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LOS0516 PLASMA CALPROTECTIN WAS ASSESSED IN MULTIPLE BIOLOGICAL TREATMENT STRATEGIES FOR EARLY RHEUMATOID ARTHRITIS

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Background: Plasma calprotectin is a sensitive inflammatory marker in patients with rheumatoid arthritis (RA) and reflects activation of granulocytes and macrophages. Plasma calprotectin has not previously been studied in a head-to-head trial of multiple biological mechanisms of action versus active conventional therapy (ACT) with methotrexate and prednisolone.

Objectives: To assess the effect of treatment on plasma calprotectin levels in patients with early RA, by determining the 24-week change in the four arms of the NOR-STAR Study, a large multicenter randomized head-to-head clinical trial of ACT versus tumor necrosis factor inhibitor, T-cell co-stimulation inhibition, and interleukin-6 inhibition (1).

Methods: Calprotectin was analyzed in plasma samples at baseline, week 4 and week 24 from 400 treatment naive patients with early RA in the NOR-STAR Study. Samples were analyzed using a calprotectin ELISA alcalase phosphatase (ALP) kit from CalproLab (Oslo, Norway) in a Dynex DS2 processing system (normal levels <910 µg/L). Patients were assessed by clinical (CRP, 28 SJC/TJC, physician global) and patients' reported assessments. Crude and adjusted linear regression analyses were performed in R 4.0.3 with calprotectin levels at week 24 as the outcome. The four arms were represented by three dummy variables. The adjustment variables were age, sex, anti-CCP status and country. Both analyses were adjusted for baseline calprotectin levels.

Results: At baseline, the mean time since diagnosis was 15.7 days (SD) (22.9), mean age 53.7 (15.0) years, ACPC positive 81%, and female 66%. Mean calprotectin levels were 1931 (1495) µg/L at baseline, 866 (951) µg/L at week 4, and 629 (681) µg/L at week 24. At baseline, normal calprotectin levels (<910 µg/L) were observed in 27% of all patients (ACT 22%, certolizumab-pegol and methotrexate 30%, abatacept and methotrexate 25%, tocilizumab and methotrexate 31%). At week 24, normal calprotectin levels were observed in 82% of all patients (ACT 68%, certolizumab-pegol and methotrexate 91%, abatacept and methotrexate 80%, tocilizumab and methotrexate 90%). Observed calprotectin levels at week 24 were significantly lower in patients treated with certolizumab-pegol and methotrexate -336µg/L (97) (p < 0.006) or tocilizumab and methotrexate -284 (99) (p < 0.004), versus ACT when adjusted for age, sex, anti-CCP status, baseline calprotectin level, and country; however, a significant difference was not observed in patients treated with abatacept and methotrexate -110 (96) (p = 0.25). The Figure 1 shows the average percentage change in calprotectin levels from baseline to week 24 for all treatment groups.

LOS0517 IGA ACPA ARE ASSOCIATED WITH PROGRESSION TO RHEUMATOID ARTHRITIS IN INDIVIDUALS AT-RISK AND DECLINE IN LEVELS AROUND THE DISEASE ONSET

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Background: Anti-citrullinated protein antibodies (ACPA) can precede the diagnosis of rheumatoid arthritis (RA) up to a decade. However, while some ACPA-positive individuals rapidly develop the disease, a considerable proportion are not progressing to RA, and the events triggering the disease outbreak are still poorly understood. While a lot is known about ACPA of IgG class, the role of IgA ACPA is still not defined.

Objectives: We aimed to look into IgA ACPA isotypes in individuals at-risk for RA and their role in RA development.

Methods: IgA1 and IgA2 ACPA were measured cross-sectionally in 30 seropositive (IgG ACPA-positive) RA patients, 29 seronegative RA patients, 63 individuals at-risk for RA (positive for IgG ACPA and/or anti-modified citrullinated vimentin antibodies and with joint complaints) and 32 healthy controls. In addition, IgA ACPA levels were compared in 24 RA at-risk individuals who developed RA during a follow-up of 14 months and in 21 individuals who did not. Furthermore, longitudinal measurements of IgA1 and IgA2 ACPA levels 1-28 months prior to, at and 1-18 months after the onset of RA were performed in 14 at-risk individuals and in 9 individuals from a confirmation retrospective cohort of RA patients from the Medical University of Vienna. Cut-offs were set based on the comparison of

Figure 1. Average percentage change in calprotectin levels from baseline to week 24. ACT: active conventional therapy. CZP+MTX: certolizumab-pegol and methotrexate, ABA+MTX: abatacept and methotrexate, TCZ+MTX: tocilizumab and methotrexate.