AB0306

EXPERIENCE WITH RITUXIMAB BIOSIMILAR BCD-020 IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL PRACTICE ACCORDING TO DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

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Background: The introduction of perspective anti-rheumatic biologic agents into clinical practice has not only increased therapy efficacy and improved medical prognosis in patients with rheumatoid arthritis (RA), but also resulted in a dramatic increase in treatment cost and, therefore, in a reduced accessibility of the innovative treatment for patients. For this reason, over the last years, there has been a huge interest towards developing biosimilars [1,2].

Objectives: To assess the effectiveness and safety of switching from reference rituximab (RTX_{ref}) to rituximab biosimilar (RTX_{bs}) BCD-020 in patients with RA in real clinical practice according to the data from MUAR.

Methods: Patients with RA who treated by RTX_{ref} at the onset and then switched to RTX_{bs} (BCD-020) were enrolled in the study. For all patients were performed: swollen and tender joints count, ESR, CRP, biochemistry and immunologic blood analyses. Assessment of dynamic of DAS28, RAPID3, HAQ-DI was performed. The great attention was given to the therapy safety assessment. RTX_{ref} effectiveness and safety profile was assessed at the moment of switching; data for RTX_{bs} (BCD-020) were collected not earlier than 6 months after switching.

Results: 46 patients with RA were enrolled, 80.5% were women; the mean age was 59.5±12.2 years; 91.3% were RF-positive, 63% - ACCPA-positive, the disease activity at the moment of switching was moderate, the mean DAS28 was 3.5. The duration of RTX_{ref} therapy until switching was 36.8 ± 26.8 months; the duration of the follow-up period for BCD-020 biosimilar was 12.1 ± 6.18 months. In 43.5% of patients, previously inefficiency or intolerance of other biologics was discovered. The proportion of patients who received concomitant therapy with glucocorticoids or methotrexate (MTX) was 45.7% and 43.5%, respectively. The mean MTX dose was 13.6 mg/wk. The mean dose of RTX_{ref}/BCD-020 was 1000 mg. The stability dynamic of clinical parameters was retained after switching to biosimilar (Tab.1) without significant difference between the rituximab products (p>0.05).

Table 1. Comparison of Efficiency Parameters for the Reference Rituximab and Biosimilar BCD-020

Parameter	Reference rituximab	Biosimilar BCD-020
DAS28 (ESR)	3.39	3.34
HAQ-DI	1.48	1.44
RAPID3	12.9	12.6

The safety profile of RTX_{ref} and RTX_{bs} (BCD-020) was also similar. None of the patients discontinued BCD-020 therapy for reasons related to safety or inefficiency.

Conclusion: Within the framework of routine clinical practice, switching from reference rituximab to BCD-020 biosimilar is not accompanied by a change in efficiency and safety profile of the therapy and does not pose a risk of discontinuation, which is coherent with the results of the registration clinical trial for BCD-020. [3]

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AB0307

DOES FCGR2A, FCGR3A AND FCGR3B POLYMORPHISM CAN PREDICT ANTI-DRUG ANTIBODIES APPARITION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TNF-BLOCKERS?

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Background: Fc gamma receptors (FcγRs) play a major role in the regulation of humoral immune responses. Single-nucleotide polymorphisms (SNPs) of FCGR2A and FCGR3A and FCGR3B can impact the expression level, IgG affinity and function of the CD32 and CD16 FcγRs in response to their engagement by the Fc fragment of IgG. It was described in patient treated for rheumatoid arthritis (RA), that such a polymorphism may influence patients response to TNF-blockers.

Objectives: In this study, we aimed to investigate whether the FCGR2A H131R (rs1801274), FCGR3A F158V (rs396991), and FCGR3B NA1/NA2 polymorphisms can be involved in the genesis of anti-drug-antibody ADA_b to anti-TNF therapy in RA patients under etanercept (ETA), adalimumab (ADL) and infliximab (INF).

Methods: We included 47 patients treated for RA under TNF-blockers. To assess the association between the FCGR2A H131R (rs1801274), FCGR3A F158V (rs396991), and FCGR3B NA1/NA2 polymorphisms and immunogenicity of TNF-blockers, we used allele contrast, the recessive model, the dominant model, and the homozygote contrast. Quantitative measurements of the ADA_bs was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®) after 6 months of treatment.

Results: We involved 18 patients treated with ETA, 13 patients with ADL and 16 under INF. None of the patients under ETA has developed ADA_b and respectively 1 and 7 patients developed immunogenicity with ADL and INF. We excluded patients under ETA from statistical study since they didn't develop ADA_b. A significant association was revealed between FCGR2A H131R polymorphism and immunogenicity of INF and ADL (table 1).

Table 1. Association between FCGR2A polymorphism and immunogenicity to INF and ADL

FCGR2A association with ADA_b
(n=29, crude analysis)

Genotype	ADA _b =0	ADA _b =1	OR (95% CI)	P-value
H/H	1 (4.8%)	3 (37.5%)	1.00	0.031
H/R-R/R	20 (95.2%)	5 (62.5%)	0.08 (0.01-0.98)	

There weren't significant associations between ADA_b's development and FCGR3A F158V and FCGR3B NA1/NA2 polymorphism.

Conclusion: FCGR2A R allele carriers show less susceptibility to develop ADA_b to ADL and INF with follow-up times of 6 months. Our results provide an explanation for controversies in the relationships between FCGR2A H131R polymorphism and TNF-blockers response. Further studies with larger population of RA patients should be undertaken to confirm this hypothesis.

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AB0308

NO SIGNS OF CONGESTIVE HEART DISEASE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS ON IL-6 RECEPTOR ANTAGONIST AFTER 12 MONTHS TREATMENT

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Background: N-terminal pro-brain natriuretic peptide (NT-proBNP) is a known marker of heart dysfunction, mainly described in patients with high activity of rheumatoid arthritis (RA). Further knowledge of the influence of the IL-6 receptor

antagonist, tocilizumab (TCZ), on NT-proBNP levels and systolic heart function is yet to be obtained.

Objectives: Access the effect of 12 months TCZ therapy on NT-proBNP levels, transthoracic echocardiography results and analyze the association between congestive heart disease progression and RA activity.

Methods: 37 RA patients (pts) (31F/6M); median age 56,5 [48; 63,5] years; disease duration 48 [6; 348] months; DAS28 score 6,15 [5,44; 6,45]; rheumatoid factor (RF)+100%; anti-citrullinated protein antibody (ACPA) + 79,6% were treated in an open-label study with TCZ (8mg/kg every 4 weeks). Identification of NT-pro-BNT in blood serum, transthoracic ultrasound evaluation of left ventricle ejection fraction (LVEF), E/A ratio performed at baseline and 12 months.

Results: 11 (29,7%) pts had congestive heart disease (CHD) (II functional class of NYHA), 7 (18,9%) pts having signs of mild left ventricular dysfunction (LVD) as dyspnea, shortness of breath, cardiotropic treatment remained the same in the course of the study. After 12 month TCZ treatment as RA activity lowered (DAS28 2.32 [1,75; 3,15], $p < 0,05$), NT-proBNP levels decreased (100,95 [57,9; 117,6] pg/ml to 90,46 [33,62; 106,6] pg/ml), along with elevation of LVEF (60,75 [60; 70]% to 67,68 [62,5; 73,5], $p = 0,001$). Increase of E/A (0,97 [0,8; 1,17] to 1,04 [0,7; 1,42] correlated with decrease of NT-proBNP level ($r = -0,63$, $p = 0,036$). Raise of LVEF over 12 months correlated with decrease of RA activity according to SDAI scale ($r = -0,670$, $p < 0,05$). No significant relationship between NT-proBNP levels, LVEF, E/A and other scales measuring RA activity was found. Clinically all patients had improvement in evaluation of their health and no signs of CHD or RVD progression were found.

Conclusion: Use of TCZ in patients with active RA showed none to positive influence on heart condition, specifically, lowering NT-proBNP levels, improving LVEF and reducing clinical signs of LVD.

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AB0309

MEASURING THE DIFFERENCE: COMPARISON OF MEASUREMENT OF FREE INFILIXIMAB ANTI-DRUG ANTIBODIES

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Background: Infliximab (IFX) was one of the first TNF alpha inhibitors to be licenced in inflammatory arthritis and is still commonly used today. Studies have shown that approximately 50% of primary IFX responders will suffer from secondary loss of response within the first 12 months of treatment (1). The development of Anti-Drug Antibodies (ADAs) plays a significant role in this treatment failure (2).

Monitoring of ADAs helps identify those patients who fail to respond to treatment due to low IFX trough levels. In this scenario the presence of ADAs can aid decision-making regarding increasing IFX dosing or switching biologic therapy to optimise treatment. (3).

Objectives: Despite their potential importance the detection of ADAs varies widely depending on the type of assays used. The aim of this study was to determine the qualitative concordance of three commercially available ELISA kits for measurement of free ADAs to IFX on the Grifols Triturus analyser.

Methods: 150 patient samples from patients with inflammatory conditions and low IFX trough drug levels ($\leq 0,6\mu\text{g/ml}$) were analysed for free ADAs using Promonitor, Lisa Tracker and IDKmonitor kits on the Grifols Triturus automated ELISA analyser.

Results: Kappa coefficient (κ) analysis indicated a moderate agreement between the Promonitor and IDKmonitor assays ($\kappa = 0,484$ (95% CI, 0.357 to 0.611)) and the IDKmonitor and Lisa Tracker assays ($\kappa = 0,485$ (95% CI, 0.348-0.621)) as well as substantial agreement between the Promonitor and Lisa

Tracker assays ($\kappa = 0,768$ (95% CI, 0.667-0.870)). Figure 1 shows the distribution of samples identified as free ADA positive by each kit.

Figure 1. Distribution of samples identified as free ADA positive by Promonitor, Lisa Tracker, and IDKmonitor assays. Fifty samples were considered positive by all assays. Three samples were considered positive by Promonitor and Lisa Tracker, and eight samples were considered positive by Lisa Tracker and IDKmonitor. No samples were considered positive by Promonitor and IDKmonitor. One sample was considered positive by Promonitor only, seven samples were considered positive by Lisa Tracker only, and twenty-six samples were considered positive by IDKmonitor

Conclusion: All kits appear amenable for utilisation in a high-throughput laboratory though a true quantitative comparison between these kits was precluded by the absence of any certified reference material for free ADAs to IFX.

Although broad qualitative agreement was found between the three kits, they should not be used interchangeably for patient management.

Further research is required to estimate the impact of free ADAs on efficiency of IFX treatment and patient management.

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AB0310

TROUGH CONCENTRATION AND ESTIMATED CLEARANCE CAN DETECT IMMUNOGENICITY TO ADALIMUMAB IN RA PATIENTS: A PROSPECTIVE LONGITUDINAL MULTICENTRE STUDY

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