bind the soluble TNF. To date, very few data are available concerning the use of biosimilar drugs in a real-life setting. Results from DANBIO registry suggested a lower retention rate in RA patients switchers from Etanercept originator (ETA) to biosimilar (SB4) versus the historic ETA cohort and higher in comparison with historic SB4 patients (1).

**Objectives:** To compare the efficacy of ETA versus SB4 in a cohort of RA patients in a real life setting.

**Methods:** In this monocentric case-control prospective study, we consecutively enrolled RA patients starting ETA or SB4 treatment from 2015. RA diagnosis was made according with ACR/EULAR 2010 criteria (2). Data were collected and entered into a standardized, computerized, electronically filled-in form. We included patient demographics, date of diagnosis, comorbidities and previous and concomitant medications. The clinical evaluation included the count of swollen and tender joints and the patient’s and physician’s global disease assessment based on a visual analogue scale (VAS; range, 0 to 100 mm). Disease activity was measured according to the disease activity score in 28 joints (DAS28ESR) (3). The patients were asked to fill in the Health Assessment Questionnaire (HAQ). All the patients were evaluated at the beginning of treatment (T0) and after 4 (T1) and 12 months (T2). Clinical response to treatment was evaluated by using EULAR criteria (4).

**Results:** We evaluated 35 RA patients treated with SB4 (M/F 2/33; mean age 63 years, IQR 21; median disease duration 108 months, IQR 138) and 40 with ETA (M/F 5/35; median age 60.5 years, IQR 20; median disease duration 102 months, IQR 141). Biologic drug was prescribed as first-line biological treatment in 71.4% of SB4 cohort and in 80.0% of ETA. At T0 no significant differences were observed among the two groups in terms of DAS28ESR [SB4 median 4.6 (IQR 1.9), ETA 4.3 (IQR 1.9), p=ns] and HAQ [SB4: median 1 (IQR 1.05), ETA median 1 (IQR 0.85), p=ns]. In both groups we observed a significant reduction of DAS28 values at T1 (SB4 p=0.01; ETA p=0.0001) and T2 (SB4 p=0.0002; ETA p=0.0002; Figure 1A). When evaluating the remission rate (DAS28ESR<2.6) at T1, we observed a significant higher rate in ETA (53.8%) versus SB4 (26.7%; p=0.0002; Figure 1B). No differences were found after 12 months of treatment.

**Conclusion:** The results of our study confirmed in a real-life setting the efficacy of SB4 in RA patients, as demonstrated by the significant reduction of DAS28ESR values after 4 and 12 months of treatment, similarly to ETA. Nonetheless, ETA seems to be able to induce a remission status earlier than SB4.

**REFERENCES**


**Disclosure of Interests:** Ramona Lucchetti: None declared, Fulvia Ceccarini: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Simona Truglia: None declared, Francesca Miranda: None declared, Manuela Di Franco: None declared, Valeria Ricciere: None declared, Rossana Scivo: None declared, Antonio Sili Scavalli: None declared, Francesca spinelli: None declared, cristiano alessandri: None declared, Guido Valesini: None declared, Roberta Priori: None declared, fabrizio conti: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8031

**Disclosure of Interests:** None declared

**AB0390**

**CORRELATION BETWEEN TNF-BLOCKERS BIOAVAILABILITY AND FCGRIIA H131R POLYMORPHISM IN TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA)’s prognosis drastically improved with the introduction of TNF-blockers. However, reasons behind therapeutic failure in some patients remain unclear. Several factors might influence pharmacokinetics of these drugs by reducing their half-life and, consequently, their effectiveness. Considering Fc-containing biologics like infliximab (IFX) and adalimumab (ADL), Fc gamma receptors (FcγR) polymorphism would be an interesting genetic candidate to focus on.

**Objectives:** The aim of our study was to determine the influence of low affinity allele FcγRIIA-131R on ADL and IFX bioavailability.

**Methods:** We enrolled RA patients treated with IFX and ADL for over six months. Blood samples were collected for each patient immediately prior to drug administration. Quantitative measurements of the residual drug concentration (DC) was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®). Then, we identified patients with DC above therapeutic cut-off (DC+) for each biologic. EULAR criteria were considered to determine treatment outcome. FcγRIIA H131R polymorphism was genotyped using PCR-SSP.

**Results:** Twenty-nine patients were included (13 treated with ADL and 16 with IFX). We identified 31.3% and 23.1% non-responders among patients treated with IFX and ADL respectively. Patients with DC+ were more frequent in ADL group (76.9%) than IFX group (43.75%). For IFX, DC+ was significantly correlated with the presence of FcγRIIA-131-R (p=0.033). In fact, none of the HH-genotyped patients had DC+. Furthermore, an association between FcγRIIA-131-R allele and poor response to IFX was noted (p=0.059) while all HH-genotyped patients responded to IFX. For ADL, no correlation was found with both of residual DC and response to treatment.

**Conclusion:** The presence of FcγRIIA-131 R allele might be a predictive factor of non-responsiveness to TNF-blockers. It also appears to be associated to a higher residual DC. That might be explained by a reduced biologic clearance due to a lower binding affinity to Fc portion compared to wild allele FcγRIIA-131-H. Therefore, FcγRIIA polymorphism assessment in RA patients would be a decision-making parameter to consider, as part of the personalized medicine approach.

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**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8031

**AB0392**

**ASSOCIATION BETWEEN FCGRIIA R131H, FCGRIIA NA1/NA2 AND FCGRIBB V159F POLYMORPHISM AND RESPONSIVENESS TO BIOLOGICS IN RHEUMATOID ARTHRITIS TUNISIAN PATIENTS**

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**Background:** Even though biologics have been used for several years in treatment of rheumatoid arthritis (RA), little is known about factors that modify their pharmacokinetics and therefore their efficacy. Polymorphisms (SNPs) in receptors for constant region of Fc of IgG (FcγR) might influence the therapeutic outcome of molecules that incorporate an Fc fragment in
their structure such as etanercept (ETA), adalimumab (ADL) infliximab (IFX) and rituximab (RTX).

**Objectives:** The aim of our study was to determine whether the presence of low affinity allele of FcgRII (FcgRIIa-131R, FcgRIIa-158F and FcgRIIb-NA2) influences efficiency and immunogenicity of ETA, ADL and IFX in RA Turkish patients.

**Methods:** We included RA patients treated with biologics for at least six months. Response to treatment was assessed according to EULAR criteria. Quantitative measurement of antidrug antibodies (ADAbs) for each biologic agent was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®). To do so, blood samples were collected for each patient right before drug administration. FcgRIIA, FcgRIIa and FcgRIIb SNPs was genotyped for all patients using PCR-SSP and direct sequencing process.

**Results:** Seventeen RA patients treated with biologics were enrolled (18 with ETA,13 with ADL,16 with IFX and 32 with RTX). Regardless of biologic type, 61 patients (77.2%) responded to treatment and 14 patients (17.7%) developed Adab. Genotypic study revealed a correlation between poor response to treatment and the presence of at least one FcgRIIa 131-R allele (94.7% for RH/RH genotypes versus 5.3% for HH genotype). But, the difference was not statistically significant (p=0.25). Besides, this mutant allele was significantly associated to the presence of ADAb (71.4% of ADAb positivity for RH/RH genotypes versus 28.6% for HH genotype; p=0.041). The haplotypic study shows that the risk allele combination of FcgRI IIA-131R/IIIA-158F/IIIB-NA2 was more frequent in ADAb+ (27%) compared to ADAb- subjects (23%) and in non-responders (27%) versus good responders (23%). But, neither of these associations was statically significant.

**Conclusion:** Our study suggests that RA patients FcgRIIa-131R allele carriers are more susceptible to develop ADAb than those with HH wild genotype. That could be explained by a higher biologic clearance in H- carriers patients, resulting in a decreased half-life and ultimately a lower risk of ADAb formation. Thus, FcgRI polymorphism genotyping may be a useful marker for predicting response to Fc-containing biologics in Tunisian RA patients. Further studies need to be done on larger population.

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Disclosure of Interests: None declared


**AB0394**

**SEUMAL CALPROTECTIN AS A PREDICTIVE MARKER OF THERAPEUTIC RESPONSE TO ADALUMAB IN RHEUMATOID ARTHRITIS**

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**Background:** Adalimumab significantly reduces the activity of rheumatoid arthritis (RA), but reliable biomarkers of inflammation are still lacking to predict and evaluate the therapeutic response. Serum calprotectin is a mainstay of endogenous activation of the inflammatory response that can be useful as a marker of response to treatment in RA.

**Objectives:** To compare the evolution over time of serum calprotectin and C-Reactive Protein (CRP) after initiation of adalimumab.

**Methods:** Serum levels of calprotectin, CRP and adalimumab concentra-

**Results:** By using this method, the percentage of loaded drug, resulted by the encapsulation of micellar/niosomes was found to be 99 ± 0.2% for 5% of SSZ weight in total ingredients weight of micellar/niosomal vesicles (w/ w). The drug-entrapped sulfasalazine niosomes (SSZN) nanofluidulations indicated controlled release of drugs in phosphate buffer saline (PBS) at pH 7.2 making these nanofluidulations ideal for colon-targeted drug delivery. It was also seen that a slower rate of the SSZ releasing of the drug encapsulated niosome was, in the range of 2-24 hours at PH 4.5-7.2. TEM examinations also confirmed the formation of 15-25 nm thick walls for the prepared SSZN particles. MTT assay revealed that the blank niosomes exhibited excellent biocompatibility. The in vitro drug loading and release behavior study indicated the as prepared nano-niosome presented ultrahigh preparation and drug carrier. The cytotoxicity assay was carried out by Hela cell line and ADAB+ cell demonstrating that fewer cellular inhibition concentration (IC50) of SSZ to 162 μM and 173 μM, respectively.

**Conclusion:** Niosomal formulation are introduced as a novel nano drug carriers to design effective drug delivery systems. They offer a greater opportunity for loading hydrophilic, lipophilic drugs, or both drugs together. Niosomal formulation has been evaluated as a safe drug delivery system. In this study, we showed that SSZN has more stability and more efficiently affect the cancer cells. It seems that SSZN is a great candidate for future in vitro and in vivo researches for evaluating potential clinical applications.

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Disclosure of Interests: None declared


**AB0393**

**IMPROVING DRUG SOLUBILITY FOR INFAMMATORY ARTHRITIS TREATMENT: SULFASALAZINE NIOSOME**

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**Background:** Newly, many studies have been assumed upon vesicular drug delivery systems like niosomes to make an effective formulation of drugs in soluble state that can lead to enhance bioavailability as well as to provide controlled drug release [1]. Niosomes due to their capability and efficient mechanism have been proposed to explain the ability of those as potential nanocarriers for poorly soluble drugs [2].

**Objectives:** In this study, niosomes have emerged as a drug delivery system to load sulfasalazine (SSZ) that is used to treat rheumatoid arthritis. Molecules were prepared by amphiphilic self-assembly of tween 80 and squalene through thin film hydration method. The optimal hydration condition that maximizes noisome yield was hydration duration of 24 hours at 30-35 °C. The encapsulation of sulfasalazine drug into niosome was characterized by Fourier transform infrared spectroscopy (FT-IR), UV-visible, Zeta potential, particle size, field emission scanning electron microscopy (FE-SEM), and transmission electron microscopy (TEM) to evaluate size, charge, morphology and functional properties.

**Conclusion:** Our methods using this method, the percentage of loaded drug, resulted by the encapsulation of micellar/niosomes was found to be 99 ± 0.2% for 5% of SSZ weight in total ingredients weight of micellar/niosomal vesicles (w/ w). The drug-entrapped sulfasalazine niosomes (SSZN) nanofluidulations indicated controlled release of drugs in phosphate buffer saline (PBS) at pH 7.2 making these nanofluidulations ideal for colon-targeted drug delivery. It was also seen that a slower rate of the SSZ releasing of the drug encapsulated niosome was, in the range of 2-24 hours at PH 4.5-7.2. TEM examinations also confirmed the formation of 15-25 nm thick walls for the prepared SSZN particles. MTT assay revealed that the blank niosomes exhibited excellent biocompatibility. The in vitro drug loading and release behavior study indicated the as prepared nano-niosome presented ultrahigh preparation and drug carrier. The cytotoxicity assay was carried out by Hela cell line and ADAB+ cell demonstrating that fewer cellular inhibition concentration (IC50) of SSZ to 162 μM and 173 μM, respectively.

**Disclosure of Interests:** None declared