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HOW TO CITE THIS ARTICLE
Antoni C, Krueger G G, de Vlam K, et al Infliximab Improves Signs and Symptoms of Psoriatic Arthritis: Results of the IMPACT 2 Trial Ann Rheum Dis Published Online First [date of publication]*. doi: 10.1136/ard.2004.032268

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Infliximab Improves Signs and Symptoms of Psoriatic Arthritis: Results of the IMPACT 2 Trial

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Manuscript category: Extended Report

Running title: Infliximab improves psoriatic arthritis

Word count: 251 (abstract), 3792 (manuscript)

Key words: psoriatic arthritis, TNFα, infliximab, enthesopathy, dactylitis
ABSTRACT

Objectives: This phase III, double-blind trial further evaluated the efficacy of infliximab in active psoriatic arthritis (PsA), as observed in the smaller IMPACT trial.

Methods: Two hundred patients with active PsA unresponsive to prior therapy were randomized to infusions of infliximab 5 mg/kg or placebo at weeks 0, 2, 6, 14, and 22. Patients with inadequate response entered early escape at week 16. The primary measure of clinical response was ACR 20. Other measures included Psoriatic Arthritis Response Criteria (PsARC), Psoriasis Area and Severity Index (PASI), and dactylitis and enthesopathy assessments.

Results: At week 14, 58.0% of infliximab patients and 11.0% of placebo patients achieved an ACR 20 response and 77% of infliximab patients and 27.0% of placebo patients achieved PsARC (both p<0.001). Among the 85% of patients with at least 3% body surface area psoriasis involvement at baseline, 63.9% of infliximab patients had at least 75% improvement in PASI compared with 2.3% of placebo patients at week 14 (p<0.001). These therapeutic effects were maintained through the last evaluation (week 24). Fewer infliximab patients than placebo patients had dactylitis at week 14 (18.2% versus 30.0%; p=0.025) and week 24 (11.8% versus 34.0%; p<0.001). Fewer infliximab patients (22.2%) than placebo patients (33.7%) had active enthesopathy at week 14 (p=0.016); corresponding figures at week 24 were 20.4% and 37.2% (p=0.002). Infliximab was generally well tolerated, with a similar incidence of adverse events in each group.

Conclusions: Infliximab 5 mg/kg through 24 weeks significantly improved active PsA, including dactylitis and enthesopathy, and associated psoriasis.
INTRODUCTION
Psoriatic arthritis (PsA) is a chronic and inflammatory arthritis that occurs in association with skin psoriasis. The prevalence of psoriasis in the general population is approximately 1 to 3% (1, 2), and approximately 6 to 42% of psoriasis patients develop PsA (3, 4). In the United States (US), an estimated 4.5 million adults suffer from psoriasis and approximately 1 million have PsA (5). Interactions between T-cells and monocytes/macrophages, the primary source of proinflammatory cytokines, including tumor necrosis factor alpha (TNFα), play an important role in the pathogenesis of PsA. Increased levels of TNFα have been detected in joint fluid and in psoriatic skin lesions in patients with PsA (6, 7). The effects of TNFα inhibition in psoriasis and PsA have been studied extensively with etanercept, a soluble TNF receptor antagonist (8, 9), and infliximab, an anti-TNFα monoclonal antibody (10-17).

In patients with PsA, data from several published studies suggest that infliximab provides fast and dramatic improvement in both arthritis and psoriasis. Results of these studies indicated that infliximab, with or without concomitant disease-modifying antirheumatic drugs (DMARDs), may be an appropriate therapy for arthritis and skin lesions in patients with PsA (10-15). Data from the first double-blind trial of infliximab in PsA (IMPACT), in which 104 patients were studied over 1 year, confirmed the efficacy of infliximab in PsA (16).

The present study, IMPACT 2, was undertaken to examine the efficacy and safety of infliximab in a larger patient population with active PsA and associated psoriasis. In addition to assessing the improvement in arthritis and psoriasis, IMPACT 2 evaluated the efficacy of infliximab in the treatment of 2 characteristic features of PsA, dactylitis and enthesopathy, as well as the treatment effect on the quality of life in patients with this disabling condition.

METHODS
Eligibility
Two hundred adult patients with active PsA diagnosed at least 6 months prior to the first infusion of study drug were enrolled in this study. Active articular disease was defined as 5 or more swollen joints and 5 or more tender joints and either C-reactive protein (CRP) levels of at least 1.5 mg/dL and/or morning stiffness lasting 45 minutes or longer. Patients were required to have had an inadequate response to current or previous DMARDs or nonsteroidal anti-inflammatory drugs (NSAIDs). In addition, patients had to have active plaque psoriasis with at least one qualifying target lesion at least 2 cm in diameter. Patients also were required to have a negative test for rheumatoid factor in their serum.

Patients were excluded from this study if they had evidence of latent or active tuberculosis (i.e., they had to have a clear chest x-ray and a negative purified protein derivative skin test); had chronic or clinically significant infection, malignancy, or congestive heart failure; or if they had used TNFα inhibitors previously. Concomitant MTX treatment (up to 25 mg/week) was allowed at least 3 months prior to the first
infusion and was maintained at a stable dose for at least 4 weeks prior to the first infusion. Oral corticosteroid use was permitted at a stable dose equivalent to no more than 10 mg prednisone per day. The use of DMARDs (other than MTX) or intra-articular corticosteroids was prohibited within 4 weeks prior to the first infusion, and DMARD use other than MTX was not allowed during the trial. Concurrent use of topical or systemic medications/treatments for psoriasis was not permitted during the study, with the exception of low potency topical corticosteroids on the face or groin.

**Study Design**
This study was conducted at 36 centers: 19 in the US, 9 in Europe, and 8 in Canada. The first patient was enrolled on December 20, 2002, and the last patient completed the week 24 visit on January 22, 2004. Institutional Review Boards at the participating sites approved the study, and written informed consent was obtained from all patients before any protocol-specific procedures were performed.

This was a Phase III, double-blind, placebo-controlled, randomized, parallel-group study in which patients were randomly assigned in a 1:1 ratio to receive infusions of either placebo or infliximab 5 mg/kg at weeks 0, 2, and 6 followed by maintenance dosing at weeks 14 and 22. Randomization was stratified by investigational site and baseline MTX usage and was performed using a dynamic patient allocation algorithm. To offer active treatment to patients randomized to placebo, any patient with less than 10% improvement from baseline in both swollen and tender joint counts entered early escape and received infliximab 5 mg/kg at weeks 16, 18, and 22. To maintain the blind, patients randomized to infliximab who had less than 10% improvement received additional placebo infusions at weeks 16 and 18. Patients were assigned to this early escape using a blinded procedure that was part of an interactive patient allocation algorithm so that the option for early escape was not at the discretion of the patient or the physician.

**Study Agent**
Study medication was prepared by an unblinded research pharmacist. Infliximab (REMICADE®, Centocor, Malvern, PA) was supplied in single-use 20-mL vials containing 100 mg of the lyophilized powder. Placebo was identically formulated except that it did not contain infliximab. Study medication infusion was initiated within 3 hours of reconstitution. The infusion solution was administered by blinded investigators over a 2-hour period.

**Study Procedures and Evaluations**
The primary efficacy assessment included components of the American College of Rheumatology (ACR) core set, which was developed originally for rheumatoid arthritis (18). These components were assessed at weeks 2, 6, 14, and 24. Additional efficacy response evaluations, which were assessed at most visits from screening through week 24, included: Psoriatic Arthritis Response Criteria (PsARC; 19) and duration of morning stiffness (minutes) during the previous week. In addition, the following were assessed at weeks 0, 14, and 24: the presence of dactylitis in the hands and feet; the presence/absence of enthesopathy in the feet; and the Short Form 36 (SF-36) questionnaire.
The severity of psoriasis at baseline was defined based on body surface area (BSA) involvement: mild (less than 5% BSA), moderate (5% to less than 10% BSA), and severe (at least 10% BSA). In patients with at least 3% BSA psoriasis involvement at baseline, psoriasis activity was assessed using the Psoriasis Area and Severity Index (PASI) at baseline and weeks 2, 6, 14, and 24. PASI is a composite score, ranging from 0 to 72, used for assessing and grading the severity of psoriatic lesions and their response to therapy. PASI includes assessments of the extent of skin involvement, erythema, plaque thickness, and the degree of scaling (20). In addition, the target lesion score (erythema, plaque induration, and scaling rated on a scale of 0-4 each) was assessed at weeks 0, 14, and 24 in all patients, irrespective of baseline PASI scores.

**Safety Evaluations**

Safety evaluations, including the monitoring of adverse events (AEs) and routine laboratory tests of hematology and chemistry parameters, were performed at every visit through week 24. Blood samples were obtained to determine the presence of antibodies to infliximab using previously described enzyme immunoassay methods (21) prior to infusion at baseline and at week 22. Additionally, blood samples were obtained to determine antinuclear antibodies (ANA; titer of 1:160 or more was considered positive) using the Indirect Fluorescent Antibody test on Hep 2 cells method prior to infusion at baseline and week 24. Among the samples positive for ANA, the number that were positive for antibodies to double-stranded DNA (anti-dsDNA) are reported (22, 23).

**Statistical Methods**

The primary endpoint was the achievement of at least 20% improvement according to ACR criteria (ACR 20) at week 14. The sample size of 200 patients was chosen to ensure an adequate safety evaluation. This sample size also ensured that there was 90% power to detect a significant difference in the proportion of ACR 20 responders between the 2 treatment groups using a chi-square test at a significance level of 0.05, assuming 20% and 42% of patients in the placebo and infliximab treatment groups, respectively, achieved an ACR 20 response. To confirm these power calculations, results of the chi-square test were simulated using the Cochran-Mantel-Haenszel test stratified by baseline MTX usage; the power ranged from 0.9 to 0.99 for all simulated cases.

The Cochran-Mantel-Haenszel chi-square test stratified by baseline MTX usage was used to analyze the primary endpoint and other secondary endpoints with categorical data. Continuous data were compared using a 2-sided F-test using an ANOVA method with baseline MTX use as a factor on the van der Waerden normal scores (24).

Subjects with missing ACR 20 and PsARC data at weeks 14 and 24 were considered nonresponders in these analyses, and data for subjects with missing PASI 75 at these time points were imputed with last observation carried forward. At week 24, early escape subjects were treated as nonresponders for ACR 20, ACR 50, ACR 70, and PsARC; the last observation before early escape at week 16 was carried forward for other assessments.
The primary efficacy and selected secondary efficacy analyses were based on the treatment to which patients were randomized (intent-to-treat), while safety (AEs and postbaseline laboratory abnormalities) analyses were based on the actual treatment received and included patients who received at least 1 study infusion. Safety is reported through week 24 for the combined infliximab group, which included all infliximab-randomized patients as well as all placebo-randomized patients who entered early escape at week 16 or received infliximab in error.

RESULTS

Patient Disposition and Baseline Characteristics

Of the 320 patients who were screened for eligibility, 200 were enrolled; of these, 185 (93%) completed the study through week 24 (Figure 1). The specific reasons for discontinuation are presented in Figure 1.

The placebo and infliximab groups were generally well balanced with regard to demographic and baseline disease characteristics (see Table 1). As evidenced by baseline levels for ACR components, patients enrolled in this trial had active disease. A substantial proportion of the patients had dactylitis and/or enthesopathy. The majority of patients (170 of 200; 85%) had at least 3% BSA psoriasis involvement. When the baseline BSA was considered, the vast majority (more than 70%) had moderate or severe psoriasis. Patients’ baseline SF-36 physical and mental component summary scores indicated reduced quality of life in the enrolled patients compared to the general US population (25), and their HAQ scores indicated impaired physical function. Similar proportions of patients were receiving MTX at baseline (45% and 47% in the placebo and infliximab groups, respectively) at a mean dose of 15 mg/week in the placebo group and 16 mg/week in the infliximab group.

Efficacy

Arthritis Response

As shown in Figure 2, the ACR response to infliximab therapy was evident as early as week 2 and responses were maintained throughout the study. Significantly (p<0.001) higher proportions of infliximab-treated patients achieved an ACR 20 response at week 14 (58.0%) and week 24 (54.0%) than did placebo-treated patients (11.0% and 16.0% at weeks 14 and 24, respectively). At week 14, 36.0% of infliximab-treated patients achieved ACR 50 response and 15.0% achieved ACR 70 response, compared with 3.0% and 1.0%, respectively, of placebo-treated patients (p<0.001; Figure 2). ACR 50 and ACR 70 responses increased from week 14 to week 24, at which time 41.0% of infliximab-treated patients achieved ACR 50 response and 27.0% achieved ACR 70 response, compared with 4.0% and 2.0%, respectively, of placebo-treated patients (p<0.001; Table 2).

The percentage of patients who achieved an ACR 20 response at week 14 was 59.6% among patients receiving MTX at baseline (MTX users) and 56.6% among those not receiving MTX (MTX nonusers). Fewer MTX users than MTX nonusers achieved ACR 50 response (27.7% versus 43.4%) and ACR 70 response (8.5% versus 20.8%) at week...
Results at week 24 were similar between MTX users and nonusers for ACR 20 response (57.4% versus 50.9%), ACR 50 response (42.6% versus 39.6%), and ACR 70 response (21.3% versus 32.1%). The generally lower ACR 50 and ACR 70 responses among MTX users are likely related to the small number of patients included in these analyses and should be interpreted with caution. In general, the concomitant use of MTX did not appear to affect efficacy among patients in the infliximab group. As with the overall study population, the differences in ACR response between the infliximab and placebo groups were significant within both the MTX user and MTX nonuser subgroups (data not shown).

Results for assessments of joint disease other than the ACR core set confirmed the efficacy of infliximab. Significant improvements from baseline to weeks 14 and 24 were observed for the individual components of the ACR 20 among patients in the infliximab group compared with those in the placebo group (Table 2). At week 14, 77.0% of infliximab-treated patients were improved according to the PsARC, compared with 27.0% of placebo-treated patients (p<0.001); similar findings were observed at week 24 (70.0% versus 32.0%; p<0.001). Although similar numbers of placebo- and infliximab-treated patients (41.0% and 40.0%, respectively) had dactylitis of one or more digits at baseline, fewer infliximab-treated patients had digits with dactylitis when compared with placebo-treated patients at week 14 (18.2% versus 30.0%; p=0.025) and week 24 (11.8% versus 34.0%; p<0.001). In addition, while 42.0% and 35.0% of patients in the infliximab and placebo groups, respectively, had enthesopathy at baseline, a significantly lower proportion of infliximab-treated patients had enthesopathy compared with placebo-treated patients at both week 14 (22.2% versus 33.7%; p=0.016) and week 24 (20.4% versus 37.2%; p=0.002).

Skin response
Among the 170 patients who had psoriasis involvement of at least 3% BSA at baseline, significantly higher proportions of infliximab-treated patients experienced at least 50%, 75%, and 90% improvement in PASI from baseline to week 14, when compared with placebo-treated patients (p<0.001; Figure 3). The proportion of patients with at least a 75% improvement in PASI was significantly higher in the infliximab group than in the placebo group at week 14 (63.9% versus 2.3%; p<0.001) and week 24 (60.2% versus 1.1%; p<0.001). Findings at week 14 were similar to those at week 24 for all PASI results (Table 2). As shown in Figure 3, the skin response to infliximab therapy was evident as early as week 2 and improvement was maintained through week 24. Patients treated with infliximab also experienced a significant (p<0.001) improvement from baseline to week 14 in the target lesion score relative to placebo-treated patients (65.6% versus -0.3%; p<0.001), with response maintained at week 24 (Table 2).

Effect on Physical and Mental Function
The physical and mental components of the SF-36 summary scores were significantly improved from baseline to week 14 in patients treated with infliximab (p<0.001, Table 2) relative to those treated with placebo. Results were similar for the physical (p=0.001) and mental (p=0.047) components at week 24. Furthermore, at week 14, the proportion of patients who achieved a clinically meaningful change in HAQ (i.e., at least a 0.3
decrease) (26) was significantly higher in the infliximab group compared with the placebo group (58.6% versus 19.4%, p<0.001); this response was sustained at week 24 (52.1% versus 20.0%; p<0.001).

Adverse Events
Infliximab was generally well tolerated through week 24. The incidences of AEs, serious adverse events, infections, and infusion reactions were similar between treatment groups (see Table 3). The percentage of patients who experienced AEs leading to withdrawal in the combined infliximab group was higher than that in the placebo group (4.0% versus 1.0%). Overall, few clinically significant abnormal laboratory findings were reported. Aminotransferase elevations occurred more frequently in infliximab-treated patients compared with placebo-treated patients. The majority of these elevations were less than 3 times the upper limit of normal. Markedly abnormal alanine transaminase (ALT) and/or aspartate transaminase (AST) values (predefined as > 150 IU/L and ≥ 100% increase from baseline) were reported in a total of 5 patients in the combined infliximab group compared to no patients in the placebo group. All 5 patients discontinued study infusions. One patient was lost to follow-up, but ALT/AST levels returned to normal or less than 1.5 times the upper limit of normal in all 4 patients for whom follow-up data were available. None of these elevations was associated with signs of liver failure. One of the 5 patients was receiving concomitant MTX.

Through week 24, no deaths occurred and no opportunistic infections, including tuberculosis, were reported. No congestive heart failure, demyelinating or new autoimmune disorders, serious infusion reactions, anaphylaxis, or delayed hypersensitivity reactions were reported. One placebo-treated patient developed a basal cell carcinoma of the skin. A small percentage (4.5%) of patients in the combined infliximab group were positive through week 22 for antibodies to infliximab. Newly positive ANA (defined by titer ≥ 1:160) were detected in 9.9% of patients in the combined infliximab group compared with 2.6% in the placebo group. Newly positive anti-dsDNA antibodies were detected in 3 ANA-positive patients treated with infliximab and no ANA-positive patients treated with placebo. No patient developed a lupus-like condition.

DISCUSSION
One-quarter of the patients with PsA are dissatisfied with the treatment they receive (5). The disease manifests first in relatively young patients (age 30-55 years) (3, 27), compared to other rheumatic disease such as rheumatoid arthritis (RA), and is associated with impaired physical function (28), reduced quality of life (28), and increased mortality (29, 30). Therefore, PsA profoundly affects individual well being and socioeconomic status (28-32). Some of the current treatments for PsA, including sulfasalazine (19), leflunomide (33), and etanercept (8, 9) have been well assessed; many of the other commonly used therapies have been adapted from treatment of RA and their use in PsA is not supported by clinical trial data. Furthermore, the use of some traditional DMARDs can be associated with organ toxicity, and the incidence and severity of these toxicities may be different in PsA patients compared with RA patients (34, 35). Considering the potentially disabling nature of PsA and the level of dissatisfaction with current
treatments, there is a need for additional therapies. The results of the IMPACT 2 study demonstrate that infliximab is both effective and well tolerated for the treatment of both the joint and skin components of PsA.

The patients enrolled in IMPACT 2 represented a disease population with well-defined features of PsA, such as arthritis, psoriasis, and rheumatoid factor-negative status. Patients in both treatment groups had characteristic features of PsA, including the presence of dactylitis and enthesopathy. All patients had psoriasis with substantial skin involvement, and psoriasis was frequently rated as moderate to severe as measured by baseline BSA involvement.

In the present study, infliximab was significantly more effective than was placebo when evaluated using ACR 20 response at week 14 (the primary endpoint) and was superior across many other PsA evaluations, including ACR 50, ACR 70, individual ACR components, PsARC, and assessments of dactylitis and enthesopathy. Specifically, ACR 50 and ACR 70 responses were significantly greater in the infliximab group relative to the placebo group by week 2 and 6, respectively, and continued to improve through the 24-week study period. The substantial percentage of patients who achieved an ACR 70 response (27%) indicates that infliximab is highly effective in a significant number of patients. Further, concomitant use of MTX did not appear to affect the efficacy. Finally, two distinctive and common clinical manifestations of PsA, dactylitis and enthesopathy, which have not commonly been included as outcomes in PsA clinical studies, were present in a substantial proportion of patients at baseline and improved significantly at both week 14 and 24 in patients receiving infliximab.

The concomitant and dramatic improvement in psoriasis in this study is noteworthy. Patients treated with infliximab experienced rapid, substantial, and sustained improvement in psoriasis, when measured by PASI improvement in patients with more significant disease and by target lesion score in those with less as well as more significant disease. As early as week 2, the proportion of patients with at least a 75% improvement in PASI from baseline in the infliximab group was significantly greater than that in the placebo group. Marked improvement was observed by week 14 (63.9%) and sustained through week 24 (60.2%). While this was not an active comparator study, when the PASI 75 scores are compared with those achieved by similar patient populations receiving etanercept 25 mg twice weekly in two randomized and controlled studies, the response to etanercept is not as profound; only 26% and 23% of etanercept-treated patients, respectively, achieved the PASI 75 endpoint at weeks 12 and 24 (8, 9). The results for PASI response in IMPACT 2 were substantiated by the mean percent improvement in target lesion score. Significantly, the efficacy results across all endpoints for improvement of both psoriasis and PsA for the IMPACT 2 study of 200 patients at 36 centers confirm those reported previously in the smaller IMPACT study of 104 patients at 9 centers (16).

In addition to the positive impact of infliximab on standard assessments of joint and skin disease, this study documented an improvement in quality of life and physical function. Results of the SF-36 questionnaire indicated a significantly greater improvement in the
physical and mental component summary scores from baseline to weeks 14 and 24 in the infliximab group compared with the placebo group. Accordingly, HAQ results showed that patients in the infliximab group experienced improvement in physical function. Furthermore, the proportion of patients who achieved a clinically meaningful change in HAQ was significantly higher in the infliximab group compared with the placebo group. These findings are especially relevant to patients with PsA, given the potential debilitating nature of the disease and the psychosocial effect of the disease state in many patients with psoriasis (36).

Infliximab was well tolerated through week 24, with generally similar AE profiles in the infliximab and placebo groups. Through week 24, the overall incidences of AEs, SAEs, infections, and infusion reactions were similar between the treatment groups. The type and incidence of infections were not notably different from those reported in previous studies of infliximab in other indications (37, 38). Transient elevations in ALT and AST values, which were not associated with concomitant significant elevations in bilirubin or with other evidence of hepatotoxicity, were reported more frequently in the infliximab group compared with the placebo group. Elevations of aminotransferases have been seen previously with infliximab treatment in RA subjects (37). A comprehensive review of postmarketing data is currently underway. As with any new patient population, the relative significance of these elevations in patients with PsA will require additional evaluation over the long-term.

In summary, the results of the IMPACT 2 trial confirm that treatment with infliximab for up to 6 months is effective in patients with active PsA. Infliximab 5 mg/kg, given at weeks 0, 2, 6, and every 8 weeks thereafter through 24 weeks, reduced clinical signs and symptoms of PsA, including dactylitis and enthesopathy, and improved psoriatic skin disease, physical function, and quality of life in this patient population. Treatment with infliximab was generally well tolerated, with an AE profile similar to that observed in other indications.
ACKNOWLEDGMENTS
The IMPACT 2 study was funded by Centocor, Inc. in Malvern, Pennsylvania. Drs. Antoni, Kavanaugh, and Birbara have received research support from Centocor, and Drs. Antoni, Kavanaugh, and Krueger have served as consultants for Centocor. Drs. Beutler, Guzzo, Zhou, and Dooley are employed by Centocor. The authors wish to acknowledge C. Arnold for her writing assistance in preparing this manuscript.

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REFERENCES


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<td>Patients taking NSAIDs (%)</td>
</tr>
</tbody>
</table>

*Plus-minus values are means ± SD
<table>
<thead>
<tr>
<th>TABLE 2. CLINICAL RESPONSES AT WEEK 14 AND WEEK 24*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 14</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Patients randomized</td>
</tr>
<tr>
<td>ACR criteria</td>
</tr>
<tr>
<td>20% improvement (%)**</td>
</tr>
<tr>
<td>50% improvement (%)**</td>
</tr>
<tr>
<td>70% improvement (%)**</td>
</tr>
<tr>
<td>Achieving PsARC (%)</td>
</tr>
<tr>
<td>Percentage improvement**</td>
</tr>
<tr>
<td>Number of swollen joints</td>
</tr>
<tr>
<td>Number of tender joints</td>
</tr>
<tr>
<td>CRP</td>
</tr>
<tr>
<td>Physician's global assessment of disease activity (VAS)</td>
</tr>
<tr>
<td>Patient's global assessment of disease activity (VAS)</td>
</tr>
<tr>
<td>Patient's assessment of pain (VAS)</td>
</tr>
<tr>
<td>HAQ disability index</td>
</tr>
<tr>
<td>Duration of morning stiffness</td>
</tr>
<tr>
<td>Patients with ≥ 1 dactylitis digits (%)</td>
</tr>
<tr>
<td>Patients with enthesopathy (%)</td>
</tr>
<tr>
<td>PASI response</td>
</tr>
<tr>
<td>Patients with ≥ 3% BSA affected with psoriasis (baseline)</td>
</tr>
<tr>
<td>≥50% improvement (%)**</td>
</tr>
<tr>
<td>≥75% improvement (%)**</td>
</tr>
<tr>
<td>≥90% improvement (%)**</td>
</tr>
<tr>
<td>Percentage improvement in target lesion score**</td>
</tr>
<tr>
<td>Change in SF-36**</td>
</tr>
<tr>
<td>Physical component</td>
</tr>
<tr>
<td>Mental component</td>
</tr>
</tbody>
</table>

*Plus-minus values are means ± SD; **Change or improvement from baseline
## Table 3. ADVERSE EVENTS THROUGH WEEK 24

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Combined a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients treated</td>
<td>97</td>
<td>150</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>65 (67.0%)</td>
<td>100 (66.7%)</td>
</tr>
<tr>
<td>Common adverse events b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>15 (10.0%)</td>
<td>14 (14.4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>5 (5.2%)</td>
<td>9 (6.0%)</td>
</tr>
<tr>
<td>Increased ALT/SGPT</td>
<td>1 (1.0%)</td>
<td>9 (6.0%)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>4 (4.1%)</td>
<td>8 (5.3%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>4 (4.1%)</td>
<td>8 (5.3%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5 (5.2%)</td>
<td>6 (4.0%)</td>
</tr>
<tr>
<td>Adverse events leading to withdrawal c</td>
<td>1 (1.0%)</td>
<td>6 (4.0%)</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>6 (6.2%)</td>
<td>13 (8.7%)</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>6 (6.2%)</td>
<td>11 (7.3%)</td>
</tr>
</tbody>
</table>

a The combined group included all infliximab-randomized patients as well as all placebo-randomized patients who entered early escape at Week 16 or incorrectly received infliximab.
b Common adverse events are adverse events with event rate ≥ 5% in the placebo group or the infliximab group. Adverse events are sorted by decreasing frequency in the infliximab column.
c Adverse event was the primary reason for withdrawal in these patients.
Figure Legends

**Figure 1.** Summary of patient disposition, including number of patients who were randomized to each treatment, entered early escape, discontinued treatment, and/or completed the study, in a controlled trial of infliximab and placebo in patients with psoriatic arthritis.

**Figure 2.** Time pattern of arthritis response, as measured by various degrees of American College of Rheumatology (ACR) response in patients with psoriatic arthritis treated with infliximab or placebo.

**Figure 3.** Time pattern of skin response, as measured by various degrees of Psoriasis Area and Severity Index (PASI) improvement in patients with psoriatic arthritis treated with infliximab or placebo.
200 patients randomized

100 assigned to placebo

- 9 discontinued treatment**
  - Adverse event in (1)
  - Unsatisfactory therapeutic effect in (2)
  - Lost to follow-up in (1)
  - Prohibited change of PsA plaques/medication in (2)
  - Other reasons in (3)
  - 6 discontinued study

- 47 entered early escape at Week 16

- 2 discontinued treatment**
  - Adverse event in (1)
  - Unsatisfactory therapeutic effect in (1)
  - Lost to follow-up in (5)
  - Prohibited change of PsA plaques/medication in (5)
  - Other reasons in (1)
  - 2 discontinued study

- 65 (63.4%) completed Week 24

100 assigned to infliximab 5 mg/kg

- 9 entered early escape at Week 16

- 12 discontinued treatment**
  - Adverse event in (5)
  - Unsatisfactory therapeutic effect in (5)
  - Lost to follow-up in (2)
  - Prohibited change of PsA plaques/medication in (5)
  - Other reasons in (1)
  - 6 discontinued study

- 8 (80.0%) completed Week 24

**Three patients in the placebo group received infliximab at the first infusion in error and were not included in the safety analysis of the placebo group.

**Patients who discontinued treatment could remain in the study and return for evaluations.

†All patients who discontinued from the study are counted in the total patients who discontinued treatment.
Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial

Christian Antoni, Gerald G Krueger, Kurt de Vlam, Charles Birbara, Anna Beutler, Cynthia Guzzo, Bei Zhou, Lisa T Dooley and Arthur Kavanaugh

Ann Rheum Dis published online January 27, 2005

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Notes

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