cytokines and chemokines including IL-12B (P=0.07), IL-6 (P=0.07), IL-10 (P=0.12), IL-18 (P=0.19), and IL-4 (P=0.63).

Conclusion: This study illuminates the downstream effects of neutralizing TNFα not previously investigated. Adalimumab had a pronounced effect on downregulation of the inflammatory CXCL family subfamily chemokines IL-8, CXCL5, CXCL9, and CXCL10. This helps explain findings of diminished inflammatory cell migration into joints seen in the first trials with TNFα inhibitors and could be an important mechanism of action of TNFα inhibitors.[2] Further characterization of downstream effects of multiple DMARDs used for the treatment of immune mediated inflammatory arthritis will help guide treatment strategies for these patients.

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AB0070 THE RELATIONSHIP BETWEEN THE LEVEL OF NESFATIN-1 AND THE CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS
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Background: Nesfatin-1 is actively studied in the pathogenesis of metabolic disorders. An excess of this factor in the brain leads to loss of appetite, a feeling of fullness, as well as a decrease in body weight. Similarly, elevated levels of nesfatin are associated with depressive disorders [1]. We studied the level of nesfatin in the serum of patients with rheumatoid arthritis (RA) and found a relationship with systemic inflammation and functional impairment [2].

Objectives: To study the relationship of serum nesfatin-1 levels with the clinical manifestations of RA.

Methods: To identify the relationship between serum nesfatin-1 and the clinical manifestations of rheumatoid arthritis, all patients were divided into 2 groups. The first group - 1 (66 patients) with elevated serum nesfatin (>37.95 ng/ml). The second group - 2 (44 patients) - with normal values (<37.95ng/ml). In both groups, we studied the clinical manifestations of RA. The level of nesfatin-1 was analyzed by ELISA. The level of nesfatin was compared with the level of inflammatory markers.

Results: A high level of nesfatin in RA patients was typical for patients with a higher degree of activity in DAS28 (χ² = 8.37; p = 0.04), seropositivity for the rheumatoid factor (RF) - (χ² = 5.53; p = 0.02), duration of the disease is more than 10 years (χ² = 9.53; p = 0.01). At the same time, there was no significant correlation between the level of nesfatin and the extra-articular manifestations of RA (χ² = 2.09; p = 0.14) and the degree of radiological damage to the joints (χ² = 4.45; p = 0.21).

Conclusion: This study shows that serum nesfatin-1 levels are significantly higher in patients with more unfavorable RA, than in RA with minimal clinical manifestations. These data confirm the pathogenetic role of Nesfatin-1 in the development of clinical manifestations associated primarily with RA activity, but to a lesser extent with organ lesions in RA. The relationship of the level of nesfatin with the duration of the disease is of particular interest, since there is no correlation with the degree of X-ray damage to the joints and organ damage. These data are also important for the development of new drugs targeting nesfatin-1 for RA.

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AB0071 SERUM S100A8/A9 (CALPROTECTIN) IN FAMILIAL MEDITERRANEAN FEVER DOES NOT CORRELATE WITH DISEASE ACTIVITY
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Background: Familial Mediterranean Fever (FMF) is caused by mutations in MEFV. The protein product pyrin is expressed in monocytes, neutrophils and eosinophils. Autoinflammatory attacks are accompanied by a dramatic hepatic acute phase response. S100A8/A9 is damage associated molecular pattern and a TLR4 ligand expressed in neutrophils, monocytes and early infiltrating macrophages. We aimed to investigate S100A8/A9 in 39 patients with FMF, 45 healthy carriers and wild type controls.

Objectives: To measure S100A8/9 in patients with FMF, carriers and healthy controls.

Methods: All patients were genotyped. Patients and healthy controls (HC) serum S100A8/A9 levels, cell surface expression on monocytes and neutrophils as well as intracellular peripheral blood mononuclear cells (PBMC) expression were measured by flow cytometry (FACS). CD14 cells were isolated and following overnight incubation with or without LPS, S100A8/A9 was measured in the supernatants by ELISA. Patients and HC monocyte apoptosis was compared.

Results: Serum levels were measured in 84 samples from 31 patients with homozygous or compound mutations (median 9039ng/ml [range 300-380470], 79 samples from 39 symptomatic patients who were MEFV heterozygotes (median 3934ng/ml [range 1744-38119], 80 samples from 45 individuals with MEFV variants but without clinical features of FMF (median 10939ng/ml [range 2447-4000], there was no difference in calprotectin concentrations between the different mutations. All the groups described had significantly higher levels than healthy controls (n=16 median 2836ng/ml [range 1058-6175])(p<0.001).Minimal monocyte and neutrophil cell surface expression was detectable. Following LPS stimulation there was significantly more S100A8/A9 detected in the supernatants in patients than healthy control CD14. There was also a trend to an increased intracellular monocyte S100A8/A9 expression.

BIOMARKER CHANGES FOR PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB WITH METHOTREXATE OR GLUCOCORTICOIDS VS TOFACITINIB MONOTHERAPY

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Herpes zoster is more common in patients (pts) with RA vs the general population.1 This risk increases with tofacitinib use2 and appears to be further increased with concomitant use of csDMARDs such as methotrexate (MTX), or glucocorticoids (GC).3 The mechanism for these increases in risk may be linked to treatment-induced interferon (IFN) suppression,4 given that replication of the varicella zoster virus appears to be limited by IFN activity.4

Objectives: To evaluate whether treatment of RA with tofacitinib + MTX or GC suppresses IFN pathway proteins to a greater extent than treatment with tofacitinib monotherapy.

Methods: This was a post hoc analysis of pooled data from 1 Phase (P2; Japan study [NCT00687193]) and 2 P3 (ORAL Scan [NCT00847613]; ORAL Start [NCT01039888]) tofacitinib studies. Serum samples were collected at baseline (BL), Week (W)12 and/or W24 from pts with RA treated with tofacitinib 5 or 10 mg BD, given as monotherapy (Japan study; ORAL Start) or with stable doses of MTX (15–25 mg weekly for ≥6 weeks; ORAL Scan) and/or GC (≤10 mg/day prednisone or equivalent; all studies). A total of 376 proteins associated with cellular and inflammatory processes, including 6 IFN pathway proteins (CXCL10, CXCL9, CXCL11, IL-12, IFNγ and IL-20), were measured using a homogeneous solution-based assay (Olink ProseekTM Multiplex Assay, Uppsala, Sweden). Changes in protein levels from BL to W12 (Japan study, ORAL Scan) and/or W24 (ORAL Scan, ORAL Start) were compared for tofacitinib monotherapy vs tofacitinib + MTX or GC using linear regression models. The dependent variable was change from BL in protein levels at W12 or W24. The independent variable was MTX or GC status. Age, gender, GC status (in MTX model) and BL protein levels and tofacitinib dose were covariates. Regressions were performed separately for each study; results for GC were combined via meta-analysis using fixed and random effect models. Significance was considered at p<0.1 after controlling for false discovery rate (FDR). Data quality control included accounting for plate/batch effects and limits of detection, and removal of sample/analytes with excessive missing data.

Results: In total, 659 serum samples were collected from 321 pts. Of the 6 IFN pathway proteins, 2 (IFNγ and IL-20) were below the limit of detection. There was no strong evidence suggesting statistical differences between tofacitinib monotherapy and tofacitinib + MTX or GC in changes in levels of the 4 detectable IFN pathway proteins (CXCL10, CXCL9, CXCL11 and IL-12) from BL to W12 and/or W24. Significant differences were observed for 2 of the 370 other proteins: MMP-1 (FDR adjusted p=0.08) and IL1Rα (FDR adjusted p=0.09), where levels decreased from BL to W12 for tofacitinib + MTX to a greater extent than for tofacitinib monotherapy.

Conclusion: The results of this post hoc analysis suggest that tofacitinib + MTX or GC may not suppress circulating serum levels of IFN pathway proteins to a greater extent than tofacitinib monotherapy. Although there were differences at W12 for tofacitinib + MTX vs tofacitinib monotherapy in MMP-1 and IL1Rα, it is not yet clear whether these observations may be attributable to differences in the ethnicities of the study populations receiving these two treatment regimens (global vs Japan). Further analyses of biomarker changes with tofacitinib are ongoing.