duration at baseline ($R=0.466$, $p=0.009$). There were no other significant correlations.

Conclusions One year tofacitinib therapy effectively reduced disease activity and systemic inflammation. The therapy also improved functional capacity. JAK inhibition significantly decreased the number and ratio of CD3+ and CD4+ T cells and increased number and ratio of CD19+ B cells in 12 months. Tofacitinib is a safe and effective treatment for rheumatoid arthritis. It makes an effect, partly, via modifying lymphocyte subsets.

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Disclosure of Interest None declared.

P134/032 SELECTIVE EXPANSION OF A THYMIC-DERIVED AND FUNCTIONALLY COMPETENT REGULATORY T CELL POPULATION BY LOW-DOSE IL-2 THERAPY IN PATIENTS WITH REFRACTORY SLE

¹JY Humrich*, ²C von Spee-Mayer, ³E Siegert, ⁴M Bertolo, ³A Rose, ³D Abdirama, ⁴P Enghard, ³B Stuhlmüller, ³F Hiepe, ³T Alexander, ³E Feist, ⁵A Radbruch, ³G-R Burmester, ¹G Riemekasten. ¹Department of Rheumatology and Clinical Immunology, University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck; ²Center for Chronic Immunodeficiency (CCI), University Hospital Freiburg, Freiburg; ³Department of Rheumatology and Clinical Immunology; ⁴Department of Nephrology and Intensive Care Medicine, Charité – University Medicine Berlin; ⁵German Rheumatism Research Center (DRFZ) Berlin, Berlin, Germany

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Career situation of first and presenting author Instructor.

Objectives An acquired deficiency of interleukin-2 (IL-2) and related defects in regulatory T cell (Treg) homeostasis play a crucial role in the pathogenesis of SLE. Here, we report the responses of Treg and other lymphocyte subsets to low-dose IL-2 therapy observed during an open-label, uncontrolled, dose adaption, phase 1/2a single-center clinical trial in patients with active and refractory SLE.

Methods 12 patients with active and refractory SLE (SLEDAI ≥ 6) were treated at our site with a low-dose IL-2 regimen consisting of four separate treatment cycles each with daily subcutaneous injections of recombinant human IL-2 (aldesleukin) at single daily doses of either 0.75, 1.5 or 3.0 million IU for five consecutive days. Cells from peripheral blood were analyzed by flow cytometry before and one day after each treatment cycle.

Results All patients showed highly significant cycle- and dose-dependent increases in the proportions and absolute numbers of CD3+CD4+FoxP3+CD127^{lo} Treg and of CD25^{hi} expressing cells among Treg. By contrast, we observed no relevant changes in the absolute numbers of CD3+CD4+FoxP3 conventional T cells (Tcon), of CD3+CD8+ T cells, of CD3+CD56+NK T cells and of CD3-CD56+NK cells. The IL-2 expanded Treg population displayed a preserved suppressive capacity and expressed high levels of the Treg-associated molecules Helios, CD39 and CD137. In addition, we noted robust and dose-dependent increases in the proportions of Treg expressing the proliferation marker Ki67. Although significant increases in the proportions of Ki67⁺ cells among Tcon and also among other lymphocyte subsets were observed at the end of each treatment cycle, the calculated ratio between Ki67⁺ Treg and Ki67⁺ Tcon continuously increased and was significantly higher at the end of the treatment phase, suggesting a preferential targeting of the Treg population.

Conclusions Low-dose IL-2 therapy promotes the selective expansion of a functionally competent and thymic-derived Treg population in patients with refractory SLE. This study also provides novel insights into the pharmacodynamics and the broad biologic effects of low-dose IL-2 therapy.

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P136 THE EFFECTS OF LY294002, THE PHOSPHOINOSITIDE 3-KINASE INHIBITOR, ON NEUTROPHIL APOPTOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND COLLAGEN-INDUCED ARTHRITIS IN MICE

X Huang, T Li*, S Zheng, W Deng, Y Huang, Z Huang, Q Huang, Z Huang. Department of Rheumatology and Immunology, Guangdong Second Provincial General Hospital, Guangzhou, China

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Career situation of first and presenting author Young investigator.

Introduction Neutrophils act as a first line in host defense, they also play important roles on acute and chronic inflammation. Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by persistent joint inflammation.¹ Previous studies have shown that delayed apoptosis of neutrophils correlated with the pathogenesis of RA.²

Objectives The aim of this study was to investigate the effects of LY294002, the phosphoinositide 3-kinase (PI3K) inhibitor, on neutrophil apoptosis in RA patients and collagen-induced arthritis (CIA) in mice.

Methods The peripheral blood from untreated RA patients who satisfy the 1987 ACR classification criteria for RA (n=20) and healthy volunteers (HC) (n=10) were used to isolate neutrophils by density gradient centrifugation. The neutrophils were cultured with or without LY294002 *in vitro* for 18 hour. The rate of neutrophils apoptosis were analyzed by flow cytometry. The intracellular protein levels of PI3K-Akt pathway in neutrophils were measured by Western blot. CIA mice were treated with vehicle or LY294002, and the incidence, arthritis score, histological assessment as well as the apoptosis rate of neutrophils from peripheral blood and marrow were analyzed.

Results The peripheral blood neutrophils apoptosis delayed in RA patients as compared with neutrophils from HC. As compared with the HC, the expression of phosphorylation PI3K (p-PI3K) and p-Akt were increased in RA patients. LY294002 could significantly promote neutrophils apoptosis in peripheral blood from RA patients. LY294002 blocked the activation of PI3K-Akt and inhibited the expression of p-Akt. Moreover, LY294002 treatment delayed the onset, reduced the severity of arthritis in CIA mice. We also found that neutrophils from both peripheral blood and bone marrow delayed apoptosis in CIA mice as compared with the control group, and LY294002 treatment facilitated the neutrophil apoptosis from peripheral blood and marrow in CIA mice.

Conclusions This data suggested that delayed apoptosis of neutrophils, which might through the activation of PI3K-Akt