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)

and Δ HAQ-DI are presented. The area under the curve (AUC) was calculated for ACR-n up to Month 12 (in months), and an analysis of covariance model was used to assess treatment effects in terms of the AUC of ACR-n at Month 12; there was no adjustment for multiplicity for this post hoc analysis.

Results: The cumulative probability plots of ACR responses at Month 12 indicated that the proportion of patients who achieved responses of ACR20, ACR50 and ACR70 was similar for tofacitinib + MTX and adalimumab + MTX, but was numerically smaller for tofacitinib monotherapy (figure, A). Responses of approximately $\geq$ ACR80 were achieved by a similar proportion of patients in each treatment group. Least squares mean (standard error) AUC of ACR-n up to Month 12 (in months) was similar for tofacitinib + MTX (437 [35]) and adalimumab + MTX (402 [35]), but was smaller for tofacitinib monotherapy (319 [35]; $p < 0.05$). The cumulative probability plots of Δ HAQ-DI suggested that, in general, reductions from baseline in HAQ-DI were similar across treatment groups (figure, B), although a slightly higher proportion of patients who received tofacitinib monotherapy reported an increase in HAQ-DI vs other treatments.

ACR-n, American College of Rheumatology response, where n represents the minimum % response achieved by each patient; BID, twice daily; Δ HAQ-DI, change from baseline in Health Assessment Questionnaire-Disability Index; MTX, methotrexate; Q2W, once every 2 weeks; SC, subcutaneous

Figure 1 Cumulative probability plot of A) ACR response and B) Δ HAQ-DI at Month 12. Two outliers for ACR response are not shown: tofacitinib 5 mg BID monotherapy, ACR-n=1700, cumulative probability=0.0003; adalimumab 40 mg SC Q2W + MTX, ACR-n=463, cumulative probability=0.003

Conclusions: These data support the primary ORAL Strategy findings,¹ indicating that in patients with RA, clinical efficacy, based on ACR response, was generally similar for tofacitinib + MTX and adalimumab + MTX, while a smaller proportion of patients who received tofacitinib monotherapy achieved ACR response in general, and particularly for $<$ ACR80. Functional efficacy, based on Δ HAQ-DI, was generally similar across all treatment groups. Cumulative probability analyses for CDAI will be further evaluated.

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SAT0253 DOSE REDUCTION OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING SUSTAINED DISEASE CONTROL: RESULTS OF A PROSPECTIVE STUDY

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Background: In patients with rheumatoid arthritis (RA) and inadequate response (IR) to DMARDs, ph3 studies demonstrated efficacy of baricitinib (Bari) (2-mg and 4-mg).

Objectives: To investigate the effects of Bari dose step-down in patients who achieved sustained disease control with Bari 4-mg.

Methods: Patients with RA participating in the Bari ph3 long-term extension study who received Bari 4-mg for ≥ 15 months and who achieved sustained low disease activity (LDA) – CDAI score ≤ 10 or remission (REM) – CDAI ≤ 2.8 ≥ 3 months apart were re-randomised in a blinded manner to continue Bari 4-mg or step down to 2-mg. Patients could rescue to Bari 4-mg. Efficacy and safety were assessed through 48 weeks (wks) following re-randomisation.

Patients Originating from RA-BEAM, RA-BUILD, RA-BEACON Combined [†]						
	Wk 12		Wk 24		Wk 48	
	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376	Continued Bari 4-mg N=374	Stepped Down to Bari 2- mg N=376
Efficacy measure	NRI after rescue or for missing data					
CDAI LDA ≤10	338/374 (90.4)	310/376 (82.4)**	327/374 (87.4)	280/376 (74.5)***	300/374 (80.2)	254/376 (67.6)***
CDAI REM ≤2.8	149/374 (39.8)	134/376 (35.6)	161/374 (43.0)	130/376 (34.6)*	145/374 (38.8)	121/376 (32.2)
	NRI only for missing data (observed data used after rescue)					
CDAI LDA ≤10	338/374 (90.4)	310/376 (82.4)**	334/374 (89.3)	304/376 (80.9)**	321/374 (85.8)	295/376 (78.5)**
CDAI REM ≤2.8	149/374 (39.8)	134/376 (35.6)	164/374 (43.9)	137/376 (36.4)*	149/374 (39.8)	134/376 (35.6)
Safety measure	Wks 0–48					
n [EAIR]	Continued Bari 4-mg N=374			Stepped down to Bari 2-mg N=376		
SDEAE	235 [69.30]			202 [63.46]		
Infection	108 [31.85]			78 [24.50]		
SAE	27 [7.96]			26 [8.17]		
Serious infection	10 [2.95]			4 [1.26]		
AE	9 [2.64]			12 [3.74]		
→discontinuation						

Efficacy and safety data are n/N (%), and n [EAIR], respectively. [†]RA-BEAM=MTX-IR patients; RA-BUILD=csDMARD-IR patients; RA-BEACON=bDMARD-IR patients; EAIR=exposure-adjusted incidence rate; NRI=nonresponder imputation; SDEAE=step-down emergent adverse event; * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$ vs. continued Bari 4-mg