Results: Sample: 2055 RA patients, female=85.1%, median disease duration=6.02 yrs; mean (SD) age=50.3 (12.1) yrs; mean (SD) DAS28=5.3 (5.1); seronegative RA=14.1%; median follow-up duration=3.9 yrs. In total, 565 patients received 664 courses of the MTX-LEF combination (median duration, 2.5 years/course; 2209 person-years). The incidence of SAE was 4.75/100 patient-years in the entire sample. There was no significant increase in the risk of any of the outcomes with the use of combined therapy (table 1) comparing with methotrexate (without leflunomide). The use of antimarial was associated with reduced risk of SAE (adjusted HR=0.62, 95% CI 0.48 to 0.79, P<0.001), while sulfasalazine (adj. HR=1.78, 1.18 to 2.68, P=0.006) and biologic DMARDS/tofacitinib (adj. HR=1.67, 1.31 to 2.12, P<0.001) increased the risk of SAE.

Table 1

<table>
<thead>
<tr>
<th>Outcome (number of SAE)</th>
<th>SAE (457)</th>
<th>SAE infections (228)</th>
<th>SAE non-myecobacterial lung infections (78)</th>
<th>SAE hepatic AE(14)</th>
<th>SAE hematologic (10)</th>
<th>SAE CV (61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (95% CI), p Value</td>
<td>1.00(0.78-1.26), p=0.970</td>
<td>1.18(0.79-1.58), p=0.538</td>
<td>0.90(0.50-1.62), p=0.732</td>
<td>1.1(0.29-4.48), NA</td>
<td>2.0(0.52-8.48), NA</td>
<td>1.2(0.65-2.30), p=0.529</td>
</tr>
<tr>
<td>p Value</td>
<td>1.06(0.83-1.35), 0.629</td>
<td>1.24(0.89-1.70), p=0.207</td>
<td>0.97(0.53-1.74), p=0.908</td>
<td>NA</td>
<td>NA</td>
<td>1.11(0.58-2.12), p=0.755</td>
</tr>
</tbody>
</table>

Conclusion: BIOBADABRASIL results suggest that the combination of methotrexate and leflunomide is safe in theraet of RA.

References:

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Disclosure of Interests: None declared


FR10143

IS PATIENT – PHYSICIAN DISCORDANCE IN ASSESSMENTS OF BURDEN OF RHEUMATOID ARTHRITIS A DETERMINANT OF M ETHOTREXATE ADHERENCE?

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Background: Accurate assessments of disease activity in rheumatoid arthritis (RA) have a crucial role in establishing disease severity and monitoring response to treatment. There is no objective, numerical measures to estimate RA severity and treatment response. A frequently used means of quantifying the overall perception of disease activity is through subjective assessments by both the patient and the physician. However, the discrepancy between these assessments is not well understood.

Objectives: The aim of the study was to explore the presence of discordance between patients’ perception of RA severity and physicians’ perception of RA severity.

Methods: In the period between May 1 and September 15, 2019, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic “Mecur Nera” randomly from Montenegro clinics were enrolled in this multi-centric cross-sectional study. The inclusion criteria were as follows: age ≥ 18 years, diagnosis of RA of at least 6 months, current methotrexate (MTX) use, current methotrexate (MTX) use for at least 1 month (with or without concomitant use of another RA drugs), and written informed consent. Non-adherence to MTX was defined as ≥1 dose missed against medical advice. The global disease activity is estimated by VAS (using a 0–10 ordinal scale), both by the patient and by the physician. The differences between groups are assessed using the Mann-Whitney U-test. The correlation between the patient – physician discordance and MTX adherence is evaluated using the Spearman rank correlation.

Results: The most of the participants (87.8%) were female with median current age of 57.5 years (range 21-83 years). The median disease duration of RA was 8 years (range 0-34 years), while the median duration of MTX treatment was 6 years (range 0-26 years). The median value of VAS score estimated both, by the patients and their physician was 5, with no statistically significant difference between these two groups (Z = 1.447, p = 0.478). The analysis of patient – physician discordance in VAS assessment showed that in concordance group the prevalence was 26.3% (20 out of 76 RA patients), while in discordance group the prevalence was 54.5% (12 out of 22 RA patients), with statistically significant difference between these two groups (Z = -5.745; p <0.001). Statistically significant correlation has been observed between presence of patient – physician discordance in VAS assessment and MTX non-adherence (r=0.427; p <0.001).

Conclusion: The results of our study have shown that the presence of patient – physician discordance in assessment of global RA activity could deeply influence the MTX adherence in a Montenegrin sample of patients with RA. This finding emphasizes the need to focus on patients perception of RA burden and values to deliver individualized patient-centered care that could potentially enhance adherence and consequently achieved optimally controlled disease control.

Disclosure of Interests: None declared


FR10144

JOINT-SPECIFIC RESPONSES TO TOFACITINIB AND ADALIMUMAB IN RHEUMATOID ARTHRITIS: A POST HOC ANALYSIS OF DATA FROM ORAL STANDARD AND ORAL STRATEGY

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Background: Inflammatory arthritis affects joints variably despite systemic inflammatory cues. Anatomical site-specific differences have been seen in the transcriptome and function of synovial fibroblasts from different joints, including evidence that some joints in rheumatoid arthritis (RA) show differential methylation of genes encoding biological pathways, such as interleukin 6 signalling via the JAK-STAT pathway. Whether such site-specific JAK-STAT sensitivity translates into joint-specific responses to therapeutic JAK inhibition is unknown. Tofacitinib is an oral JAK inhibitor for the treatment of RA.

Objectives: To explore joint-specific responses to tofacitinib and adalimumab (ADA) in RA clinical trials.

Methods: In the period between May 1 and September 15, 2019, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic “Mecur Nera” randomly from Montenegro clinics were enrolled in this multi-centric cross-sectional study. The inclusion criteria were as follows: age ≥ 18 years, diagnosis of RA of at least 6 months, current methotrexate (MTX) use, current methotrexate (MTX) use for at least 1 month (with or without concomitant use of another RA drugs), and written informed consent. Non-adherence to MTX was defined as ≥1 dose missed against medical advice. The global disease activity is estimated by VAS (using a 0–10 ordinal scale), both by the patient and by the physician. The differences between groups are assessed using the Mann-Whitney U-test. The correlation between the patient – physician discordance and MTX adherence is evaluated using the Spearman rank correlation.

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Disclosure of Interests: None declared

Methods: This was a post hoc analysis of 3-, 6- and 12-month data from the active treatment arms of Phase (P)3 study, ORAL Standard (NCT00853385; n=609) and P3b+4 study, ORAL Strategy (NCT02187055; n=1152) in patients with active RA refractory to methotrexate (MTX). Both studies included tofacitinib 5 mg BID + MTX and ADA (40 mg SC q2w) + MTX treatment arms. ORAL Standard also included a tofacitinib 10 mg BID + MTX treatment arm and ORAL Strategy, a tofacitinib 5 mg BID treatment arm. A paired joint pathology score (PJPS), a combination of bilateral tender/swollen joint counts ranging from 0 (neither side swollen/tender) to 4 (both sides swollen/tender) was calculated. Data for 33 (ORAL Standard) and 14 (ORAL Strategy) joint pairs were available. The percentage change from baseline (Δ%) in PJPS for each joint was presented in a heat map to visualise responses. To show tofacitinib-specific effects at each joint, difference in mean PJPS for each tofacitinib regimen at 3 months minus the respective ADA + MTX group was calculated.

Results: Across all treatment arms of both studies, baseline joint involvement ranged from 15.7% (5th distal interphalangeal joint of the hand) to 93.3% (wrist). All joints showed a treatment response, with 0% PJPS ranging from −36 to −94% (Figure). The heat map showed lower response rates in the wrist and knee vs most other joints in both studies persisting to 12 months, regardless of treatment arm. Similarly, in ORAL Standard, the ankle (not assessed in ORAL Strategy) showed a lower response vs most other joints. Tofacitinib-specific responses vs ADA + MTX (not shown) were seen (mean differences in PJPS ranged from −0.4 to 0.2) with no clear pattern in the combination therapy groups. In the tofacitinib 5 mg BID arm of ORAL Strategy, a pattern was observed in the metacarpophalangeal (MCP) joints, with tofacitinib responsiveness vs ADA + MTX increasing progressively (mean difference in PJPS increased from 0.16 in MCP1 to −0.08 in MCP5).

Conclusion: There is variation in the responsiveness of RA joints to tofacitinib ± MTX, with the wrist, knee and ankle responding less well vs other joints, irrespective of treatment mode of action. Concomitant MTX use in most treatment arms may mask joint-specific actions of tofacitinib and ADA. Observed responsiveness to tofacitinib monotherapy vs ADA + MTX increased from MCP1–5, which may be tentative evidence of differential sensitivity to JAK inhibition across embryologically imprinted functional genetic gradients. Further analyses of the monotherapy arms of randomised trials may yield additional evidence of joint-specific responsiveness, and provide a basis for personalised RA treatment.

REFERENCES:

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