AB0365

EFFICACY OF TOCILIZUMAB FOR CORTICOSTEROID AND METHOTREXATE SPARING IN RHEUMATOID ARTHRITIS

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Background: Successful management of rheumatoid arthritis (RA) depends on the early administration of DMARDs and biologic DMARDs. The biologic agent tocilizumab, an interleukin-6 receptor inhibitor, has been used for the management of RA.

Objectives: The aim was to describe a cohort of RA patients treated with tocilizumab and the effect of this treatment on the other DMARDs used, namely methotrexate and corticosteroids.

Methods: In a cohort of 80 patients with rheumatoid arthritis the biologic agent tocilizumab was administered in combination with methotrexate administered sc and 10 mg prednisolone. Within this cohort, 26 patients were on tocilizumab administered iv 8 mg/kg/4wks (maximum dose 800 mg) and 54 were on tocilizumab administered sc 162mg/wk. As corticosteroid administration is characterized by adverse effects, such as osteoporosis and diabetes mellitus, in the course of the disease, in all patients an effort was made to reduce and, if possible, withdraw corticosteroids. An effort was also made to reduce methotrexate dosage. After a year, prednisolone was either significantly reduced or withdrawn. The final dosage of prednisolone was either 2.5-5 mg or complete withdrawal. The successful reduction of methotrexate dosing schedule was also achieved. The final methotrexate dose was either 12.5 mg sc or complete withdrawal. After a period of 52 weeks in this cohort 42 of 80 patients (52.5%) were on monotherapy with tocilizumab.

Results: In a cohort of 80 patients with RA the administrations of tocilizumab, either iv or sc, proved safe and effective. Remission or low disease activity of RA was achieved. Corticosteroid dosage was reduced. Methotrexate dosage was also reduced. After 52 weeks within the group of RA patients on treatment with tocilizumab, in 42 complete withdrawal of corticosteroids and methotrexate proved feasible. Patients on tocilizumab monotherapy remained in remission.

Conclusion: It appears that tocilizumab is safe and effective for the treatment of RA. Tocilizumab treatment may permit withdrawal of both corticosteroids and methotrexate in patients with RA. The management of active RA initially with low dose corticosteroids in combination with methotrexate sc and, in the case of failure to achieve remission, with the addition of the biologic agent tocilizumab had as a result either significant corticosteroid reduction or complete withdrawal and reduction of methotrexate dosage, the disease remaining in remission.

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AB0366

COMPARISON OF THE EFFECT OF RITUXIMAB (ROCHE) AND RITUXIMAB BIOSIMILAR – BCD-020 (BIOCAD) ON INFLAMMATORY AND IMMUNOLOGICAL BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: BCD-020 (BIOCAD) is the first Russian rituximab (RTX) biosimilar which was approved for medical use in rheumatoid arthritis (RA) patients in Russia and some CIS countries

Objectives: To evaluate the changes in acute phase reactants, autoantibodies, immunoglobulins, cytokine profile and CD19+B lymphocytes in patients (pts) with RA during RTX and RTX biosimilar therapy

Methods: The study included 54 RA patients (pts), divided into two groups. The first group included 34 pts with RA (31 women, mean age 49(42-64), mean disease duration 66(36-132) months, mean DAS 28 6.2 (5.5-6.8)) who received two infusions of RTX - 35% at a dose of 500 mg, 65% of the dose of 1000 mg every two weeks in combination with DMARDs and glucocorticoids; 33 pts achieved a good/moderate EULAR response at week 24. The second group - 20 pts with RA (18 woman, mean age 61.5(54-66.5) years, mean disease duration 39.5(20-84) months, mean DAS 28 5.6(4.9-6.8)) who received two intravenous BCD-

020 infusions (600mg No 2) in combination with DMARDs and glucocorticoids; 17 pts achieved a good/moderate EULAR response at week 24. Laboratory biomarkers were assessed at baseline and weeks 12 and 24 after the first infusion of RTX. ESR (mm/hr) (Westergren method); serum concentrations of CRP (mg/L), IgM RF (IU/ml) (laser nephelometry); anti-CCP2 (U/ml), IgA RF (U/ml), anti-MCV (U/ml) (ELISA kits); cytokine profile (xMAP technology) were assessed

Results: RTX and BCD-020 induced decreases in ESR, levels of CRP, IgMRF, IgARF, anti-MCV at week 12 and 24, p<0.05 (tabl.1). At week 24 - 20% of IgMRF positive pts at baseline (in the first group) and 10% of IgMRF positive pts (in the second group) turned negative. Levels of anti-CCP2 did not reduced. At week 24 - 7% of anti-CCP2 positive pts at baseline (in the first group) and 15% of anti-CCP2 positive pts (in the second group) turned negative. Depletion of CD19+B-cells was achieved at week 12 in all patients (absolute number 0), with an increase in the level of B cells at week 24, tabl.1. The immunoglobulin level decreased at week 24, but remained normal. In the first group RTX induced reduction in proinflammatory (IL-1b, IL-2, IL-6, IL-12, IL-15, IFN-γ, TNF-α), anti-inflammatory cytokines (IL-1Ra, IL-5, IL-9, IL-10, IL-13), growth factors (IL-7, GM-CSF, FGF-basic) and chemokines (MC-1) at week 24 (fig.1). In the second group BCD-020 induced reduction in IL-1b, IL-1Ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, Eotaxin, G-CSF, IFN-γ, IP-10, MC-1, MIP-1β, TNF-α, VEGF at week 24 p<0.05, fig.1.

Figure 1

Conclusion: RTX biosimilar (BCD-020) has a similar effect on inflammatory and immunological biomarkers to the original RTX. BCD-020 therapy induced a rapid and significant improvement in ESR, levels of CRP, IgM/IgARF, anti-MCV, proinflammatory, anti-inflammatory cytokines, growth factors, chemokines levels and CD19+B cells depletion in RA pts

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AB0367

REASONS FOR DISCONTINUATION OF BIOLOGICAL DRUG AND TARGETED SYNTHETIC DRUGS AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS IN THE UNITED ARAB EMIRATES (UAE)

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Background: In routine clinical care of Rheumatoid arthritis (RA) Spondyloarthritis (SPA) and Psoriatic arthritis (PSA) there is a high rate of discontinuation of biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) due to loss of efficacy, side effects or lack of adherence. This can impact on the ability to achieve low disease activity.

Objectives: To evaluate the use of bDMARDs and tsDMARDs and analyze the reasons for discontinuation of these drugs and to compare them to our standard DMARD Methotrexate.

Methods: In this retrospective cohort analysis we included consecutive patients aged ≥ 18 years with RA/SPA/PSA attending 2 Rheumatology clinics in the UAE from August- December 2019. Statistical analysis was performed using STATA version 13 and R-studio. Continuous data were

summaries as mean and SD. Dichotomous data were presented as percentage. Chi square test, Proportion test and T-test were applied based on the data type and its distribution to calculated P-value at a 5% level of significance

Results: Of 745 patients who were included, 453 (60.8%) had RA, 165 (22.5%) SPA, and 127 (16.7%) PSA. Of these a total of 353 (47.3%) received 565 treatment courses with bDMARDs and 106 patients had (14.2%) had 110 treatment courses with tsDMARD, and 480 (64.4%) Methotrexate (MTX)

100/353 (28.3%) of patients discontinued bDMARDs; 35/106 (33.0%) of patients discontinued tsDMARDs; and 254/480 (52.9%) MTX. 52% of treatment courses of bDMARD and 36% courses of tsDMARD were discontinued. Reasons for discontinuation are in table 1.

Factors such as age, gender, ethnicity were not significantly associated with the rate of discontinuation of medications (Chi-square test). 647/745 (86.6%) of patients had medical insurance, however lack of insurance did not lead to discontinuation of bDMARDs (OR=0.54 95% CI (0.22 to 1.32)) and tsDMARDs (OR= 1.59 95% CI: (0.3 – 8.3)). A significant proportion of patients (15% -18%) in all the three groups have stopped the drugs of their own choice. We did not observe any statistical significant difference between the active and discontinued categories with respect to disease activity scores DAS 28 for RA; BASDAI for SPA and HAQ score for PSA.

Table 1. Distribution of different medications

Number of patients	bDMARDs (n=353)		tsDMARDs (n=106)		Methotrexate (n=480)		P value
Actively on Rx	253	72%	71	67%	226	47%	<0.001*
Discontinuation	100	28%	35	33%	254	53%	
Total	353	100%	106	100%	480	100%	
Reasons for Discontinuation							
Unknown reason	8	8%	4	11%	18	7%	0.66
Side effect	8	8%	4	11%	92	36%	<0.001*
Primary loss of efficacy	10	10%	9	26%	18	7%	0.001*
Secondary loss of efficacy	27	27%	10	29%	46	18%	0.101
Doctors choice	7	7%	1	3%	11	4%	0.486
Patient choice	17	17%	1	3%	37	15%	0.118
Pregnancy	5	5%	0	0%	24	9%	0.075
Remission	10	10%	3	9%	8	3%	0.025*
Financial	6	6%	3	9%	0	0%	<0.001*
Infection	2	2%	0	0%	0	0%	0.001*
Total	100	100%	35	100%	254	100%	

P value is computed using proportion test

* statistical significance difference at 5%

Conclusion: A significantly higher proportion of patients discontinued MTX as compared to bDMARDs and tsDMARDs. Major reason for stopping MTX was side effects while bDMARDs and tsDMARDs were mainly stopped due to loss of efficacy or financial reasons. Safety and tolerability of bDMARDs and tsDMARDs was good in our cohort of patients.

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AB0368

SAFETY OF COMBINATION THERAPY WITH TWO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: About 20% to 40% of patients with rheumatoid arthritis (RA) treated with biologic therapies fail to achieve remission consequently

requiring additional treatment (1-4). Combining different biologic agents could be a promising therapeutic strategy. However, the safety and tolerability of combining different biologic agents is one of the major concerns of this treatment approach.

Objectives: We performed a systematic review and meta-analysis of the current literature to assess the safety of combining two bDMARDs (biologic disease-modifying anti-rheumatic drugs) in the treatment of patients with RA.

Methods: We searched PubMed, the Cochrane Library, Scopus, Clinical-Trials.gov, and the WHO International Clinical Trials Registry platform through 12/18/17. Our eligibility criteria included human RCTs or observational or non-randomized comparative studies in adults (≥ 18 years of age) that recorded safety of combination therapy with two bDMARDs in RA patients. We used R version 3.1.2 to perform meta-analysis between groups on combination therapy and placebo/single therapy alone using random effect model calculating odds ratio (OR) as well as 95% confidence interval (CI). Cochran Q statistic and I^2 statistic was used to identify heterogeneity between studies. The primary outcome was the rate of major serious events. Additional outcomes were the rate of total adverse events, total infectious events and major infectious events.

Results: Six studies with a total of 623 patients (410 on combination therapy and 213 on single therapy) were included for meta-analysis. Median follow-up was 9.5 months (range 6-12 months). There was a significant increase in SAEs in the combination group (14.9 vs 6.0%, OR 2.51, 95% CI 1.29-4.89, I^2 0%) as well as in total adverse events (94.6 vs 89.1%, OR 2.07, 95% CI 1.11-3.86, I^2 0%). When performing subgroup analysis in patients receiving only full-dose of both bDMARDs there was a significant increase in serious infections (6.7 vs 0.6%, OR 5.58, 95% CI 1.25-24.90, I^2 0%) and the risk of SAEs remained significantly higher (17.1 vs 6.2%, OR 2.72, 95% CI 1.30-5.69, I^2 0%).

Conclusion: Our findings suggest that combination therapy with two bDMARDs in RA patients appears to increase the risk of SAEs during the first twelve months of treatment.

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AB0369

SAFETY, EFFICACY AND RETENTION RATE OF BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (bDMARDs) IN ASSOCIATION WITH DENOSUMAB: COMPARISON OF COMBINATION AND MONO-THERAPY REGIMENS

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Background: Osteoporosis is a frequent complication of rheumatic muscle-skeletal diseases (RMD), with high impact from steroid treatment. It is known that bDMARD impact positively on patients' prognosis and this is also known for Denosumab, a monoclonal antibody for osteoporosis. The combination treatment with two monoclonal antibodies, bDMARD & denosumab, has addressed the problem of safety and efficacy, with incomplete answers from the available literature.

Objectives: to evaluate the impact of the combination treatment bDMARD + Denosumab (COMBO group), compared to mono-therapy with bDMARD (MONO group), on clinical efficacy, safety and treatment retention of bDMARD in patients with RMD.