

Raising the Bar in Psoriasis: The Role of TNF Inhibitors



Introduction

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Psoriasis and Hepatitis C: A Case Presentation

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A Mechanistic Approach to Differentiating Biologic Agents

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Clinical Evidence for the Use of Anti-TNF Therapy in Dermatology Practice

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Target Audience

This activity has been developed for dermatologists and other health care professionals involved in the treatment of patients with psoriasis and psoriatic arthritis (PsA).

Educational Needs

Psoriasis and its frequent complication, PsA, can cause considerable morbidity and disability. The availability of new biologic agents that inhibit the proinflammatory cytokine tumor necrosis factor (TNF) represents a major step forward in the safe and effective treatment of both psoriasis and PsA. Dermatologists need to be aware of how TNF-inhibiting drugs work in psoriasis/PsA, what is involved in introducing the use of these agents in the average dermatology practice, and the clinical results that can be expected with anti-TNF therapy.

Learning Objectives

By reading and studying this supplement, participants should be able to:

- Briefly explain the role of TNF in psoriasis and PsA.
- Identify the role that anti-TNF therapy plays in the treatment of psoriasis and PsA.
- Discuss the efficacy of etanercept in PsA, as demonstrated in clinical trials.
- Discuss the safety of anti-TNF therapy, based on the data accumulated for etanercept over a 5- to 6-year period.

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. Caro has received clinical grants from and is a consultant to Amgen Inc., Centocor, Inc., Genentech, Inc., and Biogen. He discusses the investigational use of etanercept, infliximab, and efalizumab for treating psoriasis. **Dr. Goffe** has received clinical grants from Amgen and discusses the investigational use of etanercept for treating psoriasis. **Dr. Gottlieb** has received clinical grants from and is a consultant to Wyeth and Amgen. She discusses the investigational use of etanercept for treating psoriasis. **Dr. Lebwohl** has received clinical grants from Amgen, Wyeth, Centocor, Biogen, and Genentech, and is a consultant to Biogen and Centocor. He discusses the investigational use of infliximab and etanercept for treating psoriasis.

Introduction

Mark G. Lebwohl, MD

The relatively recent availability of biologic agents has created a changing paradigm in the management of patients with psoriasis. Indeed, the title of the symposium on which this supplement is based, “Raising the Bar in Psoriasis,” reflects the potential for the future. For many patients, these new therapies will mean effective and safer long-term management of their disease, with significant improvement in quality of life as well as clinical benefits.

The tumor necrosis factor (TNF) inhibitors etanercept and infliximab are currently indicated for adult rheumatoid arthritis (RA), and etanercept has an additional indication for juvenile RA.

Recently, adalimumab, also a TNF-targeting biologic agent, was approved for the treatment of RA. Additionally, etanercept is indicated for psoriatic arthritis and infliximab is indicated for Crohn’s disease. Alefacept, a non-TNF biologic, is indicated for the treatment of moderate to

severe plaque psoriasis, and both etanercept and infliximab currently are being investigated for the treatment of psoriasis, as well as a number of other disorders of interest to dermatologists, including Sjögren’s disease, scleroderma, Behçet’s syndrome, sarcoidosis, and graft-versus-host disease.

Because dermatologists are trained and skilled in treating patients with psoriasis and other diseases with cutaneous manifestations, it is becoming increasingly clear that it is appropriate and, in fact, imperative for dermatologists to learn how to use etanercept, infliximab, and the other biologic agents that have become available recently or are nearing approval by the U.S. Food and Drug Administration. Some of these agents are administered by intramuscular injections in the clinician’s office. Infliximab is given by intravenous (IV) infusion. Etanercept is self-administered by patients as a subcutaneous injection, and the learning

process is fast for both patients and office staff. In our experience with the clinical trials, all patients were able to self-administer the medication at the time of the second injection.

Administering IV infusions and teaching patients to self-inject medications have not been traditional services in dermatology practices, but if dermatologists are to provide care with the full range of available medications—which now includes the biologics—we must incorporate these techniques into our practices. If we do not, we risk losing patients with psoriasis to practitioners in other specialties, primarily rheumatologists, a change that would not be in the best interest of patients.

In the articles in this supplement, experts with many years of both clinical and research experience with TNF inhibitors discuss how these agents have raised the bar in the treatment of psoriasis and psoriatic arthritis.

Psoriasis and Hepatitis C: A Case Presentation

Mark G. Lebwohl, MD

Treatment of patients with psoriasis and hepatitis C is problematic for two main reasons. The first is that when such patients are treated with interferon for hepatitis C, their psoriasis worsens. The second is that very few treatments are available to safely treat psoriasis in patients with hepatitis C. This case illustrates the potential importance of the new biologic agents to manage psoriasis in these patients.

Assessing Treatment Options

Traditional PUVA—that is, administration of systemic psoralen prior to

ultraviolet A light exposure—was not used in this patient because the referring

“This case illustrates the potential importance of the new biologic agents to manage psoriasis in these patients.”

physician was concerned about possible hepatotoxicity. This concern was based on the publication of several papers indicating that methoxsalen is hepatotoxic¹⁻³;

however, these are isolated case reports, and two liver biopsy studies showed little or no hepatotoxicity from PUVA.^{4,5}

Methotrexate does lead to hepatic fibrosis in some patients and should be avoided in patients with hepatitis C.⁶

A high proportion of patients with hepatitis C develop cirrhosis of the liver requiring liver transplantation, after which they are treated with either FK506 or cyclosporine. The conclusion of several papers on this issue is that cyclosporine and FK506 are associated with recurrence and progression of hepatitis C and are associated with the need for retransplantation in 10% to

25% of patients within 5 years.^{7,8} As a result, immunosuppressants such as cyclosporine, commonly used to treat psoriasis, probably should rarely, if ever, be used in patients with hepatitis C. Mycophenolate mofetil also is associated with progression of hepatitis C and is not a safe choice to treat psoriasis in patients with hepatitis C.⁹

Acitretin occasionally causes elevations of values on liver function tests. However, Roenigk and colleagues¹⁰ performed a study in which liver biopsies were performed over a 2-year period in patients treated with acitretin. The study showed that acitretin is not hepatotoxic on liver biopsy, and this agent appears to be a safe treatment for psoriasis in patients with hepatitis C as long as liver function tests are not elevated.

Etanercept is the first among the biologics about which data have been published in patients with hepatitis C. In one study,¹¹ patients with hepatitis C who had been treated with interferon and ribavirin were treated with either etanercept or placebo. At 6 months, hepatitis C virus RNA was absent in 12 of 18 (67%) of the patients treated with etanercept, compared to 8 of 25 (32%) of the placebo-treated patients ($P = 0.040$). The beneficial effect of etanercept treatment was statistically significant. This agent seems either to exert its own antiviral effect or to enhance the antiviral effect of interferon and ribavirin. Liver biopsies were performed as well, and the investigators found regression of fibrosis in 6 of 11 (55%) of the etanercept-treated

patients, compared to 2 of 6 (33%) of the placebo-treated patients, a trend in favor of the etanercept group.

Brief Report of a Case

The patient is a 43-year-old male with hepatitis C, psoriasis on 40% of his body surface area, and psoriatic arthritis. He was treated for hepatitis C with interferon and had to stop therapy prematurely because of a severe flare of psoriasis. To manage the psoriasis flare, he was treated with ultraviolet B and narrow-band phototherapy, as well as soaks in a psoralen bath followed by exposure to ultraviolet A light (bath PUVA), alone and in combination with acitretin. None of these strategies yielded a clearance of psoriasis.

The patient refused another course of interferon because of the previous experience and he was given monotherapy with etanercept. By 6 weeks of follow-up, the patient's hepatitis C virus titers had decreased by 66%, a reduction that persisted at 10 weeks of follow-up, the latest point for which data are currently available. In addition, his liver function tests have remained at or near the upper limit of normal or within the normal range, and the improvement in the Psoriasis Area Severity Index is greater than 50% after 10 weeks.

Conclusion

In the case presented here, the benefit in psoriasis clearance was an expected result of etanercept therapy, but the decrease in hepatitis C virus titers was

not expected. A great deal of additional study is required before etanercept is shown to be safe and effective in patients with hepatitis C, but this case demonstrates that biologic agents may offer these patients hope for control of their psoriasis without further liver damage.

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Table. TNF Inhibition: Research in Nonrheumatic Diseases

PUBLISHED REPORTS	UNDER STUDY
<ul style="list-style-type: none"> • Sarcoidosis • Myelodysplastic syndromes • Graft-versus-host disease • Hematologic malignancies • Cochleovestibular disorders • Macrophage activation syndrome 	<ul style="list-style-type: none"> • Psoriasis • Asthma • Interstitial lung • Hepatitis C • Pulmonary fibrosis

A Mechanistic Approach to Differentiating Biologic Agents

Ivor Caro, MD

Tumor necrosis factor (TNF) is a proinflammatory cytokine, the major sources of which are activated monocytes, macrophages, keratinocytes, activated T cells, dendritic cells, and dermal mast cells. Under normal circumstances, the body naturally produces soluble TNF receptors that inhibit TNF activity and are therefore antiinflammatory. But in diseases of chronic inflammation, this natural inhibitory mechanism for TNF is overwhelmed and chronic inflammation ensues. In psoriasis, the resulting inflammation leads to keratinocyte proliferation and, finally, to signs and symptoms of the disease (Figure 1).

Importance of TNF in Psoriasis and Psoriatic Arthritis

In psoriatic arthritis (PsA), elevated TNF levels are responsible for multiple destructive effects leading to a variety of clinical manifestations, including pain, fatigue, stiffness, impaired function, joint destruction, and psoriatic skin lesions.¹

Three key areas of clinical evidence demonstrate the importance of TNF in psoriasis. First, it is known that TNF is elevated in serum and psoriatic plaques.² Second, a direct correlation has been established between TNF levels and the severity of the Psoriasis Area Severity Index.³ Third, studies have shown that serum and plaque levels of TNF decrease after effective treatment.⁴

Biologic Agents Currently Available

Etanercept is one of the TNF inhibitors currently available, along with infliximab and adalimumab. Etanercept is a fully human soluble

TNF receptor consisting of the extracellular domain of two p75 receptors fused to the Fc portion of human immunoglobulin G, subclass 1. As a

“Under normal circumstances, the body naturally produces soluble TNF receptors that inhibit TNF activity and are therefore antiinflammatory. But in diseases of chronic inflammation, this natural inhibitory mechanism for TNF is overwhelmed and chronic inflammation ensues.”

result, etanercept mimics the action of natural TNF receptors, supplementing the body’s process of regulating TNF and, in fact, binding with a greater

affinity than do the natural serum receptors, which are monomeric.⁵

The phase III studies with the use of etanercept in psoriasis are nearing completion. Preliminary data show that 59% of subjects treated with 50 mg twice weekly reached at least 75% improvement in the Psoriasis Area Severity Index at 24 weeks.⁶ (See “Clinical Evidence for the Use of Anti-TNF Therapy in Dermatology Practice,” page 8, for a discussion of safety issues associated with etanercept.)

Infliximab is a chimeric monoclonal antibody that also binds to TNF. Unlike etanercept, which is administered twice weekly as a subcutaneous injection, infliximab is administered by intravenous infusion at week 0, week 2, and week 6, and then every 8 weeks thereafter.

Although infliximab is very effective, its use is associated with a risk of infusion reactions and the formation of neutralizing antibodies. Its use in psoriasis and PsA is investigational at this time.

Figure 1. TNF and Psoriatic Inflammation

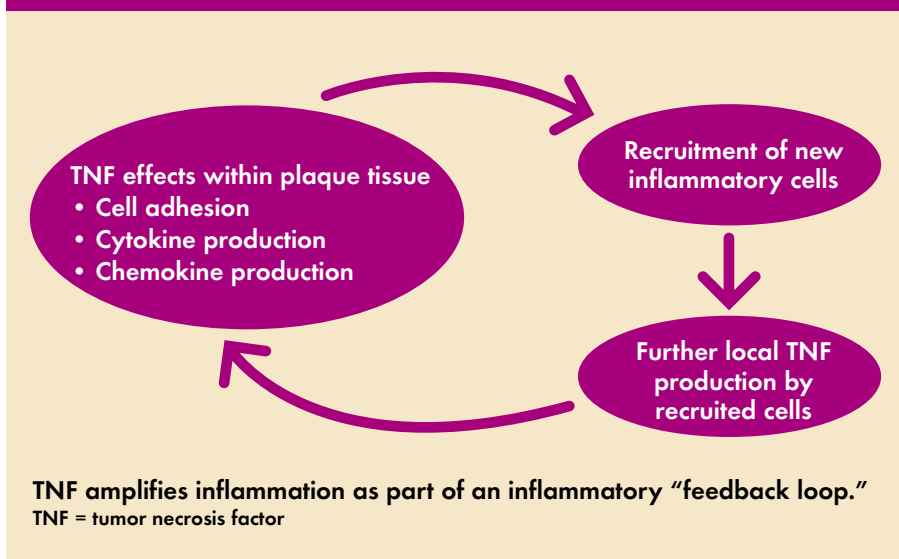
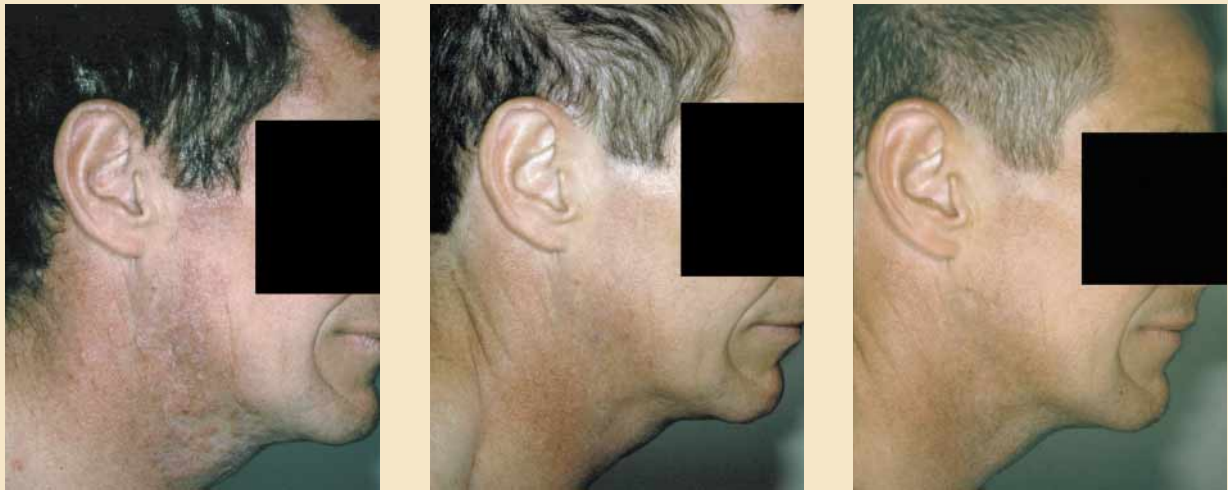


Figure 2. Psoriatic Lesion Clearance With Anti-TNF Therapy



This patient had psoriasis over most of his face and neck (right side of face and neck shown above, left). By week 4 (center), clearance was significant. At week 12 (right), the clinical improvement over baseline was dramatic.

Other Biologics: Non-TNF-Targeting Agents

Alefacept has recently been approved by the U.S. Food and Drug Administration to treat moderate to severe psoriasis. It is a recombinant fusion protein that binds to CD2 on memory-effector T lymphocytes, inhibiting their activation and reducing their numbers. It is administered either as an intravenous bolus injection or as an intramuscular injection weekly for 12 weeks.

Efalizumab is a humanized monoclonal antibody against CD11a. It blocks the interaction between leukocyte function-associated antigen-1 and intercellular adhesion molecule-1. This reduces T-cell trafficking into the skin and T-cell activa-

tion. It is administered once weekly as a subcutaneous injection.

Conclusion

Immunobiologic therapy for psoriasis and PsA represents a new paradigm for clinicians. With these new agents, it is now possible to modify the disease and its progression and modify what happens to patients. The availability of anti-TNF therapy has ushered in an era of safe and effective long-term control of psoriasis and PsA.

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Clinical Evidence for the Use of Anti-TNF Therapy in Dermatology Practice

Alice B. Gottlieb, MD, PhD

The drugs traditionally used for psoriasis—including methotrexate and cyclosporine—are administered according to an intermittent protocol because all of these agents are toxic. As a result, patients with psoriasis have been forced to live with a cycle of control and flare-up of disease. The biologic agents that have been developed over the last 2 decades, and which have recently become available for psoriasis treatment, offer hope for safe and effective long-term management of this life-altering and disabling disease.

Infliximab is a chimeric anti-tumor necrosis factor (anti-TNF) monoclonal antibody that is approved for Crohn's disease and rheumatoid arthritis (RA). Adalimumab is a human anti-TNF monoclonal antibody that was approved recently for RA. Etanercept is indicated for RA, juvenile rheumatoid arthritis for children 4 years of age or older, and for psoriatic arthritis (PsA). Etanercept also has been studied for a variety of other rheumatologic and nonrheumatologic diseases, and phase III trials in psoriasis are nearing completion.

Psoriatic Arthritis

The most common form of PsA is asymmetric inflammatory arthritis, the hallmark signs of which are pain, stiffness, and swelling of the affected joints. Approximately 40% of patients with psoriasis have psoriatic arthritis.¹ The skin disease precedes the joint disease in 85% of patients, occurs concurrently in 10% of patients, and follows joint disease in 5% of patients.¹ Although many patients with PsA have moderate to severe psoriasis, severity of psoriasis is not predictive of the development or severity of PsA, and the possibility of joint disease in

patients with mild to moderate skin disease should not be overlooked.

In most cases, PsA can be diagnosed and treated by dermatologists, with referral of difficult cases to rheumatologists as required. The diagnosis of PsA involves examination for inflammatory arthritis, which is often asymmetric, dactylitis ("sausage digits"), tender and swollen joints, and enthesitis. Examples of the

"The biologic agents that have been developed over the last 2 decades...offer hope for safe and effective long-term management of this life-altering and disabling disease."

latter include otherwise-unexplained Achilles tendonitis, tennis elbow, or heel pain. Patients with psoriasis should be asked about morning stiffness (or stiffness after any period of immobility, such as riding in a car), persistent joint pain or other arthritic symptoms, and a family history of psoriasis and/or PsA.

The traditional therapies for PsA include methotrexate and cyclosporine, which are toxic; oral corticosteroids, which may destabilize psoriasis; and antimalarials, which may cause psoriasis to flare.² Etanercept has been shown to improve PsA signs and symptoms, including x-ray signs, and to improve psoriatic skin disease as well.

Phase III Clinical Trial in PsA

The 6-month, double-blind, placebo-controlled trial³ that led to the U.S. Food

and Drug Administration's approval of etanercept for PsA involved 205 patients. They were randomized to receive either etanercept (101 patients) or placebo (104 patients) (See Figure). Twenty percent of patients were on concomitant therapy with prednisone, and 40% to 50% in both the experimental and the placebo groups were on methotrexate. The etanercept dosage was 25 mg twice weekly, given subcutaneously.

Patients were evaluated at the primary end point of 12 weeks and the secondary end point of 24 weeks according to the American College of Rheumatology (ACR) response criteria.⁴ An ACR 20, ACR 50, or ACR 70 response indicated at least a 20%, 50%, or 70% improvement, respectively. The investigators found that, by week 12, 59% of patients in the etanercept group had achieved ACR 20, versus 15% of those in the placebo group ($P \leq 0.01$). At that same point, 38% of patients who received etanercept had achieved an ACR 50, versus 4% of those in the placebo group ($P \leq 0.01$). Eleven percent of patients in the etanercept group achieved an ACR 70, whereas no patients in the placebo group had at least a 70% improvement in ACR ($P \leq 0.01$).

At 24 weeks, 92 patients were evaluated in the etanercept group and 69 patients were assessed in the placebo group. The ACR responses were as follows: ACR 20, 50% in the etanercept group and 13% in the placebo group ($P \leq 0.0001$); ACR 50, 37% in the etanercept group and 4% in the placebo group ($P \leq 0.0001$); ACR 70, 9% in the etanercept group and 1% in the placebo group ($P = 0.009$).⁴

In addition, consistent, significant improvements were seen in measures of arthritis activity from baseline to 12

weeks in the etanercept group versus the placebo group. These parameters included physician and patient assessments, pain measured according to a visual analog scale, morning stiffness, and C-reactive protein values (all differences were $P < 0.0001$).⁴

X-Ray Progression Inhibited

The Sharp scoring method is a measure that uses an erosion score and a joint space narrowing score to assess radiographic progression of disease (e.g., joint destruction). Significant inhibition of joint destruction was observed as early as 6 months in those patients who had been using etanercept since the inception of the double-blind study.

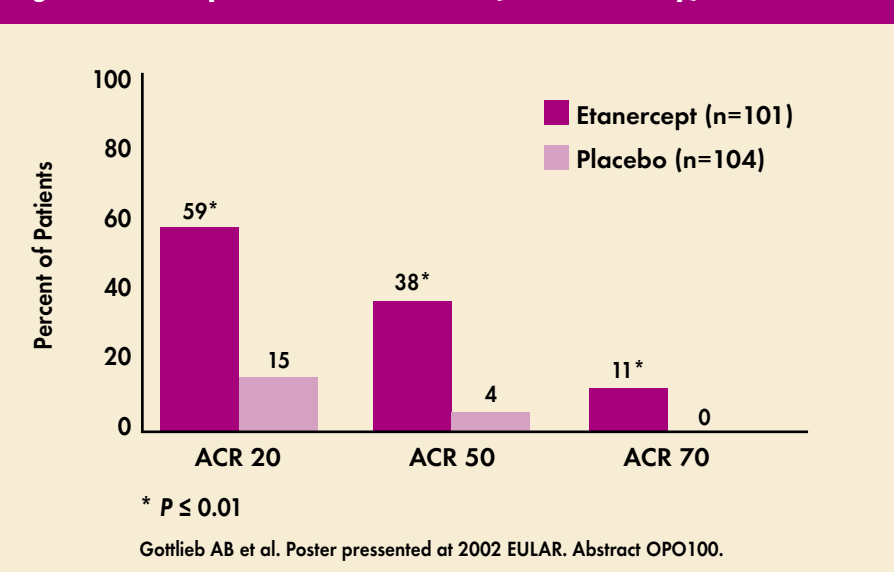
Safety Data in the PsA Trial

The only adverse event seen in the treatment group that was different from what was observed in patients who received placebo—36% versus 9%, respectively—was a clinically insignificant ($P < 0.001$) injection-site reaction consisting of macular erythema, which responded to cold compresses and/or topical hydrocortisone, 1%.⁴ No deaths occurred, and there were no infections requiring hospitalization or intravenous antibiotics. Also, there were no significant laboratory abnormalities, hematologic problems, or antibodies to etanercept. In addition, the incidence of cancer was not increased. As a result, no monitoring is required for patients on etanercept therapy.

Anti-TNF Treatment in Psoriasis

The phase II trial of etanercept in psoriasis was a 6-month study⁵ involving 112 patients who underwent a washout period of 4 weeks for prednisone and methotrexate and 2 weeks for topical corticosteroids. Patients were then randomized to receive either placebo ($n = 55$) or etanercept ($n = 57$), 25 mg twice weekly, administered subcutaneously. The primary

Figure. Etanercept in Psoriatic Arthritis (Phase III Study)



end point was the proportion of patients who achieved a 75% improvement in Psoriasis Area Severity Index (PASI) score (PASI 75) at 12 weeks.

“Significant inhibition of joint destruction was observed as early as 6 months in those patients who had been using etanercept since the inception of the double-blind study.”

The PASI 75 score in the etanercept-treated group was 30% at 12 weeks and 56% at 24 weeks ($P < 0.0001$ for both time periods).

The adverse event profile was unremarkable, with injection-site reactions being the most commonly reported side effect.

5- to 6-Year Safety Experience

Long-term safety data is available for etanercept. It was studied first in RA, and data over a period of 5 to 6 years are now available. More than 230,000

patient-years of experience have been amassed with this agent.³

Despite the fact that RA is a disease in which the incidence of lymphoma is increased, to date there has been no increased incidence of any malignancies in patients treated with etanercept.³ No increase in serious infections—that is, infections requiring hospitalization or parenteral antibiotics—has been seen in etanercept-treated patients. The background incidence of such infections in patients with RA is 0.03 to 0.09 patients/year; postmarketing reports show an incidence of 0.007 patients/year, and the incidence in the clinical trials was 0.04.^{6,7}

However, there are isolated cases in the RA population of opportunistic infection, and it is known that TNF is an important factor in the natural immunity against intracellular infections. As a result, it is not advisable to administer a TNF blocker in patients with active infections such as coccidioidomycosis or active tuberculosis (TB) before the primary infection is under control.

The incidence of TB in patients on etanercept therapy in postmarketing surveillance is not higher than what is expected in the general population,⁸

and no cases of TB have occurred in the etanercept clinical trials.³ Thus, a purified protein derivative test is not required prior to initiating treatment with etanercept. However, the incidence of TB is greater than what would be expected in the general population in patients treated with infliximab and adalimumab. The labeling for these other agents carries a warning about the increased risk for infection, including TB, and requires that a TB skin test be performed prior to the initiation of therapy.

Demyelination has been reported in association with the use of TNF-targeting drugs. Cases have been reported of flares of multiple sclerosis (MS) or reactivation of latent MS in patients on TNF inhibitors.⁹ Patients should be asked whether they have received a diagnosis of MS or if they have symptoms that may suggest the possibility of MS: trouble with vision, tingling in hands or feet, loss of muscle control, or muscle weakness. Five cases of aplastic anemia have been observed, whereas the expected background incidence is two cases. Thus, it is not unreasonable to obtain an occasional complete blood count while patients are using anti-TNF drugs.

Conclusion

Dermatologists will see patients with PsA an average of 10 years before rheumatologists see them with PsA. As a result, it is the dermatologist who is in the best position to provide treatment that can inhibit not only signs and symptoms of arthritis, but also the x-ray changes and disability.

“Patients should be asked whether they have received a diagnosis of MS or if they have symptoms that may suggest the possibility of MS: trouble with vision, tingling in hands or feet, loss of muscle control, or muscle weakness.”

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Practical Applications of Anti-TNF Therapy in Dermatology Practice

Bernard S. Goffe, MD

Clinical investigation with the first soluble tumor necrosis factor (TNF) receptor, etanercept, began in 1992. Data from trials in rheumatoid arthritis (RA) were published in 1997, leading to approval of etanercept by the U.S. Food and Drug Administration for this indication. At that point, trials were initiated using etanercept to treat juvenile rheumatoid arthritis (JRA), and, the following year, clinical studies began in patients with psoriatic arthritis (PsA). Etanercept is now approved for RA, PsA, and JRA. Studies using this agent in patients with psoriasis have been completed, and data currently are being analyzed and disseminated.

Importance of Safe and Effective Treatment

Morbidity and disability from psoriasis are significant. The interference with normal activities such as sleeping, sexual activity, use of hands, and walking, as well as the contemplation of suicide, are increased in patients with psoriasis.^{1,2} A quality-of-life analysis conducted by the National Psoriasis Foundation (NPF) shows that the physical and mental disabilities associated with psoriasis are on a par with those seen in other major illnesses, including depression, diabetes, and heart disease.³

An estimated 1 to 2 million patients with psoriasis will develop PsA, which will lead to even greater disability and other adverse effects on quality of life. Approximately 30% of patients develop PsA while under the care of a physician. About 80% of patients with PsA develop symptoms within 10 years of the onset of skin disease. Between 40% and 57% of patients have deforming erosive arthropathy, 17% have five or more deformed

joints, and 11% to 19% have PsA-associated disability.^{4,5}

In addition, once joint deformities develop, the process is not reversible. Drugs such as methotrexate that traditionally have been used to alleviate symptoms do not stop progression of joint disease. Further, mortality is

“According to the NPF, patients with psoriasis perceive that they are not adequately treated for their skin disease.”

increased in the population of patients with PsA, and, for reasons that have not yet been explained, patients with PsA have a higher incidence of cancer and heart disease.^{4,5}

Patient Satisfaction with Treatment

According to the NPF, patients with psoriasis perceive that they are not adequately treated for their skin disease.¹ About half of the NPF survey respondents reported that they had seen three or more physicians for their PsA within the previous 2 years, and 25% were dissatisfied with their treatment. Krueger and colleagues² reported that among patients with severe disease who were surveyed, 59% felt that physicians could be more helpful in assisting them to live with psoriasis, and 40% said they were frustrated with the ineffectiveness of therapies. Thirty-two percent said they believed their treatments were not aggressive enough.

Conclusion

The widespread prevalence of PsA is becoming increasingly apparent. Fortunately, effective and safe therapy for PsA now exists. As clinical trials with etanercept have demonstrated, anti-TNF therapy does halt the process of joint destruction and improves psoriatic skin lesions.⁶ Therefore, to prevent disability, early identification and treatment of patients are crucial. The availability of biologic agents to treat PsA presents a new treatment paradigm in which the dermatologist plays an increasingly important role. Clinicians in the dermatology specialty, more than ever before, must be aware of the signs and symptoms of arthritis.

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Raising the Bar in Psoriasis: The Role of TNF Inhibitors

CME Post-Test and Evaluation

The SKIN & ALLERGY NEWS supplement "Raising the Bar in Psoriasis: The Role of TNF Inhibitors" is recognized by the American Academy of Dermatology for 1 hour of AAD Category 1 credit and may be used toward the American Academy of Dermatology's Continuing Medical Education Award.

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

- In some patients with hepatitis C and psoriasis
 - Cyclosporine should be used rarely, if ever.
 - Large clinical trials have shown PUVA to be hepatotoxic.
 - Methotrexate is an acceptable alternative to PUVA.
 - Mycophenolate mofetil is an acceptable alternative to methotrexate.
- Concerning the cited Mayo Clinic study of patients with hepatitis C who had been treated with interferon and ribavirin followed by either etanercept or placebo, which one of the following statements is not true?
 - At 6 months, hepatitis C virus RNA was absent in significantly more patients in the etanercept group versus the placebo-treated group.
 - At 6 months, hepatitis C virus RNA was significantly reduced in the etanercept group versus the placebo group.
 - Etanercept may enhance the antiviral effect of interferon and ribavirin or may have its own antiviral effect.
 - Liver biopsies demonstrated a regression of fibrosis in both groups.
- According to the National Psoriasis Foundation study published by Krueger et al, what percentage of patients felt that physicians could be more helpful in assisting them to live with their psoriasis?
 - Almost 20%
 - Almost 40%
 - Almost 60%
 - Almost 80%
- Preliminary data from phase III studies with use of etanercept in psoriasis show that ___ of subjects treated with 50 mg twice weekly reached at least 75% improvement in the Psoriasis Area Severity Index at 24 weeks.
 - 19%
 - 39%
 - 59%
 - 79%
- Studies of tumor necrosis factor in patients with psoriasis have shown that
 - Patients with the highest tumor necrosis factor levels have the lowest Psoriasis Area Severity Index (PASI) score.
 - Tumor necrosis factor is decreased in psoriatic plaques.
 - Tumor necrosis factor is decreased in serum.
 - Tumor necrosis factor levels in psoriatic plaques decrease after effective treatment.
- The most common adverse event seen in the psoriatic arthritis phase III trial of etanercept was
 - Antibodies to the anti-TNF agent.
 - Injection-site reactions.
 - Laboratory abnormalities.
 - Upper respiratory infection.
- What percentage of patients with psoriasis also have psoriatic arthritis?
 - 20%
 - 40%
 - 60%
 - 80%
- In the phase III trial of etanercept in psoriatic arthritis, what percentage of patients in the active treatment group achieved the primary end point of an ACR 20 score at week 12?
 - Almost 20%
 - Almost 40%
 - Almost 60%
 - Almost 80%

PROGRAM EVALUATION

We would appreciate your answering the following questions in order to help us plan for other activities of this type.

- How would you rate the clarity of the presentation of the material?

(Please check one)

	Excellent	Good	Fair	Poor
Text	_____	_____	_____	_____
Images	_____	_____	_____	_____
Post-Test	_____	_____	_____	_____

- How would you rate the clinical relevance of the material?

- How would you rate this material, compared with similar independent study presentations in print form?

- Was this a fair and balanced presentation? Please comment on the scientific rigor, fairness, and balance of the material.

- Do you believe such materials, supported by educational grants from industry, are appropriate and useful? Please rate from 0 (not appropriate/useful) to 10 (very appropriate/useful).

- What topics would you find useful for future programs?

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