# Limited association between scalp psoriasis and psoriatic arthritis severity and treatment response

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*Received on December 8, 2015; accepted in revised form on May 16, 2016.*



**Key words:** psoriasis, scalp, psoriatic arthritis, anti-TNF, etanercept

*Trial registration PRESTA: ClinicalTrials.gov NCT00245960.*

*Funding: this study was funded by Pfizer. Medical writing support was provided by Jennica Lewis of Engage Scientific Solutions and was funded by Pfizer.*

*Competing interests: K. de Vlam has been a consultant for Abbott, Celgene, Janssen, Pfizer, and UCB, and has been on the speaker's bureau for Abbott, Celgene, Janssen, Pfizer, and UCB.*
*L. Mallbris was an employee of Pfizer at the time the work was done.*
*A. Szumski is an employee of inVentiv Health and was contracted by Pfizer to provide statistical support for the development of this paper.*
*H. Jones is an employee of Pfizer.*

## ABSTRACT

**Objective.** *We evaluated whether scalp psoriasis (PsO) is associated with psoriatic arthritis (PsA) severity and/or with treatment response to etanercept.*

**Methods.** *Patients with moderate-to-severe PsO and active PsA received etanercept 50 mg once weekly for 24 weeks. Patients were stratified according to whether scalp PsO was present at baseline. Demographics and disease characteristics were compared at baseline and after 12 and 24 weeks of treatment with etanercept.*

**Results.** *Scalp PsO was present in 273/373 (73.2%) patients; they were significantly younger and a higher proportion were male versus those without scalp PsO. At baseline, the patient global assessment psoriasis score was significantly higher for patients with scalp PsO versus without (67.0 vs. 57.9, p<0.01); tender joint count was significantly higher for patients without scalp PsO (6.0 vs. 5.0, p<0.05). A higher proportion of patients without versus with scalp PsO achieved enthesitis ≤1 at Week 12 (91.5% vs. 81.7%, p<0.05) and dactylitis ≤1 at week 24 (93.9% vs. 85.6%, p<0.05). Patients with scalp PsO showed significantly greater improvements in fatigue and joint pain at weeks 12 and 24, and a greater proportion achieved a score ≤0.5 in the health assessment questionnaire at week 12 (65.2% vs. 53.0%, p<0.05).*

**Conclusion.** *Scalp PsO was not clearly associated with PsA severity, and it did not affect treatment response. Patients without scalp PsO exhibited greater improvements in objective joint outcomes, whereas patients with scalp PsO experienced better outcomes in patient-reported outcomes.*

## Introduction

Psoriasis (PsO) is often associated with other inflammatory diseases, such as spondyloarthritis and psoriatic arthritis (PsA) (1-5). The estimated prevalence of PsA in the general population is 0.02%–0.25%, increasing to approximately 30% in patients with PsO (reported range of 6%–48%) (1-3, 5). PsA can cause clinical and radiological damage to joints and may lead to decreases in function and quality of life (1, 2, 5). Therefore, clinicians need to know whether particular manifestations of PsO are associated with a risk of developing PsA. Extensive evidence from published studies indicates that nail PsO is a risk factor for PsA (6-10). However, the relationship between PsA and other manifestations of PsO, such as scalp PsO, are less clear. Some studies have found scalp PsO to be a risk factor for the development of PsA (6, 10) and even predictive of PsA development (11), whereas other studies have noted no correlation (7, 12) or a negative correlation between scalp PsO and PsA (9). A systematic literature review concluded that although scalp PsO appears to be a risk factor for PsA, additional studies are needed to better understand the relationship (8).

We are not aware of any studies that have evaluated patients with both scalp PsO and PsA to determine whether an association exists between scalp PsO and the severity of PsA or response to treatment. Such information might assist dermatologists and rheumatologists in the management of patients. We evaluated data from a clinical study of patients with both PsO and PsA to determine whether the presence of scalp PsO is associated with PsA severity and/or with treatment response to the tumour necrosis factor (TNF) inhibitor, etanercept.

## Materials and methods

The Psoriasis Randomised Etanercept STudy in Patients with Psoriatic Arthritis (PRESTA) was a large, randomised, 24-week, multicentre study to evaluate the effects of etanercept on skin and joint disease in patients with both PsO and PsA (13). Patients had moderate-to-severe PsO involving >10% body surface area (BSA), active PsA for ≥3 months, and had never received TNF inhibitor therapy. Patients were randomised to double-blind etanercept 50 mg twice weekly or once weekly (QW) for 12 weeks. Then, all patients received open-label etanercept 50 mg QW for 12 weeks. This post hoc analysis includes the patients initially randomised to etanercept 50 mg QW. The study received independent ethics committee or institutional review board

approval and was conducted in accordance with the International Conference on Harmonisation guideline for good clinical practice and the ethical principles of the Declaration of Helsinki. All patients signed an approved informed consent form.

For this analysis, patients were stratified according to the presence or absence of scalp PsO at baseline, and the following demographic and disease characteristics were evaluated: age, gender, duration of PsO and PsA, location of PsO, and prior medication use. Additionally, several disease characteristics were compared at baseline and after 12 and 24 weeks: C-reactive protein (CRP), BSA of PsO, psoriasis area and severity index, physician global assessment, patient global assessment (PtGA) of PsO and arthritis, disease activity score in 28 joints, tender and swollen joint counts (TJC, SJC), dactylitis, enthesitis, American College of Rheumatology 70% improvement, minimal disease activity, and the patient-reported outcomes (PROs) of fatigue, joint pain visual analogue scale (VAS), health status using the EuroQoL-5 dimensions, and function using the health assessment questionnaire (HAQ).

The modified intent-to-treat population was analysed using a last observation carried forward analysis. Demographics and baseline characteristics were compared for the patients with and without scalp PsO using one-way analysis of variance for continuous variables and $\chi^2$ tests for dichotomous variables. Dichotomous endpoints for patients with and without scalp PsO were compared at weeks 12 and 24 using Cochran-Mantel-Haenszel. Change between baseline and weeks 12 and 24 was analysed using both the Wilcoxon-Mann-Whitney non-parametric test and the analysis of covariance with factors for PsO scalp status and baseline values as covariates.

## Results

Scalp PsO was present in 273/373 (73.2%) patients in the etanercept 50 mg QW cohort. The mean (SD) duration of PsO in the patients with *versus* without scalp PsO was 18.1 (10.7) years *versus* 19.8 (13.1) years, respectively, $p$=ns; duration of PsA was 7.4 (7.2) years *versus* 6.5 (6.5) years, respectively, $p$=ns (Table I). The patients with scalp PsO were significantly younger and a higher proportion was male *versus* those without scalp PsO. Significantly more patients with scalp PsO had PsO in other areas of the body and had previously used certain topical and oral PsO and PsA medications, including topical corticosteroids, vitamin D analogues, leflunomide, and anthralin compounds. No significant difference was reported in the prior use of disease-modifying anti-rheumatic drugs overall. Baseline PtGA psoriasis score was significantly higher for patients with scalp PsO *versus* without (67.0 *vs*. 57.9, $p$<0.01, Table II). Patients without scalp PsO had significantly more tender joints at baseline (6.0 *vs*. 5.0, $p$<0.05).

**Table I.** Demographics and baseline disease characteristics for patients without *vs*. with scalp PsO.

| | No scalp PsO (n=100) | Scalp PsO (n=273) | $p$-value* |
|---|---|---|---|
| Age, years | 49.4 (12.2) | 46.0 (11.0) | 0.010† |
| Male, n (%) | 48 (48.0) | 182 (66.7) | 0.001‡ |
| Duration of PsO, years | 19.8 (13.1) | 18.1 (10.7) | ns |
| Duration of PsA, years | 6.5 (6.5) | 7.4 (7.2) | ns |
| PsO body location, n (%) | | | |
| Head | 36 (36.0) | 196 (71.8) | <0.001 |
| Neck | 5 (5.0) | 103 (37.7) | <0.001 |
| Arms | 64 (64.0) | 233 (85.4) | <0.001 |
| Hands | 31 (31.0) | 163 (59.7) | <0.001 |
| Anterior body | 47 (47.0) | 217 (79.5) | <0.001 |
| Back | 43 (43.0) | 204 (74.7) | <0.001 |
| Legs | 72 (72.0) | 238 (87.2) | <0.001 |
| Buttocks | 33 (33.0) | 198 (72.5) | <0.001 |
| Ankles | 25 (25.0) | 139 (50.9) | <0.001 |
| Feet | 23 (23.0) | 144 (52.8) | <0.001 |
| Prior medication, n (%) | | | |
| Any DMARD§ | 8 (8.0) | 43 (15.8) | ns |
| Any topical PsO agent | 52 (52.0) | 183 (67.0) | 0.008 |
| Topical corticosteroid | 35 (35.0) | 148 (54.2) | 0.001 |
| Vitamin D analogue | 12 (12.0) | 68 (24.9) | 0.007 |
| Leflunomide | 1 (1.0) | 21 (7.7) | 0.015 |
| Anthralin compound | 0 | 11 (4.0) | 0.042 |

Values are mean (SD) unless otherwise stated. Modified intent-to-treat population.
*$\chi^2$; †one-way analysis of variance with treatment as a factor. ‡Fisher's exact test (2-tail); §includes oral gold, injectable gold, hydroxychloroquine, leflunomide, sulfasalazine, and other DMARDs (not otherwise specified); DMARD: disease-modifying anti-rheumatic drug; ns: non-significant; PsA: psoriatic arthritis; PsO: psoriasis.

After 12 and 24 weeks, patients in both groups showed improvements in all outcomes (Table II). Patients without scalp PsO demonstrated significantly greater improvements in tender and swollen joints after 12 weeks; this continued to 24 weeks for tender joints. Significantly more of these patients achieved an enthesitis score ≤1 at week 12 (91.5% *vs*. 81.7%, $p$<0.05) and a dactylitis score ≤1 at week 24 (93.9% *vs*. 85.6%, $p$<0.05). Conversely, patients with scalp PsO showed significantly greater improvements in the PROs of fatigue and joint pain VAS at weeks 12 and 24, and more of them achieved a HAQ score ≤0.5 at week 12 (65.2% *vs*. 53.0%, $p$<0.05).

## Discussion

The association between nail PsO and PsA is well established. However, the relationship between scalp PsO and PsA has demonstrated conflicting results in clinical studies, similar to the relationship between intergluteal PsO and PsA (8, 10). Although no immunologic relationship between scalp PsO and PsA has been established, several studies have found an association between the two.

We conducted an analysis to investigate whether the presence of scalp PsO in patients with both PsO and PsA corresponds with the severity of PsA or with response to anti-TNF therapy. Our data do not show a clear relationship be-

**Table II.** Improvement for patients without scalp PsO *vs*. patients with scalp PsO.

| | BL | | Improvement from BL to week 12 | | Improvement from BL to week 24 | |
|---|---|---|---|---|---|---|
| | No scalp PsO (n=100) | Scalp PsO (n=273) | No scalp PsO (n=100) | Scalp PsO (n=273) | No scalp PsO (n=100) | Scalp PsO (n=273) |
| CRP, mg/L, median (Q1, Q3) | 7.8 (4.0, 16.9) | 5.6 (4.0, 15.9) | –3.0 (–12.8, 0) | –1.1 (–11.4, 0) | –3.0 (–12.3, 0) | –0.9 (–11.7, 0) |
| Affected BSA, % | 27.9 (20.2) | 31.2 (22.8) | –12.7 (12.9) | –14.4 (16.8) | –17.3 (16.6) | –20.5 (20.7) |
| PASI (0–72) | 17.6 (8.9) | 19.6 (10.1) | –11.3 (6.8) | –12.1 (9.0) | –13.0 (7.9) | –14.4 (10.1) |
| PGA psoriasis (0–5) | 3.5 (0.6) | 3.7 (0.7) | –1.6 (0.9) | –1.6 (1.0) | –1.9 (1.0) | –2.0 (1.1) |
| PtGA psoriasis (0–100) | 57.9 (28.3) | 67.0 (24.5)* | –25.5 (36.1) | –34.9 (33.2) | –28.9 (39.0) | –39.6 (33.4) |
| Tender joints (0–28), median (Q1, Q3) | 6.0 (3.0, 12.0)† | 5.0 (2.0, 10.0) | –3.0 (–7.0, –1.0)† | –2.0 (–5.0, 0) | –4.5 (–10.0, –2.0)† | –3.0 (–7.0, –1.0) |
| Swollen joints (0–28), median (Q1, Q3) | 4.0 (2.0, 6.0) | 3.0 (1.0, 6.0) | –2.0 (–5.0, –1.0)† | –2.0 (–4.0, 0) | –3.0 (–5.0, –1.0) | –2.0 (–5.0, –1.0) |
| PGA arthritis (0–100) | 49.3 (20.6) | 50.2 (20.9) | –31.4 (18.8) | –30.8 (22.2) | –36.6 (21.7) | –37.0 (23.3) |
| PtGA arthritis (0–100) | 59.8 (24.2) | 62.4 (24.9) | –28.7 (32.2) | –34.9 (30.3) | –32.3 (31.9) | –38.2 (30.4) |
| Fatigue (0–100 VAS) | 51.2 (27.6) | 56.1 (27.4) | –11.6 (27.9) | –20.9 (30.5)‡ | –16.9 (30.0) | –25.7 (29.6)‡ |
| Patient assessment of joint pain (0–100 VAS) | 60.9 (23.8) | 62.3 (25.7) | –25.9 (32.1) | –33.5 (30.7)‡ | –31.4 (32.0) | –38.4 (30.1)‡ |
| EQ-5D (0–1) | 0.48 (0.31) | 0.49 (0.33) | –0.24 (0.33) | –0.24 (0.31) | –0.24 (0.36) | –0.26 (0.35) |
| | | | Patients at week 12, n/N (%) | | Patients at week 24, n/N (%) | |
| PASI75 | — | — | 37/100 (37.0) | 98/271 (36.2) | 63/100 (63.0) | 168/271 (62.0) |
| DAS28 ≤2.6 | — | — | 36/94 (38.3) | 114/260 (43.8) | 55/96 (57.3) | 151/264 (57.2) |
| ACR70 | — | — | 26/97 (26.8) | 53/263 (20.2) | 38/97 (39.2) | 94/263 (35.7) |
| Dactylitis ≤1 | — | — | 86/98 (87.8) | 213/269 (79.2) | 92/98 (93.9)§ | 232/271 (85.6) |
| Enthesitis ≤1 | — | — | 86/94 (91.5)§ | 219/268 (81.7) | 90/98 (91.8) | 241/271 (88.9) |
| Minimal disease activity | — | — | 8/99 (8.1) | 12/271 (4.4) | 16/98 (16.3) | 43/266 (16.2) |
| HAQ ≤0.5 | — | — | 53/100 (53.0) | 178/273 (65.2)§ | 59/100 (59.0) | 190/273 (69.6) |

All values are mean (SD) unless otherwise stated. Modified intent-to-treat population, last observation carried forward analysis.
*$p<0.01$; one-way ANOVA; †$p<0.05$ between groups; Wilcoxon-Mann-Whitney test; ‡$p<0.05$, analysis of covariance with factors for PsO scalp status and baseline value as covariate; §$p<0.05$; Cochran-Mantel-Haenszel test of with *vs*. without scalp PsO.
ACR70: American College of Rheumatology 70% improvement; BL: baseline; BSA: body surface area; CRP: C-reactive protein, DAS28: disease activity score in 28 joints; EQ-5D: EuroQoL-5 dimensions; HAQ: health assessment questionnaire; PASI75: Psoriasis Area Severity Index 75% improvement; PGA: physician global assessment; PsO: psoriasis; PtGA: patient global assessment; Q: quartile; VAS: visual analogue scale.

tween the presence of scalp PsO and the severity of PsA. At baseline, the PtGA psoriasis score was higher in patients with scalp PsO and the TJC was higher in the patients without scalp PsO; however, many measurements of disease activity did not differ significantly between the two groups, including CRP, PtGA arthritis, SJC, and the patient assessment of joint pain. Additionally, treatment response did not vary according to the presence or absence of scalp PsO; only a few clinical outcomes demonstrated a significant difference between patients with and without scalp PsO. Patients without scalp PsO exhibited greater improvements in objective joint outcome measures, whereas patients with scalp PsO experienced better outcomes in several PROs.

The results of this analysis may be confounded by the finding that significantly more patients with scalp PsO at baseline also had PsO in other areas of the body. Thus, patients with scalp PsO appear to be part of a distinct population of patients with widespread PsO across the body and a more severe PtGA psoriasis score at baseline than patients without scalp PsO. Similar improvements in PsO for patients with and without scalp PsO indicate that treatment was effective regardless of scalp PsO status.

An important point to remember is that our study evaluated patients with PsO who had already been diagnosed with PsA; the mean duration of PsA was 7.1 years. As noted in Langenbruch, *et al*. (7), although scalp PsO may be associated with a risk for the development of PsA, it may not be correlated with PsA once PsA is present.

In summary, our study did not find a clear relationship between the presence of scalp PsO and the severity of PsA or the response to treatment with etanercept.

## Acknowledgements

We wish to thank all the patients who participated in this study as well as the investigators and medical staff at all of the participating centres.

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