

Responses to Adalimumab in Patients with Active Psoriatic Arthritis Who Have Not Adequately Responded to Prior Therapy: Effectiveness and Safety Results From an Open-label Study

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ABSTRACT. Objective. To evaluate the effectiveness and safety of adalimumab in patients with active psoriatic arthritis (PsA) and an inadequate response to prior therapy.

Methods. Patients were treated with subcutaneous injections of adalimumab 40 mg every other week in addition to their standard antirheumatic therapies in a 12-week, open-label study. Effectiveness evaluations at Week 12 included American College of Rheumatology (ACR) and Psoriasis Area and Severity Index (PASI) response rates, Psoriatic Arthritis Response Criteria (PsARC), active dactylitis, enthesitis, and target lesion assessment. Physical function was evaluated using the Health Assessment Questionnaire Disability Index (HAQ-DI).

Results. A total of 127 patients were enrolled. At Week 12, patients achieved ACR20, ACR50, and ACR70 response rates of 78.0%, 55.9%, and 21.3%, respectively. PASI50 and PASI75 response rates were 64.7% and 47.1%. A PsARC response was experienced by 70.1% of patients. Between baseline and Week 12, clinically and statistically significant reductions occurred in the mean total plaque score of the target lesion as well as in the percentages of patients with active dactylitis and enthesitis. A mean improvement in HAQ-DI was also observed (-0.44 ; $p < 0.001$). Three serious adverse events were reported, but none was considered related to adalimumab therapy.

Conclusion. Adalimumab-treated patients achieved significant improvements in both skin and joint manifestations of PsA, as well as in physical function. Adalimumab was well tolerated and had a safety profile similar to that observed in other clinical trials of adalimumab for the treatment of PsA. ClinicalTrials.gov identifier: NCT00427362. (First Release July 1 2010; J Rheumatol 2010; 37:1898–906; doi:10.3899/jrheum.100069)

Key Indexing Terms:

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CLINICAL TRIAL
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Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. PsA affects men and women equally and has an estimated prevalence between 0.3% and 1% of the general population¹. Although originally described as a disease less severe than rheumatoid arthritis, it is now apparent

that PsA is more aggressive than previously thought and that the majority of patients with PsA experience a chronic, progressive course². Approximately one-fifth of patients with PsA will develop a destructive, disabling form of arthritis over time¹.

Elevated concentrations of the proinflammatory cytokine tumor necrosis factor (TNF) have been found in the joint synovium and lesional skin of patients with PsA^{3,4,5}. Subsequently, TNF has been validated as a therapeutic target in PsA and several other immune-mediated inflammatory diseases⁶. Anti-TNF biologic therapies, including the fully human monoclonal antibody adalimumab, have been demonstrated to significantly reduce the signs and symptoms of PsA^{7,8,9,10}.

Data from the Canadian population are still lacking regarding the effectiveness of adalimumab used to treat PsA in a routine clinical practice setting. Because the patient populations studied in clinical trials are selected according to strict eligibility criteria, clinical trial populations may not be representative of those patients who would receive adal-

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imumab during usual care. Further, randomized controlled trials may exclude patients with active disease who have not adequately responded to prior biologic therapy. Results of open-label trials conducted in a clinical practice setting can be used to confirm the findings of randomized controlled trials and to gather effectiveness data on other disease-specific domains.

The ACCLAIM trial (A Canadian Open-Label Study to Evaluate the Safety and Effectiveness of Adalimumab When Added to Inadequate Therapy for the Treatment of Psoriatic Arthritis) was an open-label multicenter Phase IIIb study conducted in Canada in care settings that reflected usual practice. Study enrollment criteria were consistent with the eligibility requirements for Canadian patients with PsA to receive biologic therapies. The objectives of ACCLAIM were to evaluate the effectiveness and safety profiles of adalimumab for treatment of patients with active PsA and an inadequate response to standard therapy, including methotrexate and, for some patients, biologic therapies.

MATERIALS AND METHODS

Patients. Adults at least 18 years of age were eligible to enroll in the study if the following criteria were met: Patients must have had active PsA (Moll and Wright criteria¹¹), defined by ≥ 3 tender or painful joints and ≥ 3 swollen joints despite standard PsA therapy. Patients must have had an unsatisfactory response or intolerance to therapy for PsA as defined by individual provincial requirements or private insurance requirements for the reimbursement of biologic TNF inhibitors (generally ≥ 3 or ≥ 5 tender or swollen joints despite therapy, depending on the province). If not applicable, the patient must have had an unsatisfactory response to or contraindication for/intolerance of at least 2 prior or ongoing disease-modifying antirheumatic drugs (DMARD; 1 of which had to have been methotrexate unless contraindicated). Women of childbearing potential were required to use contraception.

Exclusion criteria encompassed treatment within 4 weeks before baseline with any investigational agents, methotrexate-leflunomide combination, cyclosporine, tacrolimus, or intraarticular injection or intravenous infusion of corticosteroids. Treatment with infliximab and etanercept was prohibited within 8 weeks and 3 weeks before baseline, respectively. Patients were not permitted psoralen and ultraviolet A light phototherapy or topical psoriasis therapy within 2 weeks before baseline (with the exception of medicated shampoos and low-potency topical steroids used for palms, soles of feet, axilla, and groin area only).

Patients with active skin disease other than psoriasis that would interfere with the assessment of a target lesion were excluded from the study. Additional exclusion criteria included a history of or current acute inflammatory joint disease of origin other than PsA; history of cancer or lymphoproliferative disease; uncontrolled diabetes; unstable ischemic heart disease; congestive heart failure; active inflammatory bowel disease; chronic leg ulcer; recent stroke; positive serology for hepatitis B; positive human immunodeficiency virus status; neurological symptoms suggestive of central nervous system demyelinating disease; history of active tuberculosis (TB), histoplasmosis, or listeriosis; and latent TB or previous exposure to TB without prophylaxis.

Study design. Institutional review boards at each participating medical center approved the protocol, and all patients provided written informed consent before any study-related procedures were performed. There were 3 study visits: at screening, at baseline, and at Week 12 (± 7 days). Patients subcutaneously self-administered adalimumab 40 mg (Abbott Laboratories, Abbott Park, IL, USA) every other week in addition to their preexisting PsA treatment for a study period of 12 weeks.

Concomitant use of DMARD, nonsteroidal antiinflammatory drugs, and other PsA-related medications including prednisolone equivalent to ≤ 10 mg/day was allowed at stable, prestudy dosages throughout the course of the trial. However, the use of tacrolimus, cyclosporine or other calcineurin inhibitors, psoralen and ultraviolet A light phototherapy, any investigational agents, and live vaccines was prohibited during the study.

The primary efficacy measure was at least 20% improvement in the American College of Rheumatology response criteria (ACR20) at Week 12¹². A patient achieved an ACR20 response with at least a 20% improvement in both tender joint count (TJC; 78 joints assessed) and swollen joint count (SJC; 76 joints assessed) and at least a 20% improvement in 3 of the 5 remaining ACR core set measures: Patient's Global Assessment of Pain (PaGA Pain), Patient's Global Assessment of Disease Activity (PaGA), Physician's Global Assessment of Disease Activity (PhGA), erythrocyte sedimentation rate, and the Health Assessment Questionnaire Disability Index (HAQ-DI). The PaGA Pain, PaGA, and PhGA were each based on a visual analog scale of 0 to 100 mm¹².

Secondary efficacy measures included the following rheumatic components: ACR50 and ACR70 response, Psoriatic Arthritis Response Criteria (PsARC)¹³, change in the percentages of patients with fingers and toes with active dactylitis in ≥ 4 digits (fingers or toes), and change in the percentages of patients with enthesitis (tenderness of Achilles tendon and plantar fascia upon pressure). Patients were evaluated for dactylitis of the hands and feet using a total score of 0 to 60, with each digit rated 0 (absent) to 3 (severe). Enthesitis of the proximal insertion of the Achilles tendon and plantar fascia was evaluated with a score of 0 to 4, with each insertion rated 0 (enthesitis absent) or 1 (enthesitis present).

Secondary efficacy outcomes for psoriatic components included percentages of patients who achieved at least 50% and 75% improvement from baseline Psoriasis Area and Severity Index scores (PASI50 and PASI75 responses, respectively) at Week 12. PASI responses were assessed only for those patients with psoriasis involving at least 3% of body surface area at study entry. Change in psoriasis target lesion assessments were conducted for patients with a lesion that, at baseline, was at least 2 cm in diameter and had a plaque score of at least 6. Target lesions were assessed for erythema, induration, and scaling, each on a scale of 0 (best) to 5 (worst), with a total plaque score of 0 to 15.

Physical function and health-related quality of life was measured with the HAQ-DI¹⁴. The HAQ-DI has 20 questions divided among 8 categories. The total HAQ-DI score ranges from 0 to 3 and is calculated as the average of the worst score in each of the 8 categories.

As an exploratory tertiary efficacy measure, the Work Limitations Questionnaire (WLQ) evaluated the influence of adalimumab treatment on work-related productivity indices. The WLQ is a 25-item, self-administered questionnaire that measures the effects of disease on productivity of currently employed patients. The 25 WLQ items converge into 4 scales measuring difficulty in time-related demands (Time), physical impairment (Physical), cognitive function and interpersonal interactions (Mental/Interpersonal), and ability to successfully meet output demands (Output)^{15,16}.

In a post-hoc analysis, the response to adalimumab was evaluated using the Psoriatic Arthritis Joint Activity Index (PsAJAI), a new scoring tool designed to assess the response rate of patients with active PsA^{17,18}. The PsAJAI score is calculated as a weighted sum, measuring change from baseline in the following variables: TJC, C-reactive protein (CRP), PhGA, PaGA, PaGA Pain, and HAQ-DI. A reduction by $\geq 30\%$ from baseline values in each variable contributes 1 point, with the exception of TJC, CRP, and PhGA, which contribute 2 points. Scores range from 0 to 9, and scores ≥ 5 indicate response. PsAJAI responder analyses were performed by age (< 50 years vs ≥ 50 years), concomitant DMARD use, disease duration (≤ 3 years vs > 3 years), and sex.

Safety evaluations, including vital signs, laboratory evaluations, and chest radiographs, were conducted. Treatment-emergent adverse events (AE) were recorded, and AE data were collected during the study and through 70 days after the last dose of adalimumab.

Statistical analysis. All patients received at least 1 dose of adalimumab and were included in the intention-to-treat analysis. Descriptive statistics were generated for demographic and baseline variables, study outcome variables, and patient subgroups defined according to history of biologic treatment. No imputation methods were used for replacing missing data. The minimum level of statistical significance was defined a priori as 5%. Statistical significance of within-group changes in outcome measures between the baseline and Week-12 assessments was analyzed with the Student t-test for paired samples for continuous variables and McNemar chi-square test for categorical variables. Between-subgroup differences with respect to continuous variables were assessed for statistical significance with one-way analysis of variance and with the chi-square test for categorical variables. All analyses were conducted with SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Patient disposition. The study enrolled 127 patients at 24 sites in Canada between April 2006 and April 2007. Enrollment by province was as follows: Alberta, 11 (8.7%); British Columbia, 14 (11.0%); Manitoba, 9 (7.1%); Newfoundland, 16 (12.6%); Nova Scotia, 7 (5.5%); Ontario, 57 (44.9%); and Quebec, 13 (10.2%). All 127 patients received at least 1 dose of adalimumab, and effectiveness data are presented for those patients. Three patients were discontinued from the study for reasons of serious AE, protocol violation and abnormal test result, and noncompliance.

Patient characteristics at baseline. The mean age of the

ACCLAIM population was 48.8 years, 54.3% were men, and 89.8% were white (Table 1). Patients in ACCLAIM had a mean duration of PsA of 11.1 years and a mean duration of psoriasis of 21.1 years (Table 1). Shown for comparison in Table 1 are the patient characteristics of the adalimumab-treatment group in the ADalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT), as well as subgroups of ACCLAIM patients who were anti-TNF-naïve and anti-TNF-experienced. Numbers and percentages of patients who had received prior and ongoing traditional DMARD therapies are reported in Table 2. A total of 42.5% (54 of 127) of patients reported prior use of biologic agents. Etanercept was the most used prior biologic (18.1% of patients), followed by infliximab (12.6% of patients) (Table 2).

Effectiveness. A total of 78.0% (99 of 127) of patients with PsA achieved an ACR20 response following treatment with adalimumab for 12 weeks. An ACR20 response was achieved by 70.3% (26 of 37) of patients with prior biologic exposure and 81.1% (73 of 90) of patients who were naïve to biologic therapy (Figure 1a). The ACR20 response rate was not statistically significantly different between patients who had previously received biologics and those who had not. At Week 12, ACR50 and ACR70 responses were achieved by 55.9% (71 of 127) and 21.3% (27 of 127) of all

Table 1. Baseline demographics and disease characteristics of adalimumab-treated patients. Values are mean \pm SD unless otherwise noted.

Characteristic	ADEPT Adalimumab Patients, N = 151	ACCLAIM All Patients, N = 127	ACCLAIM Anti-TNF-naïve Patients, N = 90	ACCLAIM Anti-TNF-Experienced Patients, N = 37	p*
Age, yrs	48.6 \pm 12.5	48.8 \pm 10.7	48.3 \pm 11.1	50.1 \pm 9.7	0.402
Male, n (%)	85 (56.3)	69 (54.3)	46 (51.1)	23 (62.2)	0.328
White, n (%)	147 (97.4)	114 (89.8)	78 (86.7)	36 (97.3)	0.106
Body weight, kg	86.0 \pm 20.6	90.5 \pm 21.7	87.5 \pm 19.8	97.6 \pm 24.4	0.016
Duration of psoriatic arthritis, yrs	9.8 \pm 8.3	11.1 \pm 8.8	10.6 \pm 8.6	12.1 \pm 9.3	0.381
Duration of psoriasis, yrs	17.2 \pm 12.0	21.1 \pm 11.8	19.5 \pm 11.4	24.8 \pm 11.9	0.021
Arthritis subtype, n (%)					
Symmetric polyarthritis	97 (64.2)	89 (70.1)	63 (70.0)	26 (70.3)	0.999
Asymmetric oligoarthritis	37 (24.5)	22 (17.3)	20 (22.2)	2 (5.4)	0.036
Distal interphalangeal arthropathy	15 (9.9)	11 (8.7)	4 (4.4)	7 (18.9)	0.013
Spondylitis	1 (0.7)	3 (2.4)	2 (2.2)	1 (2.7)	0.999
Arthritis mutilans	1 (0.7)	0	0	0	—
Tender joint count (0–78)	23.9 \pm 17.3	25.4 \pm 16.4	23.5 \pm 16.7	30.1 \pm 15.0	0.037
Swollen joint count (0–76)	14.3 \pm 12.2	16.5 \pm 10.9	15.7 \pm 10.8	18.3 \pm 11.3	0.232
Physician's global assessment of disease activity (0–100-mm VAS)	53.8 \pm 15.7	60.9 \pm 20.8	57.7 \pm 21.7	68.7 \pm 16.1	0.002
Patient's global assessment of disease activity (0–100-mm VAS)	47.1 \pm 23.2	58.2 \pm 24.4	53.7 \pm 24.5	69.3 \pm 20.7	0.001
Patient's global assessment of pain (0–100-mm VAS)	51.1 \pm 21.4	55.9 \pm 24.5	51.0 \pm 25.0	67.7 \pm 18.5	< 0.001
Psoriasis Area and Severity Index score (0–72)	7.4 \pm 6.0	11.7 \pm 8.0	10.0 \pm 6.5	14.3 \pm 9.5	0.047
C-reactive protein, mg/dl	1.4 \pm 2.1	1.3 \pm 1.8	1.3 \pm 2.0	1.5 \pm 1.9	0.486
Health Assessment Questionnaire Disability Index	1.0 \pm 0.6	1.1 \pm 0.7	1.0 \pm 0.7	1.3 \pm 0.7	0.062

* P values comparing anti-TNF-naïve and anti-TNF-experienced patients based on chi-square test for categorical variables and independent samples t-test for continuous variables. VAS: visual analog scale.

Table 2. Prior and concomitant therapies.

Treatment	All Patients, N = 127	
	Prior Therapies n (%)	Concomitant Therapies n (%)
Methotrexate	82 (64.6)	56 (44.1)
Traditional disease-modifying antirheumatic drug		
0	0	44 (34.6)
1	28 (22.0)	56 (44.1)
2	43 (33.9)	21 (16.5)
3	22 (17.3)	6 (4.7)
≥ 4	34 (26.8)	0
Biologic agent		
Etanercept	23 (18.1)	—
Infliximab	16 (12.6)	—
Alefacept	9 (7.1)	—
Efalizumab	6 (4.7)	—
Other systemic therapy		
Corticosteroid	17 (13.4)	20 (15.7)
Retinoid	6 (4.7)	0
Phototherapy		
Ultraviolet B light	16 (12.6)	0
Psoralen and ultraviolet A light	2 (1.6)	0
Topical treatment		
Corticosteroid	56 (44.1)	24 (18.9)
Vitamin D analog	24 (18.9)	8 (6.3)
Other	6 (4.7)	17 (13.4)

patients, respectively (Figure 1a). Although response rates were somewhat greater for the subgroup of patients who were naive to biologic agents compared with those previously treated with biologics, these differences were not statistically significant (Figure 1a).

A PsARC response was experienced by 70.1% (89 of 127) of patients in the study (Figure 1b). A total of 64.9% (24 of 37) of patients who had received prior biologic treatment attained a PsARC response, compared with 72.2% (65 of 90) of patients who were biologic-naïve (Figure 1b). PASI responses were assessed only for those patients with at least 3% of body surface area affected by psoriasis at study entry. At Week 12, 64.7% (44 of 68) of patients achieved a PASI50 response and 47.1% (32 of 68) of patients achieved a PASI75 response (Figure 1c). PASI response rates were statistically significantly different between patients with and those without a history of prior biologic treatment. Those without prior biologic exposure experienced greater response rates than patients previously treated with biologics (Figure 1c).

Clinically significant changes were observed in the percentages of patients with active dactylitis of fingers and/or toes. At baseline, 33.9% (43 of 127) of patients exhibited active dactylitis in ≥ 4 digits (fingers or toes). Following 12 weeks of adalimumab treatment, 11.0% (14 of 127) of patients had active dactylitis ($p < 0.001$) (Figure 2a). The mean \pm SD total dactylitis score for patients in the study decreased from 7.04 ± 6.45 at baseline to 2.49 ± 4.68 at Week 12 ($p < 0.001$). Further, the percentages of patients

with dactylitis scores of 0 increased from 53.5% (68 of 127) at baseline to 75.6% (96 of 127) at Week 12 ($p < 0.001$).

A decrease in the percentages of patients with enthesitis was also observed during the study. The percentages of patients with tenderness of the Achilles tendon decreased from 29.9% (38 of 127) at baseline to 14.2% (18 of 127) at Week 12 ($p = 0.004$). Percentages with tenderness of the plantar fascia declined from 24.4% (31 of 127) at baseline to 11.0% (14 of 127) at Week 12 ($p = 0.008$) (Figure 2b). Target lesion assessment was performed for the 80 patients with a lesion having a total plaque score of at least 6 at baseline. These patients experienced a statistically and clinically significant change in mean total plaque score. At baseline, mean \pm SD total plaque score was 8.9 ± 2.2 , and at Week 12 it had decreased to 5.1 ± 3.3 ($p < 0.001$; Figure 2c).

A statistically and clinically significant mean improvement in the HAQ-DI from baseline to Week 12 was observed (-0.44 ± 0.53 ; $p < 0.001$). Approximately 50% of patients (63 of 127) experienced a change in the HAQ-DI that exceeded the minimum clinically important difference reported for PsA (-0.3). The WLQ was completed by patients who were employed (99 of 127) during the study. Results from this assessment demonstrated significant decreases (improvement) from baseline to Week 12 in 3 of the 4 domains [Physical ($p < 0.001$), Time ($p < 0.001$), and Output ($p = 0.003$)] (Figure 3).

Overall, 75.6% (96 of 127) of patients achieved PsAJAI scores ≥ 5 at Week 12, indicating response to adalimumab. The mean \pm SD PsAJAI at Week 12 was 6.0 ± 2.5 . A therapeutic response to adalimumab as measured by the PsAJAI was observed for all subgroup categories: age, concomitant DMARD use, disease duration, and sex (Figure 4).

Safety. During the study, 63.8% (81 of 127) of patients experienced at least 1 AE (Table 3). Most AE were mild. Infections and infestations were the most frequently reported nonserious AE, occurring in 18.1% (23 of 127) of those enrolled (Table 3). There were 2 infections (candidiasis and systemic mycosis) that were significant AE of interest, but both patients were treated and continued in the study. The only individual AE with incidences $> 4\%$ in the study were upper respiratory infection and headache (Table 3). Three serious AE unrelated or not likely to be related to adalimumab occurred, 1 during the 12-week treatment period and 2 during the 70-day followup period. A cerebrovascular accident was reported in a 73-year-old woman on Day 72. Study medication was discontinued. A 31-year-old woman experienced a cerebral venous thrombosis on Day 94 and was hospitalized. A 53-year-old man reported psoriatic arthropathy on Day 105 and was hospitalized for treatment. Overall, no deaths and no cases of malignancy, congestive heart failure, demyelinating disease, or TB were reported in the study.

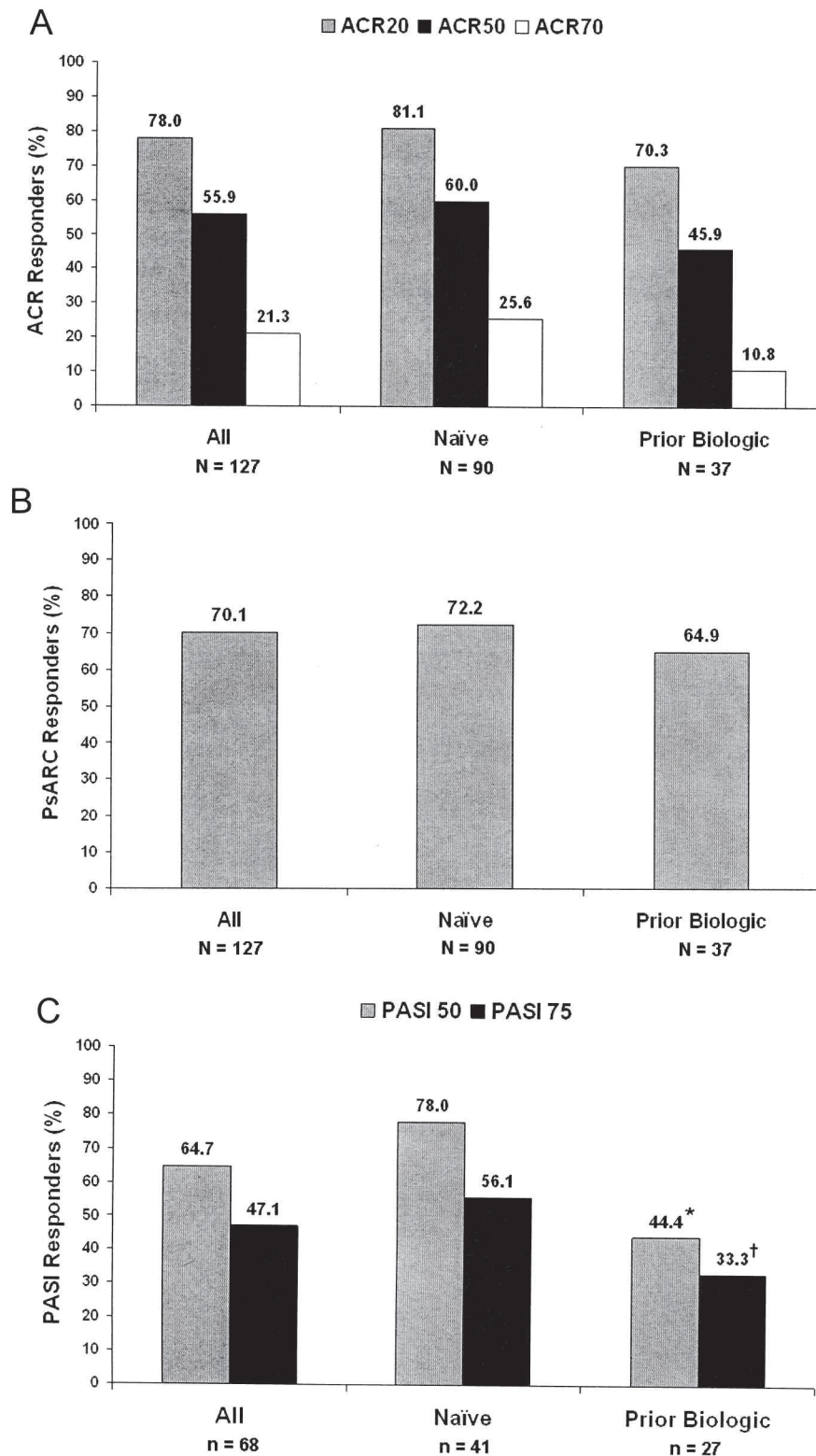


Figure 1. Percentages of patients achieving clinical responses at Week 12 by history of prior biologic treatment. American College of Rheumatology (ACR) criteria (A); Psoriatic Arthritis Response Criteria (PsARC) (B); at least 50% and 75% improvement from baseline Psoriasis Area and Severity Index score (PASI50 and PASI75). *p = 0.007 versus patients naïve to biologics; [†]p = 0.086 versus patients naïve to biologics. PASI responses based on 68 patients with body surface area \geq 3% at baseline (C). All data are observed.

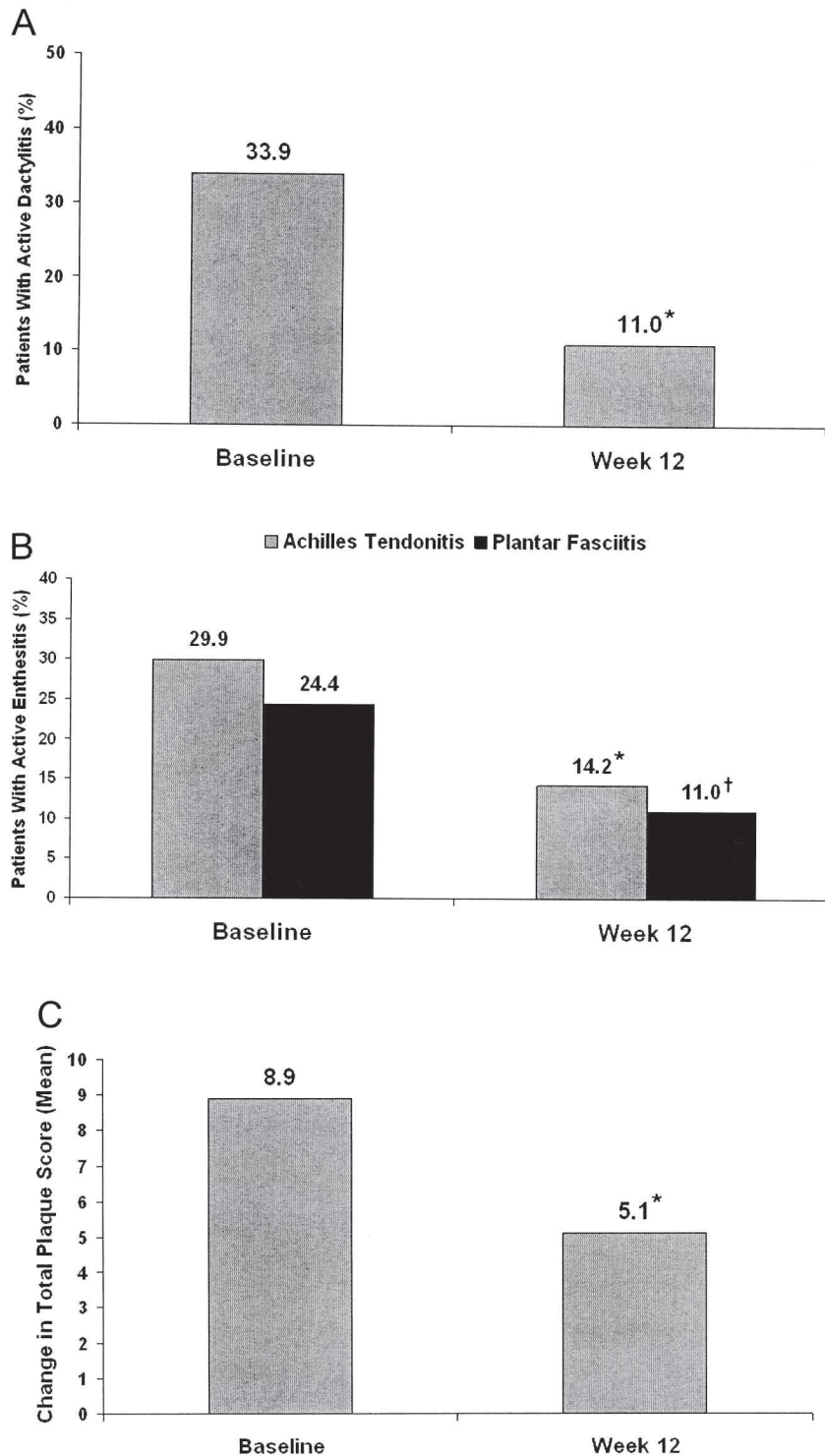


Figure 2. A. Percentages of patients with active dactylitis in ≥ 4 digits (fingers or toes) at baseline and Week 12. * $p < 0.001$ versus baseline. Data are observed. B. Percentages of patients with enthesitis of the proximal insertion of the Achilles tendon and plantar fascia at baseline and Week 12. * $p = 0.004$ versus baseline; † $p = 0.008$ versus baseline. Data are observed. C. Mean change in total plaque scores of assessed target lesions between baseline and Week 12. * $p < 0.001$ versus baseline. Data are observed values based on 80 patients with a total plaque score ≥ 6 at baseline.

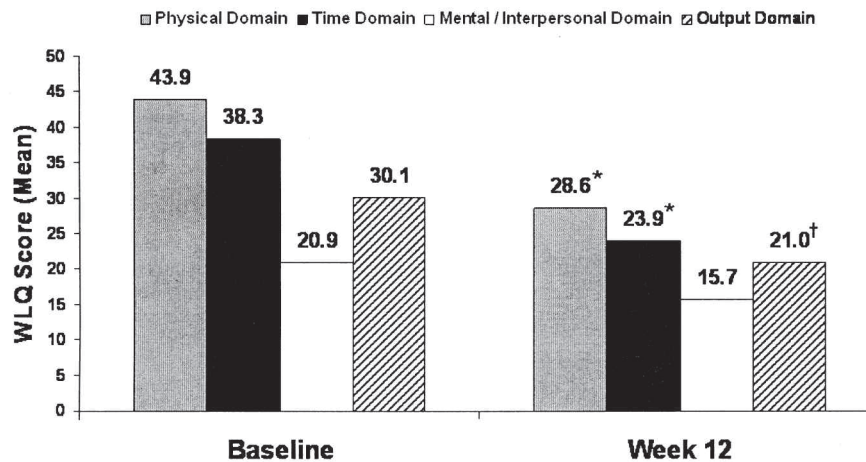


Figure 3. Changes in Work Limitations Questionnaire domains from baseline to Week 12. * $p < 0.001$ versus baseline; † $p = 0.003$ versus baseline. Data are observed.

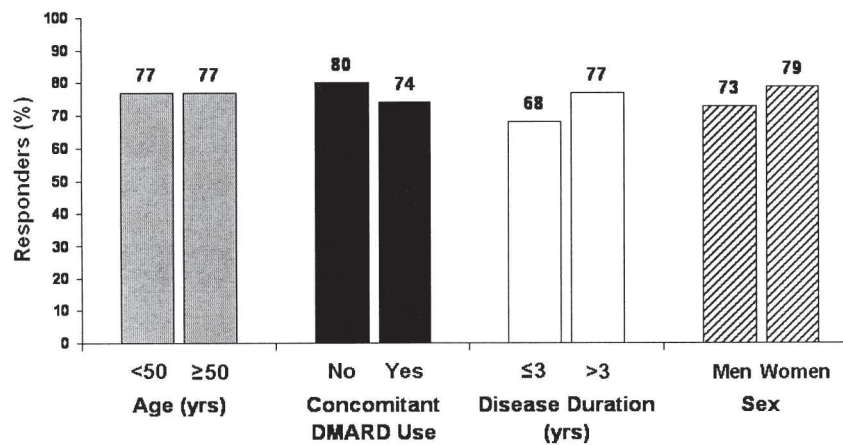


Figure 4. Percentages of patients achieving Psoriatic Arthritis Joint Activity Index (PsAJAI) responses at Week 12. Scores range from 0 to 9, and scores ≥ 5 indicate response. Scores were calculated using observed data. DMARD: disease-modifying antirheumatic drug.

DISCUSSION

ACCLAIM was a Canadian multicenter, Phase IIIb, open-label study of patients with active PsA who had not adequately responded to prior PsA treatments. Designed to reflect typical clinical practice settings in Canada, ACCLAIM enrollment criteria were consistent with Canadian eligibility requirements for the use of TNF antagonists in the treatment of PsA. The results of ACCLAIM affirmed the findings of previous randomized, controlled, pivotal trials of adalimumab in PsA as well as those of open-label studies. Patients in ACCLAIM achieved Week 12 ACR20, ACR50, and ACR70 response rates of 78%, 56%, and 21%, respectively. In ADEPT, a randomized, placebo-controlled trial, patients treated with adalimumab experienced Week-12 ACR20, ACR50, and ACR70 response rates of 58%, 36%, and 20%, respectively⁹. In STEREO, a

12-week, open-label, uncontrolled study of adalimumab, patients achieved ACR responses that closely mirrored those of ACCLAIM, with ACR20, ACR50, and ACR70 response rates of 74%, 51%, and 32%, respectively¹⁹.

Most characteristics of patients enrolled in ACCLAIM were very similar to those of the adalimumab treatment group in the ADEPT study, despite the fact that ADEPT had more strict criteria for study entry. For example, in ADEPT, methotrexate use was allowed during the trial only if it had been taken for at least 3 months before study entry. In addition, ADEPT exclusion criteria included concurrent treatment with methotrexate at dosages > 30 mg/week, use of DMARD other than methotrexate, and any prior use of anti-TNF biologic therapy. In ACCLAIM, concomitant use of traditional DMARD, nonsteroidal antiinflammatory drugs, and other PsA-related medications including pred-

Table 3. Adverse events.

Event	All Patients, N = 127 n (%)
Any adverse event	81 (63.8)
Mild adverse event	55 (43.3)
Moderate adverse event	38 (29.9)
Severe adverse event	5 (3.9)
Serious adverse event	3 (2.4)
Infection or infestation	23 (18.1)
Adverse event leading to withdrawal	1 (0.8)
Individual adverse event with > 4% incidence	
Upper respiratory tract infection	6 (4.7)
Headache	6 (4.7)

Mild adverse event: transient and easily tolerated by the patient; moderate adverse event: causes patient discomfort and interrupts the patient's usual activities; severe adverse event: causes considerable interference with patient's usual activities and may be incapacitating or life-threatening.

nisolone equivalent to ≤ 10 mg/day was allowed at stable, prestudy dosages throughout the course of the trial. Patients in the 2 studies were closely matched in age, duration of psoriasis and PsA, and distribution of PsA subtypes. However, the ACCLAIM population had more severe disease as measured by baseline PhGA, PaGA, PaGA Pain, and PASI scores. The percentage of patients with dactylitis at baseline in ACCLAIM was in the range (30% to 40%) observed in other PsA studies, including ADEPT and STEREO for adalimumab and IMPACT 2 for infliximab^{7,9,19}.

Thirty-seven of the 127 patients in ACCLAIM (29.1%) had a history of exposure to biologic agents. Insufficient clinical study data exist regarding the likelihood of clinical improvement of PsA following a switch from one biologic treatment to another²⁰. Patients in ACCLAIM experienced favorable ACR, PsARC, and PASI responses following adalimumab treatment. Compared with study patients who were biologic-naïve, these clinical responses were only modestly reduced for patients who had received prior biologic treatment.

Other clinical trials in rheumatoid arthritis, ankylosing spondylitis (AS), and PsA have demonstrated that patients with a history of prior TNF-antagonist therapy experienced clinical benefit upon transition to treatment with adalimumab. In the Research in Active Rheumatoid Arthritis Trial (ReAct), a large, 12-week, open-label study of adalimumab involving 899 patients with a history of etanercept and/or infliximab therapy, adalimumab treatment was effective, with 60% of patients achieving an ACR20 response and 33% experiencing an ACR50 response²¹. In an ongoing 5-year postmarketing observational study (ReAlise) of patients who had completed ReAct, among 408 of 3433 who were TNF-antagonist-experienced, 77% had achieved ACR20 and 53% had achieved ACR50 by 3 years of adalimumab therapy²². The Review of Safety and Effectiveness

With Adalimumab in Patients With Active Ankylosing SpOnDylitis (RHAPSODY) and STEREO studies were 12-week, open-label studies of adalimumab for patients with active AS or PsA, respectively^{19,23}. Of 326 patients with AS with prior exposure to anti-TNF agents, 40.8% achieved at least 50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index. Of 66 patients with PsA previously treated with TNF antagonists, 71.2% experienced a PsARC response. At Week 12 of STEREO, ACR20, ACR50, and ACR70 responses were achieved by 66.7%, 41.7%, and 25.0%, respectively, of patients with PsA with a history of anti-TNF therapy, compared with 75.0%, 52.3%, and 33.0% of those who were TNF-antagonist-naïve²⁴.

For patients with PsA, both the skin and joint components of the disease negatively influence quality of life^{9,10}. A statistically and clinically significant decrease in the HAQ-DI from baseline to Week 12 of ACCLAIM demonstrated improvement in physical function and health-related quality of life. The mean improvement in the HAQ-DI observed for patients in ACCLAIM (−0.44) was very similar to the −0.40 mean change in the HAQ-DI observed in ADEPT following 12 and 24 weeks of blinded adalimumab treatment⁹. Approximately 50% of patients in ACCLAIM (63 of 127) experienced a change in the HAQ-DI of at least −0.3, exceeding the minimum clinically important difference reported for PsA²⁵.

The reliability and validity of the self-administered WLQ have been demonstrated in rheumatoid arthritis, osteoarthritis, and PsA^{15,16}. Responses from ACCLAIM patients who were employed (99 of 127) demonstrated statistically and clinically significant decreases in the WLQ from baseline to Week 12 in 3 of the 4 domains (Physical, Time, and Output), indicating that adalimumab was effective in reducing patient impairment in work-related productivity.

The PsAJAI, a new scoring tool that assesses the responses of patients with active PsA, measures change from baseline in TJC, CRP, PhGA, PaGA, PaGA Pain, and HAQ-DI^{16,17}. A total of 75.6% (96 of 127) of patients in ACCLAIM experienced a response to adalimumab based on PsAJAI scores ≥ 5 at Week 12. PsAJAI responses to adalimumab treatment were observed for the majority of patients in all subgroups evaluated, including age, concomitant DMARD use, disease duration, and sex.

This study was limited by its relatively short 12-week duration, small patient enrollment, and open-label design. ACCLAIM was to have enrolled up to 400 patients who fulfilled study eligibility criteria. However, adalimumab became commercially available for the treatment of PsA in Canada before this number was reached, and enrollment continued only until the date of marketing approval. In addition, the response rates for several of the clinical outcome measures in ACCLAIM were somewhat greater than those reported in the randomized, placebo-controlled ADEPT trial, possibly because of differences in baseline disease

severity and other clinical characteristics, the open-label design of the study of ACCLAIM, and other differences in study requirements. By design, the ACCLAIM study did not assess the effectiveness of adalimumab for patients with < 3 tender and swollen joint counts (i.e., those with oligoarticular, axial, isolated enthesitis disease, etc.), as that patient population does not meet Canadian eligibility requirements for receiving anti-TNF therapy.

Adalimumab-treated patients in ACCLAIM achieved significant improvements in both the skin and joint manifestations of PsA, as well as in measures of physical function, quality of life, and work productivity. Adalimumab was generally well tolerated, with a safety profile similar to that observed in other clinical trials in PsA. These results, obtained from a clinical study conducted in a care setting that reflected routine practice, are consistent with findings from other trials of adalimumab in the treatment of PsA.

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