TNF Inhibition in Psoriasis and Psoriatic Arthritis:
Improving Disease Management and Quality of Life

A Case for Joining Prebiologic and Biologic Therapies for Optimal Outcome
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Psoriatic Arthritis: What Dermatologists Need to Know
Bruce E. Strober, MD, PhD
Associate Director, Dermatopharmacology Unit
New York University School of Medicine

Treatment of Psoriatic Arthritis and Psoriasis With TNF Inhibitors
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Learning Objectives
By reading and studying this activity, participants should be able to:
• Discuss the role that biologic treatments play in the management of patients with psoriasis and psoriatic arthritis.
• Recognize the early signs and symptoms of psoriatic arthritis in patients with psoriasis.
• List the currently available biologic agents for psoriasis and psoriatic arthritis and briefly explain their mechanisms of action.
• Discuss the efficacy and safety of anti-TNF biologic agents in patients with psoriasis and psoriatic arthritis.

Faculty and Unapproved Use Disclosures
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 Koo has received support and is a consultant to Genentech, Inc., and Biogen, Inc. He is also a consultant to Amgen, Inc., and Centocor, Inc. He discusses the unlabeled use of etanercept, cyclosporine, and acitretin for combination use. Dr Strober has received support from and is a consultant to Amgen, Inc., and Biogen. He discusses the unlabeled uses of etanercept for psoriasis, efalizumab and adalimumab for psoriatic arthritis, and infliximab for psoriasis and psoriatic arthritis.
A Case for Joining Prebiologic and Biologic Therapies for Optimal Outcome

John Y. M. Koo, MD

Physicians and clinical investigators traditionally have relied on body surface area (BSA) involvement and the Psoriasis Area and Severity Index (PASI) as an indication of how aggressively an individual patient with psoriasis should be managed. However, the impact of psoriasis on quality of life can be severe even when the BSA involved is relatively small. In addition, a quality-of-life survey reported by Rapp and colleagues revealed that patients with psoriasis experience both mental and physical suffering that is comparable to that of patients with diseases that are generally perceived by laypeople and health professionals to be “more serious.” These include arthritis, chronic lung disease, hypertension, myocardial infarction, and cancer, among others.

Prebiologic Systemic Therapy and the Issue of Undertreatment

Despite these facts, many dermatologists have been reluctant to use anything other than topical therapy to treat patients with psoriasis. This is somewhat understandable, because, in the era before biologic therapy, the typical systemic treatments available were agents such as methotrexate and cyclosporine. Dermatologists who were willing to use treatments other than topical were faced with forcing patients to choose between convenient therapies (ie, oral agents) with potential organ toxicities (Table 1) and inconvenient treatments (ie, phototherapy) that posed no risk for systemic organ toxicity. The potential organ toxicities associated with some systemic prebiologic agents are listed in Table 2 on page 4.

According to data on physician prescribing habits from IMS Health, approximately one third of dermatologists today use no prebiologic systemic agents, one third use systemic therapy if they feel “pushed against a wall,” and the remaining one third account for more than 95% of all systemic psoriasis therapy prescribed in the United States. In a nationwide study of a group of patients with generalized psoriasis, Krueger and colleagues asked which treatments were being used for severe psoriasis. While 87% said they were using creams or ointments, only 21% were having phototherapy or light treatment, and only 18% were on oral medication. It is not uncommon for psoriasis patients with whole-body involvement to be given only a prescription for topical medication, leading to gross undertreatment (Figure 1 on page 4).

Fortunately, today, some of the biologic agents offer patients with psoriasis efficacy, safety, and convenience all in one drug. In addition, the tumor necrosis factor (TNF) inhibitors are effective in treating both psoriatic skin disease and psoriatic arthritis.

Biologics Have Different Efficacy and Toxicity Profiles

According to studies that demonstrate efficacy based on 75% or greater improvement in PASI after 3 months of treatment, the biologic agents that are currently approved for psoriasis or psoriatic arthritis tend to be less effective than some of the prebiologic treatments, such as psoralen-ultraviolet light (PUVA) therapy, cyclosporine, high-dose methotrexate, the Goeckerman regimen, narrow-band ultraviolet-B (UVB) radiation, and possibly broadband UVB. In addition, the use of some biologic agents carries potential concerns not noted with prebiologic agents, such as the increased risk for opportunistic infections and the reactivation of tuberculosis. However, the safer biologic agents have safety profiles superior to those of the major prebiologic systemic agents, namely cyclosporine and methotrexate.

The longest experience with the use of biologic agents has been with the patient self-administered drug etanercept, with approximately 10 years’ worth of safety and efficacy data collected to date, with 5 of those 10 years as a US Food and Drug Administration (FDA)-approved treatment for rheumatoid arthritis. The data on etanercept involves more than 300,000 patient-years in almost 250,000 patients. Etanercept currently is approved by the FDA for the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis (in children as young as 4 years of age), anklyosing spondylitis, and psoriatic arthritis.

Unlike drugs such as nonsteroidal antiinflammatory agents, which can

Table 1.
A Deficiency of Prebiologic Therapies for Psoriasis: Making the Patient Choose Between Convenience and Safety

<table>
<thead>
<tr>
<th>Convenient But Potentially Systemically Toxic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cyclosporine</td>
</tr>
<tr>
<td>• Methotrexate</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Systemically Safe But Inconvenient</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Goeckerman therapy</td>
</tr>
<tr>
<td>• Broad-band UVB therapy</td>
</tr>
<tr>
<td>• Narrow-band UVB therapy</td>
</tr>
<tr>
<td>• Psoralen and ultraviolet A (PUVA) light</td>
</tr>
</tbody>
</table>

UVB = ultraviolet B light.

TNF Inhibition in Psoriasis and Psoriatic Arthritis

“Fortunately, today, some of the biologic agents offer patients with psoriasis efficacy, safety, and convenience all in one drug.”
help only with pain and stiffness, etanercept is regarded as a disease-modifying antirheumatic drug (DMARD). DMARDs not only help to relieve pain and stiffness but also prevent progressive destruction of bone and other structures in the joints.

To date, the only proven adverse event associated with the use of etanercept is an injection-site reaction, which is a local reaction resembling that from an insect bite. It is classified as a category B drug for pregnant women.

Infliximab, the second TNF-inhibiting biologic agent currently available, requires intravenous infusion. In addition, some questions regarding safety have emerged, as noted above, with tuberculosis and opportunistic infections. However, these concerns should not preclude the use of this drug in patients with psoriasis; indeed, infliximab is the only biologic that works like cyclosporine in a patient in crisis.

Alefacept, the first biologic agent approved for psoriasis, is a T-cell modulator which is given as weekly intramuscular injections for 12 weeks per course of therapy. Like etanercept, no serious side effects have been proven with intramuscular alefacept. However, the experience with this agent is far less extensive.

The second T-cell modulator to be approved for psoriasis, efalizumab, has been associated with rare rebound of psoriasis, and more study is needed to scientifically determine how to manage or minimize this.

### Table 2. Limitations of the Prebiologic Psoriasis Therapies: Major Organ Toxicities

<table>
<thead>
<tr>
<th>Acute Toxicities</th>
<th>Cumulative Toxicities</th>
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</thead>
<tbody>
<tr>
<td>Acute bone marrow suppression</td>
<td>Bone marrow suppression</td>
</tr>
<tr>
<td>Acute hepatitis</td>
<td>Liver fibrosis and cirrhosis</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>Nephrotoxicity</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Teratogenicity</td>
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<tr>
<td>Headache</td>
<td>Hypertension</td>
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<tr>
<td>Malaise</td>
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<td>Mucocutaneous symptoms</td>
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<tr>
<td>Nausea</td>
<td></td>
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<tr>
<td>Paresthesias</td>
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</table>

### Considering New Algorithms for Psoriasis Therapy

The traditional paradigm for the treatment of psoriasis involved a linear progression, from topical therapy, to phototherapy, and then—to stave off the risk for major organ toxicity as long as possible—to systemic therapy as a last resort. However, the availability of the safer biologics calls for a new algorithm. Topical therapy should be the first-line treatment whenever possible and appropriate, with either phototherapy or the safer biologics or safer prebiologics (ie, acitretin) as second-line therapy. If the second-line treatment fails, other systemic therapy—with the prebiologics or with biologic agents considered to carry a higher safety risk—is warranted.

Further, consideration should be given to combination therapy for patients experiencing a severe flare of their disease, using safer biologic agents with more efficacious (although potentially more toxic) prebiologic treatments in a sequential manner (Figure 2 on page 5). In contrast to rotational therapy, in which one drug is stopped before the other is started, sequential therapy involves three overlapping steps: step 1, clearance; step 2, transition; and step 3, maintenance.

For example, as is shown in Figure 2 on page 5, cyclosporine, in adequate dosage (ie, 4 or 5 mg/kg/day), would be given to bring the flare under rapid control, then etanercept would be added and the combination treatment would be given for several months. The length of the transition period is a matter of clinical judgment, but remember that it takes 3 to 6 months for most of the benefit from etanercept to become manifest. Depending on how well the patient responds to the transition regimen (and after cyclosporine has been tapered off), the choices for maintenance include etanercept alone, etanercept plus UVB or an oral retinoid, or other safe regimens that may even include all of these oral agents plus the optimal topical regimen.

Note that such combination therapy has not been evaluated in controlled clinical trials and is not approved by the FDA. The question with a regimen such as the one described here is whether the patient’s immune system would be compromised. However, the experience reported in the rheumatology literature with methotrexate and infliximab, a commonly used combination, suggests that such an approach can be used with confidence. The fact that this is an empiric use of these agents should be made clear to patients in whom it is contemplated, and consent should be fully informed and documented. I tell patients frankly that without a transition period of combination therapy after a clearance with cyclosporine or methotrexate, a flare is likely to recur and the therapeutic
The safety and efficacy data on some of the biologic agents should provide a level of comfort that allows dermatologists to take the step beyond topical therapy and to ensure that patients with psoriasis are not undertreated when systemic treatment is indicated.

The availability of biologic agents such as the TNF inhibitor etanercept, with a track record of 5 years as an FDA-approved agent for rheumatoid arthritis, has prompted a new look at how biologic systemic agents may be incorporated into patients’ treatment regimens. In particular, sequential use of safer TNF inhibitors and prebiologic agents such as cyclosporine and methotrexate may be used in the future. Combinations that take advantage of the best qualities of the prebiologic and biologic agents are currently being explored.

The prebiologic psoriasis therapies are quite effective and still valuable. Many of these older therapies are more effective and convenient to use. Dermatologists who have been reluctant to use systemic treatments in their patients with psoriasis should consider that safer biologics answer a critical need.

In patients who are already on prebiologic therapies, if at all possible, initiation of treatment with biologic agents should involve addition of the latter agent to the existing regimen rather than abrupt cessation of the prebiologic therapy before the biologic therapy is started. If prebiologic therapy is abruptly cut off, the patient may be at risk for a flare of psoriasis before the biologic agent has a chance to “kick in.” Utilizing a period of combination therapy is likely to result in a smoother transition than if an abrupt substitution is made.

In summary, in many ways, the patient’s best interest is served when biologics join the prebiologic therapies.

References

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Psoriatic Arthritis: What Dermatologists Need to Know

Bruce E. Strober, MD, PhD

Approximately 10% to 40% of patients with psoriasis have psoriatic arthritis, with skin disease preceding the arthritic signs and symptoms in about 80% of cases.1 For this reason, dermatologists are in a unique position to recognize psoriatic arthritis and to intervene before irreversible, debilitating joint damage occurs.

Features of Psoriatic Arthritis

Morning stiffness of the joints—such as fingers, cervical spine, lower back, or shoulders—often persisting for more than an hour, is a common symptom of psoriatic arthritis. Signs of the disease include inflammation and swelling; joint involvement is often asymmetric. Nail disease often accompanies inflammation of the distal interphalangeal joints (Figures 1 and 2 on pages 6 and 7, respectively); approximately 80% of patients with psoriatic arthritis have psoriatic nail disease.2

Another common feature of psoriatic arthritis is dactylitis, often referred to as "sausage digits" (Figure 1). Additionally, inflammation at the point of insertion of ligaments or tendons into bone—enthesopathy—is a major component of psoriatic arthritis. Among the examples seen most frequently are plantar fasciitis, carpal tunnel syndrome, tennis elbow, and Achilles' tendinitis. Enthesopathy is often the only feature of psoriatic arthritis in an individual with psoriasis.

Another symptom of psoriatic arthritis is back pain, which would suggest spondylitis or sacroiliitis. The cervical spinal column also can be involved, and is a possibility that should be considered if the patient has limited range of motion in the neck.

The consequences of late diagnosis and treatment of psoriatic arthritis often are debilitating, particularly when the hands are affected. A rare, late manifestation of psoriatic arthritis of the hands is arthritis mutilans, characterized by severe bone and cartilage destruction.

Early Detection of Psoriatic Arthritis

Patients do not often associate joint symptoms with psoriasis and, in fact, many are not aware of the existence of psoriatic arthritis. Patients tend to trivialize joint discomfort and attribute early symptoms, such as morning stiffness, to the natural consequences of aging. As a result, these joint symptoms may not be reported to the dermatologist and, therefore, appropriate and effective therapy may be delayed.

By periodically asking a short list of questions in follow-up visits with patients with psoriasis, the dermatologist can detect the coexistence of psoriatic arthritis in most cases (Table on page 7).

Management Options for Patients With Psoriatic Arthritis

Psoriatic arthritis is considered a rheumatologic disease, but referral to a rheumatologist often is not necessary if the dermatologist is familiar with and willing to prescribe effective systemic therapy that will treat both skin and joint disease.

For mild to moderate cases of psoriatic arthritis and significant psoriasis, methotrexate is a good first-line therapy. For patients who are not candidates for methotrexate or who have an inadequate response to this agent, a drug that inhibits tumor necrosis factor (TNF) should be used.
used. TNF-inhibiting agents often are effective when methotrexate fails.3

When both skin and joint disease are severe, the combination of methotrexate and a TNF inhibitor may be the ideal treatment.4 In clinical trials of patients with rheumatoid arthritis, the combination of either infliximab4 or etanercept5-7 and methotrexate was found to be more effective than either TNF inhibitor alone in preventing further joint damage.

If the skin disease is mild and controllable by topical medications yet the joint disease is significant, referral to a rheumatologist is warranted. In such circumstances, the treatment of choice may be methotrexate, hydroxychloroquine, or sulfasalazine, agents that rheumatologists use routinely.

The TNF inhibitors currently available include adalimumab, etanercept, and infliximab. Etanercept is the only one among these approved to date by the US Food and Drug Administration for use in the treatment of patients with psoriatic arthritis. Other biologic agents, such as efalizumab and alefacept, which work by targeting pathologic T cells, are approved for the treatment of psoriasis and currently are being investigated for use in psoriatic arthritis.

Conclusion

Dermatologists who see patients with psoriasis are in a unique position to diagnose and treat those who develop psoriatic arthritis. Early detection and treatment are essential to the prevention of irreversible joint disease and improvement in the quality of life of these patients. Fortunately, safe and effective systemic therapy is available that treats skin symptoms, alleviates discomfort, and has the potential to prevent future disability.

References


Laboratory and clinical studies of biologic agents have demonstrated that agents that inhibit tumor necrosis factor (TNF) play an important role in the treatment of immune-mediated inflammatory diseases (IMIDs). Among the IMIDs in which anti-TNF agents have been studied are rheumatoid arthritis, Crohn’s disease, psoriasis, and psoriatic arthritis. The rationale for the use of anti-TNF biologic drugs in psoriasis and psoriatic arthritis arose from the growing understanding of the mechanism by which TNF induces important inflammatory mediators—including pro-inflammatory cytokines—in both the skin and joints.

To date, three anti-TNF agents have been developed: adalimumab, etanercept, and infliximab. The US Food and Drug Administration (FDA) has approved etanercept for the treatment of rheumatoid arthritis, juvenile rheumatoid arthritis (in children as young as 4 years of age), ankylosing spondylitis, and psoriatic arthritis. Adalimumab (approved for rheumatoid arthritis) and infliximab (approved for rheumatoid arthritis and Crohn’s disease), continue to be studied for psoriasis and psoriatic arthritis but have not yet been approved by the FDA for use in these conditions.

Other biologic agents—efalizumab and alefacept—have been approved by the FDA for the treatment of psoriasis, but there is insufficient data from controlled clinical trials regarding their possible use in psoriatic arthritis. These two drugs are not TNF inhibitors, but belong to a new class called T-cell-targeted molecules.

**Anti-TNF Mechanism of Action**

The main mechanism of action that anti-TNF agents have in common is the inhibition of TNF through specific TNF binding. The anti-TNF agents differ in structure and in how they bind TNF. Adalimumab is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody to TNF. Infliximab is a chimeric monoclonal antibody to TNF that is composed of murine regions and the human IgG1:Fc region. Etanercept is a fully human receptor fusion protein composed of a human TNF type II receptor and the human IgG1:Fc region.

**Data Demonstrate Efficacy of TNF Inhibitors in Psoriatic Arthritis**

The experience with etanercept in controlled trials of psoriatic arthritis illustrates the benefits of TNF inhibition in clinical use. Etanercept has demonstrated maximum efficacy for psoriatic arthritis at the standard dose of 25 mg twice weekly. In clinical trials, it has been shown to eliminate or substantially reduce the signs and symptoms of psoriatic arthritis within 3 months of the start of therapy.

In one of the phase III clinical trials that led to FDA approval of etanercept for the indication of psoriatic arthritis,1 205 patients were randomized to receive either the active drug (n = 101) or placebo (n = 104) for 24 weeks. The primary end point for efficacy was a minimum of 20% improvement on the American College of Rheumatology index (ACR 20) at 12 weeks, the midpoint of the study. The criteria for an ACR 20 response are summarized in **Table 1**.

At week 12, ACR 20 was achieved by 59% of the patients (n = 60) in the treatment group versus 15% (n = 16) of those in the placebo group (P < 0.0001). At week 24, 50% of the patients had achieved ACR 20 compared with 13% of the placebo group (P < 0.0001). A 50% improvement in the ACR index (ACR 50) was achieved by 37% of the treatment group at week 24, compared with 4% of the placebo group (P < 0.0001). Nine percent of patients in the etanercept group achieved a 70% response in the ACR index (ACR 70) at week 24.

**Table 1. Criteria for ACR 20 Response**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 20% improvement in tender and swollen joint counts</td>
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<tr>
<td>≥ 20% improvement in at least three of the following five criteria:</td>
<td></td>
</tr>
<tr>
<td>Patient’s assessment of</td>
<td></td>
</tr>
<tr>
<td>– pain</td>
<td></td>
</tr>
<tr>
<td>– disease activity</td>
<td></td>
</tr>
<tr>
<td>– physical function</td>
<td></td>
</tr>
<tr>
<td>Physician’s global assessment of disease activity</td>
<td></td>
</tr>
<tr>
<td>Acute phase reactant levels (CRP or ESR)</td>
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</table>

ACR = American College of Rheumatology; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.
versus 1% of those in the placebo group ($P = 0.009$).

Psoriatic skin disease also was measured in this study in patients with greater than 3% body surface area (BSA) involvement (66 patients in the etanercept group and 62 in the placebo group). The response was documented according to Psoriasis Area and Severity Index (PASI) criteria. Significant improvements were seen in PASI scores in the etanercept subgroup at weeks 4, 12, and 24 compared with the placebo subgroup ($P < 0.001$). It is important to note that patients enrolled in this study who had been on stable dosages of 25 mg/wk or less of methotrexate, 10 mg/day of systemic corticosteroids, and/or non-steroidal antiinflammatory drugs were not required to stop using these medications during the course of the trial.

**Efficacy of T-Cell-Targeted Molecules in Psoriasis**

Three biologic agents currently are approved by the FDA for the treatment of moderate-to-severe psoriasis: the T-cell-targeted molecules alefacept and efalizumab. The TNF inhibitors etanercept and infliximab are likely to be approved soon.

Alefacept is a fusion protein that prevents the activation of T cells by antigen-presenting cells and causes the depletion of activated T cells by forming bridges between these and natural killer cells. This drug is given intramuscularly, at a dosage of 15 mg once weekly for 12 weeks, and the patient is followed for 12 weeks. In a phase III clinical study, 21% of patients achieved a 75% improvement in PASI (PASI 75), compared with 5% in the placebo group. A total of 33% of patients achieved PASI 75 at some point during either the 12-week treatment or 12-week observation period, compared with 13% in the placebo group ($P < 0.001$).

Efalizumab is a humanized monoclonal antibody that binds to CD11a on T cells, resulting in the blockage of T cell activation and reactivation, and the inhibition of trafficking of T cells into the skin. Efalizumab is given as a subcutaneous injection, with an initial conditioning dose of 0.7 mg/kg followed by 1 mg/kg injections once weekly thereafter.

Gordon and colleagues reported that in a 3-month, double-blind, placebo-controlled study, 37% of patients receiving efalizumab and 4% of those in the placebo group achieved PASI 75. The efficacy of efalizumab was confirmed in a 6-month study by Menter and colleagues in which 27% of patients achieved PASI 75 after 3 months of treatment and 44% achieved this score after 6 months on efalizumab.

**TNF Inhibition Effective in Psoriasis**

A phase III clinical study was completed recently for etanercept as monotherapy in psoriasis.

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treated. This relatively extensive postmarketing experience has provided valuable information about the potential side effects of the drug and allows for the rational selection of patients who are appropriate candidates for etanercept treatment.

Patients who receive etanercept should be advised that an injection-site reaction has been seen in approximately 25% of all patients who have used this agent. The reaction is mild and usually requires no treatment. Patients who experience discomfort may apply cold compresses or ice or can be given a prescription for a midpotency topical steroid.

Anti-TNF agents, including etanercept, should not be given to patients with a personal history of multiple sclerosis, transverse myelitis, or optic neuritis. TNF inhibitors also should not be used in patients with congestive heart failure, chronic infections, or a history of multiple infections.

The incidence of lymphoma in patients receiving TNF-inhibiting drugs has been a controversial issue. Analysis of patients receiving etanercept for rheumatoid arthritis in ongoing clinical trials shows no evidence that the relative risk for developing lymphoma (or any malignancy) is greater than the background risk for a matched population of patients with rheumatoid arthritis not receiving etanercept. The primary point of this analysis is that patients with rheumatoid arthritis already have an increased risk for lymphoma, and this risk is not augmented by etanercept.

Finally, laboratory testing is not necessary prior to or during treatment with etanercept. I routinely administer a purified protein derivative (PPD) of tuberculin test before beginning treatment with any systemic antipsoriatic agent (including methotrexate or cyclosporine), although a PPD is not required before starting etanercept. The reason I obtain a PPD is that in New York City, where I practice, the average incidence of tuberculosis is about 20-fold that of the national average, and our knowledge of the risk for tuberculosis reactivation during treatment with the higher dose of etanercept (50 mg twice weekly) is limited.

**Conclusion**

Dermatologists today are in the fortunate position of having available an FDA-approved TNF-inhibiting agent that we can use in our patients with psoriatic arthritis. This agent, etanercept, also has been shown to be safe and effective in treating psoriatic skin disease in these patients. For those who achieve good control of both problems on one therapy, treatment is simplified for the physician and the patient.

The other anti-TNF biologic agents, adalimumab and infliximab, are currently being investigated for efficacy in both psoriasis and psoriatic arthritis. Data from preliminary phase II clinical trials are encouraging, with both of these agents showing impressive efficacy in treating psoriasis. Ultimately, dermatologists should become familiar with the TNF-inhibiting biologic therapies, as these agents will enable us to safely control moderate to severe psoriasis and psoriatic arthritis.

**References**


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Instructions: For each question or incomplete statement, one answer or completion is correct. Circle the most appropriate response. Five of 6 correct responses are required for credit.

1. All of the following are inhibitors of tumor necrosis factor except:
   a. adalimumab c. etanercept
   b. alefacept d. infliximab

2. Which one of the following biologic agents is in the class of drugs known as T-cell-targeted molecules?
   a. adalimumab c. etanercept
   b. efalizumab d. infliximab

3. In the phase III clinical trials that led to US Food and Drug Administration approval of etanercept for the treatment of psoriatic arthritis, 15% of patients in the placebo group achieved the primary end point of 20% improvement in the American College of Rheumatology index (ACR 20). What percentage of patients in the treatment group achieved ACR 20?
   a. 29% c. 49%
   b. 39% d. 59%

4. _____ is often the only feature of psoriatic arthritis in a patient with psoriasis.
   a. dactylitis c. nail disease
   b. enthesisopathy d. tendinitis

5. Ninety-five percent of all systemic psoriasis therapy prescribed by dermatologists in the United States today:
   a. is for the new biologic treatments
   b. is for patients with moderate to severe disease
   c. is for the prebiologic agents such as cyclosporine
d. is prescribed by approximately one third of dermatologists

6. The overlapping steps of clearance, transition, and maintenance describe a psoriasis treatment protocol commonly known as:
   a. cyclic therapy
   b. linear therapy
c. rotational therapy
d. sequential therapy

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