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.

Figure 1. Final mediation model

Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo); pain was measured by Patient's Assessment of Arthritis Pain (VAS, 0–100 mm); inflammation was measured by CRP.

BID, twice daily; CRP, C-reactive protein; ISI, Itch Severity Index; LEI, Lead Enthesitis Index; VAS, Visual Analogue Scale

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AB0839

RELIABILITY OF COMPOSITE MEASURES FOR THE ASSESSMENT OF PSORIATIC ARTHRITIS

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Background: Composite measures of disease activity have been developed for use in Psoriatic Arthritis (PsA) to capture the wide spectrum of disease but there is a lack of consensus regarding which to adopt for routine practice. It is recognised that more data is required to understand the measurement properties of existing instruments and consider the impact of modifications that may improve face validity, responsiveness or feasibility. It is important to have an estimate of a measurement instrument's reliability in the setting of stable disease in order to understand measurement error and responsiveness. To our knowledge no data exists on the stability of composite measures in PsA.

Objectives: To measure test re-test reliability of composite measures of disease activity in PsA.

Methods: Clinical and patient reported outcomes to enable the calculation of composite measures were administered to 141 patients with PsA at five time points in a UK multicentre observational study. All patients fulfilled the CASPAR criteria. Twenty-nine patients with clinically stable disease and receiving no treatment intervention underwent repeat assessment by the same examiner within 2 weeks. Patients in high and low disease were included. Reliability was evaluated by intra-class correlation coefficient (ICC) and Bland Altman plots.

Results: Of the 29 patients included 15 were male, the mean age was 52.4 years (SD 13.39), mean disease duration at T₀ was 9.2yrs (SD 8.11). The mean swollen joint count was 3.4 (SD 5.1), tender joint count 11.3 (SD 15.03) and PASI 1.0 (SD1.04). The ICC (95% CI) for tender and swollen joint counts were 0.94 (0.87-0.97) and 0.91 (0.80-0.96) respectively. The ICC for PASI was 0.95 (0.90-0.98). All composite measures demonstrated high levels of test-retest reliability with ICC >0.85, table. The most reliable measure was the PADAS ICC 0.98 (95% CI 0.954-0.991). The individual ICC for each composite measures are reported in the table and Bland Altman plots, figure.

Conclusion: All composite measures show high levels of test-retest reliability in this cohort. The PASDAS was the most stable measure. Modifications to these instruments can now be tested and the impact compared to the original versions.

Table. Test Re-Test reliability of each composite measure

Intraclass Correlation Coefficient (95% Confidence Interval)	
GRACE	0.929 (0.842-0.968) *
CPDAI	0.852 (0.635-0.940) *
PASDAS	0.978 (0.954-0.991) *
DAPSA	0.922 (0.831-0.964) *
3VAS	0.915 (0.815-0.960) *
RAPID3	0.899 (0.782-0.953) *

Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS), Composite Psoriatic Disease Activity Index (CPDAI), GRAppa Composite Exercise (GRACE), 3 Visual Analogue Scale (3VAS), Routine Assessment of Patient Index (RAPID3), *P<0.001

Figure. Bland Altman plots for each composite measure

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