Abstract AB0468 – Figure 1. PDUS evaluation of two cohorts with ACPA positive

Conclusions: The treatment with Abatacept, administered in the first or second or third line, has shown significant efficacy in reducing the synovial inflammation in patients with RA, monitored with clinical and ultrasonographic outcome. Moreover, we have not demonstrate statistically significant differences between two groups into the timing of improvement.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7304

AB0469 EFFICACY AND SAFETY OF INTERLEUKIN 6 INHIBITORS IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

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Background: Interleukin 6 (IL-6) inhibitors constitute a therapeutic option for patients with rheumatoid arthritis (RA). Currently, apart from Tocilizumab (TCZ), we have data from other drugs targeting the IL-6 pathway.

Objectives: To review published evidence on safety and efficacy of IL-6 inhibitors in RA.

Methods: We performed sensitive systematic literature searches in Medline and Cochrane (up to October 2017), screened EULAR and American College of Rheumatology meeting-abstracts. An expert librarian designed the strategies that included Mesh and text word terms. The search was limited to human RA, adults and the English and Spanish language. The inclusion criteria were as follow: 1) RA patients on IL-6 Inhibitors including TCZ, sarilumab (SAR), olokizumab, sirukumab and clazakizumab; 2) Placebo and an active comparator were accepted as comparators; 3) Articles including typical efficacy and safety variables such as DAS-28, radiographic progression or the infections rate; 4) Only meta-analyses, systematic reviews and clinical trials were selected. Two reviewers screened the titles and abstracts of the retrieved articles independently. They also collected the data from the studies included by using ad hoc standard forms. All collection was double by article and independent. Subsequently, a secondary manual search of the bibliography of the articles that were finally included was performed. Evidence tables were produced. The quality was evaluated with the Oxford 2009 scale.

Results: We included 64 articles of moderate-high quality, variable duration, between 12 and 108 weeks. These articles analysed more than 8000 patients with RA, most of them with established RA (although there are data on early RA), with high disease activity and severity criteria. More than a half of the studies are of TCZ. IL-6 inhibitors were effective both in the short and long term in terms of clinical remission, RA activity, radiographic progression, function, fatigue, bone metabolism, morning stiffness, pain, quality of life, or anaemia. They also decreased and even normalised CRP values in a rapid and sustained manner. The efficacy of blocking IL-6 has been seen in RA refractory to DMARD or anti-

TNFα and in MTX-naïve patients, as well as in the intravenous and subcutaneous formulations (TCZ). TCZ and SAR are more effective than adalimumab in monotherapy. In general, no statistically significant differences were found between combined therapy and monotherapy. In terms of safety, the rate of adverse events increased over time and with the concomitant use of DMARDs. Infections and hypersensitivity reactions were the most frequent adverse events and infections the most frequent serious adverse events. IL-6 inhibitors were associated with a rapid and subsequently sustainable increase in serum lipid parameters, although this was not associated with a higher prevalence of cardiovascular events and related mortality, nor was it associated with neoplasms. Transaminase elevations were generally mild and without serious disorders. The incidence of gastrointestinal perforations was very low, and it was associated with a previous history of diverticulitis.

Conclusions: IL-6 inhibitors are effective to control RA activity and symptoms and to prevent radiographic damage in different disease profiles, with an acceptable safety profile.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5376

AB0470 INFLUENCE OF USING ADALIMUMAB IN COMPLEX TREATMENT ON FREQUENCY OF EYES INVOLVEMENT IN PATIENTS WITH JIA

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Background: Extra-articular organs involvement in JIA is frequent and mostly includes rheumatoid uveitis in ANA-positive oligoarthritis. In Ukraine almost 10% of children with JIA during systematic ophthalmologic examination have signs of ocular involvement. Early treatment with biological agents can influence inflammation progression in eyes of the JIA patients

Objectives: Objective of the study was to investigate the frequency of recurrences of uveitis in patients with JIA and eyes involvement on methotrexate alone and methotrexate with adalimumab.

Methods: There were 23 patients with JIA and rheumatoid uveitis involved into the study. Mean age was 9,6 (4–16) years. Among them there were 14 (61%) girls and 9 (39%) boys. Serological characteristic included 17 (74%) patients with positive ANA, and 3 (13%) children with positive HLA-B27. All patients received 15 mg/m2/week of SC methotrexate. During onset and recurrence of uveitis all children received glucocorticoids with slowly tapering dosage (from 1 mg/kg/day to 0.2–0.1 mg/kg/day) until uveitis remission. Of 23 patients 11 (47,8%) received adalimumab in standard doses. Study were hold for 5 years during which every child were investigated by ophthalmologist every 3 months irrespectively of clinical status.

Results: During 5 year follow up in "methotrexate" group (n=12) there were 15 episodes of uveitis recurrence (0,25 episodes per patient/year). Of them 10 (66,6%) were revealed only by ophthalmological assessment and had no obvious clinical signs (subclinical uveitis). Same time only 2 episodes of uveitis recurrence were registered in "methotrexate +adalimumab" group (0,04 episodes per patient/year) (p<0.05).

Conclusions: Adding adalimumab to methotrexate in complex treatment of patients with JIA and eyes involvement allows decreasing frequency of both clinically evident and subclinical recurrences of rheumatoid uveitis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4148

AB0471 BIOSIMILAR MEDICINE IS ACCEPTABLE TO PATIENTS IF RECOMMENDED BY A RHEUMATOLOGIST IN AN AUSTRALIAN TERTIARY RA COHORT

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Background: Advancement in biological disease-modifying antirheumatic drugs (bDMARDs) has greatly improved the prognosis of patients with rheumatoid arthritis. Their high costs, however, pose a significant health-economic challenge. Biosimilars are being adopted in Australia and worldwide to improve affordability and access to treatment. While the predominant focus of current literature has been on physicians' awareness and confidence of biosimilars, an effective introduction of biosimilars requires an understanding of patient acceptance of these products.

Objectives: To investigate patient awareness and attitudes to biosimilar medicine in a tertiary hospital RA clinic.

Methods: A cross-sectional study of 127 patients with rheumatoid arthritis was performed in Melbourne, Australia. A brief education on biosimilars was provided. Patients rated concerns regarding biosimilar efficacy, side-effect profile, operation

of the medication, and general attitude towards the new medication on a ten-point scale.

Patients willing to take generic medicines

Patients unhappy to take generic medicines

Abstract AB0471 – Figure 1

Results: 45.2% of our cohort have received biological DMARDs. Although only 5.6% have some knowledge of biosimilars, 75.4% would accept biosimilars if their rheumatologist recommends it, with only 5.6% refusing to switch. 19% of patients were unsure. Of those refusing biosimilars, the main concerns related to efficacy and general concerns about change. In our RA cohort, 61.9% took generic medicines regularly and 84.6% of these they would also be comfortable taking biosimilars. In those refusing generic medicines (27%), 61.8% would be still comfortable taking biosimilars. 15.9% and 12.7% of patients had great concerns about the efficacy and safety profile of biosimilars, respectively. 26.2% were significantly worried that their physician may be unaware if they were receiving the biosimilar or reference product.

Conclusions: Despite being unfamiliar with biosimilars, most patients in our cohort would be comfortable taking biosimilars if recommended by their rheumatologist, highlighting the role of trust in doctor-patient relationships. Of patients usually refusing generic medicines, nearly two-thirds would still accept biosimilars. Almost a quarter of the patients were unsure about the use of biosimilars and many patients indicated that they would like more information regarding these products. This patient group offered the opportunities to improve the uptake rate of biosimilars by allaying their concerns through information-education strategies. The current legislation in Australia allows pharmacists to substitute biological DMARDs in consultation with the patient without informing the prescriber. This concerns nearly all (89%) prescribers in Australia. The majority of patients in our study were not concerned, whilst approximately one quarter were worried about unrecognised switching. A successful introduction of biological DMARDs is likely to improve patient access to effective biological therapy and to ensure sustainability of the healthcare budgets.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3233

AB0472

PHARMACODYNAMIC EFFECT AND SAFETY OF SINGLE-DOSE SARILUMAB SC OR TOCILIZUMAB IV OR SC IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Two studies (PDY14191 [NCT02404558]: randomised, open-label, Japanese patients; 6R88-RA-1309 [NCT02097524]: randomised, open-label, non-Japanese patients) assessed the pharmacodynamic profiles of two monoclonal antibody blockers of IL-6Rα, sarilumab and tocilizumab.

Objectives: To evaluate the pharmacodynamics of absolute neutrophil count (ANC), C-reactive protein (CRP), IL-6, soluble IL-6R (sIL-6R), and safety after a single dose of subcutaneous (SC) sarilumab, or intravenous (IV) or SC tocilizumab in patients with RA.

Methods: 30 Japanese patients (PDY14191) were randomised 1:1 and received a single injection with SC sarilumab 150 mg or SC tocilizumab 162 mg without background medication. 101 non-Japanese patients (6R88-RA-1309) were randomised 1:1:1:1 and received a single dose of SC sarilumab (150 or 200 mg) +methotrexate (MTX), or IV tocilizumab (4 or 8 mg/kg)+MTX. Pharmacodynamic and safety outcomes were assessed through Week 6.

Results: Baseline demographics were comparable between studies except for higher mean body weight in non-Japanese patients (mean 83 vs 57 kg). Although there were numeric differences in baseline pharmacodynamic parameters in the two studies, onset of effects on ANC, CRP, IL-6, and sIL-6R during the first week after a single drug dose were similar regardless of drug, dose, or route of administration in both studies. Within both studies, maximal effects on ANC and CRP nadir and on IL-6 and total sIL-6R peaks were comparable for sarilumab and tocilizumab (table 1). The pharmacodynamic response was more prolonged with IV tocilizumab. Time for pharmacodynamic effects to return to baseline was consistent with the dosing intervals for SC sarilumab (q2w), and IV (q4w) and SC (q2w) tocilizumab. The safety profiles of sarilumab and tocilizumab were generally similar and both drugs were associated with laboratory effects consistent with their mechanism of action (ie, decrease in neutrophil count). There was a dose-dependent effect on ANC<1.0 Giga/L in study 6R88-RA-1309 and numeric differences in ANC<1.0 Giga/L between sarilumab and tocilizumab in PDY14191. The decrease in ANC was not associated with increased risk of infections.

Abstract AB0472 – Table 1. Baseline and change in pharmacodynamic parameters, and safety in studies 6R88-RA-1309 and PDY14191

	6R88-RA-1309 (non-Japanese patients)*				PDY14191 (Japanese patients)	
	SC Sarilumab 150 mg + MTX (N=26)	SC Sarilumab 200 mg + MTX (N=26)	IV Tocilizumab 4 mg/kg + MTX (N=25)	IV Tocilizumab 8 mg/kg + MTX (N=24)	SC Sarilumab 150 mg (N=15)	SC Tocilizumab 162 mg (N=15)
Neutrophils						
Baseline, mean±SD, Giga/L	4.32±1.53	4.72±1.96	4.04±1.36	4.52±2.48	3.45±1.11	3.81±0.99
Nadir, mean±SD (min-max), Giga/L	1.55±0.56 (0.61–3.07)	1.76±1.04 (0.21–3.97)	1.78±0.60 (0.96–2.92)	1.64±0.89 (0.69–4.51)	1.11±0.51 (0.3–1.9)	1.78±0.56 (0.9–2.9)
Time to nadir, median, days	3.5	4.0	5.0	3.0	2.0	4.0
CRP						
Baseline, median, mg/L	5.50	6.05	4.28	5.87	0.85	0.49
Nadir, median* (min-max), mg/L	0.67 (0.10–8.82)	0.49 (0.10–5.13)	0.43 (0.10–1.73)	0.31 (0.10–1.35)	0.06 (0.0–0.2)	0.15 (0.0–0.6)
Time to nadir, median, days	7.0	7.0	15.0	15.0	10.0	10.0
IL-6						
Baseline, mean±SD, pg/mL	71.9±58.4	9.86±10.5	7.33±11.1	22.1±45.4	1.97±5.42	5.75±15.5
Peak, mean±SD (min-max), pg/L	159±356 (22–1844)	177±234 (17–1079)	143±160 (23–644)	183±246 (25–1095)	44.0±42.2 (11–169)	48.4±67.7 (7–231)
Time to peak, median, days	5.0	4.5	6.0	6.5	5.0	7.0
sIL-6R						
Baseline, mean±SD, ng/mL	42.9±11.9	42.9±13.7	43.3±14.4	43.8±15.7	36.0±7.9	36.6±11.6
Peak, mean±SD (min-max), ng/mL	274±72.7 (125–406)	334±72.5 (159–442)	415±109 (230–603)	481±120 (340–704)	265±54.6 (155–344)	291±83.6 (206–469)
Time to peak, median, days	11.0	13.0	19.0	22.0	14.0	14.0
AEs						
Patients with TEAEs, N (%)	10 (38.5)	12 (46.2)	8 (32.0)	12 (50.0)	7 (46.7)	4 (26.7)
SAE, N (%)	0	0	0	1 (4.2)	1 (6.7)	0
Patients with ANC <1.0 Giga/L, N (%)	4 (15.4)	7 (26.9)	3 (12.0)	6 (25.0)	5 (33.3)	1 (6.7)
ANC grade						
ANC maximum grade: Grade 3 ≥0.5 to <1.0 Giga/L, N (%)	4 (15.4)	6 (23.1)	3 (12.0)	6 (25.0)	2 (13.3)	1 (6.7)
ANC maximum grade: Grade 4 <0.5 Giga/L, N (%)	0	1 (3.8)	0	0	3 (20.0)	0

*83.2% of patients were white. *Concentrations for CRP were not normally distributed, thus concentrations were summarized by median.

Conclusions: The pharmacodynamic and safety profiles observed after a single-dose of sarilumab SC or IV/SC tocilizumab are consistent with results anticipated in patients with RA administered an IL-6R inhibitor.

Acknowledgements: Study funding and medical writing support (Julie Grey, Adelphi Group) was provided by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: T. Ishii Paid instructor for: GSK, Janssen, Speakers bureau: Mitsubishi-Tanabe, Janssen, Chugai, Ono, Sanofi, Abbvie, Eisai, Astellas, UCB, Teijin, Daiichi-Sankyo, Pfizer, Takeda, Asahi Kasei Pharma, Y. Sato Consultant for: SRL, Paid instructor for: Bristol-Myers Squibb, Y. Munakata: None declared, M. Kajiwara Employee of: Sanofi K.K., Y. Takahashi Employee of: Sanofi K.K., F. Anwar Employee of: Sanofi, A. Paccaly Shareholder of: Regeneron, Sanofi, Amgen, Employee of: Regeneron, P. Kovalenko Shareholder of: Regeneron, Employee of: Regeneron, J. Parrino Shareholder of: Regeneron,