Figure 2. (A) Proportion of Patients Reporting Improvements $\geq$ MCID and (B) Scores $\geq$ Age- And Gender-Matched Normative Values at Week 12

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AB0836 PREVALENCE AND DETERMINANTS OF FATIGUE IN PSORIATIC ARTHRITIS IN AN ASIAN POPULATION

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Background: Fatigue is one of the core domains to be measured in all clinical trials for psoriatic arthritis (PsA). Studies of fatigue in PsA in Asia are scarce.

Objectives: To describe the prevalence and evaluate the factors associated with fatigue in PsA patients within a multi-ethnic Asian population.

Methods: We used data from the PRESPOND registry for PsA patients attending an outpatient clinic of a tertiary institution in Singapore. Demographics data and disease characteristics were evaluated. Fatigue was assessed by question 1 of BASDAI (BASDAI-F) and the vitality domain of SF-36 (SF-36 VT).

Results: 131 patients (50.4% men, 63.4% Chinese, median PsA duration 1.78 years) with completed data for fatigue were included. The median (IQR) tender and swollen joint count was 2 (5) and 1 (3) respectively. 45 patients (34%) experienced high fatigue (defined by BASDAI-F $\geq 6/10^{1,2}$). 5 clusters of factors were identified using principal component analysis that explained 66.2% of the variance of all factors, which mapped to disease activity, disease chronicity, demographics (ethnicity and gender), and BMI (Figure 1). Of these, disease activity and chronicity were significantly associated with BASDAI-F and SF-36 VT. In a multivariate analysis, back pain, peripheral joint pain and patient global assessment were associated with BASDAI-F, whereas peripheral joint pain, HAQ-DI, age and BMI were associated with SF-36 VT (Table 1).

Table 1. Multivariable analysis for variables associated with fatigue

	BASDAI-F				SF-36 VT			
	b	95% CI	β	p	b	95% CI	β	p
Back pain (0-10)	0.335	(0.180, 0.490)	0.356	<0.001	-	-	-	-
Peripheral joint pain (0-10)	0.027	(0.012, 0.042)	0.268	0.001	-2.296	(-3.410, -1.182)	-0.320	<0.001
PGA (0-100)	0.211	(0.061, 0.361)	0.236	0.006	-	-	-	-
HAQ-DI (0-3)	-	-	-	-	-12.74	(-17.97, -7.51)	-0.386	<0.001
Age, y	-	-	-	-	0.260	(0.065, 0.456)	0.179	0.009
BMI, kg/m ²	-	-	-	-	-0.644	(-1.183, -0.105)	-0.165	0.020

Figure 1. Principal component analysis with 5 components and residuals (in dotted lines). Only factor loadings with magnitudes greater than 0.40 are shown.

Conclusion: PsA-associated fatigue is prevalent in this Asian PsA cohort and is associated with disease activity and chronicity.

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AB0837 ITCH AS THE MAJOR MEDIATOR OF THE EFFECT OF TOFACITINIB ON HEALTH-RELATED QUALITY OF LIFE IN PSA: A MEDIATION ANALYSIS

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Background: PsA is a chronic, systemic inflammatory disease with signs and symptoms across multiple domains, including cutaneous manifestations, which can impact health-related quality of life (HQoL). Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. In two Phase 3 randomised studies, patients (pts) with active PsA treated with tofacitinib experienced greater improvements in various dermatologic endpoints, compared with placebo. As pruritus is a bothersome symptom of skin disease in pts with PsA, we sought to determine how tofacitinib affects HQoL via clinical improvements in skin symptoms including itch.

Objectives: To determine the relationships between tofacitinib treatment, dermatologic symptoms and pt-reported HQoL related to skin disease in PsA.

Methods: Analyses used data (mean scores from Months 1 and 3) from two Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) of pts with active PsA treated with tofacitinib 5mg twice daily or placebo; pts

were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response (IR) to ≥ 1 TNFi. All pts were treated continuously with a single conventional synthetic DMARD. Mediation modelling, a statistical method used to assess mechanisms underlying observed relationships between different variables via other explanatory variables (mediators), was applied. The mediation model included: treatment, as the independent (explanatory) binary variable (tofacitinib 5 mg BID vs placebo); HQoL, measured by Dermatology Life Quality Index (DLQI), as the dependent (outcome) variable; and two mediators, pt-reported Itch Severity Index (ISI) and Physician's Global Assessment of Psoriasis (PGA-PsO) (a latent variable represented by erythema, induration and scaling). The initial model designated the treatment effect on DLQI mediated via ISI and PGA-PsO as an indirect effect, and treatment effects not attributable to ISI or PGA-PsO as a direct effect (Figure 1).

Results: Data were collected from 468 pts, pooled from both studies. In the initial model (pooled data), the effect of tofacitinib treatment on DLQI was largely mediated by itch (measured by ISI) and PGA-PsO (indirect effect) ($p < 0.0001$); the effect of treatment attributable to factors other than ISI and PGA-PsO (direct effect) was not statistically significant ($p = 0.66$). Results were consistent for pooled and individual study data. Because the direct effect was small and not statistically significant, the model was re-specified to exclude the direct effect of tofacitinib treatment on DLQI. In the revised model (pooled data), 17.7% of the indirect effect was attributable to PGA-PsO ($p = 0.0006$) and 82.3% was attributable to itch (assessed by ISI) ($p < 0.0001$) (Figure 2). Analyses of individual studies using the revised model gave results generally consistent with pooled data.

Conclusion: Dermatology-focused mediation modelling showed that a majority of the effect (~80%) of tofacitinib treatment on DLQI is mediated by improvements in itch, with ~20% mediated via improvements in PGA-PsO.

Figure 1. Initial mediation model

Figure 2. Revised mediation model

Treatment is represented by a binary variable (tofacitinib 5 mg BID vs. placebo). DLQI, Dermatology Quality of Life Index; ISI, Itch Severity Index; PGA-PsO, Physician's Global Assessment of Psoriasis.

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AB0838

IDENTIFYING MEDIATORS OF PAIN REDUCTION IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH TOFACITINIB: ROLE OF INFLAMMATION ASSOCIATED WITH PERIPHERAL ARTHRITIS, ENTHESITIS AND SKIN DISEASE

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Background: Treatment effect on pain is a priority for patients (pts) with psoriatic arthritis (PsA) and physicians. As pain is multidimensional, there is growing interest to understand the mechanisms of pain relief during treatment. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. Previous analyses showed that the effect of tofacitinib on pain in pts with PsA was partially mediated through improvement of inflammation as assessed by C-reactive protein (CRP) and Swollen Joint Count (SJC). Additional potential inflammation-associated mediators that might contribute to tofacitinib's effect on pain include enthesitis and skin disease.

Objectives: To describe the interrelationship between pain, tofacitinib treatment and potential inflammatory-associated outcomes, using mediation modelling.

Methods: Data from two Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) of pts with active PsA treated with tofacitinib 5 mg twice daily (BID) or placebo were used; pts were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response to ≥ 1 TNFi. All pts were treated continuously with a single conventional synthetic DMARD. Analyses were completed using pooled and individual study data at Months 1 and 3 (using mean scores across visits). Mediation modelling seeks to explain mechanisms underlying observed relationships between independent and dependent variables via other variables (mediators). This initial model included: treatment as the independent (explanatory) binary variable (tofacitinib 5 mg BID vs placebo); pain, measured by Patient's Assessment of Arthritis Pain (VAS, 0–100 mm), as the dependent (outcome) variable; mediators were: pt-reported Itch Severity Index (ISI); CRP; SJC; Psoriasis Area and Severity Index (PASI); and enthesitis, measured by Leeds Enthesitis Index (LEI) or Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). The final model was revised based on results of the initial model.

Results: The initial model (N=329; pooled data) showed that tofacitinib treatment affects pain mainly indirectly via ISI, CRP, SJC, PASI and enthesitis (LEI), with 16.0% ($p = 0.53$) attributable to the direct effect. The indirect effect via SJC ($< 1\%$) was not significant ($p = 0.99$); the indirect effect via PASI was contradictory (-14.4% , $p = 0.10$). The final model (Figure 1) excluded SJC and PASI. Analysis of the final model (N=468; pooled data) revealed that 29.5% ($p = 0.0579$) of tofacitinib treatment effect on pain was attributable to the direct effect, and 70.5% ($p < 0.0001$) was attributable to the indirect effect. ISI, LEI and CRP mediated 37.4% ($p = 0.0002$), 17.8% ($p = 0.0157$) and 15.3% ($p = 0.0107$) of the tofacitinib treatment effect on pain, respectively. Results for individual studies were consistent with pooled data, as were those when enthesitis was represented by SPARCC in the model.

Conclusion: The majority of tofacitinib treatment effect on pain in pts with PsA is collectively mediated by itch, enthesitis and CRP, with itch being the main mediator of treatment effect (~37%), using mediation modelling analyses.