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FRI0020 CLINICAL TREATMENT RESPONSE STILL DOES NOT MATCH PATIENT REPORTED IMPROVEMENT, EVEN IN EARLY RHEUMATOID ARTHRITIS

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Background: Commonly used disease activity scores in rheumatoid arthritis (RA) include one patient reported outcome (PRO) -the patient's global health assessment (PGA). Exploratory factor analysis (EFA) was performed on data from the 2 year Care in early Rheumatoid Arthritis (CareRA) trial to explain the evolution of disease burden extracting 3 factors.[1]

Objectives: To assess the evolution and relative responsiveness over time of clinical, laboratory and patient assessments included in composite scores, together with other PROs like pain, fatigue and functionality in patients with early RA (≤1 year) treated to target (T2T) within the CareRA trial.

Methods: DMARD naïve patients with early RA (n=379) were included, randomized to remission induction with COBRA-like treatment schemes (n=332) or MTX monotherapy (n=47) and T2T.

Components of disease activity scores (swollen/tender joint count (S/TJC), C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), and physician (PhGH) or patient (PGA) global health assessment), pain and fatigue (both on 0-100 scale) and HAQ were recorded at every visit.

Missing data was handled with multiple imputation (n=15). Clustering was removed with multiple outputation (n=1000), then each of the 15 000 datasets was analyzed by EFA with principal component extraction and oblimin rotation. The analyses were combined after re-ordering the factors by maximizing factor congruence. The 3 extracted factors and their individual components (with their loadings) were: 1. Patient containing PGA (0.87), pain (0.86), fatigue (0.90) and HAQ (0.5) 2.Clinical with SJC (0.92), TJC (0.89) and PhGH (0.76) and 3.Laboratory with CRP(0.87) and ESR (0.78).[1](Pazmino, ACR 2019 abstract, Table 3)

Afterwards, variables were first normalized to a 0-1 scale, then multiplied -weighted- by the factor loadings previously obtained.[1] For each Patient, Clinical and Laboratory severity score, the weighted variables belonging to each score were summed together and then re-scaled to 0-1 (higher values suggest more burden).

The percentage (%) improvement from baseline to week 104 and the area under the curve (AUC) across time points were calculated per factor.

Differences in % improvement and AUC were compared between patients not achieving and achieving early and sustained (week 16 to 104) disease activity score remission (DAS28CRP <2.6) with ANOVA. Bonferroni correction was used for multiple testing.

Results: Severity scores of Patient, Clinical and Laboratory factors improved rapidly over time (Figure 1). In patients achieving sustained remission (n=122), Patient, Clinical and Laboratory scores improved 56%, 90% and 27% respectively. In patients not achieving sustained remission (n=257) the improvement was 32%, 78% and 9% respectively (p<0.001 only for clinical improvement).

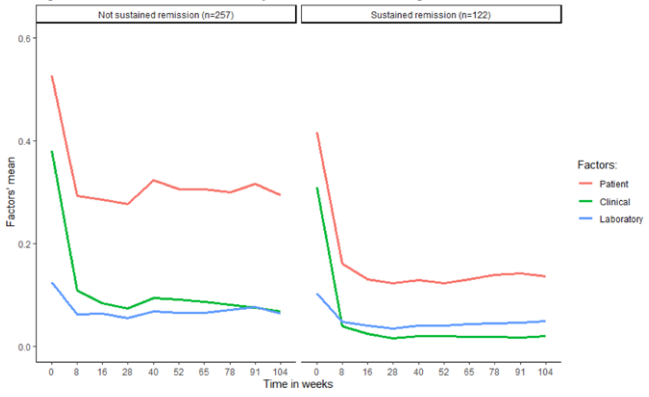
Patients in CareRA who achieved sustained remission had an AUC of 15.1, 3.4 and 4.7 in Patient, Clinical and Laboratory scores respectively, compared to 32.3, 10.0, and 7.2 in participants not achieving sustained remission (p<0.001 for all comparisons).

Conclusion: Patient, Clinical and Laboratory severity scores improved rapidly over time in patients achieving rapid and sustained disease control. However, overall, Patient burden seemed not to improve to the same extent as Clinical burden. Patient's unmet needs in terms of pain, fatigue, functionality and overall well-being should thus be given more attention, even in patients in sustained remission.

References:

[1] Pazmino S, *et al.* Including Pain, Fatigue and Functionality Regularly in the Assessment of Patients with Early Rheumatoid Arthritis Separately Adds to the Evaluation of Disease Status [abstract]. ACR. 2019.

Figure1: Mean factor evolution over 2-year CareRA trial achieving or not sustained DAS28CRP<2.6



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FRI0021 SHOULD WE USE GLUCOCORTICOID IN EARLY RHEUMATOID ARTHRITIS?: RESULTS AT 5 YEARS FROM THE ERA LOUVAIN BRUSSELS COHORT

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Background: The EULAR recommendations, updated in 2016, propose the initiation of glucocorticoid (GC) therapy in combination with cDMARDs background therapy for every patient with early rheumatoid arthritis (ERA).[1]

Objectives: The aim of this study is to evaluate the proportion of patients with ERA who have been treated with GC in daily practice, to analyse the baseline characteristics of these patients, and to assess the clinical benefit and side effects of GC during 5 years of follow-up.

Methods: We included patients with ERA from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to cDMARDs. Treatments were initiated based on the decision of a senior rheumatologist. We retrospectively collected patient characteristics prior to the introduction of cDMARDs with or without GC. Efficiency and serious adverse events were analysed at 6 months, 1 year, 3 years and 5 years.

Results: Data from 474 eligible ERA patients were collected. The average age of the population is 48.9 years. 70.5% of the patients are women. 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA).

178 patients (37.7 %) initiated GC compared to 294 patients (62.3%) who received only NSAIDs and/or analgesics in combination with cDMARDs.

At baseline, the elevation of CRP is the main factor that favors the initiation of GC (CRP 2.9 vs 2.0 mg/dl, p = 0.015) followed by smoking habits (34.2% vs 23.3%, p = 0.018), the absence of ACPA (37.2% vs 27.6%, p = 0.037), the prescription of methotrexate as a monotherapy (70.6% vs 50.5%, p <0.001), and the age (50.6 vs 48.0, p = 0.050). Other parameters such as swollen joint count, tender joint count, DAS28-CRP, HAQ or baseline erosion were similar between groups.

5 years follow-up of DAS28-CRP, HAQ or VAS pain values did not differ between the two groups (Fig 1A).

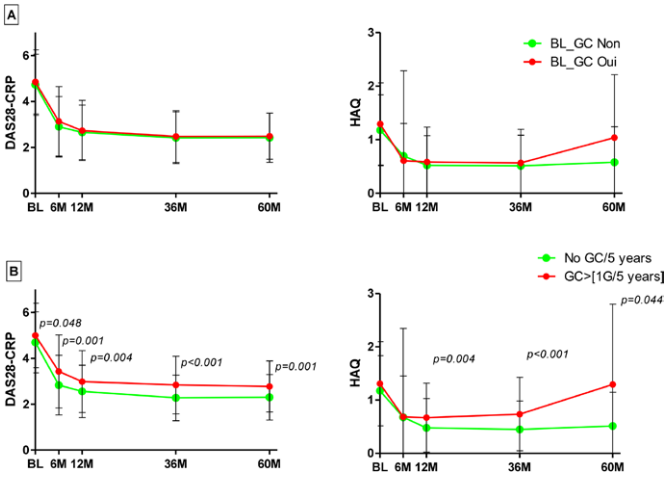

Figure 1. Comparison of DAS28-CRP and HAQ scores evolution. **(A)** in two groups of patients: treated with GC (BL-GC Yes) or without GC (BL_GC No) in combination with cDMARDs as first line treatment. **(B)** in two groups of patients: never treated with GC during 5 years follow-up (No GC/ 5 years) and those who received a high cumulative dose of GC ≥ 1 g/5years (GC>[1G/5years]).

Interestingly, patients not exposed at baseline to GC showed a higher remission rate (DAS28-CRP< 2.6) of 48.4% vs 44.3% at 6 months.

We also analysed a subgroup of patients (n=139) who received a cumulative dose of more than 1 g of prednisolone during the 5 years period. We confirmed the baseline differences for CRP, smoking habits, age and found in this subgroup more males (36.7% vs 28.2%, p=0.021) and higher DAS-28CRP values (5.0 vs 4.7, p=0.048).

During the 5 years follow up, DAS-28CRP, VAS pain and HAQ remained significantly higher leading to a higher number of bioDMARDs prescribed in this group (Fig 1B).

More severe infections were reported in this subgroup (11.5% vs 4.2%). Bone densitometry values, number of fractures, and cardiovascular profiles were similar between groups.

Conclusion: In our ERA cohort, initiation of GC treatment does not add additional benefit for the short and long-term control of the disease.

GC were more prescribed in seronegative RA patients with higher level of inflammation and we confirm that patients exposed to higher cumulative doses of GC are at higher risk to develop severe infections.

Further studies are needed to support that GC induction therapy should not be offered to all ERA patients.

References:

[1] Smolen JS, Landewé R, Bijlsma J, et al., EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Jun;76(6):960-977.

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FRI0022 THE ANALYSIS OF THE INVOLVEMENT OF TRANSFORMING-GROWTH INTERACTING FACTOR POLYMORPHISMS IN THE BONE METABOLISM OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that mainly invades synovial membranes and further damage to articular cartilage and bone. The abnormal activation of transforming-growth factor β (TGF-β) in the subchondral bone is related to the onset of RA joint cartilage degeneration and transforming-growth interacting factor (TGIF) is a negative regulator of TGF-β signaling, while there is no literature addressing the relationship between TGIF polymorphisms and the bone metabolism of RA.

Objectives: The aim of the study was to comprehensively explore the possible association for single nucleotide polymorphisms (SNPs) in the TGIF gene with serum bone metabolism markers and RA susceptibility.

Methods: Three SNPs within the TGIF gene were genotyped in 155 RA patients and 168 healthy controls by high resolution melting (HRM) analysis in a case-control study. The serum levels of osteocalcin, bone alkaline phosphatase (BALP) and β type I collagen-crosslinked C telopeptide (β-CTX) were detected by electrochemical luminescence in 108 RA patients randomly selected from RA patients group.

Results: Genotypes and alleles frequency analysis showed rs7362020 was associated with bone erosion in RA (P=0.012, P=0.003, respectively) and individuals carrying T allele for rs7362020 showed a decreased RA risk (OR=0.59, 95% CI = 0.42-0.84; P= 0.003). In the gender-specific analysis, rs73620203 polymorphism was associated with bone erosion of female RA patients (P values of the distribution of genotypes and alleles were 0.022 and 0.006, respectively). In addition, RA patients with CC, CT and TT genotypes at rs73620203 locus had statistically significant differences in serum osteocalcin and BALP (P=0.006, P=0.037, respectively) and the serum levels in TT genotype RA patients were significantly lower than CC and CT genotype RA patients. The serum levels of β-CTX in rs85440 AA genotype male RA patients were significantly higher than female RA patients (P=0.001), while the serum levels of osteocalcin and BALP in genotype AA, AG and GG female and male RA patients were not significantly different (P all>0.05).

Conclusion: Our study provided the first evidence that rs73620203 is associated with bone erosion of RA and provided new insight into the relationship between three SNPs within TGIF gene and regulation of bone metabolism in RA patients of different genders.

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FRI0023 TREATING EARLY AND INTENSIVELY IS ASSOCIATED WITH LOWER FATIGUE LEVELS ON THE LONG TERM, EVEN IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS CONSIDERED TO HAVE A FAVOURABLE RISK PROFILE

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Background: Fatigue is reported in up to 90% of patients with established Rheumatoid Arthritis (RA). Fatigue has a large impact on patient`s life and is perceived difficult to manage in many patients. The early disease course could constitute a window of opportunity to tackle fatigue.

Objectives: To explore that, if RA can be controlled rapidly, complaints of fatigue could be less in the long run, even in patients considered at low risk to develop a severe disease course.

Methods: Patients with a low risk profile recruited in the 2-year pragmatic Care in Early Rheumatoid Arthritis (CareRA) trial were used in this analysis. This low risk profile was based on the absence of erosions, rheumatoid factor, anti-citrullinated protein bodies or low disease activity status. The low-risk group was randomised to either a tight step-up starting with 15mg MTX weekly in monotherapy (MTX-TSU) or COBRA Slim, consisting of 15 mg MTX weekly and a prednisone step-down scheme starting at 30 mg. Fatigue was measured by the multi-dimensional fatigue inventory (MFI), a self-report instrument consisting of 20 questions with a Likert scale from 1-5 as answer. These 20 questions can be subdivided in five subscales (0-20) of four questions (higher scores indicating higher fatigue levels): general fatigue, mental fatigue, physical fatigue, reduced activity and reduced motivation. General fatigue means the general feeling of being tired. Mental fatigue implicates concentration and memory problems. Physical fatigue implicates a lack of energy and strength. Reduced activity means that patients can do less activities for example on one day. Reduced motivation means that patients don't want to plan or do things due to lack of motivation. MFI was obtained at baseline, at week 16, week 52 and week 104. Cobra Slim was compared with MTX-TSU by Mann-Whitney-U test. The 5 domains of the MFI of the two groups were compared by a generalized estimating equation (GEE) over 2 years adjusting for baseline MFI domain score and DAS28.