The most prevalent polymorphism (84.6% [IC95%; 84.0%-85.1%]) and in cases (86.0% [IC95%; 79.4%-92.5%]) was homozygous CC (ITPase-c94a); in controls homozygous GG (GGH-T401C) (87.5% [IC95%; 81.5%-93.4%]).

There were no significant differences in the parameters of activity between groups, in both, patients were best basally controlled than at the start of the MTX income and/or bDMARD.

Being homozygous-AA for the DHFR gene was significantly associated (p<0.05) with the appearance of AE (none of the 4 homozygous AA patients for that gene had AE).

In MLR, homozygous GG (ref. heterozygous AG) in polymorphism GGH-T401C, being homozygous CC (ref. heterozygous TC) in polymorphism ABC2-C24T and PCR (mg/dL) at the start of bDMARD resulted independent predictive factors of MTX intolerance.

Conclusion: Polymorphisms T401C for the GGH gene and C24T for the ABC2 gene and PCR at the start of the bDMARD resulted independent predictive factors of MTX intolerance.

Polymorphism homozygous AA for DHFR gene was related to significant protection against appearance of AE.

Disclosure of Interests: Alejandro Escudero Contreras: None declared, Rafaela Ortega Castro: None declared, Jerusalem Calvo Gutierrez: None declared, Natalia Mená-Vázquez: None declared, Rafael Calzó Càlic: None declared, Eduardo Collantes Estevez Grant/research support from: ROCHE and Pfizer, Speakers bureau: ROCHE, Lilly, Bristol and Celgene, Antonio Fernandez-Nebro: None declared, María del Carmen Abalós-Aguilera: None declared, Chary Lopez-Pedrana Grant/research support from: ROCHE and Pfizer., Mª Teresa Ruiz Jimenez Employee of: Roche Farma, SPAIN, Font Ugarte Pilar: None declared.

DOI: 10.1136/annrheumdis-2020-eular.4003

AB0340 EFFECT OF BARICITINIB ON RANKL SERUM CONCENTRATION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: RANKL (receptor activator of nuclear factor xB ligand) and osteo-protegerin, the main regulators of bone metabolism, are involved in osteoblasts/osteoclasts balance in inflammatory disease, such as Rheumatoid Arthritis (RA). Janus kinase (JAK) inhibitors (baricitinib and tofacitinib) can reduce the progression of structural damage in patients with moderate to severe RA. Previous studies suggest a link between JAK inhibition, production of RANKL and osteoclastogenesis.

Objectives: To investigate the effect of baricitinib on RANKL serum concentration in unselected RA patients.

Methods: Patients affected by RA according to 2010 ACR criteria, starting treatment with baricitinib as clinically indicated, were consecutively enrolled. Demographic, clinical and laboratory data were collected at baseline (T0) and after three months of therapy (T3). RANKL serum concentration was analyzed by ELISA at the same timepoints. All patients underwent ultrasound (US) examination at T0 and T3. According to OMERACT definitions, the presence of synovial effusion, hypertrophy and power Doppler were assessed and scored on a semi-quantitative scale (0=absent, 1=mild, 2=moderate, 3=severe), obtaining a total US score (0-18), representing the joint inflammatory status (15); erosions were registered. Data were expressed as median (interquartile range); Mann-Whitney and Spearman tests were performed for comparisons and p values < 0.05 were considered statistically significant.

Results: We prospectively followed up 33 RA patients starting treatment with baricitinib [M/F: 8/25, age 58(9) years; disease duration 165(150) months; 22/33 (67%) ACPA-anti-citrullinated protein antibody positive; 24/33 patients (73%) RF-negative] and RANKL compared to baseline (p<0.0001). The US inflammatory score showed a significant improvement at T3 (p<0.0001). The serum concentration of RANKL showed a significant decrease after three months of therapy from 44 (25.9) to 27.5 (35.3) pg/mL (p<0.0256 (Figure 1). While in 67% of patients RANKL decreased after treatment, in 33% of patients no decrease or an increase of RANKL was detected. Those patients showing an increase of RANKL had similar RANKL compared to baseline, CDAI and SDAI compared to baseline (p>0.0001). The US inflammatory score showed a significant improvement at T3 (p<0.0001). The serum concentration of RANKL showed a significant decrease after three months of therapy from 44 (25.9) to 27.5 (35.3) pg/mL (p<0.0256 (Figure 1). While in 67% of patients RANKL decreased after treatment, in 33% of patients no decrease or an increase of RANKL was detected. Those patients showing an increase of RANKL had similar RANKL compared to baseline, CDAI and SDAI, but had significantly less swollen joints, compared to those in which RANKL decreased (p=0.0364). At baseline, the concentration of RANKL significantly correlated with the swollen joint count (p=0.0117) and ESR (p=0.0492), but not with RANKL compared to baseline, CDAI and SDAI not with the US inflammatory score. Nevertheless, the reduction of RANKL was not significantly associated with the achievement of low disease/remission after three months of treatment, with ACPA/RF positivity or the presence of erosions detected by US.

Conclusion: This is the first study demonstrating that baricitinib reduces in vivo the serum levels of RANKL, regardless the correlation with disease activity reduces. The discrepancy between the levels of RANKL and the clinical response is in line with previous data in the literature, demonstrating that, under treatment with anti-TNF and anti-IL1, the decrease of RANKL did not
influence the local or systemic inflammatory parameters, even if still preventing bone loss3.

References:

Disclosure of Interests: Cristina Garufi: None declared, Francesca Romana Spinelli Grant/research support from: Pfizer, Consultant of: Novartis, Gilead, Lilly, Sanofi, Celgene, Speakers bureau: Lilly, Fulvia Ceccarelli: None declared, Silvia Mancuso: None declared, cristiana barbati: None declared, Tania Colasanti: None declared, cristiano alessandri Grant/research support from: Pfizer, Fabrizio Conti Grant/research support from: Pfizer, Consultant of: Sanofi
DOI: 10.1136/annrheumdis-2020-eular.4399

AB0341 SURVIVAL OF REMISSION OR LOW DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB. RESULTS OF RUSSIAN NATIONAL REGISTER

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Background: Tofacitinib is an oral Janus Kinase inhibitor for the treatment of rheumatoid arthritis (RA). The survival of remission or low disease activity (LDA) in RA patients, treated with tofacitinib remain unknown.

Objectives: To evaluate the survival of DAS28 remission or low disease activity in RA patients treated with tofacitinib.

Methods: Data from 102 patients from Russian national register of patients with RA treated with tofacitinib (OREL), achieved DAS28 remission (DAS28<2.6, n=92) or LDA (DAS28<3.2, n=102) were analyzed. Number of patients with increased disease activity, time of disease activation were registered. Statistical analysis performed with statistical programs SPSS2017 and GraphPadPrizm. p-value < 0.05 considered as significant.

Results: Baseline characteristics of the patients are presented in table 1.

Table 1. Baseline characteristics of the patients with RA (n=102).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LDA (n=102)</th>
<th>Remission (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>19 (18.6)</td>
<td>15 (16.3)</td>
</tr>
<tr>
<td>Age, years (mean ±SD)</td>
<td>53.5±13.46</td>
<td>52.4±12.56</td>
</tr>
<tr>
<td>Symptoms duration, month (mean±SD)</td>
<td>170±111.92</td>
<td>169±110.93</td>
</tr>
<tr>
<td>Positive rheumatoid factor, n (%)</td>
<td>41 (40.19)</td>
<td>36 (39.13)</td>
</tr>
<tr>
<td>Erosions of hand joints (X-rays), n (%)</td>
<td>45 (42.15)</td>
<td>41 (44.56)</td>
</tr>
<tr>
<td>BMI, kg/m²(mean ±SD)</td>
<td>25.6±2.22</td>
<td>26.8±2.19</td>
</tr>
<tr>
<td>Smokers (current and in the past), n (%)</td>
<td>9 (8.82)</td>
<td>9 (9.78)</td>
</tr>
</tbody>
</table>

p-value ≥ 0.05 for all the differences.

The remission failed in 45 from 92 patients (48.91%), LDA failed in 65 from 102 of patients (63.72%), table 2.

Table 2. Median for the time of survival of remission or LDA in RA patients treated with tofacitinib.

<table>
<thead>
<tr>
<th>Time, month</th>
<th>Me</th>
<th>Standard error</th>
<th>95% Confidential Interval from</th>
<th>To</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDA (n=102)</td>
<td>12.000</td>
<td>2.021</td>
<td>8.039</td>
<td>15.961</td>
</tr>
<tr>
<td>Remission (n=92)</td>
<td>10.312</td>
<td>6.000</td>
<td>0.796</td>
<td>4.440</td>
</tr>
</tbody>
</table>

Proportions of survival of remission or LDA are presented at figure 1 and figure 2 respectively.