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AB0420

DRUG SURVIVAL ON CERTOLIZUMAB AND PREDICTORS THEREOF IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, AND AXIAL-SPONDYLOARTHRITIS FROM THE APULIAN BIOPURE REGISTRY

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Background: In BIO.PU.RE. Registry are collected data from patients being treated with Biologics from rheumatologic centres in Apulia (Southern Italy).

Methods: We analysed longitudinal data of consecutive patients, affected with RA, PsA or axial-SpA starting a treatment with certolizumab (CTZ) in the time frame from 1st January 2011 to 30th June 2017. Demographic and disease related characteristics were collected at baseline and at last observation visit. Primary endpoint was the persistence on CTZ, and secondary endpoint was the search of baseline predictors of drug survival and clinical outcomes. Drug survival was evaluated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs, 95% confidence intervals (CI)) of drug discontinuation or achievement of low-disease/remission in RA, and minimal disease activity (MDA) in PsA at last visit, adjusted for patient's demographics, disease characteristics and prior biologic treatments were computed by Cox-regression stepwise backward models.

Results: 345 patients were included in this analysis (table 1). Global median survival time (95% CI) was 30 [23–36] months. Drug survival rate was significantly higher in SpA (63.9%, p=0.009) than in RA (54.0%) or PsA (54.5%). Within each disease, naïve-CTZ patients showed higher survival rates than biologic-experienced patients in RA (63.4% vs 45.7%, p=0.0001), but not in PsA (59.1% vs 52.3%, p=0.60), or SpA (62.5% vs 64.4%, p=0.94). In the whole cohort, the only negative predictor of drug discontinuation was the CTZ-naïve status (HR 0.62, 95 CI 0.40–0.96, p=0.03). This association was even stronger for RA (HR 0.45, 95 CI 0.26–0.77, p=0.004). In SpA, patient's age at baseline was weakly correlated to CTZ stopping (HR 0.96, 95 CI 0.93–0.99, p=0.02), but no predictor of CTZ discontinuation was detected in PsA. No factor did correlate to the achievement of low disease/remission in RA, while co-medication with MTX was significantly associated to the achievement of MDA (HR 3.82, 95 CI 1.26–11.54, p=0.01) in PsA. Globally, the causes of discontinuation were: ineffectiveness (nr 94, 27.2%), adverse event (nr. 40, 11.6%), pregnancy (nr.1, 0.3%), remission (nr. 3, 0.9%), others (nr.13, 3.8%).

Abstract AB0420 – Table 1

	All (nr. 345)	RA (nr. 172)	PsA (nr.88)	Ax- SpA (nr.83)
Age (mean)	46.9±11	48.8±12	44.4 ±10	45.7 ±11
Female	72.9%	86.2%	71.6%	43.3%
BMI (mean)	27.3±5	26.4±4	29.4±5	26.7±5
Dis Durat (mean)	8.8±8	8.7±8	8.6±7	9.2±9
Naïve	37.1%	47.1%	25.0%	28.9%
Prior biologics	62.9%	52.9%	75.0%	71.1%
Glucocorticoids	64.6%	79.3%	50.0%	41.0%
Methotrexate	60.3%	73.0%	45.5%	27.3%
Comorbidities	62.3%	58.0%	68.2%	65.1%
DAPSA (mean)			22.8 ±12	
DAS28 (mean)		4.8±1		5.4±2
Extra-articular				21.7%
HLA-B27 (nr.44)				64.8%
RF/ACPA +		72.4%		

Conclusions: In our real-life experience CTZ seems to have better drug survival in PsA rather in RA and SpA; in all these polyarthritis was observed CTZ-naïve status as negative predictor of drug discontinuation.

Disclosure of Interest: None declared

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AB0421

LOW RATES OF RETENTION OF BIOLOGIC DMARD MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL LIFE SETTINGS

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Background: A number of cross-sectional studies have shown that approximately one quarter of rheumatoid arthritis (RA) patients are being treated with biologic disease modifying anti-rheumatic drugs (bDMARDs) as monotherapy. Data regarding the retention of bDMARD monotherapy in real-life settings are limited.

Objectives: To study the survival rate of bDMARD monotherapy in RA patients in daily clinical practice.

Methods: Multicenter (11 hospital, 3 private office practices), prospective, RA epidemiological study in Greece. At baseline and after one year of follow-up, demographics, disease characteristics, treatments, co-morbidities and serious events (serious infections, cardiovascular events, neoplasms, osteoporotic fractures) were collected via a web-based platform.

Results: 1,323 RA patients with paired evaluations one year apart (mean interval: 13.2±3.7 months) were included. Among 611 bDMARD treated patients, 155 patients (25%) were on bDMARD monotherapy (women: 87%, mean age: 60.4 years, mean disease duration: 15 years, RF and/or anti-CCP positive: 66%, TNFi therapy: 57%). The majority had been previously on and had discontinued their csDMARDs (90%). During follow-up, 15% (n=24) discontinued their bDMARD; most of them stayed off any type of therapy (83%) while the rest continued with synthetic DMARD (csDMARD) monotherapy (17%). From the remaining 131 patients, 96 (73%) remained on bDMARD monotherapy (85%, n=82 on the same biologic) while in 27% (n=35) a csDMARD was added. Serious events occurred in 7.7% of patients (n=12). Overall, at the end of 1st year, approximately half of patients (53%, n=82) remained on their initial bDMARD monotherapy. Factors associated with continuation of the same bDMARD by multivariate analysis were a low HAQ score (OR=0.48, 95% C.I.=0.23–0.99, p=0.047) and corticosteroid use (OR=2.2, 95% C.I.=1.02–5.1, p=0.044) at baseline as well as the absence of a serious event during the 1st year of follow-up (OR=0.14, 95% C.I.=0.016–1.3, p=0.094).

Conclusions: In real life settings, only half of patients who are on bDMARD monotherapy continue the same agent one year later. Low HAQ score, corticosteroid use and absence of a serious event during therapy predicted bDMARD monotherapy survival.

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AB0422

COST EFFECTIVENESS ANALYSIS OF MODIFIED DOSING REGIMEN OF BIOLOGICAL THERAPY IN CHRONIC INFLAMMATORY DISORDER: AN OBSERVATIONAL STUDY

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Background: Cost of biologics in rheumatology is a prime concern in India. Due to lack of reimbursement system, a majority of the patients need to pay from their pocket for the therapy.

Objectives: Our objective was to estimate the cost-effectiveness in patients with the chronic inflammatory disorder on biological therapy with modified dosing regimen in patients of a tertiary care clinic.

Methods: In this retrospective observational study, data were captured from patients' record in a tertiary care centre located in North India who received biological therapy in rheumatology care practice between 1 January 2013 and 31 December 2017. Modification in the dosing pattern was carried out in the patients and cost of therapy were estimated. These patients, who carried out the therapy, were monitored for any safety outcomes for up to 72 weeks.

Results: During the study period, 342 patients received modified dosing of biologics indicated for rheumatoid arthritis and spondyloarthritis. The cost comparison of biologics is shown in table 1. Among all, 44 (12.86%) patients got reimbursement/claims from central and state government agencies. There were 73 (21.34%) patients who were followed up to 72 weeks (minimum possible) of the period for safety assessment. These patients achieved remission or low disease activity and after six months, mean DAS28 (mean $\pm$ SD) was 2.26 ± 0.83 , BASDAI (mean $\pm$ SD) was 2.32 ± 0.98 and DAPSA (mean $\pm$ SD) was 3.11 ± 1.05 . A total 11 (3.21%) cases of known adverse events including hematuria (1.05% patient with etanercept), pneumonia (4.34% patient with tocilizumab), sinusitis (3.63% patient with infliximab), mild fungal infection (1.81% patient with infliximab) and urinary tract infection (5.26% patient with adalimumab) were reported. One patient (1.05% patient with rituximab) diagnosed with tuberculosis and diabetes after 37 months of initiation of rituximab and one case of hospitalisation was seen due to community-acquired pneumonia in the patient receiving infliximab. Two cases of mortality were reported in patients receiving etanercept after 18 months (due to clinical parkinsonism with aspirational pneumonia) and adalimumab after one month (reason unknown). After modified dosing, the patients tend to remain longer on therapy with no new safety signal.

Abstract AB0422 – Table 1. Cost Comparison of biologics in protocolled vs modified dosing

Biologics	Number of Patients (%) n=342	Monthly Cost of Protocol Driven Dosing (euro/month)	Monthly Cost of Modified Dosing (euro/month)	Cost Benefit for the Patient (euro/month)
Etanercept	112 (32.7%)	303.12 €	151.56 €	151.56 €
Rituximab	95 (27.7%)	118.09 €	58.98 €	59.11 €
Adalimumab	57 (16.6%)	290.49 €	145.25 €	145.25 €
Infliximab	55 (16%)	252.60 €	151.56 €	101.04 €
(3 mg/kg body weight)				
Tocilizumab	23 (6.7%)	353.64 €	176.82 €	176.82 €
(8 mg/kg body weight)				

Conclusions: In developing countries, out of pocket biological cost can be brought down with a lower dose than suggested. In this study, our data show comparable safety and efficacy of biologics achieved till 72 weeks with modified dosing regimen.

Disclosure of Interest: None declared

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AB0423 SEVERE INFECTIONS IN RHEUMATOID ARTHRITIS (RA) ARE RELATED TO THE USE OF BIOLOGIC DMARDS. ASSESSMENT OF REAL-LIFE PATIENTS

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Background: Current strategies for treatment of RA promotes early use of synthetic (s-)DMARDs, their combination, or biologic (b-)DMARDs to achieve remission or low-disease activity. However, such strategies are related to a wide variety of adverse effects, from mild to life threatening. Infections could be detected more frequently among patients with b-DMARDs, although comorbidities, steroid use, chronic accumulated damage, or disease activity could bias such conclusions.

Objectives: To investigate the frequency and severity of infections comparing RA patients users of s-DMARDs or b-DMARDs in a long-term period.

Methods: Patients were selected from our RA Clinic. Those with at least 5 years using b-DMARD were compared with patients on s-DMARD, each one matched by disease duration, age, and comorbidities in a 1:1 ratio. Demographic features, disease characteristics, number and nature of infections during the follow-up, as well as disease activity, and treatment were recorded. Infections were considered as severe when it required hospitalisation or intravenous antibiotics. Comparison between groups was made with X² or t-test as required.

Results: A total of 200 patients were prospectively assessed, 100 per group, mean age was 63.5 ± 12.03 year-old, 91% were female, 78% were RF or ACPA positive, 20% had diabetes mellitus, and 3% other relevant comorbidities. When patients starting the use of b-DMARD, they had more active disease than those in the s-DMARD group (DAS28= 4.99 ± 1.5 vs. 3.91 ± 1.2 ; $p=0.01$). Throughout 5 years of follow-up, there were 18 episodes of severe infections in the b-DMARDs group, and 2 episodes in the s-DMARD group ($p=0.01$); number of non-severe infections was 569 vs. 577 in such period, respectively ($p=NS$). No association was observed between severe infections and presence of diabetes mellitus, cumulative annual dose of prednisone, or DAS28, which did not differ in any other measure between groups. Sixteen patients in b-DMARD had severe infections: 6 acute pyelonephritis, 4 pneumonia, 4 acute bronchitis, 1 infectious diarrhoea, 1 emphysematous cystitis, 1 septic arthritis, and 1 haemorrhagic dengue compared with two severe infections in the s-DMARDs group: 1 pneumonia and 1 infectious diarrhoea. Median of hospitalisation days was 4.5, and no deaths were recorded. Infectious agents isolated were *E. coli*, *C. albicans*, *Salmonella* sp., and *P. aeruginosa*. The most frequent non-severe infections were upper respiratory disease, urinary tract infection, herpes zoster, acute diarrhoea, and bacterial vaginosis. Notoriously, 11 episodes of severe infection occurred in the first 2 years of b-DMARD use (7 in first, and 4 in second year), the other 7 in remaining 3 years. b-DMARDs more frequently used were etanercept, rituximab, adalimumab, certolizumab pegol, and tocilizumab, without association between severe infections and any biologic agent.

Item	b-DMARD group	s-DMARD group	p value
Gender M/F (n%)	6/94 (6%/94%)	12/88 (12%/88%)	NS
Age years (mean $\pm$ SD)	62.64 $\pm$ 10.14	64.43 $\pm$ 13.63	NS
BMI Kg/m ² (mean $\pm$ SD)	27.23 $\pm$ 4.61	26.95 $\pm$ 4.81	NS
Disease duration months (median)	156	156	NS
Initial DAS28 (mean $\pm$ SD)	5.14 $\pm$ 1.37	3.99 $\pm$ 1.26	0.001
Average cumulative annual prednisone dose	388.12	378.77	NS
Diabetes mellitus yes/no (n%)	22	21	NS
Other comorbidities yes no (n%)	5	2	NS
Severe infections yes/no (n%)	18	2	.003
Average patient's annual non-severe infections	1.154	1.138	NS

Abstract AB0423 – Figure 1

Conclusions: b-DMARDs use in our setting, combined with low dose methotrexate, reach higher frequency of severe infections than s-DMARDs, irrespective of comorbidities, steroid use or disease characteristics including disease activity.

Disclosure of Interest: None declared

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AB0424 IL-6 RECEPTOR BLOCKADE INDUCED A DIFFERENT IMMUNE RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT REMISSION

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Background: Tocilizumab (TCZ) is a humanised antibody that blocks IL-6 receptor. Despite its effectiveness in rheumatoid arthritis (RA), there are patients that do not respond to the IL-6R blockade. The immune characteristics that would explain this lack of response are not known.

Objectives: Our aim was to determine the tocilizumab-induced changes in CD4 + T cells of patients that achieve, or not, remission at 12 m.

Methods: Prospective, multicenter study in 47 RA patients treated with TCZ during one year following standard clinical practice. Demographic, disease and treatment characteristics were collected at each visit. Ultrasound (US) grey scale and power doppler were assessed for joints and tendons using a semiquantitative scale from 0–3 points. Phenotyping of T lymphocytes was determined by flow cytometry and the plasma cytokine concentration was quantified by ELISA.

Results: Forty seven patients were treated with a mean age of 54 ± 11 y and 85% were women. Years of disease were 13 ± 8 . We segregated patients according to the DAS28-remission. 44% achieved remission at month 12. We observed that absolute counts of neutrophils and CD4 + T lymphocytes decreased significantly in the remission group but not in the other one. Both memory and naïve CD4 + T