AB0243

CONSIDERING THE COMBINATION OF TWO BIOLOGICS IN CASE OF FAILURE OF THE MONOTHERAPY IN JUVENILE ONSET RHEUMATOID ARTHRITIS

A. Haddouche¹, K. Ait Bellabas¹, W. F. Hamrani¹, S. Sahraoui¹, R. Fatma¹, F. Rahal², S. Slimani³, F. Henni¹. ¹EHS Ben Aknoun, Rheumatology, Algiers, Algeria; ²CHU Beni Messous, Rheumatology, Algiers, Algeria; ³Private Practice Office, Rheumatology, Batna, Algeria

Background: The management of rheumatoid arthritis refractory to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) is currently well codified and includes different types of biologics and even targeted sDMARDs. A rotation of biologic therapies is recommended in order to better control the disease.

Methods: We report the case of a 20-year-old patient followed in our hospital for the management of a deforming and erosive seropositive rheumatoid arthritis (FR +, ACPA +) with a juvenile onset at the age of 8 years. The diagnosis of an immunopositive polyarticular form of JIA was retained in 2010 (9 years old); the patient was treated with methotrexate (MTX) at a dose of 10mg per week and methylprednisolone at doses varying between 4 and 10mg per day. Following the failure of MTX, etanercept was introduced for 6 months without success, followed by tocilizumab in 2012 at a dose of 8mg/kg/month for a year, without good response. In 2014, a course of rituximab (RTX) at a dose of 2 shots of 500mg, 2 weeks apart was prescribed followed 9 months later by etanercept at a dose of 50mg a week for 3 years then by adalimumab (40mg/ week) because of the multiple treatment failures.

In 2018, the repetition of RTX at a dose of 1g, renewed 15 days later, improved the patient for only 3 months. Then, a combination of two biologics, namely RTX (2 x 1g, 15 days apart) and adalimumab 1 month later (40mg / week) was received by the patient with a good response at 3 months. The latter was maintained for 7 months even after stopping the adalimumab following confinement for COVID-19. In September 2020, flares occurred and the adalimumab (ADA) has been delivered but without success during 3 months, stopped later for a benign form of COVID-19 (15 months after RTX). In January 2021, the association RTX + ADA was given again and we hope that it will be as effective as the first prescription.

Results: The clinical and biological severity of our patient's rheumatoid arthritis led us to give a combination of two biological treatments. Indeed, we do not have other therapeutic classes to deliver to her, that encouraged us to rotate between all the available biological therapies in our country. The combination of a CD20 inhibitor (RTX) with a TNF blocker (ADA) was safe and made possible, for the first time, the achievement of clinical and biological remission during 7 months, even after stopping the TNF blocker. Greenwald *et al.* reported the safety of the combination of RTX + TNF inhibitors in a randomized clinical trial in 51 patients. Its efficacy, a secondary goal of the study, was suggested at 24 weeks by the percentage of ACR 20 and ACR 50 responses that was greater than in the RTX placebo group.

Conclusion: The combination of RTX with a TNF blocker can be a real alternative therapy in rheumatoid arthritis with failure to a biological monotherapy.

Disclosure of Interests: None declared

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AB0244

INFLUENCE OF BIOLOGICAL DRUGS ON HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Jriti¹, S. Boussaid¹, S. Reki¹, M. Abbes¹, M. Ben Majdoub¹, S. Jemmal¹, H. Sahli¹, M. Elleuch¹. ¹RABTA, Rheumatology, Tunis, Tunisia

Background: The level of the Health-related quality of life (HRQL) in patients with rheumatoid arthritis (RA) is often neglected in their medical care. While, these patients are suffering from a precarious quality of life, resulting from pain, impaired physical function and fatigue. The use of biological agents for treating this disease is then a challenge, leading to the possibility of reducing the consequences of the disease.

Objectives: The main purpose of this study was to compare the level of HRQL in patients with rheumatoid arthritis (RA) during therapy applying disease-modifying antirheumatic drugs (DMARDs) with conventional synthetics (csDMARDs) or with csDMARDs in combination with biological drugs (bDMARDs).

Methods: The study involved 120 patients with RA, divided into two groups: group I –treated using csDMARDs (combination therapy: methotrexate and salazopyrine), group II – using csDMARDs in association with bDMARDs which included TNF inhibitors (etanercept and adalimumab). All the studied patients were surveyed with the use of the following questionnaires: *the short-form health survey (SF-36)* for HRQL that assesses eight domains: functional capacity (ten items), physical aspects (four items), pain (two items), general health (five items), vitality (four items), social aspects (two items), emotional issues (three items)

and mental health (five items), in addition to one item to compare current health status and that of the previous year, *The AIMS2-SF*, and *Health Assessment Questionnaire (HAQ)*. The questionnaires were filled out at the consultation after patient's consent. The 28-Joint Disease Activity Score (DAS-28) was calculated.

Results: Group I consisted of 72 persons including 55 women and 17 men with a mean age of 58.4 years. Group II contained 48 patients where females predominated (sex ratio: 0.3), the mean age was 52.4 years. The majority of patients (53.3%) had been diagnosed with RA for more than five years. Most of the SF-36 domains showed significant improvement in the second group ($p < 0.01$), highlighting the social aspects, pain, physical functioning, emotional issues, vitality and physical aspects. The mean score of HAQ II decreased from 1.97 up to 1.23 with biological therapy ($p < 0.01$). The highest AIMS scores were comparatively in the two groups (I vs II): in social activity (6.49 ± 1.93 vs 6.23 ± 1.56), pain (4.70 ± 2.04 vs 4.01 ± 2), depression (4.70 ± 2.23 vs 4.66 ± 2.03), and physical activity (4.03 ± 2.10 vs 4.01 ± 2.08). The DAS-28 value, the number of swollen joints, and the duration of morning stiffness were significantly smaller among patients from group II ($P = 0.04$). After logistical regression, treatment with bioterapy was isolated as a fundamental independent factor influencing the mental component of SF-36 scale with an OR of 1.59.

Conclusion: we conclude that the use of biologic therapy in patients with RA proved to be an important pharmacological strategy for improving HRQL and functional capacity as assessed by the HAQ II and SF-36 instruments. The intensity of the activity of RA as well as experiencing pain and the duration of morning stiffness were smaller among patients applying csDMARDs plus bDMARDs compared with patients treated only with csDMARDs.

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AB0245

ANALYSIS OF THE CLINICAL AND ANTIDESTRUCTIVE EFFECTS OF RITUXIMAB DEPENDING ON GENDER IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Kudryavtseva¹, G. Lukina¹, E. Aronova¹, G. Gridneva¹, S. Glukhova¹, A. Smirnov¹. ¹V.A.Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Monitoring the Safety of Therapy, Moscow, Russian Federation

Background: Rheumatoid arthritis is a chronic autoimmune disease characterized by inflammation of the synovial tissue and destruction of the underlying cartilage and bones. It was found that RA more often affects women than men, with a sex ratio of 3: 1. And the question of the influence of gender on the outcomes and course of RA remains controversial, there is no consensus on whether RA is worse in women or men. Recent reports indicate that women are less likely to achieve remission than men. Women suffer from RA at an earlier age and have higher markers of disease activity such as DAS28 and HAQ. Rituximab is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells, it has been successfully and widely used for the treatment of rheumatoid arthritis, so it is of interest to assess whether gender influences the therapeutic and radiological effects of RTX.

Objectives: The aim of this study was to analyze the impact of gender on the response to rituximab (RTX) in patients with RA.

Methods: Initially, 221 women(w), 27 men(m), were examined to assess the clinical and X-ray effect (88w/6m), who received RTX treatment (1000 mgx2 or 500 mgx2). Both groups were comparable in terms of the main clinical and laboratory characteristics (age, duration of the disease, the number of preceding DMARDs, in both groups most patients were RF + and ACCP +, a high degree of activity according to DAS 8 - men - 5.6 [4.6-6.7], women - 6.04 [5.2-6.63] Initially, the degree of radiological changes in men is slightly higher than in women ($p > 0.05$). Clinical effect was scored by EULAR criteria, radiographic progression was assessed using Sharp/van der Heijde modified scoring method.

Results: When assessing the clinical effect after 48 weeks in men, a significantly better effect of RTX treatment was noted in comparison with women (Δ DAS28, a significantly better effect was noted in men - Δ DAS28 = $3.75 [2.8-4.14]$, and Δ DAS28 = $1.3 [0.37-2.72]$ in women, ($p = 0.04$). Analyzing the X-ray effect after 48 weeks of RTX treatment: the absence of progression in terms of the total score in 83.33% of men and 60.98% of women; there was no progression in narrowing of the joint space in 83.33% of men and 65.85% of women, noteworthy that the account of erosion practically reaches statistical significance - inhibition of destruction in 100% of men and 74.31% of women ($p = 0.06$).

Conclusion: Thus, having analyzed the clinical and antidestructive effects of RTX therapy depending on gender, we can conclude that the effect is significantly

higher in the male group. Also, there is a tendency towards more effective inhibition of radiographic progression in men.

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AB0246

COMORBIDITIES APPEARING UNDER BIOLOGIC THERAPY: PREVALENCE AND ASSOCIATED FACTORS

T. El Joumani¹, T. Latifa¹, I. Hmamouchi^{2,3}, S. Ahid⁴, R. Abouqal⁵, L. Achemlal⁶, I. El Bouchti⁷, A. El Maghraoui⁸, I. Ghoulani⁹, H. Hassikou¹⁰, T. Harzy¹¹, I. Linda¹², O. Mkini¹³, R. Niamane¹⁴, R. Bahiri¹⁵, H. Rkain¹, F. Allali¹. ¹El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Department of Rheumatology B, Rabat, Morocco; ²Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco; ³Provincial Hospital of Temara, Morocco, Department of Rheumatology, Rabat, Morocco; ⁴Mohammed V University, Rabat, Morocco, Research Team of Pharmacoeconomics & Pharmacoepidemiology, Rabat, Morocco; ⁵Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco, Laboratory of Biostatistical, Clinical and Epidemiological Research, Rabat, Morocco; ⁶Military Hospital Mohammed V, Ibn Sina University Hospital, Rabat, Morocco, Department of Rheumatology, Rabat, Morocco; ⁷Arrazi University Hospital, Marrakech, Morocco, Department of Rheumatology, Rabat, Morocco; ⁸Private Medical Office, Rabat, Morocco, Rheumatology, Rabat, Morocco; ⁹University Hospital of Agadir, Morocco, Department of Rheumatology, Agadir, Morocco; ¹⁰Military Hospital Moulay Ismail, Hassan II University Hospital, Meknes, Morocco, Department of Rheumatology, Meknes, Morocco; ¹¹Hassan II University Hospital, Fes, Morocco, Department of Rheumatology, Fes, Morocco; ¹²Mohammed VI University Hospital, Department of Rheumatology, Oujda, Morocco; ¹³Ibn Rochd University Hospital, Department of Rheumatology, casablanca, Morocco; ¹⁴Military Hospital Avicenne, Mohammed VI University Hospital, Department of Rheumatology, marrakech, Morocco; ¹⁵El Ayachi Hospital, Ibn Sina University Hospital, Department of Rheumatology A, Salé, Morocco

Objectives: The aims of our study are to determine the new comorbidities appearing under biologic therapy, their prevalence, and the factors implicated in their appearance.

Methods: It's a multicentric historical-prospective cohort including 10 rheumatology departments of Moroccan University Hospitals. The data were collected from the national register of patients under biologic therapy supervised by the Moroccan Society of Rheumatology. An electronic follow-up questionnaire is completed every 6 months by the investigator.

Results: The study included 418 patients: 224 with Rheumatoid Arthritis (RA) who represented 53.6% and 194 with spondyloarthropathy (SP) who represented 46.4%.

The prevalence rate of comorbidities appearing after one year of treatment with biologic therapy was 15.7% in RA and 8.4% in SP. The rate of cardiovascular diseases was 12.9% (arterial hypertension, myocardial infarction and/or ischemic stroke), 6.4% was the same value of hypercholesterolemia and depression, diabetes 3.3%, ulcer 3.2%, and osteoporosis 9.7%. The sedentary rate was 54.8% and smoking was about 3.3%.

No patient had developed hypertriglyceridemia or chronic obstructive pulmonary disease.

In the group of patients with RA, the average age of the patients who had developed a new comorbidity was 51.8 ± 11.3 years, women represented 87.5%, the average of Body Mass Index (BMI) was 27.6 ± 5.9 and the average duration of the disease was 14.1 ± 9.2 years. The disease activity score (DAS28) had an average of 3.15 ± 1.47 .

59.6% of patients used Rituximab, 23.8% Tocilizumab, 8.1% Etanercept, 5.8% Adalimumab, 0.18% Infliximab, and 0.9% Golimumab.

In the group of patients with SP, the average age of the patients who had developed a new comorbidity was 40.2 ± 13.7 years, men represented 63.4%, and the average of BMI was 24.3 ± 4.94 .

The activity of the disease, had an average Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of 2.62 ± 1.79 and ankylosing Spondylitis Disease Activity Score (ASDAS) of 1.93 ± 1.09 .

Regarding the type of biologic therapy, 33.2% of patients used Etanercept, 30.1% Adalimumab, 24.9% Infliximab, 9.8% Golimumab, 1.6% Secukinumab, and 0.5% Tocilizumab.

Conclusion: Our study showed a high prevalence of cardiovascular disease in patients under biologic therapy. This can be explained by the sedentary lifestyle secondary to rheumatic disease.

Disclosure of Interests: None declared

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Rheumatoid arthritis - non biologic treatment and small molecules

AB0247

ANALYSIS OF THE IMPACT OF TOFACITINIB TREATMENT ON WEIGHT IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Wollenhaupt¹, J. Morel², C. Daien², A. Ruysen-Witrand³, C. Lukas², C. Richez⁴, A. Shapiro⁵, D. Chapman⁶, M. Cros⁷, J. L. Rivas⁸, G. Citera⁹. ¹Struenseehaus Centre for Rheumatology and Clinical Immunology, Hamburg, Germany; ²CHU Montpellier and University of Montpellier, Department of Rheumatology, Montpellier, France; ³Hopital Purpan, CHU Toulouse, Department of Rheumatology, Toulouse, France; ⁴Groupe Hospitalier Pellegrin-CHU de Bordeaux, Department of Rheumatology, Bordeaux, France; ⁵Pfizer Inc, Inflammation and Immunology, Peapack, NJ, United States of America; ⁶Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America; ⁷Pfizer Inc, Inflammation and Immunology, Paris, France; ⁸Pfizer SLU, Inflammation and Immunology, Madrid, Spain; ⁹Instituto de Rehabilitación Psicosfísica, Section of Rheumatology, Buenos Aires, Argentina

Background: A prior post hoc analysis of tofacitinib clinical trial data reported improvements in rheumatoid arthritis (RA) outcomes with tofacitinib vs placebo (PBO) through Month (M)6, regardless of baseline (BL) body mass index (BMI).¹

Objectives: To assess change from BL (Δ) in BMI, and disease activity by BL BMI status, in patients (pts) with moderate/severe RA receiving tofacitinib through M12.

Methods: This post hoc analysis included data pooled from Phase 3 and 3b/4 studies of pts who were methotrexate-naïve (NCT01039688) or inadequate responders to conventional synthetic (cs) or biologic DMARDs (NCT00960440; NCT00847613; NCT00814307; NCT00856544; NCT00853385; NCT02187055; NCT02831855). Pts received ≥ 1 dose of tofacitinib 5 or 10 mg twice daily (BID) or 11 mg once daily (QD), $\pm$ csDMARDs, or PBO. Least squares (LS) mean Δ BMI (linear mixed model repeated measures; observed cases) was summarised for all treatment groups at M3/6/12 (M3/6 only for tofacitinib 11 mg QD and PBO). Other assessments at M3/6/12 included Δ BMI $\pm$ BL concomitant glucocorticoids (GCs) or antidepressants (descriptive statistics), LS mean Δ DAS28-4(ESR) stratified by BL BMI status (<25 , ≥ 25 – <30 , ≥ 30), and correlations between LS mean Δ BMI and Δ DAS28-4(ESR).

Results: In total, 2349, 1611, 694 and 681 pts received tofacitinib 5 mg BID, 10 mg BID, 11 mg QD or PBO, respectively. Demographics/baseline characteristics were generally similar across treatments, except for some numerical differences in the tofacitinib 11 mg QD group, eg fewer female pts, more White pts and fewer pts receiving concomitant GCs, compared with other treatment groups. At M3/6, LS mean BMI significantly increased from BL with all tofacitinib doses vs PBO (all $p < 0.05$); LS mean Δ BMI was greatest with 10 mg BID and lowest with 11 mg QD (Figure 1a). LS mean Δ BMI was greater in pts receiving tofacitinib as monotherapy vs combination therapy at M3/6/12 (Figure 1b). Δ BMI was generally similar in pts receiving treatment $\pm$ concomitant GCs or antidepressants (data not shown). Improvements in DAS28-4(ESR) were observed in each BL BMI status group at M3/6/12 and were greatest with all tofacitinib doses vs PBO. LS mean Δ DAS28-4(ESR) was generally numerically highest for pts with BMI <25 and numerically lowest for pts with BMI >30 , for all tofacitinib doses. LS mean Δ DAS28-4(ESR) was generally greatest with tofacitinib 10 mg BID and 11 mg QD vs 5 mg BID across BL BMI status groups (Figure 1c). Across treatments, model-adjusted associations between LS mean Δ DAS28-4(ESR) and Δ BMI were weak (correlation coefficients all <0.3 ; Table 1).

Table 1. Correlations between LS mean Δ DAS28-4(ESR) and Δ BMI through M12

	Tofacitinib 5 mg BID			Tofacitinib 10 mg BID			Tofacitinib 11 mg QD			PBO		
	N	Correlation coefficient		N	Correlation coefficient		N	Correlation coefficient		N	Correlation coefficient	
M3	2021	0.1169		1348	0.1240		641	0.0907		554	0.0783	
M6	1918	0.1305		1270	0.1397		611	0.0438		150	0.1556	
M12	1455	0.1213		874	0.1826		-	-		-	-	

Slopes for associations between LS mean Δ BMI and Δ DAS28-4(ESR) were significantly different from 0 at M3/6/12 with tofacitinib 5 and 10 mg BID (all $p < 0.05$). Correlations were analysed by a general linear model method, which included BL age, gender, race and RA duration. For pts receiving tofacitinib 11 mg QD in ORAL Shift (NCT02831855), only data to M6 were included. Pts who advanced from PBO to tofacitinib were not analysed post-advancement-DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; N, number of pts analysed