The secondary endpoint was to analyze the characteristics of patients who remain for a longer period of time in an optimized dose regimen.
Methods: In our Rheumatology Unit we are treating 271 RA patients with BT, the dose was deintensificated for 62 (23%) patients in remission or low disease activity for at least 6 months. We have selected 32 patients with BT reduced for at least 6 years in an observational, descriptive, longitudinal and retrospective study. Disease activity was measured by the DAS 28 index. Structural damage was evaluated by SENS method.
Results: We analyze 32, 20 female, 12 male, mean age at diagnosis 42.6 years old; BT was started after RA evolution of 98.63 months. Drug reduction was performed after full BT for 62 months, mean DAS 28 was 2,47.
Patients were 75% FR positive and 56.7% ACPA positive. Etanercept was the BT more commonly reduced 59.4%, followed by adalimumab 21.9%, infliximab 12.5% and certolizumab 6.3%.
BT dose returned to normal for 11 patients because of disease activity worsening after an average time of 15.90 months.
For 21 patients remaining on reduced doses, the mean DAS28 at time for analysis was 2.67.
BT reduction as different drugs: none infliximab reduced dose patients required return to normal dose. All certolizumab reduced (2 patients) patients needed to back to normal dose. Etanercept in 36,8% and adalimumab 28,6%.
The mean of SENS score before the optimization was 8.78 and at time for analysis 10.67 for both kind of patients, who continued reduced and those who needed to increase BT dose.
For the secondary endpoint 10 out of 12 male continue with deintensificated BT (83%) in the other hand only 11 out of 20 female (55%) maintained reduced dose.More negative for FR (69,2%) and ACPA (75%) patients keep on reduced dose regimen.
Conclusions: We have deintensificated 62 out of 271 RA patients on BT (23%). All patients were in clinical remission at the beginning of BT dose reduction for more than 6 months.
Most patients (65%) analyzed remain long time with reduced BT in clinical remission.
We have not observed significant X-ray progression for reduced patients, even if they increase disease activity and need to back to the original BT dose.
The increase in disease activity was the main reason to interrupt the optimization regime.
Infliximab was the drug that remained more time optimized.
According to the results of our study, male patients negative for ACPA and FR remain longer with reduced doses
Disclosure of Interest: None declared
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AB0385 STRATEGIES FOR THE OPTIMIZATION OF BIOLOGICAL THERAPY IN PATIENTS WITH JOINT INFLAMMATORY DISEASE: ANALYSIS OF CLINICAL RESULTS AT 4 YEARS

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Background: Biological therapies optimization in joint inflammatory diseases is indicated in patients who have more than six months in clinical remission. The main objective is to limit the occurrence of adverse effects, which are dosage-dependent. In addition, the cost savings suppose a better access of new patients to these treatments. Given the increasing importance of this topic in recent years, we present the optimization experience in our center at the last 4 years
Objectives: 1.To analyze the clinical evolution evaluated by DAS28 in patients with rheumatoid arthritis (RA) and polyarticular psoriatic arthritis (PPSA) in biological therapy (BT) followed in a university hospital in the south of Spain which are performed in optimization of BT. 2.To analyze the optimization strategies used with the different BT
Methods: Observational, longitudinal, retrospective and descriptive study by the review of clinical records, between January 2013 and January 2017, of patients with RA and PPSA who underwent BT optimization for more than 6 months at follow-up (DAS28 $<$2.6) or minimal activity (DAS28 2.6–3.2). We analyze demographic data, time of evolution of illness before the use of BT, time of TB until optimization, clinical evaluation by DAS28 and therapeutic strategies. Statistical analysis was performed with the IBM SPSS Statistics program
Results: From 294 patients in BT (174 RA and 120 PPsA), 95 (32.3%) were submitted to optimization treatment: 58 in RA group and 37 in PPSA group. 57 were women and 38 men, with 56±12 years mean age. The mean treatment time at optimized doses was 32±17 months. At the optimization time, 85 (89.5%) patients presented DAS28 remission and 10 (10.5%) had low activity; at the study cut time, 67 (70.5%) of them continue at clinical remission,14 (14.7%) low activity, 11 (11.6%) moderate and 3 (3.2%)high activity according to DAS28. A 69.5% (66) of the patients continued with optimized doses at the end of the study. From the 58 patients included in the RA group, 14 (5 with adalimumab 40 mg/21 days, 8 with etanercept 25 mg/7–10 days or 50 mg/10 days and 1 with certolizumab 200 mg/month) need the standard dose of the drug for disease control; a patient receiving etanercept discontinued the treatment after the diagnosis of breast cancer, as well as three other patients treated with adalimumab who were diagnosed of pancreatic cancer, septic arthritis and cognitive impairment respectively. On the other hand, 9 patients from of the PPSA group needed to restart the treatment at standard doses, either for articular (4) or cutaneous (5) worsening, 3 of them being treated with adalimumab and 6 with etanercept. In addition, a patient had to be discontinued due to the diagnosis of decompensated liver cirrhosis; another patient suspended it voluntarily
Conclusions: After 4 years, we can conclude that in our cohort of patients with inflammatory joint disease in BT that have been submitted to dose optimization because they were in remission or low disease activity, a high percentage (69.5%) remain in the same clinical situation for an average of 32 months. The response rate obtained for optimization in the RA group and in the PPSA group are comparable. The most frequent optimization strategies employed were adalimumab 40mg/21 days, etanercept 25mg/7 days and etanercept 50mg/10 days.
Disclosure of Interest: None declared
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AB0386 A STUDY OF RETENTION AND SWITCHING RATES OF 1ST LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS

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Background: Since the introduction of biologics for rheumatoid arthritis (RA) treatment, significant improvements in joint inflammation control, prevention of bone/joint destruction, activities of daily living (ADL), and quality of life (QOL) have been observed. Tumor necrosis factor (TNF) inhibitors, such as anti-TNF drugs and TNF receptor drugs, accounted for the majority of biologics. However, the use of non-TNF inhibitors, including interleukin (IL)-6 receptor antibodies and selective modulators of T-cell co-stimulation, has been approved, and their efficacy has been demonstrated.
Objectives: This study aimed to analyze the effective usage retention rate of TNF inhibitors and non-TNF inhibitors in RA patients.
Methods: Among 475 RA patients who were administered biologics up to the end of 2015, 329 patients who had been treated for more than 5 years (treatment initiated before the end of December 2010) since the first introduction of biologics (1st line) were included in this study. These patients were divided into TNF inhibitor (infliximab: IFX, etanercept: ETN, and adalimumab: ADA) and non-TNF inhibitor groups (tocilizumab: TCZ, and abatacept: ABT) to investigate the number of patients who progressed to 2nd or 3rd line therapy by 5 years after introduction, and which biologic was administered as the 2nd or 3rd line therapy in each group.
Results: Of 329 patients, 67 were men and 262 were women. Patient age ranged between 22 and 83 years with a mean of 58.7±13.5 years. RA disease duration ranged between 1 and 50 years with a mean of 9.6±8.1 years. TNF inhibitors and non-TNF inhibitors were used as 1st line therapy in 278 and 51 patients respectively. In the TNF inhibitor group, IFX, ETN, and ADA were administered to 145, 87, and 46 patients respectively. In the non-TNF inhibitor group, TCZ and ABT were administered to 48 and 3 patients respectively. In the TNF inhibitor group, 94 of 278 patients (33.8%) progressed to 2nd line therapy owing to efficacy attenuation and adverse events. Thirty-four of these patients were switched to TNF inhibitors and 60 to non-TNF inhibitors. Conversely, 6 of 51 patients in the non-TNF inhibitor group (11.8%) advanced to 2nd line therapy, with 2 switching to TNF inhibitors and 4 to non-TNF inhibitors. Additionally, 25 and 3 patients advanced to 3rd line therapy in the TNF inhibitor and non-TNF inhibitor groups respectively. Throughout the 5 years, 154 (55.4%) patients in the TNF inhibitor group did not change their treatment agent while 69 (24.8%), 24 (8.6%), and 1 (0.4%) switched once, twice, or 3 times or more, respectively. Thirty (10.8%) patients discontinued biologic usage. In the non-TNF inhibitor group, 3 (5.9%), 2 (3.9%), and 1 (2.0%) patients switched once, twice, or 3 times, respectively. Six (11.8%) patients discontinued biologic usage, and no change in treatment occurred in 39 (76.5%) patients. The mean number of biologic agent switches per patient in each group over 5 years was 0.43 times in the TNF inhibitor group and 0.20 times in the non-TNF inhibitor group, indicating that the number was significantly lower in the non-TNF inhibitor group (p=0.0032).
Conclusions: While the sample size was small and patient characteristics varied, it appears that non-TNF inhibitors are not inferior to TNF inhibitors as 1st line therapy biologics in terms of retention rate and number of switches to TNF inhibitors.
Disclosure of Interest: None declared
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AB0387 COMPARISON OF ETANERCEPT IN MONOTHERAPY AND COMBINATION WITH SYNTHETIC DMARDS: DATA FROM ATTRA REGISTRY

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Background: Etanercept (ETN) is an established bDMARDs for therapy of rheumatoid arthritis and some other inflammatory diseases. In rheumatoid arthritis patients ETN could be given in combination therapy with sDMARDs as well as in monotherapy.

Objectives: To investigate and compare etanercept monotherapy versus combination with sDMARDs in RA patients regarding survival on drug, efficacy, quality of life and reason for discontinuation.
Methods: Observational, open, long-term study of patients from the ATTRA registry starting the ETN therapy since 2010 either on monotherapy or in combination with sDMARDs (n=605). 461 patients (80.7%) were females, rheumatoid factor was positive in 429 (76.6%), anti CCP antibodies in 412 (74.5%) patients. The following groups of patients were assessed: Etanercept monotherapy (ETN-mono, n=83), combination with methotrexate (Combo-MTX, n=378), combination with other sDMARDs (Combo-other sDMARDs, n=110).
Mean ± SD and absolute/relative frequencies were used to describe continuous and categorical variables, respectively. P-value of Pearson Chi-square test and Kruskal-Wallis test is given when assessing differences between groups in categorical and continuous variables. Results are presented as hazard ratio (HR) with corresponding p-value. Statistical evaluation was processed by IBM SPSS Statistics ver. 24.
Results: In the first measurement of activity after 3 months, there were significantly lower disease activity in both Combo groups compared to ETN mono (3.2±0.1 resp. 2.9±0.1 versus 3.7±0.2, $p<0.001$). However since the month 6 the differences lost their significance and the disease activity were comparable in all groups up to the month 24.
The HAQ value was significantly higher already at the time of ETN onset at month 0 in the ETN-mono group (1.7 versus 1.4 resp. 1.5, $p<0.001$) and stayed significantly higher at the month 3 and 12.
The hazard ratio (HR) for ETN discontinuation was higher in ETN mono group compared to Combo-MTX (HR=1.330) and also compared to Combo-other sDMARDs (HR=1.098), even if the differences did not reach statistical significance (p=0.131, resp. 0.671). Similar trend was evident, if the etanercept was given in the first and any subsequent line of biological therapy. The HR for ETN discontinuation was also numerically higher in Combo-other sDMARDs than in Combo MTX group (HR=1.211, p=0.244).
The patients on ETN mono have higher risk of discontinuation due to inefficacy compared to Combo-MTX (HR=1.415) and also to Combo-other sDMARDs (HR=1.670). The patients of combo-other sDMARDs group had lower risk of discontinuation due to inefficacy also in comparison with combo-MTX (HR=0.847). None of the differences reach statistical significance.
The patients on ETN mono have higher risk of discontinuation due to adverse event compared to Combo-MTX and also to Combo-other sDMARDs. This trend is higher, if ETN is given in the subsequent line of biological therapy, but not in first line. Nevertheless like in other situations, the differences showed some trend, but were not statistically significant.
Conclusions: Results support the evidence of advantages of ETN combination with methotrexate – quicker onset of efficacy and give some evidence of better survival on etanercept therapy in combination with methotrexate.
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Disclosure of Interest: None declared
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AB0388 RESULTS AT 3 YEARS OF AN OPTIMIZATION GUIDELINE OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS. CREATE RECORD RESULTS

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Background: Dose optimization, such as dose reduction or dose spacing, is nowadays presented as a therapeutic strategy to be followed in patients with rheumatoid arthritis (RA) who have managed to reach and maintain clinical remission for a while. This strategy reduces the frequency of adverse effects and promotes cost savings
Methods: Patients with RA (Criteria ACR 1987) of the CREATE registry (patients who was treated in real life conditions) who had clinical remission (DAS28 <2.6) of at least 6 months of duration on November 1, 2013, constituted the cohort of patients who were optimized for the dose received. According to the consensus of the Spanish Societies of Rheumatology and Hospital Pharmacy, the optimization of doses meant the reduction of between 20 and 50% of the same.
A multidisciplinary team of rheumatologists and clinical pharmacists in a third-level hospital was involved in decision-making on treatment and dose reduction, which involved the application of protocols and the follow-up of patients at least every two months.
Results: A prospective follow-up of 70 patients with RA who had received optimized doses of biological therapy for 3 years, with a mean age of 56.9 (13.7) years, of which 78.6% were women, 68.8% were positive rheumatoid factor and 66.7% ACPA +.
The relapse occurred in 41.8% (at first year), 56.7% (at second year) and 62.7% (at third year). There were no statistical differences between these last 2 percentages. The median survival time of the optimization regimen was 15.24 (4.65) months (95% CI: 4.66–25.83). No statistically significant differences were found when comparing patients according to the optimized drug (antiTNF versus non-anti-TNF) (test log.rank: 0.239, p: 0.625).
When relapse occurs, the patient returns to normal doses prior to optimization of the drug. Our data show that 62.7% of the patients in whom the relapse occurs at 3 years, maintains DAS28 <2,6 ($P<0.05$) when dose was returned to the manufacturer recommended dose.
The 37.3% (95% CI: 26.72%, 49.28%) patients maintained the optimization pattern throughout the follow-up without relapse, with an average DAS28 of 1.99 (1.07) at 3 years. Comparing these patients with those who relapse, they achieved significantly lower DAS28 values at both (p: 0.028) and at three years (p: 0.025)
Conclusions:
- The strategy of dose reduction of biological therapies in patients with established RA that achieve sustained remission is possible in 37.3% of cases in real clinical practice (CREATE Registry) and it was maintained for 3 years.
- The probability of occurrence of relapse decreases after 2 years of treatment with an optimized regimen in those patients who have not relapsed before.
- This strategy is possible in patients with persistently controlled disease and in view of our results, it is independent of the drug administered (antiTNF versus non-antiTNF).
- After 3 years of follow-up, all patients maintained clinical remission (DAS 28 <2.6) despite relapses, and after resumption of the usual dose, all of them reached the therapeutic goal again.
- Patients who maintain clinical remission for 3 years achieve DAS28 values statistically lower than those who did not after 2 years.

Disclosure of Interest: None declared
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AB0389 THE IMMUNOGENICITY OF BRANDED AND BIOSIMILAR INFLIXIMAB IN RHEUMATOID ARTHRITIS ACCORDING TO TH9-RELATED RESPONSES

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Background: There are many evidences that Th9 lymphocytes take part to the pathogenesis of rheumatoid arthritis (RA), however it is unclear whether these cells are implicated in the immunogenicity of biologic agents.
Objectives: We aimed to evaluate the immunogenicity of branded and biosimilar infliximab by detecting changes in Th9 percentages following an *"in vitro"* stimulation test.
Methods: PBMCs from 55 consecutive RA outpatients (15 drug-free, 20 successfully treated with branded infliximab and 20 failing branded infliximab) and from 10 healthy controls were collected. PBMCs were cultured with/without 50 μg/mL infliximab originator (Remicade®) or 50 μg/mL infliximab biosimilar (Remsima®), 50 μg/mL Human IgG1kappa and 50 μg/mL recombinant Human IgG Fc for 18 hours. Th9 lymphocytes were identified by means of flow cytometry as PU.1+, IRF4+, IL9+ CD4+ cells. Furthermore, the markers CCR7 and CD45RA were used to distinguish naive from memory IL-9-producer cells.
Results: In unstimulated condition, RA patients showed the highest percentages of Th9 lymphocytes. Following stimulation with branded infliximab, the percentage of PU.1+, IRF4+ Th9 cells, CCR7+, CD45RA- central memory and CCR7-, CD45RA- effector memory IL-9 producer cells significantly increased in the group of infliximab non responder RA patients. On the contrary, no significant variation was observed after biosimilar exposure. Figures 1,2,3,4 resume the results.

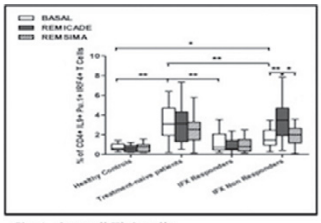

Fig.1 Overall Th9 cells

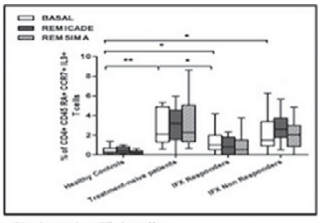

Fig.2 Naive Th9 cells

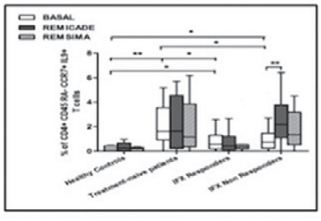

Fig.3 Central memory Th9 cells

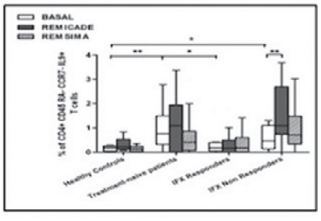

Fig.4 Effector memory Th9 cells

Conclusions: According to our results, Th9 cells seem to be involved in the immune response against the epitopes of branded but not biosimilar infliximab and this condition could rely on the recall and the stimulation of both central and effector memory cells. Further studies are indeed needed to confirm these data.
Disclosure of Interest: None declared
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