

AB0453 **RED RICE YEAST. AN ALTERNATIVE IN RHEUMATOID ARTHRITIS AND HYPERLIPIDEMIA**

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Background: Lipid profile control is essential in patients diagnosed with inflammatory disease such as rheumatoid arthritis (RA), since cardiovascular events (CV) are still the first cause of mortality. According to the EULAR recommendations on CV risk, in those patients with a low or moderate CV risk index, for whom diet and exercise have not been effective to diminish low density lipoprotein (LDL) cholesterol below 190 and 100 respectively, we must prescribe a statin. These are the most commonly used drugs with undoubted benefits shown in medical literature. However, often-polymedicated patients may present intolerances or adverse side effects that limit their use. Red rice yeast, whose main active ingredient is monacolin K, has been used in traditional Chinese medicine since 800 AD as a remedy to reduce the total cholesterol level (TC) in blood, LDL and triglycerides (TG). In addition, some studies underline its anti-inflammatory effect and its benefit in patients with inflammatory pathology. In recent years, its use has spread throughout the western world.

Objectives: To evaluate the efficacy of red rice yeast in patients with elevated levels of TC and LDL in rheumatology clinic.

Methods: Prospective study that includes two cohorts of 30 patients with similar demographic characteristics. One cohort with RA patients and the other one without inflammatory disease. Both groups present high levels of TC and LDL. We study the demographic, clinical and lipid levels. A standard dose of red rice yeast is administered to every patient and we evaluate the analytical response after 3 and 6 months of treatment. For the statistical analysis, we used the SPSS program 22.0 version. Quantitative variables are presented as means \pm standard deviation and qualitative variables as percentages. The comparisons between the quantitative variables are made with the Student's T-test. We compared the mean values for each visit with the Anova test. A $p < 0.05$ is considered significant.

Results: In the group of patients without inflammatory pathology ($n = 30$), 73% are women with an average age of 63.9 ± 7 years. The mean of baseline TC is $265.2 \text{ mg/dL} \pm 13.7$ and LDL 176.4 ± 16 . After 3 and 6 months of treatment, a significant decrease in both values was obtained (TC 231 ± 19 and 209.8 ± 19 F: 26.71 $p < 0.000$ and LDL 143.9 ± 20 and 123.6 ± 19 F 22.51 $p < 0.000$)

In the cohort of patients with RA ($n = 30$), 66% were women with an average age of 62.1 ± 10 . The mean baseline TC is 258.2 ± 14 and LDL is 176.7 ± 10 . After 3 and 6 months of treatment a significant decrease of both values was obtained (TC 224 ± 24 and 196.1 ± 28 F: 21.55 $p < 0.000$ LDL 149.5 ± 12 and 122.4 ± 25 F: 28.28 $p < 0.000$)

There were no significant changes in HDL or TG levels. Neither adverse effects were detected nor treatment was abandoned.

Conclusion: The red rice yeast significantly decreases the levels of TC and LDL in the two cohorts. In patients with RA and mild or moderate CV risk, where a close control is necessary, the use of red rice yeast could be an effective therapeutic alternative free of adverse side effects. More studies are needed with a greater number of patients to corroborate these data

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AB0454 **FREQUENCY AND DURATION OF EARLY NON-SERIOUS ADVERSE EVENTS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB 5 MG TWICE DAILY AS MONOTHERAPY AND COMBINATION THERAPY**

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Background: Tolerability remains ill-defined in clinical trials and commonly refers to non-serious adverse events (AEs) impacting patient (pt) satisfaction and treatment adherence. Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: This update to a previously published post hoc analysis¹ describes the frequency and duration of the most common tolerability-related non-serious AEs in pts with RA receiving tofacitinib 5 mg BID as monotherapy or with conventional synthetic (cs)DMARDs in Phase (P)3 and P3b/4 studies.

Methods: Data were pooled from: ORAL Step (NCT00960440); ORAL Solo (NCT00814307); ORAL Scan (NCT00847613); ORAL Sync (NCT00856544); ORAL Standard (NCT00853385); and ORAL Strategy (NCT02187055). This post hoc analysis included data from pts receiving tofacitinib 5 mg BID monotherapy (ORAL Solo, ORAL Strategy), placebo (PBO; ORAL Solo), or tofacitinib 5 mg BID or PBO with csDMARDs (all studies except ORAL Solo). Non-serious AEs (affecting pts' day-to-day experience and ability to tolerate therapy) with incidence rates (IRs, pts with events/100 pt-years) ≥ 5 were evaluated up to Month (M)3. Infections, laboratory test abnormalities, general disorders or events not directly reported by pts, and musculoskeletal disorders likely due to underlying RA, were excluded.

Results: Of the 2657 pts included in the analysis, 1976 received tofacitinib 5 mg BID (monotherapy: N=627; combination: N=1349) and 681 received PBO (monotherapy: N=122; combination: N=559). The most frequent non-serious AEs up to M3 are shown in the Table. IRs ≥ 10 were seen for headache and diarrhoea (tofacitinib 5 mg BID monotherapy, combination therapy and PBO monotherapy), and nausea (PBO monotherapy and PBO combination therapy). Non-serious AE duration was ≤ 4 weeks for most pts with headaches, diarrhoea or gastric discomfort (any gastrointestinal pain, dyspepsia, epigastric discomfort or abdominal discomfort/pain). With tofacitinib 5 mg BID and PBO, respectively, duration of AEs was ≤ 2 weeks for 43.2% and 64.7% of pts with headaches; 66.1% and 81.3% with diarrhoea; and 36.2% and 58.6% with gastric discomfort. Most non-serious AEs were mild/moderate.

Table. Non-infectious, treatment-emergent non-serious adverse events* in Phase 3 and Phase 3b/4 studies up to Month 3

Non-serious AE, n (%), IR [95% CI]	Monotherapy		Combination therapy		Overall	
	Tofacitinib 5 mg BID (N=627)	PBO ^b (N=122)	Tofacitinib 5 mg BID (N=1349)	PBO ^c (N=559)	Tofacitinib 5 mg BID (N=1976)	PBO ^c (N=681)
Headache	21 (3.3) 13.7 [8.5, 21.0]	3 (2.5) 10.1 [2.1, 29.4]	50 (3.7) 15.3 [11.5, 20.1]	13 (2.3) 9.5 [5.1, 16.3]	71 (3.6) 14.8 [11.5, 18.6]	16 (2.3) 9.6 [5.5, 15.6]
Diarrhoea	18 (2.9) 11.7 [7.0, 18.5]	3 (2.5) 10.0 [2.1, 29.2]	41 (3.0) 12.5 [8.9, 16.9]	13 (2.3) 9.5 [5.1, 16.3]	59 (3.0) 12.2 [9.3, 15.8]	16 (2.3) 9.6 [5.5, 15.6]
Nausea	15 (2.4) 9.8 [5.5, 16.1]	3 (2.5) 10.0 [2.1, 29.2]	29 (2.1) 8.8 [5.9, 12.6]	15 (2.7) 11.0 [6.2, 18.2]	44 (2.2) 9.1 [6.6, 12.2]	18 (2.6) 10.8 [6.4, 17.1]
Vomiting	7 (1.1)	2 (1.6)	18 (1.3) 5.4 [3.2, 8.6]	8 (1.4) 5.8 [2.5, 11.4]	25 (1.3) 5.1 [3.3, 7.6]	10 (1.5) 6.0 [2.9, 11.0]
Dyspepsia	4 (0.6)	4 (3.3)	20 (1.5) 6.0 [3.7, 9.3]	7 (1.3) 5.1 [2.1, 10.5]	24 (1.2)	11 (1.6)
Abdominal pain upper	7 (1.1)	0 (0.0)	17 (1.3) 5.1 [3.0, 8.2]	6 (1.1) 4.4 [1.6, 9.5]	24 (1.2)	6 (0.9)

*Defined as AEs with an IR (pts with events per 100 pt-years) ≥ 5 in at least one treatment group under monotherapy, combination therapy or overall therapy. IRs (and 95% CI) that did not meet this criterion (ie. IR < 5) are not shown. ^bPts receiving PBO without background csDMARDs in ORAL Solo (only concomitant antimalarial medications were allowed). ^cIncludes pts receiving PBO with background csDMARDs in Phase 3 and Phase 3b/4 studies.

AE, adverse event; BID, twice daily; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IR, incidence rate; PBO, placebo; pt, patient

Figure 1

Conclusion: Overall, non-infectious non-serious AEs were mild/moderate and the majority were self-limiting. Non-serious AE frequency was similar for tofacitinib monotherapy and combination therapy, and for tofacitinib and PBO.

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AB0455

FACTORS ASSOCIATED WITH DAS28 RESPONSE IN BIOLOGIC-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: 10 YEAR FOLLOW-UP

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Background: Access to adequate care is limited in Mexico as biologics or targeted therapies are unavailable for a proportion of patients with rheumatoid arthritis (RA) and only methotrexate and other conventional (c) DMARDs are employed as therapeutic options in many cases.

Objectives: To determine the factors associated to DAS28 response in patients with rheumatoid arthritis followed up to 10 years and who never received biologic or targeted therapy, being treated only with cDMARDs.

Methods: We analyzed a prospective cohort of 543 patients with RA followed for 10 years (March 2006 to February 2016) at the Hospital General de Cuernavaca, in central México. Demographic data, shared epitope (SE; HLA-DR*0101, *0102, *0401, *0404, *0405, *0408, *0410, *1001, *1402) status, date since onset of disease and treatment, clinical and disease activity characteristics as well as treatment data was obtained and followed through time. Patients were seen by a rheumatologist every three months and blood samples obtained on each visit. The DAS28 score was determined on each visit and treatment adjusted accordingly. They were treated with prednisone (PDN; ≤ 10 mg/day), Methotrexate (MTX; 7.5-25 mg/week), Cloroquine (CLQ; 150-300 mg/day), Sulphasalazine (SSZ; 1-3 gr/day) or a combination of these. Descriptive statistics were used for the analysis of demographic data and parametric correlation tests (Spearman) were employed in the analysis.

Results: Of the 543, 94.3% of patients were women; mean age at baseline was 54.1 years (23-89; SD 12.4), mean time since onset of disease was 6.6 years (0-49; SD 7.9) and mean time since onset of treatment was 3 years (1-9; SD 2.12). HLA was determined in 57 patients and 36.8% of these patients were SE positive (one or two alleles). Most patients received treatment on the baseline visit based mainly on MTX (72.7%) combined with CLQ (63%) and low-dose PDN (76.4%). Less than 5% was under treatment with a non-MTX cDMARD. Baseline mean DAS28 was 4.9 (0.9-8.3; SD 1.41). At 6 months since DMARD-onset mean DAS28 was 3.8 (0.42-8.0; SD 1.46), at 12 months mean DAS28 was 3.6 (0.14-7.6; SD 1.34). At 2 years of follow-up, mean DAS28 remained at 3.6 (1.27-7.43; SD 1.35). Over the course of the next 8

years patients maintained a mean DAS28 between 3.5-3.6, with no significant changes in spite of continuing cDMARD treatment. Apart from being under treatment, which correlated with a better DAS28 score, being female correlated with a poorer DAS28 response ($p < 0.05$). The other baseline factor significantly associated to an improved long-term outcome regarding disease activity was time since onset of disease, which correlated with a higher DAS28 score during the first two years of follow up but tapered after two years of follow-up ($p < 0.001$). One of the limitations of the study was the significant drop-out rate ($> 20\%$) seen during follow up.

Conclusion: DAS28 response occurs mainly in the first 2 years of treatment. After that, cDMARD treatment is associated to a stationary effect over DAS28 in patients with no access to biologics or targeted therapies. This is an important factor to consider when establishing long-term therapeutic strategy from a cost-effective point of view.

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AB0456

PERCEPTIONS OF GLUCOSTEROID SIDE EFFECTS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Most of the new recommendations proposed for the management of Rheumatoid arthritis (RA) emphasize the involvement of patients in therapeutic decision-making. This should encourage us to evaluate their level of information, fears and beliefs about the different treatments especially corticosteroids.

Objectives: The aim of this study was to evaluate the fears and beliefs of Tunisian patients with RA regarding corticosteroids.

Methods: A prospective study including 35 RA patients according to the ACR/EULAR 2010 criteria was performed. All of them were treated with corticosteroid therapy in addition to DMARDs and their usual long-term treatment. Every patient included in the study completed a questionnaire, containing sociodemographic component and evaluating corticosteroid modality use as well as side effects[1].

Results: The study included 35 patients with female predominance (74, 3%). The mean age was 57 years (29-72). The mean duration of the disease was 8 years (2-13 years). All RA patients were immunopositive for rheumatoid factor and/or for Anti-cyclic citrullinated peptide antibody (anti-CCP). Twenty-six patients were on Methotrexate, 6 on Infliximab, and 3 on Rituximab. Corticosteroid therapy was prescribed at a mean dose of 7.5 mg prednisone (5 to 10 mg). The level of education of our patients was generally low: 17 were illiterate, 10 had received a primary or secondary education, only 8 attended college. None of them was part of a medical or paramedical profession. Twenty patients, of whom eight diabetic, had an idea about the potentially harmful effect of corticosteroids on glycemic equilibrium (14 patients reported hyperglycemia and six patients mentioned hypoglycemia). Forty percent were aware of obesity as an effect correlated with corticotherapy. Moreover, 34.3% of patients talked about the hypertensive peak as a serious complication. Osteoporosis was mentioned in 17.1% of cases. About 10 patients had no idea about the adverse effects of steroids. When asking them about their source of information: they mentioned respectively television and radio programs with medical informative content, environment and medical or paramedical medical staff.

Conclusion: This study highlights the insufficiency of the level of information provided for RA patients regarding corticosteroids side effects. New awareness-raising materials should be reinforced and adapted to make full use of their potential with less likelihood of adverse effects.