with tofacitinib 5 mg twice daily (BID) or placebo; pts were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response (IR) to ≥ 1 TNFi. All pts continued on a stable dose of a single conventional synthetic DMARD. Analyses used pooled and individual trial data (mean scores from Months 1, 2 and 3). Mediation modelling seeks to explain mechanisms underlying an observed relationship between independent and dependent variables via other explanatory variables (mediators). In this model, pain (100 mm visual analogue scale) was the designated dependent variable, treatment (tofacitinib 5 mg BID vs placebo) the independent variable and inflammation, measured by swollen joint count (SJC) and C-reactive protein (CRP), was a mediator. The primary model designated treatment effect on pain mediated via CRP/SJC as an indirect effect and treatment effect not attributable to CRP/SJC as a direct effect. Models were re-specified based on initial results; model invariance by population (TNFi-naïve vs TNFi-IR pts) was assessed.

Results: In the pooled analysis (N=469), 25.9% ($p<0.01$) of the tofacitinib treatment effect on pain was mediated by CRP/SJC (indirect effect), of which changes via CRP and SJC were 17.8% ($p<0.01$) and 8.1% ($p>0.05$), respectively. The treatment effect on pain not attributable to CRP/SJC (direct effect) was 74.1% ($p<0.0001$). In TNFi-naïve and TNFi-IR pts, indirect effects via SJC were not statistically significant. In the re-specified model with CRP as sole mediator, the indirect effect was 21.3% for pooled data ($p<0.01$; Figure A) and 36.1% ($p<0.05$) and 16.7% ($p<0.05$) for TNFi-naïve and TNFi-IR pts, respectively (Figures B, C); the 19.4% difference between TNFi-naïve vs TNFi-IR pts was not statistically significant.

Conclusion: While inflammation, as assessed by CRP/SJC, was a significant mediator of the overall treatment effect on pain in tofacitinib-treated pts with PsA, the majority of the treatment effect was not attributable to CRP/SJC changes. When mediators were assessed individually, only CRP was a significant mediator in the pooled analysis. In the re-specified model, CRP-mediated effects differed in TNFi-naïve vs TNFi-IR pts, but this was not statistically significant. These results suggest that CRP/SJC-associated inflammation only partially explains pain in PsA; other potential mediators need to be identified to better understand the treatment effect of tofacitinib on pain.

Figure. Mediation effects: A. Overall treatment effects on pain, and indirect effect of CRP; B. Indirect effects of CRP in OPAL Broaden; C. Indirect effects of CRP in OPAL Beyond

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ENTHESITIS, DACTYLITIS, AND AXIAL DISEASE IN PSORIATIC ARTHRITIS (PSA): IMPACT ON PATIENT QUALITY OF LIFE AND WORK PRODUCTIVITY

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Background: PsA is a chronic, inflammatory disease characterised by peripheral arthritis, axial disease, enthesitis, dactylitis and skin and nail psoriasis. The impact of skin and joint components of the disease on quality of life and work productivity has been studied (1,2) but the impact of other manifestations has not.

Objectives: To assess the impact of enthesitis, dactylitis, and axial disease on quality of life and work productivity in PsA patients.

Methods: Cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Physicians recorded (Yes/No) if patients currently presented with enthesitis, dactylitis, inflammatory back pain (IBP), and sacroiliitis (identified by x-ray or MRI). Multiple linear regression analyses were used to examine the impact of these manifestations on patient reported outcomes (PROs) including EQ-5D index, EQ-5D VAS, HAQ-DI, PsAID12, and WPAI. Models were adjusted for age, gender, number of joints affected, and time since diagnosis. There was no imputation of missing data.

Results: The sample included 1103 patients: mean age 47.6 [SD 13.2] years, 46% were female, 58% were working full time. Mean number of joints affected by PsA was 3.8 (SD 5.2), and 54.9% were receiving biologic treatment. Enthesitis (present in 6.3% of patients), dactylitis (8.0%) and IBP (12.6%) were associated with worse outcomes overall (Table 1); sacroiliitis (3.9%) was linked to worse physical function and quality of life.

Conclusion: In a multi-national, real-world PsA population, enthesitis, dactylitis, IBP, and sacroiliitis were significantly associated with worse patient quality of life and/or work productivity across a range of PROs independent of the number of joints affected. These manifestations should be considered alongside skin and joint components in order to optimize patient outcomes.

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Table 1. Impact of manifestations on PROs: Adjusted* regression coefficient and p-values

Outcome measure (N patients with data available)	Manifestation	Coef.	P value
EQ-5D Index (N=771)	Enthesitis	-0.12	0.002
	Dactylitis	-0.07	0.010
	IBP	-0.07	0.001
	Sacroiliitis	-0.06	0.259
EQ-5D VAS (N=784)	Enthesitis	-8.86	0.013
	Dactylitis	-4.31	0.123
	IBP	-4.10	0.073
	Sacroiliitis	-10.19	0.043
HAQ DI (N=744)	Enthesitis	0.17	0.096
	Dactylitis	0.17	0.024
	IBP	0.20	0.003
	Sacroiliitis	0.30	0.035
PsAID12 (N=750)	Enthesitis	1.32	0.002
	Dactylitis	1.09	0.003
	IBP	0.47	0.060
	Sacroiliitis	0.59	0.243
WPAI: Productivity (N=485)	Enthesitis	14.40	0.034
	Dactylitis	4.36	0.128
	IBP	4.07	0.185
	Sacroiliitis	-3.86	0.332

*Adjusted for age, gender, number of joints affected, time since diagnosis.

FRI0464 **EFFECT OF BIOLOGICS ON ENTHESITIS AND DACTYLITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: Enthesitis and dactylitis are hallmarks for patients with psoriatic arthritis and mechanical injury are common risk factor for enthesitis and dactylitis [1-4]. Biologic disease modifying anti-rheumatic drugs (bDMARDs), including tumor necrosis factor alpha (TNF- α), interleukin (IL), phosphodiesterase type 4(PDE-4), Janus kinase (JAK) blockers and abatacept have shown efficacy on enthesitis and dactylitis in patients with PsA.

Objectives: The aims of this study are to summarize the efficacy of the bDMARDs on enthesitis and dactylitis in patients with PsA.

Methods: Systematically review of articles published up to Jan 2019 in Medline and Web of Science, and abstracts from the two last European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) meetings. Primary endpoint was the proportion of patients with resolution of enthesitis or dactylitis from week 12 to 24. Secondary

endpoint was the mean change in different enthesitis score (Leeds Enthesitis Index [LEI, 0-6], Maastricht Ankylosing Spondylitis Enthesitis Score [MASES, 0-13], PsA modified MASES [0-15]) and dactylitis score (Leeds Dactylitis Index [LDI, 0-60], dactylitis severity score [DSS, 0-60], [DSS, 0-20]) from week 12 to 24. Odds ratio (OR) and standardized mean difference (SMD) with 95% CIs across studies were synthesized.

Results: Nineteen studies (8,208 patients), 10 drugs (adalimumab, infliximab, certolizumab pegol, golimumab, secukinumab, ustekinumab, ixekizumab, abatacept, tofacitinib and apremilast) and 22 treatments were evaluated. Patients treated with bDMARDs were more likely to achieve resolution of enthesitis compared with placebo (OR for pooled: 1.99, 95% CI:1.74, 2.27; OR for IL blocker: 2.06, 95%CI:1.78, 2.38; OR for abatacept:1.82, 95%CI:1.05,3.14; OR for PDE4 blocker:1.67, 95%CI:1.14, 2.45) (Figure 1) and have significant improvement in terms of LEI (SMD for pooled: -2.17, 95%CI: -2.87, -1.46; SMD for tofacitinib: -3.83, 95%CI: -5.24, -2.43; SMD for TNF blocker: -1.43, 95%CI: -2.38, -0.48; SMD for ixekizumab: -1.47, 95%CI: -2.42, -0.52; Figure 2A), MASES (SMD for apremilast: -1.50, 95%CI: -2.80, -0.21; Figure 2B), PsA modified MASES (SMD for golimumab: -0.32, 95%CI: -0.52, -0.12; Figure 2C) compared with placebo. Patients treated with bDMARDs were more likely to achieve resolution of dactylitis compared with placebo (OR for pooled: 3.26, 95% CI:2.45, 4.33; OR for IL blocker: 3.88, 95%CI:2.97, 5.06; OR for abatacept:1.54, 95%CI:0.71, 3.34; OR for PDE4 blocker:1.50, 95%CI:0.97, 2.33) (Figure 3) and have significant improvement in terms of LDI (SMD for pool: -1.73, 95%CI: -3.07, -0.40; SMD for TNF blocker: -1.67, 95%CI: -3.72, 0.38; SMD for ixekizumab: -1.67, 95%CI: -3.69, 0.12; Figure 4A), DSS [0-60] (SMD for pool: -2.10, 95%CI: -3.11, -1.10; SMD for tofacitinib: -3.39, 95%CI: -4.95, -1.83; SMD for TNF blocker: -0.84, 95%CI: -1.48, -0.20; Figure 4B), DSS [0-20] (SMD for apremilast: -1.20, 95%CI: -2.07, -0.34; Figure 4C) compared with placebo.

Conclusion: Biologic DMARDs was effective for PsA patients with enthesitis and dactylitis. IL blocker is probably the optimal option to consider when patients present with predominant enthesitis and dactylitis

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Figure 1. Risk estimates of resolution of enthesitis