Clinical Remission in Patients with Active Psoriatic Arthritis Treated with Adalimumab and Correlations in Joint and Skin Manifestations

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ABSTRACT. ***Objective.*** Adalimumab (ADA) was evaluated for its efficacy in patients with moderate to severely active psoriatic arthritis (PsA) and for the presence of correlations in disease change variables.

Methods. Patients with inadequate response to standard PsA therapy were given 40 mg of ADA every other week for up to 12 weeks or 20 weeks. Outcome variables encompassed tender joint count (TJC), swollen joint count (SJC), physician's global assessment (PGA) of psoriasis, Health Assessment Questionnaire (HAQ), patient's global assessment (PtGA) of disease activity and pain, C-reactive protein, as well as composite measures of disease activity. Patients with inactive skin disease symptoms at baseline were excluded from the remission analyses.

Results. Of 268 patients with active baseline joint and skin disease and data available at Week 12 following open-label ADA therapy, 73 achieved joint remission (27.2%, TJC ≤ 1 + SJC ≤ 1) and 144 achieved skin remission criteria (53.7%, PGA = clear/almost clear). Simultaneous joint and skin remission criteria were achieved in 16.0% and 24.8% of patients at weeks 12 and 20, respectively. In patients who did not achieve skin and/or joint remission, 12-week ADA treatment improved mean clinical and functional scores. Joint remission was more frequently associated with achieving clinically relevant outcomes including HAQ, PtGA disease activity, and PtGA pain compared to skin remission. No correlation between improvement in skin and joint disease was observed.

Conclusion. ADA was effective in achieving strict criteria for remission in joint or skin disease in many patients with active PsA within 12 weeks and sustained through 20 weeks. (NCT00235885) (First Release April 1 2015; J Rheumatol 2015;42:952–9; doi:10.3899/jrheum.140312)

Key Indexing Terms:
PSORIATIC ARTHRITIS
ADALIMUMAB
REMISSION INDUCTION
MINIMAL DISEASE ACTIVITY

Psoriatic arthritis (PsA) manifests articular and cutaneous symptoms of disease, although not all patients demonstrate these symptoms at all times. Flares caused by increased inflammation affect individual patients differently. For example, some patients may present worsening in scaly, painful, cutaneous patches, while others will present increased symptoms in 1 or more joints that may change locations with recurring episodes[1]. Different patterns of joint involvement, including peripheral or axial arthritis, enthesitis, and dactylitis, are commonly experienced by patients. Despite symptom variability, articular and cutaneous aspects of PsA should be treated simultaneously as deemed necessary by the treating physician and patient to prevent impairment and improve patient quality of life[2,3].

New and effective treatments for PsA[4,5,6,7] have assured physicians and patients alike that low disease activity or remission is a realizable goal, although formal definition and validation of remission criteria are not yet agreed upon[8,9,10]. The heterogeneity among PsA manifestations presents serious challenges in remission definition. Remission criteria have been suggested for other autoimmune diseases, including rheumatoid arthritis (RA). In 2011, an American College of Rheumatology/European League Against Rheumatism committee proposed a Boolean-based remission criteria for RA as the simultaneous improvement in tender joint count (TJC ≤ 1), swollen joint count (SJC ≤ 1), C-reactive protein (CRP ≤ 1 mg/dl), and patient's global assessment [PtGA ≤ 10, 0–100 mm visual analog scale

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AbbVie Inc. sponsored the study (NCT00235885), contributed to its design, participated in the collection, analysis, and interpretation of the data, and in the writing, reviewing, and approval of the final manuscript. F. Van den Bosch has received consulting fees and speaker's fees from AbbVie Inc. A. Kavanaugh has received grant/research and/or provided expert advice to AbbVie Inc. P.J. Mease has received consulting fees, research grants, and/or speaker honoraria from AbbVie Inc. M. Kron and H. Kupper are full-time employees of AbbVie Deutschland GmbH & Co. KG and may hold stock or stock options.

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Accepted for publication January 21, 2015.

(VAS)], or remission could be defined by a score on the Simplified Disease Activity Index (SDAI) ≤ 3.3[11]. Unfortunately, using strict RA remission definitions to assess PsA is insufficient because they neglect to address the skin disease manifestations of PsA (psoriasis and nail disease), as well as typical articular manifestations such as dactylitis and enthesitis. As a result, composite methodologies have been developed to define PsA minimal disease activity (MDA), an admirable treatment goal[8,9]. PsA MDA criteria includes simultaneous achievement of joint and skin symptom improvement. A patient is classified as achieving MDA when meeting 5 of the following 7 criteria: TJC ≤ 1; SJC ≤ 1; Psoriasis Activity and Severity Index (PASI) ≤ 1, or body surface area ≤ 3%; PtGA of pain ≤ 15 mm VAS; PtGA of disease activity ≤ 20 mm VAS; Health Assessment Questionnaire–Disability Index (HAQ-DI) ≤ 0.5; and tender entheseal points ≤ 1[8]. The 7-point physician's global assessment (PGA) scale (ranging from "severe" to "clear") and PASI have proven to be interchangeable based on high correlation[12] and previous assessment in a modified MDA[13].

Of the many clinical signs of PsA, the severities of peripheral arthritis and psoriasis have strong influences on the ultimate impairment and the intensity of therapy recommended by the physician. Tumor necrosis factor (TNF) antagonists have emerged as a viable antiinflammatory treatment option directed at disease control for PsA[4,5,7,14,15,16] and psoriasis[17,18]. The purpose of this posthoc study was to evaluate the efficacy of 12- and 20-week treatments with adalimumab (ADA), a fully human monoclonal antibody against TNF, in achieving clinical PsA remission while borrowing remission criteria cutoffs from RA and criteria for skin clearance for the psoriatic component of the disease. Because of the spectrum of PsA manifestations, correlations of therapeutic improvement in joint and skin symptoms following treatment were also investigated.

MATERIALS AND METHODS

Study design and patients. STEREO (SafeTy and Efficacy of ADA in patients with active PsA — a multinational study to evaluate the Response to Every-Other week ADA when added to insufficient standard therapy including patients who failed prior treatment with other TNF inhibitors; NCT00235885) was a 12-week study of open-label (OL), subcutaneous, self-administration of ADA (40 mg) every other week (eow), followed by an optional 8-week extension (up to 20 weeks), depending on the availability of commercial ADA and the opinion of the investigator. Primary study results have been presented previously[4]. A total of 442 patients with moderate to severely active PsA were enrolled in STEREO and were not diversified into different treatment groups; all received 40 mg ADA eow. STEREO inclusion criteria consisted of adults ≥ 18 years of age with diagnosed active PsA, TJC ≥ 3, SJC ≥ 3, and unsatisfactory or intolerance to at least 1 prior or ongoing disease-modifying antirheumatic drug (DMARD). Patients with or without active skin psoriasis at baseline were enrolled. Main exclusion criteria included the following: prior treatment with any investigational agent within 30 days, or 5 half-lives of the product, whichever was longer; treatment with infliximab or etanercept within 2 months or 3 weeks prior to trial initiation, respectively; treatment within 4 weeks prior to trial initiation with a combination of methotrexate and leflunomide, or any combination of a DMARD with cyclosporine. Continuation of prestudy PsA therapy, including traditional DMARD, nonsteroidal antiinflammatory drugs, and glucocorticoids (≤ 10 mg prednisone equivalent/day) was permitted concomitant with ADA 40 mg eow, provided that dosage remained stable from trial initiation.

Clinical and functional assessments. Outcome measures to investigate PsA clinical remission in psoriatic joint disease included TJC (0–78 joints), SJC (0–76 joints), PtGA of disease activity (VAS 0–100 mm), PtGA of pain (VAS 0–100 mm), PGA of disease activity (VAS 0–100 mm), 28-joint Disease Activity Score (DAS28), MDA, SDAI, Clinical Disease Activity Index (CDAI), and HAQ-DI. Skin disease was assessed using PGA and total plaque score; CRP (mg/dl) was also assessed, but enthesitis was only measured at screening. For the purpose of our study, skin remission was defined as clear or almost clear PGA. For most analyses, joint remission was defined as SJC ≤ 1 and TJC ≤ 1 with assessments of the proportions of patients in DAS28 (≤ 2.6), MDA (achieving 5 of the following 6 criteria: TJC ≤ 1, SJC ≤ 1, PGA = clear, PtGA of pain ≤ 15, PtGA of disease activity ≤ 20, HAQ-DI ≤ 0.5), SDAI (≤ 3.3), CDAI (≤ 2.8), or Boolean remission (TJC ≤ 1, SJC ≤ 1, CRP ≤ 1, PtGA ≤1).

Statistical analyses. Patients who received at least 1 dose of ADA, completed 12 weeks of OL treatment, and had available data were included in the main analyses. Patients with data available at Week 20 were assessed at weeks 12 and 20 for the presence of remission over time. Patients at baseline without active disease (i.e., patients with PGA clear/almost clear or SJC < 3) were removed from analyses presented, except for the analyses presented in Figure 1. Patients were stratified by joint and skin remission status at Week 12 for analyzing baseline and Week 12 patient demographics and disease characteristics. Four distinct subgroups were established based on remission status at weeks 12 and 20: joint and skin remission, joint remission only, skin remission only, and neither joint nor skin remission. Correlation analyses were performed comparing joint and skin variables. The biserial correlation coefficient was used to correlate the change from baseline in quantitative variables TJC, SJC, and DAS28 with the dichotomous variable improvement of PGA of psoriasis (yes vs no). Correlation for changes from baseline in quantitative variables was performed using the Spearman rank correlation coefficient, specifically the change in total plaque score with changes in SJC, TJC, and DAS28. Correlation coefficients > 0.3 were considered evidence for at least weak correlation.

RESULTS

Subgroups based on remission status at Week 12. Following treatment with OL ADA, 412 of 442 patients (92.8%) who initiated the trial had data available at Week 12. Among these 412 patients, 143 (34.7%) had minimal or no skin involvement at baseline (i.e., PGA clear/almost clear) and 1 patient possessed fewer than 3 swollen joints at baseline (Figure 1, gray bars). At Week 12, 282 of all patients (68.4%) were PGA clear/almost clear. Nearly half of the patients who achieved skin remission at Week 12 had inactive skin symptoms at baseline. For this reason, data for the 143 patients with baseline PGA clear/almost clear and 1 patient with SJC < 3 were removed from further analyses presented.

Of the 268 patients with active baseline disease, 174 (64.9%) achieved remission of joint and/or skin symptoms, and 73 achieved joint remission (27.2%, TJC ≤ 1 + SJC ≤ 1), irrespective of skin remission fulfillment (Figure 1, black bars) and irrespective of concomitant corticosteroid use (data not shown). Skin remission (PGA = clear/almost clear) irrespective of joint remission status was observed in 144 patients (53.7%). Joint and skin remission were simultaneously achieved in 43/268 patients at Week 12 (16.0%),

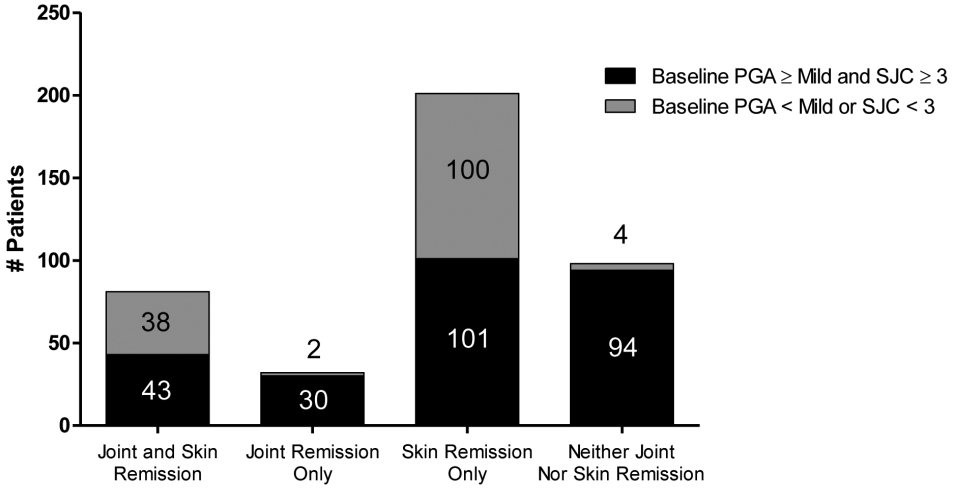

Figure 1. Remission status at Week 12. Subgroups based on the Week 12 remission status of patients with data available who received at least 1 dose of ADA. Black bars represent patients with active baseline skin disease, while gray bars represent patients who were PGA = clear/almost clear (n = 143) or had SJC < 3 (n = 1) at baseline. Joint remission is defined as TJC ≤ 1 + SJC ≤ 1. Skin remission is defined as PGA = clear/almost clear. PGA: physician's global assessment; SJC: swollen joint count; TJC: tender joint count.

whereas failure to attain remission in either was observed in 94 patients (35.1%).

Subgroup baseline demographics and disease characteristics. STEREO subgroups based on Week 12 remission status demonstrated similar duration of psoriasis, although patients who failed to achieve simultaneous skin and joint remission possessed the longest mean psoriasis, arthritis, and PsA disease durations (Table 1). Conversely, the joint remission subgroup presented arthritis and PsA symptoms for the shortest duration at baseline compared to other subgroups. Patients failing to achieve joint remission at Week 12 had higher baseline SJC and TJC. For the patients who achieved Week 12 skin remission, baseline psoriasis tended to be less active, as indicated by the differences comparing the

Table 1. Baseline demographics and disease characteristics of Week 12 response subgroups (n = 268). Values are mean ± SD or n (%) unless otherwise specified.

Variable	Joint[a] and Skin[b] Remission, n = 43	Joint Remission Only[a], n = 30	Skin Remission Only[b], n = 101	Neither Skin nor Joint Remission[c], n = 94
Age, yrs	45.6 ± 10.8	39.4 ± 10.2	48.2 ± 11.3	46.5 ± 10.7
Female	17 (39.5)	8 (26.7)	48 (47.5)	35 (37.2)
Psoriasis duration, yrs	19.5 ± 11.6	18.1 ± 11.1	20.1 ± 12.3	22.0 ± 13.7
Arthritis duration, yrs	10.4 ± 7.7	7.4 ± 7.0	11.9 ± 8.5	12.1 ± 9.0
PsA duration, yrs	10.2 ± 7.7	7.3 ± 7.0	11.2 ± 7.8	11.8 ± 8.8
Previous anti-TNF, ETN and/or IFX	7 (16.3)	5 (16.7)	9 (8.9)	17 (18.1)
Concomitant DMARD	34 (79.1)	15 (50.0)	83 (82.2)	64 (68.1)
CRP, mg/dl	1.87 ± 1.80	1.46 ± 1.33	1.62 ± 1.97	1.96 ± 2.23
TJC, 0–78, n ± SD	14.0 ± 7.6	12.5 ± 9.0	22.7 ± 13.7	21.0 ± 14.4
SJC, 0–76, n ± SD	8.9 ± 4.9	9.3 ± 8.9	11.9 ± 9.3	10.7 ± 7.6
PGA				
Mild	14 (32.6)	5 (16.7)	40 (39.6)	16 (17.0)
Mild to moderate	14 (32.6)	6 (20.0)	22 (21.8)	14 (14.9)
Moderate	10 (23.3)	7 (23.3)	29 (28.7)	32 (34.0)
Moderate to severe	3 (7.0)	7 (23.3)	8 (7.9)	24 (25.5)
Severe	2 (4.7)	3 (7.0)	2 (2.0)	8 (8.5)
PGA disease activity, VAS 0–100 mm	49.7 ± 17.3	54.0 ± 21.3	51.8 ± 17.8	56.1 ± 17.6
PtGA disease activity, VAS 0–100 mm	66.7 ± 17.6	62.5 ± 20.5	63.6 ± 19.0	60.8 ± 19.7
PtGA pain, VAS 0–100 mm	63.2 ± 21.8	59.2 ± 24.0	65.4 ± 20.8	60.9 ± 20.8
HAQ-DI	1.07 ± 0.59	1.02 ± 0.62	1.30 ± 0.61	1.25 ± 0.57

[a] TJC ≤ 1 + SJC ≤ 1. [b] PGA = clear/almost clear. [c] TJC > 1 + SJC > 1 + PGA > clear/almost clear. PsA: psoriatic arthritis; anti-TNF: anti-tumor necrosis factor; ETN: etanercept; IFX: infliximab; DMARD: disease-modifying antirheumatic drug; CRP: C-reactive protein; TJC: tender joint count; SJC: swollen joint count; PGA: physician's global assessment of psoriasis; VAS: visual analog scale; PtGA: patient's global assessment; HAQ-DI: Health Assessment Questionnaire–Disability Index.

proportion of patients with mild baseline symptoms and similar differences in the proportion of patients with moderate to severe PGA. Nearly three-fourths of the patients failing to achieve skin remission had baseline body surface areas with psoriasis ≥ 3%, whereas the subgroups achieving PGA = clear/almost clear at Week 12 reported half of the patients had body surface areas with psoriasis ≥ 3% (data not shown). Baseline PGA of disease activity was lower than PtGA disease activity, although the levels were largely consistent between Week 12 remission subgroups. Similarly, differences in patient-reported pain and disease activity means were minimal between the subgroups.

Joint remission subgroup analysis. In a daily-life setting, a rheumatologist may weigh swollen joints as more clinically informative than tender joints, especially because there may be multiple reasons for joints being tender (e.g., aging, degenerative disease). Among patients who met joint remission criteria (TJC ≤ 1 and SJC ≤ 1), 71 of 113 possessed both a TJC and SJC of 0 (62.8%); 94 patients (83.2%) possessed an SJC = 0. The overall mean TJC in patients without a swollen joint was 3.9 ± 7.7, whereas the mean SJC in patients lacking a tender joint was 0.7 ± 1.7. For all patients, 254 of 414 possessed either a TJC or SJC ≤ 1 following a 12-week ADA treatment (61.4%).

Achievement of additional stringent remission variables. Incorporating additional criteria commonly used to define RA remission, ADA 12-week treatment was assessed to meet additional stringent efficacy variables within the subgroups. ADA was effective in achieving additional clinically and functionally relevant outcomes (e.g., PtGA pain, PtGA disease activity, TJC, SJC, CRP, HAQ-DI) for many patients. Joint remission subgroups (TJC ≤ 1 + SJC ≤ 1) were more strongly associated with achieving 1 additional RA remission variable, including HAQ-DI (≤ 0.5), pain (≤ 10 mm), and disease activity (≤ 10 mm) scores, compared to skin remission subgroups at Week 12 (Table 2). Using higher, thus less stringent, cutoffs from the PsA MDA composite index (PtGA pain ≤ 15 mm and PtGA disease activity ≤ 20 mm) similarly yielded better association of joint remission subgroups with achieving these additional variables when compared to skin remission (data not shown). More patients achieving joint remission simultaneously achieved RA remission criteria for PtGA pain (60.3%), PtGA disease activity (56.2%), or HAQ-DI (74.0%), irrespective of simultaneous skin remission; skin remission subgroups were less frequently able to meet 1 additional remission variable. The CRP RA remission criterion of ≤ 1 mg/dl was achieved at Week 12 by 81.1–92.9% of patients across the subgroups. This RA remission assessment seemed to be easily achievable in patients with PsA following ADA treatment because a large majority of patients met CRP ≤ 1 mg/dl despite failure to meet simultaneous joint and skin remissions. Using the modified PsA definition of MDA (meeting at least 5 of the 6 remission criteria) was achieved by 17.9% of patients when using the more strict RA remission cutoffs for PtGA pain and disease activity; meeting all 6 of the MDA criteria assessed in STEREO was achieved by 21/268 of patients (7.8%). Using the RA Boolean criteria, 14.6% of patients achieved remission; additionally, 35.2% of patients met SDAI ≤ 3.3 and 33.6% of patients met CDAI ≤ 2.8 remission criteria (Figure 2). Further, more than half of patients (58.4%) satisfied DAS28-CRP ≤ 2.6. Most patients who satisfied the various joint-based remission criteria also satisfied the skin remission criteria. These responses were sustained beyond Week 12 and further improved to Week 20 in the population receiving 20 weeks of ADA therapy (Figure 2).

Clinical and functional outcomes. Following 12 weeks of ADA treatment, mean CRP was ≤ 1 mg/dl for all subgroups

Table 2. Week 12 PsA remission outcomes with additional variable criteria. Values are n (% of subgroup, % of total).

Variable	Joint[a] and Skin[b] Remission, n = 43	Joint Remission Only[a], n = 30	Skin Remission Only[b], n = 101	Neither Skin nor Joint Remission[c], n = 94
One additional variable				
PtGA pain ≤ 10 mm	26 (60.5, 9.7)	18 (60.0, 6.7)	36 (35.6, 13.4)	22 (23.4, 8.2)
PtGA disease activity ≤ 10 mm	27 (62.8, 10.1)	14 (46.7, 5.2)	35 (34.7, 13.1)	13 (13.8, 4.9)
HAQ-DI ≤ 0.5	31 (72.1, 11.6)	23 (76.7, 8.6)	50 (49.5, 18.7)	40 (42.6, 14.9)
CRP ≤ 1 mg/dl[d]	39 (90.7, 14.9)	26 (89.7, 9.7)	92 (92.9, 35.2)	73 (81.1, 28.0)
Two additional variables				
PtGA pain ≤ 10 mm + PtGA disease activity ≤ 10 mm	24 (55.8, 9.0)	14 (46.7, 5.2)	25 (24.8, 9.3)	12 (12.8, 4.5)
HAQ-DI ≤ 0.5 + PtGA pain ≤ 10 mm	22 (51.2, 8.2)	16 (53.3, 6.0)	26 (25.7, 9.7)	20 (21.3, 7.5)
HAQ-DI ≤ 0.5 + PtGA disease activity ≤ 10 mm	24 (55.8, 9.0)	13 (43.3, 4.9)	23 (22.8, 8.6)	11 (11.7, 4.1)
Three additional variables				
HAQ-DI ≤ 0.5 + PtGA pain ≤ 10 mm + PtGA disease activity ≤ 10 mm	21 (48.8, 7.8)	13 (43.3, 4.9)	18 (17.8, 6.7)	10 (10.6, 3.7)

[a] TJC ≤ 1 + SJC ≤ 1. [b] PGA = clear/almost clear. [c] TJC > 1 + SJC > 1 + PGA > clear/almost clear. [d] No. patients achieving joint and skin remission, joint remission only, skin remission only, and neither skin nor joint remission are 43, 29, 99, and 90, respectively. PsA: psoriatic arthritis; PtGA: patient's global assessment; HAQ-DI: Health Assessment Questionnaire–Disability Index; CRP: C-reactive protein; TJC: tender joint count; SJC: swollen joint count; PGA: physician's global assessment.

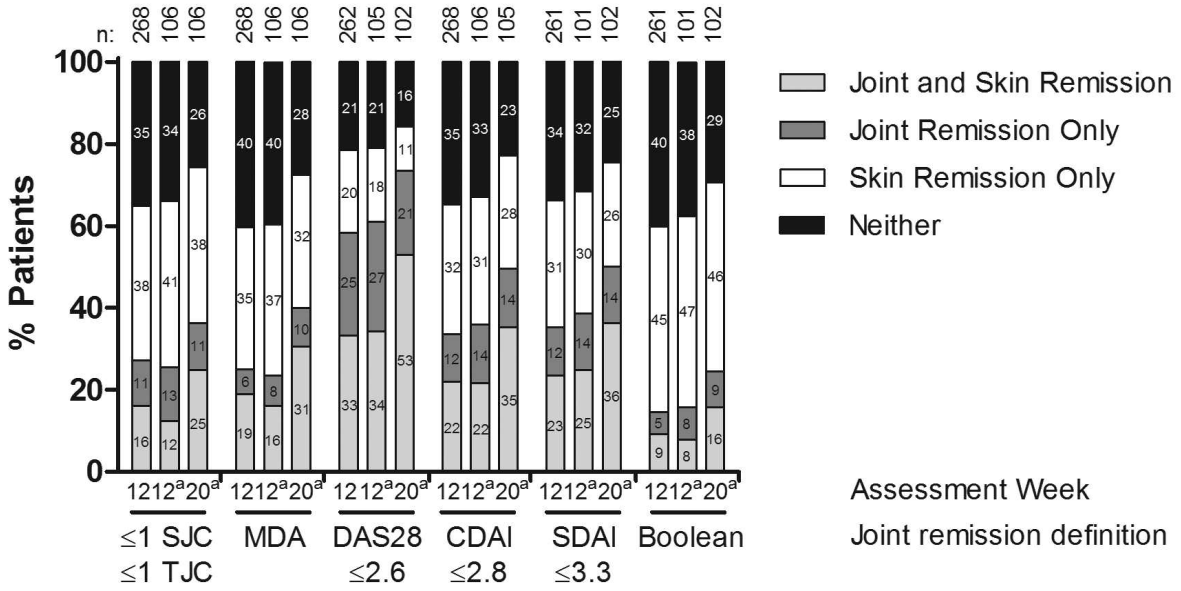

Figure 2. Achievement of various composite remission criteria for patients with data available at Week 12 or weeks 12 and 20. Subgroups based on the Week 12 or Week 20 remission status of patients with data available who received at least 1 dose of ADA. Joint remission variables were defined as indicated or as follows: Boolean (TJC ≤ 1, SJC ≤ 1, CRP ≤ 1, and PtGA ≤ 1), CDAI (≤ 2.8), DAS28 (≤ 2.6), MDA (achieving 5 of the following 6 criteria: TJC ≤ 1, SJC ≤ 1, PGA = clear, PtGA of pain ≤ 15, PtGA of disease activity ≤ 20, and HAQ-DI ≤ 0.5), and SDAI ≤ 3.3. Skin remission was defined as PGA = clear/almost clear. [a] Patients with data available through Week 20. Numbers within columns refer to the proportions in the remission categories. ADA: adalimumab; TJC: tender joint count; SJC: swollen joint count; CRP: C-reactive protein; PtGA: patient's global assessment; CDAI: Clinical Disease Activity Index; DAS28: 28-joint Disease Activity Score; MDA: minimal disease activity; PGA: physician's global assessment; HAQ-DI: Health Assessment Questionnaire-Disability Index; SDAI: Simplified Disease Activity Score.

independent of whether joint or skin remission was achieved (Table 3). Similarly, improvements were observed in PtGA of pain and disease activity from baseline, although patients achieving joint remission reported lower Week 12 scores than those who achieved skin remission only. Joint remission irrespective of skin remission also yielded lower HAQ-DI scores. In patients who failed to achieve joint remission at Week 12, mean functional scores still improved by 38–45% from baseline.

Correlation of joint and skin variables. Correlation analyses of changes in continuous variables of joint disease with changes in variables measured by PGA or total plaque score were assessed. The biserial correlation coefficient was calculated between continuous variables (SJC, TJC, change in DAS28) and the dichotomous variable of improved PGA (yes vs no). No correlation was identified when comparing improvement in skin disease activity with changes in joint disease (Table 4). The Spearman rank correlation also did not reveal a correlation between changes in total plaque score and SJC or TJC, although a weak correlation was found with change in DAS28.

DISCUSSION

PsA is a chronic disorder with worldwide prevalence ranging from 0.25% to 1%[19,20]. Discrepancies in prevalence are commonly attributed to the heterogeneity in disease manifes-

Table 3. Response outcomes following 12-week ADA treatment. Data are mean ± SD.

Variable	Joint[a] and Skin[b] Remission	Joint Remission Only[a]	Skin Remission Only[b]	Neither Skin nor Joint Remission[c]
CRP, mg/dl	0.39 ± 0.62	0.54 ± 0.96	0.51 ± 1.02	0.66 ± 0.91
PtGA pain, VAS 0–100 mm	16.6 ± 20.7	14.7 ± 18.9	22.8 ± 21.0	36.2 ± 27.1
PtGA disease activity, VAS 0–100 mm	14.0 ± 18.7	15.9 ± 15.5	22.6 ± 19.9	38.7 ± 24.8
HAQ-DI	0.36 ± 0.49	0.35 ± 0.59	0.71 ± 0.63	0.78 ± 0.63

[a] TJC ≤ 1 + SJC ≤ 1. [b] PGA = clear/almost clear. [c] TJC > 1 + SJC > 1 + PGA > clear/almost clear. ADA: adalimumab; CRP: C-reactive protein; PtGA: patient's global assessment; VAS: visual analog scale; HAQ-DI: Health Assessment Questionnaire–Disability Index; TJC: tender joint count; SJC: swollen joint count; PGA: physician's global assessment.

Table 4. Correlation of changes in articular and cutaneous variables of PsA. Correlation coefficients > 0.30 are considered evidence of at least weak correlation.

Variable	n	Biserial Correlation Coefficient
PGA improved, yes vs no		
With change in SJC	268	–0.16
With change in TJC	268	–0.19
With change in DAS28	247	–0.22
Variable	**n**	**Spearman Rank Correlation Coefficient**
Change in total plaque score		
With change in SJC	253	0.26
With change in TJC	253	0.28
With change in DAS28	234	0.31

PsA: psoriatic arthritis; PGA: physician's global assessment; SJC: swollen joint count; TJC: tender joint count; DAS28: 28-joint Disease Activity Score.

tations, as well as diagnosis tools used. Patients may present different degrees of skin lesions, nail disease, peripheral arthritis, spondylitis, enthesitis, and dactylitis. For these reasons, the multifaceted nature of PsA presents challenges in defining remission.

For the purpose of our posthoc study, remission of skin symptoms was defined by the absence of psoriasis (PGA = clear/almost clear), and joint remission by the lack of tender and swollen joints (TJC ≤ 1 and SJC ≤ 1) or by well-documented and composite measures of arthritic disease activity. ADA was successful at inducing remission of joint and/or skin symptoms in 64.9% of 268 patients with longstanding PsA disease after only 12 weeks of OL treatment. Simultaneous remission of both skin and joint symptoms occurred in 16–25% of patients who had active baseline skin disease. Nearly two-thirds of patients achieving joint remission did so with the complete absence of tender and swollen joints.

As many as 30% of patients with psoriasis develop PsA[19,21,22]. This observation is indirectly evidenced in the STEREO study by mean psoriasis duration having persisted longer than additional joint symptoms. The joint remission only subgroup had a shorter duration of joint symptoms, as one may expect, although interestingly, the subgroup achieving simultaneous joint and skin remission had mean arthritis duration more similar to the subgroups not achieving joint remission. Baseline predictors for achieving joint remission criteria included TJC and HAQ-DI, and SJC to a lesser extent[4]. Increased baseline joint counts would seem to indicate more advanced disease that is also evidenced by elevated baseline CRP and disease duration in patients who had neither skin nor joint remission at Week 12 compared to other subgroups.

It should be noted that although 143 of the 412 patients (34.7%) were PGA clear or almost clear at baseline, over half of the remaining patients became PGA clear or almost clear at Week 12, demonstrating the ability of ADA to treat skin symptoms of PsA. Nearly all patients who failed to meet the skin remission criteria had active psoriasis at baseline (124/130). However, active baseline psoriasis was also reported in 144 patients who achieved skin remission at Week 12 with these patients manifesting milder symptoms at baseline. Inclusion of patients with inactive baseline disease in the analyses of meeting additional remission criteria yielded similar proportions within the subgroups (data not shown).

A potential limitation of our study is its duration. Twelve weeks may not be long enough to fully alleviate skin lesion symptoms or reduce TJC and SJC ≤ 1. However, the trial design followed the UK National Institute for Health and Clinical Excellence guidance on length of anti-TNF therapy prior to efficacy evaluation[23]. One may deduce from previous TNF inhibitor studies that further improvements may have been observed with increased study duration[16,24], a hypothesis that appears to have been verified by examining those patients who continued in STEREO through Week 20. A further limitation of the study is the absence of enthesitis, dactylitis, and nail psoriasis assessments in the present analysis, all of which can have a significant effect on overall patient quality of life.

Depending on the joint remission definition applied, between 9% and 33% of patients obtained skin and joint remission at Week 12, although these percentages increased in patients receiving ADA through Week 20. Still, improvement in disease symptoms was observed even in patients who did not achieve 1 or both remission criteria. The lack of rheumatologist-assessed swollen joints was observed in 38.6% of all patients at Week 12. All subgroups reported substantially improved patient's mean physical function scores; HAQ-DI improved by 66.4%, 65.7%, 45.4%, and 37.6% for the joint and skin remission, joint remission only, skin remission only, and neither joint nor skin remission subgroups, respectively. Among the patients in the joint remission subgroup, mean Week 12 HAQ-DI scores reflected clinically relevant normal function and were lower than those of the skin remission subgroup, which may have been expected given the focus of the disability index questions on joint involvement and also the observed reduced baseline HAQ-DI scores for the joint remission subgroups. Lastly, patient-reported assessments of pain and disease activity following 12 weeks of ADA treatment were improved in all subgroups. Patients achieving neither joint nor skin remission had the highest Week 12 patient-reported pain and disease activity scores compared to those achieving 1 or both remission criteria, suggesting that these patient-reported measures accurately account for articular and cutaneous disease manifestations. Improvements in patient-reported pain were more impressive in patients achieving joint remission criteria.

Our posthoc study also attempted to correlate observed improvements in joint and skin symptoms of PsA to broaden understanding of disease manifestations and assess the extent to which ADA therapy can successfully treat both conditions.

Despite the ability of ADA to meet articular and cutaneous remission criteria in many patients, improvement in joint and skin manifestations were not correlated in the STEREO population for the 12-week observation period, with the exception of weak correlation between change in DAS28 and change in total plaque score. This would seem to suggest that skin and joint symptoms should be monitored independently to maximize individual patient efficacy.

Defining MDA and remission criteria for rheumatic diseases is an attempt to address chronic inflammation, clinical, and functional aspects of disease[9]. Meeting strict remission or MDA criteria in PsA is challenging because of the multifaceted nature of disease symptoms. Implementing additional remission criteria to the previously mentioned joint and skin disease measures (lack of skin and joint symptoms) attempts to address deficiencies in accounting for patient physical function, pain, and disease activity. In our study, patients who achieved joint remission irrespective of skin remission demonstrated a higher likelihood of meeting additional remission criteria, including pain, disease activity, and HAQ-DI. Simultaneous achievement of increasing numbers of remission criteria variables proved more challenging, especially given the lack of correlation in disease symptoms. PsA remission criteria should attempt to address all aspects of disease symptoms; therefore, the number of required criteria likely extends beyond joint and skin variables. Based on the results presented, the 5 most eligible candidates would seem to be HAQ-DI ≤ 0.5 and PtGA pain ≤ 10 mm, in addition to TJC ≤ 1, SJC ≤ 1, and PGA = clear/almost clear (Table 2). The absence of PtGA disease activity follows Studenic, *et al's* observations that patient-reported disease activity most commonly limited the achievement of the Boolean remission criteria[25].

With respect to patient-reported pain and disease activity scores, this posthoc analysis used the more stringent RA remission criteria cutoffs, as opposed to the suggested PsA MDA criteria. Interestingly, this modified PsA MDA criteria resulted in similar rates when compared to both the RA Boolean remission and SDAI remission. From these analyses, ADA is effective at achieving a broad range of remission criteria addressing both skin and joint disease symptoms in many patients with longstanding PsA.

ACKNOWLEDGMENT

We thank Douglas E. Dylla, PhD, a full-time employee of AbbVie Inc., for his support in medical writing.

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