Methods: A retrospective observational study was conducted including patients with RA treated in a tertiary hospital between June 2006 and May 2017 who had received at least one RTX cycle. At RTX initiation we analysed: age, sex, comorbidities and Charlson score, disease duration, presence of rheumatoid factor (RF)/anti-citrullinated protein antibodies (ACPA), disease activity (DAS28), acute phase reactants (CRP, ESR), previous biological treatments; concomitant treatment (csDMARD/glucocorticoids (GC)). Serum Ig levels before every RTX cycle, the number of RTX cycles and adverse events (AE), including serious and opportunistic infections were also analysed.

Results: We included 53 patients (86.8% women, mean age 55.5±13.5 years), 58% with a Charlson score ≥3. Mean disease duration was 16±9.1 years; 84.9% and 92.5% were RF and ACPA positive, respectively.

Before starting RTX, 81% of patients had received other biologic drugs (58.5% ≥ 2), 88% received concomitant csDMARD, (52% methotrexate and 32% leflunomide) and 81% were treated with GC (median dose 10 mg, P₂₅₋₇₅ 5–10 mg). The median number of RTX cycles received per patient was 5 (P₂₅₋₇₅ 2–6).

80 AE were reported: 12 infusion reactions, 8 cases of neutropenia, 51 infections (18 respiratory, 8 urinary, 4 skin and soft tissues, 8 gastrointestinal, 4 cases of non-disseminated *herpes zoster*, 1 bacteremia, 2 septic shock and 6 other) of which 19 were serious, and 5 malignancies (2 melanomas, 2 cervix, and 1 bladder) were also notified. No opportunistic infections were reported.

Ig levels were obtained for 41 subjects: 7, 5 and 1 patients had low levels of IgG, IgM and IgA, respectively.

Patients who developed infections received a greater number of RTX cycles (p<0.0002) and had more frequently low levels of serum IgG during follow-up (p<0.044) than those who did not have infections.

Conclusions: Long-term exposure to RTX showed a good safety profile with a low incidence of serious infectious and no opportunistic infections.

Factors associated with the development of infections were the number of cycles received and low serum levels of IgG at any point during follow-up.

Acknowledgements: The authors would like to thank Dr. García de Yébenes who provided statistical support

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3634

AB0467

SUSTAINED CLINICAL RESPONSE IN REFRACTORY RHEUMATOID ARTHRITIS PATIENTS WITH A LOW-DOSE RITUXIMAB RETREATMENT REGIMEN

S.D.L.C. Rodríguez García, R. Castellanos-Moreira, M.V. Hernandez-Miguel, A. Cuervo, V. Ruiz-Esquivé, J. Ramírez, O. Camacho, J.D. Cañete, J. Gomez Puerta, R. Sanmartí. *Rheumatology, Hospital Clinic de Barcelona, Barcelona, Spain*

Background: The standard dose of rituximab (RTX) in rheumatoid arthritis (RA) is two intravenous (iv) 1 g infusions, separated by two weeks. Recently, the efficacy of a low-dose of RTX for retreatment in RA patients has been reported.¹

Objectives: Our aim was to assess the long-term sustained effectiveness of a low-dose of RTX in daily clinical practice.

Methods: Observational retrospective study including all RA patients treated on a tertiary hospital who had received at least one cycle of RTX, at the standard dose, between June 2006 and May 2017. We selected those patients who achieved a good or moderate EULAR response and thereafter were down-titrated to a low-dose regimen (1 g). Variables analysed: age, sex, disease duration, presence of ACPA (antiCCP2) and rheumatoid factor (RF), glucocorticoid (GC) and conventional synthetic DMARD (csDMARD) use and dosage before and after RTX treatment, number of biologic DMARD (bDMARD) used prior to initiating RTX. Disease activity was measured using DAS28 index (prior to first RTX infusion, at low-dose regimen initiation and at last follow-up visit).

Results: 53 patients received, at least, one cycle of 2 g RTX, 70% achieved a good or moderate EULAR response and were stepped-down to a low dose retreatment regimen. Baseline characteristics of patients receiving low-dose RTX were: mean age 56.4±10.9 years; 13.5% male, mean disease duration 12.7±9.8 years, 91.9% RF + and 97.3% ACPA +; mean DAS28 prior to RTX initiation 5.79 ±1.17.

73% of patients had received other bDMARD before RTX, 48% 2 or more. 92% were on cs-DMARDs, 51.4% methotrexate (MTX) and 37.8% leflunomide (LEF) and 86.5% were receiving concomitant GC (median dose 10 mg, P₂₅₋₇₅ 5–10 mg). 73% of subjects received only one standard cycle before RTX dose reduction.

Mean DAS28 decreased significantly between the first visit on 1 g RTX vs the last follow-up visit (4.08 vs 3.04; p<0.0001). Additionally, 11 patients (8 MTX, 3 LEF) were able to reduce csDMARD dosage, 56.3% of patients receiving GC at the initiation of low-dose retreatment were able to reduce the dose (median 10 mg vs 5 mg; p<0.0001), and 28% discontinued GC therapy.

After a mean follow-up of 3±1.8 years, RTX was withdrawn in 10 patients: 8 due to adverse events (recurrent infections in 4) and 2 cases due to loss of efficacy.

Conclusions: A sustained clinical response was observed with the 1 gr retreatment of RTX after a long-term follow-up period.

REFERENCE:

[1] Mariette X, et al. *Ann Rheum Dis* 2014;73:1508–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4008

AB0468

CLINICAL AND ULTRASONOGRAPHIC EFFECTIVENESS IN TWO COHORTS OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT: A REAL LIFE STUDY

S. Parisi, M.C. Ditto, M. Scarati, M. Priora, C.L. Peroni, E. Fusaro. *Rheumatology Unit, AOU Città della Salute e della Scienza di Torino, Turin, Italy*

Background: Synovitis in Rheumatoid Arthritis (RA) is a phenomenon related to the development of erosions and progressive structural damage; early synovitis improvements are successfully associated with long-term clinical and structural outcomes.

Objectives: The aim of this study was to evaluate the efficacy of abatacept in two cohort of patients treated with Abatacept as the first and second or third line of treatment.

Methods: We evaluated patients affected by RA (according to ACR 2010 criteria) and were divided into two groups:

Group A: patients with moderate or severe active RA, non-responders to Methotrexate (MTX), bDMARDs naïve, treated with Abatacept 125 mg/wk;

Group B: patients with moderate or severe active RA, non-MTX and anti-TNF responders, treated with Abatacept 125 mg/wk;

The concomitant treatment with MTX was maintained unchanged in those patients who were taking it at stable doses before the start of the study (10–15 mg/week for ≥28 days); concomitant therapies such as low-dose systemic CS (prednisone ≤7.5 mg/day) and NSAIDs have been maintained for at least 4 weeks if stable. The activity of RA was calculated with the DAS28-CRP according to the clinical practice protocol (week 0,4,12,24). The Ultrasound (US) evaluation of the synovitis was done according to the Omeract criteria (Grey Scale and PDUS score: 0 to 3).

Results: We recruited consecutively 34 patients with RA, 16 pts (male n=4; 25.00%) took Abatacept as the first line (Group A), and 18 pts (males n=5; 27.70%) took Abatacept as followed by another anti-TNF drugs (Group B). The mean age was 57.2±10.7 years (median 60, range 45–72); mean of DAS28 at baseline was 4.8±0.9 (median 4.7; range 3.9–5.6); mean duration of the disease was 15.3±5.7 years (median 10; range 3–22). Tab.1

A constant improvement of the DAS28 score is shown in both groups examined until the end of the follow up, resulting respectively -Δ 2.0 for Group A (p<0.05) and -Δ 2.1 (p<0.05) for Group B. The total PDUS score decreased in both groups from week 4, with a mean change (95% CI) compared to baseline of -0.8 (range -1.4/-0.2) and progressive mean significant improvement until follow-up (Gr.A p<0.05; Gr.B p<0.05). No serious adverse events or infections were observed. Patients with ACPA positive showed a greater improvement trend compared to other patients in both groups (p: 0.068). Figure 1.

Abstract AB0468 – Table 1. Cohort of patients at baseline

Characteristics	Group A (Abatacept 1 st line)	Group B (Abatacept 2 nd or 3 rd line)
Patients (n.)	16	18
Age (mean±SD), yy	44,20 (±8,7)	56,10 (±10,6)
Female (%)	76,00%	77,00%
Disease Duration (mean±SD), yy	7,60 (±5,3)	12,70 (±5,6)
DAS28-CRP (mean±SD)	5,10 (±0,9)	4,90 (±1,1)
PDUS score (mean±SD)	12,30 (±2,5)	12,60 (±3,1)

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.

REFERENCE:

- [1] D'Agostino T, et al. Early Response to Abatacept Plus MTX in MTX-IR RA Patients Using Power Doppler Ultrasonography: an open label Study. *Ann Rheum Dis* 2012;71:18.

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

T. Oton¹, E. Loza², R. Sanmarti³, J. Tornero Molina⁴. ¹Instituto de Salud Musculoesquelética; ²Instituto de Salud Musculoesquelética, Madrid; ³Rheumatology, Hospital Universitari Clínic, Barcelona; ⁴Rheumatology, Hospital de Guadalajara, Guadalajara, Spain

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-

TNF α 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

T. Marushko, O. German, J. Golubovska. *National Academy of postgraduate education named after P.L. Shupik, Kyiv, Ukraine*

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

T. Kovitwanichkanont^{1,2}, D. Wang^{2,3}, S. Raghunath^{2,3}, L. Kyi², N. Walpole³, S. Pignataro², S. Morton², E. Morand^{2,3}, M. Leech^{2,3}. ¹University of Sydney, Sydney; ²Monash Health; ³Monash University, Melbourne, Australia

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