whether changes in these levels and/or presence associates with SDFR.

Methods In sera of 399 seropositive RA patients in the IMPROVED study,¹ we measured, at 4 month intervals over the first year of treatment: IgG, IgM, and IgA isotypes for anti-cyclic citrullinated peptide-2 (anti-CCP2) and anti-carbamylated protein antibodies (anti-CarP), IgM and IgA for rheumatoid factor (RF), and IgG autoantibodies against 4 citrullinated and 2 acetylated peptides. We investigated whether changes in antibody levels and seroconversion from positive to negative for each individual antibody was favourable for SDFR (drug-free DAS44 <1.6 lasting ≥1 year until last follow-up).

Results For all 14 antibodies, median levels decreased significantly between baseline and 4 months and then stabilised. Most seroconversion to negative happened within the first 4 months of treatment (with prednisone and methotrexate), after which some patients converted back to seropositive. The prevalence of seroconversion varied substantially depending on the autoantibody. The percentage of baseline autoantibody positive patients that became seronegative by 12 months was: anti-CCP2 IgG (2%), IgM (29%), IgA (29%); RF IgM (21%), IgA (31%); anti-CarP IgG (51%), IgM (49%), IgA (66%); anti-acetylated-lysine-vimentin IgG (24%), anti-acetylated-ornithine-vimentin IgG (10%); anti-cit-vimentin 59–74 IgG (21%); anti-cit-fibrinogen α27–43 IgG (45%), anti-cit-fibrinogen β36–52 IgG (20%), and anti-cit-enolase 5–20 IgG (22%). We hypothesised that greater level decreases and seroconversion to negative, reflecting disappearance of the underlying immunopathology, might be favourable for the long-term outcome SDFR, but surprisingly, greater median decreases in levels were not associated with higher chance of SDFR for any antibody. Furthermore, we found no evidence that rates of SDFR were higher in patients who seroconverted to negative compared those who stayed seropositive, for any of the 14 antibodies analysed.

Conclusions Autoantibody levels decrease and seroconversion from positive to negative occurs under treatment, but these changes do not translate to apparent clinical long-term benefits with regard to SDFR. This suggests that the disappearance of measurable serological autoimmunity does not lead to eradication of disease.

REFERENCE

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Disclosure of interest None declared

P008

METHOTREXATE AND BAFF INTERACTION PREVENTS IMMUNISATION AGAINST TNF-A INHIBITORS BY INCREASING ADENOSINE AND REGULATORY B-CELLS

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Introduction TNFα inhibitors (TNFi), frequently used in patients with autoimmune diseases, can induce anti-drug antibodies (ADA) in one third of cases, leading to secondary resistance. Methotrexate (MTX) is known to decrease

immunisation against TNFi. In BAFFtg mice, a model of autoimmune disease in which immunisation against biologic drugs is high, we investigated a new way of tolerization using a single course of MTX and we identified the mechanisms involved in this tolerization.

Objectives To assess the potential interaction between BAFF and tolerization induced by MTX.

Methods BAFFtg mice treated with TNFi with or without MTX were monitored for drug concentration and ADA. WT and BAFFtg mice were compared for B-Cell surface markers involved in MTX-related purinergic metabolism, adenosine production or B-regulatory cells (Bregs). Then, BAFF levels, MTX treatment and ADA were assessed in the human ABIR-ISK cohort of patients with chronic inflammatory diseases.

Results In BAFFtg but not in WT mice, a single course of MTX prevented immunisation against TNFi and maintained drug concentration for over 52 weeks. BAFFtg mice B-cells expressed more CD73 and CD39 leading to more adenosine production and to increase in Breg. MTX-induced tolerization was reversed *in vivo* using anti-CD73 antibodies. In patients treated with TNFi for chronic inflammatory diseases, high BAFF serum level was protective against ADA formation to TNFi only in patients co-treated with MTX but not in patients on TNFi monotherapy.

Conclusions This data supports an interaction between MTX and BAFF via increase in CD73 to prevent ADA formation in mice and humans. Treatment increasing CD73 could potentialize the role of MTX to prevent immunisation.

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P009

TRANSCRIPTOMIC ANALYSIS OF PLASMACYTOID DENDRITIC CELLS FROM RHEUMATOID ARTHRITIS PATIENTS REVEALS NOVEL TARGETS FOR THERAPY

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Introduction Reestablishing immune tolerance and long term remission represent major therapeutic goals in rheumatoid arthritis (RA). Our laboratory previously demonstrated that plasmacytoid dendritic cells (pDCs) from RA patients in remission have the ability to induce IL-10 producing regulatory T cells *in vitro*. However, the molecular pathway of RA pDC-mediated Treg induction remains elusive.

Objectives Herein, we sought to identify the molecular mechanism through which pDCs contribute to restoration of tolerance in RA.

Methods pDCs were isolated from peripheral blood of RA patients responding to anti-TNF therapy (DAS28 <5.1) and