Prevalence and Predictors of Methotrexate-Associated Adverse Events in Patients with Rheumatoid Arthritis

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Background: Methotrexate (MTX) is the first-choice treatment for rheumatoid arthritis (RA), but the exact prevalence rates and predictors of important adverse events (AEs) associated with MTX treatment are less well investigated.

Objectives: To determine the prevalence of MTX AEs (gastrointestinal (GI), mucocutaneous, neurological, haematological, pulmonary, and liver enzymes elevation), and to identify baseline demographic, clinical and drug related predictors of liver and GI AEs.

Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a UK multicentre prospective cohort study of patients with RA commencing MTX for the first time. Relevant demographic, medical, clinical and disease related data, and blood samples were collected from patients at baseline. Data on MTX therapy and occurrence of AEs were reported at six and twelve month follow-ups, and include recorded laboratory values of alanine transaminase (ALT) enzyme.

The prevalence rates of AEs were calculated based on the number of patients who reported the AE at either 6 or 12 month follow-up visits. The association between candidate baseline predictors and occurrence of GI or liver AEs was assessed using multivariable logistic regression.

Results: In total, 2089 participants were included (mean age=58.4±13.5 years; 1390 (65.5%) women). Of those, 1816 and 1584 completed their visits at 6 and 12 months, respectively.

The frequency of abnormal ALT values (>1xULN) was 10.8% (183/1685) and 1.03 (1.02, 1.04) – 0.53 (0.42, 0.67)

Conclusion: GI events were the most commonly reported AEs among patients with RA in the first year of MTX treatment, followed by neurological, mucocutaneous and pulmonary AEs. Identifying predictors of AEs may help to optimise drug therapy in RA by tailoring the dosing strategy or frequency of monitoring. This may lead to increased adherence and consequently improved effectiveness.
available. In the future, machine learning applications may allow fast and reliable decisions on flare prediction in RA patients. These data can guide decisions about DMARD tapering at in real time during the physician-patient contact and allow to reduce costs not only by selective treatment tapering but also by sparing additional laboratory examinations.

References:

Disclosure of Interests: Asmir Vodencarevic Shareholder of: Siemens Health- care GmbH. Siemens Healthcare GmbH is a medical technology company (NOT a pharmaceutical company)., Employee of: Siemens Healthcare GmbH. Siemens Healthcare GmbH is a medical technology company (NOT a pharmaceutical company)., Employee of: Siemens Healthcare GmbH. Siemens Healthcare GmbH is a medical technology company (NOT a pharmaceutical company)., Fabian Hartmann: None declared, Michaela Reiser: None declared, Sara Bayat Speakers bureau: a pharmaceutical company)., Koray Tascilar: None declared, Fabian Hartmann: None declared, Melanie Hagen: None declared, Axel Novartis, Larissa Valor: None declared, Melanie Hagen: None declared, Axel Hueber Grant/research support from: Novartis, Lilly, Pfizer, Consultant of: Abbvie, BMS, Celgene, Gilead, GSX, Lilly, Novartis, Speakers bureau: Abbvie, BMS, Celgene, Lilly, Novartis, Roche and UCB, David Simon Grant/research support from: Elsei Köner-Memorial Scholarship, Novartis, Consultant of: Novartis, Lilly

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SAT0057 INITIAL PRESENTATION OF RHEUMATOID ARTHRITIS (RA) – IS IT STILL “SYMMETRIC POLYARTHRITIS”? T Sokka-Islér1, K Paalanen1, M Kauppi1, E Nikiphorou2, KSSHP, Jyväskylä, Finland; 2PHHYKY Lahti, Finland; 3King’s College Hosp., London, United Kingdom

Background: RA is traditionally described as a symmetric polyarthritis. The ACR/EULAR 2010 criteria are met if patient has high positive ACPA, symptoms >=6 wks and one small joint swollen. The public and all steps of health care have been informed for many years that RA should be found early.

Objectives: To study variations in patients on first presentation of RA.

Methods: All patients with the new diagnosis of RA were extracted from the GoTreatIT clinical database between 2008 to 2019 at a single RA clinic that covers a population of 250,000. Demographic data, clinical variables, labs, x-rays, joint status and PROs at baseline were included in the analysis. Appropriate parametric/non-parametric tests were used to study differences between groups.

Results: A total of 1044 (73.5% CCP+) patients with no prior diagnosis of RA were included; 683 (66%) female, mean age 56.361 (35%) male, mean age 61. At initial presentation in 2008, 60% had >=6 swollen joints (Figure) and a mean DAS28 of 4.4 compared to 22% and 3.8 respectively, in 2019 (p<0.007). Duration of symptoms prior to diagnosis decreased from 6 to 4 months (p=0.033), and the proportion of patients with erosions from 20% in 2008 to 14% in 2019 (ns). Symptoms (PROs) such as pain, fatigue and global health were similar/slightly worse in 2018 compared to 2008.

Conclusion: RA cannot be marketed as “symmetric polyarthritis” as more than half of the patients have a maximum of 2 swollen joints at the time of the diagnosis at the most recent years. Patients with RA can be identified earlier, with less disease activity and damage, compared to previous years.

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SAT0057 PREDICTING INADEQUATE RESPONSE TO JAK INHIBITORS BY CLUSTER ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS M Sugawara1, Y Fujieda1, A Noguchi2, S Tanimura3, Y Shimizu4, I Nakagawa5, M Kono5, M Kato5, K Oku5, T Atsumi5, 1Graduate School of Medicine and Faculty of Medicine, Hokkaido University, Department of Rheumatology, Endocrinology and Nephrology, Sapporo, Japan; 2Japanese Red Cross Kitami Hospital, Department of Internal Medicine and General Medicine, Kitami, Japan; 3Tomakomai City Hospital, Department of Internal Medicine, Tomakomai, Japan; 4Hokkaido P.W.F.A.C Obihiro-Kosei General Hospital, Third Department of Internal Medicine, Obihiro, Japan; 5Takikawa Municipal Hospital, Department of Internal Medicine, Takikawa, Japan

Background: Oral Janus kinase inhibitors (JAKi) have dramatically altered outcomes in patients with rheumatoid arthritis (RA). However, there remains some proportion of patients who respond to inadequately JAKi treatment (JAKi-IR) [1,2]. The characteristics in RA patients associated with JAKi-IR have not been fully demonstrated.

Objectives: To clarify the characteristics of JAKi-IR in patients with RA by cluster analysis.

Methods: This retrospective study comprised 120 RA patients who were treated with JAKi (Tofacitinib or Baricitinib) between July 2013 and September 2019 in five facilities. The disease status at the baseline, at 12 weeks after JAKi treatment and at the time point of withdrawing JAKi was assessed using the Disease Activity Score (DAS28) and the American College of Rheumatology (ACR) response criteria. JAKi-IR was defined as follows, primary non-response at 12 weeks after JAKi treatment: withdrawal of JAKi with ACR20 non-response or non-improvement in DAS28-CRP (ΔDAS28-ΔCRP<12 from baseline), secondary non-response: withdrawal of JAKi without clinical remission after 12 weeks. Hierarchical cluster analysis was performed with the following variables: gender, age, disease duration, bone erosion, ACR functional classification (Class ≥3), comorbid rheumatoid arthritis related interstitial lung disease (RA-ILD) or other autoimmune disease (AID), anti-citrullinated protein antibody (ACPA) positivity, rheumatoid factor (RF) at baseline, use/dose of methotrexate (MTX) and prednisolone (PSL), serum ESR/CRP, tender/swollen joint counts (TJC/SJC), visual analog scale by patients (VAS-Pt), and prior of biologic DMARDs.

Results: The 120 enrolled patients were classified into 4 groups by cluster analysis (Figure1). The characteristics of each group are as follows, Group A(n=21): female + bone erosion + RF/ACPA positive + AID + MTX non-user, Group B(n=36): male + older age + RA-ILD + RF/ACPA positive + MTX non-user, Group C(n=35): RF/ACPA positive + absence of RA-ILD + MTX user, Group D (n=28): seronegative + MTX user + absence of RA-ILD + history of biologic DMARDs failure. The rate of JAKi-IR was A:9%, B:8%, C:20%, D:32%, and the significant difference between Group B and D was identified (p=0.02). In multiple comparison of 4 groups, no significant difference was identified (p=0.08) (Figure2).

Conclusion: JAKi-IR would be more likely to be seronegative, MTX user, absence of RA-ILD and history of biologic DMARDs failure. Cluster analysis is an exploratory tool that aids in the analysis of huge amount of data.