1.28) and outpatient bronchitis: 0.80 (0.57, 1.14). Results remained unchanged with sensitivity analyses.

Conclusions: In this real-world study of patients with RA and COPD, the incidence of pre-specified respiratory SAEs was not significantly increased in patients using abatacept compared with those using other bDMARDs or tofa. The safety signal based on the subgroup of 54 patients from the ASSURE trial could not be confirmed in this large and long-term cohort study of over 5000 patients.

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Disclosure of Interest: S. Suissa Consultant for: Bristol-Myers Squibb, P. Ernst: None declared, S. Dell'Aniello: None declared, S. Shen Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, T. A. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2018-eular.1505

FRI0140 INDIVIDUALISED INFlixIMAB TREATMENT: A TREATMENT STRATEGY BASED ON THERAPEUTIC DRUG MONITORING

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Background: Infliximab (INX) and other targeted therapies have greatly improved the treatment of patients with RA, SpA and PsA, but a significant proportion of patients either do not respond sufficiently to therapy or loose efficacy over time. Recent advances in assay development have revealed an extensive individual variation in serum drug concentrations suggesting both under- and overtreatment of a substantial proportion of patients. Many patients develop anti-drug antibodies (ADAb) during therapy, contributing to reduced drug levels, inefficacy and adverse events. Therapeutic drug monitoring (TDM), i.e. individual dose adjustments according to serum drug levels, can probably increase effectiveness of treatment with INX and other biological drugs.

Objectives: To develop an individualised treatment strategy based on TDM in order to optimise efficacy of INX treatment.

Methods: The treatment strategy has been developed by the steering committee of the NORwegian DRUG Monitoring study (NOR-DRUM), based on a systematic literature review (SLR), unpublished data and expert opinion. A SLR was performed in May 2016 to identify the therapeutic range. In Norway neutralising ADAb are measured with an "in house" assay. For this assay, ADAb levels >50 µg/L are defined as "high" leading to a recommendation to switch therapy. This cut-off is based on own s-INX and ADAb data (Diakonhjemmet Hospital during 2015–2016) and clinical experience. The proposed strategy has been developed through a series of meetings in the project group consisting of national leading experts in this field (both clinicians experienced with TDM and laboratory physicians) and with additional input from international key experts in the scientific advisory board of the NOR-DRUM study.

Serum INX level (µg/ml)	<2.0 and high ADAb (>50 µg/L)	<2.0	2.1–2.9	3.0–8.0	8.1–10.0	>10.0
Action	Switch therapy if possible to another TNFi	Increase dose if no ADAb or low level ADAb (<50 µg/L)	Consider increasing dose	No action	Consider decreasing dose	Decrease dose
Guideline for action	Increase the dose by increasing the dose by 2–2.5 mg/kg to a max dose of 10 mg/kg or by decreasing the dose interval by 2 weeks to a min of 4 weeks	Consider increasing the dose based on clinical judgement and the patients factors given below*	Within target range. Continue with the same dose and dosing interval	Consider to decrease the dose based on clinical judgement and the patients factors given below*	Decrease the dose by increasing the dose interval by 2 weeks to a max of 30 weeks or by decreasing the given dose by 2–2.5 mg/kg	

*Patient factors to be considered when making the treatment decisions in the yellow zones: Disease activity and trend in disease activity, the trend of the trough level over time, previous drug interval changes, availability of alternative drug, diagnosis (RA patients are expected to have lower trough levels due to lower recommended dosing)

Results: The treatment strategy from infusion number 4 onwards is depicted in the figure 1. The therapeutic range for serum INX (through levels) is defined as 3–8 µg/ml (figure 1, green zone). During the induction phase (infusion 1–3) the recommendation is to keep the level >20 µg/ml at infusion 2 and >15 µg/ml at infusion 3. A guideline for action according to levels outside the therapeutic range is given in the figure 1. Dose modifications may be performed either as changes in doses or intervals as stated in the figure 1. If the patients develop high levels of ADAb the recommendation is to switch therapy.

Conclusions: An individualised treatment strategy based on TDM has the potential to optimise therapy with infliximab and other biological drugs by: 1) prevention of treatment failure by identification of patients with drug levels below the therapeutic range, 2) reduction of overtreatment, which predispose to side effects and increase costs, and 3) early identification of ADAb development, with the possibility to detect treatment failures prior to a clinical flare and to prevent hypersensitivity reactions. This approach has high face validity, and the effectiveness compared to regular care is being investigated in an ongoing randomised clinical trial, NOR-DRUM (NCT03074656).

Disclosure of Interest: S. Syversen Consultant for: Roche, G. Goll Consultant for: AbbVie, Biogen, Boehringer Ingelheim, Orion Pharma, Eli Lilly, Novartis, Pfizer, Roche, UCB, K. Jørgensen Consultant for: Tillot, Celltrion, Intercept, Ø. Sandanger: None declared, J. Gehin Consultant for: Roche, C. Mørk Consultant for: AbbVie, Novartis, LEO Pharma, ACI hud Norge, Cellegene AS, Galderma Nordic AB, T. K. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Epirus, Hospira, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, J. Jahnson Consultant for: AbbVie, Celltrion, Takeda, Napp Pharm, AstroPharma, Hikma, Orion Pharma, Pfizer, N. Bolstad Consultant for: Pfizer, Roche, Orion Pharma, Napp pharm, Takeda, E. A. Haavardsholm Consultant for: AbbVie, Pfizer, MSD, Roche, UCB

DOI: 10.1136/annrheumdis-2018-eular.1433

FRI0141 VACCINATION DECISIONS AND INCIDENCE OF NEONATAL INFECTIONS IN MOTHERS EXPOSED TO BIOLOGICALS DURING PREGNANCY

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Background: Rheumatologic diseases commonly affect women of childbearing age.^{1,2} There is currently limited data available regarding the safety of vaccinations in infants after in utero exposure to biologics.

Objectives: To determine the vaccination decisions of mothers with rheumatologic diseases exposed to biologics during pregnancy and the incidence of serious neonatal infections after third trimester exposure.

Methods: All Australian women with inflammatory arthritis, exposed to biologics during the preconception, antenatal and/or postpartum periods, were invited to participate in the Pregnancy Exposed to Biological (PEB) study from May 2009 – Jan 2018. Recruitment was via direct invitation from patients treating rheumatologists, community groups, and via social media. Following self-referral to the study, retrospective data was collected, including biological exposure, vaccination history and the incidence of serious neonatal infections, defined as infection requiring hospitalisation.

Results: Preliminary data is available regarding 35 offspring from 28 mothers. 34 of 35 offspring were vaccinated. 29 received vaccinations in accordance with the Australian National Immunisation Program Schedule. 1 mother declined to immunise her infant due to personal preference.

13 infants were exposed to a tumour necrosis factor inhibitor (TNFi) during the third trimester. Of these, 4 had Rotavirus vaccine delayed from 2 to 4 months and 1 infant until 6 months. 1 infant did not receive the Rotavirus vaccine at 2 months due to exposure to a TNFi while breastfeeding. There were no incidences of serious neonatal infections.

Conclusions: Current guidelines recommend deferring live vaccines, such as rotavirus, until after 6 months if exposed to a biologic in the third trimester.^{3–5} Compliance with these recommendations was only observed in one infant in our study. One infant received delayed Rotavirus vaccination due to concern about TNFi exposure during breastfeeding; this is not in keeping with current guidelines. Of the 12 infants exposed to a biologic during the third trimester who did not delay live vaccination until after 6 months, there were no incidents of serious neonatal infections, in keeping with the findings of current published case series.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5162

FRI0142

THE COMPARISON OF THE ULTRASONOGRAPHIC SYNOVIAL FINDINGS BETWEEN INTRAVENOUS ADMINISTRATION AND SUBCUTANEOUS INJECTION OF TOCILIZUMAB

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Background: Biologic disease-modifying anti-rheumatic drugs (bDMARDs) that target cytokines and cytokine receptors such as tumour necrosis factor (TNF) alpha and interleukin (IL) 6 have been established as a standard therapy in patients with rheumatoid arthritis (RA). Tocilizumab (TCZ) that targets IL-6 receptors has two administration routes such as intravenous administration (IV) or subcutaneous injection (SC). The effect of TCZ-SC therapy demonstrated comparable efficacy and safety to TCZ-IV therapy in clinical study.^{1,2} However, there have been no reports that evaluate the effect of TCZ-IV and SC for synovitis by imaging modality.

Objectives: The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by TCZ-IV and SC.

Methods: All patients with RA who treated with TCZ in Osaka City University RA registry (1140 patients with RA and 390 patients using bDMARDs) were included in this cross-sectional study. US examination was performed in MCP, PIP, wrist and MTP joints and finger flexor tendon and wrist extensor tendon, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18–6 MHz). The grey scale (GS) and power Doppler (PD) findings were assessed by the semi-quantitative method (0–3). GS score and PD score (both 0–156 points) were defined as the sum total of each score.

Results: We analysed total 76 patients who treated TCZ, 27 patients in IV group and 49 patients in SC group (mean age: 62.9±14.0 vs 66.0±13.2 years, p=0.343, mean duration of RA: 17.1±11.1 vs 13.7±12.3 years, p=0.218). The duration of TCZ use was significantly longer in IV (4.6±2.2 vs 3.0±2.4 years, p=0.004).

Clinically, DAS28-ESR improved from 5.3±1.5 at baseline to 2.4±1.1 at US examination in IV group, and it improved from 5.2±1.4 to 2.8±1.5 in SC group. US findings were not significantly differenced in both groups, GS score: 11.7±12.5 vs 10.9±9.6 (p=0.751), PD score: 5.3±8.1 vs 5.7±6.8 (p=0.832), max PD grade: 1.3±0.9 vs 1.4±0.9 (p=0.571) in IV and SC respectively.

Abstract FRI0142 – Table 1. The comparison of demographic and ultrasonographic findings between TCZ-IV and SC patients with rheumatoid arthritis.

	TCZ-IV group (n=27)	TCZ-SC group (n=49)	P value
Age (years old)	62.9±14.0	66.0±13.2	0.343
Disease duration (years)	17.1±11.1	13.7±12.3	0.218
Duration of TCZ use (years)	4.6±2.2	3.0±2.4	0.004
DAS28-ESR at baseline	5.3±1.5	5.2±1.4	0.780
DAS28-ESR at ultrasound examination	2.4±1.1	2.8±1.5	0.175
CDAI at baseline	21.8±14.5	22.8±14.4	0.787
CDAI at ultrasound examination	7.3±5.9	10.6±10.4	0.082
Total GSUS score	11.7±12.5	10.9±9.6	0.751
Total PDUS score	5.3±8.1	5.7±6.8	0.832
Maximum PDUS grade	1.3±0.9	1.4±0.9	0.571

Conclusions: We compared the ultrasound findings between patients with RA treated by TCZ-IV and SC. Ultrasound findings between IV and SC were not significantly differenced. Both administration routes of TCZ are effective for the treatment in patients with RA.

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Acknowledgements: We wish to thank Tomoko Nakatsuka for clinical assistant, Setsuko Takeda, Emi Yamashita and Yuko Yoshida for their special efforts as a sonographer and collecting data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.1851

FRI0143

INFLUENCE OF LOW-DOSE GLUCOCORTICOID TREATMENT ON PERSISTENCE ON BIOLOGIC DMARDS THERAPY: REAL-LIFE DATA FROM THE ITALIAN GISEA REGISTRY

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Background: The use of glucocorticoid (GC) in Rheumatoid arthritis (RA) is recognised by the current treatment approach as a valid adjunct to DMARDs therapy. Despite its efficacy, safety of GC is still an issue and the best strategy of use is still debated, including patients under bDMARDs therapy

Objectives: To analyse in RA the differences of GC users versus non-users of baseline features, response to therapy and persistence in bDMARDs from the Italian biologics registry GISEA (Italian Group for the Study of Early Arthritis)

Methods: Consenting patients satisfying 1987 or 2010 ACR criteria for RA included in the Italian GISEA registry were enrolled. Data recorded comprehend demographic and clinimetric variables. Data are collected at baseline and 6 monthly during follow-up. To be included in the study patients needed a minimum follow-up time of 12 months and if data were not updated after 2012 patients were considered lost to follow-up. EULAR and HAQ responses were calculated. Statistical analysis included descriptive measures, parametric and nonparametric comparisons between groups and univariate analysis of survival on therapy

Results: A total of 8545 patients were enrolled, of them 4193 (49%) using a variable dose of GC. In 3035 (72%) the dose was ≤5 mg. Baseline demographic and disease-specific features at the start of bDMARD therapy were not different between GC users and non-users, both in 1 st and 2nd line bDMARDs RA patients. EULAR response rates were generally better in GC users at 6 and 12 months, but without statistical significance: good/moderate EULAR responses at 6 months were attained in 76.5% of GC users versus 67% in non users, while at 12 months in 81.5% vs 73% respectively (both Ps not significant). Similarly, HAQ responses (<0.5) were slightly better in users vs non users at 6 (42.5% vs 37.4%) and 12 months (46.5% vs 42%) but again without statistical significance. Finally, mean survival on bDMARDs therapy after 2 years was significantly influenced by GC with better survival curves in steroid-treated patients (55.8% vs 47%, p<0.001). This difference was also maintained subanalysing patients in 1 st or 2nd bDMARD lines of therapy (56.2% in users vs 48% in non users in 1 st line and 55.3% vs 45.9% in 2nd line, both Ps <0.001).

Conclusions: Our data show that GC are used in a high percentage of RA patients on bDMARD therapy. GC significantly improve the persistence on bDMARDs therapy in 1 st and 2nd line. No obvious other differences are evident in baseline, EULAR and HAQ response rates. This fact should be kept in mind when evaluating the persistence on bDMARD treatment reported in different registries. Safety evaluations in individual patients should be further analysed to guide the use of GC in this setting

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4321

FRI0144

PATIENT-REPORTED OUTCOMES WITH SARILUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE SIMILAR REGARDLESS OF PRIMARY OR SECONDARY FAILURE WITH TUMOUR NECROSIS FACTOR INHIBITORS

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Background: Sarilumab is a human monoclonal antibody that binds membrane and soluble IL-6 and was recently approved for the treatment of moderate-to-severe rheumatoid arthritis. Among inadequate responders to a TNF inhibitor (TNFi), patients may respond differently to sarilumab depending on whether they had a primary (1st) failure or initially responded but then subsequently lost response (secondary [2nd] failure).