POS0290
THE EFFECTS OF TREATMENT RESPONSE AND RISK FACTOR TO INHIBIT THE CLINICAL RESPONSE IN PATIENTS WITH DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS TREATED WITH IL-6 RECEPTOR INHIBITOR, ABATACEPT AND JAK INHIBITOR
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Background: Recently, the disease activity of rheumatoid arthritis (RA) was improved due to the ‘treat-to-target’ strategy. However, some patients remain various symptoms despite recommended treatment was performed. Then, the term of ‘difficult-to-treat RA (D2TRA)’ is widely recognized. It is unknown how the difference of type of biological disease-modifying anti rheumatic drugs (bDMARDs)/Janus kinase inhibitor (JAKi) will affect clinical efficacy in patients with D2TRA. Moreover, the risk factor to inhibit the clinical response in patients with D2TRA is unknown.

Objectives: The aim of this study was to evaluate the treatment response in patients with D2TRA who were treated with interleukin 6 receptor inhibitor (IL-6Ri), abatacept and JAKI.

Methods: This study used the multicenter database included 673 RA patients treated with bDMARDs/JAKi (tocilizumab 240, sarilumab 67, abatacept 146, tofacitinib 101, baricitinib 83, upadacitinib 20, peficitinib 14, filgotinib 2). Two hundred forty-two patients were treated as first line bDMARDs/JAKi (IL-6Ri 117, abatacept 63, JAKi 62), 211 patients were treated as second line bDMARDs/ JAKi (IL-6Ri 117, abatacept 37, JAKi 57), 220 patients were treated as third and more bDMARDs/JAKi. In these 220 patients, 82 patients did not meet D2TRA criteria (IL-6Ri 42, abatacept 15, JAKi 25) and 138 patients met D2TRA criteria (IL-6Ri 31, abatacept 31, JAKi 76). In all patients, we analyzed 138 patients with D2TRA (113 female, mean age was 63.1 ± 13.7 years). Drug retention rate and effectiveness of bDMARDs/JAKi in patients with D2TRA were evaluated for 24 weeks. Multivariate linear regression analysis was performed to clarify the risk factors to inhibit the clinical response.

Results: Drug retention rate of patients with D2TRA at 24 weeks was 67.7% in IL-6Ri group, 74.2% in abatacept group, 61.8% in JAKi group. Drug retention rate in patients with D2TRA was not different between groups (IL-6Ri vs abatacept: p=0.86, IL-6Ri vs JAKi group: p=0.39, abatacept vs JAKi group: p=0.33). DAS28- CRP at 4, 12, 24 weeks decreased in all group (Figure 1). Abatacept showed lower improvement ratio of DAS28-CRP at 24 weeks compared to IL-6Ri group (IL-6Ri vs abatacept: p<0.01, IL-6Ri vs JAKi: p<0.01, abatacept vs JAKi: p=0.07). Good responder (defined as decrease in DAS28-CRP score > 1.2 with a score < 3.2) was 52.4% patients in IL-6Ri, 17.4% patients in abatacept, 29.8% patients in JAKi. SDAI and CDAI at 4, 12, 24 weeks decreased in all group (Figure 1). There were no differences between the groups in improvement ratio of SDAI (IL-6Ri vs abatacept: p=0.11, IL-6Ri vs JAKi: p=0.81, abatacept vs JAKi: p=0.08) and CDAI (IL-6Ri vs abatacept: p=0.31, IL-6Ri vs JAKi: p=0.08, abatacept vs JAKi: p=0.13) at 24 weeks. HAQ was 1.42, 1.15, 1.39 at baseline, 1.27, 1.07, 1.52 at 4 weeks, 1.17, 1.07, 1.17 at 12 weeks, 1.26, 1.06, 1.14 at 24 weeks in IL-6Ri group, abatacept and JAKi, respectively. Multivariate linear regression analysis revealed that high HAQ (β=0.28, p=0.02) and high dosage of glucocorticoid (β=0.67, p<0.01) inhibited the improvement of DAS28-CRP. Type of bDMARDs/JAKi (β=0.09, p=0.36) did not affect the DAS28-CRP improvement for 24 weeks.

Conclusion: Drug retention rate and clinical efficacy of D2TRA patients were not different among IL-6Ri, abatacept and JAKi. D2TRA patient with functional disorder and high dosage of glucocorticoid were risk factor to inhibit the clinical response.

Disclosure of Interests: None declared

Table 1. Multivariate linear regression analysis of risk factor to inhibit the clinical response in patients with D2TRA.

<table>
<thead>
<tr>
<th>β</th>
<th>95% CI</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>-0.037</td>
<td>-0.025, 0.017</td>
</tr>
<tr>
<td>Male</td>
<td>-0.047</td>
<td>-0.788, 0.486</td>
</tr>
<tr>
<td>Disease durations (years)</td>
<td>-0.048</td>
<td>-0.028, 0.017</td>
</tr>
<tr>
<td>RF (U/ml)</td>
<td>-0.082</td>
<td>-0.004, 0.0002</td>
</tr>
<tr>
<td>Anti CCP antibody (U/ml)</td>
<td>0.111</td>
<td>-0.005, 0.002</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>-0.093</td>
<td>-0.228, 0.042</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.279</td>
<td>0.059, 0.717</td>
</tr>
<tr>
<td>MTX (mg/day)</td>
<td>0.136</td>
<td>-0.018, 0.081</td>
</tr>
<tr>
<td>Glucocorticoid dose (mg/day)</td>
<td>0.669</td>
<td>0.174, 0.324</td>
</tr>
<tr>
<td>Type of bDMARDs/JAKi</td>
<td>-0.088</td>
<td>-0.415, 0.151</td>
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POS0291
OLOKIZUMAB IMPROVED PATIENT REPORTED OUTCOMES IN TNF INCOMPLETE RESPONDER (TNF-IR) RHEUMATOID ARTHRITIS PATIENTS: RESULTS FROM THE PHASE 3 RANDOMIZED CONTROLLED TRIAL, CREDO 3
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Background: Olokizumab (OKZ) is an interleukin-6-inhibitor for treatment of rheumatoid arthritis (RA). In these analyses we present patient reported outcomes (PROs) reported by TNF-IR patients with moderate to severely active RA receiving OKZ or placebo in a phase 3 randomized controlled trial (RCT) (ClinicalTrials.gov number, NCT02760433).

Objectives: To assess the effect of OKZ treatment compared with placebo in patient global assessment of disease activity (PGA), pain, physical function (HAO-DI), fatigue (FACIT-F) and health related quality of life (SF-36 physical (PCS) and mental (MCS)) component summary and domain scores) at 12 weeks.

Methods: 368 patients were randomized 2:2:1 to receive subcutaneously administered OKZ 64 mg every two weeks (q2w), OKZ 64 mg q4w, or placebo, plus self-reported medical information in a prospective cohort event monitoring system. Rheumatology (Oxford), 2020;59(6):1253-61.

Disclosure of Interests: Jette van Lin: None declared, Naomi Jessurun: None declared, Sander Tas Consultant of: Gebro, GSK, AbbVie, Galvani, Arthrogen/ MeiraGTx, Galapagos, Grant/research support from: Pfizer, GSK, Celgene, BMS, Genentech, AstraZeneca, Harald Voskamp, Speakers bureau: AbbVie, Celgene, BMS, Celgene, Galapagos, GSK, Janssen-Cilag, Lilly, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB, Grant/research support from: AbbVie, Sanofi-Genzyme, Frank Hoentjen Speakers bureau: served on advisory boards or as speaker for AbbVie, Janssen-Cilag, MSD, Takeda, Celtrion, Teva, Sanofi and Dr Falk, Consultant of: Celgene, Grant/research support from: Funding (Grants/Honoraria): AbbVie, Janssen-Cilag, AbbVie, Takeda, Martin van Doorn Speakers bureau: AbbVie, Janssen, LEO Pharma, Pfizer, Novartis, Paid instructor for: LEO Pharma, Consultant of: AbbVie, Janssen, LEO Pharma, Pfizer, Celgene, Novartis, TEVA, MSD, Sanofi, AstraZeneca, Grant/research support from: Novartis, Janssen, Michael Nurmohamed Speakers bureau: AbbVie, Janssen, Celgene, Consultant of: AbbVie, Grant/research support from: AbbVie, Amgen, Pfizer, Galapagos, BMS, Bart van den Bermt Speakers bureau: UCB, Pfizer, Sanofi-Aventis, Galapagos, Amgen en Eli Lilly

Table 1. Mean baseline values and LSM changes from baseline to week 12 for PROs

<table>
<thead>
<tr>
<th></th>
<th>OKZ q2w, N=138</th>
<th>OKZ q4w, N=161</th>
<th>Placebo, N=69</th>
<th>12 weeks LSM changes (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline, mean (standard deviation)</td>
<td></td>
<td></td>
<td>OKZ q2w, N=138</td>
</tr>
<tr>
<td>PIGA-VAS (mm)</td>
<td>64.8 (20.5)</td>
<td>68.1 (19.1)</td>
<td>72.1 (18.5)</td>
<td>-24.9 (2.1)</td>
</tr>
<tr>
<td>Pain-VAS (mm)</td>
<td>672 (19.5)</td>
<td>693 (19.1)</td>
<td>69.6 (21.9)</td>
<td>-28.2 (2.2)**</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.79 (0.53)</td>
<td>1.78 (0.56)</td>
<td>1.78 (0.64)</td>
<td>-0.40 (0.05)*</td>
</tr>
<tr>
<td>SF-36 PCS score</td>
<td>31.4 (6.8)</td>
<td>30.6 (7.2)</td>
<td>30.5 (6.9)</td>
<td>6.0 (0.7)**</td>
</tr>
<tr>
<td>SF-36 MCS score</td>
<td>44.3 (12.6)</td>
<td>44.5 (11.1)</td>
<td>45.1 (10.2)</td>
<td>4.1 (0.8)*</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>29.9 (7.9)</td>
<td>29.8 (8.5)</td>
<td>29.6 (8.4)</td>
<td>6.1 (0.8)</td>
</tr>
<tr>
<td>Role physical</td>
<td>32.8 (6.9)</td>
<td>33.1 (7.4)</td>
<td>33.7 (6.8)</td>
<td>6.0 (0.7)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>34.5 (6.9)</td>
<td>33.2 (6.0)</td>
<td>33.0 (6.6)</td>
<td>8.5 (0.7)**</td>
</tr>
<tr>
<td>General health</td>
<td>38.3 (8.3)</td>
<td>36.5 (8.6)</td>
<td>36.9 (8.5)</td>
<td>4.7 (0.7)*</td>
</tr>
<tr>
<td>Vitality</td>
<td>40.8 (10.1)</td>
<td>40.7 (9.5)</td>
<td>41.1 (8.1)</td>
<td>5.7 (0.8)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>38.8 (9.9)</td>
<td>38.7 (9.8)</td>
<td>39.6 (9.3)</td>
<td>6.7 (0.8)**</td>
</tr>
<tr>
<td>Role emotional</td>
<td>39.1 (12.5)</td>
<td>39.1 (12.2)</td>
<td>38.9 (11.1)</td>
<td>4.3 (0.9)*</td>
</tr>
<tr>
<td>Mental health</td>
<td>41.4 (11.6)</td>
<td>41.4 (10.5)</td>
<td>42.2 (10.3)</td>
<td>4.4 (0.8)</td>
</tr>
<tr>
<td>FACT/Gil- Fatigue</td>
<td>270 (10.2)</td>
<td>266 (10.6)</td>
<td>273 (9.9)</td>
<td>7.8 (0.9)*</td>
</tr>
</tbody>
</table>

Figure 1. SF-36 domain changes from baseline to week 12. *p<0.05, **p<0.01, ***p<0.001 for OKZ q2w vs placebo; *p<0.05, **p<0.01, ***p<0.001 for OKZ q4w vs placebo; AGNorms, age- and gender-matched normative values; BL, baseline.

Conclusion: Treatment with OKZ over 12 weeks resulted in statistically significant improvements in PROs vs placebo reported by TNF-IR RA patients. Benefits were more frequently reported by patients receiving OKZ q2w than q4w in this phase 3 RCT of limited size in treatment experienced patients.

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Disclosure of Interests: Vibeke Strand Consultant of: Abbvie, Amgen, Arena, AstraZeneca, Bayer, BMS, Boehringer, Ingelheim, Chemocentryx, Celtrion, Galapagos, Genentech/Roche, Gilead, GSK, Horizon, Inmedix, Janssen, Kinksa, Lilly, Novartis, Pfizer, Regeneron, Rheos, R-Pharm, Samsung, San-do, Sanofi, Scipher, Servier, Setpoint, Sorrento, Synthex, UCB, Ernesto,sky Consultant of: Abbvie, Amgen, Bristol Myer Squibbs, Chugai Pharma, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Regeneron, RPharm, Roche, Sanofi, and UCB., Grant/research support from: Bio-Cancer, Biogen, Novartis, Pfizer, Roche, Sanofi and UCB, Evgeny Nasonov Consultant of: AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Tatiana Listysyna: None declared, Alexander Lila Consultant of: Abbvie, Amgen, Bayer, Biotechnos, Eli Lilly, Galapagos, Gilead, Jans- sen, Novartis, Pfizer, RPharm, Roche, Sanofi, Stada, Viatris and UCB, Grant/ research support from: Novartis, Pfizer, Sofia Kuzkina Employee of: R-Pharm, Mikhail Samsonov Employee of: R-Pharm, Eugen Feist Consultant of: Abbvie, Eli Lilly, Galapagos, Medac, Novartis, Sanofi, Sobi, R-Pharm, Grant/research support from: Eli Lilly, Novartis, Pfizer


POS0292

INCREASE OF PRO-INFLAMMATORY CYTOKINES IS ASSOCIATED WITH ANTI-IDIOYPE EVENTS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH INFlixIMAB OR ADALIMUMAB

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Background: A significant percentage of rheumatoid arthritis (RA) patients undergoing Infliximab (IFX) or Adalimumab (ADA) treatment develop antidrug antibodies with potential negative effects over their clinical activity; however, it is unknown if these anti-idiotpe events could be associated with changes in cytokines levels

Objectives: To evaluate the association between blood cytokine levels, anti-idio- type events and clinical activity in RA patients treated with IFX or ADA.

Methods: All patients complied with ACR/EULAR 2021 criteria for RA and received anti-TNFa agents. Blood samples were collected during the drug trough and kept at -75ºC until analysis. Clinical activity was based on DAS28-ESR. Specific anti-drug antibodies to IFX and ADA were evaluated by sandwich ELISA. Cytokine blood levels were quantified using a multiplex system or sandwich ELISA.

Results: 57 patients with RA were recruited, 17 treated with IFX and 40 with ADA. According to the presence of anti-drug antibodies and sub-optimal levels of the biologic drug, patients were classified as immunogenic (29.8%; n=17) and non-immunogenic (70.2%; n=40), the first showed significantly higher ESR (p<0.001) and DAS28 (p<0.009). A significant association was seen between antidrug antibodies and increases of IFNg (2.1 OR, C195%:1.2-3.8, p<0.01); MCP-1 (3.9 OR, C195%:1.1-14.5, p<0.05); MIF (2.8 OR, C195%:1.3-5.7, p<0.01) and TNFa 3.0 OR, C195%:1.3-6.6, p<0.01 (see Table 1). Although anti-idiotpe events were more frequent in IFX treated patients (41%), a significant difference was not seen when comparing with ADA treated patients (25%).