Table 1

Dynamics of symptoms in TOFA treated pts with or without MRI-SI

Symptoms	MRT-SI (+)			MRT-SI (-)		
	(n=14)			(n=26)		
	Baseline	After 6 months	p	Baseline	After 6 months	p
Number of digits with dactylitis	2 [0; 4]	0 [0; 0]	0.008	0 [0; 2]	0 [0; 0]	0.003
ESR (mm/h)	47 [26; 76]	12 [6; 16]	0.006	20 [6; 37]	8 [6; 16]	0.001
WPAI (%)	80 [60; 84]	0 [0; 20]	0.007	20 [0; 60]	0 [0; 10]	0.128

After 6 months of TOFA therapy, no differences were found between groups of pts with and without MRI-SI in the number of digits with dactylitis ($p=0.47$), in ESR ($p=0.79$) and in WPAI ($p=0.93$).

Conclusion: In PsA pts significant association of active MRI-SI was found with dactylitis, high ESR level and WPAI. Use of TOFA in pts with both active MRI-SI and dactylitis demonstrated its high efficacy in reduction of SI inflammation and dactylitis; it also significantly improved pts' work productivity. These findings are important for personalized approach to treatment of PsA.

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SAT0420

EFFICACY OF NON-TUMOUR NECROSIS FACTOR BIOLOGICS AND TARGETED SYSTEMIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN THE TREATMENT OF PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Psoriatic arthritis (PsA) is a systemic, inflammatory condition presenting in approximately 30% of patients with psoriasis and associated with functional impairment and a reduced health-related quality of life. Current treatment guidelines recommend non-steroidal anti-inflammatory drugs, conventional Disease Modifying Anti-Rheumatic Drugs (cDMARDs) and Tumour Necrosis Factor α inhibitors (TNFi). Recent research has focused on alternative biologic medications which target interleukin (IL) 6, 12/23, 17A, 23 and T Cell co-stimulation, as well as targeted synthetic DMARDs (tsDMARDs) including Janus Kinase inhibitors (JAKi) and Phosphodiesterase 4 inhibitors (PDE4i). Evidence of the safety and efficacy, measured using the American College of Rheumatology-20 (ACR20), has been demonstrated leading to the inclusion of several biologics and tsDMARDs in guidelines. However, it can be argued that ACR50, indicating a 50% improvement in disease, is a more clinically relevant outcome measure.

Objectives: To conduct a systematic review and meta-analysis of the efficacy (ACR50 response) of non-TNFi biologics and tsDMARDs in the treatment of PsA. **Methods:** A systematic literature search of Embase, MedLine and Web of Science was undertaken to identify randomised controlled trials (RCTs) investigating efficacy and safety of non-TNFi biologics and tsDMARDs published in English from the inception of the databases to September 2019. The Cochrane Risk of Bias tool was used to assess methodological rigour of included trials. A meta-analysis was performed using a random effects model to estimate odds ratios of ACR 50 response vs placebo. A subgroup analysis was performed using patients with previous TNFi exposure.

Results: 21 RCTs were eligible with 6389 participants. Evaluation periods ranged from 12 to 24 weeks. JAKi, PDE4i, IL6i, IL12/23i, IL17Ai and IL23i treatments were more efficacious than placebo for ACR50 response ($p<0.001$) (Figure 1). Only tofacitinib (JAKi), secukinumab (IL17Ai) and ixekizumab (IL17Ai) were able to

demonstrate efficacy at the ACR50 level in participants with prior TNFi exposure ($p<0.0001$) (Figure 2). All treatments demonstrated an adequate safety profile.

Figure 1. Forest plot of achieving American College of Rheumatology-50 with treatment versus placebo M-H, Mantel-Haenzel; CI, confidence interval; JAKi, Janus Kinase inhibitor; PLA, placebo; df, degrees of freedom; IL6i, Interleukin 6 inhibitor; IL12/23i, Interleukin 12/23 inhibitor; IL17Ai, Interleukin 17A inhibitor; TNFi, Tumour necrosis factor inhibitor; IL23i, Interleukin 23 inhibitor

Figure 2. Forest plot of achieving American College of Rheumatology-50 with treatment versus placebo in tumour necrosis factor inhibitor-exposed subgroup M-H, Mantel-Haenzel; CI, confidence interval; JAKi, Janus Kinase inhibitor; PLA, placebo; df, degrees of freedom; PDE4i, Phosphodiesterase 4 inhibitor; IL6i, Interleukin 6 inhibitor; IL12/23i, Interleukin 12/23 inhibitor; IL17Ai, Interleukin 17A inhibitor; IL23i, Interleukin 23 inhibitor

Conclusion: Non TNFi biologics and tsDMARDs are able to demonstrate 50% improvement with adequate safety profiles. These therapies are often used in patients who are inadequate responders to TNFi but there is less robust data in this specific patient group. Studies with clinically relevant primary endpoints should be considered in this patient population.

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SAT0421

GUSELKUMAB DEMONSTRATED AN INDEPENDENT TREATMENT EFFECT ON FATIGUE AFTER ADJUSTMENT FOR CLINICAL RESPONSE (ACR20) IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM PHASE-3 TRIALS DISCOVER 1 & 2

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Background: DISCOVER 1 and 2 are phase-3 trials of guselkumab (GUS, a monoclonal antibody that specifically binds the p19-subunit of IL-23) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (ACR20) as well as in other measures of arthritis and psoriasis at week (W) 24.^{1,2}

Objectives: To evaluate the effect of GUS on fatigue in DISC 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.³

Methods: DISC 1 & 2 enrolled patients with active PsA, despite nonbiologic DMARDs and/or NSAIDs, who were mostly biologic naïve except for ~30% of patients in DISC 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100mg at W0 and W4 then every (q) 8W, to GUS 100mg q4W, or to matching PBO. Concomitant treatment with select non-biologic DMARDs, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO instrument assessing fatigue and its impact on daily activities and function over the past seven days, with a total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is identified as clinically meaningful.³ Change from baseline in FACIT-Fatigue was analyzed using MMRM (Figure). Independence of treatment effect on FACIT-Fatigue from effect on ACR20 was assessed using Mediation Analysis⁴ (Table) to estimate the natural direct effect (NDE) and natural indirect effect (NIE) mediated by ACR20 response.

Results: At baseline in DISC 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating moderate to severe fatigue. In

Figure. Week-24 Changes from Baseline in FACIT-Fatigue in the DISCOVER 1 and 2 Trials of Guselkumab in Patients with Psoriatic Arthritis

*P vs. PBO ≤0.013, **P vs. PBO <0.001

FACIT=Functional Assessment of Chronic Illness Therapy, GUS=guselkumab, PBO=placebo, Wk=Week
 Analysis of changes from baseline in FACIT-Fatigue scores used Mixed-Effect Model Related Measures (MMRM), with factors including treatment group, baseline use of non-biologic DMARDs, CRP status (>2.0 or ≤2.0 mg/dL), and for DISCOVER 1 only, prior use of TNF inhibitors.

Table. Mediation Analysis of the Effect of ACR 20 Response on Change from Baseline in FACIT-Fatigue Score at Week 24

Effect		GUS 100 mg q8W vs. PBO	GUS 100 mg q4W vs. PBO
		Estimate (95% CI)	Estimate (95% CI)
DISCOVER 1	NDE	0.36 (-1.7, 2.4)	2.60 (0.6, 4.5)*
	NIE	2.75 (1.4, 4.3)*	1.20 (0.3, 2.3)*
	Total Effect	3.12 (1.0, 5.2)*	3.79 (1.9, 5.4)*
	Proportion Independent	11.7%	68.5%
	Proportion Mediated	88.3%	31.5%
DISCOVER 2	NDE	1.44 (-0.1, 3.0)	2.49 (1.0, 4.1)*
	NIE	2.53 (1.6, 3.6)*	1.09 (0.4, 1.9)*
	Total Effect	3.97 (2.4, 5.5)*	3.58 (2.1, 5.0)*
	Proportion Independent	36.3%	69.7%
	Proportion Mediated	63.7%	30.3%

*P vs placebo<0.02

NDE=Natural Direct Effect (effect on FACIT-F beyond effect on ACR20), NIE=Natural Indirect Effect (effect on FACIT-F mediated by ACR20)

Mediation analysis⁴ used linear and logistics regression models with Bootstrapping method

both DISCOVER 1 & 2 trials, treatment with GUS led to improvements in FACIT-Fatigue scores compared with PBO as early as W8 (Figure). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue (P≤0.003). Mediation analysis revealed that the independent treatment effects on fatigue after adjustment for ACR20 response (Natural Direct Effect [NDE], Table) were 12-36% in the q8W GUS dosing group and 69%-70% in the q4W GUS group.

Conclusion: In 2 phase-3 trials, treatment with GUS of patients with active PsA led to significant improvements compared to PBO in fatigue, including substantial effects on FACIT-Fatigue that were independent of the effects on ACR 20, especially for the q4W dosing group.

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SAT0422

FIRST-LINE CSDMARD MONOTHERAPY RETENTION IN PSORIATIC ARTHRITIS: METHOTREXATE OUTPERFORMS SULFASALAZINE

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Background: Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) are the first-line treatment for psoriatic arthritis (PsA), but there is conflicting data regarding their efficacy and scarce reports describing the duration of use (drug retention) of csDMARD in this population. Their position in treatment recommendations is a matter of growing debate due the availability of alternative treatment options with higher levels of evidence.