Lilly & Company, Merck, Roche, Seattle Genetics, UCB, Consultant of: AbbVie, Actelion, Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eicos Sciences, Eli Lilly & Company, Emerald, Gilead Sciences, Inc., Janssen, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, UCB, Speakers bureau: UCB, Carter Thorne Consultant of: Abbvie, Centocor, Janssen, Lilly, Medexus/Medac, Pfizer, Speakers bureau: Medexus/Medac, Diane Tin: None declared, Vivian Bykerk: None declared

DOI: 10.1136/annrheumdis-2020-eular.3415

SAT0054

PREVALENCE AND PREDICTORS OF METHOTREXATE-ASSOCIATED ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Sherbini¹, J. Gwinnutt¹, K. Hyrich¹, S. Verstappen¹ on behalf of RAMS Co-Investigators. ¹The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom

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 multi-centre prospective cohort study of patients with RA commencing MTX for the first time. Relevant demographic, medication, 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 [66.5%] 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 11.6% (170/1461) at 6 and 12 month follow-up visits, and 15.5% (286/1845) for either visits. The number of patients who reported GI AEs was 777 (40.6%) within 1 year of follow-up. The prevalence of mucocutaneous, neurological, haematological and pulmonary AEs were 441 (23.1%), 487 (25.5%), 116 (6.1%), and 406 (21.3%), respectively.

Male sex, having high ALT at baseline and a history of diabetes were all associated with increased risk of ALT elevation during the study period (Table 1). Contrarily men were 47% less likely to report GI AEs compared to women. Furthermore, younger age and higher baseline disease activity score (DAS28-CRP) were associated with increased risk of GI AEs occurrence.

Table 1. Baseline predictors of elevated alanine transaminase (ALT) and gastrointestinal (GI) adverse events

Variable	Elevated ALT	GI adverse events
	Adjusted Odds Ratio (95% CI)	
Age (years)	1.00 (0.99, 1.01)	0.99 (0.98, 1.00)
Male sex	1.39 (1.02, 1.90)	0.53 (0.42, 0.67)
Drink alcohol	1.23 (0.88, 1.73)	1.09 (0.86, 1.37)
Current or past smoking	1.10 (0.80, 1.49)	1.10 (0.88, 1.37)
BMI (kg/m ²)	1.01 (0.98, 1.03)	1.02 (1.00, 1.03)
Symptoms duration (months)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
RF positivity	0.81 (0.60, 1.10)	0.93 (0.75, 1.16)
DAS28-CRP	0.97 (0.87, 1.08)	1.13 (1.04, 1.23)
ALT at baseline (IU)	1.03 (1.02, 1.04)	—
History of diabetes	1.94 (1.22, 3.08)	0.91 (0.62, 1.34)
History of liver disease	1.73 (0.43, 6.95)	—
History of renal disease	1.29 (0.42, 3.96)	1.13 (0.50, 2.52)
MTX starting dose (mg/week)	1.03 (0.98, 1.08)	1.03 (0.99, 1.06)

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.

Disclosure of Interests: Ahmad Sherbini: None declared, James Gwinnutt Grant/research support from: BMS, Kimme Hyrich Grant/research support from: Pfizer, UCB, BMS, Speakers bureau: Abbvie, Suzanne Verstappen Grant/research support from: BMS, Consultant of: Celltrion, Speakers bureau: Pfizer
DOI: 10.1136/annrheumdis-2020-eular.1485

SAT0055

PREDICTION OF FLARES FOR RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC DMARDS USING MACHINE LEARNING AND SUBSETS OF VARIABLES AVAILABLE TO PHYSICIANS, PATIENTS AND PAYERS

A. Vodencarevic¹, K. Tascilar², F. Hartmann², M. Reiser², S. Bayat², J. Knitza², L. Valor², M. Hagen², A. Hueber^{2,3}, A. Kleyer², M. Zimmermann-Rittereiser¹, G. Schett², D. Simon². ¹Digital Health, Siemens Healthcare GmbH, Erlangen, Germany; ²Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany; ³Section Rheumatology, Sozialstiftung Bamberg, Bamberg, Germany

Background: Today approximately 50 percent of patients with RA reach sustained remission. In a specific subset of RA patients in stable remission, biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) may be successfully tapered. However, it remains challenging to predict the patients' individual flare risk. As we have recently shown, machine learning based on extensive clinical and laboratory data could be used to estimate individual flare risk [1].

Objectives: In this study we aimed to investigate the performance of machine learning models trained with variables that are typically (1) immediately available to a physician during patient visits (clinical and demographic variables without laboratory values and composite disease activity scores), (2) theoretically available to patients at home and (3) available to payers in large health-system databases.

Methods: Longitudinal clinical data of RA patients on bDMARDs from the first interim analysis of the phase-3, multicentre, randomised, open, prospective, controlled, parallel-group RETRO study (EudraCT number 2009-015740-42) was used [2] to build a predictive model for estimating the flare probability within 3 months from the current patient visit. A flare was defined as a DAS-28 ESR score over 2.6. Four different models (log. regression, random forest, k-NN and naïve Bayes) were trained which output the flare probability at each patient visit. These probabilities were used as an input for a stacking logistic regression meta-classifier [3]. The final model performance expressed as the AUROC was assessed using nested cross-validation [4]. We applied this method to three variable subsets (physician, patient, payer, Table 1).

Table 1. List of variables used in three subsets:

Variable / Role	Physician	Patient	Payer
Gender (m/f)	x	x	x
Disease duration (years)	x	x	x
Methotrexate co-use (yes/no)	x	x	x
Other DMARDs co-use (yes/no)	x	x	x
Drug ATC code	x	x	x
IV-administration (yes/no)	x	x	x
Dose percentage	x	x	x
Age	x	x	x
Body mass index	x	x	x
Dose percentage change	x	x	x
Swollen joint count	x		
Tender joint count	x		
VAS_GH (pat. global disease activity)	x	x	
HAQ (health assessment questionnaire)	x	x	
Smoking status (yes/no/ex)	x	x	
Alcohol consumption (yes/no)	x	x	
Previous flares (yes/no)	x		

Results: Data from 135 follow-ups of 41 patients were used. The measured AUROC of the best performing model using all RETRO variables was 0.802 (95%CI 0.717 – 0.887) [1]. When a subset based on demographic and clinical variables is used that is available to a physician immediately during a patient visit the AUROC drops about 5 percent points. When only variables theoretically available to patients at home are used, the performance drops about 10 percent points comparing to the original model. Similar observation holds for the variable subset typically available to payers (Figure 1).

Conclusion: This study shows that predictive models for flares have the potential to support physicians in making decisions immediately during the patient visit, even though laboratory values and respective activity scores are not yet

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:

- [1] Vodencarevic A. et al. *Arthritis Rheumatol.* 2019; 71
- [2] Haschka J et al. *Ann Rheum Dis* 2016; 75:45-51.
- [3] Tang J et al. *CRC Press* 2015; 498-500
- [4] Cawley GC et al. *J Mach Learn Res* 2010; 11:2079-2107

Figure 1: AUROC curves for three variable subsets. A: Variables available to a clinician immediately at patient visits, B: Variables available to a patient at home, C: Variables available to a payer.

Disclosure of Interests: Asmir Vodencarevic Shareholder 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)., Koray Tascilar: None declared, Fabian Hartmann: None declared, Michaela Reiser: None declared, Sara Bayat Speakers bureau: Novartis, Johannes Knitz Grant/research support from: Research Grant: Novartis, Larissa Valor: None declared, Melanie Hagen: None declared, Axel Hueber Grant/research support from: Novartis, Lilly, Pfizer, Consultant of: Abbvie, BMS, Celgene, Gilead, GSK, Lilly, Novartis, Speakers bureau: GSK, Lilly, Novartis, Arnd Kleyer Consultant of: Lilly, Gilead, Novartis, Abbvie, Speakers bureau: Novartis, Lilly, Marcus Zimmermann-Ritterer Shareholder 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)., Georg Schett Speakers bureau: Abbvie, BMS, Celgene, Janssen, Eli Lilly, Novartis, Roche and UCB, David Simon Grant/research support from: Else Kröner-Memorial Scholarship, Novartis, Consultant of: Novartis, Lilly

DOI: 10.1136/annrheumdis-2020-eular.1553

SAT0056 INITIAL PRESENTATION OF RHEUMATOID ARTHRITIS (RA) – IS IT STILL “SYMMETRIC POLYARTHRITIS”?

T. Sokka-Isler¹, K. Paalanen¹, M. Kauppi², E. Nikiphorou³. ¹KSSH, Jyväskylä, Finland; ²PHYKY, 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 pattern 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 (65%) 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 2019 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.

Figure:

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2652

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. Kono¹, M. Kato¹, K. Oku¹, T. Atsumi¹. 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 (Δ DAS28-CRP<1.2 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 $\geq$ 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=0.06) (Figure2).

Conclusion: JAKi-IR would be more likely to be seronegative, MTX use, 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.