Table 1. Key endpoints at week 12.

	DAS28(CRP) ^a (mean change from BL to week 12)	ACR20/50/70 ^b (% achieving at week 12)	HAQ-DI ^b (mean change from BL to week 12)
PBO	-1.36 (1.044)	40.9/22.7/13.6	-0.39 (0.389)
GS-9876 10 mg	-0.78 (1.119)	25.0/20.0/15.0	-0.18 (0.800)
GS-9876 30 mg	-1.26 (1.276)	35.0/20.0/5.0	-0.46 (0.480)
FIL 200 mg	-2.46 (1.242); *p=0.002	81.0/47.6/38.1	-0.70 (0.649)

^aPrimary endpoint; ^bSecondary endpoint; *p (compared to PBO).

Conclusion: Clinical efficacy of GS-9876 in RA was not observed, but GS-9876 was safe and well-tolerated over a 12-week period in patients with RA on MTX. FIL showed favorable safety and clinical efficacy consistent with prior data, validating the study concept and design. Additionally, biomarker changes with GS-9876 support the continuation of studies in lupus-related diseases.

REFERENCES:

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FRI0151

THE RELATIONSHIP BETWEEN THE EFFECTIVENESS OF METHOTREXATE (MTX) IN RHEUMATOID ARTHRITIS (RA) AND MTX POLYGLUTAMATES LEVELS (MTXPGS) IN RED BLOOD CELLS BY TANDEM CHROMATOMASS SPECTROMETRY (PILOT STUDY)

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Background: Therapeutic control of the level of MTXPGs in erythrocytes may be an objective marker of its effective dose in RA treatment.

Objectives: To evaluate the relationship between the level of MTXPGs in erythrocytes and the effectiveness of the dose of MT used by RA patients.

Methods: The study included 60 random selected RA patients over the age of 18, 16 men and 44 women. The diagnosis in all cases met the criteria of ACR/EULAR 2010. All pts received MTX at a constant dose of at least 20 mg per week subcutaneously for at least the last 12 weeks. Patients were divided into 2 groups depending on the presence (group 1, n = 30) or absence (group 2, n = 30) of the therapeutic effect of MTX, according to the criteria of the EULAR response to therapy. The groups were comparable in age, sex, alcohol intake, smoking, body mass index (BMI), ACP positivity, incidence of unwanted reactions to MTX, single dose of MTX, duration of MTX treatment course. The groups differed in duration of the disease at the beginning of the current course of continuous therapy: 5.5 [2.0, 12.0] months in group 1 and 12.0 [3.0, 60.0] months in group 2; in group 2 patients received glucocorticoids (GK) orally 17 (57%) against 9 (30%) in group 1. Blood sampling was performed no later than 36 hours after the last administration of methotrexate. From each patient 2 ml of hemolysed blood were examined using an Agilent 6410 chromatograph (Agilent Technologies) - a quantitative measurement of methotrexate polyglutamate by liquid chromatography-spectrometry.

Results: It was established that the levels of total MTXPG and MTXPG1,2,3,5 in erythrocytes did not depend on the effectiveness of MTX, the dose of which was comparable in all patients. At the same time, the level of MTXPG4 was significantly higher (p = 0.023) in patients of group 1 (26.4 ± 6.1 nmol/l) compared with patients in group 2 (22.1 ± 6.8 nmol/l). Evaluation of the ROC curve showed that MTXPG4 values below 22.5 nmol/l corresponded to the absence of the therapeutic effect of MTX. The area under the curve was 0.672, (CI 95 0.536-0.808); p = 0.022. Sensitivity - 77%, specificity - 53.3%.

Conclusion: For effective treatment of RA patients, it is necessary to administer such doses of MTX so that the achieved level of MTXPG4 in erythrocytes is not less than 22.5 nmol/l.

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FRI0152

METHOTREXATE TREATMENT PATTERNS IN ADVANCED THERAPY-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS IN THE CORRONA REGISTRY

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Background: Methotrexate (MTX) is one of the most commonly used drugs in the treatment of rheumatoid arthritis (RA). Some patients may discontinue MTX therapy due to lack of efficacy or intolerance and may or may not restart MTX. There is a need to better understand the patterns of MTX use, the characteristics of these patients, and how the patterns of use are related to outcomes.

Objectives: To assess patterns of MTX use in a clinical practice setting, describe baseline demographic and clinical characteristics for groups defined by patterns of MTX use, and assess the association of patterns of MTX use with clinical outcomes and side effects during the 2 years after MTX initiation.

Methods: This observational study included patients from the US Corrona RA registry who initiated MTX from 01 October 2001 to 31 October 2018, were biologic/targeted synthetic disease-modifying antirheumatic drug (bDMARD/tsDMARD)-naïve and did not start bDMARD/tsDMARD through 2 years of follow-up. Patients were divided into 3 cohorts: those who discontinued and restarted MTX, those who discontinued without restarting MTX and those who persisted on MTX. Descriptive statistics were used to evaluate patient demographics and disease activity at MTX initiation and side effects during follow-up. Changes in clinical outcomes from baseline to 2 years were calculated for all groups. Differences in outcomes were assessed using Kruskal-Wallis one-way analysis of variance for continuous or ordinal-dependent variables and chi-square test for categorical variables.

Results: Among 785 MTX initiators, 34 (4.3%) discontinued/restarted MTX, 174 (22.2%) discontinued MTX, and 577 (73.5%) persisted on MTX within the 2-year follow-up period. Overall, mean age was 59.7 years; 72.7% were female; mean duration of RA was 4.8 years; and 52.9% were conventional synthetic DMARD-naïve. Generally, in patients who discontinued/restarted, discontinued, or persisted on MTX, those who discontinued/restarted therapy had more comorbidities at MTX initiation: hypertension (35.3%, 32.8%, or 29.3%, respectively), malignancy (14.7%, 9.2%, or 8.7%, respectively), chronic obstructive pulmonary disease (10.0%, 3.9%, 1.9%, respectively), or asthma (5.0%, 4.7%, or 2.9%, respectively). At end of follow-up, mean Clinical Disease Activity Index (CDAI) was 15.6, 10.1, and 8.8 for those who discontinued/restarted, discontinued, and persisted, respectively. Disease activity according to CDAI improved during the 2-year follow-up for all 3 groups, but less improvement was observed in those who discontinued/restarted MTX (Table). Overall, the most common side effects while on MTX therapy were elevated liver enzymes (65.4%) and fatigue (43.1%). Patients who discontinued/restarted MTX vs those who persisted had higher rates of hair loss (35.3% vs 18.9%), loss of appetite (32.4% vs 17.3%) stomach pain (26.5% vs 14.6%), mouth sores (20.6% vs 16.3%), diarrhoea (11.8% vs 9.5%), and myelosuppression (8.8% vs 2.1%).

Conclusion: More than 26% of patients who initiated MTX therapy either discontinued and did not restart or discontinued and restarted therapy during 2 years of follow-up. Patients who discontinued/restarted MTX therapy had less improvement in disease activity, experienced more side