Conclusions: The IR of ADR was 16.2%, being similar in all age categories. Gastrointestinal was the main cause of ADR followed by infections. We have found differences in discontinuation rates among DMARD due to ADR, being Abatacept, Gold and Leflunomide the drugs with the highest risk. Methotrexate had a lower risk of ADR compared to other DMARD. Caution should be taken in patients receiving combined therapy and with certain comorbidities

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2473

Saturday, 16 JUNE 2018

Rheumatoid arthritis - biological DMARDs

SAT0165

REASONS FOR bDMARD CESSATION AND SUBSEQUENT PERSISTENCE OF SECOND LINE TREATMENT IN A LARGE REAL WORLD RHEUMATOID ARTHRITIS REGISTRY

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Background: The current recommendations for treating Rheumatoid Arthritis (RA) patients (pts) who fail on conventional disease modifying anti-rheumatic drugs (DMARDs) is to use biologic (b) or targeted synthetic (ts) DMARDs. Pts who fail first (1st) line b/tsDMARDs are recommended to go on other b/tsDMARDs; however, reasons for stopping or switching between bDMARDs according to mode of action and the persistence on treatment are not well characterized in real world patient populations.

Objectives: The primary objective was to identify the reasons for stopping 1st line b/tsDMARDs in RA pts treated in the clinical practice setting. The secondary objectives were to identify second (2nd) line b/tsDMARDs choices in pts who stop TNF inhibitors (TNFis) within 6 months (mo) due to lack of efficacy and the persistence on these treatments.

Methods: Pts ≥ 18 years with confirmed RA who were treated with 1st line b/tsDMARDs, from 1 August 2010 to 30 June 2017, by physicians participating in the OPAL-QUMI database, were included in the analyses. Reasons for stopping b/tsDMARDs were recorded by the treating physician during routine visits. The following b/tsDMARDs were included abatacept (ABA), adalimumab, certolizumab pegol, etanercept, golimumab, infliximab and tocilizumab (TCZ), rituximab (RTX) and tofacitinib (TFB). Data were analysed using descriptive statistics for continuous variables and frequency counts for categorical variables. Persistence on treatment was summarised using Kaplan-Meier (K-M) methodology. Individual TNFis were combined for simplicity.

Abstract Sat0165 – Table 1. Patients receiving 1st line treatment by mechanism of action.

First-line Treatment	RTX	TCZ	TFB	ABA	TNFis
Started, n	230	555	518	609	5002
Stopped, n(%)	51(22)	238(43)	105(20)	233(38)	2029(41)
Stopped within 6 months; n(%) ^a	11(22) ^a	41(17) ^{a*}	57(54)	72(31) ^a	733(36) ^{a*}

^apercentage relative to subset stopped treatment
^{*}p<0.001: RTX vs TFB; TCZ vs ABA; TNFis vs TFB
^{*}p<0.0001: TCZ vs TFB; TNFis/ABA vs TFB

Abstract Sat0165 – Table 2 K-M. estimates of persistence on 2nd line b/tsDMARDs after discontinuation of 1st line TNFis due to lack of efficacy.

	RTX	TCZ	TFB	ABA	TNFis
N	13	49	25	92	130
6 months, %	75	78	71	61	60
12 months, %	75	57	ND	49	40

ND=not determined

Results: A total of 6914 pts received 1st line b/tsDMARDs. Median age was 61 years, median disease duration (RA onset to last visit) was 10 years. The majority

(75%) were females. Treatment was stopped in 2656 pts (38%); 914 (34%) of these stopped within 6 mo of treatment initiation. The highest and lowest percentage of pts stopping treatment within 6 mo was in pts receiving TFB (54%) and TCZ (17%), respectively (table 1). The most common reasons for stopping therapy within 6 mo were lack of efficacy (45%>ABA, 44%>TNFis, 33%>TFB and 27%>TCZ) and adverse reactions (21%>TFB, 20%>TCZ, 15%>TNFis, 13%>ABA). Stopping due to lack of efficacy-primary failure was highest for TFB (23%). The percentage of pts remaining on 2nd line b/tsDMARD treatment after stopping 1st line TNFis due to lack of efficacy was the highest for TCZ (78%) at 6 mo and RTX (75%) at 12 mo (table 2). Median time to stopping 2nd line treatment was 48 mo (95% CI:17–74) for RTX, 21 mo (95% CI:11–62) for TCZ, 21 mo (95% CI:6–21) for TFB; 11 mo (95% CI:8–22) for ABA and 9 mo (95% CI:7–12) TNFis.

Conclusions: The primary failure rate is lower than previously reported. In pts who failed 1st line TNFis within 6 mo of commencement due to lack of efficacy, 2nd line TNFis resulted in the lowest treatment persistence. These real world data will assist clinicians with treatment choices post primary TNFis failure.

Acknowledgements: Sponsored by Roche Products, Pty. Limited. Medical Writing provided by Dr Joseline Ojaimi from Roche.

Disclosure of Interest: P. Youssef: None declared, B. Marcal Employee of: Roche Products, Pty. Limited, P. Button Consultant for: Roche Products, Pty. Limited, M. Truman Consultant for: Roche Products, Pty. Limited, P. Bird: None declared, H. Griffiths: None declared, L. Roberts Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Pfizer, Roche Products, Pty. Limited, UCB, K. Tymms Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Pfizer, Roche Products, Pty. Limited, UCB, G. Littlejohn Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Pfizer, Roche Products, Pty. Limited, UCB

DOI: 10.1136/annrheumdis-2018-eular.6022

SAT0166

WHICH BIOLOGIC AGENT IS MOST SUITABLE FOR AN EXTENDED-INTERVAL TREATMENT FOR RHEUMATOID ARTHRITIS ? RESULTS FROM A MULTICENTER STUDY

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Background: Biological disease-modifying antirheumatic drugs (bDMARDs) have made apparent development of treating rheumatoid arthritis (RA). However, prescription of them appeared to be relatively difficult due to high cost. The newest EULAR recommendation advocates tapering of bDMARDs when RA activity is controlled.

Objectives: A multicenter clinical study on a longer interval treatment with three bDMARDs, Golimumab (GOL), which is one of TNF inhibitors, and two of non-TNF inhibitor, Tocilizumab (TCZ) and Abatacept (ABT) was investigated.

Methods: Patients, who were maintained at low disease activity by DAS28 score for more than 3 months treated with GLM, TCZ, ABT, were enrolled. These selected patients were treated with these drugs with 1.5 fold longer interval of standard schedule for 60 weeks, and the rate of patients, who preserved low disease activity were determined. The patients who were not tolerated these drugs because of the side effects or adverse events, were withdrawn from this study.

Results: One hundred thirty-one patients treated with GLM, 149 with ABT (S.C. 61, I.V. 88) and 299 with TCZ (S.C. 87, I.V. 212) were enrolled. Among these, 57 patients treated with GLM (43%), 40 with ABT(26%, S.C 18, I.V 22), 93 with TCZ (31%, S.C 21, I.V 72) were successfully maintained at low disease activity with

this 1.5 folds longer interval treatment, respectively. The age of patients in ABT group was 73.5±10.6, and significantly higher than those in TCZ (58.8±13.9) and GOL (58.1±14.7) groups. At 60 weeks, DAS28 in ABT group was 3.1±0.5, and significantly higher than those in TCZ (2.6±0.7) and GLM (2.6±0.7) groups. On the other hand, CDAI in GOL was 6.6±3.4, and was significantly higher than those in TCZ (4.4±2.6) or ABT (4.6±2.3) groups. Accordingly, successive rate at 60th week in ABT group was 52% and significantly lower than those in TCZ (69%) or in GOL (73%) groups as shown in figure. Finally, no significant difference in successive rate was observed between s.c. and i.v.

Conclusions: This study clarified that TCZ and GLM had higher successive rate than ABT for maintaining low disease activity for 60 weeks by longer interval treatment. This effectiveness might relate to the high therapeutic efficacy of TCZ and low antigenicity of GOL.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1464

SAT0167

COMPARISON OF THE EFFICACY AND TOLERABILITY OF TOCILIZUMAB, SARILUMAB, AND SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: A humanized, anti-human IL-6 receptor monoclonal antibody, tocilizumab, was developed to block IL-6 signaling and has been used as an effective therapeutic agent for patients that do not respond to methotrexate (MTX) or tumor necrosis factor (TNF) inhibitor. The successful use of tocilizumab in RA stimulated the development of other biologics targeted to the IL-6 pathway, such as anti-IL-6R (sarilumab) or anti-IL-6 (sirukumab) antibodies.

Objectives: The relative efficacy and tolerability of tocilizumab, sarilumab, and sirukumab were assessed in patients with rheumatoid arthritis (RA) and an inadequate response to MTX or TNF inhibitors.

Methods: We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tocilizumab, sarilumab, and sirukumab in RA patients and an inadequate MTX or TNF inhibitor response.

Results: Fourteen RCTs, comprising 9,753 patients, met the inclusion criteria. Tocilizumab 8 mg combined with MTX or as monotherapy was the most effective treatment for active RA with an inadequate MTX or TNF antagonist response, followed by sarilumab and sirukumab, regardless of MTX combination. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that tocilizumab 8 mg+MTX had the highest probability of being the best treatment to achieve the ACR50 response rate, followed by tocilizumab 8 mg, sarilumab 200 mg, sarilumab 200 mg+MTX, sirukumab 100 mg, tocilizumab 4 mg +MTX, sirukumab 100 mg+MTX, sirukumab 50 mg+MTX, sarilumab 150 mg +MTX, adalimumab 40 mg, and sirukumab 50 mg, and placebo+MTX. No significant differences were observed in withdrawals owing to adverse events after treatment with tocilizumab 8 mg+MTX, sirukumab 100 mg+MTX, or sarilumab 200 mg+MTX.

Conclusions: In RA patients with an inadequate MTX or anti-TNF therapy response, tocilizumab 8 mg as monotherapy and combined with MTX showed acceptable tolerability and the highest performance based on the ACR50 response rate, followed by sarilumab and sirukumab.

REFERENCES:

- [1] Smolen JS, Beaulieu A, Rubbert-Roth A, Ramos-Remus C, Rovinsky J, Alecock E, Woodworth T, Alten R, Investigators O. Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomised trial. *The Lancet* 2008;371:987–997.
- [2] Genovese M, Fleischmann R, Fiore S, Radin A, Fan C, Huizinga T. SAT0117 Sarilumab, a Subcutaneously-Administered, Fully-Human Monoclonal Antibody Inhibitor of The IL-6 Receptor: Relationship Between Euler Responses and Change from Baseline of Selected Clinical Parameters. *Annals of the Rheumatic Diseases* 2013;72:A620-A620.
- [3] Xu Z, Bouman-Thio E, Comisar C, Frederick B, Van Hartingsveldt B, Marini JC, Davis HM, Zhou H. Pharmacokinetics, pharmacodynamics and safety of a human anti-IL-6 monoclonal antibody (sirukumab) in healthy subjects in a first-in-human study. *British journal of clinical pharmacology* 2011;72:270–281.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1644

SAT0168

MRI RESULTS FOLLOWING DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

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Background: Although previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO) for the treatment of rheumatoid arthritis (RA),^{1,2} changes in active intra-articular inflammation after discontinuation of methotrexate (MTX) in patients achieving good clinical control with TCZ + MTX have not been evaluated. Magnetic resonance imaging (MRI) effectively images synovitis and osteitis and can detect changes in bone erosion with greater sensitivity than radiography.³

Objectives: This study used MRI to assess differences in joint damage between patients with RA who achieved low disease activity with TCZ + MTX and then continued or discontinued MTX in the COMP-ACT trial (NCT01855789).

Methods: US patients with RA who were inadequate responders to MTX were enrolled; initial combination therapy included MTX (≥ 15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly or every 2 weeks. Patients who achieved DAS28-ESR ≤ 3.2 at week 24 were randomized 1:1 to receive TCZ-MONO or continue TCZ + MTX until week 52 (double blind). A subset of these patients was included in this MRI substudy; 1.5 Tesla MRI was used to obtain images of bilateral hands and wrists at Weeks 24 and 40. Two independent radiologists evaluated images at a central reading facility using RAMRIS (synovitis, osteitis, erosion) and CARLOS (cartilage loss). Outcomes included changes in MRI scores from Week 24 to 40 and the proportion of patients with progression of each score.

Results: Of the 296 patients who achieved DAS28 ≤ 3.2 at Week 24 and were randomized to TCZ + MTX or TCZ-MONO, 79 were enrolled in the MRI substudy (n = 41 and 38, respectively); 74.7% were women, and the mean (SD) age was 56.3 (12.8) years. Patient demographics in the MRI substudy were similar to overall study demographics. Mean changes from Week 24 to 40 in bone erosion, synovitis, osteitis, and cartilage loss scores were not significantly different between the TCZ + MTX and TCZ-MONO groups for both bilateral hands and the dominant hand (table 1). There were no significant differences between the groups in the proportion of patients with no progression in each outcome measure (range, 89.7% to 97.4% with TCZ + MTX and 87.9% to 100.0% with TCZ-MONO).

Table 1 MRI Changes in Patients Receiving TCZ in Combination With MTX or TCZ as Monotherapy

Mean change from Week 24 to 40*	Both Hands			Dominant Hand		
	TCZ + MTX (n = 41)	TCZ-MONO (n = 38)	Difference (95% CI) (TCZ-MONO minus TCZ + MTX)	TCZ + MTX (n = 41)	TCZ-MONO (n = 38)	Difference (95% CI) (TCZ-MONO minus TCZ + MTX)
Bone erosion score (0-250), mean (SE)	-0.06 (0.18)	0.18 (0.19)	0.24 (-0.21 to 0.68)	0.06 (0.24)	0.49 (0.25)	0.43 (-0.14 to 1.01)
Synovitis score (0-24), mean (SE)	-0.24 (0.15)	-0.18 (0.15)	0.06 (-0.30 to 0.41)	-0.22 (0.12)	-0.11 (0.12)	0.11 (-0.18 to 0.40)
Osteitis score (0-75), mean (SE)	-0.16 (0.34)	0.37 (0.36)	0.53 (-0.30 to 1.36)	-0.39 (0.52)	0.69 (0.54)	1.07 (-0.18 to 2.33)
Cartilage loss score (0-100), mean (SE)	0.20 (0.14)	-0.03 (0.15)	-0.23 (-0.58 to 0.11)	0.11 (0.18)	-0.05 (0.19)	-0.16 (-0.59 to 0.27)

MTX, methotrexate; TCZ, tocilizumab; TCZ-MONO, TCZ monotherapy.

* ANCOVA model for estimated means includes Week 24 bone erosion as a covariate, treatment group and the randomization stratification factors: DAS28 remission status at Week 24 (< 2.6, ≥ 2.6 to < 3.2), patient anti-TNF exposure (Yes or No) and baseline weight-by-dosing group (< 80 kg q2w, 80 to < 100 kg q2w, 80 to < 100 kg qw, ≥ 100 kg qw).

Conclusions: In patients who achieved low disease activity with TCZ + MTX, MRI changes were minimal and showed no difference in the response of active intra-articular inflammation in patients who discontinued MTX vs those who continued TCZ + MTX within the period of observation, consistent with the result of similar mean change in DAS28 between the groups in the primary analysis.

REFERENCES:

- [1] Jones G, et al. *J Rheumatol* 2017;44(2):142–146.
- [2] Dougados M, et al. *Ann Rheum Dis* 2013;72(1):43–50.
- [3] Strand V, et al. *Arthritis Rheum* 2013;65(10):2513–2523.

Acknowledgements: This study was funded by Genentech, Inc.

Disclosure of Interest: C. Peterfy Consultant for: Roche, Employee of: Spire Sciences, Inc., J. Kremer Shareholder of: Corrona, LLC, Consultant for: Abbvie,