AB0486 SUBCUTANEOUS METHOTREXATE DISCONTINUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Gridneva, Y. Muraviev. Federal State Budgetary Institution «Research Institute of Rheumatology» under the Russian Academy of Medical Sciences, Moscow, Russian Federation

Background: Safety of methotrexate (MT) therapy remains the most important issue of early rheumatoid arthritis (RA) therapy.

Objectives: A prospective evaluation of most common causes of MT discontinuation in RA patients with disease duration <3 years.

Methods: An open 1 year study included 106 patients with active RA meeting ACR/EULAR 2010 or ACR 1987 (DAS28 >3.2) criteria, naïve to subcutaneous (SC) MT. All pts were administered SC MT, starting with 10–15 mg/week dose, and following 5 mg up-titration each 1–2 weeks (to max 30 mg/week) until achieving the target (remission or minimum disease activity) or emergence of adverse reactions (AR). Pts' monthly monitoring procedures included physical examination, blood analysis and biochemistry panel. T. Woodworth et al. inventory was used to assess the severity of ARs, and Naranjo scale was used to assess casual relationship of MT with an AR.

Results: Totally 12 (11%) MT discontinuations for the period of >3 weeks were analysed. Permanent discontinuation occurred in 9 pts (8%), and temporary (from 4 weeks to 4 months)—in 3 (3%). 83% of all cases of withdrawal took place during the first 3 months. In 3 patients MT was discontinued because of an AR and inefficiency. Combination of drug failure with AR was the reason for permanent SC MT discontinuation in 3 pts.

The causes led to SC MT discontinuation were: skin reactions in 3 pts (25%), "after-dose reactions"—in 2 (17%), allergic rash—in 2 (17%), diarrhoea—in 2 (17%), elevated liver enzymes—in 3 (25%), leukopenia—in 1 (8%), breast abscess—in 1 (8%). Some patients manifested multiple ARs. Two ARs (17%) were serious (grade 4 severity). Grade 3 ARs were documented in 4 cases (30%), Grade 2 ARs—in 4, and Grade 1 (mild) ARs—in 2 (17%) pts.

Skin lesions became the underlying cause for SC MT discontinuation, such as active dermatitis (n=1) and lichenoid skin reaction (n=1).

Totally 12 (11%) MT discontinuations for the period of >3 weeks were analysed. Permanent discontinuation occurred in 9 pts (8%), and temporary (from 4 weeks to 4 months)—in 3 (3%). 83% of all cases of withdrawal took place during the first 3 months. In 3 patients MT was discontinued because of an AR and inefficiency. Combination of drug failure with AR was the reason for permanent SC MT discontinuation in 3 pts. The causes led to SC MT discontinuation were: skin reactions in 3 pts (25%), "after-dose reactions"—in 2 (17%), allergic rash—in 2 (17%), diarrhoea—in 2 (17%), elevated liver enzymes—in 3 (25%), leukopenia—in 1 (8%), breast abscess—in 1 (8%). Some patients manifested multiple ARs. Two ARs (17%) were serious (grade 4 severity). Grade 3 ARs were documented in 4 cases (30%), Grade 2 ARs—in 4, and Grade 1 (mild) ARs—in 2 (17%) pts. Skin lesions became the underlying cause for SC MT discontinuation, such as active dermatitis (n=1) and lichenoid skin reaction (n=1).

Conclusions: Skin reactions were the most common cause for SC MT discontinuation. Therapeutic failure as the leading cause for drug discontinuation was not documented in a single patient.

REFERENCES:

- [1] Standardizing assessment and reporting of adverse effects in rheumatology clinical trials II: the Rheumatology Common Toxicity Criteria v.2.0.
- [2] Thasia Woodworth, Daniel E Furst, Rieke Alten, Clifton Bingham, David Yocum, Victor Sloan, Wayne Tsuji, Randall Stevens, James Fries, James Witter, Kent Johnson, Marissa Lassere, Peter Brooks. The Journal of Rheumatology Jun 2007;34(6):1401–1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1483

AB0487 MULTICENTER 24-WEEK STUDY TO ASSESS THE EFFICACY AND SAFETY OF TACROLIMUS IN ACTIVE RHEUMATOID ARTHRITIS PATIENTS

J. Hur¹, S. Hong², S. Kim³, G. Kim⁴, S. Choi⁵. ¹Internal medicine, Eulji university college of medicine; ²Internal medicine, Kyunghee university school of medicine, Seoul; ³Internal medicine, Ulsan university college of medicine, Ulsan; ⁴Internal medicine, Kosin university college of medicine, Busan; ⁵Internal medicine, Korea university college of medicine, Ansan, Korea, Republic of Ireland

Background: Rheumatoid arthritis (RA) is characterised by persistent synovitis and structural joint damage with T cell-driven inflammation. Tacrolimus suppress activation of T cells through the inhibition of calcineurin.

Objectives: We evaluated the efficacy and safety of tacrolimus in Korean active RA patient who had inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including Methotrexate (MTX).

Methods: During the study period from Aug. 2012 to Jan. 2016 in this open labelled, multicenter study, 115 patients were enrolled with DAS28 ≥3.2. Patients received tacrolimus during 24 weeks. The initial dose was 1 mg once daily and was increased to 3 mg by every 4 weeks. The disease activity and safety was assessed.

Results: Data from 97 patients were evaluated in full set analysis. At week-24, EULAR response rate were 83.5% (81 of 97) with improvements from week-16 in 74.2% (72 of 97). Mean DAS28-ESR was continuously decreased of 5.64 at baseline, 4.14 (±1.22, p<0.001) at week-16 and 3.66 (±1.39, p<0.001) at week-24. Efficacy rates according to SDAI were 89.7% (87 of 97) and KHAQ-20 score decreased -2.42 (±4.37, p<0.001) from baseline 7.27 (±4.59) at week-24. Mean ESR was decreased -10.97 (±24.16, p<0.001) at week-16, -14.77 (±24.57, p<0.001) at week-24 from baseline 46.05 (±23.22). Mean CRP was decreased from 2.86 (±7.85, p=0.0578) at baseline to 1.34 (±3.02, p=0.0367) at week-24. In serious adverse events (6 of 108, 5.56%), two cases (pneumonia, high glucose level) were related with tacrolimus and recovered with treatment.

Conclusions: This study demonstrated the efficacy of add on tacrolimus therapy to MTX in patients with active RA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5094

AB0488 DISEASE ACTIVITY AT ONE YEAR AFTER ADDITION OF IGURATIMOD OR SULFASALAZINE TO METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS

K. Tokunaga¹, A. Shiraiishi², H. Oshikawa¹, N. Hagino³, S. Tohma⁴. ¹Department of Rheumatology, JAPANESE RED CROSS KUMAMOTO HOSPITAL, Kumamoto-City Higashi-ku; ²Emergency Department, Kameda Medical Center; ³Department of Rheumatology, Teikyo University Chiba Medical Center, Chiba; ⁴Department of Rheumatology, Tokyo National Hospital, National Health Organization, Tokyo, Japan

Background: Igruratimod (IGU) is a small-molecule disease-modifying anti-rheumatic 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 assess the disease activity at one year after addition of IGU in comparison with SSZ to MTX in typical clinical practice.

Methods: We analysed data from 16,988 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2012 to March 2017.¹ 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 ±0.2 calliper and no replacement. We used the standardised difference to measure covariate balance, whereby a standardised 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 113 patients; the other group that received SSZ in addition to MTX included 244 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics.

One hundred and nine patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 45.0% (49/109 patients) and 54.1% (59/109 patients; p=0.22), and drug retention rate was 79.8% (87/109 patients) and 78.9% (86/109 patients; p=1.00), in the IGU and SSZ groups, respectively.