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 as 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, ClinicalTrials.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.

Methods: RMD patients treated with COMBO therapy were enrolled from a single centre rheumatology unit; for each case, at least one MONO therapy control (matched per age $\pm$ 5 years, sex, bDMARD, RMD, without osteoporosis) was enrolled. Data on clinical efficacy (3-points Likert scale for physician and patient – improved/stable/worse), safety (local reaction, serious and non-serious adverse events) and bDMARD treatment retention at 12, 18 and 24 months.

Results: Out of 129 eligible patients, 77 were enrolled in the protocol: 49 in the MONO and 28 in the COMBO group. The two groups were different of age (slightly higher in the COMBO group), for tender joint count, erythrocyte sedimentation rate and c-reactive protein (higher in the MONO group). Efficacy analysis showed higher percentage of clinical improvement at 12 months in the MONO group at 12 months, being not significant at 18 and 24 months (possibly explained by a different disease activity at baseline visit, corresponding to the overlap of denosumab on top of bDMARD in the COMBO and to the initiation of bDMARD in the MONO group). Between the 2 groups, no difference about safety and retention rate was found.

Conclusion: the efficacy of COMBO treatment is similar to MONO therapy. Moreover, the data show that also safety and retention rate are similar. Therefore, the COMBO treatment with 2 different monoclonals can be safely employed in the treatment of RMDs and osteoporosis.

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AB0370 EFFICACY AND SAFETY OF BIOLOGIC TREATMENT IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS: A WIDE COHORT STUDY

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Background: Given the data on efficacy and safety of biologic treatment in rheumatoid arthritis (RA), more and more patients older than 65 years are starting these drugs.

Objectives: This study aims to evaluate safety and efficacy of biologics in elderly patients.

Methods: four-hundred and thirteen patients with RA were enrolled and divided in two group, i.e. older or younger than 65 years old. Data on disease characteristics, treatment and adverse reactions were collected. In addition, comorbidities were evaluated by the Rheumatic Disease Comorbidity index (RDCl).

Results: Seventy-seven patients were male and 87 were older than 65 years. The elderly patients had a higher RDCl as compared to those younger than 65 years (1.0 ± 3.0 vs. 0.0 ± 10 respectively, $p < 0.001$). Mean DAS28 at the beginning of biologic treatment was 4.46 ± 1.16 . Most of patients started etanercept (41.4%) or adalimumab (26.9%) and 37.1% were on monotherapy. None of these variables were statistically different between age groups. The figure shows the differences in retention rate of first biologic at 60 months in the two groups that was found to be significantly higher in older than younger patients (43.3 vs. 48.5, $p = 0.023$). This result was confirmed also after correcting for comorbidities as defined by RDCl ($p = 0.014$). On the contrary, no differences were found in retention rate on any biologic (i.e. not only first line) between age groups ($p = 0.509$). The main reason for biologic treatment discontinuation was inefficacy in both groups (74.7% in <65 years old and 58.6% in ≥ 65 years old, $p = 0.161$). The most common side effects in elderly patients were hematological complications (30.4%) while in younger patients muco-cutaneous (32.4%) adverse reactions. Infections were a reason for discontinuation in 17.4% in old patients and 20.6% in younger ones ($p = 1.000$).

Conclusion: RA patients aged over 65 years have been found to have even a better retention rate at first biologic than younger one, probably because of less strict targets in disease control and a more frequent follow up. In addition, safety has been found to be as good as in younger patients. Comorbidities do not seem to affect retention rate.

Figure. Retention rate in patients <65 years old (blue line) vs patients ≥ 65 years old (green line) ($p = 0.023$).

Figure 1

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AB0371 LONG TERM RITUXIMAB PERSISTENCE FOR RHEUMATOID ARTHRITIS IN THE REAL WORLD: THE RITAR STUDY

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Background: Rituximab (RTX) is a B-lymphocyte depleting monoclonal antibody that was approved for rheumatoid arthritis (RA) treatment in Europe in 2006.

Objectives: To analyse factors affecting long term persistence of RTX for the treatment of RA patients in daily clinical practice.

Methods: RITAR (Rituximab en Artritis Reumatoide) is a retrospective, open-label, observational study that describes the patterns of use and long term persistence of RTX in a tertiary university hospital from 2003 to 2015. We collected demographic, clinical and therapeutic variables. Patients who discontinued RTX were considered events whereas patients lost for follow-up and non-RTX-related deaths were censored. Statistical analysis was performed with STATA 12. Kaplan-Meier survival analysis, Log-rank test and Cox Regression were used. A multivariable Cox-proportional hazards model was fitted to determine which variables were most likely related to RTX persistence.

Results: 114 patients were included: 80.7% women, median age 60 years (IQR 51-69) and median RA duration 11 years (IQR 6-16). Most patients were FR/ACPA positive (93.0%). Retreatment schedule was 94.6% on demand and 5.4% fixed-retreatment every 6 months. In the 1st cycle RTX monotherapy used in 12.2% and gradually increased over time. The mean RTX dose by cycle was 1,733 mg (DE: 294): 324 x 2000 mg and 130 x 1000 mg. RTX was used as 1st biologic in 19.3%. Median response duration was 10 months (IQR 7-13).

We observed 38 events, 22 patients were censored and 54 remained on RTX treatment at the end of the study. Follow-up time in analysis was 484.84 years. Median survival was 9.98 years, withdrawal rate was 7.67/100 patients-year. Reasons for discontinuation were 21.0% ineffectiveness, 8.7% adverse events and 3.5% deaths probably related with RTX.