Mark C. Genovese Grant/research support from: Abbvie, Eli Lilly and Company, EMD Merck Serono, Galapagos, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, Pfizer Inc., RPharm, Sanofi Genzyme, Consultant of: Abbvie, Eli Lilly and Company, EMD Merck Serono, Genentech/Roche, Gilead Sciences, Inc., GSK, Novartis, RPharm, Sanofi Genzyme
DOI: 10.1136/annrheumdis-2020-eular.2237

THU0205

RESPONSE TO SMALL MOLECULES IS MOSTLY DRIVEN BY PATIENT GLOBAL ASSESSMENT OF DISEASE: A REAL WORLD OBSERVATION

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Background: Two Small molecules (Tofacitinib and Baricitinib) have been licensed in the UK for the use in rheumatoid arthritis. Their licensing came from several studies that showed good efficacy with baricitinib (1) study showing superior efficacy to adalimumab and tofacitinib showing non inferiority to TNF drugs (2). The response has also been shown in patient reported outcomes (find reference). Response when measure using the DAS score has two relatively subjective components (tender joints and patient global assessment) and two relatively objective components (Swollen joints and inflammatory markers)

Objectives: To determine in a real world setting if the response to small molecules is mostly due to a drop in subjective or objective components of the DAS score

Methods: A retrospective chart review was done on all new starters on small molecules in a district hospital in the North of England. Data were collected at baseline, three months and six months from October 2018 to date. Drop in the components of the DAS28 score was calculated and overall drop in DAS28 was modelled as the explanatory variable using linear regression modelling. This was the done Adjusting for age gender and duration of disease. Sensitivity of the model was examined using a logistic model of EULAR moderate/good response and using adjusted R squared estimates for linear model of improvement of the DAS28 score.

Results: 76 patients were included in the analysis from 85 starters on small molecules. 61 (71.8 %) were on baricitinib and the baseline median DAS28 score was .5.97 (IQR 5.35,6.55). The median drop at three months in the DAS28 score was 2.42 (IQR 1.33,3.31). and at six months was 2.77 (IQR 2.01,3.83). There was numerical relative increased efficacy of baricitinib but this was not statistically significant (DAS drop at three months 2.54 IQR 1.73,3.09 vs 2.12 IQR 1.51,3.5). The relative contribution of the individual components of the DAS score to the drop in DAS are shown in table 1 below. Sensitivity analysis looking at predictors of a DAS drop of >0.6 confirmed this finding.

Table 1. Results of the adjusted linear regression models.

Component of DAS dropping at three months	Adjusted R squared at 3 months	Adjusted R squared at six months
Swollen Joints	0.12	0.05
Tender Joints	0.28	0.18
Patient global assessment	0.31	0.48
Erythrocyte sedimentation rate	0.04	0.17

Conclusion: In this real world observational study, there was a good response to both small molecules with numerical better response to baricitinib. Tender joint count and patient global response accounted for more of the drop in DAS28 than swollen joints and inflammatory markers. At six months the biggest contributor to response was patient global assessment. This shows that JAK inhibitors might mediate their response initially mostly through pain modulation then by inflammation as exposure to drug continues.

References:

[1] N Engl J Med. 2017 Feb 16;376(7):652-662

[2] N Engl J Med. 2014 Jun 19;370(25):2377-86

Disclosure of Interests: : Clerin Joseph: None declared, Syed Mujtaba Bilgrami Speakers bureau: Pfizer, Lesley Ottewell: None declared, Leanne Gray: None declared, William Mitchell: None declared, Fiona Wood: None declared, Marco Massarotti: None declared, Marwan Bukhari Speakers bureau: Bristol-Myers Squibb, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Menarini, Sanofi-aventis, Eli-Lilly, Janssen, Amgen and Novartis.

DOI: 10.1136/annrheumdis-2020-eular.3118

THU0206

A VERY EARLY (7-28 DAYS) RESPONSE ON JAK INHIBITOR TOFACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: EFFECT ON PAIN AND CENTRAL SENSITIZATION.

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Background: The presence of central sensitization (CS) significantly burdens the course of rheumatoid arthritis (RA). JAK inhibitors block intracellular signal pathways including the ones responsible for synthesis of mediators and cytokines causing pain and CS. The application of JAK inhibitors is supposed to relieve pain and reduce CS severity promptly.

Objectives: To evaluate JAK inhibitor effect on pain and signs of CS in patients with active RA 7 and 28 days after the start of therapy.

Methods: Study group included 39 patients with RA, their age was 50.9±11.1, 79.5% of women, 89.7% of RF "+", DAS28 5.8±0.6, receiving DMARDs (methotrexate 82.0% and leflunomide 18.0%), who were administered with tofacitinib 5mg 2 times a day due to inefficiency or intolerance of genetically engineered biological drugs. There were assessed the pain severity using Brief pain inventory (BPI) questionnaire, the presence of neuropathic pain component (NPC) using PainDETECT questionnaire and signs of CS using Central Sensitisation Inventory (CSI) questionnaire at early time after tofacitinib administration.

Results: Patients initially experienced a severe pain – 5.72±2.21 according to the visual analogue scale (VAS), 53.8% had signs of central sensitization (CSI ≥ 40), 17.9% had NPC (PainDETECT ≥ 18). 7 days after tofacitinib intake there was statistically reliable reduction of pain severity – up to 4.37±2.2 (p=0.01), pain decrease of 29.4±17.9% (BPI), NPC – PainDETECT from 12.9±5.5 to 10.6±5.6 (p=0.047) and CS – CSI from 43.1±12.8 to 35.9±11.2 (p=0.01). The effect had increased after 28 days: pain level (VAS) was 2.84±1.57 (p=0.000), pain decrease of 43.6±29.6% (BPI), PainDETECT 29.8±12.4 (p=0.000), CSI 26.4±13.9 (p=0.000).

During this period there were no serious adverse reactions.

Conclusion: The application of JAK inhibitor tofacitinib allows to reach a fast analgesic effect, also due to impact on CS and NPC.

Source: National Registry patients with RA

Disclosure of Interests: : Andrey Karateev: None declared, Ekaterina Filatova: None declared, Elena Pogozheva: None declared, Vera Amirdzhanova: None declared, Evgeny Nasonov: None declared, Alexander Lila: None declared, V Mazurov: None declared, N Lapkina: None declared, Galina Lukina Speakers bureau: Novartis, Pfizer, UCB, Abbvie, Biocad, MSD, Roche, Tatiana Salnikova: None declared, Ruzana Samigullina: None declared, Diana Chakieva: None declared, Irina Marusenko: None declared, Olga Semagina: None declared, Marina Semchenkova: None declared

DOI: 10.1136/annrheumdis-2020-eular.4029

THU0207

SUSTAINABILITY OF RESPONSE TO UPADACITINIB AS MONOTHERAPY OR IN COMBINATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS

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Background: The primary treatment goal for patients (pts) with rheumatoid arthritis (RA) is a state of sustained clinical remission (REM) or low disease activity (LDA).^{1,2}

Objectives: To assess the long-term sustainability of responses to upadacitinib (UPA), a JAK inhibitor, with or without background csDMARD(s) in pts with RA.

Methods: Data are from two phase 3 randomized, controlled trials of UPA in RA pts with roughly similar baseline disease characteristics: SELECT-NEXT enrolled pts with an inadequate response (IR) to csDMARD(s) on background stable csDMARD(s) receiving UPA 15mg or 30mg once daily or placebo for 12 weeks (wks);