Background: 2022 EULAR recommendation announced that both biological disease-modifying antirheumatic drugs (bDMARDs) and janus kinase inhibitors (JAKI) are considered in the phase II treatment of rheumatoid arthritis (RA). However, we still lack reliable evidence of direct comparison between these agents regarding effectiveness and safety.

Objective: The aim of this multi-center (7 university-related hospitals) retrospective study is to clarify the factors affecting treatment retention of bDMARDs and JAKI in a real-world setting.

Methods: This study assessed 6,666 treatment courses of bDMARDs and JAKI introduced from 2001 to 2022 (TNF inhibitors [TNFi]-3,577, anti-IL-6 receptor antibody [aIL-6R]-1,497, cytotoxic T lymphocyte-associated anti- gen-4 [CTLA4-Ig]-1,139, JAKI=453; BioJAK naive cases 55.4%, baseline age 58.8 years, female 82.6%, disease duration 9.7 years, DAS28-ESR 4.3; concomitant methotrexate [MTX] 52.8%, other csDMARDs 26.0%, and oral glucocorticoid [GC] 36.4%). Reasons for discontinuation were classified into four categories by each attending physician: 1) lack of effectiveness (primary and secondary), 2) toxic adverse events (infection, malignancies, and cardiovascular events, et al.), 3) non-toxic reasons (patient preference, change in hospital, and pregnancy, et al.), and 4) remission. Remission rates of each discontinuation reason were estimated at 36 months using the Kaplan-Meier method and adjusted for potential clinical confounders (age, sex, concomitant GC, MTX, and other csDMARDs, switched number of bDMARDs or JAKI, and prior use of TNFi, aIL-6R, CTLA4-lg, or JAKI) using Cox proportional hazards modeling.

Results: Adjusted retention rates for each discontinuation reason were as follows: due to lack of effectiveness was aIL-6R=80.9%, JAKI=75.2%, CTLA4-lg=73.6%, and TNFi=66.1% (Cox P<0.001 between 4 groups) (figure 1a), due to toxic adverse events was CTLA4-lg=88.0%, JAKI=86.4%, aIL-6R=84.1%, and TNFi=83.6% (Cox P=0.052) (figure 1b), due to non-toxic reasons was aIL-6R=96.7%, TNFi=85.9%, JAKI=85.9%, and CTLA4-lg=96.7% (Cox P=0.064), and due to remission was JAKI=97.1%, CTLA4-lg=96.7%, aIL-6R=96.9%, and TNFi=94.9% (Cox P=0.18). Compared to TNFi, aIL-6R (hazard ratio [HR]=0.54, 95%CI=0.47–0.61, P<0.001), JAKI (HR=0.69, 95%CI=0.56–0.85, P<0.001), and CTLA4-lg (HR=0.75, 95%CI=0.66–0.86, P<0.001) showed lower discontinuation rate due to lack of effectiveness. Compared to TNFi, CTLA4-lg showed lower discontinuation rate due to toxic adverse events (HR=0.77, 95%CI=0.63–0.93, P=0.008) and remission (HR=0.67, 95%CI=0.46–0.98, P=0.041). Other factors increasing drug discontinuation due to lack of effectiveness was switching number of bDMARDs or JAKI (HR=1.42, 95%CI=1.24–1.63, P<0.001), concomitant GC (HR=1.17, 95%CI=1.06–1.29, P=0.0018), and prior aIL-6R use (HR=1.24, 95%CI=1.05–1.45, P=0.011). On the other hand, higher age (HR=1.01, 95%CI=1.00–1.02, P<0.001) and concomitant GC (HR=1.29, 95%CI=1.07–1.54, P=0.01) increased drug discontinuation due to toxic adverse events.

Conclusion: Adjusted by potential confounders, aIL-6R showed lowest discontinuation due to lack of effectiveness, and CTLA4-lg showed lowest discontinuation due to toxic adverse events. Besides the difference of bDMARDs and JAKI, concomitant GC increased drug discontinuation due to lack of effectiveness and toxic adverse events.

REFERENCES:
Background: Radiographic joint damage progresses in 20-30% of rheumatoid arthritis (RA) patients despite fulfilling clinical remission criteria [1]. Osteitis assessed on MRI predicts subsequent bone damage progression [2]. Therefore, targeting absence of osteitis combined with clinical remission may improve long-term radiographic outcomes.

Objectives: To investigate whether a 2-year MRI treat-to-target (MRT T2T) strategy targeting absence of osteitis combined with clinical remission, compared to a conventional T2T strategy targeting clinical remission only, could reduce radiographic joint damage progression over 5 years in RA patients.

Methods: IMAGINE-more was designed as a three-year observational extension study of the 2-year IMAGINE-RA randomized clinical trial [3]. IMAGINE-RA included 200 RA patients in clinical remission (DAS28-CRP<3.2 and no swollen joints), with erosive disease (bone erosion on conventional radiography), and treated with csDMARDs. The objective was to investigate whether an MRT T2T strategy, targeting absence of osteitis combined with clinical remission (DAS28- CRP<3.2 and no swollen joints) as compared to a conventional T2T strategy, targeting clinical remission only, could improve remission rates and prevent radiographic joint damage progression. If treatment target was not met, treatment was intensified stepwise starting with increment in csDMARDs and subsequently adding biologics. Participants in the IMAGINE-more study were managed in routine clinical practice in outpatient clinics. Clinical examinations and radiographs of hands and feet (also obtained at baseline, year 1 and 2 in IMAGINE-RA) were done year 3, 4 and 5. The primary endpoint was the proportion of patients with no radiographic progression (increase in total van der Heijde-modified Sharp score (vdHSS) ≤0) from baseline to year 5. Secondary endpoints were 0-5 years changes in total vdhss, vdhss erosion and joint space narrowing (JSN) scores. Dichotomous endpoints were estimated by logistic regression, while median differences were calculated for the continuous outcome measures.

Results: Informed consent to participation in IMAGINE-more was obtained from 131 patients (59 from the original MRI T2T group). Of these, 14 patients (24%) in the MRI T2T group and 19 patients (28%) in the conventional T2T group had no radiographic progression from baseline to year 5 (OR 0.70 [0.28 to 1.71]). As illustrated in the Table 1 and Figure 1, the median progression in total vdhss from baseline to 5 years was low, with no differences between treatment groups.

Table 1. Radiographic endpoints at 5 years (change from baseline - year 0)

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>n MRI T2T</th>
<th>n Conventional T2T</th>
<th>Difference</th>
<th>P between groups value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No radiographic progression, 59 14 (24%) 72 19 (26%)</td>
<td>OR 0.70</td>
<td>0.431</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (%)</td>
<td>(0.28 to 1.71)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key secondary endpoint</td>
<td>Change in total vdhss (0-488) 47 1.0 [0.0-3.0] 56 2.0 [0.0-4.0]</td>
<td>0.0 (1.0 to 0.0)</td>
<td>0.515</td>
<td></td>
</tr>
<tr>
<td>Other secondary endpoints</td>
<td>Change in erosion (0-280) 47 1.0 [0.0-2.0] 56 1.0 [0.0-3.0]</td>
<td>0.0 (0.0 to 0.0)</td>
<td>0.967</td>
<td></td>
</tr>
<tr>
<td>Change in JSN (0-168) 47 0.0 [0.0-0.5] 56 0.0 [0.0-1.3]</td>
<td>0.0 (0.0 to 0.0)</td>
<td>0.565</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Group contrasts are presented as No. (%) for dichotomous data and medians [IQR] for continuous data. OR (95%CI) were estimated from logistic regression adjusted for a propensity score.

Conclusion: A 2-year combined MRI T2T and clinical T2T strategy, compared with a conventional clinical T2T strategy alone, did not result in reduced radiographic progression in the long term over 5 years in RA patients with erosive disease in clinical remission.

REFERENCES:

Acknowledgements: NIL

Disclosure of Interests: Signe Møller-Bisgaard Grant/research support from: Study support from Abbvie, Kim Horslev-Petersen: None declared, Lykke Middelholt ørnørgen: None declared, Bo Ejbjerg: None declared, Merete Lund Hetland: None declared, Jakob Mollenbach Møller: None declared, Robin Christensen: None declared, Sabrina Mai Nielsen: None declared, Daniel Gilnats: None declared, Mikael Boesen Shareholder of: Minority shareholder in Image Analysis Group Ltd, London UK, Speakers bureau: Abbvie, Celgene, Eli Lilly, Image Analysis Group, Novartis, Pfizer, UCSB and Esato, Paid instructor for: Novartis and Eli Lilly, Consultant of: Novartis, Grant/research support from: Abbvie, Celgene, Novo Nordisk and Novartis, Kristian Stengaard-Pedersen Consultant of: Pfizer, Abbvie, Grant/research support from: Roche, Pfizer and Medoc., Ole Madsen: None declared, Bente Jensen: None declared, Jan Alexander Villadsen: None declared, Ellen Margrethe Hauge Shareholder of: Novartis, Abbvie, Sanofi, Sobi, Grant/research support from: eareach funding to Aarhus University Hospital from Novo Nordic Foundation, Danish Rheumatism Association, Danish Regions Medicine Grants, Roche, Novartis, Abbvie, Oliver Hendricks Speakers bureau: Pfizer, Lilly, Novartis, Hanne Merete Lindegaard: None declared, Niels Steen Krogh: None declared, Anne Grethe Junk: None declared, Henrik Thomsen: None declared, Mikkel Oestingaard Speakers bureau: Abbvie, BMS, Boehringer-ingelheim, Celgene, Eli-lilly, Galapagos, Gilead, Hospira, Janssen, MEDAC, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi and UCB, Grant/research support from: Abbvie, BMS, Merck, Novartis and UCB.

DOI: 10.1136/annrheumdis-2023-eular.711

PO0053 EARLY DIAGNOSIS, PROMPT INITIATION OF METHOTREXATE AND TREATMENT STEERED-TO-TARGET DO NOT ABROGATE THE RISK OF BEING MULTIDRUG REFRACTORY FOR PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Disease-modifying Drugs (DMARDs), Rheumatoid arthritis, Prognostic factors

B. Donorino1, V. Morandi1, F. Maggiore1, M. Di Lernia1, L. De Stefano1, C. Montecucco1, S. Bugatti1. IRCCS Foundation, Polyclinic San Matteo, Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy

Background: The management of rheumatoid arthritis (RA) has substantially improved during the last few decades; despite that, a significant proportion of patients remain refractory to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), as well as to one or more biological/target-synthetic (b/ts) DMARDs. It is estimated the overall proportion of refractory RA is around 3-17%. Refractory disease has been defined among patients with established, long-standing, RA. However, at present time, it is not known whether early diagnosis, prompt institution of DMARD within the window of opportunity and treatment steered-to-target are efficacious to prevent multidrug failure in patients with new-diagnosed RA.

Objectives: First, to assess if an Early Arthritis Clinic (EAC) background – early diagnosis and treatment within the “window of opportunity”, disease management according to treat-to-target (T2T) strategy – reduces the risk of being DMARDs refractory; secondly, to detect possible predictors of refractoriness in patients escalated to b/tsDMARDs.

Methods: Data were retrieved from a prospective monocentric cohort of 810 patients with early RA (symptoms duration <12 months at inclusion) diagnosed between 2005-2017 and treated with csDMARDs (methotrexate in 90.4% of the cases) according to a T2T strategy in the setting of an EAC. The population of interest included all patients escalated to b/tsDMARDs because of inefficacy/ intolerance to csDMARDs. The frequency and factors associated with failure to first and second b/tsDMARDs were analysed by logistic regression.

Results: A total of 135/816 (16.5%) early RA patients required treatment escalation to a b/tsDMARDs after a median (IQR) of 18.5 (11.39) months from diagnosis; of them, 117 had follow-up visits available for a median (IQR) of 96 (37-122.5) months after treatment initiation. Fifty-six patients (50.4%) failed the first b/tsDMARD after a median (IQR) of 14 (7.3-44.3) months due to inefficacy/side effects. The rates of failure of the second and third b/tsDMARD were 20.5% and 11.7%. Thirteen patients (11.1%) could be defined D2T (failed to first/second b/tsDMARDs) with a median (IQR) number of 2 (2-3) b/tsDMARDs with different mechanisms of action, and 3 (2.8-4) different b/tsDMARDs in general. By logistic regression, significant predictors of first b/tsDMARD failure were disease duration ≤24 months