naive T-, B-cells and CD16⁺ NK-cells along with a relative increase in memory lymphocytes and CD16⁺ NK-cells. These effects were also observed but less pronounced in controls.

Conclusions: Bowel cleanse and fasting in RA induces a reduction of inflammation related to monocyte activation and turnover immediately within few days. Changes in the monocyte compartment were specific for RA compared to controls and dominated the immunological changes, suggesting that innate triggering mechanisms from gut and its microbiota are etiologically relevant in RA.

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SAT0250 THE DOSING OF INTRA-ARTICULAR TRIAMCINOLONE HEXACETONIDE FOR KNEE SYNOVITIS IN CHRONIC POLYARTHRITIS – A RANDOMIZED CONTROLLED STUDY

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Background: Intra-articular glucocorticoid (IAGC) injection treatment is an easy and effective way to treat signs and symptoms of arthritis and it has been used for decades. Serious adverse reactions are rare, but IAGC therapy has impact on endocrine balances. There is limited knowledge of the adequate dosing for different joints and dosing traditions vary all over world.

Objectives: To compare the relapse rate during 6 months after IAGC for knee synovitis, between two common doses (20 mg vs 40 mg) of triamcinolone hexacetonide (THA).

Methods: A total of 159 adult patients with rheumatoid arthritis (RA) or psoriatic arthritis (Psoa) and active knee synovitis were randomized to IAGC injection with either 20 mg or 40 mg THA blinded to the participants. The primary endpoint was relapse of arthritis. When symptoms from the treated joint recurred and signs of arthritis could be confirmed on a following clinical examination a relapse was recorded and days from injection to relapse was calculated. At the end of the observation period those without relapse had a phone call to verify persistence of good treatment response.

Results: In this material there was no significant difference in patient characteristics at baseline and the proportion of relapse after 6 months were equal in the treatment arms (30% versus 32%, p=0.822). Additionally no significant differences were found in the subgroups with RA and Psoa patients.

Conclusions: To reduce the risk for endocrine side effects and as no difference in treatment outcome between the compared doses was found the lower 20 mg THA dose should be preferred in IAGC treatment for knee synovitis in chronic polyarthritis.

Disclosure of Interest: None declared

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SAT0251 SELECTIVE GLUCOCORTICOID RECEPTOR MODULATOR SHOWS POTENT ANTI-INFLAMMATORY EFFECT WITH IMPROVED METABOLIC PROFILE IN A PHASE I STUDY SUPPORTED BY IN VITRO DATA

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Background: AZD9567 is a novel oral selective glucocorticoid receptor modulator (SGRM) developed to have an improved safety profile versus prednisolone while maintaining efficacy.

Objectives: To show clinical evidence of safety differentiation for AZD9567 compared to prednisolone with respect to glucose homeostasis and to investigate the underlying effects on the glucose metabolism in human cell systems *in vitro*.

Methods: In a dose escalation study (NCT02760316), healthy volunteers were randomized to a 5-day once-daily treatment with AZD9567 (20, 40, 80, 125 mg) or prednisolone (5, 20, 40 mg). We monitored the anti-inflammatory effect by TNF α release from *ex vivo* LPS stimulated whole blood and modelled the relationship with pharmacokinetics (PKPD). Plasma glucose was measured (AUC_{0-4h}) during an oral glucose tolerance test (OGTT) before and after four days of treatment. We also studied the effects of AZD9567 and prednisolone on mRNA expression of key gluconeogenesis enzymes (tyrosine aminotransferase (TAT), phosphoenolpyruvate carboxykinase (PEPCK) and glucose 6-phosphatase (G6Pase)) in primary human hepatocytes as well as on insulin secretion in human islets microtissues.

Results: The inhibition of TNF α release increased with the plasma concentrations of AZD9567. PKPD modeling of TNF α inhibition data showed that 40 mg AZD9567 results in an anti-inflammatory activity similar to that predicted for 20 mg prednisolone.

A significantly smaller increase of the glucose AUC was observed following treatment with 20 to 125 mg AZD9567 compared to 20 mg prednisolone (p<0.05). Mean (95% CI) changes from baseline for 20, 40, 80 and 125 mg AZD9567 were 16% (6.5–26, n=7), 19% (9.3–30, n=7), 19% (9.8–30, n=7) and 34% (24–46, n=7), respectively. The corresponding values for 5, 20 and 40 mg prednisolone were 17% (10–24, n=13), 53% (43–62, n=13), and 68% (58–79, n=12), respectively. We found significant induction of TAT, PEPCK, and G6Pase mRNA in hepatocytes after prednisolone treatment. In contrast, AZD9567 did not change the expression of these enzymes and inhibited the effect of prednisolone when co-administered. Furthermore, AZD9567 showed less suppression of insulin secretion in human islets microtissues compared to prednisolone at concentrations with comparable inhibition of TNF α release, resulting in a 12-fold better therapeutic ratio.

Conclusions: In healthy individuals, AZD9567 showed significantly reduced effect on glucose homeostasis versus prednisolone at doses with similar anti-inflammatory activity. Thus, AZD9567 shows potential as an anti-inflammatory treatment with an improved metabolic safety profile compared to prednisolone.

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SAT0252 CLINICAL AND FUNCTIONAL RESPONSE TO TOFACITINIB AND ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: PROBABILITY PLOT ANALYSIS OF RESULTS FROM THE ORAL STRATEGY TRIAL

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). ORAL Strategy (NCT02187055), a 12-month, global, Phase 3b/4 study, demonstrated that in patients with RA and an inadequate response to methotrexate (MTX), tofacitinib + MTX was non-inferior to adalimumab + MTX, while tofacitinib monotherapy was not non-inferior to either combination based on American College of Rheumatology (ACR)50 response rates at Month 6.¹

Objectives: To assess clinical and functional efficacy across treatments in the ORAL Strategy trial using cumulative probability plots.

Methods: Efficacy was evaluated between patients who received tofacitinib 5 mg twice daily (BID) as monotherapy (N=384), tofacitinib 5 mg BID + MTX (N=376) and adalimumab 40 mg subcutaneously once every 2 weeks + MTX (N=386) based on ACR responses and changes from baseline in Health Assessment Questionnaire-Disability Index (Δ HAQ-DI) score at Month 12. Cumulative probability plots for ACR-n (where ACR is the % improvement from baseline in ACR components, and n represents the minimum % achieved by each patient)