Long-term use of adalimumab in the treatment of moderate to severe plaque psoriasis: a review of the literature

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Abstract: Psoriasis is a chronic T-cell-mediated inflammatory disease that primarily affects the skin and joints. Patients with moderate to severe psoriasis constitute about 30% of the psoriasis population. Treatment of this group is challenging due to the long-term side effects, toxicities and inconvenience of conventional treatments such as phototherapy, methotrexate and cyclosporine. However, recent advances in our understanding of the pathogenesis of psoriasis have led to the popular use of biologics, which offer a safer, more convenient and effective targeted therapy. Adalimumab was originally approved for treating rheumatoid arthritis. Currently, adalimumab is also approved for treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy or when other systemic therapies are medically less appropriate. Since the onset of the use of biologics, there have been concerns over safety and efficacy when used as long-term therapy. This paper reviews all publications, posters and abstracts reporting original data on the efficacy and/or safety of adalimumab in patients treated for chronic plaque psoriasis for more than 1 year.

Keywords: psoriasis, adalimumab, biologics

Introduction

Psoriasis is a chronic T-cell-mediated inflammatory disease that primarily affects the skin and joints with an estimated world-wide prevalence of 3%. Accurate diagnosis is important due to recent evidence that psoriasis may be associated with other co-morbidities such as metabolic disorders, obesity and may be an independent risk factor for cardiovascular disease.\(^1\) The most common form of psoriasis is plaque psoriasis, which constitutes around 80% to 90% of psoriasis patients. Other less common forms include inverse, erythrodermic, pustular, and guttate psoriasis.\(^2\)

Psoriatic arthritis (PsA) is an inflammatory arthritis characterized by pain, swelling and stiffness of the joints that affects between 6% to 42% of patients with psoriasis. Joint symptoms often precede skin manifestations of the disease by an average of 10 years.\(^3\)

Patients with moderate to severe psoriasis constitute about 30% of the psoriasis population. These patients are determined by a score greater than 10 on several indices including: total body surface area (TbSA 1%–100%), psoriasis area and severity index (PASI 0–72), and dermatology quality of life index (DQLI 1–30). This subset of patients presents a challenge due to the long-term side effects, toxicities and inconvenience of conventional treatments such as phototherapy, methotrexate and cyclosporine. However, recent advances in our understanding of the pathogenesis of psoriasis have led to the popular use of biologics, which offer a safer, more convenient and effective targeted therapy.\(^4\)
Recently, several studies suggest that patients with severe psoriasis may have an increased risk for cardiovascular disease, depressive illness, lymphoma (Hodgkin’s lymphoma and cutaneous T-cell lymphoma), and a decreased life expectancy.

We systematically reviewed all published articles, posters, and abstracts reporting original data concerning the efficacy and/or safety of adalimumab in chronic plaque psoriasis for more than 1 year. Relevant articles were identified by searching Medline from its inception until December, 2009 for combinations of the search terms “psoriasis” and “adalimumab”. Animal studies were excluded. No persons other than the authors of this manuscript were involved in the design, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

Pathogenesis of psoriasis

The pathogenesis of psoriasis is currently viewed as a disorder of TH1 cell-mediated immunity. Tumor necrosis factor α (TNF-α), which is a natural occurring cytokine, is elevated in the plaques as well and in the synovial joints and serum in psoriasis patients. TNF-α appears to be responsible for the keratinocyte hyperproliferation, endothelial cell regulation, and recruitment and activation of memory T cells that perpetuate the inflammatory response in psoriasis.\(^1\) TNF-α, produced by activated T-cells, promotes the inflammatory response by activating nuclear factor κB, leading to the induction of interleukin (IL1)/6/8 and to the up-regulation of adhesion molecules on endothelial cells. These interleukins are responsible for the up-regulation of adhesion molecules on endothelial cells.\(^4\) IL-23 has also been found in increased levels and stimulates the survival and proliferation of TH17 cells. More research is needed to access the role in the TH17 pathway in the pathogenesis of psoriasis, as it may play a key role in effective treatment options.\(^3\)

Anti-TNF agents

Anti-TNF-α agents block the inflammatory effects of TNF-α and include adalimumab, infliximab, and etanercept. Blocking TNF-α may also inhibit the Th17 pathway. These TNF agents have become popular treatment options for a variety of inflammatory disorders including psoriasis and PsA.\(^4\)

Pharmacology and recommended dosing of adalimumab

Adalimumab is the first fully humanized recombinant monoclonal antibody that is indistinguishable in structure and function from naturally occurring IgG1. Adalimumab binds to both soluble and cell-bound TNF-α and prevents TNF-α interaction with the p55 and p75 cell surface TNF receptors. Adalimumab lyses surface TNF expressing cells in vitro in the presence of complement and also induces apoptosis in cells expressing surface TNF-α, thereby neutralizing its effects and improving joint and skin manifestations.\(^12\)

In addition, adalimumab modulates biological responses that are induced or regulated by TNF, including changes in the levels of adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1, and ICAM-1 with an IC\(_{50}\) of 1–2 \(\times\) \(10^{-10}\) M).\(^12\)

According to the therapeutic window concept,\(^9\) the steady-state range of serum or tissue drug concentrations should be adequate for neutralization of surplus TNF, but not so high as to threaten safety because of neutralization of homeostatic concentrations of TNF required for host defense, or so low as to impair efficacy from suboptimal neutralization of TNF. Recommended dosing for the treatment of psoriasis is 80 mg given subcutaneously at week one, 40 mg given subcutaneously at week 2, followed by regular dosing of 40 mg subcutaneously administered every 2 weeks thereafter.\(^10\)

Adalimumab given 40 mg subcutaneously every other week produces steady-state serum trough concentrations of 4 to 8 \(\mu\)g/mL, which are 3 to 7 times greater than the clinically effective serum concentrations (0.8–1.4 \(\mu\)g/mL).\(^11\) The systemic clearance of adalimumab is approximately 12 mL/h. Once therapy is initiated, the drug reaches its peak around 5.5 days and has a half-life of approximately 14 days ranging from 10 to 20 days across studies. Mean serum adalimumab trough levels at steady state increases proportionally with dose following 20, 40, and 80 mg every other week and every week subcutaneous dosing.\(^10\) In long-term studies with dosing more than 2 years, no evidence exists of changes in clearance over time.

Current approval

Adalimumab is currently Food and Drug Administration (FDA) and European Medicines Agency (EMEA) approved for the treatment of PsA, rheumatoid arthritis (RA), Crohn’s disease (CD), juvenile idiopathic arthritis (JIA), ankylosing spondylitis (AS), and, more recently, moderate to severe plaque psoriasis.\(^10\) Specifically, in the US, adalimumab is approved for treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy or when other systemic therapies are medically less appropriate. Before starting treatment with adalimumab, a complete history and physical exam should be performed. Recommended labs include a complete
Efficacy and safety concerns based on previous RA studies

To date, most large-scale safety assessments of adalimumab are based on trials of patients with RA. Patients with RA are often treated with the combination of TNF inhibitors and an immunosuppressive agent such as methotrexate, while patients with psoriasis are often treated with the TNF inhibitors as monotherapy. The extrapolations on the safety of TNF inhibitors derived from this combination therapy data may actually overestimate the potential risk of these agents when used as monotherapy in psoriasis. It is important to be aware of potential adverse events that have been reported with the use of adalimumab in RA studies. Serious adverse events of concern are discussed below. However, the safety data based on RA studies should only be cautiously compared between other indications such as moderate to severe plaque psoriasis, due to differences in co-morbidities and patient populations.

Studies of RA patients have shown that the most common adverse events associated with adalimumab therapy are injection-site reactions. They are usually mild and include local erythema and pruritus. In clinical studies, 53% of adalimumab patients with RA developed infections compared with 47% of placebo-treated patients. Other common adverse events include upper respiratory tract infections, rhinitis, bronchitis and urinary tract infections.

The incidence of serious infections in studies of RA patients was under 2%. However, patients with underlying predisposing medical conditions are at a higher risk. Rare opportunistic infections, including histoplasmosis, cryptococcosis, aspergillosis, coccidioidomycosis, candidiasis, listeriosis and pneumocystis, have been reported. Most of these patients were also treated with other immunosuppressive agents, such as methotrexate, systemic corticosteroids, or both.

In the event of an infection requiring antibiotic therapy, adalimumab should be withheld and appropriate treatment should be initiated. However, in the event of more serious infections or opportunistic infections, adalimumab should be discontinued and the patient should be treated appropriately. Treatment with TNF inhibitors should be avoided if possible in patients with chronic, serious, or recurring infections.

Registry data from patients with RA and post marketing reports to the FDA have identified numerous cases of Tb reactivation associated with all TNF inhibitors. Extrapolunmonary or disseminated cases of Tb occurred in 7 patients on anti-TNF therapy during the first 534 patient-years of adalimumab exposure in clinical trials; the rate of Tb decreased by 75% in European trials after the introduction of routine Tb screening. The FDA currently recommends Tb screening with a purified protein derivation before beginning anti-TNF therapy. A tuberculin skin test (PPD) or quantitative Gold serum assay can be used to screen for Tb. For patients about to initiate anti-TNF therapy, a positive test...
is read if greater than 5 mm induration is observed at 48 to 72 hours. For a positive PPD reading, a follow-up chest X-ray is indicated to rule out an active infection. If a patient is diagnosed with a latent infection, prophylaxis with 9 months of isoniazid is warranted. Anti-TNF therapy may be initiated after 1 to 2 months only if the patient is adhering to and tolerating the isoniazid therapy. Patients with active tuberculosis should be appropriately referred to a specialist to begin the standard 4-drug treatment. Concurrent anti-TNF therapy is contraindicated in active tuberculosis.

In trials of patients with RA treated with adalimumab, the incidence rate of lymphomas was 3.1. Risk of lymphoma is substantially increased in a subset of patients with very severe RA, regardless of previous treatment types. High inflammatory activity, rather than its treatment, is a major risk determinant. Further investigation is warranted to evaluate if TNF inhibitors are associated with increased lymphoma rates.

Patients treated with adalimumab tend to have a higher incidence of demyelinating conditions, especially multiple sclerosis (MS). MS has been reported to develop in and also worsen in patients taking TNF inhibitors. However it has been suggested that psoriasis and RA patients have a higher incidence of MS compared to the general population. TNF inhibitors should be avoided in the setting of a personal history of demyelinating conditions or patients with first-degree relatives with MS.

To determine the hazard risk of developing or worsening heart failure, RA patients treated with infliximab, etanercept, or adalimumab (n = 2757) or conventional disease-modifying anti-rheumatic drugs (controls; n = 1491) in a German biologics register were studied. No evidence was found of an increased risk of heart failure with TNF-α inhibitors, especially if no concomitant treatment with glucocorticoids or cyclooxygenase 2 inhibitors is given. Since exacerbation of chronic heart failure (CHF) has been reported with TNF inhibitors, however, it has been recommended that adalimumab be avoided in patients with severe CHF (class III or IV) and discontinued in those with mild disease during a CHF exacerbation.

Data suggest there may be a risk of hepatotoxicity and hepatitis B reactivation in adalimumab patients. Whereas TNF-α may promote viral clearance in hepatitis B, it is thought to promote chronic liver injury in hepatitis C, with elevated levels of TNF-α in patients with hepatitis C compared to the general population. A few reports have stated that anti-TNF treatment in hepatitis C is safe and well tolerated by patients and may even be beneficial. Consultation with liver specialists as indicated may be appropriate when considering the use of anti-TNF therapy in this setting. There is an FDA warning suggesting that patients who have concurrent hepatitis B infection should not be treated with any of the TNF inhibitors.

The safety and efficacy of adalimumab in immunosuppressed patients have not been evaluated. HIV is listed among the relative contraindications for anti-TNF therapy. Because clinical trials have excluded patients with HIV/AIDS, limited data are available. However, in a study of 64 RA patients there was no evidence of depression of delayed-type hypersensitivity, depression of immunoglobulin levels or change the number of effector T and B cells, natural killer cells, monocytes, macrophages or neutrophils. There have been several case reports of HIV patients treated with etanercept and infliximab in which there did not appear to be an increase in morbidity or mortality. In some patients, some symptoms of HIV/AIDS such as aphthous ulcers, cachexia, dementia, and fatigue actually improved with TNF blockade. HIV/AIDS patients who are well controlled on antiviral therapy and have failed all other treatment options may be carefully selected for anti-TNF therapy under careful surveillance of their physician. However, there are no conclusive data and no specific recommendations in the current guidelines.

In a prospective cohort study, in which 289 RA patients on anti-TNF therapy were followed through the course of several years, 128 dermatological events were recorded in 72 patients. In placebo-controlled randomized clinical trials on adalimumab in RA patients, conversion rates of patients with negative ANA at baseline to positive ANA occurred in 11% to 26% of RA patients treated with adalimumab, and 5.5% to 15.2% of RA patients who received placebo. Interestingly, 5% to 44% of RA patients converted from ANA(+) to ANA(−). Presenting manifestations were mostly cutaneous lesions, photosensitivity and serositis. No evidence exists that developing ANA, anti-DNA antibodies or anticyclic citrullinated peptide antibodies while on TNF antagonist therapy increases the risk of developing clinical systemic lupus erythematosus (SLE)-type syndromes.

However, one case of clinical SLE and 2 cases of cutaneous lupus have been identified in patients shortly after initiating adalimumab in RA patients in clinical practice. VanRijthoven et al described clinical symptoms of SLE in a 56-year-old female with RA who was loss response to infliximab so then switched to adalimumab. ANA and anti-dsDNA were positive at the initiation of adalimumab therapy and clinical symptoms of lupus (no organ involvement) ensued after 4 injections of adalimumab. Resolution of
Efficacy of adalimumab in the long-term treatment of moderate to severe plaque psoriasis and psoriatic arthritis

Even though adalimumab has only been evaluated for up to 100 weeks for chronic plaque psoriasis, the efficacy and safety of adalimumab therapy has been evaluated up to 120 weeks for PsA. The ADEPT trial evaluated the long-term efficacy and safety in PsA over a 2-year period. Of particular interest is the efficacy of adalimumab in the clearance of skin lesions as well as the long-term safety profile. It is important to note that patients who were on non-steroidal anti-inflammatory agents, disease-modifying anti-rheumatic drugs or prednisone before the trial could continue these medications throughout the study. In this placebo-controlled trial, 298 patients completed a 24-week double-blind period; 285 patients were then enrolled in an open-label extension study and received 40 mg adalimumab subcutaneous every other week for up to an additional 120 weeks. Skin assessments were restricted to patients with at least 3% body surface area involvement at enrollment. Notably, greater than 20% achieved and maintained a PASI 100 at 48 weeks and 56.6% had a physicians global assessment (PGA) of clear or almost clear at 104 weeks. The percentage of patients achieving PASI 50, PASI 75, PASI 90, or PASI 100 changed by 10% or less from week 48 through 2 years of adalimumab treatment. Skin-related improvements that were present after 48 weeks of adalimumab therapy were maintained through 2 years of therapy for most patients.

To compare treatment effectiveness as well as patient satisfaction and tolerability of the TNF-α antagonists, Heiberg et al compared the discontinuation rates of adalimumab, infliximab, and etanercept in patients with PsA, RA, and AS. 150 patients were treated with 172 anti-TNF-α treatment courses in patients with PsA (adalimumab n = 28; infliximab n = 48; etanercept n = 96). Concomitant methotrexate therapy (68%) was associated with lower withdrawal rates of all three anti-TNFα agents. Discontinuation rates were lower for adalimumab (14.3%) than for infliximab (25.0%) or etanercept (24.0%). These data suggest that 86% of patients treated with adalimumab maintained acceptable efficacy, patient satisfaction, and tolerability to maintain compliance.

In phase II double-blind, randomized controlled clinical trials of adalimumab in chronic plaque psoriasis, in the open-label extension arm, patients who received adalimumab for 60 weeks for plaque psoriasis achieved PASI 75 in 56% of the every other week, 64% of the every week, and 45% of the placebo/eow groups. Total clearance (PASI 100) at week 60 was observed in 16% of the every other week group, 26% of the every week group and 19% in the placebo/every other week group.

In a phase III double-blind, randomized-controlled clinical trials of adalimumab 40 mg every other week in 1212 patients with moderate-to-severe plaque-type psoriasis, Menter et al reported initial PASI-75 response rates of 71% after 16 weeks and 70% after 24 weeks of treatment. Patients who had met the PASI-75 response criterion were re-randomized at week 33 to continue treatment with adalimumab or switched to placebo until week 52. Loss of response over the 19 weeks, defined as <PASI 50 and ≥6 point increase in PASI, was observed in 5% of patients continuing adalimumab therapy and 28% of patients switched to placebo. Based on these findings, loss of response after continuous treatment with adalimumab over 1 year was 5% while sustained efficacy was seen in 72% of patients for 19 weeks after discontinuation of adalimumab treatment.

A small retrospective study by Van et al evaluated 49 patients with moderate-to-severe plaque psoriasis who has lack of or loss of efficacy with prior biologic therapy including infliximab and/or etanercept. After 12 months of adalimumab therapy, 78% of patients were considered as “clear” or “almost clear” according to PGA of disease severity. Five patients (10%) stopped adalimumab due to lack of effectiveness. Thus, it appears that prior treatment with another TNF-α antagonist does not significantly appear to diminish response to adalimumab.
Although loss of efficacy over time has been observed in patients receiving infliximab, this does not appear to be an issue for adalimumab based on published data. In contrast, efficacy in patients with psoriasis treated continuously with adalimumab for 100 weeks sustained PASI 75 responses in 83% and PASI 100 responses in 32%, with a PGA score of “clear” or “minimal” in 70%. Similar efficacy was seen in patients with moderate to severe plaque psoriasis and PsA treated with adalimumab for 2 years.

Mentor et al also assessed for the presence of anti-adalimumab antibodies (AAAs). 8.8% had detectable AAAs during the 52-week treatment period. Three of 7 AAA-positive patients, compared with 65 of 233 AAA-negative patients, lost an adequate response. The presence of AAAs was not correlated with any treatment-related adverse events, including serious adverse events and injection-site reactions. Some patients who developed AAAs demonstrated reduced efficacy. However, because the percentage of patients who developed antibodies to adalimumab was small, the overall involvement of AAAs in reduction of efficacy was minimal.

Safety and tolerability of adalimumab in the long-term treatment of plaque psoriasis and psoriatic arthritis

The safety profile of adalimumab in phase II clinical trials during long-term treatment of PsA and psoriasis was consistent with the safety profile of previous adalimumab studies. No clinically meaningful changes in the type and frequency of adverse events were observed with 24 versus 48 weeks of adalimumab treatment. No significant changes in laboratory values were seen, besides the desired effect of a decrease in C-reactive protein. No new safety signals were seen compared to rheumatoid arthritis. Specifically, no indication of an increase in such TNF-associated adverse events such as Tb, malignancies, demyelinating disease, CHF, or SLE were observed. Through 2 years of adalimumab exposure, only 1 report of peritoneal Tb, 4 of oral candidiasis, 1 of non-Hodgkin’s lymphoma, 2 of basal cell carcinoma, and 1 with a neuroendocrine carcinoma of the skin occurred. Three deaths occurred among the 298 patients. Two patients experienced cardiopulmonary arrest from a myocardial infarction, which was probably not related to adalimumab. The third patient experienced sudden death that was attributed to acute pulmonary edema and was considered to be possibly related to adalimumab.

In phase-II clinical trials on patients receiving adalimumab for 60 weeks, adalimumab was generally well tolerated, with 9% of patients discontinuing therapy due to an adverse event. No significant laboratory abnormalities were observed. The most frequently reported side effects included nasopharyngitis and upper respiratory infection as well as pain at the injection site. Fourteen patients experienced a serious adverse event during the 60-week period, being more common in the patients receiving adalimumab weekly (11 patients). Serious adverse events included 2 cases of malignant melanoma, 1 case of squamous cell carcinoma, 2 cases of cerebrovascular events, 1 case of breast carcinoma, 1 case of gastric adenocarcinoma, 1 case of coccidiomycosis and 2 cases of Tb.

Burmester et al performed a safety analysis in 19,041 patients exposed to adalimumab using data from 36 global clinical trials through April 15, 2007, and concluded that the overall malignancy rates and the all-cause mortality rates for adalimumab treated patients were as expected for the general population. Safety data were included from adalimumab stud-

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<th>Table 1 Compiled safety data (rates per 100 patient-years) for serious adverse events for adalimumab in different FDA-approved indications</th>
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<td><strong>Established safety profile for adalimumab</strong></td>
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**Abbreviations:** CHF, congestive heart failure; SLE, systemic lupus erythematosus; PY, patient-years; Ps, psoriasis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; AS, ankylosing spondylitis; JIA, juvenile idiopathic arthritis; CD, Crohn’s disease.
ies in PsA, RA, AS, CD, and JIA. Data revealed that the average psoriasis patient treated with adalimumab was 44 years of age, which is 10 years younger than the average RA patient. Also, 61.8% of RA patients were on concomitant immunosuppressive therapy and 58.6% were on concomitant systemic steroid therapy compared to only 0.3% and 1.2% of psoriasis patients, respectively. Cumulative rates of adverse events in RA patients treated with adalimumab have remained stable over 10 years. Rates of adverse events for psoriasis patients in adalimumab trials were lower compared to those with RA in adalimumab trials, while rates of adverse events for PsA, AS, CD, and JIA were similar to or lower than rates for RA (Table 1). Overall malignancy and mortality rates for adalimumab-treated psoriasis patients were comparable to the general population.50

The monthly incidence rate of injection-site reactions in published clinical trials ranged from 1.2%41 to 3.4%34 (Table 3). Within 2 years of exposure to adalimumab, 20/298 patients with PsA discontinued treatment due to adverse events.32 Of 3 patients (1.0%) who died within the observation period, 2 had myocardial infarction, which was classified as probably not related to adalimumab, and 1 experienced sudden death after acute pulmonary edema, which was classified as possibly related to adalimumab.32 No deaths were observed in the other clinical trials included in this systematic review.34,35,43,44 Possibly from the associations of co-morbidities with psoriasis and PsA, the randomized clinical trial by Genovese et al to assess the efficacy and safety of adalimumab for PsA found significantly more adverse events in patients receiving placebo compared to those receiving adalimumab (P < 0.01).44

Despite the fact that patients were screened for latent Tb prior to inclusion and not eligible if Tb was suspected unless Tb treatment had been initiated already in clinical trials, 3 cases of Tb were observed in the randomized, placebo-controlled clinical trials (Table 2).34,35 Other severe infections observed in clinical trials assessing adalimumab for psoriasis included coccidioidomycosis (n = 1)34 and viral meningitis (n = 1)44,40,41 No cases were reported of opportunistic infections in psoriasis patients treated with adalimumab, although a series of cases with Legionella pneumophila pneumonia has been reported in RA patients treated with adalimumab.45

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Table 3 Case reports of serious adverse events in psoriasis patients treated with long-term adalimumab

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<tr>
<th>References</th>
<th>Clinical history (sex, age, concomitant medications)</th>
<th>Duration of adalimumab prior to SAE</th>
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<th>Resolution of symptoms</th>
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<td>Chung et al</td>
<td>1. Male, age 55, MTX, simvastatin, atenolol, aspirin, metformin, paroxetine, risperidone</td>
<td>1. Two months</td>
<td>1. Rapid painless decrease of central vision in one eye; MRI: retrobulbar optic neuritis</td>
<td>1. Complete resolution after discontinuation of adalimumab</td>
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<td>Deng et al</td>
<td>Male, age 54, MTX</td>
<td>One year</td>
<td>Annular erythematous papules on thighs and back, clinically and histologically consistent with interstitial granulomatous dermatitis</td>
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Abbreviations: MTX, methotrexate; SAE, serious adverse event; MRI, magnetic resonance imaging; CNS, central nervous system.

December 2009, no events of progressive multifocal leukoencephalopathy have been reported among subjects participating in controlled clinical trials on adalimumab or in medical published literature.

Because late recurrences of melanoma in RA patients receiving anti-TNF-α treatment have been reported,47 patients with a history of melanoma have not been eligible in clinical trials on adalimumab in psoriasis patients. In these double-blinded, placebo-controlled, randomized clinical trials on psoriasis patients treated with adalimumab, 10 cases of non-melanoma skin cancers and 3 cases of malignant melanoma were observed (Table 2).

In phase II clinical trials on psoriasis patients treated with adalimumab, a few patients in each treatment group (placebo, 40 mg every other week, 40 mg weekly) converted from negative to positive (5.8%, 2.2%, and 12%, respectively), although a greater number of patients converted from positive to negative (8%–10%) during the first 12 weeks of the trial.34 The most significant autoantibody induction occurs early in treatment (in the first year) and stabilizes over time. These data (as well as negative to positive shift) suggest that only short-term humoral immune responses are induced during TNF-α blockade. Through December, 2009, no cases of lupus have been reported in the medical literature after long-term treatment with adalimumab in plaque psoriasis.

Deng et al reported 5 cases of interstitial granulomatous dermatitis developing in patients treated with a variety of TNF-α antagonists, including one patient developing these erythematous annular plaques after treatment with adalimumab for 1 year (Table 3) and which resolved upon discontinuation of adalimumab.48

There have also been reports of flaring or changing forms of existing psoriasis as well development of palmoplantar pustulosis in patients with no previous history of psoriasis.49 Immuno-histochemical staining of skin biopsy specimens showed increased staining for IFN-α in anti-TNF-α-induced psoriasis compared with patients with non-drug induced psoriasis. Collamer et al reviewed all cases of pustular psoriasis occurring during anti-TNF-α therapy and concluded that new-onset psoriasis may occur any time after initiation of anti-TNF-α therapy and often presents with an uncommon morphology or distribution.50 They speculated that disruption in cytokine balance following TNF-α inhibition may trigger the upregulation of plasmacytoid dendritic cells and the subsequent production of unopposed interferon-α. Multiple reports on the induction or exacerbation of psoriasis in patients treated with TNF-α antagonists exist,51 including such cases associated with adalimumab as new onset generalized pustular psoriasis and52 pustular psoriasis of the scalp.53 Although it has been reported to cause pustular psoriasis, adalimumab has also been found to be effective in the treatment of recalcitrant generalized pustular psoriasis in adults53 and adolescents.54 Therefore, adalimumab-induced psoriasis requires discontinuation of adalimumab only in cases unresponsive to topical anti-psoriatic treatment.

**Conclusion**

Adalimumab has demonstrated excellent efficacy in moderate to severe plaque psoriasis. Based on the current literature on the use of adalimumab for plaque psoriasis, no significant increase in risk of serious infections is observed, in contrast to what has been previously reported in the treatment of RA. Due to differences in co-morbidities, adalimumab treatment
for patients with moderate to severe plaque psoriasis may have less adverse effects compared to RA patients. Prior to initiation of adalimumab therapy, however, patients should be evaluated for active/latent tuberculosis, serious infections, and other contraindications.

**Disclosures**

The authors declare no conflicts of interest.

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