significant differences in RA duration, %stage III+IV, %class 3+4 and PSL concomitant rate between group A and B.

Conclusion: D2T RA occurred in 9.4% of patients treated with b/tsDMARDs. Incidence rate was increased to 39.1% after the treatment with ≥ 2 b/tsDMARDs. The patients with D2T RA tended to be older, have a long RA duration, be treated

without concomitant MTX, be treated with concomitant PSL, and have higher disease activity at the time of starting the b/tsDMARD treatment. The baseline patient characteristics in group C were similar to those in group A. In the future, we suggest that patients with D2T RA be included in group C.

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Figure1. Incidence rate of difficult-to-treat rheumatoid arthritis

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POS0451

SERUM FETUIN-A AND VISFATIN LEVELS IN WOMEN WITH RHEUMATOID ARTHRITIS DEPENDING ON DISEASE ACTIVITY

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Background: In recent years, the systemic effects of a number of cytokines have been actively studied, in particular, fetuin-A is considered a negative protein of the acute phase response, and visfatin, on the contrary, affects the activation of the cytokine cascade and has a pro-inflammatory effect. Taking into account that women suffer from rheumatoid arthritis (RA) more often, we investigated the levels of fetuin-A and visfatin in the blood serum of females in comparison with a group of healthy individuals and depending on the activity of the disease.

Objectives: to study the levels of fetuin-A and visfatin in the blood serum of women suffering from RA, depending on the activity of the disease

Methods: The study included 110 women with RA and 30 apparently healthy individuals. The inclusion criteria were: a diagnosis of RA verified based on the criteria of the American College of Rheumatology/European Anti-Rheumatic League (ACR/EULAR) 2010. The patients' age ranged from 18 to 90 years. The control group included 30 conventionally healthy individuals. Serum fetuin-A and visfatin levels were determined by indirect enzyme-linked immunosorbent assay using commercial kits. RA activity was determined by the DAS28-CRP index. Activity 0-I was in 33 (30%) patients, grade II in 67 (60.9%), grade III in 10 (9.09%) patients.

Results: The normal level of fetuin-A was calculated using the formula $M \pm 2\sigma$ in the group of conventionally healthy individuals and ranged from 653.55 to 972.19 $\mu\text{g/ml}$. In patients with grade 0-I RA activity according to DAS28, the mean serum fetuin-A level was $843.92 \pm 130.73 \mu\text{g/ml}$, in patients with grade II activity - $742.37 \pm 98.85 \mu\text{g/ml}$, with III the degree of activity - $663.9 \pm 123.7 \mu\text{g/ml}$ ($p < 0.001$).

The average level of visfatin in the blood serum in healthy individuals was $2.43 \pm 0.17 \text{ ng/ml}$. The level of normal values of visfatin in healthy individuals, defined as $M \pm 2\sigma$, ranged from 0 to 5.07 ng/ml . The average level of visfatin in patients with RA was $6.27 \pm 0.18 \text{ ng/ml}$, which is significantly higher than in healthy individuals ($p < 0.001$).

In patients with 0-I degree of RA activity according to DAS28, the average level of visfatin in blood serum was $4.94 \pm 0.02 \text{ ng/ml}$, in patients with degree II activity - $5.08 \pm 0.02 \text{ ng/ml}$, with III degree of activity - $6.82 \pm 0.23 \text{ ng/ml}$ ($p < 0.001$).

Conclusion: Thus, the level of fetuin-A in the blood serum of patients with RA is significantly lower in the case of a high degree of disease activity. The level of visfatin in the blood serum in women with RA is significantly higher in patients with a higher degree of disease activity. Therefore, the concentration values of fetuin-A and visfatin in the blood serum of patients with RA can be used in an integrated assessment of the prognosis of disease activity.

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POS0452

SYNOVIAL MYELOID-STROMAL PATHOTYPE PREDICTS ONE-YEAR RADIOGRAPHIC PROGRESSION IN ACTIVE RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a heterogeneous disease with variable prognosis. The cellular composition in synovium is the driving force of joint destruction in RA, and the predictive values of histopathological assessments on the clinical outcomes of RA have been identified. However, current synovial histopathological assessments mainly focus on the infiltrated immunocytes to distinguish RA synovium into different synovial pathotypes. Whether addition of stromal cells improve the accuracy of histopathological assessments remains unknown.

Objectives: To distinguish synovial pathotypes of RA based on intercellular connection and explore their predictive value on one-year radiographic progression.

Methods: Active RA patients who underwent needle synovial biopsy at baseline were recruited from a real-world prospective cohort. Clinical data were evaluated at baseline and 1, 3, 6, 12 months. Histopathologic assessments included Krenn synovitis score and semiquantitative score of immunohistochemical staining for CD20, CD38, CD4, CD8, CD68, CD31 and CD90. Cluster analysis was used to distinguish synovial pathotypes. The primary outcome was one-year radiographic progression defined as a change in total Sharp/van der Heijde modified score ≥ 0.5 units.

Results: 1. Among 134 RA patients who received synovial biopsy at baseline and finished one-year follow-up, 105 had qualified synovial tissue. The mean age was 50.2 ± 13.3 years with 77.1% female. The median disease duration was 24 (9-120) months. All patients were active RA, and 64.8%, 26.7% and 8.6% patients in high, moderate and low disease activity, respectively. There were 41 (39%) patients who have never been treated with corticosteroids or disease-modifying anti-rheumatic drugs.

2. During one-year follow-up, there were 48.6%, 63.8%, 71.4%, and 69.5% patients achieved CDAI LDA target, and 12.4%, 30.5%, 34.3%, and 32.4% patients achieved CDAI remission after 1, 3, 6, and 12 months, respectively. A total of 33 (31.4%) patients had radiographic progression.

3. All patients were divided into three clusters using cluster analysis based on the seven synovial cellular scores. Patients in cluster 1 ($n=50$, 47.6%) had higher scores of sublining CD68+ macrophages, CD31+ endothelial cells and CD90+ fibroblasts, thus named as myeloid-stromal pathotype. Patients in cluster 2 ($n=26$, 24.8%) had higher scores of CD20+ B cells, CD38+ plasma cells, CD4+ T cells and CD8+ T cells, thus named as lymphoid pathotype. Patients in cluster 3 ($n=29$, 27.6%) had lower scores of all seven cell types, thus named as pauci-cellular pathotype (Figure 1).

4. RA patients with baseline synovial myeloid-stromal pathotype showed higher rate of one-year radiographic progression versus lymphoid and pauci-cellular pathotypes (48% vs. 16.4%, $P<0.001$), whereas there was no difference between lymphoid and pauci-cellular pathotypes (11.5% vs. 20.7, $P=0.475$). Adjusted for confounding factors including age, sex, smoking, disease duration, RF status, ACPA status, CDAI, HAQ-DI and mTSS at baseline, multivariate logistic regression analysis showed that baseline synovial myeloid-stromal pathotype independently predicted one-year radiographic progression ($AOR=3.602$, 95%CI:1.257-10.324, $P=0.017$, Table 1).

Conclusion: Baseline synovial myeloid-stromal pathotype in RA can predict one-year radiographic progression.

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Figure 1 Representative HE staining and immunohistochemistry of three synovial pathotypes

POS0453

VALIDATION OF THE SIMPLIFIED DISEASE ACTIVITY INDEX (SDAI) WITH A QUICK QUANTITATIVE C-REACTIVE PROTEIN ASSAY (SDAI-Q) IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONAL, MULTICENTER STUDY

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Background: Therapeutic decisions in RA patients should be based on regular disease activity assessment using scores like the Simplified Disease Activity Index (SDAI) or the Clinical Disease Activity Index (CDAI) [1]. The CDAI has the benefit of being immediately available, while the SDAI encompasses with the C-reactive protein (CRP) an acute phase reactant and therefore is the recommended score for the use in clinical trials. However, CRP determination takes hours to days, thus hindering the treat-to-target concept using the SDAI. Quick quantitative CRP (qCRP) tests allow CRP measurement within a few minutes. Therefore, qCRP based SDAI (SDAI-Q) could combine the advantages of both scores.

Objectives: To validate the SDAI-Q in a prospective, multicenter study of RA patients.

Methods: The study was conducted in five centers in Berlin, Germany. Consecutive adult (≥ 18 years) RA patients were included. In addition to a rheumatological assessment, including patient reported outcomes, routine CRP was measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument“ (Aidian Oy, Finland) was performed locally (measurement range 0.5 - 200 mg/l). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen's kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for CRP, qCRP, SDAI, SDAI-Q and CDAI.

Results: In this study 100 RA patients were included (mean age: 60.9 years, mean disease duration: 11.4 years, 73.0% were female, 63.0% RF positive, 57.0% ACPA positive, 49.0% positive and 29% negative for both parameters). 75.0% patients were treated with csDMARD, 15% with tsDMARDs, 39.0% with bDMARDs and 40% with glucocorticoids (mean prednisolone equivalent: 5.4 mg prednisolone/d). Mean CRP and qCRP-levels were 6.97 and 7.89 mg/l, respectively (ICC 0.992; 95%CI: 0.987; 0.995). Comparing SDAI-Q and SDAI, all patients (100%) achieved the same disease activity status (Table 1A); weighted Cohen's kappa was 1.000 (95%CI: 1.000; 1.000). ICC for SDAI-Q- and SDAI-values was 1.000 (95%CI: 1.000; 1.000). The agreement of SDAI-Q and SDAI is shown in a Bland-Altman plot (Figure 1). When comparing the CDAI with the SDAI-Q 93 patients (93%) were assigned to the same disease activity category (Table 1B); weighted Cohen's kappa was 0.929 (95%CI: 0.878; 0.981). ICC for numerical values of SDAI-Q and CDAI was 0.989 (95%CI: 0.978; 0.994).

Conclusion: SDAI-Q showed an absolute agreement with SDAI on the assignment to disease activity categories with the important advantage of time. With SDAI-Q, rheumatologists could base their clinical decision-making immediately on an index-based disease activity measurement by using a composite score considering acute phase reactants. Consequently, SDAI-Q can be integrated in clinical routine and clinical trials and could be implemented into the treat-to-target concept in RA patients.

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