indirect, yet powerful indicator of the impact of MTX therapy on patients' quality of life.

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AB0337

TOFACITINIB MONOTHERAPY OR COMBINED WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS SHOW SIMILAR RETENTION OVER FOUR YEARS. REPORT FROM RHUMADATA ®

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Background: Since the introduction of biologic agents around the turn of the century, the scientific evidence shows that the majority of agents, independent of the therapeutic target, have a better outcome when used in combination with methotrexate (MTX). In 2014, tofacitinib (TOFA), an agent targeting Janus kinase 1 and 3, has reached the Canadian market with data showing that the combination with MTX may not be necessary [1,2].

Objectives: To evaluate the efficacy and retention rate of TOFA in real-world patients with rheumatoid arthritis (RA).

Methods: Two cohorts of patients prescribed TOFA was created. The first cohort was formed of patients who were receiving MTX concomitantly with TOFA (COMBO) and the other of patients using TOFA in monotherapy (MONO). MONO patients either never use MTX or were prescribed MTX post-TOFA initiation for at most 20% of the time they were on TOFA. COMBO patients received MTX at the time of TOFA initiation or were prescribed MTX post-TOFA initiation for at least 80% of the time. For all those patients, baseline demographic data definitions. Disease activity score and HAQ-DI were compared from the initiation of TOFA to the last visit. Time to medication discontinuation was extracted, and survival was estimated using Kaplan-Meier calculation for MONO and COMBO cohorts.

Results: Overall, 194 patients were selected. Most were women (83%) on average younger than the men (men: 62.6 ± 11.0 years vs. women: 56.9 ± 12.1 years, p-value=0.0130). The patient's assessments of global disease activity, pain and fatigue were respectively 5.0 ± 2.7, 5.2 ± 2.9, 5.1 ± 3.1 in the COMBO group and 6.2 ± 2.5, 6.5 ± 2.6, 6.3 ± 2.8 in the MONO group all differences being significant across groups. HAQ-DI at treatment initiation was 1.3 ± 0.7 and 1.5 ± 0.7 in the COMBO and MONO groups, respectively, p-value=0.0858. Similarly, the SDAI score at treatment initiation was 23.9 ± 9.4 and 25.2 ± 11.5, p-value=0.5546. Average changes in SDAI were -13.4 ± 15.5 (COMBO) and -8.9 ± 13.5 (MONO), p-value=0.1515, and changes in HAQ -0.21 ± 0.63 and -0.26 ± 0.74, p-value 0.6112. At treatment initiation, DAS28(4)ESR were 4.4 ± 1.4 (COMBO) and 4.6 ± 1.3 (MONO), p-value 0.5815, with respective average changes of -1.06 ± 2.07 and -0.70 ± 1.96, p-value=0.2852. The Kaplan-Meier analysis demonstrated that the COMBO and MONO retention curves were not statistically different (log-rank p-value=0.9318).

Conclusion: Sustainability of TOFA in MONO or COMBO are not statistically different as are the changes in DAS28(4)ESR and SDAI. Despite this result, some patients may still benefit from combination with MTX.

References:

- [1] Product Monograph - XELJANZ® (tofacitinib) tablets for oral administration Initial U.S. Approval: 2012.
- [2] Reed GW, Gerber RA, Shan Y, et al. Real-World Comparative Effectiveness of Tofacitinib and Tumor Necrosis Factor Inhibitors as Monotherapy and Combination Therapy for Treatment of Rheumatoid Arthritis [published online ahead of print, 2019 Nov 9]. *Rheumatol Ther*. 2019;6(4):573–586. doi:10.1007/s40744-019-00177-4.

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AB0338

EVALUATION OF THE ASSOCIATION OF ALLELES OF INTOLERANCE RISK TO METOTREXATE IN RHEUMATOID ARTHRITIS PATIENTS UNDER TREATMENT WITH BIOLOGIC THERAPIES

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Background: Metotrexate (MTX) is the first-line treatment for rheumatoid arthritis (RA) both in monotherapy and in combination with biologic disease-modifying antirheumatic drugs (bDMARDs), it usually well tolerated but AEs may appear that causing toxicity that requires suspension of the treatment

Objectives: Determine the prevalence of certain polymorphisms among patients that receive bDMARD in monotherapy or in combination with MTX to confirm its relevance as biomarkers of intolerance. Evaluate the influence of certain polymorphisms in the effectiveness of monotherapy or combined treatment in patients, through "Disease Activity Score 28" (DAS28), SDAI Simple disease activity index (SDAI), Clinical disease activity index (CDAI) and each one of its components

Methods: Retrospective observational multicentric study (University Hospital Complex, Granada, Carlos de Haya Hospital, Málaga and University Hospital Reina Sofía, Córdoba), of cases-control of 227 patients with RA (criteria ACR/ EULAR), of which 120 received MTX and bDMARD combined therapy (cases) and other with only bDMARD (controls). All of them had been or were currently treated with MTX, remained with stable doses of bDMARD, and had a DNA sample stored before the inclusion in the study

DNA was isolated from total peripheral blood and by fluorescent probe Hyb-Probe and/ or Taqman, 10 polymorphisms of 10 protein coding genes were determined involved in the metabolism and toxicity of MTX according to current evidence

Besides the type of polymorphism, data on the activity of the disease were analysed (DAS28VSG, DAS28PCR, SDAI, CDAI, at the start of the MTX income, of the BT, and in the inclusion visit

A descriptive and comparative study was carried out on all that and afterwards an assessment was made through a multiple logistic regression analysis (MLR) on the risk of intolerance to MTX

Results: An analysis was carried out on 227 patients (120 cases and 107 controls) with an average age of 60 (12,1) being women 78,4%, with a time of evolution since diagnosis of 14,84 (7,78) years

48,9% registered adverse events (AE) MTX related, mainly gastrointestinal, hepatobiliary and skin-subcutaneous tissue. The percentage of AE appearance was superior in the monotherapy group than in the group with combined therapy

The most prevalent polymorphism (84,6% (IC95%: 84,09%-85,11%) and in cases (86,0% (IC95%: 79,43%-92,57%) was **homozygous CC (ITPase-c94a)**; in controls **homozygous GG (GGH-T401C)** (87,5% (IC95%:81,58%-93,42%)

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 **ABCC2-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 ABCC2 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

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AB0339 THE IMPORTANCE OF THERAPEUTIC COMPLIANCE: ADHERENCE TO METHOTREXATE AND ITS ROLE IN IMMUNOGENICITY

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Background: Immunogenicity against adalimumab leads to loss of response and secondary failure to biologic therapy; however, concomitant use of methotrexate (MTX) seems to reduce the development of anti-drug antibodies (ADAbs) in a dose-dependent manner. Suboptimal adherence to MTX may favour ADAbs appearance.

Objectives: To evaluate the relationship between MTX adherence and ADAbs development.

Methods: Observational study among adult patients with chronic inflammatory arthropathy, followed in a tertiary care centre, who were in treatment with MTX and adalimumab. ADAbs formation in relation to MTX adherence was assessed.

Results: 33 patients were included, with a MTX adherence overall mean of 82.13 (12.45%-100%, median adherence 92.19%). Only 9.09% (n=3) of the patients developed ADAbs, being its MTX adherence mean of 60.95% (46.47%-70%, median adherence 66.39%); ADAbs negative group showed an average MTX adherence of 84.23% (12.45%-100%, median adherence 94.29%). A statistically significant result ($p<0.05$) between groups was found.

	n	Adherence mean	
ADAbs (+)	3 (9.09%)	60.95%	p<0.05
ADAbs (-)	30 (90.91%)	84.23%	
Total	33 (100%)	82.13%	

No statistically significant differences ($p>0.05$) involving MTX adherence and its dose were found.

Conclusion: While the sample is small, this study suggests that ADAbs development may be influenced by MTX adherence, thereby promoting adequate MTX adherence should be a priority in the daily practice of every rheumatologist.

References:

- [1] World Health Organization. Adherence to long term therapies: evidence for action. 2003.

- [2] Krieckaert CL, Nurmohamed MT, Wolbink GJ. Methotrexate reduces immunogenicity in adalimumab treated rheumatoid arthritis patients in a dose dependent manner. *Annals of the Rheumatic Diseases*. 2012;71:1914-1915.
- [3] Zhang J, Xie F, Delzell E, et al. Impact of biologic agents with and without concomitant methotrexate and at reduced doses in older rheumatoid arthritis patients. *Arthritis Care Res (Hoboken)*. 2015;67(5):624-632. doi:10.1002/acr.22510
- [4] Jani M, Barton A, Warren RB, Griffiths CE, Chinoy H. The role of DMARDs in reducing the immunogenicity of TNF inhibitors in chronic inflammatory diseases. *Rheumatology (Oxford)*. 2014;53(2):213-222. doi:10.1093/rheumatology/ket260.

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

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Background: RANKL (receptor activator of nuclear factor κ B ligand) and osteoprotegerin, 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^{1,2}.

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 with 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 (0-198), 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-rheumatoid factor positive]. After three months of therapy we observed a significant reduction of DAS28_{CRP}, 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 DAS28_{CRP}, CDAI, 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 ($p=0.0482$), but not with DAS28_{CRP}, CDAI, SDAI nor 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 indices. 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