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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

A. Pieren[1], C. Plasencia[1], D. Pascual-Salcedo[2], M.B. Paredes[1], A. Balsa[1].
[1]Rheumatology; [2]Immunology, Hospital la Paz, Madrid, Spain

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

A. Martinez-Feito[1], C. Plasencia[2], B. Hernandez-Breijo[1], A. Jochems[1], C. Diego[3], A. Villalba[2], D. Peiteado[2], L. Nuño[2], P. Nozal[3], A. Balsa[2], D. Pascual-Salcedo[1]. *[1]Immuno-Rheumatology research group; [2]Rheumatology; [3]Immunology, University Hospital la Paz, madrid, Spain*

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.
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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?

B.I. Gavrila[1], C. Ciofu[1], C. Mihai[1], G. Udrea[1], M. Bojinca[1], V. Stoica[1], E. Panaitescu[2]. *[1]Department of Internal Medicine and Rheumatology Cantacuzino Hospital; [2]Medical Informatics and Biostatistics, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

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).