ORIGINAL ARTICLE

Efficacy of adalimumab across subgroups of patients with moderate-to-severe chronic plaque psoriasis of the hands and/or feet: post hoc analysis of REACH

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Abstract

Background   The Randomized Controlled Evaluation of Adalimumab in Treatment of Chronic Plaque Psoriasis of the Hands and Feet (REACH) trial demonstrated that adalimumab was efficacious and well-tolerated for the treatment of hand and/or foot psoriasis through 28 weeks.

Objective   To evaluate the effects of patient baseline characteristics on efficacy of adalimumab treatment of hand and/or foot psoriasis.

Methods   Patients with moderate-to-severe chronic plaque psoriasis of the hands and/or feet were randomized 2 : 1 to adalimumab or placebo during the 16 week, double-blind period of REACH. Primary endpoint was percentage of patients achieving Physician's Global Assessment of the hands and/or feet of clear/almost clear at week 16. Post hoc analyses evaluated effects of baseline patient characteristics on the primary endpoint. Patients with nail psoriasis at baseline were assessed for association of Nail Psoriasis Severity Index (NAPSI) 50 response with efficacy outcomes at week 16.

Results   Seventy-two patients (49 adalimumab : 23 placebo) were analysed. Greater percentages of adalimumab-treated patients achieved the primary endpoint vs. placebo across all subgroups. Among 31 patients with nail psoriasis, a greater percentage of adalimumab-treated patients achieved NAPSI 50 (56.5%) vs. placebo (12.5%) at week 16. In adalimumab-treated patients, greater percentages of NAPSI 50 Responders vs. Non-responders achieved the primary endpoint, and had greater improvements in erythema, scaling, induration and fissuring, Dermatology Life Quality Index, and pain scores.

Conclusions   Adalimumab was efficacious in treating chronic plaque psoriasis of the hands and/or feet over 16 weeks, regardless of baseline characteristics. Marked improvement in nail psoriasis among adalimumab-treated patients correlated with significant improvements in skin disease and patient-reported outcomes.

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Conflict of interest

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to the data and were involved with data analysis and interpretation, had input into the decision to submit the publication, contributed to content development, and reviewed and approved the publication.

Previous Presentations

A portion of the data in this manuscript was presented as a poster at the 69th Annual Meeting of American Academy of Dermatology in New Orleans, Louisiana, February 4–8, 2011. (Langley RG, Crowley J, Unnebrink K, Goldblum O. Improvement in Nail Psoriasis is Associated With Improved Efficacy Outcomes in Hand and/or Foot Psoriasis in Adalimumab-treated Patients: Subanalysis of REACH. J Am Acad Dermatol. 2011;64[2, Supp 1]:AB7.)

Introduction

Plaque psoriasis is a chronic, recurring condition that varies in severity and body surface area (BSA) affected. It can manifest from few localized areas to complete body coverage, and can also primarily involve the hands and feet, including nails. Of the 1–3% of the general population who have psoriasis, an estimated 3–41% have chronic plaque psoriasis of the hands and/or feet,[1] and approximately 50% of psoriasis patients have nail involvement.[2] Despite the relatively small BSA that is affected by psoriasis of the hands and/or feet, quality of life for these patients can be disproportionally poor due to pain, discomfort, and limitations in performing activities of daily living.[1,3–7] Nail psoriasis can alter the sense of touch and reduce manual dexterity.[8] Psoriasis of the hands and/or feet can also cause embarrassment due to the unsightly appearance of scales and fissures on the skin, and pitting, discoloration and crumbling of the nail.[6]

Published information related to specific treatment of hand and/or foot psoriasis focuses mainly on palmoplantar psoriasis. Although topical therapies, including corticosteroids, retinoids, calcipotriol, salicylic acid, and coal tar, are widely used, palmoplantar psoriasis is often resistant, and prolonged corticosteroid use can have undesirable side-effects.[9–11] Common light therapies, including topical psoralen plus long-wave ultraviolet A (PUVA), broadband ultraviolet B, and narrowband ultraviolet B (NB-UVB), have also been used, but published, definitive conclusions about the effectiveness of NB-UVB on localized psoriasis are lacking.[9] In addition, the multiple clinic visits for treatment can be inconvenient.[11]

Established systemic therapies are typically employed when the disease is severe or refractory to topical treatment. These include PUVA with oral psoralen, methotrexate, cyclosporine, and retinoids; however, adverse effects can limit long-term use in patients with psoriasis of the hands and/or feet.[12] Patients with localized psoriasis may need multiple treatment agents, which include a combination of topical and systemic medications, during the course of disease to achieve treatment benefit.[9,10] Biologics approved for the treatment of chronic plaque psoriasis have also been used successfully to treat hand and/or foot psoriasis, although none are currently approved specifically

for this condition, and most of the evidence is limited to small clinical studies and case reports.[13–22]

Adalimumab, a fully human monoclonal antibody that neutralizes tumour necrosis factor (TNF) and modulates TNF-related biological responses, is approved in the United States and Europe for multiple indications, including psoriatic arthritis (PsA) and moderate-to-severe chronic plaque psoriasis.[23,24] Recently, REACH (ClinicalTrials.gov NCT00735787), a phase 4, 16 week, multicenter, randomized, double-blind, placebo-controlled trial with an additional 12-week open-label period, demonstrated that adalimumab was efficacious and well-tolerated for the treatment of psoriasis of the hands and/or feet for up to 28 weeks.[25] Following adalimumab treatment, significant improvements were seen in scores evaluating efficacy and pain. These included erythema, scaling, induration, and fissuring (ESIF); Nail Psoriasis Severity Index (NAPSI); and plaque psoriasis and PsA pain Visual Analogue Scale (VAS) scores.

This post hoc analysis REACH evaluated the effects of baseline demographic and disease characteristics on the efficacy of adalimumab compared with placebo for the treatment of
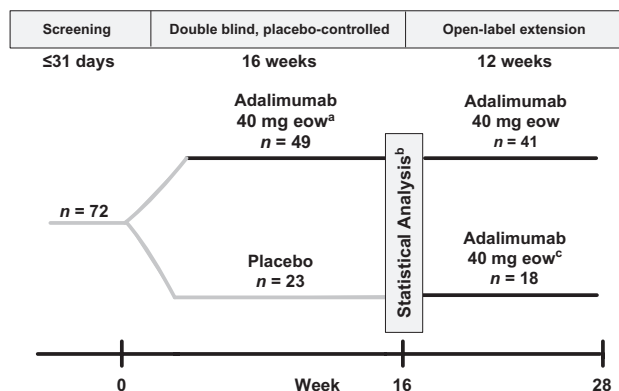

Figure 1 Study design. [a]From week 1, after an 80 mg dose at week 0. [b]Primary Endpoint was proportion of patients with Physician's Global Assessment of hands and/or feet (hfPGA) of clear or almost clear at week 16. [c]From week 17, after an 80 mg dose at week 16. n: efficacy analysis set.

chronic plaque psoriasis of the hands and/or feet during the 16-week double-blind period.

Materials and methods

The REACH study design is illustrated in Figure 1; a detailed description has been published.[25] Patients had moderate-to-severe chronic plaque psoriasis involving the hands and/or feet. In the 16-week placebo-controlled period, patients were randomized 2 : 1 (adalimumab:placebo) to adalimumab 80 mg at week 0, and 40 mg every other week from weeks 1–15 or matching placebo. Washout periods were conducted for investigational and biologic agents, other systemic psoriasis therapies, phototherapy, excessive sun exposure or tanning-bed use, and topical therapies on the hands and feet.[25]

Study population

Criteria for including or excluding patients have been previously described.[25] Briefly, patients were adult (at least 18 years of age) men and women who had been diagnosed with moderate-to-severe chronic plaque psoriasis of the hands and/or feet for at least 6 months, and had evidence of psoriatic disease on at least one other cutaneous area. Patients had a baseline score of at least three on the Physician's Global Assessment of hands and/or feet (hfPGA). A score of zero or one indicated either no signs of plaque psoriasis ('clear') or perceptible erythema and scaling ('almost clear'), a score of two indicated light-pink erythema and minimal scaling with or without pustules ('mild'), a score of three indicated dull-red erythema with diffuse scaling, and some skin thickening with or without fissures or pustules ('moderate'), and a score of four indicated deep, dark-red erythema with obvious, diffuse scaling, thickening, and numerous fissures, with or without pustules ('severe'). The main exclusion criteria included previous treatment with adalimumab or the presence of palmoplantar pustulosis or other active skin diseases.

Efficacy assessments

The primary endpoint of REACH was the proportion of patients achieving an hfPGA score of clear or almost clear at week 16. The post hoc analyses reported here include evaluation of patients for the effects on the primary endpoint of baseline demographic and clinical characteristics, including age (<40 years, 40–64 years, and ≥65 years), gender, weight (<88 kg, ≥88 kg), Psoriasis Area Severity Index (PASI) score (<10, ≥10), disease duration (<4.7 years, ≥4.7 years), PsA history, prior systemic treatment, smoking history and nail involvement. The population median for bodyweight (88 kg) and disease duration (4.7 years) determined the dichotomization for baseline weight and disease duration.

All patients with nail psoriasis at baseline were also evaluated for improvement of target nail (most severely involved fingernail) at week 16 by NAPSI 50 response and concomitant improvement in psoriasis of the hands and/or feet. Patients were grouped by NAPSI 50 response at week 16; those who achieved or did not achieve NAPSI 50 (at least a 50% improvement from baseline in NAPSI score) were defined as 'Responders' or 'Non-Responders' respectively. At week 16, both subgroups were then evaluated for the proportion who achieved hfPGA score of clear or almost clear, and improvements from baseline in ESIF, Dermatology Life Quality Index (DLQI), and plaque psoriasis and PsA pain Visual Analogue Scale (VAS) scores. Only adalimumab-treated patients were included in the subgroup analyses by NAPSI 50 response.

Statistical analyses

The intent-to-treat (ITT) population consisted of all randomized patients who received at least one dose of study medication. Due to investigator non-compliance at one study centre, all of that centre's patients ($N = 9$) were excluded from all analyses in REACH (decided pre-database lock), and were not included in this post hoc analysis.[25] Missing or incomplete data were handled using non-responder imputation for categorical data and last observation carried forward for continuous data. Due to the small numbers of patients in each subgroup, all analyses in this publication are descriptive.

Results

Baseline characteristics

Eighty-one patients with chronic plaque psoriasis of the hands and/or feet were enrolled in REACH and 72 (49 adalimumab, 23 placebo) were included in the analyses (see Materials and methods). Of the 72 patients, 31 (23 adalimumab, 8 placebo) with nail psoriasis at baseline and data available through week 16, were evaluated for nail improvement.

Overall, patient baseline demographics and clinical characteristics were similar between treatment groups (adalimumab and placebo) across the three studied populations (ITT, NAPSI 50 Responders, NAPSI 50 Non-Responders). The majority of patients had moderate disease and a relatively low percentage of affected BSA (Table 1). NAPSI 50 Responders reported a longer duration of psoriasis at baseline than NAPSI 50 Non-Responders (20.6 ± 20.06 vs. 15.1 ± 14.42 years). A greater percentage of NAPSI 50 Non-Responders compared with NAPSI 50 Responders had an hfPGA score of severe at baseline (47.1% vs. 14.3%) and psoriasis only on the palms (23.5% vs. 0%).

Week 16 results in all patients with hand and/or foot psoriasis ($N = 72$)

A significantly greater percentage of adalimumab-treated patients achieved the primary endpoint (hfPGA score of clear or almost clear at week 16) compared with placebo-treated patients (30.6% vs. 4.3%; $P = 0.014$).[25]

Table 1 Baseline demographics and clinical characteristics

| | ITT study population | | Patients with nail psoriasis at baseline and data available through week 16 | | | | |
| | | | NAPSI 50 responders at week 16 | | NAPSI 50 non-responders at week 16 | | Overall (*N* = 31) |
	ADA (*N* = 49)	PBO (*N* = 23)	ADA (*N* = 13)	PBO (*N* = 1)	ADA (*N* = 10)	PBO (*N* = 7)	
Age, years, mean (SD)*	49.0 (11.41)	54.8 (11.40)	56.7 (9.48)	54.0	52.9 (9.24)	56.6 (12.26)	55.4 (9.74)
Age groups, *n* (%)							
<40 years	11 (22.4)	1 (4.3)	1 (7.7)	0	1 (10.0)	0	2 (6.5)
40 to <65 years	34 (69.4)	19 (82.6)	10 (76.9)	1 (100)	8 (80.0)	6 (85.7)	25 (80.6)
≥65 years	4 (8.2)	3 (13.0)	2 (15.4)	0	1 (10.0)	1 (14.3)	4 (12.9)
Male, *n* (%)*	21 (42.9)	8 (34.8)	5 (38.5)	0	5 (50.0)	3 (42.9)	13 (41.9)
White, *n* (%)*	45 (91.8)	20 (87.0)	12 (92.3)	0	9 (90.0)	6 (85.7)	27 (87.1)
Bodyweight (kg), mean (SD) *	90.4 (19.65)	86.9 (18.66)	84.8 (18.82)	76.0	92.9 (22.41)	95.4 (26.76)	89.5 (21.53)
Bodyweight, *n* (%)							
<88 kg	21 (42.9)	14 (60.9)	8 (61.5)	1 (100)	3 (30.0)	3 (42.9)	15 (48.4)
≥88 kg	28 (57.1)	9 (39.1)	5 (38.5)	0	7 (70.0)	4 (57.1)	16 (51.6)
Duration of psoriasis (years), Mean (SD)*	14.9 (16.16)	11.5 (9.94)	20.4 (20.87)	23.0	15.9 (17.11)	14.1 (10.62)	17.6 (17.11)
Duration of psoriasis hands/ feet (years), Mean (SD)*	10.0 (12.36)	7.2 (6.69)	8.6 (8.91)	7.0	14.6 (17.57)	9.8 (7.82)	10.7 (12.01)
Duration of psoriasis hands/ feet, *n* (%)							
<4.7 years	24 (49.0)	12 (52.2)	5 (38.5)	0	5 (50.0)	2 (28.6)	12 (38.7)
≥4.7 years	25 (51.0)	11 (47.8)	8 (61.5)	1 (100)	5 (50.0)	5 (71.4)	19 (61.3)
Psoriatic arthritis, *n* (%)*	7 (14.3)	1 (4.3)	0	0	1 (10.0)	1 (14.3)	2 (6.5)
Evidence of nail involvement, *n* (%)*	28 (57.1)	8 (34.8)	13 (100)	1 (100)	10 (100)	7 (100)	31 (100)
hfPGA, *n* (%)*							
Moderate	37 (75.5)	17 (73.9)	11 (84.6)	1 (100)	5 (50.0)	4 (57.1)	21 (67.7)
Severe	12 (24.5)	6 (26.1)	2 (15.4)	0	5 (50.0)	3 (42.9)	10 (32.3)
Psoriasis of palms and soles, *n* (%)*	39 (79.6)	14 (60.9)	13 (100)	0	8 (80.0)	4 (57.1)	25 (80.6)
ESIF (0–48), Mean (SD)*	25.9 (10.35)	23.7 (9.11)	27.9 (6.53)	13.0	30.7 (12.19)	26.9 (9.39)	28.1 (9.46)
Target nail NAPSI (0–8), Mean (SD)*·†	3.9 (1.95)	3.3 (1.75)	3.2 (2.08)	2.0	4.8 (1.75)	3.4 (1.81)	3.7 (1.99)
Prior systemic therapy, *n* (%)	23 (46.9)	8 (34.8)	7 (53.8)	0	6 (60.0)	5 (71.4)	18 (58.1)
Smoker, *n* (%)	16 (32.7)	9 (39.1)	4 (30.8)	0	4 (40.0)	2 (28.6)	10 (32.3)
PASI score (0–72), mean (SD)*	8.8 (8.23)‡	5.7 (4.52)	11.2 (12.40)	22.2	12.0 (9.51)	3.4 (3.64)	10.0 (10.42)
PASI score (0–72), *n* (%)							
<10 at baseline	37 (75.5)	20 (86.9)	9 (69.2)	0	6 (66.7)‡	6 (85.7)	21 (70.0)‡
≥10 at baseline	11 (22.4)	3 (13.4)	4 (30.8)	1 (100)	3 (33.3)‡	1 (14.3)	9 (30.0)‡
% BSA (0–100), Mean (SD)‡	8.9 (11.88)	5.1 (6.96)	12.6 (17.80)	35.0	13.1 (15.22)	3.6 (3.15)	11.4 (15.24)
DLQI (0–30), Mean (SD)*	11.2 (6.95)	13.3 (7.31)	10.9 (8.67)	12.0	14.5 (6.47)	10.4 (4.89)	12.0 (7.11)
VAS (0–100), Mean (SD)*·§	44.1 (27.63)	55.3 (26.69)	43.1 (23.61)	39.0	53.0 (36.61)	54.7 (19.73)	48.8 (27.10)

ITT, intent to treat population; ADA, adalimumab; PBO, placebo; SD, standard deviation; hfPGA, Physician's Global Assessment of hands and/or feet; ESIF, Erythema, Scaling, Induration and Fissuring scale; NAPSI, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; BSA, body surface area; DLQI, Dermatology Life Quality Index; VAS, visual analogue scale of plaque psoriasis and psoriatic arthritis (PsA) pain.
*Data for ITT population previously reported.[25]
†For patients with nail involvement at baseline.
‡Data missing for one patient.
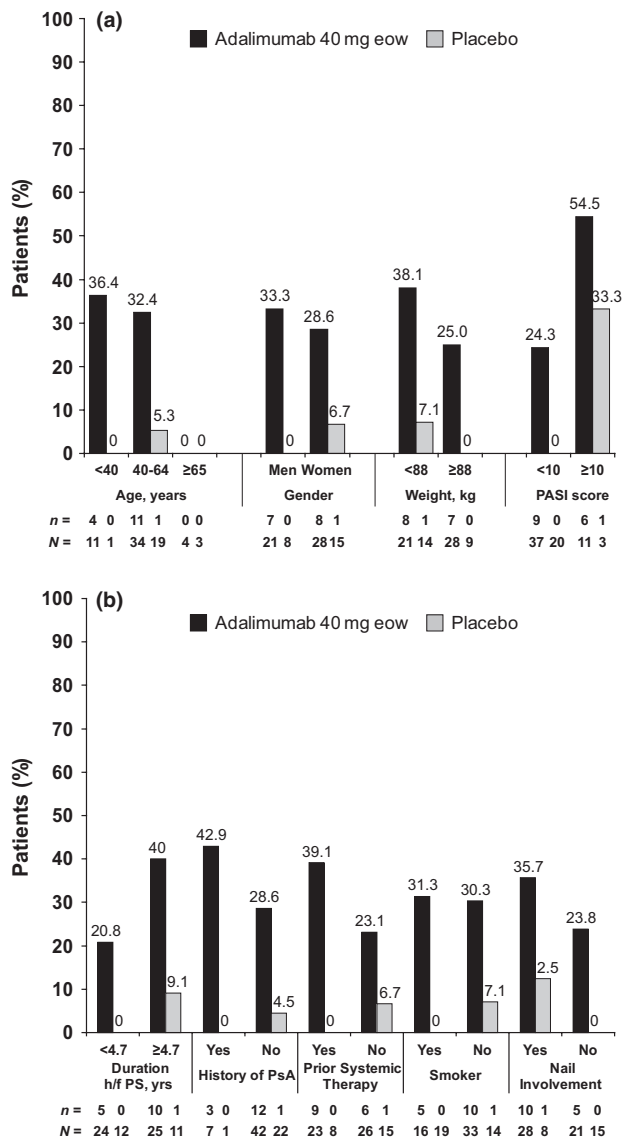§Includes VAS for plaque psoriasis and PsA pain.

Figure 2 Percentages of patients with week 16 hfPGA score of clear or almost clear by baseline characteristics. (a) Age, gender, weight, and psoriasis area severity index (PASI) score. Analysed by non-responder imputation. (b) Duration of hand and/or foot psoriasis, history of psoriatic arthritis (PsA), prior systemic therapy, smoking status, and nail involvement. Analysed by non-responder imputation. *N* = number of patients with the corresponding characteristic at baseline; *n* = number of patients with week 16 hfPGA score of clear or almost clear.

Week 16 results of post hoc analyses by baseline characteristics

In examining the effects of baseline characteristics on the efficacy of adalimumab at week 16, greater percentages of patients treated with adalimumab achieved hfPGA scores of clear or almost

clear at week 16 across all of the evaluated subgroups, compared with placebo-treated patients. The effectiveness of adalimumab treatment was similar across the <40 year and 40–64 year age groups, in which 36.4% and 32.4% of patients, respectively, achieved hfPGA scores of clear or almost clear. None of the patients in the ≥65-year age group, which comprised only 10% of the study population, achieved the primary endpoint in either of the treatment groups (Fig. 2a). Although more women were enrolled in the trial, adalimumab was similarly effective across genders, with 33.3% of men and 28.6% of women achieving hfPGA scores of clear or almost clear at week 16 (Fig. 2a). Analysis of efficacy by baseline weight (median 88 kg) showed that adalimumab-treated patients in the <88 kg subgroup (38.1%) had a clinically significantly greater hfPGA response than those in the ≥88 kg subgroup (25.0%) (Fig. 2a). While all patients in the study had moderate-to-severe disease, a great majority had a PASI score of <10 at baseline. Adalimumab-treated patients in the ≥10 PASI subgroup (54.5%) responded better than patients in the <10 PASI subgroup (24.3%) (Fig. 2a).

Patients treated with adalimumab demonstrated improvements in both shorter- and longer-duration psoriasis of the hands and/or feet (median 4.7 years). Patients treated with adalimumab with longer disease duration (≥4.7 years) showed a better hfPGA response (40.0%) than those with shorter duration (<4.7 years, 20.8%) (Fig. 2b). Adalimumab was also more efficacious in patients with PsA history; 42.9% and 28.6% of patients with or without PsA history, respectively, achieved an hfPGA score of clear or almost clear at week 16 (Fig. 2b).

Nearly half (46.9%) of adalimumab-treated patients included in this analysis had previously used systemic therapies, biologic or non-biologic, for their recalcitrant disease. Nonetheless, adalimumab was efficacious regardless of prior use of such therapies, resulting in a marked difference between the proportion of adalimumab-treated patients who used prior systemic therapies (39.1%) compared with those who did not (23.1%) (Fig. 2b). Adalimumab was also equally effective in smokers (31.3%) and non-smokers (30.3%) (Fig. 2b). Half of the patients in the study had psoriatic nail disease at baseline; 35.7% of patients with nail psoriasis and 23.8% of patients without nail psoriasis achieved an hfPGA score of clear or almost clear at week 16 (Fig. 2b).

Week 16 results in patients with nail psoriasis (*N* = 31)

Among patients with nail psoriasis at baseline, a greater percentage of adalimumab-treated patients (56.5%) compared with placebo-treated patients (12.5%) achieved NAPSI 50 at week 16 (Fig. 3a). Improvement in nail psoriasis at week 16 following treatment with adalimumab is shown in Fig. 4. Further evaluation showed that in adalimumab-treated patients, a greater percentage of NAPSI 50 Responders (61.5%) achieved an hfPGA score of clear or almost clear compared with NAPSI 50 Non-Responders (20.0%) (Fig. 3b). In addition, NAPSI 50
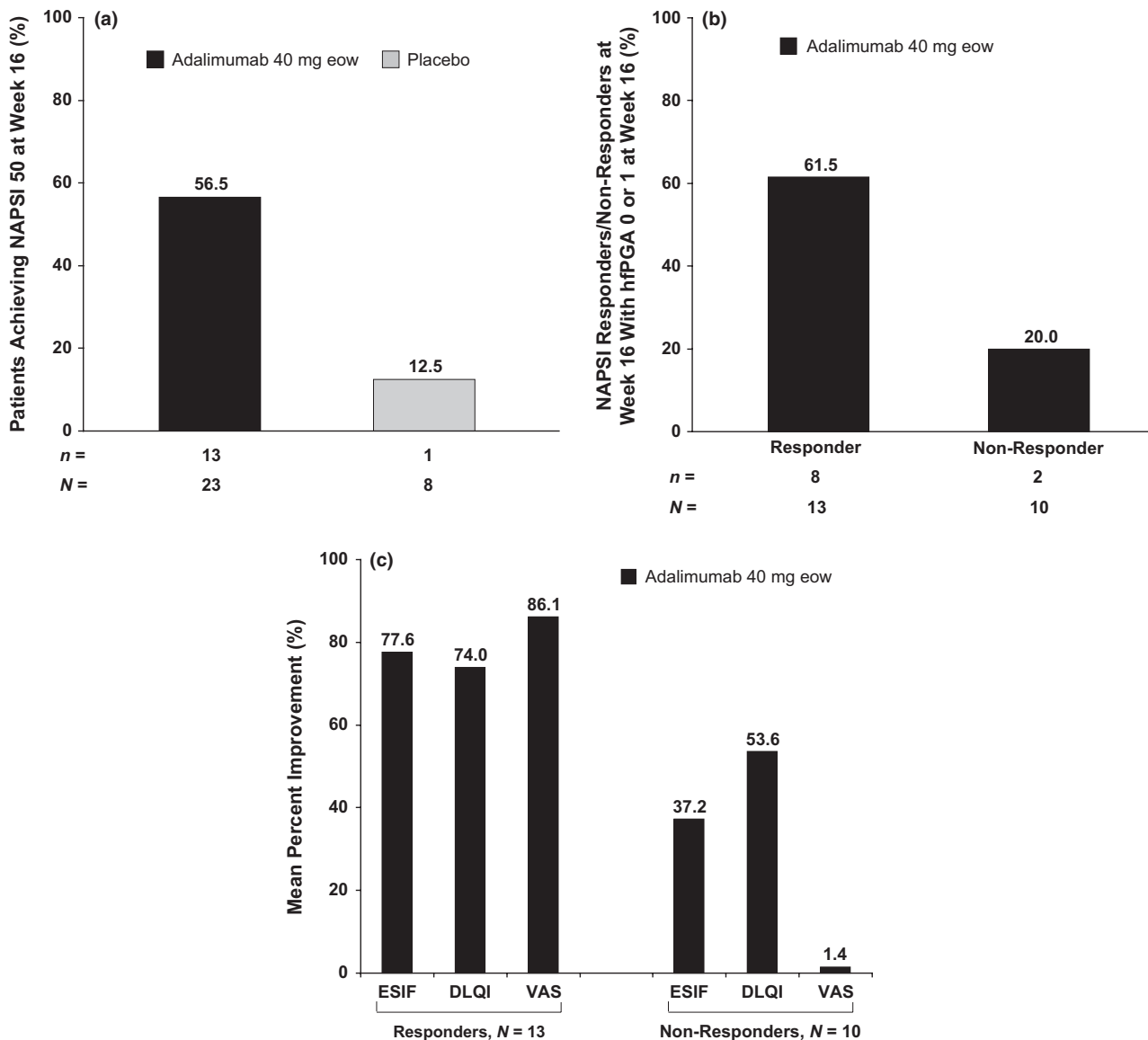
Figure 3 Results for patients by Nail Psoriasis Severity Index (NAPSI) 50 response at week 16. (a) Percent of patients achieving NAPSI 50 at week 16 (Responders), among 31 patients with nail psoriasis at baseline. As observed. (b) Percentages of NAPSI 50 Responders and Non-Responders at week 16 who achieved hfPGA score of clear or almost clear at week 16. Non-responder imputation. (c) Mean percent improvements from baseline in ESIF, DLQI and pain Visual Analogue Scale (VAS) scores for NAPSI 50 Responders and Non-Responders at week 16. Patients receiving PBO were not included in these analyses due to the small number (Responders, $N = 1$; Non-Responders, $N = 7$). ESIF, Erythema, Scaling, Induration and Fissuring; DLQI, Dermatology Life Quality Index; VAS, visual analogue scale. Last observation carried forward.

Responders among adalimumab-treated patients demonstrated greater mean percent improvements in ESIF scores (77.6%) and DLQI scores (74.0%) compared with NAPSI 50 Non-Responders (37.2% and 53.6% respectively) (Fig. 3c). Finally, NAPSI 50 Responders experienced a greater mean reduction in pain VAS score (86.1%) than NAPSI 50 Non-Responders (1.4%) among patients treated with adalimumab (Fig. 3c).

Discussion

This post hoc analysis of the REACH 16-week period demonstrated that overall, patient baseline demographic and disease characteristics did not affect the efficacy of adalimumab for the treatment of chronic plaque psoriasis of the hands and/or feet. Adalimumab showed greater efficacy compared with placebo for the primary efficacy measure (hfPGA score of clear or
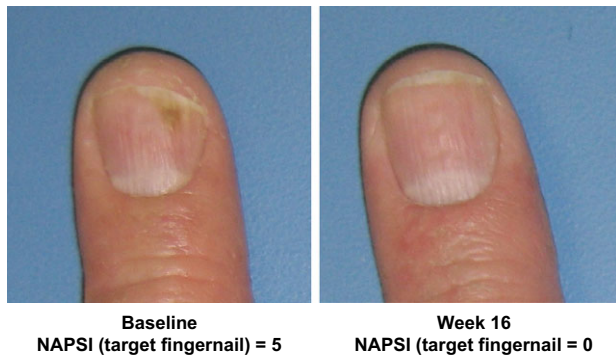
Baseline
NAPSI (target fingernail) = 5

Week 16
NAPSI (target fingernail = 0

Figure 4 Nail psoriasis improvement in one patient. Images from a white, 63-year-old male patient, illustrate improvement in the patient's nail psoriasis (left hand, digit 4) from baseline to week 16 following adalimumab treatment. This patient was previously treated with corticosteroids and infliximab, but did not achieve response with infliximab. Nail Psoriasis Severity Index target fingernail scores range from 0 to 8.

almost clear), regardless of age, gender, weight, PASI score, disease duration, PsA history, prior systemic treatment, smoking history, or nail disease. This is the first analysis of the impact of baseline patient demographic and disease characteristics on the efficacy of a TNF-antagonist for hand and/or foot psoriasis in a double-blind, controlled trial. The clinical responses observed with adalimumab treatment are consistent with the overall results of the placebo-controlled period of REACH[25] and with adalimumab data for the treatment of psoriasis elsewhere on the body. Adalimumab also was efficacious in treating nail disease in patients with hand and/or foot psoriasis; marked improvement in nail disease correlated with significant improvements in skin disease and patient-reported outcomes.

All patients demonstrated improved responses following adalimumab treatment, but greater response was seen in patients of younger age (<65 years), lighter bodyweight (<88 kg), with higher PASI scores (≥10), longer disease duration (≥4.7 years), history of PsA, prior systemic treatment, and nail involvement. Such response differences may be due to the small number of patients included in this analysis. Higher response rates have been reported in younger compared with older (<65 vs. ≥65 years of age) adalimumab-treated patients with moderate-to-severe psoriasis not limited to hands and/or feet.[26] Also, higher response rates in patients of lower weight have been reported in the treatment of psoriasis elsewhere in the body with adalimumab[26] and with other fixed-dose systemic biologics such as alefacept and etanercept.[27] While a higher response rate was noted in patients with PASI score ≥10, this finding does not necessarily indicate that patients with more severe disease responded better to adalimumab compared with those of

less-severe disease; this is based on limitations of the PASI scoring method (compounded weighted averaging of all components), which can hide potential response differences.[28] Patients with longer disease duration characteristically do not respond as well to systemic treatment as those with shorter disease duration. The results of this post hoc analysis, however, suggest that adalimumab is efficacious even in patients with well-established psoriasis of the hands and/or feet. Patients who had received prior systemic therapy also had a better response to adalimumab than patients with no prior systemic treatment, suggesting that patients had not become refractory to adalimumab treatment despite failing other systemic agents, including biologics. In patients with psoriasis, there is an increased prevalence of smoking, which is a known risk factor for incident psoriasis.[3] The response to adalimumab treatment in this analysis did not appear to be affected by patient smoking status, although the small number of patients does not allow a comparison to the general psoriasis population.

Nail involvement can contribute significantly to the burden of illness in patients with hand and/or foot psoriasis. In this study, nail psoriasis at baseline was identified for about half of all patients, which is similar to reports of nail involvement in patient populations with all types of psoriasis, including plaque psoriasis (35–50%).[3] A marked improvement in nail disease after 16 weeks of adalimumab treatment was associated with marked improvements in both skin disease (hfPGA) and in patient-reported outcomes (ESIF, DLQI, pain VAS scores). Several other studies of biologic agents, including TNF inhibitors, for treatment of patients specifically with nail psoriasis have shown concomitant improvements in nail response and psoriatic skin and/or quality of life.[29–31] While NAPSI responses reported in this analysis are only through week 16, further improvements in nail psoriasis and quality of life with longer duration of adalimumab therapy have been reported.[25,32,33] Improvement in nail psoriasis has also been correlated with improvement in moderate-to-severe psoriasis elsewhere in the body following treatment with infliximab, etanercept and adalimumab,[34] and with ustekinumab.[35] Small studies comparing the efficacy of anti-TNF agents in nail psoriasis show that patients treated with infliximab experience greater NAPSI improvement early in therapy compared with etanercept and adalimumab, although the differences among these biologics become less pronounced after 48 weeks of therapy.[30,36]

Few large, prospective randomized studies have been published about the effect of biologic agents on psoriasis of the hands and/or feet. Studies of systemic treatment for hand and/or foot psoriasis are often accomplished as subanalyses of studies in psoriasis generally affecting the entire body and can exclude patients with psoriasis that manifests only on the hands and/or feet when inclusion criteria limits psoriasis involvement to ≥10% of BSA.[4] REACH is one of the first randomized, placebo-controlled trials that focused specifically on chronic plaque

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psoriasis of the hands and/or feet. Other biologics, including etanercept,[13] infliximab,[14,15] ustekinumab,[16,17] alefacept,[18–20] and efalizumab[21,22] (withdrawn from approval due to safety issues) have demonstrated clinical improvement in patients with psoriasis of the hands and/or feet, although the majority of these studies were case studies showing no statistically significant improvements. In a randomized, double-blind, placebo-controlled trial of patients with non-pustular palmoplantar psoriasis, an improved response with infliximab was observed compared with placebo, although the study did not meet its primary efficacy endpoint.[15]

The hfPGA scale used in this study to measure psoriasis severity, employed a 5-point scale (0 = clear; 4 = severe) to evaluate psoriatic lesions on all surfaces of the hand and foot. Despite being a subjective scale, the consistent efficacy observed among adalimumab-treated patients through various secondary endpoints in REACH support the primary endpoint (hfPGA of clear or almost clear) result.[25] In addition, the use of this scale resulted in a more comprehensive assessment of localized psoriasis on the hands and feet, compared with other studies that mostly used the palmoplantar pustular PASI (PPPASI) score,[37,38] or modification thereof.[39] The PPPASI score evaluates only the palmar and plantar aspects of the hands and/or feet, and includes a score for pustules, which replaces the regular PASI score of induration. In a recent clinical trial, a measure similar to the hfPGA was used, but only for palmar and/or plantar evaluation based on a 5-point scale (0 = clear, 5 = most severe).[17]

This study is limited by the small number of patients included in the analyses. As a result, statistical comparisons of responses could not be made between adalimumab and placebo-treatment subgroups for the primary endpoint, or between NAPSI 50 Responders and Non-Responders for improvements in patient-reported outcomes among patients with psoriatic nail involvement at baseline. In addition, patients with pustular psoriasis were excluded from the trial, which limits generalization of the results of this analysis to non-pustular forms of hand and/or foot psoriasis. Finally, the analyses were conducted within a relatively short period of 16 weeks during the double-blind controlled period of the trial.

Conclusions

Psoriasis affecting the hands and/or feet has a negative impact on patient quality of life due to its visibility and resultant disability. Thus, achieving optimal clearance of psoriatic lesions is of high importance for these patients. After 16 weeks, adalimumab was efficacious for the treatment of chronic plaque psoriasis of the hands and/or feet regardless of patient baseline demographics and disease characteristics. Adalimumab was also efficacious in treating nail disease, with a marked improvement in nail psoriasis correlating with significant improvements in both skin disease and patient-reported outcomes.

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