and 406 (36.09%) biologic therapy. The frequency of use of the biologic therapy was: abatacept (73 patients/6.49%), etanercept (66/5.87%), tocilizumab (60/5.33%), adalimumab (54/4.8%), infliximab (50/4.44%), rituximab (49/4.36%), golimumab (37/3.29%), certolizumab (17, 1.51%). The time of use of the biological drugs is presented in table 1.

Abstract AB0417 – Table 1. Time (in years) of use of biological drugs in patients with rheumatoid arthritis

DRUG	MEAN	MAXIMUM
ABATACEPT	1.95	8
ADALIMUMAB	1.70	12
CERTOLIZUMAB	0.63	2.0
ETANERCEPT	1.49	9.0
GOLIMUMAB	0.65	2.0
INFLIXIMAB	1.56	9.0
RITUXIMAB	1.27	6.0
TOCILIZUMABE	2.0	6.0

Conclusions: The therapeutic profile of this cohort of Brazilian RA patients shows some interesting results. The relatively high number of patients on biologics, compared to other studies, may be related to fact that the centres involved were reference centres, probably dealing with more difficult cases.

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AB0418 THE EFFECT OF CONCOMITANT METHOTREXATE ON SERUM TNF INHIBITORS LEVELS AND CLINICAL RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS IS DOSE DEPENDENT AND GREATER THAN OTHER DMARDS

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Background: Several factors influence on the pharmacokinetics(PK) of TNF inhibitors(TNFi). One of the most relevant influencing factors is the development of antidrug- antibodies(ADA), which is associated with low circulating drug levels and loss of clinical efficacy. Previous studies, mostly about Adalimumab (Ada), have demonstrated a beneficial effect of concomitant use of methotrexate(MTX) in patients(pts) under TNFi therapy by reduction of immunogenicity. There are other csDMARDs(OD) as leflunomide, hydroxycloroquine or sulfasalazine which may have also an effect on PK.
Objectives: To investigate the effect of csDMARDs on the presence of serum TNFi levels and on the clinical response during the first year of Ada or Infliximab (Ifx) treatment in RA pts. Secondly, to evaluate if MTX has a dose-dependent effect on these outcomes.
Methods: This is an inception cohort including pts with RA starting Ifx or Ada in a tertiary hospital since 1999. At baseline, 6 and 12 months clinical(DAS28, EULAR response and ΔDAS28) and serological(drug and ADA levels) parameters were measured. Patients were clustered according to the use of concomitant csDMARDs at baseline in three groups: i)TNFi monotherapy;ii)TNFi +MTX;iii) TNFi +OD. Pts within the TNFi +MTX group were also classified according to the MTX dose:MTX <15 mg/week(TNFi +MTX <15) and MTX ≥15 mg/week(TNFi +MTX ≥15).
Results: A total of 92 RA pts[Ada(n=25) or Ifx(n=67)] under TNFi were included. The number and percentage of pts in each group were as follows:TNFi monotherapy,12 pts(13%);TNFi +MTX, 59 pts(64%);TNFi +OD 21 pts(23%). According to MTX dose, the distribution was:TNFi +MTX <15,18 pts(20%);TNFi +MTX ≥15, 41 pts(45%). Considering the overall of pts receiving any dose of MTX, the percentage of them with drug levels after 12 months(71%) was numerically higher than in the other groups(20% in TNFi +OD and 9% in TNFi monotherapy,p=0.1). However, after stratifying pts by MTX dose, we observed that circulating drug levels at 12 months were more frequent in higher dose of MTX(54% of the pts with TNFi +MTX ≥15) compared to patients with TNFi +MTX <15 (17%), with TNFi +OD (20%) and with TNFi monotherapy (9%);p=0.002). According to EULAR response, pts treated with TNFi +MTX(81%) achieved more frequently a good response compared with the other groups (11% on TNFi +OD and 8% on TNFi monotherapy, p=0.6). Moreover, differences on clinical response were observed depending on MTX dose. While 58% with TNFi +MTX ≥15 were good EULAR responders, 23% with TNFi +MTX <15 achieved this. Overall, the best effect on clinical response was observed in the group of MTX; p=0.4. Finally, the TNFi median survival time(mst) was significantly higher in pts with TNFi +MTX than in pts with TNFi +OD or on TNFi monotherapy(5 years vs 2 years vs 2.15 years, respectively;p=0.03). Analysing by MTX dose, drug survival was superior for high (≥15) and low MTX doses(<15) (mst 5.2 and 3.3, respectively)compared to OD and/or TNFi monotherapy although the difference was not statistically significant p=0.09.
Conclusions: In RA pts under Ifx or Ada treatment, the presence of TNFi in serum, the clinical response and the TNFi survival are influenced by MTX but not by OD. Moreover, a MTX dose-dependent effect is closely associated with these outcomes.
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AB0419 FREQUENCY OF DISEASE FLARE AND STUDY OF THE CD4+CD25+HIGHCD127LOW/- CELL POPULATIONS AFTER DISCONTINUATION OF ANTI-TNFA THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITISIN PERSISTENT REMISSION

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Background: Rheumatoid arthritis (RA) patients in a prolonged remission status represent a population whose future management has yet to be established. Treg cell function in patients with active RA is assumed to be impaired, a trend that seems to be reversed by TNFalpha antagonist therapy (aTNF). Theoretically a deeper remission may be represented by an immunological resetting of immune system, a condition which could enable to consider the possibility of a drug-free remission.
Objectives: To evaluate the incidence of disease flare after cessation of aTNF in pts in remission together with reconstitution of the CD4 +CD25highCD127low/-Tcell subset respect to those patients in the same remission status with persistent low CD4 +CD25highCD127low/-Tcell population, assuming the Treg populations as a markers of deep remission allowing a better selection of those patients at low-risk of flare after aTNF withdrawal.
Methods: inclusion criteria: patients with RA (>18 years) fulfilling the 1987 ACR classification criteria treated with aTNF and synthetic DMARDs for at least 12 months, in remission (DAS28 <2.6/DAS44 <1.6)>6 months, without glucocorticosteroid. Exclusion criteria:<18 years, glucocorticosteroids within the three months before; another inflammatory disease other than RA; ongoing infections. Intervention: aTNF drug withdrawal with continuation of DMARDs previously associated (MTX or LFN); a 24 months of follow up was performed. Serial clinical and instrumental evaluation, blood sampling and radiographs have been performed according to the scheduled protocol. Treg population and several cytokines/chemokines/growth factors were analysed (Human Cytokine/Chemokine Panel I, Millipore).
Results: 23 patients were included, mean age 53 years (SD 12.3), 68% RF +, 52% ACPA +, DAS28 medium 1.41 (SD 0.48); average duration of illness 9.62 years (SD ±5.73). During the 24 month post-suspension follow-up, for a total of 267 person-months, 11 patients presented a flare, for a flare rate of 3.74/100 person-months (CI95% 1.79–6.88). The average observed exacerbation time from aTNF withdrawal was 14.6 months (SD ±9.32). None statistical predictive value of Treg levels regarding disease outcome after aTNF withdrawal was observed IIR (95% CI) 1.38 (0.82–2.30). None significant correlation among cytokines concentrations and disease status/Treg levels was observed. A correlation was observed between the presence of a synovitis with PD1+* at the baseline and the loss of remission [HR 7.062 (1.64–30.41, p 0.009);*higher values were exclusion criteria]. All 3 patients with positive US (PD1) who had flare-up were asymptomatic at baseline.
Conclusions: 47.8% of pts maintained aTNF-induced remission at 24 months continuing only sDMARDs therapy (MTX). Only in 1 case reintroduction of Adalimumab did not allow to regain clinical remission, which was obtained using another therapeutic target (anti-CTL4). The presence of a residual synovitis, although mild (PD1), was correlated with the risk of exacerbation. Further results will be discussed.