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Table 1. Demographics, Treatment Profiles, Disease Activity, Quality of Life, and Work Productivity at Enrollment for Patients With Multidomain vs Single-Domain PsA Disease Presentations

Characteristic*	Multidomain (N = 1698)	Single Domain† (N = 617)	P Value‡
Age, years	53.5 (13.2) [1678]	54.5 (12.9) [607]	0.20
Female, n/m (%)	907/1689 (53.7)	314/610 (51.5)	0.35
Race, n (%)	n = 1655	n = 596	0.04
White	1548 (93.5)	572 (96.0)	
Black	9 (0.5)	4 (0.7)	
Other	98 (5.9)	20 (3.4)	
BMI, kg/m ²	32.0 (7.4) [1658]	31.3 (7.6) [600]	< 0.01
Symptom duration, years	11.3 (10.7) [1651]	11.0 (9.7) [594]	0.51
Disease duration, years	7.7 (8.8) [1662]	8.5 (8.1) [598]	< 0.01
Select comorbidities, n (%)			
Psoriasis	1537 (90.5)	520 (84.3)	< 0.01
Nail psoriasis	602 (35.5)	81 (13.1)	< 0.01
Depression	280 (16.5)	57 (9.2)	< 0.01
Fibromyalgia	114 (6.7)	23 (3.7)	< 0.01
Anxiety	65 (3.8)	12 (1.9)	0.03
History of biologic use, n (%)	561 (33.0)	151 (24.5)	< 0.01
History of csDMARD use, n (%)	478 (28.2)	151 (24.5)	0.08
History of prednisone use, n (%)	230 (13.5)	83 (13.5)	0.95
Current biologic use, n (%)	980 (57.7)	378 (61.3)	0.13
Current csDMARD use, n (%)	859 (50.6)	339 (54.9)	0.06
Current prednisone use, n (%)	122 (7.2)	42 (6.8)	0.75
Physician global assessment (VAS 0-100)	24.3 (21.4) [1686]	10.9 (15.0) [612]	< 0.01
Physician global assessment of psoriasis (VAS 0-100)	28.0 (22.6) [1661]	12.9 (15.0) [594]	< 0.01
Patient pain (VAS 0-100)	44.8 (29.2) [1590]	28.6 (26.9) [580]	< 0.01
Patient-reported fatigue (VAS 0-100)	45.9 (29.2) [1676]	33.8 (28.4) [602]	< 0.01
Patient global assessment (VAS 0-100)	43.1 (28.4) [1669]	36.8 (31.5) [605]	< 0.01
HAQ-DI (0-3)	0.8 (0.7) [1600]	0.5 (0.6) [586]	< 0.01
EQ-5D (0-1)	0.7 (0.2) [1592]	0.8 (0.2) [579]	< 0.01
EQ VAS (0-100)	67.4 (29.1) [1667]	75.5 (19.8) [606]	< 0.01
WPAI domains			
Current employment, n/m (%)	987/1646 (60.0)	381/595 (64.0)	0.08
% Work time missed	6.2 (17.5) [842]	2.7 (11.3) [323]	< 0.01
% Impairment while working	22.9 (24.4) [887]	12.4 (18.9) [344]	< 0.01
% Overall work impairment	26.2 (26.8) [798]	13.0 (19.5) [306]	< 0.01
% Activity impairment	34.7 (29.9) [1530]	19.1 (24.3) [549]	< 0.01

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol-5 Dimensions; EQ VAS, EuroQol visual analogue scale; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis; WPAI, Work Productivity and Activity Impairment questionnaire; VAS, visual analogue scale.

* All values were calculated based on available data and are presented as "mean (SD) [n]" unless otherwise stated.

† Single-domain disease presentations for PsA overall (N = 617) included skin disease (53.8%), peripheral arthritis (29.0%), nail psoriasis (10.9%), axial disease (3.4%), enthesitis (1.8%), and dactylitis (1.1%).

‡ Test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher's exact test for categorical variables.

Table 2. Multidomain vs Single-Domain Impact on Outcomes—Multivariable Regression Coefficients Estimating the Association of Presence of Multidomain Presentations With Selected PsA Disease Activity, Quality of Life, and Work Productivity and Activity Measures Relative to Single-Domain Presentations in Patients With PsA

Outcomes*	β Coefficient (95% CI)	P Value
Physician global assessment	12.16 (10.30, 14.01)	< 0.001
Physician global assessment of psoriasis	14.03 (12.03, 16.04)	< 0.001
Patient pain	14.02 (11.26, 16.78)	< 0.001
Patient-reported fatigue	10.09 (7.38, 12.81)	< 0.001
Patient global assessment	5.65 (2.81, 8.49)	< 0.001
HAQ-DI	0.26 (0.20, 0.32)	< 0.001
EQ-5D	-0.07 (-0.09, -0.06)	< 0.001
% Work time missed	2.71 (0.57, 4.84)	0.013
% Impairment while working	8.63 (5.72, 11.55)	< 0.001
% Overall work impairment	11.02 (7.69, 14.36)	< 0.001
% Activity impairment	13.47 (10.65, 16.29)	< 0.001

BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; EQ-5D, EuroQol-5 Dimensions; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis.

* Single-domain disease is the reference group. Adjusted for age, sex, race, BMI, disease duration, and current and prior biologic, csDMARD, and prednisone use.

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FRI0461

GENETIC ANALYSIS OF THE NF-KB PATHWAY CAN BE USEFUL TO DISTINGUISH PATIENTS AT RISK OF PSORIATIC ARTHRITIS WITHIN THE SPECTRUM OF PSORIATIC DISEASE

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Background: Psoriasis and psoriatic arthritis (PsA) are the main manifestations of what is now known as psoriatic disease. Both entities share common genetic pathways, but they also differ. The NF-Kb pathway has been implicated in the genesis of psoriatic disease, but the differential contribution of this genetic pathway to the risk of psoriasis and PsA is not fully understood¹.

Objectives: Our aim was to study the association of common polymorphisms at genes of the NF-Kb pathway in patients with psoriatic disease.

Methods: The study involved a total of 690 psoriatic disease patients (187 of them with PsA) and 550 controls. We genotyped three common polymorphisms in *NFKB1* (rs230526), *NFKBIA* (rs7152376) and *NFKBIZ* (rs3217713 indel) and compared allele and genotype frequencies between cases and controls.

Results: The rare *NFKBIA* rs7152376 C was significantly more frequent in the PsA group vs. controls (0.42 vs. 0.36; p=0.04, OR=1.29, 95% CI=1.02-1.63). Compared to skin psoriasis, PsA patients showed a significantly higher frequency of the rs7152376 C (0.42 vs. 0.31; p<0.001). In reference to the genotypes, carriers of rs7152376 C (CC+CT) were non-significantly more frequent in PsA compared to controls (0.66 vs. 0.58; p=0.06). However, the frequency of these carriers was significantly higher in PsA vs. skin psoriasis (p=0.004). Thus, our data showed significant association between the rare *NFKBIA* rs7152376 C allele and PsA, and a trend toward the opposite effect for skin psoriasis. Neither *NFKB1* rs230526 or *NFKBIZ* rs3217713 indel were associated with the risk of developing psoriasis or PsA.

Conclusion: We found a significant association between *NFKBIA* variants and PsA. Our study shows that alterations in the same genetic pathway may have differential effects on different manifestations of psoriatic disease. Additional studies from larger cohorts and different populations are necessary to validate these results.

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FRI0462

UNDERSTANDING MEDIATORS OF PAIN REDUCTION IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH TOFACITINIB: ROLE OF INFLAMMATION

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Background: Pain is a priority for patients (pts) with psoriatic arthritis (PsA) and physicians. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. As pain is a multidimensional phenomenon, there is growing interest in understanding mechanisms of pain relief during treatment.

Objectives: To examine the potential role of inflammation in the effect of tofacitinib on pain in pts with PsA, using mediation modelling.

Methods: Data were from the Phase 3 OPAL Broaden (NCT01877668) and OPAL Beyond (NCT01882439) studies of pts with active PsA treated

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, dactylitis, enthesitis 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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