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

Disclosure of Interests: None declared

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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 & Pharmacoeconomics, 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), ± csDMARDs, or PBO. Least squares (LS) mean ΔBMI (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 ΔBMI ± BL concomitant glucocorticoids (GCs) or antidepressants (descriptive statistics), LS mean ΔDAS28-4(ESR) stratified by BL BMI status (<25, ≥25–<30, ≥30), and correlations between LS mean ΔBMI and ΔDAS28-4(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 ΔBMI was greatest with 10 mg BID and lowest with 11 mg QD (Figure 1a). LS mean ΔBMI was greater in pts receiving tofacitinib as monotherapy vs combination therapy at M3/6/12 (Figure 1b). ΔBMI was generally similar in pts receiving treatment ± 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 ΔDAS28-4(ESR) was generally numerically highest for pts with BMI <25 and numerically lowest for pts with BMI >30, for all tofacitinib doses. LS mean ΔDAS28-4(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 ΔDAS28-4(ESR) and ΔBMI were weak (correlation coefficients all <0.3; Table 1).

Table 1. Correlations between LS mean ΔDAS28-4(ESR) and ΔBMI 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 ΔBMI and ΔDAS28-4(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

Figure. a) LS mean Δ BMI in pts with RA receiving tofacitinib 5 or 10 mg BID, tofacitinib 11 mg QD or PBO* by LS mean Δ BMI in pts with RA receiving tofacitinib monotherapy or tofacitinib in combination with csDMARDs; and c) LS mean Δ DAS28-4(ESR) in pts with RA, stratified by BL BMI status*

Conclusion: LS mean Δ BMI was greater with tofacitinib (all doses) vs PBO at M3/6, and with tofacitinib monotherapy vs combination therapy at M3/6/12. Improvements in DAS28-4(ESR) were seen across all BL BMI status groups. BMI increases with tofacitinib were only weakly associated with DAS28-4(ESR) improvements. The relationship between disease activity and Δ BMI requires further investigation.

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AB0248

INFLUENZA ADVERSE EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE TOFACITINIB CLINICAL PROGRAMME

K. Winthrop¹, A. Yndestad², D. Henrohn³, H. Jo⁴, S. Marsal⁵, M. Galindo-Izquierdo⁶, A. Diehl⁷, A. Shapiro⁸, S. B. Cohen⁹. ¹Oregon Health & Science University, Portland, OR, United States of America; ²Pfizer Inc, Inflammation and Immunology, Oslo, Norway; ³Pfizer Inc, Inflammation and Immunology, Sollentuna, Sweden; ⁴Pfizer Inc, Inflammation and Immunology, New York, NY, United States of America; ⁵Vall d'Hebron Hospital, Rheumatology Department, Barcelona, Spain; ⁶Hospital Universitario 12 de Octubre, Rheumatology Unit, Madrid, Spain; ⁷Pfizer Inc, Inflammation and Immunology, Collegeville, PA, United States of America; ⁸Pfizer Inc, Inflammation and Immunology, Peapack, NJ, United States of America; ⁹Metrolplex Clinical Research Center, Dallas, TX, United States of America

Background: Patients (pts) with rheumatoid arthritis (RA) have an increased susceptibility to seasonal influenza and its complications.¹ In light of the COVID-19 pandemic, there is a need to better understand acute respiratory viral RNA infections, such as influenza, in pts with RA.

Objectives: To present a comprehensive summary of data on influenza adverse events (AEs) occurring in the tofacitinib RA clinical programme.

Methods: Influenza AEs were evaluated in pts with RA from 21 Phase (P)1-3b/4 trials and two open-label, long-term extension (LTE) studies from 2005-2019. These were analysed as two cohorts: P2-3b/4 cohort (pts who received tofacitinib 5 or 10 mg twice daily [BID] as monotherapy or with conventional synthetic [cs]DMARDs, adalimumab, methotrexate or placebo, in P2-3b/4 controlled studies) and Overall cohort (pts who received ≥ 1 tofacitinib dose, as monotherapy or with csDMARDs, in P1-3b/4 and LTE studies; data were summarised by average tofacitinib dose [average tofacitinib 5 or 10 mg BID based on average total daily dose of <15 or ≥ 15 mg,

respectively]). Incidence rates (IRs; unique pts with events/100 pt-years of exposure; censored at day of first event or up to last dose +28 days) were evaluated for influenza AEs, influenza complication AEs, influenza-like illness (all composites of several MedDRA preferred/verbatim terms) and overall influenza AEs (composite of all preferred/verbatim terms included under influenza AEs, influenza complication AEs and influenza-like illness). In the Overall cohort, the incidence of serious non-influenza AEs within 28 days of the start of an overall influenza AE and time taken to resolution of overall influenza AEs by action taken were summarised descriptively.

Results: In total, 7964 pts were included; 517 (6.5%) pts reported overall influenza AEs, three of which occurred outside the risk period. In the P2-3b/4 cohort (N=6690), IRs for influenza AEs, influenza-like illness and overall influenza AEs generally appeared similar across treatment arms (Figure 1a). In the Overall cohort, IRs for influenza AEs and influenza-like illness were similar between tofacitinib doses (Figure 1b), and IRs for overall influenza AEs were similar between tofacitinib doses and pt age groups (Figure 1c). No influenza complication AEs (eg pneumonia/encephalitis/influenza) were reported in either cohort. Among pts with overall influenza AEs, nine (1.7%) had serious overall influenza AEs (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=3). Of these pts, eight (1.5%) were hospitalised (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=2) and two (0.4%) died (average tofacitinib 5 mg BID, n=1; average tofacitinib 10 mg BID, n=1). Both deaths occurred in pts with H1N1 Influenza A. Twelve (2.3%) pts had a serious non-influenza AE within 28 days of the start of the overall influenza AE (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=6). The most common serious non-influenza AEs (one event each in average tofacitinib 5 and 10 mg BID groups) were acute respiratory distress syndrome and pneumonia. In most pts with overall influenza AEs, no change to tofacitinib treatment was made (70.2%, n=363) or treatment was stopped temporarily (28.2%, n=146) for a mean duration of 11.0 days. The mean number of days to resolution of overall influenza AEs was numerically similar, ranging from 10.4-11.8 days across tofacitinib doses, irrespective of these actions.

Figure. IRs (95% CI) for influenza AEs in patients with RA in the a) Phase 2-3b/4 cohort, b) Overall cohort and c) Overall cohort stratified by age group

IRs were calculated as the number of unique pts with events (per 100 PY) during the time between the first and last dose +28 days, divided by the pt time accrued during the first and last dose +28 days, or up to the first event, whichever occurred earlier. 95% CI are based on the Exact Poisson method adjusted for exposure time.
*Total PY of study drug exposure for all pts in treatment group.
*Included all PTs under the high-level term "influenza viral infections", and a collection of VTs for influenza AEs.
*Included the PT "influenza-like illness" and a collection of VTs for influenza-like illness.
*Included all PTs and VTs included under influenza AEs, influenza complication AEs and influenza-like illness; no events of influenza complication AEs were reported.
ADA, adalimumab; CI, confidence interval; MTX, methotrexate; PT, preferred term; PY, pt-years; VT, verbatim term

Conclusion: This post hoc analysis of influenza AEs across the tofacitinib RA clinical programme, over 14-15 influenza seasons, showed generally similar rates between treatment groups, and between tofacitinib doses and pt age groups. Limitations include varying exposure across treatment arms in the P2-3b/4 cohort. Most influenza AEs were non-serious (98.3%), and were not associated with changes to tofacitinib treatment.

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