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Effectiveness of adalimumab in the treatment of scalp and nail affection in patients with moderate to severe plaque psoriasis in routine clinical practice

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Abstract

Introduction: Data on the effectiveness of biologics the treatment of nail and scalp psoriasis (PSO) in a routine clinical setting are scarce. The aim of this study was therefore to evaluate the effectiveness of adalimumab in the treatment of nail and scalp psoriatic lesions in routine dermatologic practice.
Methods: Five hundred one patients were analyzed in this observational study; 157 patients had nail involvement (nail PSO set; NPS) and 404 had scalp involvement (scalp PSO set; SPS). Patients treated with adalimumab were observed for up to 12 months. Outcomes were evaluated via changes in the Nail Psoriasis Severity Index (NAPSI), Psoriasis Scalp Severity Index (PSSI), Psoriasis Area and Severity Index (PASI), and QoL (using the Dermatology Life Quality Index).
Results: Eighty-four percent of the patients in the NPS and 93.8% in the SPS achieved a good clinical response upon treatment with adalimumab. Complete clearing of local symptoms was achieved by 33.3% of the patients with nail involvement and 66.7% of the patients with scalp involvement. There was also a marked improvement in QoL.
Conclusion: Adalimumab appears to be an effective treatment for scalp and nail PSO in patients with moderate to severe plaque PSO. No new clinical concerns were established.

Keywords: psoriasis, nail psoriasis, scalp psoriasis, adalimumab, routine clinical practice

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Introduction

Psoriasis is an immune-mediated chronic inflammatory disease that primarily affects the skin (1); however, in severe forms, psoriasis is associated with an increased risk of metabolic syndrome, cardiovascular diseases, depression, and decreased life expectancy (2–7). Psoriasis may cause substantial psychological and social distress and reduced quality of life (8). Scalp and nail disorders are common symptoms of psoriasis but are often overlooked by the treating physician.

The scalp is one of the most common sites involved in patients with plaque psoriasis. Scalp psoriasis occurs in 50% to 80% of patients with psoriasis, but may also be the sole manifestation of disease. Scalp psoriasis may be associated with pruritus, pain, and social stigma, and can severely impact quality of life due to external exposure (9).

Up to 50% of patients with plaque psoriasis also have concurrent nail psoriasis, with an estimated lifetime incidence of 80% to 90%. Nail psoriasis occurs more often in patients with severe disease, such as those with concomitant psoriatic arthritis. These patients have a 70% to 80% prevalence of nail psoriasis. In the longer term, nail involvement may be a signal of a more severe form of psoriasis or a precursor to psoriatic arthritis (10).

Nail involvement may place a significant burden on patients as a result of functional impairment of manual dexterity, pain, and psychosocial embarrassment (11). Historically, the nails and the scalp are among the most problematic areas to treat. These areas are also poorly represented in measures of skin severity, such as the Psoriasis Area and Severity Index (PASI), and are usually not the focus of therapeutic clinical trials.

Since the approval of biologic agents for treating moderate to severe plaque psoriasis, interest has been renewed in revisiting unsatisfactory treatment modalities for nail and scalp psoriasis, with the goal of finding better treatment options. The clinical efficacy and safety of the tumor necrosis factor (TNF) inhibitor adalimumab in patients with moderate to severe chronic plaque psoriasis have been demonstrated in several randomized, double-blind, controlled clinical trials; however, data on the effectiveness of biologics in treating nail and scalp psoriatic lesions in routine clinical practice are scarce (12, 13).

Materials and methods

Study design and patients

This was a multi-center, multi-country, single-arm prospective postmarketing study conducted in Slovenia, Hungary, Slovakia, Romania, Israel, the Czech Republic, Ukraine, and Estonia. A total of 72 dermatological medical centers were included in the study.

Adult patients with moderate to severe plaque psoriasis eligible for adalimumab therapy (according to the local product label and prescription/reimbursement guidelines) with a Nail Psoriasis

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Severity Index (NAPSI) score of the hands and feet of ≥ 10 and a Psoriasis Scalp Severity Index (PSSI) score of ≥ 10 were included in the study. The decision to treat patients with adalimumab was made prior to and independent of participation in this study. Three patient populations were analyzed: the full analysis set (FAS), the nail psoriasis set (NPS), and the scalp psoriasis set (SPS). The FAS included patients with any data available in the case report form regarding treatment with adalimumab. The NPS included patients from the FAS that had a NAPSI score of the hands and feet of ≥ 10 at Visit 0 (V0). The SPS included patients from the FAS that had a PSSI value of ≥ 10 at V0.

Each patient included in the study was to be observed during treatment for a maximum of 12 months. The follow-up visits were not interventional and were not strictly scheduled, but rather left to the judgment of each investigator. To optimize data collection, five patient visits were indicated within the 12-month observation period: the baseline visit (V0) and then follow-up visits at months 3 (V1), 6 (V2), 9 (V3), and 12 (V4).

Objectives

The primary objective of this study was to evaluate the improvement of nail and scalp psoriasis in patients with moderate to severe plaque psoriasis after treatment with adalimumab. The improvement of nail psoriasis was measured using the NAPSI and the improvement of scalp psoriasis was measured using the PSSI. Secondary objectives included evaluation of general improvement in psoriasis, changes in quality of life, the association between general and nail or scalp improvement during adalimumab therapy, and the association between general, nail, or scalp improvement and patient quality of life. General improvement in psoriasis was evaluated using the PASI and changes in quality of life were evaluated using the DLQI. During the study, physical examinations, diagnostic measures (erythrocyte sedimentation rate and C-reactive protein), and observations were entered into case report forms by the investigator or staff.

Statistical analysis

All statistical analyses were carried out using SAS® version 9.2 (SAS Institute, Cary, NC, USA) and are described in detail in the respective statistical analysis plan from July 9th, 2013. Only descriptive analyses were performed. For correlation analyses, Spearman's rank correlation coefficient was applied. The analyses presented herein are based on all available data. In addition, an analysis using the last observation carried forward (LOCF) was used. This analysis was based on patients that provided the respective V0 value and ≥ 1 follow-up assessment. The last of these assessments was used for the analysis.

Results

Baseline characteristics

Five hundred six patients were included in the study; however, five patients were lost to follow-up after the baseline visit and were excluded from the analysis. Of these patients, 157 had nail involvement (NPS) and 404 had scalp involvement (SPS), with an overlap of 119 patients (NPS and SPS; Fig. 1).

Almost all of the patients in the FAS were Caucasian (99.6%); 62.7% of the patients were male and the mean age of patients was 47.0 years. For approximately one-third of the patients in the FAS (34.0%), psoriasis was confirmed by biopsy. The mean time since diagnosis of psoriasis at V0 was 15.7 years. Concomitant psoriatic arthritis was diagnosed in 36.3% of the patients in the FAS.

Efficacy data: primary objectives

The vast majority of patients in the FAS (96.6%) received 40 mg of adalimumab every other week without any change in dose during the course of the study. The mean value of the NAPSI in the NPS at V0 was 13.0 (range, 10–16; 16 is the maximum NAPSI value). This mean value decreased during the course of the study to 2.5 at V4 (Fig. 2). The mean percentage change in the NAPSI score was –81.6% from V0 to V4.

The number of patients with a good clinical response (i.e., the rate of patients with an improvement of ≥ 50% in the NAPSI score compared with V0 values) increased during the course of the study: at V4, 90.4% of patients in the NPS had a good clinical response. Complete clearing of the nails (i.e., a NAPSI score of 0) was achieved by 40.0% of patients at V4.

The mean PSSI at V0 in the SPS was 26.8 (range, 10–72; 72 is

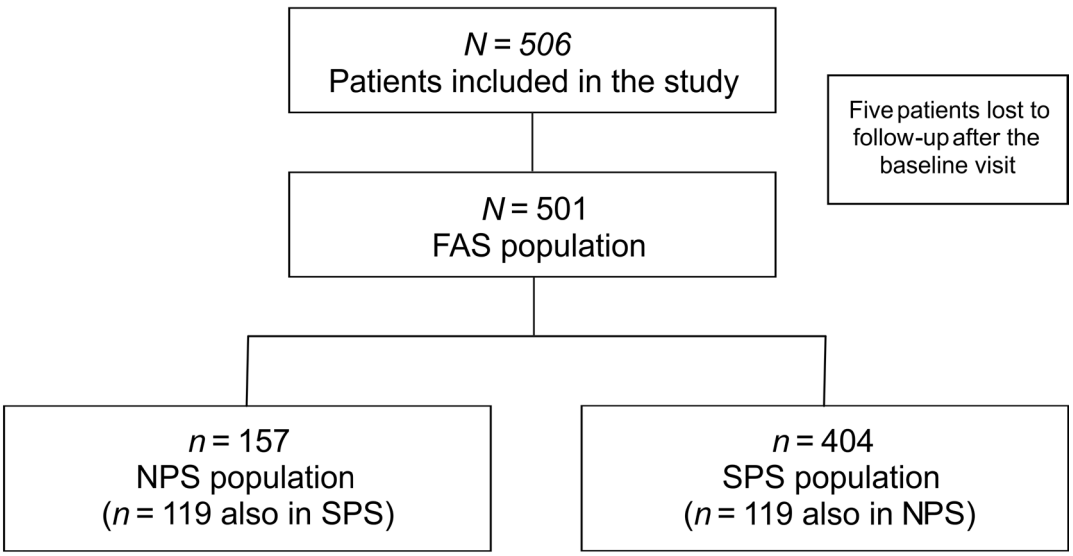

Figure 1 | Patient disposition in the study.*
Abbreviations: FAS = full analysis set; NPS = nail psoriasis set; SPS = scalp psoriasis set.
*There was an overlap of 119 patients that were included in both the NPS and the SPS.

the maximum PSSI value). During the course of the study, the mean value decreased to 1.2 at V4 (Fig. 3), yielding a mean percentage change of –94.8%. Good clinical response at V4 (i.e., an improvement in the PSSI of ≥ 50% compared with values at V0) was achieved by 98.3% of all patients. The rate of patients with complete clearing of the scalp (i.e., a PSSI of 0) was 71.7% at V4.

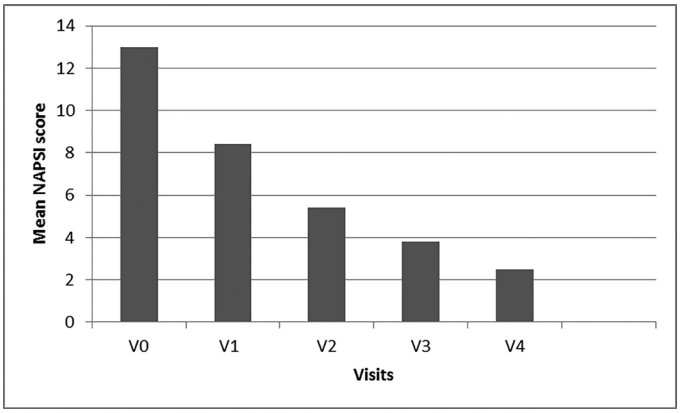

Figure 2 | Mean NAPSI scores through the course of the study.
Abbreviations: NAPSI = Nail Psoriasis Severity Index.

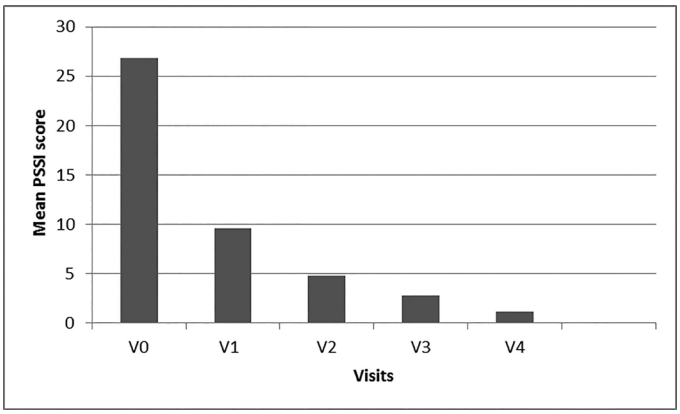

Figure 3 | Mean PSSI scores through the course of the study.
Abbreviations: PSSI = Psoriasis Scalp Severity Index.

Efficacy data: secondary objectives

In the FAS, mean PASI scores decreased from 22.0 at V0 to 1.8 at V4. The mean percentage change from V0 to V4 was –91.0% in the FAS, –87.4% in the NPS, and –91.5% in the SPS.

An improvement in quality of life was observed during the course of the study: the mean DLQI score decreased significantly in all patient populations (Table 1). The average improvement in quality of life was similar in the SPS and less distinct in the NPS compared to the FAS. The percentage of patients in which psoriasis had no or only a small effect on quality of life (i.e., DLQI scores ≤ 5) changed in the FAS from 3.3% at V0 to 94.1% at V4. In the NPS, 90.8% of the patients had a DLQI score ≤ 5 at V4; in the SPS, the proportion was 94.0% at V4 (Table 2).

Associations between general, nail, or scalp improvement and quality of life were evaluated using Spearman's rank correlation coefficient. As a rule of thumb, a correlation coefficient < 0.2 is considered as no or only a weak association, between 0.2 and 0.5 as a moderate association, between 0.5 and 0.8 as a strong association, and > 0.8 as a very strong association. The association between improvement in quality of life and improvement in nail psoriasis in the NPS resulted in moderate to strong correlations between 0.25 at V1 and 0.6 at V4-LOCF. The association with the improvement of scalp psoriasis in the SPS yielded correlation coefficients between 0.49 at V4 and 0.63 at V1 and V2. In the FAS, the associations between general improvement of psoriasis and improvement in quality of life were strong throughout the study: the respective correlation coefficients ranged between 0.69 at V1 and 0.78 at V4-LOCF.

Table 1 | **Change in quality of life with respect to DLQI (metrical).**

	FAS			NPS			SPS		
	V0	V4	% change	V0	V4	% change	V0	V4	% change
Mean DLQI score	20	1.5	–91.2%	20.2	2.2	–87.7%	20.6	1.5	–92.2%

Abbreviations: DLQI = Dermatology Life Quality Index; FAS = full analysis set; NPS = nail psoriasis set; SPS = scalp psoriasis set.

Table 2 | **Change in quality of life with respect to DLQI (dichotomous).**

DLQI* score	FAS		NPS		SPS	
	V0 %	V4 %	V0 %	V4 %	V0 %	V4 %
≤ 5	3.3	94.1	4.3	90.8	1.6	94.0
› 5	96.7	5.9	95.7	9.2	98.4	6.0

Abbreviations: DLQI = Dermatology Life Quality Index; FAS = full analysis set; NPS = nail psoriasis set; SPS = scalp psoriasis set.
*A DLQI score of 0 to 5 means no effect or a small effect on patient quality of life.

Safety

Adverse events (AEs) that occurred during the study are presented in Table 3. The most common AEs were skin and subcutaneous tissue disorders (5.8%) and infections and infestations (1.6%). Serious AEs (SAEs) included exacerbations of psoriasis (n = 4), myocardial infarction (n = 1; the patient died), and lung cancer and alcoholic polyneuropathy (n = 1; the patient died). A causal relationship to the study drug was not indicated in any of the patient deaths. One patient had a SAE of psoriasis that was considered to be probably related to treatment by the investigator. No new clinical concerns were established with regard to the incidence of adverse drug reactions and no new safety signals were observed.

Table 3 | **Overview of AEs**

Type of event	*N*	%
Any AE	48	9.6
Serious AE	5	1
Adverse drug reaction*	30	6
AE leading to drug withdrawal	35	7

Abbreviations: AE = adverse event.
*AE with a causal relationship to the study drug judged as possible or probable.

Discussion

Nail psoriasis is notoriously difficult to treat because nails are slow to heal and conventional treatments are generally difficult to administer, are considered inconvenient by patients, are limited by AEs, and often lose efficacy over time. Overall, there is no consistent treatment approach to nail psoriasis. There is also a lack of controlled study data related to existing treatment modalities. Relatively effective conventional systemic treatments for nail psoriasis (cyclosporine, methotrexate, and acitretin) have a serious toxicity potential (10). Treatment of scalp psoriasis is even less well established. All conventional topical therapies are difficult to administer and affect the cosmetic hair condition, resulting in reduced patient compliance. In patients with recalcitrant scalp changes, systemic immunosuppressive therapy is recommended; however, the toxicity of these drugs limits their long-term use (9). Despite the fact that biologics have been used for more than a decade in the treatment of various forms of psoriasis, data on the efficacy and safety of these drugs in the treatment of scalp and nail psoriasis are rather limited. A few case reports can be found in the literature; however, there are no published data from non-interventional studies (9, 10), such as postmarketing observational studies, reflecting data on routine clinical practice.

The results of this study clearly indicate the beneficial effect of

adalimumab with regard to the primary objective: improvement of scalp and nail psoriasis after 12 months of treatment. In 90% of patients, no additional anti-psoriatic medication was taken during the observation time.

Data on the effectiveness of adalimumab are in accordance with results of several previous studies, including the open-label STEREO study, describing a pronounced improvement in patients with nail psoriasis treated with adalimumab (12), and the randomized, controlled BELIEVE study, which reported the effectiveness of treatment for scalp psoriasis as a secondary outcome (13). In the BELIEVE study, the mean NAPSI score at baseline was 25.3 (in this study, the mean score was 13.0), and the mean PSSI score was 16.3 (in this study, the mean score was 26.8), suggesting a more severe scalp affliction in this study (comparisons with regard to the NAPSI score are hard to draw). Overall, improvement in disease scores correlated well with improvement in quality of life. The average improvement in the NPS was slightly less pronounced compared with the overall population for both indications, suggesting that nail psoriasis may be more recalcitrant to treatment. The favorable association of the effects of adalimumab with general quality of life ratings has been režported previously, further supporting the results of this study in routine dermatological practice (14–16). Although data from an observational study are of a lower evidence level than data retrieved from a randomized clinical trial, data gleaned from general dermatological practice more readily allow generalization and deductions for the real-world treatment of patients with psoriasis.

Adalimumab appears to be an effective treatment for scalp and nail psoriasis in patients with moderate to severe plaque psoriasis, improving both objective clinical indices (NAPSI and PSSI) and patients' quality of life. No new clinical concerns were established and no new safety signals were observed in the study. This observational study provides the rationale for further randomized clinical trials in the quest for an improved treatment regimen in patients with nail and scalp psoriasis.

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Conflict of interest disclosures

KKh: speakers bureau of AbbVie/Abbott, Astellas, and GlaxoSmithKline; IL: employee of AbbVie; AS: paid consultant for Janssen, Novartis, speaker for Janssen, Novartis, AbbVie, and Ewopharma; LP has received consultancy/speaker honoraria from AbbVie, Janssen-Cilag, Novartis, Pfizer, Neopharm, and Dexon pharma; TL: speakers bureau / advisory board of AbbVie, Celgene, Eli Lilly, Janssen-Cilag, MSD, Novartis, and Pfizer; KK has served as a principal investigator in clinical studies sponsored by Celgene, Mitsubishi Pharma, Novartis, Merck, Regeneron, AbbVie, and Sandoz; JM: speakers bureau of AbbVie; JP received consultancy fees from AbbVie, Janssen-Cilag, Novartis, Pfizer, and Teva; MB: employee of AbbVie; MH: employee of AbbVie.

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