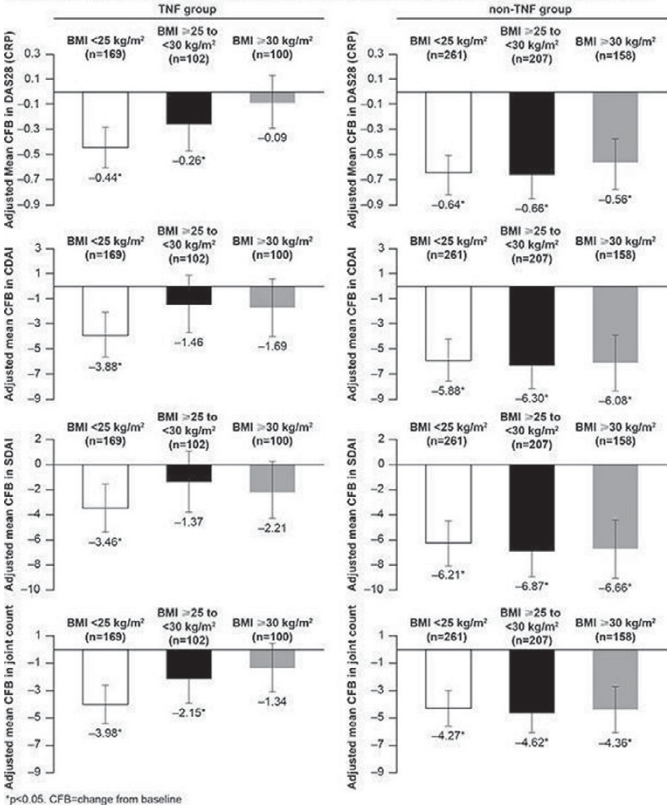
from treatment exposure. Treatments were categorized into TNF and non-TNF, which included conventional DMARDs and other non-TNF biologics. Multivariate linear regression analyses were used to evaluate impact of BMI on treatment outcomes controlling for baseline covariates of age, sex, disease duration, co-morbidities, baseline disease activity and serostatus. Separate models were run for the TNF and non-TNF groups.

Results: A total of 997 (78%) pts in the registry had baseline BMI values and were included in the analysis. Around 37% (n=371) had TNF exposure and were included in the TNF cohort; the remainder (63%; n=626) were included in the non-TNF cohort. Proportions of pts in the normal, overweight and obese groups for the TNF cohort were 45.5% (n=169), 27.5% (n=102) and 27.0% (n=100), respectively. For the non-TNF cohort, these were 41.7% (n=261), 33.1% (n=207) and 25.2% (n=158), respectively. In both cohorts, pts with normal BMIs were younger vs the overweight and obese BMI groups. However, obese BMI pts had higher disease activity measures at baseline (mean [SD] CDAI: 22.8 [17.8] for TNF and 24.9 [17.3] for non-TNF) vs the normal BMI pts (17.5 [15.9] for TNF and 19.9 [16.7] for non-TNF) and overweight BMI pts (20.9 [16.5] for TNF and 20.5 [15.0] for non-TNF). Adjusted mean change from baseline in disease activity in the TNF cohort was significantly reduced across all disease activity measures for the normal BMI group ($p<0.05$), but not for the overweight and obese groups (Fig). There were significant reductions in disease activity measures for all BMI groups (all $p<0.05$) in the non-TNF cohort (Fig).

Figure. Association between BMI and Treatment Outcomes DAS28 (CRP), CDAI, SDAI and Joint Count



*p<0.05. CFB=change from baseline

Conclusions: Independent of BMI, non-anti-TNF therapy demonstrated similar outcomes in pts with RA. However, obese and overweight pts with RA (vs normal weight) had less improvement in disease activity (as measured by DAS28 [CRP]) with anti-TNF therapy.

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SAT0198 TOCILIZUMAB FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS: DISCONTINUATION DUE TO INEFFICACY AND TOXICITY – EXPERIENCE FROM A LARGE TEACHING HOSPITAL

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Background: Tocilizumab (TCZ) is a humanised anti interleukin-6 receptor antibody licensed for use for the treatment of moderate to severe Rheumatoid Arthritis (RA) as monotherapy or in combination with methotrexate (MTX).

Objectives: To describe the use of TCZ for RA in a large UK teaching centre and examine reasons for treatment discontinuation.

Methods: A retrospective case note review of all adult patients receiving TCZ either alone or in combination with DMARDS, for the treatment of RA between April 2009 and January 2017 in Sheffield, UK.

Results: 132 patients received TCZ for RA. 71% were female. 61% were CCP positive. Mean disease duration was 15.6 years (range 1.5–43). 46 (34.6%) received TCZ as monotherapy, 55 (42.1%) in combination with MTX and 31 (23.3%) other DMARDS. 23% of patients received concomitant oral prednisolone. Median duration of TCZ treatment was 27 months across the whole cohort, and 19 months in those who discontinued treatment.

Overall 44 (33%) patients discontinued TCZ; 5 due to primary and 10 secondary inefficacy, 27 patients due to adverse events (8 recurrent infection, 5 abnormal LFT, 4 malignancy, 3 rash, 7 other including 1 death whilst on treatment). A logistic regression model, including gender, smoking status, disease duration, DMARD use, steroid treatment and number of prior biologics was constructed to examine association with treatment discontinuation. Of these factors, disease duration ($p=0.05$) and number of previous biologics ($p=0.09$) were weakly associated with persistence of TCZ and in particular there was no association of concomitant DMARD or steroid treatment with discontinuation either due to lack of efficacy or adverse events. Table 1 demonstrates the proportion of patients stopping treatment, and treatment duration according to previous biologic treatment received. We have not seen any cases of infusion reaction, diverticular perforation or reactivation of tuberculosis.

Table 1. Proportion of Patients Continuing TCZ and Treatment Duration According to Previous Biologic Treatment

		Previous Biologics Received			
		0	1	2	3 or more
Continued	N (%)	15 (83%)	31 (66%)	24 (51%)	12 (60%)
	Treatment Duration (Mths)*	46	27	26	58
Discontinued	N (%)	3 (17%)	16 (34%)	23 (49%)	8 (40%)
	Treatment Duration (Mths)	4.5	14	24	18
	Lack of Efficacy/Toxicity	2/1	7/9	9/14	3/5

*To date.

Conclusions: Our real world data on the use of TCZ in the treatment of adult patients with RA is consistent with clinical trial data for efficacy and safety and is similar to other biological drugs used in the treatment of RA. We have seen a relatively low rate of withdrawal due to primary and secondary treatment failure.

Disclosure of Interest: None declared

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SAT0199 SUBCUTANEOUS TOCILIZUMAB MONOTHERAPY OR COMBINED WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: TOZURA, A POOLED ANALYSIS OF PHASE IV STUDIES IN 22 COUNTRIES

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Background: Tocilizumab administered subcutaneously (TCZ-SC) has been approved for the treatment of rheumatoid arthritis (RA) both as mono- and combination therapy.

Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs) over 24 weeks in adult patients (pts) with moderate to severe RA.

Methods: TOZURA is a multinational, open-label, single-arm umbrella program comprising 7 single-country and 4 regional multicountry protocols (total 22 countries). Pts enrolled were inadequate responders to DMARD, and previous biologic DMARDs were allowed in 8 of 11 protocols. Pts received TCZ-SC 162 mg qw for 24 weeks administered at the investigator's discretion as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (CS), ≤10 mg/day prednisone or equivalent, were allowed. Efficacy and safety were evaluated at weeks 1, 2, 4 and every 4 weeks for 24 weeks (plus 8 weeks for safety). Propensity score-based matching was used for between-group tests.

Results: Of 1804 pts treated, 353 (19.6%) received monotherapy (mono) and 1451 (80.4%) combination therapy (combo); 349 pts (19.3%) had received a prior biologic DMARD. Background characteristics: 81.6% female; mean age, 54.1

years; mean RA duration, 7.7 years; and 82.7% seropositive –similar between treatment groups. Baseline CS was less frequent in the mono vs combo group (41.1% vs 51.2%); however, the mean prednisone equivalent daily dose was similar (6.6 vs 6.5 mg/day, respectively). Pts who continued TCZ to week 24 based on Kaplan-Meier estimates (95% CI) were 79.3% (74.7%>83.2%) for mono and 85.6% (83.7%>87.3%) for combo. DAS28 scores decreased comparably from baseline to week 24 in both groups (mean change: mono −3.40 and combo −3.46), with no significant difference between groups (P =0.61). Results were similar for the Clinical Disease Activity Index (CDAI, mean change by week 24: −23.5 and −23.8, with no significant difference between groups: P=0.42). The proportion of pts who achieved DAS28 or CDAI-based remission, low disease activity or ACR20/50/70/90 responses was similar between groups (Figure 1). In all, 18.2% of pts withdrew; 6.4% did so for safety reasons (mono 9.1%, combo 5.8%). AE rates were similar between groups (Table). Serious AE (SAE) rates were 14.6/100 PY (mono: 22.8/100 PY, combo: 12.8/100 PY). Serious infection and infestation rates were 3.6/100 PY (mono: 4.0/100 PY, combo: 3.5/100 PY) – similar between groups. Six deaths occurred (0.64/100 PY), 1 in the monotherapy group (0.57/100 PY) and 5 in the combination (0.65/100 PY) group.

Figure 1: DAS28 and CDAI Disease Activity and ACR Responses*

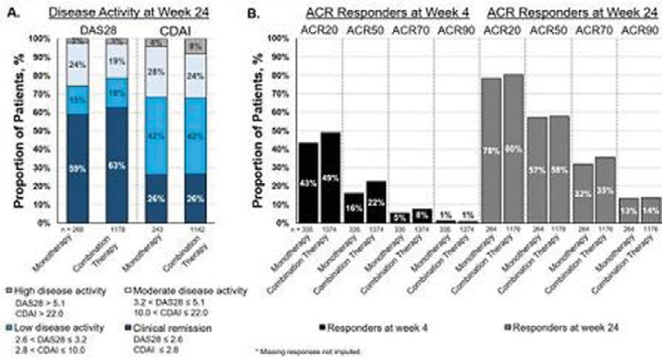

Table: Summary of Relevant Adverse Events

		Total Population (N = 1804; 943.3 PY)	Monotherapy (n = 353; 175.7 PY)	Combination Therapy (n = 1451; 767.6 PY)
Adverse events	Total patients with ≥ 1 AE, n (%)	1508 (83.6%)	282 (79.9%)	1226 (84.5%)
	Rate of AEs per 100 PY	622.4	622.1	622.5
Serious adverse events	Total patients with ≥ 1 SAE, n (%)	105 (5.8%)	29 (8.2%)	76 (5.2%)
	Rate of SAEs per 100 PY	14.6	22.8	12.8
Serious infections and infestations	Total patients with ≥ 1 SAE, n (%)	27 (1.5%)	6 (1.7%)	21 (1.4%)
	Rate of SAEs per 100 PY	3.6	4.0	3.5
Withdrawals due to insufficient therapeutic response	Total patients with ≥ 1 reason, n (%)	40 (2.2%)	9 (2.5%)	31 (2.1%)
Withdrawals due to safety reasons*	Patients, n (%)	116 (6.4%)	32 (9.1%)	84 (5.8%)
Deaths	Number of deaths, n (%)	6 (0.3%)	1 (0.3%)†	5 (0.3%)‡
	Rate of deaths per 100 PY	0.64	0.57	0.65

AE, adverse events; SAE, serious adverse events; PY, patient-year.
* Deaths, anaphylaxis and hypersensitivity reactions not included.
† Coronary artery disease.
‡ Myocardial infarction, pneumonia, pulmonary fibrosis, sepsis, septic shock.
Note: TOZURA trial numbers: NCT01995201, NCT02046603, NCT02011334, NCT02031471, NCT02001987, NCT01941095, NCT01941940, NCT02046616, NCT01988012, NCT01987479, NCT01951170.

Conclusions: TCZ-SC demonstrated convincing and comparable efficacy as mono- and combination therapy in pts with RA as was previously observed with TCZ-IV. The safety profile of TCZ-SC is consistent with the known safety profile of TCZ as monotherapy and in combination with csDMARDs.

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SAT0200 BIOLOGIC THERAPY RETENTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ACCORDING TO THE MOSCOW ARTHRITIS REGISTRY (MAR)

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Background: The use of biologics significantly improved results of the therapy of RA pts who did not achieve the target disease activity level on traditional DMARDS treatment. However the biologic therapy is in many cases withdrawn due to inefficacy or side effects (seldom because of sustained remission). Retention on treatment is a good integral index of efficacy and safety of biologics used in the real clinical practice.

Objectives: To assess the treatment survival of various biologics in RA pts in the real clinical practice.

Methods: Patients from MAR with RA receiving biologics were enrolled. Cases with missed results were excluded. A Cox proportional hazards regression model was used to determinethe predictors of the treatment discontinuation risk. Comparison of biologics retention rates for different biologicswas performed by means of Kaplan-Meier survival curves. Bonferroniadjustment was applied because of multiplicity of comparisons.

Results: 306 RA pts (mean age 54,5 years, mean age of disease onset 39,6 years, 86,5% women, 18% smokers, RF-positive 83,7%) were included in the study and 394 treatment courses (263 retrospective and 131 prospective) were analyzed. It was shown that significant independent predictors of discontinuation risk were: the biologic drug, the sequence number of the biologic drug in the patient and the age of RA onset. Risk of withdrawal was minimal by the use of the first biologic and increased by administration of the next ones. It also increased in pts with late onset of RA. Mass body index, age of the patient and the dose of methotrexate did not show significant correlations. Abatacept (ABA) demonstrated significant superiority over adalimumab (ADA) ($p<0.001$), infliximab (INF) ($p<0.001$), rituximab (RTM) (p=0.004) and etanercept (ETA) (p=0.035) when they was used as the first biologic drug. The treatment survival of tocilizumab was significantly higher compared to INF (p=0.02). As a second-line biological therapy ADA was maintained significantly longer than the INF (p=0.048).

Conclusions: Results of the real clinical practice trial show the significant differences in the retention rates of some biologics. It is reasonable to take these differences into consideration by the planning of the biologic treatment of RA pts.

Disclosure of Interest: None declared

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SAT0201 ABATACEPT BUT NOT TNF INHIBITORS BLOCK AUTOANTIBODY-MEDIATED CYTOKINE PRODUCTION BY MONOCYTES

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Background: The anti-inflammatory effect of abatacept (CTLA4-Ig) is most pronounced in patients with high-titer autoantibodies (including anti-citrullinated protein antibodies, ACPA, and rheumatoid factor, RF) even exceeding the effect of TNF inhibitors (TNFi)[1]. Considering that autoantibodies trigger inflammatory cytokine production by monocytes[2] and that abatacept bind to monocytes influencing their functional state[3] we hypothesized that abatacept, in contrast to TNFi, may effectively inhibit the production of several different cytokines by ACPA-or RF-challenged monocytes.

Objectives: (i) To test whether abatacept inhibits the production of TNFa, IL-1b, IL-6 and IL-8 by monocytes exposed to ACPA or RF, (ii) to compare these effects of abatacept with those of TNFi and (iii) to investigate whether the effect of abatacept on cytokine production is based on IDO induction in monocytes.

Methods: CD68+ monocytes were isolated from peripheral blood and stimulated with MCSF for 24 hours before exposing them to random IgG alone (negative control), 10mg/mL purified anti-citrullinated vimentin antibodies (ACPA), 10mg/mL RF or LPS (positive control) in cell culture plates coated with citrullinated vimentin (to allow ACPA immune complex formation). ACPA and RF stimulation was done in the presence or absence of abatacept or TNF-antibody (adalimumab) with or without IDO inhibitor 1-MT. Supernatants were analyzed for four key pro-inflammatory cytokines TNFa, IL-1b, IL-6 and IL-8 by cytokine array (R&D Proteome Profiler) after 24h.

Results: Exposure to ACPA or RF dramatically induced the production of TNFa (20 fold and 27-fold, respectively) IL-1b (each 4-fold), IL-6 (12-fold and 11-fold, respectively) IL-8 (43-fold and 30-fold, respectively) in human monocytes. Abatacept significantly inhibited this up-regulation of inflammatory cytokine production with TNFa reduced by 79%, IL-1b by 74%, IL-6 by 88% and IL-8 by 83%. In contrast, TNFi did not influence autoantibody-induced production of IL-1b, IL-6 and IL-8. Inhibition of IDO by 1-MT reversed the effect of abatacept and unlocked cytokine production in the presence of ACPA and RF.

Conclusions: These data show that abatacept interferes with autoantibody mediated cytokine production by induction of IDO. The fact that several different