AB0288

GLUCOCORTICOID SPARING EFFECT OF THE BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS IN TUNISIAN REAL LIFE PRACTICE

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Background: Glucocorticoids (GCs) are still widely prescribed in rheumatoid arthritis (RA). Despite their disease-modifying properties, they are associated with significant adverse effects. The international guidelines recommend the lowest effective dose and the lowest duration of GCs. Previous studies have shown that biologic disease modifying anti-rheumatic drugs (bDMARDs) can have a GC-sparing effect in RA.

Objectives: The aim of the study was to assess the impact of the bDMARDs on glucocorticoids use in rheumatoid arthritis Tunisian patients, in real life practice.

Methods: RA patients (according to the American College of Rheumatology criteria) who started their first bDMARDs (Tumour necrosis factor(TNF) α inhibitors, Tocilizumab and Rituximab) between January 2016 and august 2019, were recruited from the BINAR« Biologic National Registry», a prospective national Tunisian biologic registry. Oral prednisone intake was compared at inclusion (M0), at 3 months (M3) and at 6 months (M6) after bDMARDs initiation.

Results: 175 patients were included (149 females / 26 males). The mean age was 54.1 years $\pm$ 12.6 and the mean disease duration was 6.7 years $\pm$ 3.5. The TNF inhibitors, the Tocilizumab and the Rituximab were prescribed, respectively, in 79.4%, 17.7% and 8.6%. The mean DAS28 index activity was 4.9 $\pm$ 1.5 at M0, 4.5 $\pm$ 1.5 at M3 and 4.2 $\pm$ 1.1 at M6 (p=0.78). At inclusion, 150 patients (85.7%) were taking oral prednisone and the mean dose was 8.2 $\pm$ 5.4 mg/day. Overall, a significant decrease of oral prednisone use was observed at M3 (78%) and M6 (67.6%). The mean daily dose of oral prednisone was 8.9 $\pm$ 4.3 mg at M3 (p>0.05) and 8.1 $\pm$ 2.7 mg at M6 (P>0.05). At M3 and M6, 4% and 2% of patients (p>0.05) had lowered prednisone doses, respectively. Prednisone discontinuation was observed in 17.7% at M3 and 18.1% at M6. Increased prednisone doses were noted in 2.7% at M3 and 2.6% at M6. The bDMARDs use wasn't associated with oral prednisone decrease at M3 (TNFi p=0.51; Tocilizumab p=0.54; Rituximab p=0.77) and at M6 (TNFi p=0.61; Tocilizumab p=0.39; Rituximab p=0.64).

Conclusion: This study showed a small glucocorticoids sparing-effect of bDMARDs at 3 months and 6 months in rheumatoid arthritis patients with a decrease of oral prednisone use of 18.1% at 6 months.

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AB0289

EFFICACY, SAFETY AND IMMUNOGENICITY IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARING PF-06410293 (ADL-PF), AN ADALIMUMAB (ADL) BIOSIMILAR, AND REFERENCE ADL: RESULTS FROM WEEK 26–52 OF A DOUBLE-BLIND, RANDOMISED PHASE 3 STUDY INCLUDING PATIENTS WHO SWITCHED FROM ADL-PF TO REFERENCE ADL AT WEEK 26

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Background: PF-06410293 (ADL-PF) is an adalimumab biosimilar approved for the treatment of several inflammatory and autoimmune indications.¹ The efficacy, safety and immunogenicity of ADL-PF and reference adalimumab sourced from the European Union (ADL-EU) in patients with rheumatoid arthritis (RA) have been demonstrated to be similar in a randomised controlled trial up to 26 weeks (wks; treatment period 1 [TP1]).²

Objectives: To evaluate the efficacy, safety and immunogenicity of ADL-PF and ADL-EU in patients with moderate to severe RA on longer-term treatment, and following a treatment switch from ADL-EU to ADL-PF in a subset of patients.

Methods: This multinational, randomised, double-blind, parallel-group study compared ADL-PF and ADL-EU in essentially biologic-naïve patients with active RA despite methotrexate (MTX) (NCT02480153). In TP1, patients were randomised (1:1) to ADL-PF or ADL-EU (40 mg subcutaneous injection every 2 wks) for 26 wks while continuing MTX (10–25 mg/wk). The primary endpoint

was achievement of American College of Rheumatology response (ACR20) at Wk 12. At Wk 26, the start of treatment period 2 (TP2), patients receiving ADL-EU were blindly re-randomised (1:1) to remain on ADL-EU or switch to ADL-PF for 26 wks while patients receiving ADL-PF continued treatment in a blinded manner. Secondary efficacy endpoints at Wks 26, 30, 36, 44 and 52 (ACR20/50/70, European League Against Rheumatism [EULAR] response, Disease Activity Score [DAS] 28-4[CRP] <2.6 and ACR/EULAR defined remission), safety events and percentage of patients with anti-drug antibodies (ADA) were assessed.

Results: In TP1, 597 patients were randomised to ADL-PF (n=297) or ADL-EU (n=300). At Wk 26, 552 patients were re-randomised for TP2 (continued ADL-PF, n=283; continued ADL-EU, n=135; switched from ADL-EU to ADL-PF, n=134). Patients who demonstrated at least minimal efficacy continued in TP2. Observed ACR20 rates were comparable between treatment groups at all visits during TP2 (Figure). Other measures of deep response (ACR70, EULAR good response, DAS28-4[CRP] <2.6 and ACR/EULAR defined remission) showed maintained efficacy during TP2 in all treatment groups. Incidences of treatment-emergent adverse events were comparable between treatment groups (Table). Overall, incidences of ADA through Wk 52 were comparable between treatment groups (47.3%, 54.1% and 45.9% for patients who continued ADL-PF, continued ADL-EU or switched from ADL-EU to ADL-PF, respectively). In patients who switched from ADL-EU to ADL-PF compared with patients who continued ADL-EU, the increase in ADA incidence over TP2 was 0.8% (from 45.1% to 45.9%) versus 6.7% (from 47.4% to 54.1%), respectively.

Conclusion: TP2 results demonstrated comparable efficacy, safety and immunogenicity between ADL-PF and ADL-EU was maintained up to Wk 56 and was unaffected by a blinded switch from ADL-EU to ADL-PF at Wk 26.

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Figure ACR20 response rates by visit: Treatment Period 2 (ITT population)

ACR20, $\geq 20\%$ improvement in American College of Rheumatology response; ADL-EU, adalimumab sourced from the European Union; ADL-PF, adalimumab biosimilar PF-06410293; ITT, intent-to-treat.

Table. All-causality TEAEs: Treatment Period 2 (Safety population)

	Continued ADL-PF (n=283)	Continued ADL-EU (n=135)	Switched from ADL-EU to ADL-PF (n=133)
Number of AEs	243	112	100
Patients with events, n (%)			
AEs	123 (43.5)	60 (44.4)	51 (38.3)
Serious AEs	4 (1.4)	6 (4.4)	3 (2.3)
$\geq$ Grade 3 AEs	7 (2.5)	7 (5.2)	4 (3.0)
TEAEs leading to treatment discontinuation	6 (2.1)	8 (5.9)	2 (1.5)
Deaths	0	0	0

ADL-EU, adalimumab sourced from the European Union; ADL-PF, adalimumab biosimilar PF-06410293; AE, adverse event; TEAE, treatment-emergent AE.

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AB0290

HERPES ZOSTER INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS EXPOSED TO BIOLOGICAL AGENTS AND JAK INHIBITORS. REAL-WORLD EVIDENCE.

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Background: The overall occurrence of Herpes zoster (HZ) infections in patients with rheumatoid arthritis (RA) is greater than in the general population although is controversial whether the use of the different disease-modifying antirheumatic drugs (DMARDs) increases this risk.

Objectives: To investigate the incidence and factors associate to HZ infections in patients with RA exposed to biologic agents (BA) and small molecule JAK inhibitors (JAKi), and to describe RA disease features at the moment of HZ infection.

Methods: Retrospective longitudinal study was conducted. We included RA patients seen at the rheumatology outpatient clinic of tertiary hospital, commencing BA (anti-TNF therapy and no anti-TNF therapy) or JAKi from Jan 2007 until Dec 2017, and followed up until end of study (Dec 2019). The outcome of interest was the occurrence of HZ infection, the diagnosis of HZ events was based on the rheumatologist's report. Covariables: sociodemographic, clinical, and concomitant treatments including glucocorticoids, conventional synthetic DMARDs (csDMARDs). Survival techniques were used to estimate the incidence of HZ (IR), per 1000 patient-year (PYs) with the respective Confidence Interval [95%CI]. Cox multivariate regression model to compare the risk of HZ was performed. Results were expressed in Hazard ratio (HR).

Results: 474 RA patients were included, starting 881 different courses of treatment (1954.86 patients-years of follow-up). 382 (80.6%) were women with a mean (SD) age of 56.9 (15.0) years at first BA. Across all groups of treatments, a total 18 HZ were recorded, events were non-serious and involved 1 or 2 dermatomes. The mean age (SD) at moment of the infection was 62 (11) years and 10 cases were on prednisone > 7.5 mg/day. 13 HZ cases (72.2%) occurred on treatment with anti-TNF treatment (6 with adalimumab, 4 with certolizumab and 1 with infliximab), 4 (22.2%) cases were on treatment with rituximab one occurred during tocilizumab prescription. The overall incidence of HZ was 9.20 cases per 1000PYs [5.80-14.61]. The crude IR was similar between gender, increased with age (Patients < 46 years: 2.17 [0.3-15.4]; >70 years 14.1 [5.8-33.8]), was higher with concomitant use of two csDMARDs (IR: 15.68 [7.8-31.7], and was similar between anti-TNF and non anti-TNF therapy. None HZ event was recorded in patients exposed to JAKi. In the multivariate analysis, age (HR: 1.05, p: 0.006), prednisone dose > 7.5 mg/day (HR: 2.83, p: 0.02) and the concomitant use of two csDMARDs (HR: 2.34 p: 0.039) increase the risk for HZ. Lymphopenia (HR: 2.6; p=0.06) achieved a trend and BA therapy dropped from the model.

Conclusion: HZ incidence rate was 9.20 cases per 1000PYs, HZ occurrence in RA patients cannot be attributed solely to the current BA or JAKi treatment and other factors involved must be taking in count as age, concomitant DMARDs prescriptions, and use of glucocorticoids. Our data suggest that preventive strategies for HZ should be developed for patients with RA.

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AB0291

RITUXIMAB MAY DELAY THE MOVEMENT OF RHEUMATOID ARTHRITIS PATIENTS ON CARDIORENAL CONTINUUM: RESULTS FROM A PROSPECTIVE OBSERVATIONAL SINGLE-CENTRE COHORT STUDY

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Background: Similarities in risk factors, initial stages, progression and final stage of both atherosclerotic cardiovascular disease (ACVD) and chronic kidney disease (CKD) allowed formulating a concept of cardiorenal continuum.¹ ACVD and CKD remain the main causes of mortality in rheumatoid arthritis (RA) patients.^{2,3}

Objectives: To evaluate the effects of rituximab (RTM) therapy on cardiorenal continuum of RA patients.

Methods: Biologics-naïve RA patients (n=92; age 49.5±9.9) were followed up for 72 months after commencing and continuing RTM therapy (1–10 standard courses) compared with 50 control RA patients (age 49.2±9.8). All control and 63% of RTM patients received methotrexate or leflunomide.

Results: There were no baseline differences between two groups – Table. At year 6, RTM patients have fewer incidences of hypertension, anxiety/depression, atherosclerosis and diastolic dysfunction than controls. RTM decreased prevalence of albuminuria and CKD.

Table. Cardiorenal continuum of rheumatoid arthritis patients (%)

Features	Rituximab group			Control group			p _{RTM-C}
	1 year n=92	3 years n=47	6 years n=31	1 year n=50	3 years n=26	6 years n=16	
Risk factors							
Hypertension	52.2	38.3	25.8 p6– 1=0.022	50.0	38.5	50.0	p6=0.032
Dyslipidaemia	44.6	36.2	38.7	48.0	46.2	50.0	>0.05
Pre-diabetes	41.3	36.2	41.9	44.0	34.6	56.3	>0.05
Metabolic syndrome	12.0	6.4	3.2	10.0	7.7	12.5	>0.05
Diabetes mellitus	3.2	0	0	2.0	0	0	>0.05
Anxiety/depression	78.3	41.5 p3– 1=0.005	35.3 p6– 1<0.001	76.0	73.1	68.8	p3=0.009 p6=0.008
Initial stages (asymptomatic organ damage)							
Atherosclerosis	34.8	21.3	12.9 p6– 1=0.045	36.0	34.6	37.5	p6=0.02
Left ventricular hypertrophy	8.7	4.3	0	8.0	7.7	0	>0.05
Diastolic dysfunction	57.6	38.3	22.6 p6– 1=0.018	56.0	50.0	56.3	p6=0.04
Albuminuria	19.6	0	0 p6– 1=0.038	12.0	0	6.3	>0.05
Kidney impairment	6.5	2.1	0	6.0	0	0	>0.05
Progression							
Angina	6.5	0	0	4.0	0	0	>0.05
Chronic kidney disease	26.1	8.5	9.7 p6– 1=0.042	12.0	0	0	>0.05
End stage							
Myocardial infarction	0	0	0	0	0	0	>0.05
Stroke	0	0	0	0	0	0	>0.05
Heart failure	4.4	0	0	0	0	0	>0.05
Acute/chronic renal failure	0	0	0	0	0	0	>0.05
Death	0	0	0	0	0	0	>0.05

There were no significant differences in frequencies of other risk factors, signs of organ damage and cases of established heart, cerebrovascular and renal diseases/complications.

Conclusion: RTM may be effective in delay of the movement of RA patients on cardiorenal continuum. The clinical implications of RTM for cardiorenal correlations in RA patients need to be confirmed in large-scale clinical outcome trials.

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