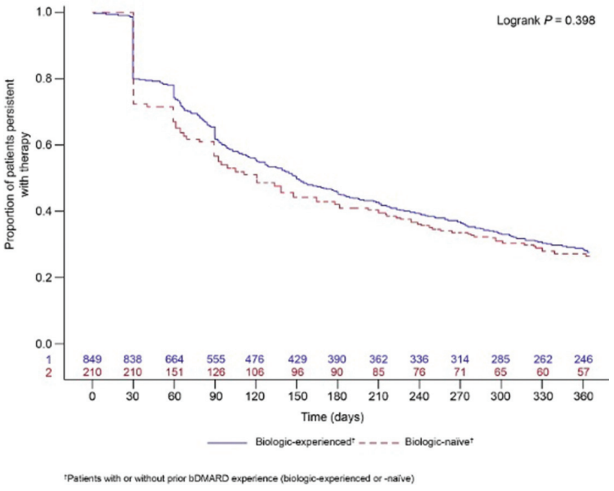


**Figure 1** Kaplan–Meier curve of persistence with JAKI therapy

**Conclusions:** Most patients (80.2%) newly initiating JAKi therapy had prior bDMARD experience. Over 70% were non-persistent with JAKi treatment for 1 year, with 39% non-persistent beyond 90 days. For non-persistent patients, the pattern of JAKi use was characterized most as interrupting with restart (42%), followed by switching (30%), and then discontinuation (28%). Reasons for the high non-persistence rate are unknown but may include suboptimal efficacy or intolerance. Further research is needed to elucidate these points.

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## SAT0178 PREDICTORS OF DRUG SURVIVAL OF ABATACEPT IN RHEUMATOID ARTHRITIS – RESULTS FROM A LARGE NATIONAL QUALITY REGISTER COHORT STUDY

G. Cagnotto[1,2], M. Willim[2,3], J.-Å. Nilsson[1,2], S. Saevarsdottir[4], C. Turesson[1,2].
*[1]Rheumatology, Department of Clinical Sciences, Malmö, Lund University, [2]Department of Rheumatology, SKÅNE UNIVERSITY HOSPITAL, Malmö, [3]Rheumatology, Department of Clinical Sciences, Lund, Lund University, Lund, [4]Rheumatology Unit, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden*

**Background:** Abatacept is a biologic disease modifying anti-rheumatic drug (bDMARD) used to treat rheumatoid arthritis (RA). There is growing experience with abatacept in many countries. National registers are useful resources for investigation of long term real world outcomes.

**Objectives:** To compare the effectiveness of abatacept in the treatment of RA between bionaïve patients and patients with previous bDMARD treatment, and to investigate predictors of remaining on treatment with abatacept.

**Methods:** This was an observational cohort study, based on a national quality register database. Patients with a diagnosis of RA who initiated treatment with abatacept between April 1, 2006 and November 20, 2017, were included. Patients were censored at abatacept discontinuation, death, migration, or the end of the study period. Analyses were stratified by previous exposure to bDMARDs. Survival on drug was estimated using the Kaplan-Meier method. Predictors of discontinuation of abatacept were investigated in Cox Proportional Hazards analyses, with significance-based backwards stepwise selection of variables for the final multivariate model.

**Results:** A total of 2716 patients with RA (80 % females, mean age 59 years, mean duration of RA 14 years) started abatacept during the study period. Of these, 17 % had no previous bDMARD treatment (bionaïve patients), 27 % had received 1bDMARD previously, and 56 % had been treated with ≥2 bDMARDs. Fifty percent each of the patients received intravenous and subcutaneous therapy. At the time of abatacept initiation, 57 % were on methotrexate (MTX), and 48 % were treated with glucocorticosteroids. There were significant differences in drug survival across categories of previous bDMARD exposure (p=0.002). The median survival time on treatment was 2.23 years for bionaïve patients (95 % confidence interval (CI) 1.69–2.79)), 1.68 years for those with 1 previous bDMARD (95 % CI 1.34–2.01) and 1.56 years for those with ≥2 previous bDMARDs (95 % CI 1.35–1.76). At 6 months, 88 % of bionaïve patients remained on abatacept, compared to 74 % at 12 months. The corresponding figures for those with 1 or ≥2 previous bDMARDs were 78 % and 61 %, and 76 % and 59 %, respectively. In bivariate analyses, bionaïve patients were less likely to discontinue treatment compared to those treated with ≥2 previous bDMARDs previously (Table). Bionaïve patients were more often male (28 % vs 18 %) and had lower pain scores (mean Visual analogue scale score 58 vs 62) compared to those previously exposed to ≥2 bDMARDs. Measures of disease severity were associated with reduced drug survival (Table), but age, RA duration and method of administration had no significant impact on discontinuation. In the final multivariate model, pain increased the risk of abatacept discontinuation, whereas male patients and those on concurrent MTX had a reduced risk of stopping abatacept (Table).

Significant predictors for abatacept discontinuation. Cox regression analysis

| | | Unadjusted analysis HR (95 % CI) | Multivariate analysis – final model HR (95 % CI) |
|---|---|---|---|
| Sex | Male | 0.85 (0.75-0.96) | 0.86 (0.74-0.98) |
| No of previous bDMARDs | ≥ 2 bDMARDs | reference (1.0) | * |
| | Bionaive | 0.78 (0.68-0.90) | * |
| | 1 bDMARD | 0.94 (0.84-1.05) | * |
| Baseline clinical characteristics | DAS28-CRP (per SD) | 1.11 (1.04-1.17) | * |
| | VAS pain (per SD) | 1.14 (1.08-1.21) | 1.14 (1.07-1.20) |
| | Current Methotrexate | 0.86 (0.78-0.96) | 0.85 (0.76-0.95) |
| | HAQ-DI (per SD) | 1.10 (1.04-1.17) | * |

*Not included in the final model

**Figure 1**. Significant predictors for abatacept discontinuation. Cox regression analysis*Not included in the final model

**Conclusions:** Survival on abatacept was significantly longer in bionaïve RA patients compared to those previously exposed to bDMARDs. In the bionaïve subset, 50 % of the patients remained on treatment after 2.2 years. Concomitant MTX therapy, male sex and low pain scores were associated with longer drug survival for abatacept.

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## SAT0179 THE BLOOD B-CELL SUBSETS AND EFFECT OF TOCILIZUMAB THERAPY ON THEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Gerasimova[1], T. Popkova[2], A. Aleksankin[2], S. Davidyan[3], A. Martinova[2], E. Aleksandrova[2]. *[1]34A, Kashirskoe Shosse, Gerasimova Elena, [2]34A, Kashirskoe Shosse, [3]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

**Background:** The use of the IL-6 receptor antagonist, tocilizumab (TCZ), in rheumatoid arthritis (RA) produce pleiotropic effects that also involve circulating B-cells. Preliminary reports have suggested that B cell function and humoral immune responses might be modulated by TCZ treatments in RA pts.

**Objectives:** To assess the effect of 12 months (mo) TCZ therapy on B-cell phenotype and gene expression in RA and to analyze the association between B-cell subsets and RA activity.

**Methods:** 24 active RA pts (20 F/4 M); median age 55[49; 64] years; disease duration 72[24; 108]m; DAS28 score 5,8[5,3;6,3]; RF+100%, ACCP+ 87% were treated in an open-label study with tocilizumab (8 mg/kg every 4 weeks). Immunophenotyping was performed at baseline and 12 mo. Pts were assessed for B-cell subpopulations and laboratory data: ESR, RF, ACCP, CRP. CD19+B cells, memory B cells (CD19+CD27+), non-switched memory B cells (CD19+CD27+ IgD+), switched memory B cells (CD19+ CD27+IgD-), naive (CD19+CD27-IgD+), double-negative (CD19+CD27-IgD-), transitional (CD19+CD38++CD10+IgD+CD27-) B cells, and plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were analyzed using multicolor flow cytometry.

**Results:** At baseline, the absolute counts of memory B cells (CD19+CD27+) and switched memory B cells (CD19+CD27+IgD-) were lower in RA pts compared to

healthy donors: 0,0015(0,001–0,003) vs 0,003(0,001–0,007) and 0,01(0,005–0,02) vs 0,02(0,01–0,04), respectively, p<0,01 for both cases. At baseline, a significant correlation was found in RA pts between absolute counts of memory B cells (CD19+CD27+) and CRP (r=0,50, p<0,05); the percentage and absolute counts of plasmablasts (CD19+CD38+++CD27+IgD-CD20-) and RF (r=0,41 and r=0,52, p<0,05). After 12 mo of TCZ therapy, 54% of pts were categorized as good responders, 46% of pts – as moderate responders according to the EULAR response criteria. Reductions in the percentages and absolute counts of plasmablasts (CD19+CD38+++CD27+IgD-CD20-) were documented after 12 mo of TCZ therapy: 0,15%(0,1–0,3) vs 0,1%(0,01–0,1) and 0,0003(0,00007–0,004) vs 0,0001(0–0,0003), respectively, p<0,05. The median percentages/absolute counts of switched memory B cells (CD19+CD27+IgD-) were 6,8%(3,6–11,6)/0,01(0,005–0,02) at baseline; and 3,1%(1,1–4,2)/0,003(0,002–0,006) after 12 mo of TCZ therapy, p>0,05. After 12 mo of TCZ therapy, the median percentages and absolute counts of memory B cells (CD19+CD27+) and switched memory B cells (CD19+CD27+IgD-) became lower in RA pts than in the controls: 1,0%(0,7–1,2) vs 2,2%(1,1–3,0); 0,001(0,006–0,003) vs 0,003(0,001–0,007); 3,1%(1,1–4,2) vs 12,8%(9,3–17,0); 0,003(0,002–0,006) vs 0,02(0,01–0,04), respectively, p<0,05, respectively, for all cases. Other B-cell subpopulations did not changed after 12 mo of TCZ therapy as compared to baseline values.

**Conclusions:** Immunophenotyping in pts with active RA showed the decrease in the absolute counts of memory B cells (CD19+CD27+), switched memory B cells (CD19+ CD27+IgD-) as compared to healthy subjects. Positive correlation between the counts of memory B cells and plasmablasts and values of laboratory indicators of RA (CRP, RF) suggests that B-lymphocytes may be involved in RA pathogenesis. The reduction in the levels of plasmonoblasts after 12 mo of TCZ therapy was observed.

**Disclosure of Interest**: None declared

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## SAT0180 TWO-YEAR CONSOLIDATED SAFETY DATA FOR ABP 501 IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

E. Krishnan[1], N. Zhang[1], H. Wang[1]. [1]*Biosimilars Development, Amgen Inc., Thousand Oaks, United States*

**Background:** Biosimilars are expected to have similar long-term safety profiles as originator products.

**Objectives:** To describe the consolidated, 2-year safety data on ABP 501, an approved biosimilar to adalimumab.

**Methods:** We combined individual patient data from a 26-week randomized controlled head-to-head study (parent study) comparing ABP 501 with adalimumab (NCT01970475) and its 72-week open-label extension (OLE) study (NCT02114931) in which all patients received only ABP 501. Safety data were reported by exposure-adjusted incidence rate as the number of subjects with the specified adverse events *(AEs) per 100 person-years. AEs from the parent and OLE studies were summarized; for each category, patients were included only once based on the 1st event in that AE category. All comparisons were performed descriptively.

**Results:** In the parent study, 264 patients received ABP 501 and 262 patients received adalimumab reference product (RP). Of these, 229 in the ABP 501 arm and 237 in the RP arm entered and were treated in the open-label extension study. The exposure-adjusted incidence rate for treatment-emergent AEs by treatment group are shown in the Table.

| | ABP 501/ABP 501 (N = 264) | Adalimumab RP/ABP 501 (N = 262) |
|---|---|---|
| **Adverse Event Category** | **Exposure-adjusted incidence rate n/E (r)** | |
| Any AE | 187/187.6 (99.7) | 197/192.2 (102.5) |
| Any grade ≥3 AE | 32/405.2 (7.9) | 30/410.6 (7.3) |
| Any treatment-related AE | 72/345.3 (20.9) | 79/344.3 (22.9) |
| Any grade ≥3 treatment-related AE | 6/427.2 (1.4) | 5/433.6 (1.2) |
| Any serious AE | 34/407.6 (8.3) | 32/410.1 (7.8) |
| Any treatment-related serious AE | 6/427.9 (1.4) | 2/434.3 (0.5) |
| Any events of interest | 141/261.5 (53.9) | 154/254.7 (60.5) |
| Infections and infestations | 125/289.9 (43.1) | 130/287.4 (45.2) |
| Liver enzyme elevations | 25/401.4 (6.2) | 20/415.6 (4.8) |
| Hypersensitivity | 19/407.7 (4.7) | 22/412.2 (5.3) |
| Injection site reactions | 6/417.9 (1.4) | 13/418.3 (3.1) |
| Hematological reactions | 6/421.8 (1.4) | 7/426.1 (1.6) |
| Malignancies | 6/423.9 (1.4) | 3/433.6 (0.7) |
| Heart failure | 1/428.4 (0.2) | 2/435.6 (0.5) |

n = number of subjects with the specified AE; E = total subjects exposure-time (patient-years); r = exposure-adjusted incidence rate per 100 patient-years (100 * n/E).

**Conclusions:** Over the 2-year observation period, there were no meaningful differences in AEs between adalimumab reference product and ABP 501.

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## SAT0181 EFFECT OF ANTI-IL-6 THERAPY ON SERUM LEVELS OF METABOLIC SYNDROME-RELATED BIOMARKERS IN RHEUMATOID ARTHRITIS PATIENTS

F. Genre[1], S. Remuzgo-Martínez[1], R. López-Mejías[1], V. Mijares[1], J. Calvo-Alen[2], R. Blanco[1,3], J. Llorca[4], S. Castañeda[5], M. Á. González-Gay[1,3,6,7]. [1]*Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, IDIVAL, Santander,* [2]*Rheumatology Department, Hospital Universitario Araba, Vitoria,* [3]*Rheumatology Department, Hospital Universitario Marqués de Valdecilla,* [4]*Epidemiology and Computational Biology Department, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL, Santander,* [5]*Rheumatology Department, Hospital Universitario La Princesa, IIS-IPrincesa, Madrid,* [6]*School of Medicine, University of Cantabria, Santander, Spain,* [7]*Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

**Background:** Metabolic syndrome (MeS) is a pathologic state that encompasses metabolic anomalies such as hyperglycemia, dyslipidemia, obesity and hypertension and that, apart from being a cardiovascular risk factor, it has been associated with chronic inflammatory diseases such as rheumatoid arthritis (RA)[1,2]. Ghrelin and retinol binding protein-4 (RBP-4) are two biomarkers associated with MeS, and are also linked to different cardiometabolic risk factors. In this regard, it is known that ghrelin exerts an anti-inflammatory role, while RBP-4 has a pro-inflammatory role[2].

**Objectives:** Since a beneficial effect on endothelial function has been reported for anti-IL-6 therapy[3], we aimed to evaluate the effect of a single infusion of anti-IL-6 on the serum levels of ghrelin and RBP-4 in patients with RA.

**Methods:** Ghrelin and RBP-4 levels were measured in serum samples from 50 Spanish individuals with RA that fulfilled the 2010 classification criteria[4], and that were under treatment with the anti-IL-6 monoclonal antibody Tocilizumab. Patients with diabetes mellitus or plasma glucose levels >110 mg/dL were excluded. Blood samples were taken in the fasting state, immediately before (time 0) and after (time 60 minutes) Tocilizumab infusion.

**Results:** A significant increase in serum levels of ghrelin was observed after a single infusion of Tocilizumab (mean±standard deviation: 72.99±58.43 pg/mL versus 134.02±225.93 pg/mL, before and after Tocilizumab infusion, p=0.04). Serum levels of RBP-4 were not affected by the administration of Tocilizumab (mean ±standard deviation: 23.48±13.99 μg/mL versus 20.90±15.54 μg/mL, before and after Tocilizumab infusion, p=0.42).

**Conclusions:** Our results show that ghrelin levels increase after a single infusion of Tocilizumab, supporting the hypothesis that IL-6 blockade has a rapid beneficial effect on factors associated with MeS and cardiovascular risk in RA patients. Hence, long-term treatment with anti-IL-6 may reduce the risk of developing cardiovascular disease in RA.

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