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.

REFERENCES

- [1] Ebina K, et al. Drug retention and discontinuation reasons between seven biologics in patients with rheumatoid arthritis -The ANSWER cohort study. *PLoS One*. 2018 Mar 15;13(3)
- [2] Favalli EG, et al. Real-life 10-year retention rate of first-line anti-TNF drugs for inflammatory arthritides in adult- and juvenile-onset populations: similarities and differences. *Clin Rheumatol*. 2017 Aug;36(8):1747-1755.

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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.

REFERENCES

- [1] Lipsky PE, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-Tumor Necrosis Factor Trial in Rheumatoid Arthritis with Concomitant Therapy Study Group. *N Engl J Med*. 2000 Nov 30;343(22):1594-602.
- [2] Weinblatt ME, et al. Adalimumab, a fully human anti-tumor necrosis factor alpha monoclonal antibody, for the treatment of rheumatoid arthritis in patients taking concomitant methotrexate: the ARMADA trial. *Arthritis Rheum*. 2003 Jan;48(1):35-45.
- [3] Keystone EC et al. Once-weekly administration of 50 mg etanercept in patients with active rheumatoid arthritis: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2004 Feb;50(2):353-63.
- [4] Weinblatt ME, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. *N Engl J Med*. 1999 Jan 28;340(4):253-9.

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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.