Analysis of Chronological Changes in Japanese Version of Health Assessment Questionnaire Score and Factors Associated with J-HAQ Remission at 5 Years After Disease Onset in Patients with Rheumatoid Arthritis Using the IORRA Cohort

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Background: Recent advances in rheumatoid arthritis (RA) treatment including the introduction of biologics have greatly affected treatment strategies for RA, achieving remission as a realistic treatment target. However, several reports have been concerned about changes in long-term physical dysfunction among large numbers of RA patients in daily practice.

Objectives: To evaluate chronological changes in Japanese version of Health Assessment Questionnaire score (J-HAQ) score and J-HAQ remission rates at 5 years after RA onset using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort.

Methods: RA patients who developed RA between 2000 and 2010 and who first visited our hospital during the year of RA onset were divided into two groups: 1) former onset group (RA onset between 2000 and 2005) and 2) recent onset group (RA onset between 2006 and 2010). J-HAQ scores and J-HAQ remission rates at baseline and at 5 years after onset were investigated for each group, and factors associated with J-HAQ remission after 5 years were assessed by logistic regression analysis. Methotrexate (MTX), corticosteroid (steroid) and biologic DMARDs user (bDMARDs) was defined as the patients if they were used each medication during the observation period.

Results: The former onset group and recent onset group included 357 and 291 RA patients, respectively. For the former onset group, the average J-HAQ score/J-HAQ remission rate at baseline and 5 years after the onset were 0.659/54.6% and 0.430/71.4%, respectively. The recent onset group showed significant improvements relative to the former onset group in J-HAQ score/J-HAQ remission rates at baseline and 5 years after onset were 0.705/52.2% and 0.316/78.4%, respectively (p=0.011/0.044). The percentage of MTX and bDMARDs users was significantly higher in the recent onset group (former vs. recent onset group: MTX: 70.9% vs. 86.6% [p<0.0001]; bDMARDs: 5.3% vs. 23.0% [p<0.0001]). Significant factors associated with achieving J-HAQ remission at 5 years after RA onset were: patients in the recent onset group (p<0.001), male (p<0.001), younger (p<0.001), lower J-HAQ score (<0.001) at baseline, and non-steroid user (p<0.001).

Conclusion: In daily practice, J-HAQ scores for RA patients remarkably improved with recent advances in RA treatment strategies. To achieve J-HAQ remission at 5 years of RA onset, beginning treatment in the early disease stage is needed to prevent deterioration of J-HAQ and treatments that avoid steroid use appear to be important.

Disclosure of Interests: None declared, Eiichi Tanaka Speakers bureau: Bristol-Meyers Squibb, Chugai, Teijin Pharma, Bristol-Myers Squibb, Princeton, United States of America; Brigham and Women’s Hospital, Boston, United States of America; Mu Sigma, Bangalore, India

Evaluation of Rheumatoid Arthritis Treatments and Joint Outcomes in Rheumatoid Arthritis-Associated Interstitial Lung Disease

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Background: RA-associated interstitial lung disease (RA-ILD) is an extrathoracic manifestation of RA and is one of the leading causes of death in patients (pts) with RA. Previous studies have indicated that clinical factors such as age, sex, smoking and autoantibody positivity are strongly associated with RA-ILD. There is also evidence of active RA being related to increased risk for clinically apparent ILD. However, there are limited data on how pts with RA-ILD are managed for their joint conditions and joint outcomes.

Objectives: To evaluate RA treatment patterns in pts with subclinical and clinical RA-ILD compared with pts with RA without ILD, and to assess joint disease activity at baseline and change in disease activity by treatment in all cohorts.

Methods: Data from adult pts with RA enrolled in a longitudinal sequen-tial RA registry were analysed. Pts in the registry were evaluated annually by a rheumatologist for disease activity and treatment, and semi-annually on multiple clinical patient-reported outcomes (PROs) and resource utilisation parameters. Pts with chest computed tomography (CT) scans performed to evaluate clinical indications for ILD and with blood samples were included in this analysis. Pts with chest CT scans that were indeterminate for ILD were excluded from the study. Pts were then divided into two mutually exclusive groups: non-ILD RA pts and RA-ILD pts. RA-ILD pts were further divided into subclinical and clinically evident ILD. Rate of chest CT scan was considered the index date. The two cohorts were compared using descriptive statistics to summarise baseline differences in demographics, disease activity measures, serostatus and treatments. Kruskal–Wallis test for continuous variables and chi-square test for categorical variables were performed, with two-sided significance level of 0.05. Multivariable linear regression was used to evaluate change from baseline to 12 months in joint disease activity for pts with available data at baseline and follow-up.

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References:


Results: 75 pts with chest CT scans were included in the analysis. Of these, 38.7% (n=29) were non-ILD RA and 61.3% (n=46) had some manifestation of RA-ILD. Of the RA-ILD cohort, 63.0% (n=29) and 37.0% (n=17) were classified as subclinical and clinically evident RA-ILD, respectively. At the time of chest CT scan, RA-ILD (vs non-ILD RA) pts were older with longer disease duration, a greater proportion were male and had higher anti-citrullinated protein antibody and RF titres (Table 1). In terms of RA treatments, a significantly greater proportion of RA-ILD (vs non-ILD RA) pts were on corticosteroids (CS; 47.8% vs 20.7%) and a significantly greater proportion of clinically evident RA-ILD (vs non-ILD RA) were on non-TNF inhibitor (TNFi) biologics. RA-ILD (vs non-ILD RA) pts had numerically higher joint disease activity and modified HAQ score at baseline (Table 1). However, the change in joint disease activity and PROs in RA-ILD pts was numerically greater vs non-ILD RA pts. In a multivariable analysis, RA-ILD status did not impact change in joint disease activity, but baseline joint disease activity was significantly associated with reduced joint disease activity at 12 months (Table 2).

Conclusion: RA-ILD pts compared with non-ILD RA pts in clinical practice are more likely to be managed with CS therapy and non-TNFi bDMARDs. The improvement in joint disease activity was similar between RA-ILD and non-ILD RA pts. The analysis was limited by small sample size; further studies with larger patient numbers are required to confirm the findings.

Table 2. Multivariable analysis of change in disease activity (CDAI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.8</td>
<td>(−12.5, 14.0)</td>
</tr>
<tr>
<td>No ILD (vs ILD)</td>
<td>−3.9</td>
<td>(−12.8, 5.1)</td>
</tr>
<tr>
<td>RA duration, years</td>
<td>−0.1</td>
<td>(−0.5, 0.3)</td>
</tr>
<tr>
<td>Baseline CDAI score*</td>
<td>0.4</td>
<td>(0.0, 0.7)</td>
</tr>
<tr>
<td>No CS (vs CS)</td>
<td>−3.6</td>
<td>(−13.5, 6.2)</td>
</tr>
<tr>
<td>*p&lt;0.05 vs no ILD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CS=coronary/cortisone, ILD=intestinal lung disease</td>
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</tbody>
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REFERENCES


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SAT0074

DAS-28 DISEASE ACTIVITY DEFINES THE TNFR1/2 CO-EXPRESSION PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: TNF-alpha acts as main proinflammatory cytokine in rheumatoid arthritis (RA) immune processes. However, TNF-alpha activity and functions may be regulate not only by soluble receptors (which act as decoys) but also by number, density, and co-expression of its membrane-bound receptors type 1 and 2 (TNFR1 and TNFR2).

Objectives: To analyze the TNFR1/2 co-expression profile in RA patient with different disease activity in comparison to healthy donors (HD).

Methods: PBMC were analyzed from 64 HD and 64 patients with RA using flow cytometry. Patients were divided according to the DAS-28 index into groups with high (n=22, 34.4%), moderate (n=30, 46.9%) and low (n=12, 18.8%) disease activity. Co-expression of TNFR1/2 was evaluated as percentage of cell with different receptors. Number of receptors of each type per cell was counted using QuantiBrite PE beads (BD, USA). The following populations were analyzed: total monocyte pool; common pool of B lymphocytes; common pool of T lymphocytes; cytotoxic T cells (CD8+); T helper cells (CD4+), activated (CD25+) cells among CD8+ and CD4+, T memory (CD45RO+) and naïve T cells


SAT0073

STAT3/STAT5 BALANCE AS A BIOMARKER IN RA: CTLA4-IG AND T CELL DIFFERENTIATION THROUGH STAT SIGNALING

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Background: Regulatory T cells (Treg) play suppressive functions and are modulated by Abatacept (CTLA4-Ig). The aim of the study was to analyze if STAT3/STAT5 expression ratio in CD4+ T cells at baseline identify RA patients better responding to CTLA4-Ig, which decreases Treg cells.

Methods: Early RA (ERA) and long-standing RA (LS-RA) patients with conventional DMARDs insufficient response were enrolled in this observational, monocentric, non-randomized, no profit study, and treated with CTLA4-Ig in combination with methotrexate. Each enrolled RA patients underwent peripheral blood sampling and CD4+ cells isolation using magnetic micro-beads at baseline and after 6-12 months follow-up. Flow cytometric analysis (FACS) for CD4 positive cells phenotype was performed to T-regulatory cells (Treg) as CD4+CD25+CD127- and CD4+CD25+/Foxp3+, respectively. STAT3/STAT5 gene expression on CD4+ cells was performed by RT-PCR for each enrolled patient at every time-point follow-up. Low disease activity (LDA) and disease remission (DAS) achievement were assessed at 6 and 12 months follow-up (FU), respectively.

Results: A total of 35 patients were enrolled in the study (16 ERA and 19 LS-RA, respectively). Treg, baseline, ERA vs LS-RA did not differ based on clinical parameters. Eight (22.9%) withdrew from the study because of treatment failure (n=6), severe infection (n=1) and death (n=1). LDA or DAS remission within twelve months follow-up were achieved in 28/34 (82.4%) and 16/34 (47.1%) patients, respectively, without any significant difference among ERA and LS-RA. There were no significant differences in the demographic and clinical characteristics of RA patients at study based on LDA or DAS remission status achievement within 12 months FU, even stratifying patients based on disease duration. FACS analysis showed CD4+CD25+CD127- and CD4+CD25+/Foxp3- cells decrease during CTLA4-Ig treatment (p<0.01) and p<0.02, respectively after 12 months FU), despite disease duration. RT-PCR revealed that PB CD4+ cells of RA patients achieving LDA, but not DAS remission after CTLA4-Ig treatment have significantly lower endogenous expression of STAT3 and STAT5 compared to RA patients not achieving this outcome (p<0.03 and p<0.001, respectively). Moreover, baseline STAT3/STAT5 ratio in PB CD4+ cells of RA patients directly correlates with Treg cells percentages (CD4+CD25+CD127- cells (%): R=0.518, p=0.03; CD4+CD25+/Foxp3+ cells (%): R=0.549, p=0.02, respectively).

Finally, baseline CD4+STAT5 expression ratio on CD4+ cells > 0.93 (obtained by ROC analysis: AUC=0.75<+0.100; Sensitivity 75.0%, Specificity: 80.0%) arose as baseline predictor factor of LDA achievement in RA patients treated with CTLA4-Ig [OR(95% CI): 12.0 (1.98-72.89)].

Conclusion: STAT3/STAT5 expression ratio in T cells at baseline identify RA patients with better responding to CTLA4-Ig, which decreases Treg cells.

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