Potential Use of TNF Inhibitors in the Treatment of Psoriasis

The Potential of TNF Inhibitors Relative to Other Therapies
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The Role of TNF in Psoriasis and Psoriatic Arthritis
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Faculty Disclosure Faculty/authors must disclose any significant financial interest or relationship with proprietary entities that may have a direct relationship to the subject matter. They must also disclose any discussion of investigational or unlabeled uses of products.

Dr. Lebwohl has received financial support from Wyeth-Ayerst Pharmaceuticals and Immunex Corporation, is a consultant to Immunex, and discusses unlabeled use of etanercept for psoriasis and psoriatic arthritis. Dr. Cohen has received financial support from Wyeth-Ayerst Pharmaceuticals, Immunex, and Centocor. He discusses unlabeled use of etanercept and infliximab in psoriatic arthritis. Dr. Goffe has received financial support from Immunex and discusses unlabeled use of etanercept in psoriasis and psoriatic arthritis. He also discusses investigational use of TNF inhibitors.

Target Audience This activity has been developed for dermatologists and other health care professionals involved in the treatment of psoriasis and psoriatic arthritis.

Educational Needs The roles of tumor necrosis factor (TNF) and other cytokines in psoriasis and psoriatic arthritis have been under evaluation for several years, following the identification of increased levels of TNF-α and other proinflammatory cytokines in the synovial fluid and skin lesions of patients with psoriatic arthritis. These findings have more recently led to clinical evaluation of the potential benefits of TNF inhibitors in treating psoriasis and psoriatic arthritis. Emerging data from phase II clinical trials and the clinical experience of lead investigators suggest the potential of these agents to improve symptoms and disease progression in psoriatic arthritis. As clinicians who specialize in skin disorders, dermatologists should be aware of the latest developments in this area. Ongoing research on the use of TNF inhibitors in psoriasis and psoriatic arthritis is the focus of this activity.

Learning Objectives Upon completion of this activity, participants should be able to:
• Describe the role of TNF in psoriasis and psoriatic arthritis.
• Discuss emerging data on the use of TNF inhibitors in treating psoriasis and psoriatic arthritis.
• Explain the potential impact of these agents on current approaches to psoriasis and psoriatic arthritis.

Accreditation The American Academy of Dermatology certifies that this educational activity has been recognized for 1 hour of AAD Category 1 credit and may be used toward the American Academy of Dermatology’s Continuing Medical Education Award. This program was developed in accordance with the Accreditation Council for Continuing Medical Education guidelines. Term of approval, November 2001 – November 2002.
Despite growing knowledge about the pathogenesis of psoriatic arthritis—for example, the influence of genetic, immunologic, and etiologic factors—no pharmacologic interventions have been specifically approved for treating this condition. Similarly, few double-blind, placebo-controlled trials have been conducted among patients with psoriatic arthritis.

There are five major goals in the management of psoriatic arthritis (Table 1): (1) suppress joint and skin inflammation, (2) maintain musculoskeletal function, (3) prevent joint deformities, (4) prevent disability, and (5) improve quality of life. To meet these goals, clinicians have used a variety of treatments, none of which has been formally approved for psoriatic arthritis, but many of which are known to have some therapeutic effect. Certainly, some of the treatments prescribed for psoriatic skin lesions are known to cause improvements in joints as well.

**Sulfasalazine and Methotrexate**

Four controlled trials have been conducted with sulfasalazine (Table 2). Two small studies, by Farr and colleagues and Fraser and coworkers, yielded contradictory results: The former demonstrated significant improvement in painful joints; the latter showed no significant difference.

Two larger studies failed to demonstrate consistent benefit over placebo. The first of these, by Dougados and colleagues, compared sulfasalazine with placebo in a double-blind, randomized, 24-week study of patients with spondyloarthropathy who had active disease after a trial of nonsteroidal anti-inflammatory drugs. Among the 351 patients enrolled were 136 with psoriatic arthritis. The primary measures of efficacy were the physicians’ and patients’ overall assessments, pain, and morning stiffness. A subgroup analysis of the patients with psoriatic arthritis showed that the greatest beneficial effects of sulfasalazine were seen in this group, although the only end point that reached statistical significance was in the patients’ global assessment.

In the second large clinical trial comparing sulfasalazine with placebo, Clegg et al enrolled 221 patients with active psoriatic arthritis in a randomized, double-blind, 36-week multicenter study. The response rates at the end of treatment just reached statistical significance: 57.8% in the sulfasalazine group versus 44.6% in the placebo group (P = 0.05). The investigators also noted that the patients taking sulfasalazine had a greater decline in erythrocyte sedimentation rate than did those in the placebo group (P < 0.0001). However, most clinical variables, including pain and tenderness scores, did not improve.

A trend in favor of sulfasalazine over placebo (P = 0.066) with respect to improvement in skin scores also was seen.

Controlled clinical trials in patients with psoriatic arthritis have also been performed with the use of methotrexate (Table 3). Only one of two small placebo-controlled studies, from Black et al and Willkens et al, demonstrated improvement in joint swelling and tenderness with methotrexate, compared with placebo. Substantial toxicity with methotrexate also was seen.

A case-control study of methotrexate in a population of patients with psoriatic arthritis was conducted by Abu-Shakra and coworkers. Thirty-eight patients who had had psoriatic arthritis for a mean of 11.4 years were enrolled; 38 patients who had never used methotrexate were identified from a psoriatic arthritis database and served as controls. The treatment and control groups were matched according to joint damage, actively inflamed joints, gender, and disease duration. The primary outcome measure was an increase in the number of damaged joints, as seen on x-rays.

Twenty-three patients (60%) completed 24 months of methotrexate treatment. According to clinical evaluations, 45% compared with 50% of controls had at least a 40% improvement in the actively inflamed joint count at 6 months; 47% of patients and 53% of controls had at least a 40% clinical...
improvement at 24 months. However, one troubling finding was that progression of joint damage was seen on radiography in 63% of methotrexate-treated subjects and 47% of controls—not a statistical difference.

Spadaro and coworkers compared methotrexate with cyclosporin A in a 48-week, prospective, double-blind, randomized, controlled trial. The study was completed by 59% of the cyclosporin A patients and 72% of the methotrexate-treated patients. The clinical improvements were significant in both groups, as assessed by measures including number of painful joints, number of swollen joints, duration of morning stiffness, grip strength, and Psoriasis Area Severity Index. There were no significant differences between the groups in any of the parameters measured except in erythrocyte sedimentation rate, which was reduced in the methotrexate group ($P < 0.01$), and liver enzyme values, which were increased in the methotrexate group ($P < 0.01$). There were more withdrawals due to toxicity in the cyclosporin A group.

While methotrexate and sulfasalazine are beneficial in some patients with psoriatic arthritis, they are limited by toxicity and by incomplete efficacy in many patients, as well as by the absence of evidence to demonstrate that they prevent disease progression.

**Studies With Other Current Therapies**

In a 24-week comparative study of cyclosporin A, 5 mg/kg/day, versus azathioprine, 100 mg/day, cyclosporin A showed a noticeable—although not statistically significant—improvement in patients with psoriasis. Both agents are limited by their respective toxicities, especially bone marrow toxicity for azathioprine and nephrotoxicity for cyclosporine.

Palit and colleagues conducted 24-week studies of oral gold (auranofin) and intramuscular gold thiomalate in a double-blind, four-center trial in 82 patients with psoriatic arthritis. Auranofin given at a dosage of 3 mg twice daily yielded no significant difference, compared to placebo. The patients on intramuscular gold, 50 mg/week, had statistically significant decreases in pain and the Ritchie articular index.

Thus, intramuscular gold and cyclosporine may prove beneficial in selected patients, but again, toxicity and limited efficacy are drawbacks to their use.

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**Emerging data on the effects of TNF-α inhibitors provide a promising outlook for their role in treating psoriasis and psoriatic arthritis.**

**Future Directions**

More controlled clinical trials in psoriatic arthritis are needed. The clinical trials that have been published on the treatments currently in use have yielded either subtle or contradictory results. It has been suggested in many of the studies conducted to date that patients should be offered aggressive treatment early in the course of the disease to prevent progression.

A new class of agents has emerged that are designed to inhibit the inflammatory activity of tumor necrosis factor alpha (TNF-α). This class of agents represents a breakthrough in the treatment of psoriatic arthritis and skin psoriasis. Two of these agents—infliximab and etanercept—are currently approved by the U.S. Food and Drug Administration for the treatment of patients with rheumatoid arthritis.

Emerging data on the effects of TNF-α inhibitors provide a promising outlook for their role in treating psoriasis and psoriatic arthritis. Indeed, these agents may fill a considerable gap in current treatment options. Dermatologists should look to findings from ongoing prospective, placebo-controlled studies with TNF-α inhibitors to determine the specific role of these agents in patient care.

The articles that follow, by Dr. Marc D. Cohen and Dr. Bernard S. Goffe, explore and explain the role of TNF in psoriasis and psoriatic arthritis, from the perspectives of pathogenesis and clinical response.
Table 2: Published Studies of Sulfasalazine for Psoriatic Arthritis (PsA) Treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Dose (g/day)</th>
<th>Duration (weeks)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farr et al 1990</td>
<td>30</td>
<td>2</td>
<td>24</td>
<td>Significant improvement in painful joints, pain, ESR, and articular index</td>
</tr>
<tr>
<td>Fraser et al 1993</td>
<td>39</td>
<td>2</td>
<td>24</td>
<td>No significant difference between placebo and active treatment groups</td>
</tr>
<tr>
<td>Dougados et al 1995</td>
<td>351 (total)</td>
<td>136 (PsA)</td>
<td>24</td>
<td>Significant improvement only in patients’ assessment of disease activity</td>
</tr>
<tr>
<td>Clegg et al 1996</td>
<td>221</td>
<td>2</td>
<td>36</td>
<td>PsARC: 57.8% SSZ, 44.6% placebo (P = 0.05); no significant difference in individual parameters</td>
</tr>
</tbody>
</table>

ESR = erythrocyte sedimentation rate; PsARC = Psoriatic Arthritis Response Criteria; SSZ = sulfasalazine.

Table 3: Published Studies of Methotrexate for Psoriatic Arthritis Treatment

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Methotrexate Dose</th>
<th>Duration (weeks)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black et al 1984</td>
<td>21</td>
<td>1-3 mg/kg; 3 doses, 10 days apart</td>
<td>12</td>
<td>Improvement in joint swelling and tenderness; significant toxicity in 13 patients</td>
</tr>
<tr>
<td>Willkens et al 1984</td>
<td>37</td>
<td>7.5-15 mg/wk</td>
<td>12</td>
<td>Statistical improvement shown only in global assessment</td>
</tr>
<tr>
<td>Abu-Shakra et al 1995</td>
<td>76</td>
<td>7.5-20 mg/wk</td>
<td>96</td>
<td>At 96 weeks, 47% of treated subjects and 53% of controls had improved clinically; radiographic progression evaluation showed worsening damage in 63% of treated subjects and 47% of controls</td>
</tr>
<tr>
<td>Spadaro et al 1995</td>
<td>35</td>
<td>Up to 15 mg/wk</td>
<td>48</td>
<td>Comparable clinical response in number of tender/swollen joints, pain, patient and physician assessment, CRP</td>
</tr>
</tbody>
</table>

CRP = C-reactive protein.
The Role of TNF in Psoriasis and Psoriatic Arthritis

Inhibition of tumor necrosis factor alpha (TNF-α) has changed the practice of rheumatology, allowing the successful treatment of patients with rheumatoid arthritis whose disease has been heretofore refractory to medical intervention. As a result, there is much enthusiasm in the field of rheumatology concerning TNF-α inhibition for a variety of other rheumatologic diseases. Although the exact pathogenesis of psoriasis and psoriatic arthritis has not yet been established, there are now good data suggesting that TNF-α inhibition may have a role in the treatment of these conditions.

Recent studies on the immunopathogenesis of psoriasis and psoriatic arthritis have demonstrated that inflammation of both skin and synovium is characterized by elevations in the cytokines interleukin-1 (IL-1) and TNF-α. The epidermis, in particular, is a “storehouse” for IL-1 and IL-1β and TNF-α. Stimulation of the production of these cytokines leads, in turn, to stimulation of other factors that control gene products, including a circular feedback loop involving a chronic helper T lymphocyte—particularly T lymphocyte type 1—response. The result is an ongoing, self-perpetuating process that eventually results in disease.

Other lines of investigation in this area concern the controlling steps in this immunopathologic process. We now know that IL-1 and TNF stimulate the synovial cells to strongly express receptor activation of an intermediary product known as nuclear factor κB ligand (NF κB ligand), also called RANKL. It has been demonstrated that production of NF κB ligand is a controlling step in the immunopathology of psoriasis as well as several other skin conditions.

**Dermatologic and Arthritic Features of Psoriatic Arthritis**

As noted above, an insult to the skin leads to IL-1 and TNF production and activation of NF κB which, in turn, are now known to have certain effects in the epidermis and dermis. In the epidermis, cytokines and chemokines are released from keratinocytes into the dermal layer. As these products move through the venules, rolling, tethering, adhesion, and extravasation of cutaneous lymphocyte antigen (CLA) T cells occur. Finally, in the dermis, the CLA T cells bind antigen, produce cytokines, recruit inflammatory cells, and upregulate addressins and adhesion molecules.

In the joint, insult leads to activation of NF κB, resulting in effects in the synovium, cartilage, and bone. In the synovium, cellular hypertrophy and hyperplasia occur, with resultant or associated leukocytic infiltration, the release of collagenase and proliferation of fibroblasts, and the endothelial activation of E selectin, intercellular adhesion molecule, and vascular cell adhesion molecule. In the cartilage, this biochemical process leads to cartilage destruction. In the bone, the damage involves resorption, erosion of articular cartilage and marginal bone, and, subsequently, deterioration of the joint.

The bony changes of psoriatic arthritis are distinct from those seen in rheumatoid arthritis: The morphology, pattern of joint involvement, and bony erosion pattern are different in the two diseases. The reasons for these differences are not well understood. It is known that NF κB ligand binds to NF κB on the surfaces of osteoclast precursors in psoriatic bone, and this may be one of the controlling factors for osteoclast differentiation, activation, and function that lead to damage.

**Improved Treatments: Goals and Mechanisms of Action**

These advances in research concerning the pathogenesis of immunemediated inflammatory diseases—including rheumatoid arthritis, psoriasis, and psoriatic arthritis—present new challenges as investigators continue to gain the ability to interfere with these...
processes with great specificity and selectivity. For TNF-α to have any effect—that is, to cause gene transcription and production of NF-κB—this cytokine must react with its receptors in a three-dimensional interaction resembling the placement of jigsaw puzzle pieces. The molecular structure of TNF-α and its receptor has been identified. It has also been established that TNF-α is cleaved from macrophages by a cleaving enzyme, is released into the circulation, and binds to a receptor.

Manipulation of this interaction between TNF-α and its receptor can be accomplished in several ways. Options that have been identified include inhibition of TNF-α by a monoclonal antibody, blockade of the receptor, and creation of a “false” receptor to “distract” TNF-α. Two of these options have been realized in agents that are currently approved for and used in the treatment of patients with rheumatoid arthritis.

**TNF-α Inhibitors**

Etanercept and infliximab are the two drugs that are approved in the United States for use in rheumatoid arthritis—and in the case of etanercept, for juvenile rheumatoid arthritis as well. Both are potent TNF-α inhibitors (Table).

Infliximab, a monoclonal antibody against TNF-α, is a chimera of a human antibody bound to a murine portion. The murine portion—which constitutes 20% of the molecule—is the binding site for TNF-α. Infliximab targets both free and cell-bound TNF-α. Laboratory evidence demonstrates that this agent lyses the TNF-expressing cells in vitro, although the significance of this observation is not yet clear. Infliximab has a half-life of 9.5 days. It is administered via intravenous infusion every 4 to 8 weeks. Because of the murine portion, infliximab is immunogenic, causing formation of human antichimeric antibodies (HACAs). There is some controversy over whether this has an impact on the clinical efficacy of infliximab. The presence of these antibodies is also associated with a higher incidence of adverse events, including infusion reactions. To suppress HACA formation, methotrexate is used concomitantly with this agent.

In contrast, etanercept is a soluble receptor (a “false” receptor)—a fusion protein composed of the human p75 receptor and the Fc portion of an immunoglobulin G1. Etanercept binds soluble and cell-bound TNF-α and the related cytokine, lymphotoxin-alpha (LT-α). (The significance of LT-α in psoriatic arthritis is not yet clear.) Unlike infliximab, etanercept does not fix complement and does not lyse TNF-producing cells in vitro. Etanercept has a median half-life of about 4.8 days and is administered subcutaneously twice weekly.

**Summary**

Recent evidence demonstrates that TNF-α inhibition may have an important role in the treatment of psoriasis and psoriatic arthritis. Good data now exist demonstrating that TNF-α is elevated in the synovium, serum, and skin of patients with psoriasis and psoriatic arthritis.

Two TNF-inhibiting drugs—etanercept and infliximab—are currently available and are being used in patients with rheumatologic diseases. Both etanercept and infliximab are potent TNF-α inhibitors that neutralize soluble and cell-bound TNF-α. Etanercept, a soluble TNF-inhibitor, is given subcutaneously; infliximab, a chimeric antibody directly
Two tumor necrosis alpha (TNF-α) inhibitors, infliximab and etanercept, are currently under evaluation for the treatment of psoriatic arthritis and psoriasis. (See “The Role of TNF in Psoriasis and Psoriatic Arthritis,” page 6, for a discussion of the rationale for TNF-α inhibition in these conditions.) To date, only a few studies have been completed. The purpose of this presentation is to review the findings from the clinical trials.

Chimeric Monoclonal Antibody Studies

Antoni and colleagues’ conducted an open-label, 10-week study of infliximab in six patients with severe psoriatic arthritis (as determined by polyarticular disease with clinical and serologic activity). The patients were all on concomitant treatment with methotrexate, corticosteroids, and nonsteroidal anti-inflammatory drugs (NSAIDs). They were all treated with 5 mg/kg of infliximab, administered at weeks 0, 2, and 6.

Improvement was measured by the American College of Rheumatology (ACR) response criteria for 50% improvement (ACR 50) and the ACR response criteria for 70% improvement (ACR 70), which are evaluations of parameters including joint swelling and tenderness. In addition, the subjects were evaluated according to the Psoriasis Area Severity Index (PASI).

At week 10, all patients showed substantial clinical and radiologic benefit. All patients in the study achieved 50% improvement, and five of the six had 70% improvement by ACR response criteria. Although these authors did not indicate the details on the PASI, they noted that there was “rapid improvement” in all patients on this evaluation. (The PASI scores on these patients were reported in another paper, discussed below.)

Four patients were added to this original group of six for an additional 10-week, open-label study. The four new patients also had severe psoriatic arthritis. Seven of the 10 were on concomitant treatment with methotrexate, 1 patient was on sulfasalazine, and 2 were on no disease-modifying antirheumatic drugs (DMARDs).

As in the previous study, 5 mg/kg of infliximab was administered at weeks 0, 2, and 6. At week 10, all 10 patients showed a reduction in the signs and symptoms of their disease, as well as in the serologic markers of disease activity. This group has been followed for 1 year, and evaluations at that point showed that all patients were still free of joint swelling and tenderness. Of interest is the fact that one of the patients became pregnant during the study and had an uneventful pregnancy.

In a third published paper, Ogilvie and coworkers reported on the PASI scores in the same patient set in the study published by Antoni and colleagues. The mean improvement in the group was 72%.

An open-label study of infliximab by Baeton et al was conducted in patients with severe spondyloarthritis to examine the histology of synovium in this patient population. In addition to their spinal involvement, all eight patients in this study group had peripheral involvement. Three patients had ankylosing spondylitis, one had undifferentiated spondyloarthropathy, and four had psoriatic arthritis. Patients who were on DMARDs had stopped treatment with those agents at least 4 weeks prior to the start of the infliximab study. All patients were given 5 mg/kg of infliximab at weeks 0, 2, and 6. A clinical evaluation of peripheral joint inflammation at 12 weeks showed marked improvement.

The most recently published study of infliximab was a phase II, investigator-initiated, 10-week, placebo-controlled study of infliximab in patients with psoriasis. The 33 patients in the study were assigned to receive either infliximab 5 mg/kg, infliximab 10 mg/kg, or placebo, at weeks 0, 2, and 6. The primary end point was the physicians’ global assessment score.

Nine of the 11 patients in the
5 mg/kg arm (82%) were rated as having good, excellent, or clear clinical results, compared with 18% of those in the placebo group \( (P = 0.0089) \). Ten of 11 patients in the 10 mg/kg group (91%) achieved these ratings \( (P = 0.0019 \text{ versus placebo}) \), and 64% had the highest ratings—excellent or clear.

**Fusion Protein Studies**

The other TNF-inhibiting drug, etanercept, was studied in a 3-month, randomized, double-blind, placebo-controlled phase II clinical trial.\(^6\) Thirty patients with psoriasis/psoriatic arthritis were assigned to each arm of the study comparing 25 mg of etanercept, given subcutaneously twice weekly, with placebo. The entry criteria for the study included presence of psoriasis, active arthritis (defined as at least three swollen and at least three tender joints), inadequate response to current therapy, and the absence of other inflammatory rheumatic disease. Patients who were taking methotrexate and other DMARDs for psoriatic arthritis continued taking those drugs throughout the trial.

As shown in Figure 1, after 12 weeks, 87% of the patients on etanercept had achieved improvement according to the Psoriatic Arthritis Response Criteria (PsARC). The PsARC are response criteria that include the physicians’ global evaluation, the patients’ global evaluation, joint swelling, and joint tenderness.

Nineteen patients in the active treatment group and 19 of the controls who had psoriasis involving at least 3% of body surface area were evaluated for their psoriasis response. The two groups were similar in duration of psoriasis, baseline PASI scores, and concomitant use of NSAIDs and methotrexate, but more patients in the placebo group were on corticosteroid therapy.

The subgroup analysis of these patients (Figure 2) showed that, after 3 months, 46% of those in the etanercept group had a 75% or greater improvement in PASI score versus 9% in the placebo group \( (P < 0.003) \). The target lesion also showed significant improvements.

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**Figure 1: PsARC Improvements Over Baseline with Etanercept Treatment**

- **Psoriatic Arthritis Response Criteria (PsARC) scores over 12 weeks of treatment with etanercept, 25 mg twice weekly, versus placebo in patients with psoriasis and psoriatic arthritis.**

**Figure 2: Improvement in Psoriasis at 3 Months**

- **Psoriatic Arthritis Response Criteria (PsARC) scores over 12 weeks of treatment with etanercept, 25 mg twice weekly, versus placebo in patients with psoriasis and psoriatic arthritis.**

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\(^{*}P < 0.0001\)


\(^{†}P < 0.004\)


Significant improvements were seen in PASI scores and target lesions in the subgroup of patients with psoriasis over at least 3% of body surface area.
improvement in the active treatment group at the 25% ($P = 0.0098$) and 50% levels ($P < 0.004$), but not at the 75% improvement level.

At the end of that 3-month study period, an open-label extension of the trial was conducted, with ongoing surveillance for efficacy and safety. In this phase, the patients who had been in the placebo group were given the opportunity to receive etanercept. Concomitant arthritis medications—which patients were required to use without discontinuing or changing at the start of the 3-month blinded phase—were allowed during the extension phase, but adjustments in concomitant arthritis medications could be made at the discretion of the physician during the extension phase.

The improvements in both PsARC and PASI scores in patients who had been in the placebo group were rapidly seen during the extension phase. In the open-label phase, 25% of patients were able to discontinue methotrexate and 44% of patients were able to discontinue prednisone. Forty-three percent of patients were able to decrease their dose of methotrexate—on average, from about 18 mg/wk to 12 mg/wk. Prednisone use decreased in 67% of patients, by an average of 50%—from about 8 mg/day to about 4 mg/day.

The safety profile of etanercept in this patient population was similar to what has been seen in patients with rheumatoid arthritis. There have been no deaths, serious infections, or serious adverse events, and there were no discontinuations of therapy due to side effects. The most serious adverse events were injection-site reactions.

**Another Approach to TNF-α**

Infliximab and etanercept are drugs that target TNF-α once it has been produced. Another drug currently being investigated, Isis 104838, is an antisense drug—that is, an agent that blocks the RNA/DNA pathway so that TNF-α is not produced. Studies have recently been launched to test this drug in psoriasis and psoriatic arthritis.

**Summary**

Both infliximab and etanercept are under evaluation for the treatment of psoriasis and psoriatic arthritis. Early open-label studies have demonstrated their potential benefit in this arena. In a double-blind, placebo-controlled, phase II trial, etanercept was shown to be safe and effective in reducing the clinical signs and symptoms of psoriasis and psoriatic arthritis for up to 9 months.

**References**


**The Role of TNF in Psoriasis and Psoriatic Arthritis**

*Continued from page 7*

against TNF-inhibitor, is given intravenously. Investigation continues on the potential role of TNF-inhibiting agents in patients with psoriasis and psoriatic arthritis.

**References**


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INSTRUCTIONS: Six out of eight correct responses are required for credit. For each question or incomplete statement, one answer or completion is correct. Circle the most appropriate response.

1. In patients with psoriasis and psoriatic arthritis, it has been demonstrated that ________, in particular, is a “storehouse” for interleukin 1α (IL-1α) and IL-1β, as well as tumor necrosis factor alpha (TNF-α).
   a. dermis
   b. epidermis
   c. subdermal tissue
   d. all of the above

2. Which one of the following is not currently an identified and feasible option for manipulating the interaction between TNF-α and its receptors?
   a. creation of a “false” receptor
   b. destruction of the cleaving enzyme that releases TNF-α into the circulation
   c. destruction of TNF-α with monoclonal antibody
   d. TNF-α receptor blockade

3. Which one of the following characterizes the mechanism of action of infliximab?
   a. acts as a “false” receptor
   b. blocks the receptor
   c. destroys the cleaving enzyme that releases TNF-α into the circulation
   d. is a monoclonal antibody that inhibits the action of TNF-α

4. Which one of the following characterizes the mechanism of action of etanercept?
   a. acts as a “false” receptor
   b. blocks the receptor
   c. destroys the cleaving enzyme that releases TNF-α into the circulation
   d. is a monoclonal antibody that inhibits the action of TNF-α

5. In the 10-week, phase II, investigator-initiated, controlled study of infliximab in 33 patients with psoriasis, what percentage of patients receiving 5 mg/kg of infliximab were rated as having good, excellent, or clear clinical results, compared with placebo?
   a. 62%
   b. 72%
   c. 82%
   d. 92%

6. In the phase II, controlled study of etanercept in patients with psoriasis and psoriatic arthritis, what percentage of patients receiving 25 mg of etanercept twice weekly achieved improvement at 12 weeks according to the Psoriatic Arthritic Response Criteria (PsARC)?
   a. 67%
   b. 77%
   c. 87%
   d. 97%

7. Which one of the following statements is true concerning the treatments currently used for psoriatic arthritis?
   a. Intra-articular corticosteroids, NSAIDs, and methotrexate alone are approved by the FDA for the treatment of patients with psoriatic arthritis.
   b. Gold, intra-articular corticosteroids, methotrexate, and sulfasalazine alone are approved by the FDA for the treatment of patients with psoriatic arthritis.
   c. The agents listed in a and b all are approved for the treatment of psoriatic arthritis, as is sulfasalazine.
   d. There are currently no treatments approved by the FDA for the treatment of patients with psoriatic arthritis.

8. The clinical trials that have been published to date on the treatments currently in use for patients with psoriatic arthritis have yielded
   a. evidence suggesting that aggressive treatment offered early in the course of the disease may prevent progression
   b. evidence suggesting that less aggressive treatment should be offered early in the course of the disease, and that more aggressive treatment should be instituted if the disease progresses
   c. strong data supporting the use of several of the currently used agents
   d. strong data demonstrating that the currently used agents are of only modest benefit

3. Rate the information about the use of TNF inhibitors in the treatment of psoriasis.
   □ Below average □ Average □ Good □ Excellent

4. How would you rate the content?
   (Circle the letter of the appropriate answer)
   a. Will definitely change the way you practice
   b. Challenged you to think about the topics
   c. Applicable to your practice, a good review
   d. Of limited use in your practice
   e. Not applicable to your practice

5. This program was commercially supported. Did you perceive any bias?
   □ Yes □ No

6. What other continuing medical education topics would be of value to you? Please offer additional comments.