

EXTENDED REPORT

Adalimumab improves joint-related and skin-related functional impairment in patients with psoriatic arthritis: patient-reported outcomes of the Adalimumab Effectiveness in Psoriatic Arthritis Trial

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Objective: To evaluate the effects of adalimumab on patient-reported outcomes of joint-related and skin-related functional impairment, health-related quality of life, fatigue and pain in patients with psoriatic arthritis (PsA).

Methods: Patients with moderately- to severely- active PsA were treated with adalimumab, 40 mg, every other week, or placebo, in this 24-week, randomised, controlled trial. Patient-reported outcomes included the Health Assessment Questionnaire Disability Index (HAQ DI), Short-Form 36 Health Survey (SF-36), the Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue) Scale and the Dermatology Life Quality Index (DLQI).

Results: Adalimumab (n=151) and placebo (n=162) groups were comparable with respect to baseline demographics and disease severity. Significant changes from baseline in HAQ DI were reported for adalimumab v placebo (−0.4 v −0.1, p<0.001) at both 12 and 24 weeks. At week 24, significant improvements in the SF-36 domains of physical functioning, role-physical, bodily pain, general health, vitality and social functioning, as well as the physical component summary score, were observed for adalimumab versus placebo (p<0.01). These reported changes in HAQ DI and SF-36 were also clinically important. Significantly more patients treated with adalimumab had complete resolution of functional loss (HAQ DI=0) and dermatological-related functional limitations (DLQI=0) compared with placebo at weeks 12 and 24 (p≤0.001). Adalimumab led to significantly greater improvements in FACIT-Fatigue scores, pain scores, and disease activity measures versus placebo at 12 and 24 weeks (p<0.001 for all).

Conclusions: Adalimumab improved physical-related and dermatological-related functional limitations, HRQOL, fatigue and pain in patients with PsA treated for 24 weeks.

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that affects 0.3–1% of the general population and from 5% to >30% of patients with psoriasis, depending on the population studied.¹ The onset of PsA usually occurs from 30 to 55 years of age.^{1–3} Despite the small percentage of the general population affected, PsA has a marked effect on healthcare utilisation and the functional ability of patients. The disability and morbidity associated with PsA are substantial, and mortality is increased compared with the general population.^{4–7} In the US, the direct costs of caring for patients with psoriasis and PsA (including hospitalisations, doctors' visits, and drug and non-drug treatments) may be nearly US\$650 million/year.⁸ Assessments of direct costs do not quantify the functional impairment associated with PsA, including pain and emotional effect on quality of life (QOL) and work-related disability. A recent study showed a statistically significantly lower rate of employment for patients with PsA and an increased relative risk for unemployment with longer disease duration.⁹ Previous studies that have evaluated patient-reported outcomes, such as the generic health status measure, the Short-Form 36 Health Survey (SF-36) and the disease-specific Health Assessment Questionnaire Disability Index (HAQ DI), have found that PsA reduces QOL compared with that of the general population and its effect is similar to that of patients with rheumatoid arthritis.^{10–13}

Patients with PsA are primarily afflicted with progressive joint damage and skin-related physical effects that can severely affect functional ability during their productive years.^{4 6 14–16} In one study, Husted *et al*¹⁷ estimated that 72% of patients with

PsA experienced either enduring physical disability or fluctuating states of physical disability during a 10-year period. Although peripheral joint damage may be greater in patients with rheumatoid arthritis than in PsA, degrees of functional limitations and disability are often similar.¹⁸ However, Rahman *et al*¹⁹ showed no difference in radiological scores between patients with rheumatoid arthritis and those with PsA. Psoriasis also causes marked physical pain and disfigurement that may contribute to the emotional and psychosocial effects of PsA.^{16 20} One study found that 39% of patients with PsA indicated that the disease is a huge problem in everyday life.²¹ Therefore, effective treatments may considerably improve the QOL of patients with PsA.

In clinical trials, tumour necrosis factor (TNF) antagonists have shown marked improvements in skin and joint manifestations of PsA, and they have been shown to markedly improve patients' QOL.²² Adalimumab (HUMIRA; Abbott, Abbott Park, Illinois, USA) is a fully human, monoclonal antibody that binds to TNF with great specificity and affinity. It has shown

Abbreviations: ACR, American College of Rheumatology; ADEPT, Adalimumab Effectiveness in Psoriatic Arthritis Trial; BSA, body surface area; DLQI, Dermatology Life Quality Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy—Fatigue; HAQ DI, Health Assessment Questionnaire Disability Index; MCID, minimum clinically-important difference; MCS, mental component summary; MTX, methotrexate; PASI, Psoriasis Area and Severity Index; PCS, physical component summary; PsA, psoriatic arthritis; QOL, quality of life; SF-36, Short-Form 36 Health Survey; TNF, tumour necrosis factor

beneficial effects in clinical trials on the signs and symptoms and psoriatic skin lesions of PsA.²²

ADEPT (Adalimumab Effectiveness in Psoriatic Arthritis Trial), a 24-week, phase III randomised, controlled trial, was conducted to evaluate the efficacy and safety of adalimumab in patients with moderately to severely active PsA.²² Results from ADEPT showed significant responses for both 20% improvement in the American College of Rheumatology response (ACR20) and 75% improvement in the Psoriasis Area and Severity Index (PASI 75) versus placebo at 12 and 24 weeks ($p < 0.001$ for both).²² In addition, adalimumab was associated with significant inhibition of radiographic progression versus placebo at 24 weeks ($p < 0.001$). Adalimumab was generally well tolerated, with a similar incidence of adverse events compared with placebo.

Although clinical measures such as ACR20 or PASI 75 are important end points in clinical trials of PsA, to a patient, the primary goal of treatment is to reduce pain, increase the ability to function, reduce fatigue and improve well-being, allowing them to carry out normal daily activities. For this reason, it is important to also assess response to treatment from a patient's perspective through the use of disease-specific measures, as well as comprehensive generic health status measures. This paper reports on the effect of adalimumab on physical and dermatological-related functional limitations in PsA, as well as health-related quality of life (HRQOL), fatigue and pain, as quantified by well-established, disease-specific measures and generic, patient-reported outcome measures assessed during the ADEPT trial. The clinical relevance of the established patient-reported outcomes in PsA is also dealt with.

METHODS

A detailed description of the methods and results for the efficacy and safety outcomes of ADEPT has been published previously.²² ADEPT was a 24-week, randomised, double-blind, parallel-group, placebo-controlled trial of adalimumab in the treatment of patients with moderately to severely active PsA. Before randomisation, patients were stratified according to methotrexate (MTX) use (yes/no) and degree of psoriasis involvement at baseline ($\geq 3\%$ body surface area (BSA) or $< 3\%$ BSA). Treatment consisted of subcutaneous injections of adalimumab 40 mg or placebo every other week. Joint assessments were completed for all patients randomised to treatment. Skin assessments were conducted in the subgroup of patients with $\geq 3\%$ BSA affected by psoriasis. Study visits were conducted at baseline, weeks 2 and 4, and then every 4 weeks until week 24. After 12 weeks, patients who failed to have at least a 20% decrease in both swollen and tender joint counts on two consecutive visits could receive rescue treatment with corticosteroids or disease-modifying antirheumatic drugs. All patients who completed the double-blind study were eligible for long-term treatment in an ongoing, open-label extension study. The disposition of patients in the ADEPT trial has been previously reported.²²

Patient-reported outcomes

Well-established, validated patient-reported outcome measures were used in this trial. All assessments were made at weeks 12 and 24. Clinical relevance was assessed on the basis the minimum clinically-important difference (MCID), expressed as a value or range established for each patient-reported outcome measure, and considered the smallest change in score observed in a particular patient to be clinically important.

Health Assessment Questionnaire Disability Index

To determine physical function and functional loss, the HAQ DI was used.²³ The HAQ DI was validated in PsA by Husted *et al*^{20–24} for face and content validity, and for responsiveness to disease

state. Complete resolution of joint-related functional loss was defined as a HAQ DI score = 0. For PsA, the MCID for HAQ DI has been defined as ± 0.3 change from baseline on the basis of a patient's assessment and 0.4 based on a standard error of measurement (SEM).^{25–26} The authors recommended using the 0.3 MCID for characterising within-treatment group changes and the 0.4 MCID for within-patient changes. In this study, the MCID for within-treatment group changes (0.3) was used to evaluate clinically-important changes in the HAQ DI.

Short-Form 36 Health Survey

To determine functional status and general well-being, the SF-36 was used.²⁷ The SF-36 has been validated in several chronic diseases, including PsA, and has shown responsiveness over time.^{12–24, 28} The SF-36 physical component summary (PCS) and mental component summary (MCS) scores were also derived.^{12–27} Clinically meaningful changes in SF-36 scores have not been defined in patients with PsA; however, in those with rheumatoid arthritis, a 2.5–5-point change from baseline has been established as the MCID for the PCS and MCS, and a 5–10-point change from baseline has been established for the SF-36 domains, these ranges were used in this study.²⁹

Functional Assessment of Chronic Illness Therapy—Fatigue scale

To assess fatigue in PsA patients, the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue) Scale was used (<http://www.facit.org>).³⁰ The FACIT-Fatigue has been validated in the general population, in patients with rheumatoid arthritis, and, most recently, in patients with PsA.^{30–33} The MCID for FACIT-Fatigue in patients with rheumatoid arthritis was determined to be a 3–4-point change³⁰; this MCID was used in evaluating clinically meaningful changes in fatigue for patients with PsA.

Patient's assessment of pain

During the course of the ADEPT Study, patients self-assessed their pain on a weekly basis using a horizontal visual analogue scale ranging from 0 mm (no pain) to 100 mm (pain as bad as it could be).

Patient's global assessment of disease activity

To measure patients' general assessment of their disease, patients assessed their disease activity (ie, how they were doing) within a 24-h period using a visual analogue scale ranging from 0 mm (very well) to 100 mm (very poorly).

Dermatology Life Quality Index

To assess dermatological-related functional limitations in the subset of patients with $\geq 3\%$ BSA affected by psoriasis, the Dermatology Life Quality Index (DLQI) was used. The DLQI is a 10-item questionnaire assessing the effect of psoriasis on daily activities and level of disability over the previous 7 days.³⁴ DLQI questions are grouped into six subcategories: symptoms and feelings; daily activities; leisure; work/school; personal relationships; and treatment.³⁴ The reliability and validity of the DLQI has been shown previously.^{5–34–37} DLQI overall scores range from 0 to 30, with higher scores indicating a more impaired functional status. The MCID for the DLQI in patients with PsA has not been established, but in psoriasis it has been estimated to be a five-point improvement and was used in this study.^{38–40} Complete resolution of dermatological-related functional loss was defined as a DLQI score = 0.

Statistical analysis

All patients who received at least one dose of study treatment were included in the data analysis (intention-to-treat analysis).

The percentages of patients achieving ACR20 or PASI 75 responses were assessed for treatment differences using the Cochran–Mantel–Haenszel mean score test adjusted for MTX use (yes/no) and extent of psoriasis at baseline ($\geq 3\%$ BSA or $< 3\%$ BSA). Non-responder imputation was used, in which patients who discontinued participation in the study or had missing data were counted as non-responders. Patients who received rescue treatment were considered to be non-responders at the time that rescue treatment was initiated.

For continuous variables (HAQ DI, SF-36, FACIT-Fatigue, patient's assessment of pain, patient's global assessment of disease activity and DLQI), changes from baseline were compared between treatment groups using analysis of variance. The analysis of variance model included factors for treatment group and baseline MTX use/extent of psoriasis (yes/ $\geq 3\%$ BSA, yes/ $< 3\%$ BSA, no/ $\geq 3\%$ BSA, no/ $< 3\%$ BSA). All statistical tests were two sided, with an α -level of 0.05. Last observation carried forward analysis was used.

RESULTS

This trial was conducted at 50 sites in North America and Europe. A total of 315 patients were randomised to treatment, of which 313 were treated (placebo, $n = 162$; adalimumab, $n = 151$). Approximately 92% of patients from each group completed the 24-week treatment period (placebo, $n = 149$; adalimumab, $n = 140$). Baseline demographics and disease characteristics were consistent with moderate to severe PsA and were comparable between treatment groups ($p = \text{NS}$; table 1).²²

Patient-reported outcomes

Health Assessment Questionnaire Disability Index

Baseline HAQ DI scores were similar between treatment groups ($p = \text{NS}$; table 1). The mean changes from baseline in the HAQ DI at both weeks 12 and 24 were -0.4 for adalimumab and -0.1 for placebo ($p < 0.001$; table 2). For patients treated with adalimumab, the improvement was clinically meaningful, as defined by a

> 0.3 -point improvement. Approximately twice the number of patients receiving adalimumab surpassed the MCID of -0.3 for improvement in HAQ DI compared with placebo at weeks 12 and 24 (table 3). At week 12, 33.8% of patients treated with adalimumab versus 14.3% with placebo ($p < 0.001$) had complete resolution of functional loss (HAQ DI scores = 0; table 3). Results were similar at week 24 (34.0% v 13.1%, respectively; $p < 0.001$; table 3).

Short-Form 36 Health Survey

At baseline, the SF-36 PCS was comparable between treatment groups (table 1) and markedly reduced compared with US population norms (33.3% v 50.0%, respectively).²⁸ After 12 weeks, patients treated with adalimumab had significant improvements from baseline in six of the eight SF-36 domains (physical functioning, role-physical, bodily pain, general health, vitality and social functioning; table 2). However, changes in all eight domains were deemed to be clinically important, achieving or surpassing the MCID of a 5–10-point change. After 24 weeks, for patients treated with adalimumab versus placebo, the mean changes from baseline for seven of the eight domains were significant (table 2). Patients treated with adalimumab reached clinically-important improvements in seven of the eight domains, surpassing the upper limit of the MCID (10-point change), whereas patients treated with placebo did not show clinically-important changes ≥ 10 points in any domain (table 2). Compared with placebo, there were significant improvements in physical function at both weeks 12 and 24, as measured by the SF-36 PCS, in patients treated with adalimumab ($p < 0.001$ for both weeks; table 2). Patients treated with adalimumab achieved clinically meaningful improvements in PCS scores (2.5–5-point change), whereas those treated with placebo did not. At 24 weeks, more than twice as many patients treated with adalimumab (61.7%) had achieved clinically meaningful improvements in PCS scores versus those treated with placebo (30.1%; $p < 0.001$; table 3). Results were similar at 12 weeks. Changes from baseline in the

Table 1 Baseline demographics and disease severity characteristics

Characteristic*	Placebo, $n = 162$ †	Adalimumab 40 mg eow, $n = 151$ †
Age, years	49.2 (11.1)	48.6 (12.5)
Sex, male	54.9%	56.3%
Race, white	93.8%	97.4%
Psoriatic arthritis duration, years	9.2 (8.7)	9.8 (8.3)
Psoriasis duration, years	17.1 (12.6)	17.2 (12.0)
C reactive protein, mg/dl (normal < 0.287)	1.4 (1.7)	1.4 (2.1)
Patients taking methotrexate at baseline	50%	51%
Tender joint count (0–78 joints)	25.8 (18.0)	23.9 (17.3)
Swollen joint count (0–76 joints)	14.3 (11.1)	14.3 (12.2)
HAQ DI (range 0–3)	1.0 (0.7)	1.0 (0.6)
SF-36 PCS score	33.3 (9.8)	33.2 (9.9), $n = 148$
SF-36 MCS score	46.6 (12.2)	48.1 (10.2), $n = 148$
FACIT-Fatigue (range 0–52)	30.8 (12.2), $n = 161$	30.8 (12.1), $n = 150$
Patient's assessment of pain (0–100 mm VAS)	48.8 (21.7), $n = 161$	51.1 (21.4)
Patient's global assessment of disease activity (0–100 mm VAS)	48.1 (21.2), $n = 161$	47.1 (23.2)
PASI (range 0–72)‡	8.3 (7.3), $n = 69$	7.4 (6.1), $n = 69$
DLQI (range 0–30)‡	10.3 (7.5), $n = 68$	8.6 (6.6), $n = 66$
Physician's global assessment of psoriasis, % "clear" or "almost clear"‡	1.4%, $n = 70$	1.4%, $n = 70$

DLQI, Dermatology Life Quality Index; eow, every other week; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy—Fatigue Scale; HAQ DI, Health Assessment Questionnaire Disability Index; MCS, mental component summary; PASI, Psoriasis Area and Severity Index; PCS, physical component summary; SF-36, Short-Form 36 Health Survey; VAS, visual analogue scale.

*Values are mean (SD) unless specified.

† $p = \text{NS}$ for comparisons between-treatment groups for all baseline characteristics.

‡ $n = 162$ for placebo, $n = 151$ for adalimumab except where specifically noted.

§ n in patients with at least 3% body surface area psoriasis involvement.

Table 2 Changes from baseline in patient-reported outcomes in Adalimumab Effectiveness in Psoriatic Arthritis Trial*

Patient-reported outcome	Week 12			Week 24		
	Placebo	Adalimumab	p Value†	Placebo	Adalimumab	p Value‡
HAQ DI	-0.1 (0.5) (162)	-0.4 (0.5) (151)	<0.001	-0.1 (0.4) (162)	-0.4 (0.5) (151)	<0.001
SF-36 PCS	1.4 (8.7) (151)	9.3 (10.0) (136)	<0.001	1.4 (9.6) (152)	9.3 (10.1) (140)	<0.001
SF-36 MCS	1.2 (10.2) (151)	1.6 (10.1) (136)	0.708	0.6 (10.4) (152)	1.8 (9.3) (140)	0.288
Physical functioning	3.9 (23.3) (151)	14.4 (22.1) (139)	<0.001	2.9 (23.8) (152)	15.8 (22.9) (143)	<0.001
Role-physical	7.2 (34.8) (152)	30.1 (41.9) (138)	<0.001	8.9 (43.4) (152)	30.0 (38.5) (142)	<0.001
Bodily pain	3.0 (20.5) (152)	19.6 (23.4) (141)	<0.001	3.4 (18.9) (152)	21.8 (22.8) (143)	<0.001
General health	0.2 (16.7) (152)	12.4 (18.2) (139)	<0.001	-0.1 (16.8) (152)	11.6 (19.4) (143)	<0.001
Vitality	3.0 (17.2) (152)	13.7 (20.4) (138)	<0.001	1.7 (19.1) (152)	12.8 (21.0) (141)	<0.001
Social functioning	4.4 (23.4) (152)	11.8 (25.7) (140)	0.014	2.6 (25.4) (152)	11.8 (25.8) (143)	0.003
Role-emotional	4.4 (46.8) (152)	5.7 (45.3) (138)	0.762	4.6 (48.5) (152)	10.3 (40.3) (142)	0.255
Mental health	1.8 (15.0) (152)	5.1 (14.9) (138)	0.060	1.1 (14.9) (152)	4.5 (15.3) (141)	0.045
FACIT-Fatigue	0.6 (8.4) (148)	6.5 (11.1) (140)	<0.001	0.1 (9.6) (151)	7.1 (10.2) (143)	<0.001
Patient's assessment of pain‡	1.6 (24.0) (161)	-23.0 (27.0) (151)	<0.001	0.6 (24.1) (161)	-24.0 (28.3) (151)	<0.001
Patient's global assessment of disease activity§	0.4 (23.1) (161)	-19.6 (29.4) (151)	<0.001	0.6 (24.5) (161)	-21.1 (29.4) (151)	<0.001
DLQI	-0.4 (5.8) (64)	-5.6 (5.6) (66)	<0.001	-0.7 (6.7) (66)	-6.1 (6.3) (66)	<0.001

DLQI, Dermatology Life Quality Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy—Fatigue Scale; HAQ DI, Health Assessment Questionnaire Disability Index; MCS, mental component summary; PCS, physical component summary; SF-36, Short Form 36 Health Survey; VAS, visual analogue scale.
 *Values are mean (SD) (n) change from baseline, by the last observation carried forward analysis.
 †For differences between treatment groups from an analysis of variance model with treatment group, and baseline methotrexate use (yes/no) and extent of psoriasis (≥3%, <3% body surface area) as factors.
 ‡Patient's assessment of pain is based on VAS possible range of 0 (no pain) to 100 (pain as bad as it could be).
 §Patient's global assessment of disease activity is based on VAS possible range of 0 (very well) to 100 (very poorly).

MCS scores were not statistically different between treatment groups (table 2).

Functional Assessment of Chronic Illness Therapy—Fatigue Scale

The mean changes from baseline in FACIT-Fatigue were significantly greater for patients treated with adalimumab than placebo at weeks 12 and 24 (p<0.001 for both weeks; table 2). At week 12, 60.7% of patients treated with adalimumab and 30.4% of those treated with placebo achieved or surpassed the MCID of a four-point change. These results were similar at week 24 (p<0.001 for both weeks; table 3).

Patient's assessment of pain

The mean change in the visual analogue scale pain score from baseline improved significantly more with adalimumab than

with placebo at weeks 12 and 24 (p<0.001 for both weeks; table 2).

Patient's global assessment of disease activity

The mean change from baseline in the patient's global assessment of disease activity improved significantly more with adalimumab than with placebo at weeks 12 and 24 (p<0.001 for both weeks; table 2).

Dermatology Life Quality Index

Dermatological-related functional limitations were assessed with the DLQI in the subset of patients with psoriasis involving ≥3% BSA (placebo, n = 70; adalimumab, n = 70). Improvement in the DLQI total score was significantly greater in the adalimumab treatment group versus placebo at weeks 12 and 24 (p<0.001; table 2). For patients treated with adalimumab,

Table 3 Patient-reported outcomes in Adalimumab Effectiveness in Psoriatic Arthritis Trial: patients with clinically-important changes and complete resolution of functional limitations*

Patient-reported outcome	Week 12			Week 24		
	Placebo	Adalimumab	p Value†	Placebo	Adalimumab	p Value‡
HAQ DI						
Patients achieving the MCID ≥-0.3 points (%)	26.0	51.4	<0.001	26.9	52.5	<0.001
Patients with complete resolution (HAQ DI=0) (%)	14.3	33.8	<0.001	13.1	34.0	<0.001
SF-36 PCS						
Patients achieving the upper limit of the MCID ≥5 points (%)	26.5	66.9	<0.001	30.1	61.7	<0.001
FACIT-Fatigue						
Patients achieving the upper limit of the MCID ≥4 points (%)	30.4	60.7	<0.001	31.5	61.9	<0.001
DLQI						
Patients achieving the MCID ≥-5 points (%)	21.7	54.8	<0.001	23.7	55.0	0.001
Patients with complete resolution (DLQI=0) (%)	4.9	36.9	<0.001	5.0	43.6	<0.001

DLQI, Dermatology Life Quality Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy—Fatigue Scale; HAQ DI, Health Assessment Questionnaire Disability Index; MCID, minimum clinically-important difference; PCS, physical component summary score; SF-36, Short-Form 36 Health Survey.
 *Data based on observed intention-to-treat analysis.
 †p Values are versus placebo based on Cochran-Mantel-Haenszel test.

the improvement in DLQI at weeks 12 and 24 was clinically meaningful as defined as a >5-point improvement. By week 24, 55% of patients treated with adalimumab versus 23.7% of those treated with placebo achieved or surpassed the MCID of five points ($p = 0.001$). In addition, 43.6% of patients treated with adalimumab versus 5 of patients treated with placebo had complete resolution of functional loss (DLQI score = 0; $p < 0.001$) by week 24 (table 3).

DISCUSSION

With more than 300 patients enrolled, ADEPT is the largest randomised controlled trial of a TNF antagonist in the treatment of PsA. In ADEPT, adalimumab treatment led to statistically significant improvement in joint and skin manifestations of PsA, significantly inhibited radiographic disease progression, reduced disability due to joint damage and improved HRQOL.²²

In this report, further analysis of ADEPT data showed improvement in several measures of physical function, both at 12 and 24 weeks. Significant improvement in HAQ DI for adalimumab versus placebo at 12 weeks surpassed the disease-specific MCID for this measure, showing the ability of adalimumab to provide clinically meaningful improvement in physical function in patients with PsA. Moreover, more than twice as many patients treated with adalimumab had complete resolution of functional loss compared with placebo at both weeks 12 and 24. Similar observations were made with regard to the SF-36 PCS. These results signify the efficacy of treatment with adalimumab in improving the debilitating disease effects of PsA.

The SF-36 MCS scores did not change by significant or clinically-important amounts. These results are not unexpected because the MCS can be largely a measure of treatment effects in diseases that directly affect the central nervous system.^{12–27} Nonetheless, by week 24, clinically-important improvement was observed in seven of the eight SF-36 domains, with changes >10 points, indicating that improvement at the higher end of the MCID range for SF-36 was achieved. As expected, the three SF-36 domains showing the greatest magnitude of mean change were related to physical function—physical functioning, role—physical and bodily pain. These measures may be more related to the underlying disease mechanisms and are highly correlated with measures of function, pain, and disease activity.¹² Improvement with adalimumab in seven of the eight domains were also significant versus placebo. One domain, role—emotional, failed to reach significance in patients treated with adalimumab (mean change 10.3) versus those treated with placebo (mean change 4.6), despite surpassing the upper limit of MCID of 10 points for patients treated with adalimumab. This could be related to the greater variance for this domain than the other domains. The lesser degree of changes in domain scores related to mental health emotional health, and social functioning was expected, given that these outcomes are less related to the underlying mechanisms of PsA.

In the subset of patients with $\geq 3\%$ BSA affected by psoriasis, significant and clinically-important improvement in DLQI was seen with adalimumab versus placebo. The percentages of patients treated with adalimumab who reported complete resolution of dermatological-related functional loss were more than seven times that of patients treated with placebo at 12 weeks (36.9% *v* 4.9%), and nine times greater at 24 weeks (43.8% *v* 5%, respectively).

A limitation of this study is the short duration of treatment. Although the 24-week treatment duration is comparable with that of other PsA trials, longer-term results are needed for a more comprehensive assessment of the long-term benefits of adalimumab on functional outcomes, QOL and disability in

PsA. To this end, results from the long-term, open-label extension of ADEPT are being assessed. In addition, MCIDs for the HAQ DI, SF-36, DLQI, and FACIT-Fatigue in PsA need to be established and validated.

Thus, in addition to controlling disease activity, adalimumab also improves physical function, general physical health, fatigue, pain and dermatological-related functional limitations of patients with moderate to severe PsA. As patients with PsA experience disease-related deterioration in physical function during their productive years, this improvement is important and may reduce the economic burden associated with the work-related disability and other direct healthcare costs associated with PsA.

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