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

cells decreased in the remission group. The analysis of T cells classified according to chemokine receptors showed that memory (29.1 ± 4.0 vs $22.7 \pm 2.7 \times 10^4$ cells/mL; $p=0.06$) and naïve (22.6 ± 4.1 vs 17.2 ± 2.8 ; $p=0.04$) CD4 +with CXCR3 +and with CCR4 +were the subsets that decreased significantly in the remission group but not in the non-remission group. Since the expression of chemokine receptors defines the different Th subpopulations, we analysed them in the two groups of patients. Th1 tended to decreased in the remission group (3.5 ± 0.7 vs 2.5 ± 0.4 ; $p=0.06$) and Th9 decreased significantly in both groups ($R: 5.0 \pm 0.8$ vs 2.5 ± 0.3 ; $p=0.006$ and Non $R 5.5 \pm 0.8$ vs 3.1 ± 0.4 ; $p=0.001$). In regard to the cytokines produced by CD4 +T lymphocytes, IL-17 (2.1 ± 1.1 vs 1.2 ± 0.5 ng/ml; $p=0.04$) and VEGF (0.5 ± 0.2 vs 0.3 ± 0.1 ng/ml; $p=0.05$) but not IL-6 and IL-22 changed significantly in the remission group. Interestingly, IL-17 and VEGF correlated with US findings before the initiation of the treatment (grey scale $R=0.378$, $p=0.01$ and $R=0.322$, $p=0.03$; power Doppler $R=0.415$, $p=0.004$ and $R=0.320$, $p=0.03$ respectively).

Conclusions: Tocilizumab induced changes in specific subsets of CD4 +T cells and their inflammatory associated cytokines in the remission group.

Disclosure of Interest: None declared

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AB0425 PREVALENCE AND RISK FACTORS OF SERIOUS INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING THE BIOLOGIC/TARGETED SYNTHETIC DMARDS: A PROPENSITY SCORE ANALYSIS FROM THE HONG KONG BIOLOGICS REGISTRY

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Objectives: To study the prevalence and risk factors for serious infections in rheumatoid arthritis (RA) patients receiving the biologic/target synthetic (b/ts) DMARDs.

Methods: Patients who fulfilled the EULAR/ACR criteria for RA and were ever treated with b/tsDMARDs were included. Withdrawal of b/tsDMARDs due to serious adverse events (SAEs) and serious infections (SIs) was analysed. Demographic data, medical comorbidities and concomitant use of glucocorticoids and csDMARDs were retrieved and their contribution to SIs was evaluated by logistic regression. The propensity score for SIs was calculated and patients were stratified into 5 quintiles. The hazard ratios (HRs) of SIs with respect to individual b/tsDMARDs in each quintile were studied by Cox regression.

Results: Up to December 2017, 2355 courses of b/tsDMARDs were used in 1355 RA patients (83% women; age 54.0 ± 12.7 years). The usage of various b/tsDMARDs was: adalimumab (12%), etanercept (24%), infliximab (17%), golimumab (9.4%), certolizumab (0.9%), tocilizumab (19%), rituximab (6.6%), abatacept (7.7%) and tofacitinib (2.7%). After a follow-up of 5056 patient-years, 1433 courses of b/tsDMARDs were discontinued, with major reasons being inefficacy (50%), SAEs (22.4%) and cost (8.4%). Among those b/tsDMARD courses terminated because of SAEs, 32% were due to SIs (103 episodes). The rate of SIs was 1.17/100 patient-years. The commonest causes of SIs were pulmonary tuberculosis (TB) (41%), severe pneumonia (33%), soft tissue infection (6.8%), atypical TB (2.9%), urogenital sepsis (2.9%), septic arthritis (2.9%), hepatobiliary/gastrointestinal sepsis (2.9%), central nervous infection (1%), severe viral infections including herpes zoster (5.8%), and opportunistic infections (2.9%). A logistic regression model showed that increasing age (OR1.02 [1.001–1.04 per year]), male sex (OR1.88 [1.08–3.26]) and concomitant chronic obstructive pulmonary disease/asthma (OR2.55 [1.05–6.23]) were risk factors significantly associated with SIs. The rate of TB infection was highest in users of infliximab (2.32/100 patient-years), followed by tofacitinib (1.47), adalimumab (1.27), etanercept (0.62) and tocilizumab (0.36). Non-TB SIs occurred most frequently with infliximab (2.32/100 patient-years), tofacitinib (1.47) and abatacept (1.15). In the quintile of patients with the highest propensity score for SIs, infliximab had the highest withdrawal rate due to SIs (18%), followed by tofacitinib (10%), etanercept (8%), adalimumab (6%), abatacept (2.8%) and tocilizumab (2.6%). Cox regression revealed the following HRs for SIs with reference to adalimumab: infliximab (2.81 [0.80–9.88]), tofacitinib (HR 2.12 [0.19–23.4]), etanercept (HR 0.82 [0.22–3.11]), abatacept (HR 0.41 [0.04–3.98]) and tocilizumab (HR 0.38 [0.06–2.26]). Concomitant low-dose glucocorticoid was associated with an insignificantly increased risk of SIs only in the three quintiles of patients with lower propensity to SIs.

Conclusions: SIs causing withdrawal of b/tsDMARDs in patients with RA account for one-third of all SAEs. Increasing age, male sex and concomitant chronic chest conditions were independent risk factors for SIs. Infliximab was associated with the highest rates of serious TB and non-TB infection, and this observation was consistent in all quintiles of patients with different propensity to SIs.

Disclosure of Interest: None declared

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AB0426 EFFICACY OF MONOTHERAPY OF THE BIOLOGIC DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL LIFE DATA FROM THE HONG KONG BIOLOGICS REGISTRY

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Objectives: To report the prevalence and efficacy of biologic DMARD (bDMARD) monotherapy in real life treatment of rheumatoid arthritis (RA).

Methods: RA patients registered in the Hong Kong Biologics Registry who were receiving bDMARD monotherapy (without concomitant conventional synthetic DMARDs [csDMARDs] except low dose prednisolone) were identified. The efficacy (clinical response and drug retention rate) of bDMARD monotherapy was compared with bDMARD combination therapy (with csDMARDs) using statistical tests.

Results: From December 2007 to April 2017, 2123 courses of bDMARDs/tsDMARDs were used in 1250 RA patients (83% women, mean age at therapy 53.8 ± 12.7 years). Among 1881 courses of therapies with complete data, 164 (8.7%) was monotherapy at baseline. Low dose prednisolone (<10 mg/day) was used in 56% of these courses. In the combination group, the commonest csDMARDs used in combination with bDMARDs were methotrexate (79%), sulphasalazine (27%), hydroxychloroquine (25%) and leflunomide (21%). The bDMARDs/tsDMARDs most frequently used as monotherapy were tofacitinib (14.3%), tocilizumab (11.6%) and abatacept (11.2%). Overall, the non-TNF was more commonly used as monotherapy (11.2%) than the anti-TNF bDMARDs (7.4%). At 6 months of bDMARD/tsDMARD therapy, the DAS remission rate was non-significantly higher in the combination than monotherapy group (11% vs 5%; $p=0.42$). The change in DAS28 score was also non-significantly greater in the combination group (-1.95 ± 1.26 vs -1.68 ± 1.56 ; $p=0.30$). The difference in 6 month efficacy between the combination and monotherapy groups was greater in anti-TNF users. The overall cumulative withdrawal rate of the bDMARDs/tsDMARDs due to either inefficacy or serious adverse events (SAEs) was 0.55 at 3 years and 0.47 at 5 years. The anti-TNF biologics had a significantly higher withdrawal rate than the non-TNF biologics (hazard ratio [HR] 1.83 [1.56–3.14]; $p<0.001$). In Cox regression models, monotherapy of the bDMARDs was not significantly associated with drug withdrawal due to inefficacy (HR 0.95 [0.53–1.71]; $p=0.87$) or SAEs (HR 1.27 [0.51–3.19]; $p=0.61$) after adjustment for age, sex, anti-TNF (vs non-TNF) biologic use, previous use of bDMARDs (vs first time use) and DAS28 at baseline. Separate analyses of the anti-TNF and non-TNF biologics again did not reveal a significant relationship between monotherapy of the biologics with the drug withdrawal due to inefficacy or SAEs after adjustment for age, sex, previous use of bDMARDs and disease activity at baseline (HR 1.002 [0.56–1.80]; $p=0.99$ for anti-TNF and HR 1.20 [0.47–3.08]; $p=0.70$ for non-TNF biologics, respectively).

Conclusions: Monotherapy of bDMARD/tsDMARD was used in 8.7% of our RA patients in real life practice, probably due to intolerance, inefficacy or non-compliance in the csDMARDs. Short-term efficacy tended to be better with bDMARDs/csDMARDs combination, especially in the anti-TNF biologics, but the long-term drug retention rate was similar between bDMARD monotherapy and combination therapy with the csDMARDs.

Disclosure of Interest: None declared

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AB0427 COMPARATIVE SAFETY OF ABACEPT VS TOFACITINIB IN ADULTS WITH MODERATE-TO-SEVERE RA: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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Background: While targeted (biologic or synthetic) DMARDs are overall highly effective in improving symptoms and function in RA patients (pts), their comparative safety relative to each other remains inconclusive.

Objectives: Compare the safety of abatacept (ABA) and tofacitinib (TOF) through a systematic literature review (SLR) and network meta-analyses (NMA).

Methods: A comprehensive search of randomised and non-randomised clinical trials was conducted across MEDLINE, Embase and Cochrane CENTRAL databases from inception to June 2017. The PICO framework (population=moderate to severe RA pts; intervention=ABA and TOF; comparison=placebo and other RA therapies; outcome=AEs, treatment-related AEs [TrAEs], serious infections and treatment-related deaths) was used to design searches and define the eligibility of studies for inclusion. Additional searches were performed on relevant conference proceedings and the US clinical trials registry from the past 2 years (figure 1). Data configuration was performed by expert methodologists using DOC Data 2.0 (Doctor Evidence, Santa Monica, CA). NMAs using the random-effects model were used to examine the risk of AEs, TrAEs and serious infections in