escalated to the maximum tolerated dose (16 - 30 mg/week) and tapering MTX can be considered after a persistent remission¹⁾. Renal impairment is one of the major concerns in treatment with high dose MTX for malignancy, but it is still unclear whether low dose MTX administration in RA cause the renal impairment or not.

Objectives: The purpose of this study is to elucidate the association between MTX dosage and a one-year change of estimate glomerular filtration rate (eGFR) in RA patients.

Methods: Of outpatients with RA in Okayama university hospital between 2006 and 2017, 497 patients who had continued the administration of MTX for more than one year were enrolled. All patients fulfilled the ACR/EULAR 2010 Classification Criteria for RA. Patients who had nephrotic syndrome, unilateral kidney or other rheumatic disorders other than secondary Sjögren's syndrome were excluded. The primary outcome was the change of eGFR during the most recent one year in each patient. The revised Japanese equation of Modification of Diet in Renal Disease²⁾ was used to calculate eGFR. MTX dosage was defined as an average dosage of MTX during the observational period. We evaluated the association between MTX dosage and the primary outcome using univariate and multivariate analysis.

Results: Median (IQR) age was 64 (54 - 72) years, 78% were female, and median disease duration was 73 (31 - 160) months. The median dosage of MTX was 8 mg/week (6 - 10.1) and biological agents were used in 28% of the patients. The eGFR (mean $\pm$ SD) decreased by 1.2 ± 8.3 ml/min/1.73m² in one year and MTX dosage was associated with the change of eGFR significant inversely ($p < 0.0001$). The eGFR in patients treated with MTX < 8 mg/week ($n=185$), ≥ 8 and < 10 ($n=131$), ≥ 10 and < 12 ($n=86$), ≥ 12 ($n=95$) decreased 0.2 ± 0.6 , 0.6 ± 0.7 , 1.0 ± 0.9 , and 4.6 ± 0.8 ml/min/1.73m²/year, respectively. After adjusting possible confounding factors such as sex, age, concomitant use of NSAIDs, hypertension, and C reactive protein (CRP) using multiple linear regression analysis, MTX dosage was still an independent risk factor for the decrease of eGFR (beta-coefficient: -0.4, 95% confidence interval -0.12 - -0.61, $p=0.003$).

Conclusion: Careful monitoring of renal function should be required in long-time treatment for RA patients with MTX.

REFERENCES:

- [1] Smolen JS, et al. *Ann Rheum Dis*. 2017;76:960-977.
- [2] Imai E, et al. *Am J Kidney Dis*. 2007;50:927-937.

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THU0176

COMPARISON OF ADHERENCE TO MONOTHERAPY VERSUS COMBINED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Treatment adherence in Rheumatoid Arthritis (RA) patients vary from 30 to 80% (1). It is important to identify the associated factors to a low adherence, so clinicians can make interventions to obtain better therapeutic results. Adherence to treatment has been described to be affected by several factors, such as access to healthcare facilities, education, socioeconomic status, quality of communication between physician and patient, among others (2). There are no previous studies that investigate if the number of drugs received in RA patients affects this adherence. REPAIR[®] is a program designed with the purpose of improve data collection and medical practice in our outpatient clinic.

Objectives: To compare the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) among RA patients prescribed with monotherapy and combined therapy.

Methods: Cross sectional, observational, comparative study. This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, México. Consecutive patients with RA, were approached

during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs (self-report). We classified the adherence rate in 2 categories based on the days of the last month they took the indicated medication; adequate: 75%-100% (> 21 days), inadequate $< 75\%$ (< 21 days). When adherence was inadequate we interrogated about the cause. Data was obtained from REPAIR[®] (internal electronic patient record). The Kolmogorov Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number and percentage (%), and numerical variables as median and the 25th-75th percentiles (q25-q75). Chi square and Mann Whitney U test were used to compare groups and considered significant if $p < 0.05$. Data was analyzed with the statistical package SPSS version 24 (New York, USA).

Results: A total of 959 patients were included. When comparing adherence to treatment and gender between groups, no statistically significant difference was found. The main cause of inadequate adherence in the monotherapy group was the economic (30.3%) and own decision in the combined therapy group (29.1%).

Table 1:

	Monotherapy (n=346)	Combined therapy (n=613)	p
Age (years), median (q25-q75)	54 (44-63)	53 (43-59)	0.018
Women, n (%)	317 (91.6)	575 (93.8)	0.362
Inadequate adherence to treatment, n (%)	52 (15)	102 (16.6)	0.514
Adequate adherence to treatment, n (%)	294 (85)	511 (83.4)	

Conclusion: Patients with combined therapy had the same percentage of inadequate adherence as patients with monotherapy. These results may indicate that number of drugs prescribed not necessarily affects adherence to treatment. The principal causes for an inadequate adherence to treatment were: economic for monotherapy group and own decision for combined therapy group. However, long-term studies are needed to evaluate the persistence of treatment in these groups of patients.

REFERENCES:

- [1] Van den Bemt BJF, Zwicker HE, van den Ende CHM. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. *Expert Rev Clin Immunol*. 2012;8(4):337-51.
- [2] M.F. M. Improving treatment adherence in patients with rheumatoid arthritis: What are the options? *Int J Clin Rheumatol* [Internet]. 2015;10(5):345-56.

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THU0177

TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH A BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG OR JAK INHIBITOR: A NATION-WIDE STUDY IN KOREA

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Background: Limited data are available on whether patients with rheumatoid arthritis (RA) are treated with conventional disease-modifying antirheumatic drugs (cDMARDs) according to the current recommendations before they initiate biologic DMARDs (bDMARDs) or JAK inhibitors (JAKis).

Objectives: We examined the treatment patterns among Korean RA patients who received bDMARDs or JAKis in a real world setting, using the 2002-2016 Korean National Health Insurance Service database that covers the entire Korean population.

Methods: We identified RA patients who initiated bDMARDs (TNF inhibitor, abatacept, rituximab and tocilizumab) or JAKis (tofacitinib). Their treatment patterns during 1 year after RA diagnosis (defined as free of any RA diagnosis or any DMARD use for one year before the diagnosis) and prior to the initiation of index drugs (bDMARDs or JAKis) were examined regarding: initial cDMARD used, dose and parenteral use of methotrexate (MTX), use and time to combination therapy of cDMARDs, and steroid use.

Results: 10,145 RA patients were identified who used index drugs from the database (mean age 57 years, 82% female). Among them, 6,986 patients had identifiable dates for RA diagnosis (mean age 57 years, 79% female). The mean (SD) duration from RA diagnosis to index drug initiation was 1,425 (1,162) days with 1,509 (22%) patients having a duration ≤ 1 year. At diagnosis, the most common 1st cDMARD used was hydroxychloroquine (63%), followed by MTX (55%) and sulfasalazine (29%) with steroids used in 75%. During the 1 year from the diagnosis, 85% of patients eventually used MTX, 42% ever used MTX ≥ 15 mg/week, only 3% used parenteral MTX, and 85% patients used combined cDMARDs with a mean 188 days from the RA diagnosis to combination therapy. Patients whose maximal MTX dose reached 20mg/week were rare (9%) and 62% were still on steroid after 1 year.

During the 1 year prior to the index drug use ($n = 10,145$), the most common cDMARD was MTX used in 89% patients with 46% who ever used ≥ 15 mg/week and 4% of parenteral users, followed by hydroxychloroquine (55%), leflunomide (52%), sulfasalazine (38%), and tacrolimus (20%). All patients used combination therapy and 98% steroids.

Conclusion: These data indicate that a substantial proportion of RA patient did not try maximal dose or parenteral use of MTX during the 1 year post-diagnosis as recommended by the current treatment guideline. Instead, they often used cDMARDs combination therapy. During the 1 year before initiating bDMARDs or JAKis, they were treated with intensive cDMARD combination therapy rather than escalating their MTX dose.

REFERENCE:

- [1] Smolen, Josef S., et al. "EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update." *Annals of the rheumatic diseases* 76.6 (2017): 960-977.

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THU0178

THE EFFECT OF TOLEROGENIC DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SMALL PILOT TRIAL

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Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through the presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, utilization of tolerogenic DCs seems to be a promising immunotherapeutic tool to treat RA.

Objectives: The aim of our study is to evaluate the safety and tolerability of a single intra-articular injection (into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN- α /GM-CSF and tolerized with Dexamethasone in RA patients.

Methods: DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN- α in the presence dexamethasone, applied on third day. Azoximer bromides maturation stimuli was added on fourth day. Twelve RA patients with moderate and high disease activity and ultrasound-defined kneesynovitis were recruited in this study. All patients fulfilled ACR/EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine or their combination. The patients received intra-articular injections of 1×10^6 , 3×10^6 , 5×10^6 , 8×10^6 , 10×10^6 DCs in knee joints. Safety was assessed by evaluation of adverse events (AE). Acceptability was assessed by questionnaire. DAS28 and HAQ were used for assessment of treatment efficiency. This trial registered on clinicaltrials.gov (ID: NCT03337165).

Results: DCs injections were safe and well tolerated. No one participants showed worsening of symptoms in targeting knee, fever, elevation of blood pressure or other AE within 7 days after injection. All patients,

evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR > 1.2). The median DAS28-ESR decreased from 5.1 to 3.1 ($p=0.03$). The median pain VAS score decreased from 52 (41-70) mm to 42 (15-55) mm; $p=0.04$. In addition, we detected median HAQ improvement (from 1.45 to 1.0; $p=0.04$). The effect of treatment had been continued for 6 months and after that we indicated escape of effect.

Conclusion: The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and have a potential not long term efficiency and requires the repeating of procedure.

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THU0179

PATIENT AND THEIR ILLNESS – ATYPICAL SOURCES OF THERAPY RISKS. CHARACTERISTICS OF THE USE OF METHOTREXATE (MTX) AND FOLIC ACID (FA) SUPPLEMENTATION IN THERAPY LASTING MINIMUM 8 WEEKS IN ADULT PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: MTX is a well-established treatment with an anchor role in RA (1). Patients being treated for RA must pay attention to the specific dosage of drugs and the different routes of administration. Additionally they suffer from the inconvenience related to the progression of the disease.

Objectives: We observed patients diagnosed with RA, who were treated with subcutaneous (SC) MTX and possible risks associated with this therapy. The attention paid to the inconvenience for the patient associated with SC form of drug administration and the principles of MTX dosing with FA supplementation.

Methods: 32 rheumatologists were invited to non-interventional, post marketing observation. They collected information from 690 patients who already received a minimum of 1 dose of MTX SC. As part of a standard medical visit, the sociographic data of the patient and information obtained during the medical interview as well as subjective and objective examination were recorded in the prepared form. Data was collected on a weekly basis over a period of 8 weeks. The protocol was compliant with the regulatory and ethical requirements in the country.

Results: Out of 682 enrolled patients, 581 (85.2%) were sero-positive and 95 (14%) were sero-negative. The average level of anti-CCP antibodies before enrollment was 85.76 Units. The mean time from the diagnosis of the underlying disease was 28.7 months. The vast majority of patients confirmed that they had previously used FA supplementation (92.2%), only 10 patients showed DAS28 at the remission level. During each visit no adverse events (AE) were reported in over 90% of patients. The most commonly reported AE are nausea or weakness. No severe, life threatening AE were recorded.

Patients evaluated the pain of the injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Most patients assessed the pain of injections as the minimum (1) (56.5% - week 1 (W1), 52.9% - W2, 56.7% - W3, 61.5% - W4, 56.7% - W5, 53.8% - W6, 65.2% - W7, 61.8% - W8). The second most frequently mentioned pain assessment by respondents was 2 (34.6% - W1, 35.3% - W2, 34.3% - W3, 29.2% - W4, 34.3% - W5, 38.5% - W6, 26.1% - W7, 32.9% - W8). No patients reported values between 6 and 10. Patients also assessed how the pain at the site of injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Each week, more than half of the patients assessed pain at the injection site as 1 (55.9% - W1, 56.7% - W2, 56.7% - W3, 57.8% - W4, 50.8% - W5, 62.5% - W6, 60.3% - W7, 61.6% - W8). Patients did not report any value of 5-10. More than seven out of ten patients reported FA administration the day 2 of their therapy (76.5%, at W1). In remaining days FA supportive therapy reported 30.3-52.3% of patients (2).

Conclusion: Neither pain related with injection nor local AE was reported as a significant issue by patients. Adherence to FA administration recommendation is low. This should be evaluated in further studies, but there is a risk that inappropriate FA administration may reduce efficacy of MTX treatment.

REFERENCE:

- [1] Smolen JS, et al. *Ann Rheum Dis* 2017;0:1–18; 2. Todoerti M, et al., *Reumatismo*. 2013 Dec 18;65(5):207-18.