initial improvement of 30% in FACIT-F total score was 16 weeks in pts receiving tofacitinib 5 mg BID; however, in pts receiving PBO, the median time for this event was not achieved up to W16. More pts receiving tofacitinib 5 mg BID vs PBO experienced initial improvement events up to W16 (Table 1). For example, 36.1% of pts receiving tofacitinib 5 mg BID experienced 50% improvement of fatigue up to W16, compared with 19.9% of pts receiving PBO.

Table 1. Proportions of pts who experienced initial improvement events in FACIT-F total score up to W16

Fatigue improvement threshold	Initial improvement, n (%)	p value[a]
25%		
Tofacitinib 5 mg BID	82 (61.7)	0.0009
PBO	58 (42.6)	
50%		
Tofacitinib 5 mg BID	48 (36.1)	0.0031
PBO	27 (19.9)	
75%		
Tofacitinib 5 mg BID	30 (22.6)	0.0626
PBO	19 (14.0)	
100%		
Tofacitinib 5 mg BID	23 (17.3)	0.1233
PBO	15 (11.0)	

N=133 (tofacitinib 5 mg BID); N=136 (PBO) [a]Test of equality over strata log-rank test, p<0.05 n, number of pts achieving an initial improvement event; N, total number of pts in each treatment group

Study	Population	Early vs established (years)	RR (early vs established)	RRR (95%IC)	NNTs (early vs established)
ASAS20					
Landewé 2014	axSpA	<5 vs ≥5	1.5 vs 1.5	0.96 (0.53-1.73)	5.5 vs 4.8
ASAS40					
Sieper 2012	nr-axSpA	<5 vs ≥5	8.2 vs 1.6	5.24 (1.12-24.41)	2.4 vs 9.1
Kay 2019	nr-axSpA	<5 vs ≥5	5.0 vs 3.3	1.52 (0.60-3.87)	2.1 vs 3.9
			3.6 vs 3.5	1.01 (0.46-2.20)	2.1 vs 2.9
ASDAS-MI					
Kay 2019	nr-axSpA	<5 vs ≥5	5.1 vs 6.5	0.78 (0.19-3.16)	2.7 vs 4.9
			7.1 vs 6.4	1.11 (0.34-3.66)	2.1 vs 3.0

Study	Population	Symptom duration		p value
		Responders	Non responders	
ASDAS-ID				
Sieper 2019	nr-axSpA	6.1±6.2	8.3±8.1	<0.001
ASAS-PR				
Sieper 2019	nr-axSpA	5.3±5.7	8.0±7.8	<0.001

Cell colours: In favor of early disease | In favor of establish disease | Non significant

Conclusion: In pts with AS, initial improvements in fatigue, as determined by FACIT-F total score, occurred faster and were larger in magnitude with tofacitinib vs PBO up to W16. These results may help physicians better understand the speed and magnitude for fatigue benefit in pts receiving tofacitinib.

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POS0306

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS REFRACTORY TO BIOLOGIC THERAPY: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIAL

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Background: Upadacitinib (UPA) was shown to be safe and effective through 2 years in patients (pts) with active ankylosing spondylitis (AS) naïve to biologic disease-modifying antirheumatic drugs (bDMARDs) in the pivotal phase 2/3 SELECT-AXIS 1 trial.[1,2]

Objectives: To assess the efficacy and safety of UPA in pts with active AS with an inadequate response (IR) to bDMARDs.

Methods: SELECT-AXIS 2 (NCT04169373) was conducted under a master protocol and includes two separate studies (one for AS bDMARD-IR and one for non-radiographic axial spondyloarthritis [nr-axSpA]). The AS bDMARD-IR study is a randomized, double-blind, placebo (PBO)-controlled, phase 3 trial that enrolled adults ≥18 years with AS who met modified New York criteria, had BASDAI and pt's assessment of total back pain scores ≥4 (numeric rating scale 0–10) at study entry, and had an IR to one or two bDMARDs (TNF inhibitor or IL-17 inhibitor). Pts were randomized 1:1 to receive oral UPA 15 mg once daily (QD) or PBO during the 14-week (wk) double-blind treatment period. The primary endpoint was ASAS40 response at wk 14. Multiplicity-controlled secondary endpoints evaluated at wk 14 were improvements from baseline in disease activity (ASDAS [CRP], ASDAS ID [<1.3], ASDAS LDA [<2.1], BASDAI50, ASAS20, and ASAS PR), pain (total and nocturnal back pain), function (BASFI), objective measure of inflammation (SPARCC MRI score of the spine), spinal mobility (BASMI), enthesitis (MASES), and quality of life (ASQoL and ASAS HI). Non-responder imputation incorporating multiple imputation (NRI-MI) was used to handle intercurrent events and missing data for binary endpoints. Cochran-Mantel-Haenszel (CMH) test and mixed-effect model for repeated measures (MMRM) were used for analyzing binary and continuous endpoints, respectively. Treatment-emergent adverse events (TEAEs) assessed through wk 14 are reported for pts who had ≥1 dose of study drug.

Results: All 420 randomized pts with active AS received assigned treatment (UPA 15 mg, n=211; PBO, n=209); 409 (97%) received study drug through wk 14. Baseline demographic and disease characteristics were generally similar between treatment groups and reflective of an active AS bDMARD-IR population (74% male; mean age 42.4 years; mean disease duration 7.7 years; 83% HLA-B27 positive; mean BASDAI 6.8). Significantly more pts achieved the primary endpoint of ASAS40 response at wk 14 with UPA vs PBO (45% vs 18%; $P<0.0001$; Figure 1); UPA showed onset of effect in ASAS40 as early as wk 4 (nominal $P\leq0.05$). All multiplicity-controlled secondary endpoints met statistical significance for UPA vs PBO at wk 14 across multiple clinical domains of AS ($P<0.0001$; Figure 1). The rate of TEAEs was similar between treatment groups through wk 14 (UPA, 41%; PBO, 37%). TEAEs led to discontinuation in 3 (1.4%) pts treated with PBO and none with UPA. Serious infections occurred with UPA (2.4%) but not with PBO and included 4 events of COVID-19 and 1 event of uveitis. Additional events of uveitis were reported in 3 (1.4%) pts treated with PBO. Inflammatory bowel disease (IBD) occurred in 1 (0.5%) pt on UPA and none on PBO. No malignancy, major adverse cardiovascular events, venous thromboembolic events, or death were reported with UPA; 1 event of malignancy was observed with PBO.

Conclusion: UPA 15 mg QD was significantly more effective than PBO over 14 wks of treatment in pts with active AS and IR to bDMARDs. No new safety risks were identified with UPA compared with its known safety profile.[3,4] These findings are consistent with and complementary to those of SELECT-AXIS 1 (bDMARD-naïve AS population),[1,2] and support the use of UPA in pts with active AS, including those who had a previous IR to bDMARD therapy.

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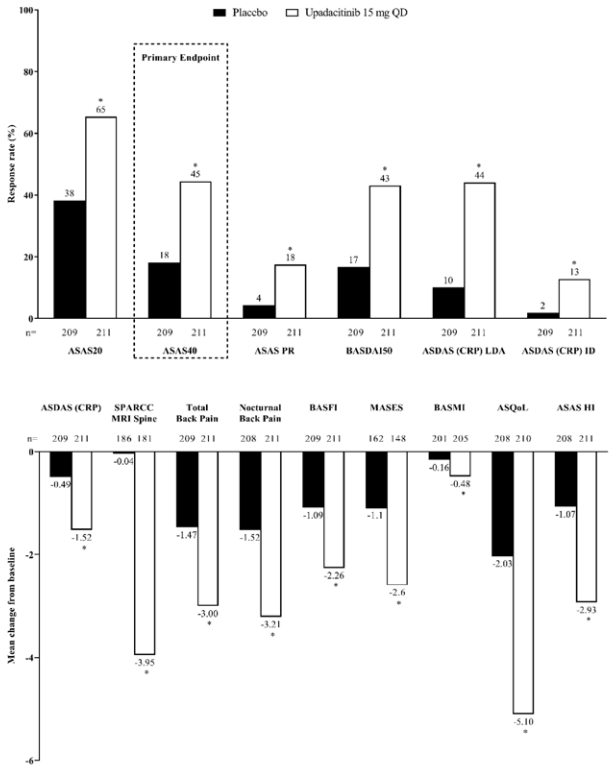

Figure. Analysis of Primary and Multiplicity-Controlled Secondary Endpoints at Wk 14

ASAS20=Assessment of SpondyloArthritis international Society 20 response; ASAS40=Assessment of SpondyloArthritis international Society 40 response; ASAS HI=Assessment of SpondyloArthritis international Society Health Index; ASAS PR=Assessment of SpondyloArthritis international Society partial remission; ASDAS (CRP)=Ankylosing Spondylitis Disease Activity Score C-reactive protein; ASDAS (CRP) ID=Ankylosing Spondylitis Disease Activity Score C-reactive protein inactive disease; ASDAS (CRP) LDA=Ankylosing Spondylitis Disease Activity Score C-reactive protein low disease activity; ASQoL=Ankylosing Spondylitis Quality of Life; BASDAI50=at least 50% improvement from baseline in Bath Ankylosing Spondylitis Disease Activity Index; BASFI=Bath Ankylosing Spondylitis Functional Index; BASMI=Bath Ankylosing Spondylitis Metrology Index; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score; QD=once daily; SPARCC=Spondyloarthritis Research Consortium of Canada.
*P<0.0001; Significant in multiplicity-adjusted analysis.
ASDAS LDA was defined as ASDAS (CRP) <2.1 and ASDAS ID as ASDAS (CRP) <1.3.
MASES was assessed in pts with baseline enthesitis.

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Clinical aspects in Psoriatic Arthritis

POS0307

IMPAIRED GLYCAEMIC CONTROL IS ASSOCIATED WITH INCREASED RISK OF PSORIATIC ARTHRITIS: MENDELIAN RANDOMISATION STUDY

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Background: Psoriatic arthritis (PsA) and psoriasis are both strongly associated with impaired glycaemic control and type 2 diabetes. The risk of developing type 2 diabetes is estimated to be ~40% higher in PsA compared to controls [1]. However, these observational findings are susceptible to bias from reverse causation: Insulin resistance and impaired glycaemic control are evident well over a decade before clinical onset of type 2 diabetes [2]. Therefore, whether impaired glycaemic control is a cause or consequence of PsA is unclear. Testing this hypothesis using traditional observational designs is challenging since longitudinal assessments of glycaemic control before PsA onset are often not available. Mendelian randomisation (MR) is an epidemiologic method that provides evidence about putative causal relationships between modifiable exposures and disease outcomes using genetic variants as instrumental variables. MR is less likely to be affected by confounding or reverse causation than conventional observational designs because genetic variants are randomly allocated at conception.
Objectives: To estimate the effect of genetically predicted glycaemic traits - glycated haemoglobin (HbA1c), 2-hour glucose after oral glucose challenge (2hG), fasting glucose (FG), and fasting insulin (FI) - on risk of PsA and psoriasis compared to controls using two-sample MR.
Methods: We selected 320 independent (r^2<0.001) genome-wide significant ($p<5x10^{-8}$) variants as instruments for HbA1c from a UK biobank genome-wide association study (GWAS) of 344,182 individuals, and 14 variants for 2hG, 67 for FG and 38 for FI from up to 200,622 individuals from a MAGIC consortium meta-analysis that adjusted for body mass index. Genetic associations for PsA were obtained from a GWAS comprising 3,609 cases (majority fulfilling CASPAR criteria) and 9,192 controls. Psoriasis data were obtained from 5,278 cases (96% European, defined using ICD and phecodes) and 650,391 controls from the UK biobank, FinnGen and BioBank Japan [3]. We used the inverse-variance weighted method to combine effect estimates from each variant using fixed-effect meta-analysis.
Results: Genetically predicted HbA1c increased risk of PsA (OR 1.18 per standard deviation (6.7 mmol/mol) increase in HbA1c; 95%CI 1.02, 1.36). 2hG (OR 1.55 per SD (0.6 mmol/L) increase; 95%CI 1.26, 1.89) and FG (OR 1.73 per SD (1.6 mmol/L) increase; 95%CI 1.35, 2.21) similarly increased PsA risk (Figure 1). FI was not associated with PsA risk. 2hG was the only glycaemic trait significantly associated with psoriasis (OR 1.21; 95%CI 1.04, 1.40).

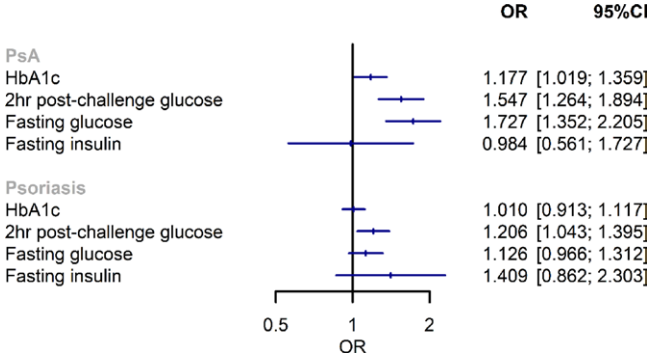

Figure 1. Mendelian randomisation estimates of the effect of glycaemic traits on risk of psoriatic arthritis and psoriasis.

Conclusion: This study provides supportive genetic evidence that impaired glycaemic control increases risk of PsA. By contrast, estimates were smaller when comparing psoriasis against controls with confidence intervals including the null. Improving glycaemic control may reduce PsA risk, although further studies are required to confirm these findings and to compare PsA directly against cutaneous only psoriasis.
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POS0308

EFFECT OF GUSELKUMAB ON SERUM BIOMARKERS IN PSORIATIC ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO TUMOR NECROSIS FACTOR INHIBITORS: RESULTS FROM THE COSMOS STUDY

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