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Rheumatoid arthritis - anti-TNF therapy

AB0374 FLARE INCIDENCE AND PREDICTIVE FACTORS IN A POPULATION OF PATIENTS WITH RHEUMATOID ARTHRITIS UNDER OPTIMISED TREATMENT WITH ADALIMUMAB AND INFLIXIMAB

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Background: Anti-TNF are nowadays widely used for the treatment of Rheumatoid Arthritis (RA),which has drastically changed the prognostic of the disease,carrying an important healthcare expense.This is why,optimisation seems a successful strategy that should not be linked to a worse become of our patients' clinical evolution.
Objectives: Describe a population of patients with RA under optimised treatment with Adalimumab (Ada) and Infliximab (Ifx).Study the incidence of flares and establish predictive factors of flares at baseline and pre-optimization.
Methods: Observational study of the prospective cohort RA-Paz. All the patients diagnosed of RA under treatment with Ifx and Ada between Jan.2000 and Dec.2016 of the day-care unit of La Paz Hospital,were included.Demographic data,clinical activity and blood sample results were collected at baseline, pre-optimization (pre-op)and at 3,6,9,12,18 and 24 months.Drug serum trough levels were measured under ELISA in each visit.Optimal range for Ifx was described as drug concentration between 1000- 4000 ng/ml and 1500- 5000 ng/ml for Ada.Optimisation was defined as drug use below standard dose.Flares were collected from the pre-op visit.Flare was described as clinical worsening which led to a therapeutic change or a DAS28>3.2 and DeltaDAS28>0,6.Predictive factors of flare at baseline and pre-op were evaluated with a uni and multivariate analysis. Statistical study was performed with the statistical program SPSS.
Results: Of the 271 patients diagnosed of RA, 74 patients were optimised (44 under Ada and 30 under Ifx). Baseline demographic caracteristics are shown in the table below.During the 24 months after the pre-op visit, 55,4% (41)of the patients presented at least one flare,with an average of 1,38 flares [1–5]. Most of the patients (53.7%,22/41),were controlled with the adjustment of non biological treatment.Only 39,0% (16) of the patients,had to go back to the previous optimised dose and 7,3% (3)to the standard dose.88% (39/41)were controlled after the dose modification.104 flares were collected,33% (34) happened at the 3rd month and 20% (21) at 24th. In the population who presented flares, we observed a persistent higher DAS Vs the patients who never presented flares (DAS pre-op 3,20±1,16 Vs 2,26±0,59;DAS 24month 3,61±1,13Vs2,10±0,65;p=0,007). A least proportion of patients with flares were in supra-optimal range (13,3% with flares vs 26% without, p=0,007). At baseline, no clinical factors were predictive of flare. Nor were blood sample results. In contrast, a higher disease activity, measured by DAS pre-op (p=0,004),a worst EULAR answer (p=0,027) and not being in supra-optimal range (p=0,032),were statistically correlated with flares development at the univariate analysis. Time to the optimisation tended to the significance (OR=1,152; p=0.08). In the multivariate analysis, only a higher DAS pre-op (OR:2,00,[1,08–3,73])and being in optimal (OR:5,90, [1,38–25,2])and sub-optimal range (OR=6,05 [1,28–28,7]), were independently correlated.

	N Total= 74
Sex	Women 83,8 % (62) Men 16,2 % (12)
Age	64,1 (+/-12,6)
Age at diagnosis	41,6 (+/-14,0)
bDMARD	Ada 59,5% (44) IFX 40,5% (30)
Time to the beginning of bDMARD (years)	10,7 (+/- 7,50)
Time to optimisation (years)	4,70 (+/-3,12)
Treatment duration (years)	8,80 (+/-4,00)
RF +	75,7% (56)
ACPA +	73,0% (54)
Smoking	No smokers 68.9% (51) Smokers 17,6% (13) Ex smokers 12,2% (9)
BMI	25,6 (+/-4,61)
Methotrexate (MTX)	74,3% (55)
Average dose MTX (mg/sem)	12,3 (+/-8,60)
Other sDMARD	54,1% (40)
sDMARD	Leflunomide 62,5% (25) Salazopyrine 15% (6) Hydroxychloquine 10% (4) Leflunomide+SZP 5% (2) Leflunomida+HCQ 5% (2) SZP+HCQ 2,5% (1)
Prednisone	37,8% (28)
Prednisone dose (mg/día)	1,89 (+/-2,62)
DAS baseline	5,03 (+/-1,35)
VSG baseline	34,7 (+/-18,9)
PCR baseline	10,2 (+/-12,5)

Conclusions: In our cohort of optimised patients, we noted a high proportion of flares. However, flares were controlled with dosage readjustment without needing a treatment change. Independently correlated predictive factors for flares were a higher disease activity measured by DAS and not being in therapeutic range in the pre-optimisation visit.
Disclosure of Interest: None declared
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AB0375 THE EFFECT OF CONCOMITANT USE OF METHOTREXATE ON THE CLINICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER ANTI-TNFTHERAPY

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Background: Several publications in rheumatoid arthritis (RA) have demonstrated a beneficial effect of concomitant methotrexate (MTX) use with TNF inhibitors (TNFi), mainly because of the MTX effect in reducing immunogenicity. In a previous work in the RA-La Paz cohort, we found that the concomitant use of MTX had a positive effect on the pharmacokinetics of serum TNFi levels, decreasing the immunogenicity of these drugs. Furthermore, the MTX effect was dose-dependent, being greater at high MTX dose. Currently, we investigate the effect of concomitant MTX use on the clinical response.
Objectives: To investigate the MTX influence on the clinical response in the RA-La Paz cohort treated with Infliximab (Ifx), Adalimumab (Ada) or Etanercept (Etn) at one year of treatment.
Methods: This is an observational study from a prospective cohort from the Biological Unit of the University Hospital La Paz, Madrid, Spain that analysed a total of 293 RA patients treated with Ifx (112 patients), Ada (71 patients) and Etn (110 patients). Patients were grouped according to the MTX dose: no MTX, low dose (LD: ≤12.5 mg/week), intermediate dose (ID: 15–17.5 mg/week) and high dose (HD: ≥20 mg/week). For this study, the clinical response was evaluated by DAS28-ESR and the clinical improvement by∆DAS28. Data were collected at baseline, 0.5 and 1 year of TNFi treatment. Statistical analysis was performed using GraphPad Prism 6.0 software.
Results: Out of 293 RA patients (pts) under TNFi treatment, 184 (71 with Ifx, 40 with Ada and 73 with Etn) were included. In this cohort, 128 (70%) pts used concomitantly MTX (91% oral administration) and 56 (30%) pts were in monotherapy. No differences in DAS28 were found at baseline between patients with or without MTX (p=0.8).
After one year of treatment, pts with TNFi +MTX have a significantly lower DAS28 than patients without MTX (3.3±1.3 vs 3.9±1.1; p=0.004). When analyzing the DAS28 values in relationship to the MTX dose, statistical differences are observed with use of HD (≥20 mg/week) (3.1±1.3 with HD vs 3.9±1.1 without MTX; p=0.001) but not with intermediate (3.4±1.2 with ID vs3.9±1.1 without MTX; p=0.06) or low MTX dose (3.8±1.6 with LD vs 3.9±1.1 without MTX; p=0.4) at 1 year of therapy.
Clinical improvement by∆DAS28 was higher in patients with TNFi +MTX than in patients without MTX (1.7±1.4 vs 1±1.3p=0.007). This effect was observed with all MTX doses (1.7±1.5 with HD vs 1±1.3 without MTX, p=0.01; 1.6±1.3 vs with ID 1±1.3without MTX, p=0.03; 1.8±1.3 with LD vs 1±1.3 without MTX, p=0.01).
Conclusions: In the RA-La Paz cohort under TNFi treatment, the concomitant use of MTX has a positive effect on the clinical activity, mainly when high dose of MTX is used. Moreover, we demonstrate a positive effect of any MTX dose on the clinical improvement at one year of treatment.
Disclosure of Interest: None declared
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AB0376 CARTILAGE OLIGOMERIC MATRIX PROTEIN, A BIOMARKER OF ARTHRITIS, COULD BE USEFUL FOR PREDICTING THE RESPONSE TO BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS?

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Background: introduction of biologic therapy has revolutionized the treatment of Rheumatoid Arthritis (RA). Despite these advances, 20–40% of the patients are declared nonresponders to at least one of the therapies (1).High costs and patient exposure to severe adverse reactions (ex. infections) determined the need to identify biomarkers that can distinguish pretreatment responders versus nonresponder patients.
Objectives: evaluating the predictive role for the response to anti tumor necrosis factor therapy (anti-TNF) of cartilage oligomeric matrix protein (COMP), a specific serological marker, which evaluates the articular cartilage degradation and its turnover.(2)
Methods: prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by conventional synthetic DMARDs.Clinical assessment was performed at 0, 6 and 12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good /moderate /nonresponder).

Results: of the 64 patients included in the study, 59 (92.2%) were women and 5 (7.8%) men, mean age 57.55±9.42 years. After 6 months, 7 patients were declared nonresponders, 38 achieved a moderate response and 19 good response.
Following baseline COMP titres and the EULAR response at 6 months, general tests identified significant differences between groups. Lower baseline titres had predictive value for achieving a good response (746.04±130.095 ng/ml) comparing with moderate responders (1032.8±188.671ng/ml) and nonresponders (1042.2±181.717 ng/ml, p=0.0000).
After 12 months 11 patients achieved moderate response, 44 a good response and just 1 patient was declared nonresponder. At this visit, even if we didn't find significant differences between baseline COMP titres and the EULAR response (p=0.1430), we observed lower baseline titres for good responders (917.8±219.943 ng/ml) versus moderate responders (1042.7±193.117 ng/ml).
Grouping patients in 2 categories (responders/nonresponders) there were no differences between groups at 6 months (937.27±218.106 ng/ml versus 1042.2±181.717 ng/ml, p=0.227) or 12 months (942.82±219.025 ng/ml versus 896.5±0.000 ng/ml, p=0.9753).
Following the status pretreatment of COMP and EULAR response at 6 months, we identified differences between groups (p=0,0001), all 7 patients declared nonresponders were COMP positive and only 13/19 (68.4%) of good responders were tested positive. At 12 months there were no differences between pretreatment status of COMP and response to treatment (p=0.2805).
Regarding the evolution of serum levels, we noticed a decrease statistically significant from baseline (948.75±215.683 ng/ml) to 12 months (740.88±227.04 ng/ml, p=0.0000).
Conclusions: COMP could be one of the biomarkers for identifying pretreatment the patients who will respond to biologic therapy in Rheumatoid Arthritis.
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AB0377 SWITCHING FROM BIO-ORIGINAL ETANERCEPT TO BIOSIMILAR ETANERCEPT SB4: PATIENT ACCEPTABILITY AND OUTCOMES IN THE REAL WORLD

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Background: A number of studies have demonstrated the efficacy of biosimilar therapies including SB4 (a biosimilar-etanercept). However, real world data of the process of switching, acceptability to patients, efficacy and safety is lacking.
Objectives: To obtain real world data of the acceptability and outcomes of patients with severe (eligible for TNFi therapy as defined by UK NICE) rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) who switch from bio-original etanercept (boDMARD-ETN) to the bsDMARD etanercept SB4 (bsDMARD-ETN).
Methods: Adult patients, with RA, PsA & AS, currently enrolled in the SMaRT study and switching from boDMARD-ETN to bsDMARD-ETN were followed for 6 months. Primary outcome was change in DAS28, PsARC response or BASDAI following switching. Additional outcomes included; % change of remission rate, HAQ-DI, CRP or ESR levels, patient satisfaction, PDUS and SAEs leading to discontinuation. All patients had severe disease and were receiving boDMARD-ETN as per local guidelines of UK NICE. Analysis was performed in a similar way to a cross-over RCT trial design where patients act as their own control with the experience in the 6 and 12 months prior to switching used as the control for experience after switching.
Patient education and support during the switch included: rheumatologist face to face discussion, letter giving details of the switch and bsDMARD-ETN information sheet, patients invited to discuss switch in clinic, helpline number with patients advised to call for further information or to report adverse events (AEs), routine review in clinic 3 months after switching, and then 6 monthly thereafter or more often if clinically necessary.
Results: Following the education and support programme 99% of patients agreed to switch to bsDMARD-ETN (one declined due to concerns about allergic reactions to previous therapies). To date 92 patients have switched from boDMARD-ETN to bsDMARD-ETN and been followed up for more than 6 months (58 RA, 15, AS, 16 PSA and 4 enteropathic arthritis; mean age 55.9 (14.9) yrs, (56 female, 36 male), mean disease duration 16.8 (10.9) yrs, duration on boDMARD-ETN before switch mean 4.85 (3.92) yrs and duration since switch 204.1 (51.4) days. After 6 months following the switch 91% of patients using bsDMARD-ETN have continued with mean last DAS28 – 2.67 (1.32) for RA patients and mean last BASDAI – 4.58 (2.47). Following the switch 8 patients stopped bsDMARD-ETN after mean of 93.6 (56.4) days, the reasons for this were 7/8 clinician/patient determined inefficacy (6 returned to boDMARD-ETN, 1 switched to certolizumab), 1/8 switched after reporting palpitations and poor concentration. In the control period 6 months before switching 17/110 patients stopped boDMARD-ETN (85% continued) including 7 due to primary failure, 7 due to secondary failure, 1 adverse event (AE), 1 patient choice, 1 death (Lung cancer in male ex-smoker with longstanding RA who had received boDMARD-ETN for 10 yrs).
Conclusions: An education programme prior to switching to a biosimilar TNFi leads to a high uptake by patients. In follow-up of 6 months after switching from boDMARD-ETN to a bsDMARD-ETN there appears to be a low rate of discontinuation due to inefficacy or AEs.
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AB0378 IMPROVED CLINICAL OUTCOMES AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ADALIMUMAB IN CENTRAL AND EASTERN EUROPE

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Background: Although physical activity has known positive impacts upon pain, disease activity and functional status in patients with rheumatoid arthritis (RA), very little is known about physical activity in patients with RA on biologic therapy.
Objectives: To evaluate the effect of adalimumab treatment on physical activity and relationship with improvements in disease activity and physical function in patients with RA in routine clinical practice.
Methods: This was a 52-week multi-center, post-marketing observational study conducted in 7 countries in Central and Eastern Europe (CEE). Eligible RA patients were prescribed originator adalimumab according to the local practice; visits were performed approximately 3 months apart. Physical activity was assessed by validated Short QUestionnaire to ASsess Health-enhancing physical activity (SQUASH)[1,2], which measures habitual physical activity across four domains: commuting, leisure time and sport, household, work and school. RA disease activity was assessed by DAS28 and physical function by HAQ-DI; clinical remission (REM) and low disease activity (LDA) were defined as DAS28<2.6 and <3.2, respectively. Descriptive statistical analyses were performed, observed data are presented.
Results: 462 patients were enrolled and 255 patients completed the study. Mean age was 53.9 (±12.1) yrs; 82.2% of enrolled patients were female; average disease duration was 7.8 (±7.5) yrs. DAS28 decreased from 6.1 (±1.1) at baseline to 2.9 (±1.0) at study end, whereas the mean HAQ-DI from 1.6 (±0.6) to 0.7 (±0.5). The proportion of patients in LDA and REM at study end was 56.0% and 31.1%, respectively. Total SQUASH score increased from 4772 (±4132) to 6104 (±4921), representing 28% improvement in overall physical activity. The largest score improvements were seen in the SQUASH domains of leisure time and sport (by 43%), followed by household activities and activities at work and school (each by 19%). The correlations between the total SQUASH score and its subscores with DAS28 were weak both at baseline and study end. A significant correlation between the total SQUASH and HAQ-DI scores was seen at baseline (r -0.30), but not at the study end (r -0.22). Correlations between SQUASH subscores and HAQ-DI were not significant. The percentage of work disabled subjects decreased from 22% to 17%. According to linear regression analysis, sociodemographic factors did not substantially influence habitual physical activity.
Conclusions: Treatment with adalimumab in clinical practice in CEE resulted in clinically meaningful improvements in disease activity and physical function as well as improvements in physical activity. The correlation between the scores for disease activity, physical function and physical activity were however poor and there was no clear influence of the standard sociodemographic factors on physical activity.
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