remission even using biological therapy. DNAse activity of the blood serum and antinuclear antibody may be useful in this context. Changes of serum DNase activity in the RA treatment by biological agents previously have been not investigated.

Objectives: The aim of this work is to study the dynamics clinical and laboratory parameters, DNAse serum activity and ANA during the RA treatment by infliximab (INF) and assess the prognostic potential of them in prediction of response to INF.

Methods: 24 RA patients were involved in the study. All patients fulfilled the EULAR/ACR 2010 RA criteria. 22/24 patients received 6 infusions of INF at a dose of 3 mg/kg according to standard protocol: at 0th, 2th, 6th and then every 8 week. 2/24 patient received 4 infusions of INF. All patients received synthetic DMARDs therapy by metotrexate (10–17,5 mg weekly), 18/24 patients received glucocorticoids (methylprednisolone 4–8 mg daily) and non-steroidal anti-inflammatory drugs. Prior to treatment by INF patients did not receive any biological agents. All patients had high disease activity before INF treatment (DAS28<5,1).

ANA determination was performed by indirect immunofluorescence on Hep-2 cells using digital system AKLIDES. ANA was measured in serum samples before 1st INF administration, at 22–30 weeks after the 1st INF administration.

To determine the DNAse activity of serum the method of rivanol clot was used. DNase activity was measured in serum samples before 1st INF administration, at 6 weeks after the 1st INF administration, at 30 week of treatment.

Results: At week 30, ACR70 improvement reached 5/22 of the patients, ACR50 - 10/22 of the patients, ACR20 – 4/24 of patients.

At 30 weeks of treatment by INF 2/22 of patients achieved remission (SDAI<3,3), 10/22 - a low disease activity (3,3 <SDAI ≤11).

13/24 patients were ANA-positive before INF treatment, 12/22 - after 24 weeks of treatment.

Levels of serum DNase activity did not differ before and during the INF treatment (p>0,05).

For assessment prognostic value of laboratory signs for INF response prediction logistic regression was used. Prognostic model, which included changes in ANA (Δ ANA) and DNAse serum activity level (Δ DNAse serum activity), anti-CCP- and RF-negativity was better (p=0,02) (area under ROC-curve =1,0; 95% CI 0,844–1,00 p=0,0001) than the model, which included only anti-CCP- and RF-negativity (area under ROC-curve =0,795; 95% CI 0,597–0,924, p=0,0141).

Conclusions: The study confirmed the efficacy of RA treatment by INF for anti-CCP and RF negative patients. DNAse serum activity and ANA may be used as additional prognostic biomarker of INF response. For the assessment DNAse activity as marker of response to therapy is needed futher investigations with more number of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6941

SAT0167 CAN INFLIXIMAB EFFICACY BE PREDICTED BASED ON BLOOD CONCENTRATION AT THE FOURTH DOSE?

M. Sato[1], M. Takemura[2], T. Tani[1], T. Ohashi[1]. *[1]Rheumatology, Ohashi and Tani Orthopedics, Gifu; [2]Advanced Diagnostic System Research Laboratory, Fujita Health University Graduate School of Health Sciences, Toyoake, Japan*

Background: Biological drugs exhibit excellent efficacy and continuity in the treatment of rheumatoid arthritis (RA) and play an important role in RA treatment. Blood concentration is an important factor in the efficacy of biological drugs, particularly antibody drugs. Infliximab (IFX) is an antibody drug against TNF-α and is reported to require a blood concentration of ≥1 μg/mL to be effective.

Objectives: To investigate whether clinical efficacy can be predicted based on blood concentrations at the fourth dose of IFX in patients with RA.

Methods: This study included 56 patients with RA who were treated with IFX. Patients included 13 men and 43 women aged from 26 to 81 years (mean, 60.3 years). The IFX concentration was measured immediately before administering the fourth IFX dose (8 weeks after administering the third dose). We then investigated the relationship between subsequent IFX efficacy and IFX concentration immediately before the fourth dose of IFX in these patients with RA. Concentrations were measured in stored frozen serum by using the ELISA method.

Results: The IFX concentration immediately before the fourth dose was ≥1 μg/mL in 32 patients (≥1 μg/mL group) and <1 μg/mL in 24 patients (<1 μg/mL group). At the fourth dose, IFX was effective in 30 patients (93.8%) in the ≥1 μg/mL group, at a mean concentration of 5.18 μg/mL, while the mean concentration was 5.69 μg/mL for the remaining 2 non-responders. IFX was also effective in 21 patients (87.5%) in the <1 μg/mL group but did not elicit any response in the other 3 patients. At this point, all 5 non-responsive patients were primary non-responders. Of all 51 responders, 58.8% were in the ≥1 μg/mL group and 41.2% were in the <1 μg/mL group. Based on the data, we observed no relationship between efficacy and IFX concentration. After 1 year of IFX treatment, 36 of the 56 patients were responsive and 20 were non-responsive. In the 2 groups, 26 responsive patients (63.9%) and 9 non-responsive patients (45.0%) had an IFX concentration of ≥1 μg/mL immediately before the fourth dose.

Conclusions: At the fourth dose, many of the patients with an IFX concentration of <1 μg/mL were also responsive to the treatment, so future efficacy was difficult to predict based on IFX concentration. In other words, during clinical evaluation, measurement of IFX concentrations is not necessary in responsive patients. However, IFX concentrations should be measured in non-responsive patients or patients with a diminished response. If the concentration is <1 μg/mL, IFX efficacy should be restored by increasing the dose or shortening the administration interval.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6072

SAT0168 DISCONTINUATION OF FIRST BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS: MAIN CAUSES AND CORRELATION BETWEEN SECONDARY INEFFICACY AND DEVELOPMENT OF IMMUNOGENICITY

P. Bogas[1], C. Plasencia[1], D. Pascual-Salcedo[2], G. Bonilla[1], E. Moral[1], C. Tornero[1], L. Nuño[1], A. Villalba[1], D. Peiteado[1], A. Martinez[2], B. Hernandez[2], A. Balsa[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitario la Paz, Madrid, Spain*

Background: Biologic therapy has been a major change in Rheumatoid Arthritis (RA) prognosis, but around 40% of patients (pts) fail to respond. Part of this treatment failure can be explained by the development of anti-drug antibodies (ADA), but the ADA-associated secondary inefficacies rate is currently unclear

Objectives: To assess in our AR cohort treated with Adalimumab (Ada), Infliximab (Ifx), etanercept (Etn), certolizumab (Czp), Tocilizumab (Tcz) and Abatacept (Abt) as 1st biologic agent, the frequency of drug suspension as well as the main causes for discontinuation and the secondary inefficacy rate associated with the development of immunogenicity

Methods: From the RA cohort that initiated their 1st biologic agent at Hospital La Paz between 2005 and 2016, only those who had suspended those drugs were included, and causes for suspension were collected. Clinical activity was measured by DAS28 and Delta-DAS28 at 6 months of treatment to classify discontinuation by primary or secondary inefficacy. Drug levels (DL) and/or ADA were also measured by ELISA at 6 months since initiating the biologic agent in 43 pts and at drug discontinuation in 59 pts. Primary inefficacy was defined as DAS28>3.2 and delta-DAS28 <1.2 at 6 months with DL present. Secondary inefficacy was defined both as DAS28>3.2 plus delta-DAS28 <1.2 at 6 months with ADA+ and Delta-DAS28>1.2 or DAS28 <3.2 at 6 months with subsequent loss of efficacy. Statistical analysis was performed using SPSS version 20.0

Results: From the 246 pts who started their first biologic therapy, 144 (58%) pts who had definitively discontinued were included. [Ifx (n 35, 24%), Ada (n 40, 28%), Etn (n 30, 21%), Czp (n 23, 16%), Tcz (n 10, 7%) y Abt (n 6, 4%)]. 116 (80,6%) were women. The mean age was 56.3±14.7 years. The mean time of biologic was 2.23±1.96 years. From the global cohort, 18 (12.5%) drop out the treatment due to primary inefficacy, 41 (28.5%) to secondary inefficacy, 57 (39.6%) to adverse effects (AE), 11 (7.6%) to remission and 17 (11.8%) to other causes (surgery, pregnancy, etc.). 12.5% pts who discontinued due to AE or other causes had also a primary or secondary inefficacy; by including those pts in these last causes for suspension, a total of 20 pts (14%) failed due to primary inefficacy and 57 pts (39.6%) to secondary inefficacy. The most frequent AEs were: infections (35%), cutaneous AEs (psoriasis, rash, etc. (10.5%), infusion reactions (9%) and neoplasia (9%). Of the 59 pts who had DL/ADA measured at drug discontinuation, 42.4% were ADA +. Within the group that failed due to secondary inefficacy and had DL/ADA determined, 50% were ADA+; nevertheless this rate was smaller in suspensions due to other causes. Likewise, in the ADA+ pts, 73% suspended due to secondary inefficacy

Demographic Characteristics	
Age (years)	64±15,4
Sex (Female)	116 (80,6%)
Smokers	25 (17,6%)
BMC	27,79±8,87
Disease duration	16,7±8,04
RF +	117 (81,3%)
Anti-CCP +	119 (85,6%)
Duration of treatment (years)	2,23±1,96
Basal DMARDs	127 (89%)
Basal Methotrexate	82 (57,3%)
Basal Leflunomide	57 (39,6%)
Basal Salazopyrine	13 (9,1%)
Basal CPR	15,14±19,4
Basal ESR	34,2±23,4
Basal DAS	5,24±1,32

Conclusions: In our RA cohort, adverse effects were the main cause for discontinuation, with infections at 1st place. The 2nd cause conditioning interruption was the secondary inefficacy, in which 50% of our pts were ADA+ at drug

discontinuation. These data suggest that the development of ADA is a frequent cause of secondary inefficacy in our RA pts
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6371

SAT0169 MAINTENANCE AND IMPROVEMENT IN CLINICAL EFFICACY BETWEEN WEEK 12 AND 24 IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB4 OR REFERENCE ETANERCEPT

P. Emery[1], J. Vencovsky[2], E. Keystone[3], J. Ghil[4], S.Y. Cheong[4], E.E. Hong[4]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; [2]Institute of Rheumatology, Prague, Czech Republic; [3]Mount Sinai Hospital, Toronto, Canada; [4]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of*

Background: SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN).
Objectives: To evaluate the maintenance and improvement in clinical efficacy between week 12 and 24 in patients with rheumatoid arthritis (RA) treated with SB4 or ETN from a post-hoc analysis of phase III results.
Methods: Patients with RA were randomised to receive 50 mg/week of either SB4 or ETN with background methotrexate. American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) responses were compared at week 12 and week 24. At week 12, patients with available assessment results were categorised as ACR responders or ACR non-responders and EULAR responders (patients with moderate or good EULAR response) or EULAR non-responders. The same was assessed for week 24 and patients with missing data at week 24 were regarded as non-responders.
Results: A total of 551 patients (283 patients from SB4 and 268 patients from ETN) completed 24 weeks of the study. In both treatment groups, efficacy was well maintained between week 12 and week 24. Among patients who were ACR20, 50, or 70 responders at week 12, 90.8% vs. 91.4%, 80.5% vs. 80.6%, and 74.5 vs. 77.5% of patients from SB4 and ETN, respectively, maintained their responses at week 24. Likewise, EULAR response was maintained by 93.1% vs. 92.6% of patients who had a good or moderate response at week 12. (Table).
The improvement in ACR responses between week 12 and 24 was comparable between SB4 and ETN group (Table). In SB4 and ETN, respectively, 42.1% vs. 50.5% of 12-week ACR20 non-responders became ACR20 responders at week 24. Similarly, 20.9% vs. 21.9% of 12-week ACR50 non-responders became ACR50 responders and 13.0% vs. 11.4% of 12-week ACR70 non-responders became ACR70 responders. The improvement in EULAR responses was also comparable between SB4 and ETN. 43.2% vs. 52.2% of 12-week EULAR non-responders in SB4 and ETN, respectively, became EULAR responders at week 24.

Table. Maintenance and improvement of efficacy between week 12 and week 24

		Week 24 responders	
		SB4 50 mg n/n' (%)	ETN 50 mg n/n' (%)
ACR20	Responder at week 12	179/196 (91.3%)	162/175 (92.6%)
	Non-responder at week 12	41/97 (42.3%)	51/105 (48.6%)
ACR50	Responder at week 12	91/114 (79.8%)	75/93 (80.6%)
	Non-responder at week 12	37/179 (20.7%)	41/187 (21.9%)
ACR70	Responder at week 12	38/51 (74.5%)	31/40 (77.5%)
	Non-responder at week 12	31/242 (12.8%)	28/240 (11.7%)
EULAR response*	Responder at week 12	231/246 (93.9%)	215/231 (93.1%)
	Non-responder at week 12	19/46 (41.3%)	24/49 (49.0%)

n, number of responders; n', number of responders or non-responders at week 12
*Patients with moderate or good EULAR response were regarded as responders.

Conclusions: Efficacy of SB4 and ETN was well maintained and the maintenance rate was comparable between week 12 and week 24. In addition, a similar and considerable proportion of patients in SB4 and ETN who did not achieve a clinical response at week 12 reached clinical response at week 24. These results suggest that etanercept non-responders at week 12 may benefit from continuing treatment up to 24 weeks.
Disclosure of Interest: P. Emery Grant/research support from: Abbvie, BMS, Pifzer, USB, MSD, Novartis, Lilly, Consultant for: Samsung Bioepis Co., Ltd., J. Vencovsky Consultant for: Samsung Bioepis Co., Ltd., Biogen, E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Janssen, Lilly, Novartis, Pfizer, Consultant for: Abbott, AstraZeneca, Biotest, BMS, Genentech, Janssen, Lilly, Merck, Pfizer, Samsung Bioepis, Speakers bureau: Abbott, AstraZeneca, BMS Canada, Janssen, J. Ghil Employee of: Samsung Bioepis Co., Ltd., S. Y. Cheong Employee of: Samsung Bioepis Co., Ltd., E. Hong Employee of: Samsung Bioepis Co., Ltd.
DOI: 10.1136/annrheumdis-2017-eular.3344

SAT0170 B-CELL PHENOTYPE AND IGD-CD27- MEMORY B CELLS ARE AFFECTED BY TNF-INHIBITORS AND TOCILIZUMAB TREATMENT IN RHEUMATOID ARTHRITIS

R.A. Moura[1], C. Quaresma[1], A.R. Vieira[1], M.J. Gonçalves[1,2], J. Polido-Pereira[1,2], V.C. Romão[1,2], N. Martins[2], H. Canhão[1,2], J.E. Fonseca[1,2]. *[1]Rheumatology Research Unit, Instituto de Medicina Molecular; [2]Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon, Portugal*

Background: The use of TNF-inhibitors and/or the IL-6 receptor antagonist, tocilizumab, in rheumatoid arthritis (RA) have pleiotropic effects that also involve circulating B-cells.
Objectives: The main goal of this study was to assess the effect of TNF-inhibitors and tocilizumab on B-cell phenotype and gene expression in RA.
Methods: Blood samples were collected from untreated early RA (ERA) patients (<1 year of disease duration), established RA patients under methotrexate treatment, established RA patients before and after treatment with TNF-inhibitors and tocilizumab, and healthy donors. B-cell subpopulations were characterized by flow cytometry and B-cell gene expression was analyzed by real-time PCR on isolated B-cells. Serum levels of BAFF, CXCL13 and sCD23 were determined by ELISA.
Results: The frequency of total CD19+ B-cells in circulation was similar between controls and all RA groups, irrespective of treatment, but double negative (DN) IgD-CD27- memory B-cells were significantly increased in ERA and established RA when compared to controls. Treatment with TNF-inhibitors and tocilizumab restored the frequency of IgD-CD27- B-cells to normal levels, but did not affect other B-cell subpopulations. TACI, CD95, CD5, HLA-DR and TLR9 expression on B-cells significantly increased after treatment with either TNF-inhibitors and/ or tocilizumab, but no significant changes were observed in BAFF-R, BCMA, CD69, CD86, CXCR5, CD23, CD38 and IgM expression on B-cells when comparing baseline with post-treatment follow-ups. Alterations in B-cell gene expression of BAFF-R, TACI, TLR9, FcγRIIB, BCL-2, BLIMP-1 and β2M were found in ERA and established RA patients, but no significant differences were observed after TNF-inhibitors and tocilizumab treatment when comparing baseline and follow-ups. Serum levels of CXCL13, sCD23 and BAFF were not significantly affected by treatment with TNF-inhibitors and tocilizumab.
Conclusions: In RA, treatment with either TNF-inhibitors or tocilizumab affects B-cell phenotype and the frequency of memory B-cell subpopulations in peripheral blood, particularly DN (IgD-CD27-) B-cells, but not B-cell gene expression or serum levels of CXCL13, sCD23 and BAFF, when comparing baseline with post-treatment follow up. Overall, our results may suggest that TNF-inhibitors and tocilizumab inhibit B-cell trafficking towards inflammatory sites, thus supporting activated B-cell recirculation from tissues through blood and lymphatic systems.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3011

SAT0171 ABP 501 BIOSMILAR TO ADALIMUMAB: FINAL SAFETY, IMMUNOGENICITY, AND EFFICACY RESULTS FROM AN OPEN-LABEL EXTENSION STUDY

S. Cohen[1], J.L. Pablos[2], H. Wang[3], G.A. Müller[4], A. Kivitz[5], A. Matsumoto[6], E. Krishnan[3]. *[1]Metroplex Clinical Research Center, Dallas, United States; [2]Instituto de Investigación Hospital, Madrid, Spain; [3]Amgen, Thousand Oaks, United States; [4]Abteilung für Nephrologie und Rheumatologie, Göttingen, Germany; [5]Altoona Center for Clinical Research, Duncansville; [6]Arthritis and Rheumatism Associates, Wheaton, United States*

Background: ABP 501 has been approved by the US FDA as the first biosimilar to the fully human recombinant monoclonal antibody, adalimumab. Totality of evidence to date suggests that ABP 501 is highly similar to adalimumab. Subjects receiving either ABP 501 or adalimumab in the active-controlled, comparative, pivotal phase 3 study in rheumatoid arthritis (parent study) continued on to this open-label extension (OLE) study if they had completed the final week 26 visit of that study.
Objectives: To describe the safety, immunogenicity, and efficacy outcomes of ABP 501 in the OLE study.
Methods: Subjects who completed the parent study were screened and were included if they met the eligibility requirements. All subjects included in the OLE were treated with ABP 501 40 mg subcutaneously every other week for 68 weeks followed by disease assessments at week 70 and the follow-up safety assessment at week 72 (or early termination). Data were summarized descriptively and no inferential analyses were performed.
Results: Of the 467 subjects enrolled in the OLE study, 466 were treated with ABP 501. Of these, 237 transitioned from the adalimumab arm of the parent study; 412/467 completed the study. Demographics and disease characteristics were balanced between subjects who transitioned from adalimumab and those who continued on ABP 501 from the parent study. Overall, the incidence of treatment-emergent adverse events (TEAEs) was 63.7% (297/466) and that of grade ≥3 TEAEs was 9.0% (42/466); incidence of TEAEs leading to discontinuation of investigational product was 3.6% (17/466). TEAEs with incidence ≥5% were nasopharyngitis (9.2%), upper respiratory tract infection (8.6%), bronchitis (6.4%), rheumatoid arthritis (6.2%), hypertension (4.7%), and pharyngitis (4.1%). The incidence of serious adverse events was 9.9% (46/466). Most common