Adalimumab for Treatment of Moderate to Severe Chronic Plaque Psoriasis of the Hands and Feet

Efficacy and Safety Results From REACH, a Randomized, Placebo-Controlled, Double-blind Trial

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Objective: To determine the efficacy, safety, and sustainability of response to adalimumab therapy for moderate to severe chronic plaque psoriasis involving hands and/or feet.

Design: Sixteen-week, randomized, double-blind, placebo-controlled evaluation of adalimumab therapy for moderate to severe chronic plaque psoriasis involving the hands and/or feet with a 12-week open-label extension (Randomized Controlled Evaluation of Adalimumab in Treatment of Chronic Plaque Psoriasis of the Hands and Feet [REACH]).

Setting: Multicenter outpatient study in the United States and Canada.

Participants: Patients with chronic plaque psoriasis on the hands and/or feet with a Physician’s Global Assessment of hands and/or feet (hfPGA) score of “moderate” or above.

Intervention: Patients were randomized 2:1 to adalimumab (80 mg at week 0, then 40 mg every other week starting at week 1) or to matching placebo.

Main Outcome Measure: Percentage of patients achieving an hfPGA score of “clear” or “almost clear” at week 16.

Results: Seventy-two patients (adalimumab [n=49]; placebo [n=23]) were evaluated. Baseline percentages of patients with moderate and severe hfPGA scores were 76% and 24%, respectively, for the adalimumab group and 74% and 26%, respectively, for the placebo group. At week 16, 31% and 4% of patients randomized to adalimumab and placebo, respectively, achieved an hfPGA score of clear or almost clear (P=.01). At week 28, 80% of the hfPGA clear or almost clear response was maintained from week 16 (25% for patients randomized to adalimumab). Adverse events in both groups were generally mild to moderate. In both periods combined, nasopharyngitis (27% and 13% for adalimumab- and placebo-treated patients, respectively) was most frequently reported.

Conclusion: Adalimumab is efficacious and well tolerated for treatment of chronic plaque psoriasis of hands and/or feet, with efficacy largely maintained to 28 weeks.

Trial Registration: clinicaltrials.gov Identifier: NCT00735787


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A number of case reports suggest that biological agents can be effective for patients with hand/or foot involvement; however, published results from randomized controlled trials are limited. In addition, paradoxical reports of psoriasis induced by anti–tumor necrosis factor (TNF) therapy, while uncommon and generally occurring in patients treated for other immunologic disorders, further complicate successful treatment.

Adalimumab is a fully human monoclonal antibody that neutralizes TNF and modulates TNF-related biological responses and is currently approved in the United States and Europe for a variety of therapeutic uses including psoriatic arthritis and moderate to severe chronic plaque psoriasis. Phase 3 trials have demonstrated its efficacy against chronic plaque psoriasis; however, REACH (Randomized Controlled Evaluation of Adalimumab in Treatment of Chronic Plaque Psoriasis of the Hands and Feet) is among the first of its kind to focus specifically on adalimumab for the treatment of psoriasis of the hands and/or feet.

This 16-week, multicenter, randomized, double-blind, placebo-controlled study with an added 12-week open-label period evaluates the efficacy and safety of adalimumab compared with placebo in adults with moderate to severe chronic plaque psoriasis involving hands and/or feet, and examines the sustainability of that response.

Institutional review boards at each participating medical center approved the protocol, and all patients provided written informed consent prior to initiation of any study-related procedures. Patients were men and women 18 years or older diagnosed as having moderate to severe chronic plaque psoriasis of the hands and/or feet for at least 6 months with a Physician’s Global Assessment of the hands and/or feet (hfPGA) score of 3 or higher at baseline and with evidence of psoriatic disease on at least 1 other area of skin outside the hands and/or feet. Patients were excluded if they had received prior treatment with adalimumab or if they had been diagnosed as having palmoplantar pustulosis; however, patients who presented with pustules were not necessarily excluded (unless the pustules were the predominant feature of psoriasis).

Sample size was calculated using nQuery Advisor 6.0 (Statistical Solutions, Saugus, Massachusetts). With a total sample size of 75 patients (2:1 randomization: adalimumab [n = 30] and placebo [n = 25]) and an expected response rate of 40% for adalimumab vs 7% for placebo, the study provides 87% power to detect the treatment difference using a 2-sided Fisher exact test with a type I error α level of .05. The randomization schedule was prepared by the Statistics Department of Abbott GmbH & Co KG, Ludwigshafen, Germany, and the study investigators, study site personnel, and patients remained blinded throughout the study.

All medications received at the time of screening and enrollment or during the study were recorded. Washout periods of 30 days or 5 half-lives (whichever was longer) were required for biological, systemic, and investigational agents prior to baseline. Psoralen and UV-A phototherapy was not allowed within 4 weeks of baseline, and topical therapies on the hands and/or feet (except low- to mid-potency corticosteroids [classes VI and VII]), UV-B phototherapy, and excessive sun exposure or tanning bed use were not allowed within 2 weeks of baseline.

As shown in Figure 1, the study was divided into 2 periods: the placebo-controlled period (week 0-16) and the extension period (week 17-28). During the placebo-controlled period, enrolled patients were randomized in a 2:1 ratio to receive either active adalimumab (initial dose of two 40-mg injections subcutaneously [SC] at week 0 followed by 40 mg SC every other week from week 1 to 15) or matching placebo (2 injections SC at week 0 followed by 1 placebo injection SC every other week from week 1 to 15). At week 16, all patients received 2 injections SC to maintain the blind. Patients from the adalimumab group received 2 placebo injections SC followed by adalimumab, 40 mg SC, every other week from week 17 to 27, and patients from the placebo group received the adalimumab initial dose of 80 mg (two 40-mg injections SC) followed by 40 mg SC every other week from week 17 to 27.

The primary end point of the study was the proportion of patients with an hfPGA score of “clear” or “almost clear” at week 16. Other efficacy measures included the Erythema, Scaling, Induration, Fissuring (ESIF) scale for characterizing palmoplantar disease, Nail Psoriasis Severity Index (NAPSI) score for characterizing nail disease, and psoriasis/psoriatic arthritis pain scores measured by visual analog scale (VAS). Safety measures included adverse events, laboratory data, physical examinations, and vital signs throughout the study.

As given in Table 1, success as determined by hfPGA required a score of 0 or 1, meaning either no signs of plaque psoriasis, or mild erythema and minimal scaling with or without pustules.
riasis ("clear") or just perceptible erythema and scaling ("almost clear"). As given in Table 2, ESIF was assessed by characterizing the severity of each attribute (erythema, scaling, induration, and fissuring) on a 4-point scale for both palms and both soles: clear (0), mild (1), moderate (2), and severe (3). The score for palms plus soles could range from 0 to 48 (4 × 4) and the score for palms or soles could range from 0 to 24 (2 × 4).

For patients with nail involvement, the most severely involved fingernail at baseline was identified as the "target fingernail," and NAPSI scores for that fingernail were assessed again at weeks 8, 16, and 28. NAPSI scores ranged from 0 (no nail disease) to 8 (nail bed and nail matrix disease in each of four nail quadrants.) Pain was assessed using a 100-mm VAS. All patients assessed their pain involving psoriatic plaques and/or psoriatic arthritis within the last week at baseline, week 16, week 28, or early termination.

All statistical analyses were 2-tailed, with the intent-to-treat population and the safety population consisting of all patients who were randomized and received at least 1 dose of study medication. Owing to investigator noncompliance at one study center, it was decided prior to database lock that all patients from that center (n=9) would be excluded from analyses. Thus, the primary efficacy and safety analyses were conducted in the respective analysis populations excluding all patients from that particular site. In the efficacy analyses, the strategy for dealing with missing or incomplete data was nonresponder imputation for categorical data (eg, hfPGA scores) and last observation carried forward for continuous data (eg, percentage improvements in ESIF and NAPSI scores).

### RESULTS

Overall, 81 patients were enrolled at 17 sites in the United States and Canada, and 72 were included in the analyses (see “Methods” section). Forty-nine patients were randomized to adalimumab and 23 to placebo (followed by adalimumab in the open-label extension). As given in Table 3, overall baseline demographics were generally similar between treatment groups. The majority of patients had moderate disease, a relatively low percentage of BSA affected, and relatively high pain scores considering the BSA affected (Table 3).

As given in Table 4, 41 of 49 patients (84%) treated with adalimumab and 18 of 23 patients (78%) treated with placebo completed the double-blind, placebo-controlled portion of the study (weeks 0-16). Of these, 40 of 41 patients (98%) in the adalimumab group and 13 of 17 patients (77%) in the placebo group (switched to adalimumab) completed the open-label extension period (weeks 17-28). The most frequent primary reason for discontinuation during each period was an adverse event.

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**Table 2. Erythema, Scaling, Induration, Fissuring Scale**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Score</th>
<th>Erythema</th>
<th>Scaling</th>
<th>Induration</th>
<th>Fissuring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>0</td>
<td>No sign (residual hyperpigmentation permitted)</td>
<td>No sign</td>
<td>No sign</td>
<td>No sign</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td>Light to dark pink appearance</td>
<td>Fine white pattern of scaling</td>
<td>Slight but definitive palpable height or corny layer, approximately 0.5-mm elevation</td>
<td>Few fissures, superficial</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>Red, but not dark red, appearance</td>
<td>Diffuse, thick; most lesions partly covered</td>
<td>Moderate, definitive induration, approximately 0.75-mm elevation</td>
<td>Multiple fissures, intermediate in depth</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
<td>Deep red to purple appearance</td>
<td>Very thick coverage, all lesions covered</td>
<td>Noticeable height, at least approximately 1-mm elevation</td>
<td>Numerous and/or deep fissures</td>
</tr>
</tbody>
</table>

**Table 3. Baseline Demographics and Clinical Characteristics of Patients With Chronic Plaque Psoriasis on the Hands and/or Feet**

<table>
<thead>
<tr>
<th>Demographic/Characteristic</th>
<th>Adalimumab Group (n=49)</th>
<th>Placebo Group (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, ya</td>
<td>49.0 (11.4)</td>
<td>54.8 (11.4)</td>
</tr>
<tr>
<td>Male, No./total (%)</td>
<td>21/49 (43)</td>
<td>8/23 (35)</td>
</tr>
<tr>
<td>White, No./total (%)</td>
<td>45/49 (92)</td>
<td>20/23 (87)</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>90.4 (19.7)</td>
<td>86.9 (18.7)</td>
</tr>
<tr>
<td>Duration of psoriasis, ya</td>
<td>14.9 (16.2)</td>
<td>11.5 (9.9)</td>
</tr>
<tr>
<td>Duration of psoriasis hands/feet, ya</td>
<td>10.0 (12.4)</td>
<td>7.2 (6.7)</td>
</tr>
<tr>
<td>Psoriatic arthritis, No. (%)</td>
<td>7/49 (14)</td>
<td>1/23 (4)</td>
</tr>
<tr>
<td>Evidence of nail involvement, No. (%)</td>
<td>20/49 (57)</td>
<td>6/23 (26)</td>
</tr>
<tr>
<td>ESIF score (range, 0-48)</td>
<td>25.9 (10.4)</td>
<td>23.7 (9.1)</td>
</tr>
<tr>
<td>ESIF score, score (range, 0-24)</td>
<td>13.4 (6.2)</td>
<td>13.9 (5.2)</td>
</tr>
<tr>
<td>ESIF score, score (range, 0-24)</td>
<td>12.5 (7.3)</td>
<td>9.8 (8.3)</td>
</tr>
<tr>
<td>Target nail NAPSI, score (range, 0-8)</td>
<td>3.9 (2.0)</td>
<td>3.3 (1.8)</td>
</tr>
<tr>
<td>PASI score (range, 0-72)</td>
<td>8.8 (8.2)</td>
<td>5.7 (4.5)</td>
</tr>
<tr>
<td>BSA, %</td>
<td>8.9 (11.9)</td>
<td>5.1 (7.0)</td>
</tr>
<tr>
<td>DLQI score (range, 0-30)</td>
<td>11.2 (7.0)</td>
<td>13.3 (7.3)</td>
</tr>
<tr>
<td>VAS plaque psoriasis and psoriatic arthritis pain (range, 0-100)</td>
<td>44.1 (27.6)</td>
<td>55.3 (26.7)</td>
</tr>
</tbody>
</table>

Abbreviations: BSA, body surface area; DLQI, dermatology life quality index; ESIF, Erythema, Scaling, Induration, Fissuring scale; hfPGA, Physician’s Global Assessment of hands and/or feet; NAPSI, nail psoriasis severity index; PASI, psoriasis area and severity index.

- Data are given as mean (SD).
- Among patients with nail involvement at baseline.
- Adalimumab (n=28); placebo (n=8).
- Adalimumab (n=48).
- Placebo (n=22).
Efficacy Results

For the primary efficacy analysis at week 16, the proportion of patients achieving an hPGA score of clear or almost clear was significantly higher for adalimumab-treated patients (15 of 49 [31%]) compared with placebo-treated patients (1 of 23 [4%]) (P = .01) (Figure 2). At week 28, 80% of the hPGA clear or almost clear response was maintained from week 16, with 25% (12 of 49) of the patients who began the study with adalimumab having an hPGA of clear or almost clear at week 4, compared with 13% (3 of 23) for placebo-treated patients (1 of 23 [4%]) (P = .01) (Figure 2). At week 28, the proportions of patients achieving Physician’s Global Assessment of hands and/or feet scores of “clear,” “almost clear,” or “mild” at weeks 2, 4, 8, 12, 16, 20, 24, and 28 for all treatment groups (placebo, adalimumab, and placebo switched to adalimumab at week 16) Intent-to-treat population; analyzed by nonresponder imputation.

Figure 2. Percentages of patients achieving Physician’s Global Assessment of hands and/or feet scores of “clear” or “almost clear” from week 0 to week 16 and from week 0 to week 28 (following switch from placebo to adalimumab at week 16). Intent-to-treat population; analyzed by nonresponder imputation.

Figure 3. Percentages of patients achieving Physician’s Global Assessment of hands and/or feet scores of “clear,” “almost clear,” or “mild” at weeks 2, 4, 8, 12, 16, 20, 24, and 28 for all treatment groups (placebo, adalimumab, and placebo switched to adalimumab at week 16). Intent-to-treat population; analyzed by nonresponder imputation.

For patients who began the study with adalimumab and for patients who were switched to adalimumab from placebo, respectively. The percentages of patients achieving greater than 50% improvement in ESIF (ESIF 50) at week 16 were 43% (21 of 49) and 17% (4 of 23) (P = .04) for adalimumab- and placebo-treated patients, respectively. At week 28, the percentages achieving ESIF 50 were 39% (19 of 49) and 13% (3 of 23) for patients who began the study with adalimumab and for patients who were switched to adalimumab from placebo, respectively.

The mean percentage improvement in total ESIF score relative to baseline demonstrated consistent improvement over time: 30%, 41%, and 48% at weeks 4, 16, and 28, respectively, for patients who began the study with adalimumab compared with 8%, 21%, and 26% for patients who were switched to adalimumab from placebo. In patients with palmar involvement, adalimumab treatment was associated with a mean percentage ESIF improvement of 47% at week 16, compared with 20% for placebo treatment (P = .01). At week 28, the mean percentage ESIF improvement for palmar disease was 53% for patients who began the study with adalimumab and 30% for patients who
were switched to adalimumab from placebo. In patients with plantar involvement, adalimumab treatment was associated with a mean percentage ESIF improvement of 41% at week 16, compared with 35% for placebo treatment ($P = .67$). At week 28, mean percentage ESIF improvement for plantar disease was 43% for patients who began the study with adalimumab and 36% for patients who were switched to adalimumab from placebo.

**Figure 4** depicts the left and right palms of a 59-year-old white woman randomized to adalimumab with psoriasis of the hands in whom previous therapy with topical corticosteroids had failed and acitretin was intolerable. The patient experienced an improvement in hfPGA score from “severe” at baseline to “mild” at week 16. Also, ESIF scores improved from baseline to week 16 on each palm, with an ESIF score of 8 reduced to 5 on the left palm (Figures 4A and B) and an ESIF score of 9 reduced to 4 on the right palm (Figures 4C and D).

Among the subset of enrolled patients with psoriatic nail disease, adalimumab-treated patients achieved significantly higher mean percentage NAPSI improvement compared with placebo-treated patients (50% vs 8%; $P = .02$) at week 16. Once switched to adalimumab, patients from the placebo group improved to 38% at week 28, while patients who began the study with adalimumab continued to improve to 54%.

Pain is a prominent symptom for patients with hand and/or foot psoriasis; therefore, improvement in pain VAS scores is a meaningful measure of therapeutic success. At week 16, mean pain scores for adalimumab-treated patients were significantly lower compared with mean pain scores for placebo-treated patients (26.6 and 43.4, respectively; $P = .048$). Among patients with a greater than zero pain score at baseline, mean percentage improvements from baseline to week 16 were 31% for adalimumab and 9% for placebo ($P = .39$). At week 28, mean pain scores for patients who began the study with adalimumab and patients who were switched to adalimumab from placebo were 27.5 and 39.8, respectively, and among patients with a greater than zero pain score at baseline, mean percentage improvements from baseline to week 28 were 35% for patients who began the study with adalimumab and 30% for patients who were switched to adalimumab from placebo.

**SAFETY**

Overall, treatment throughout the study was well tolerated. No reports of death, serious infections, tuberculosis, demyelinating disease, lupuslike syndrome, lymphoma, or nonmelanoma skin cancer were reported. During both periods combined, the most frequently reported adverse events were nasopharyngitis, headache, diarrhea, and injection site reaction; however, the majority of adverse events were mild to moderate in severity.

During the placebo-controlled period, 63% (31 of 49) of patients in the adalimumab group and 70% (16 of 23) of patients in the placebo group experienced at least 1 adverse event; however, none of the patients in the adalimumab group and 1 patient (4%) from the placebo group experienced a serious adverse event (breast cancer) (Table 5). Discontinuations due to adverse events were reported for 3 patients in the adalimumab group (pain in an extremity and paraesthesia, increases in alanine aminotransferase and aspartate aminotransferase levels, and urticaria) and 2 patients in the placebo group (gastroesophageal reflux, chest pain and dyspnea, and breast cancer). The incidence of symptomatic psoriasis flare was low (2 of 49 patients [4%] in the adalimumab group and 2 of 23 patients [9%] in the placebo group).

Of the 49 patients who began the study with adalimumab and the 23 patients who were switched to adalimumab from placebo, 21 (43%) and 9 (39%), respectively, experienced at least 1 adverse event during the extension period. Two patients (4%) who began the study with adalimumab experienced a serious adverse event: 1 patient with a history of cigarette smoking, hypertension, and diabetes experienced acute myocardial infarction and pulmonary edema (coded as congestive heart failure) (Table 5), and 1 patient experienced gastrointestinal hemorrhage 6 days after colonoscopy and polypectomy (Table 5). No patients who were switched to adalimumab from placebo experienced a serious ad-
verse event. No patients who began the study with adalimumab discontinued therapy because of an adverse event during the extension period; however, 2 patients who were switched to adalimumab from placebo discontinued because of adverse events (swollen tongue, pruritus plus urticaria, and urticaria) (Table 5).

The present study demonstrates that adalimumab is efficacious in the treatment of adults with moderate to severe chronic plaque psoriasis involving hands and/or feet, with improvement observed by 4 weeks and sustained to 28 weeks. At week 16, a significantly higher proportion of adalimumab-treated patients achieved clinically relevant success (hfPGA clear or almost clear rate of 31%) compared with placebo-treated patients (hfPGA clear or almost clear rate of 4%) (P = .01). These primary efficacy results were supported by secondary efficacy results including ESIF, NAPSI, and pain VAS scores. The percentage of patients achieving an hfPGA score of clear or almost clear is substantially lower than the percentage of patients achieving a PGA score of clear or minimal in other clinical trials of adalimumab for psoriasis, but this might be expected given the known difficulty in treating hand and/or foot psoriasis and the differences between the hfPGA and PGA scales. In addition, consistent with other adalimumab studies for the treatment of chronic plaque psoriasis elsewhere on the body, the adverse event pro-

Table 5. Adverse Events of Adalimumab vs Placebo

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Adalimumab Group (n=49)</th>
<th>Placebo Group (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weeks 0-16</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any adverse event</td>
<td>31 (63)</td>
<td>16 (70)</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>0</td>
<td>1 (4)*</td>
</tr>
<tr>
<td>Infectious adverse event</td>
<td>17 (35)</td>
<td>10 (44)</td>
</tr>
<tr>
<td>Malignant diseases, excluding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lymphoma</td>
<td>0</td>
<td>1 (4)*</td>
</tr>
<tr>
<td>Opportunistic infections, excluding</td>
<td>1 (2)b</td>
<td>0</td>
</tr>
<tr>
<td>tuberculosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic eventsc</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>2 (4)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal</td>
<td>3 (6)d</td>
<td>2 (9)h</td>
</tr>
<tr>
<td><strong>Weeks 17-28</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any adverse event</td>
<td>21 (43)</td>
<td>9 (39)</td>
</tr>
<tr>
<td>Serious adverse event</td>
<td>2 (4)1g</td>
<td>0</td>
</tr>
<tr>
<td>Infectious adverse event</td>
<td>12 (25)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1 (2)1i</td>
<td>0</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal</td>
<td>1 (2)</td>
<td>2 (9)h</td>
</tr>
</tbody>
</table>

a Breast cancer.  
b Oral candidiasis.  
c Events that are serious or led to permanent discontinuation only.  
d Pain in an extremity and paresthesia, increases in alanine aminotransferase and aspartate aminotransferase levels, and urticaria.  
e Gastroesophageal reflux, chest pain and dyspnea, and breast cancer.  
f Acute myocardial infarction: 1 (2%).  
g Gastrointestinal hemorrhage: 1 (2%).  
h Swollen tongue, pruritus plus urticaria, and urticaria.

COMMENT

The proportion of patients who were switched to adalimumab from placebo with an hfPGA of clear or almost clear at week 28 was anomalously lower (9%) compared with the proportion of patients who began the study with adalimumab (25%). Interestingly, the percentage of patients who began the study with adalimumab and the percentage who were switched to adalimumab from placebo were similar at week 24 for an hfPGA score of clear or almost clear (25% vs 22%, respectively). While the reason for this anomaly is unknown, the shorter duration of adalimumab treatment for patients initially randomized to placebo, the relatively small number of patients, the high dropout rate, and/or the imbalance in treatment allocation (as evidenced by baseline differences between the 2 groups) are possible contributing factors.

The ESIF results for patients who began the study with adalimumab demonstrated a rapid and sustained response compared with patients who began the study with placebo, and the percentages of patients achieving greater than 75% and 50% improvements in ESIF scores relative to baseline for patients who began the study with adalimumab were significantly better than for those who began the study with placebo. Psoriatic lesions on the palms were noted to respond better to treatment than lesions on the soles. While the explanation for this finding is unclear, possibilities include the increased skin thickness of the soles compared with the palms, which could limit penetration of concomitant topical drugs, or the fact that feet are likely subjected to greater daily trauma than hands that results in more frequent and sustained psoriatic outbreaks due to the Koebner phenomenon.

Because a high proportion of patients with hand and/or foot psoriasis have concomitant nail disease, an optimal therapy should improve psoriatic nails; however, despite modestly effective available therapies for this subset, no gold standard of treatment has been definitively identified. Nail psoriasis affects up to 35% of patients with cutaneous psoriasis and up to 90% of patients with psoriatic arthritis. In the present study, target fingernail NAPSI scores improved relative to baseline in patients who be-

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gan the study with adalimumab (50% and 54% at weeks 16 and 28, respectively). Patients who were switched to adalimumab from placebo at week 16 demonstrated an improvement in NAPSI as well.

As mentioned previously, the mean baseline VAS scores related to pain associated with psoriatic plaques and/or psoriatic arthritis in this study were high relative to the percentage of BSA affected, suggesting a relatively high level of pain in this population. Based on mean VAS scores at week 16, which demonstrated a statistically significant difference between adalimumab and placebo groups (P = .048), the data presented herein suggest that adalimumab may improve symptoms as well as signs of psoriasis of the hands and/or feet.

Adverse events in this study were generally mild to moderate, with nasopharyngitis occurring most frequently in both treatment groups (27% and 13% for adalimumab- and placebo-treated patients, respectively). Severe adverse events were observed infrequently and were not those characteristically associated with TNF inhibition. Importantly, the incidence of symptomatic psoriasis flare with adalimumab treatment in this study was low, even though TNF antagonist–induced psoriasis or worsening of psoriasis on the palms or soles has been reported in patients treated with TNF inhibitors for other immunologic disorders.10-13

A recent review highlighted the paucity of randomized controlled trials in assessing treatment options for palmoplantar psoriasis and proposed a possible treatment algorithm in which first-line treatment is topical therapy of potent corticosteroids combined with either calcipotriol or tazarotene, followed by phototherapy (either topical psoralen plus UV-A or narrowband UV-B) or systemic therapies such as oral retinoids, methotrexate, biological agents, or cyclosporin.23 Data supporting this algorithm are largely derived from case reports or series, open-label studies, or studies of palmoplantar pustulosis. A placebo-controlled study of efalizumab demonstrated that this agent was significantly effective in the treatment of hand and/or foot psoriasis, with 33% of patients achieving an hfPGA score of clear or almost clear,24 but efalizumab has been withdrawn from use. Smaller controlled trials with etanercept25 and infliximab26 also suggest some benefit from using these agents for this subset, although both studies failed to achieve their primary end points. The present study augments the available literature on treatment of this psoriasis subtype by providing data from a randomized, double-blinded, placebo-controlled trial in which the active therapy significantly improved disease. Accordingly, adalimumab is an appropriate alternative for patients with moderate to severe psoriasis of the hands and/or feet who are appropriate candidates for systemic therapy.

Limitations of the present study include its small patient enrollment relative to other trials of psoriasis elsewhere on the body, its lack of long-term efficacy and safety data, and its relatively high dropout rate, perhaps due to the exclusion of topical agents other than low- to mid-potency corticosteroids. In addition, the study was not restricted to patients with psoriasis of the hands and/or feet exclusively, and it did not characterize what percentage of patients did or did not have pustules at baseline, thus limiting any conclusions as to the efficacy of adalimumab in pustular or mixed forms of palmoplantar psoriasis. Accurate diagnosis of hand and/or foot psoriasis can be problematic owing to the variety of its morphologic patterns.2,27,28 It is therefore possible that some enrolled patients may not have had psoriasis on the hands or feet or that some patients had coincidental psoriasis and another hand dermatitis. Lastly, distinguishing among the 5 categories of the hfPGA scale is subjective and can be affected by interphysician variability; however, the consistent efficacy demonstrated by adalimumab-treated patients with a variety of different secondary end points supports the conclusions derived from the primary end point.

Notwithstanding these limitations, our findings regarding the safety, efficacy, and sustainability of adalimumab for treatment of chronic, plaque psoriasis of the hands and/or feet are consistent with the large body of clinical data regarding adalimumab for treatment of chronic plaque psoriasis elsewhere on the body. Despite the relatively small BSA affected, patients with psoriasis of the hands and/or feet may experience substantial impairment in quality of life, including a high level of pain associated with the disease and a reduced ability to perform simple daily tasks. This study is among the first of its kind to analyze this subset and to demonstrate that adalimumab is a useful agent for treatment of moderate to severe chronic plaque psoriasis of the hands and/or feet.

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REFERENCES


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