The impact of this debilitating disease has been largely underestimated, yet new biologic agents offer significant clinical benefit to those afflicted.

Management of Moderate to Severe Plaque Psoriasis With Biologic Therapy

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INTRODUCTION

Plaque psoriasis, also referred to as psoriasis vulgaris, afflicts upwards of seven million Americans (Koo 1996). Because psoriasis is a cutaneous disorder, many have underestimated its medical impact (Weiss 2002). Nevertheless, many patients are hospitalized each year due to complications related to psoriasis and its treatment, and approximately 350 patients die annually from related causes. The overall costs associated with psoriasis management are significant, possibly exceeding $3 billion annually (National Psoriasis Foundation 2001).

Because the manifestations of psoriasis are obvious and visible, this disease has a profound psychosocial impact. Notably, the results of a questionnaire revealed that patients with psoriasis reported reduction in physical and mental functioning similar to that observed in patients with other major medical illnesses, including cancer, arthritis, hypertension, heart disease, diabetes, and depression (Rapp 1999).

In the last decade, a new understanding about the pathophysiology of psoriasis has resulted in the development of a new class of agents for these patients: targeted biologic therapy. These novel treatments target specific immunologic processes involved in the genesis of this disease, providing significant clinical benefit to psoriasis sufferers. The American Academy of Dermatology (AAD) Consensus Statement places biologic therapies among the currently approved systemic treatments for patients with widespread disease.

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Plaque psoriasis: clinical overview

Psoriasis is a chronic lifelong condition for which no cure exists. While some patients may undergo spontaneous remissions, relapses are common and most patients require lifelong treatment following diagnosis. Psoriasis affects men and women equally. It typically manifests during the third decade, but people of any age can develop psoriasis (Lebwohl 2001a). Plaque psoriasis is characterized by circumscribed, thickened plaques that are marked by silvery scales, which occur most commonly on the elbows, knees, buttocks, scalp, and sites of local trauma (Koebner's phenomenon). Additionally, patients often experience pain, itching, burning, and bleeding from the thickened lesions (Greaves 1995).

Typically, treatment of psoriasis is based on disease severity, the extent of involvement, and response to prior treatments (Koo 1999, Odom 2000). As disease severity increases, more aggressive treatment approaches are used and risks of toxicity increase. Dermatologists are moving away from using the traditional concept of a stepped approach, in which patients' disease severity was defined as mild, moderate, or severe. Dermatologists now view disease severity in terms of localized disease, for which topical therapies are likely to be effective. For those patients with severe disease that is not controlled by topical therapies, a systemic approach to their disease is warranted. This latter group of patients comprises candidates for biologic treatment, for whom an increasing number of treatment options are available.

In clinical trials but not in routine clinical practice, disease severity is estimated by the Psoriasis Area and Severity Index (PASI) — a physician-performed assessment of overall severity and coverage of psoriasis. It takes into account the affected areas on the head, trunk, arms, and legs. Disease severity in each body region is assessed by examining the degree of plaque erythema (redness), thickness, and scaling (Fredrikksson 1978). The composite PASI score ranges from 0 (no disease) to 72 (maximal disease).

Historically, measures of psoriasis severity were not standardized, making estimations of efficacy in clinical trials and comparisons between agents difficult, if not impossible.

Recently, the Food and Drug Administration established a primary outcome measure for evaluation of new agents. This is the proportion of patients who achieve a ≥75 percent reduction in PASI score relative to baseline, often referred to as PASI-75. This standardized efficacy endpoint will facilitate comparisons between agents. To provide a point of reference, a recent study involving methotrexate (considered by some to be the gold standard of treatment) showed that 26 percent of treated psoriasis patients achieved PASI-75 (Callis 2002). While PASI-75 is the primary endpoint, most physicians and patients in clinical trials also find that PASI-50, a 50 percent reduction in PASI, affords measurable and meaningful clinical benefit.

Although PASI is used in clinical trials, it is not calculated routinely in clinical practice settings. Rather, a dermatologist's expertise and intimate familiarity with assessing the extent of disease is most important in identifying those who are candidates for biologic therapy.

The majority of patients can be successfully managed with topical therapy, but approximately 20 percent of patients will require phototherapy or systemic therapy to control their symptoms (Weinstein 1993). These patients represent a small subset of the psoriasis population and can be challenging to manage. Despite the similar appearance of psoriatic plaques among patients, response to various therapeutic modalities often varies, even for different plaques on a single patient (Koo 1999). It is therefore important that multiple viable treatment options be available for patients with moderate to severe disease.

A number of efficacious systemic agents have been approved for the treatment of psoriasis. Nevertheless, their long-term use is limited by factors including long-term toxicity, teratogenicity, need for invasive monitoring, inconvenience, and noncompliance. Table 1 summarizes the advantages, disadvantages, and important safety concerns of traditional agents, highlighting considerations when weighing the risk versus benefit of a given therapeutic option for each patient.

Despite various treatment algorithms and management techniques, many patients with moderate to severe disease fail to achieve satisfactory control of their disease. The results of a National Psoriasis Foundation patient-membership survey of more than 17,000 patients demonstrated the profound adverse impact of suboptimal disease management (Krueger 2001). Of those who responded to the survey, 79 percent reported an overall negative impact of severe psoriasis on their lives. Among patients between the ages of 18 to 34, 81 percent reported feelings of embarrassment and 90 percent reported feeling frustrated with ineffective therapies. When patients were asked about treatment effectiveness, 49 percent reported feeling "only somewhat" or "not at all satisfied" with therapy; 46 percent reported that the current regimen was working "just somewhat well" or "not well at all." There was widespread dissatisfaction with the ability of therapy to control many of the disease-related symptoms.

In another survey of 120 patients with psoriasis, nearly 40 percent of respondents reported intentional noncompliance with their prescribed psoriasis treatment (Richards 1999). These findings show that despite the availability of effective therapies, a significant population of psoriasis patients is being managed suboptimally.

Immunopathophysiology of psoriasis: the role of T cells

Until the 1980s, psoriasis was considered to be a disease resulting from abnormal regulation of keratinocyte growth and differentiation. Over time, it became clear that the immune system, specifically T cells, played a critical role in the pathogenesis of this disease (Bos 1999, Nickoloff 1999). The serendipitous finding that cyclosporine improved psoriasis in a patient receiving immunosuppressive therapy following renal transplantation provided the first evidence of T-cell involvement (Mueller 1979). Other findings, which included the discovery that targeted pathogenic probes such as denileukin diftitox (DAB_{389}IL-2) — a fusion protein that specifically kills activated T cells — resulted in clinical improvement (Gottlieb 1995). The recent identification of an animal model provided additional evidence that T cells were central to the pathogenesis of this disease (Raychaudhuri 2001).

T cells undergo three key interactions with other cell types that yield changes in the dermis and epidermis, with the end result being keratinocyte changes that are associated with psoriasis (Figure 1). The immune system is first activated when an antigen is recognized by antigen-presenting cells (APCs) in the dermis. At present, the identity of any specific psoriasis antigen is unknown. In the epidermis, APCs internalize and enzymatically process antigen. Subsequently, major histocompatibility complex (MHC) molecules present fragments of degraded antigen on the APC surface to a T-cell receptor. Activated APCs then travel to the lymph nodes where they undergo activation and clonal expansion of a population of activated memory-effector T cells. (Krueger 2002a). The initial binding of T cells with APCs in the lymph nodes is mediated by costimulatory molecules, e.g., leukocyte function-associated antigen-1 (LFA-1) and intercellular adhesion molecule-1 (ICAM-1), located on the T cell and APC, respectively. Other costimulatory pairs that are potential therapeutic targets include LFA-3/CD2, CD40/CD40L, and B7/CD28 (Krueger 2002b). T-cell activation is followed by T-cell proliferation and

cytokine production (Krueger 2002a).

In the second step, LFA-1/ICAM-1 interactions facilitate the migration of skin-homing T cells into areas of inflammation in the dermis and then into the epidermis. Finally, T cells undergo reactivation in the skin on exposure to the offending antigen. Reactivation is followed by cytokine secretion (interferon gamma [IFN-gamma] and tumor necrosis factor alpha [TNF-alpha]), keratinocyte hyperproliferation, and an inflammatory response. Again, LFA-1 and ICAM-1, on the memory T cell and activated APC, respectively, facilitate reactivation.

Advances in technology have allowed the development of therapies targeted at these specific pathogenic mechanisms, for example, biologic therapies. Biologic therapies are produced in a living organism and can be derived from various sources, including recombinant DNA technology, hybridomas, blood, or whole human cells. Given that they are typically large protein molecules, they are usually administered by injection (Singri 2002). More than 40 biologic agents are in development for the treatment of psoriasis, using strategies that target various pathogenic steps, including inhibition of T-cell activation or migration, elimination of pathologic T cells, and binding of secretory cytokines (Krueger 2002b, Singri 2002). Biologic therapies in the latest stages of clinical development are listed in Table 2.

Biologic therapies under investigation

It was postulated that inhibiting or modifying T-cell activities would provide therapeutic benefit for the management of psoriasis. As previously described, the costimulatory molecules LFA-1 and ICAM-1 facilitate various T-cell interactions. Efalizumab (Raptiva, anti-CD11a, Genentech) is a humanized monoclonal IgG_1 antibody that is directed against the alpha chain (CD11a) of LFA-1. Efalizumab blocks the interactions between LFA-1 on T cells and ICAM-1 on APCs or endothelium. This, in turn, blocks T-cell binding to endothelial cells and inhibits migration from the circulation into the dermis and epidermis, preventing T-cell reactivation (Figure 2).

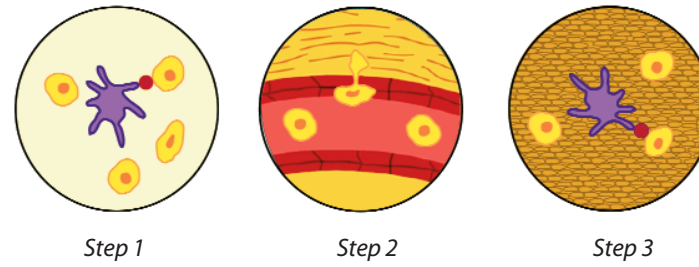

FIGURE 1 Key steps in psoriasis pathogenesis
Step 1: Antigen-presenting cells (APCs) are activated first in the epidermis, where an as-yet unidentified antigen is internalized, enzymatically processed, and presented on the APC surface. Activated APCs migrate to the lymph nodes and activate naïve T cells. *Step 2:* T cells bind to venous endothelial cells and migrate into dermal and epidermal tissue. *Step 3:* T cells are reactivated in the dermis or epidermis following repeat exposure to the antigen. This results in keratinocyte changes. Step 1 occurs only once and is followed by proliferation of activated T cells, which amplify the process. Steps 2 and 3 repeat, resulting in the cyclic persistence of the disease (Krueger 2002).

In phase 1 and 2 studies, efalizumab completely blocked CD11a staining on peripheral and lesional T cells, with staining returning to normal within 7 to 10 days following efalizumab elimination (Gottlieb 2000, Papp 2001, Gottlieb 2002a). Efalizumab significantly decreased epidermal thickness and the number of dermal and epidermal T cells in lesional plaques. ICAM-1 staining on keratinocytes and blood vessels was also decreased, as was Keratin 16 (K16), a proliferation marker. The investigators of the study postulated that the decreased ICAM-1 and K16 expression suggests that efalizumab can reverse histologic evidence of inflammation and epidermal hyperplasia. Accompanying these histologic changes, patients experienced significant reduction in PASI scores compared with baseline.

Over 2,100 patients with plaque psoriasis have been treated with efalizumab in 12 clinical trials. The FDA is evaluating this agent for treatment of moderate to severe plaque psoriasis. A Biologics Application License (BLA) for efalizumab was submitted in December 2002. In the first two of the three placebo-controlled phase 3 studies with similar study design, patients received 12 weekly subcutaneous injections of efalizumab (n=394) 1 mg/kg, 2 mg/kg (n=409), or placebo (n=292). At 12 weeks, a greater percentage of patients in the efalizumab 1-mg/kg and 2-mg/kg dose groups achieved ≥75 percent PASI improvement (29 percent and 28 percent, respectively, vs 3 percent) and ≥50 percent PASI improvement (56 percent and 55 percent, respectively, versus 15 percent) compared with placebo (Gottlieb 2002b). Importantly, efalizumab therapy resulted in rapid clinical benefit, with significant improvement observed as early as 2 weeks following initiation of therapy (Menter 2002). Efalizumab-treated patients reported greater improvement in quality of life measures than did placebo-treated patients as evidenced by decreased Dermatology Life Quality Index (DLQI) scores, from baseline to week 12 (12 to 6 vs 12 to 10). Additionally, efalizumab significantly reduced itch-

TABLE 1 Overview of traditional agents available for the management of psoriasis

Advantages	Disadvantages	Agents	Safety concerns
Topical therapy			
Widely available, limited systemic toxicity, efficacy in mild/localized psoriasis	Messy, cutaneous side effects, patient compliance issues, tachyphylaxis		
		Corticosteroids	Skin thinning/telangiectasia, rebound, HPA axis suppression
		Anthralin and tars	Staining and skin irritation
		Vitamin D analogs	Minor skin irritation, risk of hypercalcemia, pregnancy category C
		Retinoids	Persisting erythema, burning; pregnancy category X
Phototherapy			
Useful for generalized disease, efficacious, long duration of effect, useful in combination with other agents (e.g., retinoids, methotrexate)	Increased risk of skin cancer, requires frequent patient visits, cost and availability, slow onset of response, photodamage		
		Psoralen UVA	Nausea, headache, itching, redness, lentigines, aging of skin, increased risk of skin cancer
		UVB	Can burn, possible long-term skin cancer risk
		Narrowband UVB	Can cause freckling, skin aging
Systemic therapy			
Effective for generalized disease, easy to administer	Renal and hepatic toxicity limit duration of therapy, monitoring required, contraindications due to concomitant diseases, potential for drug-drug interactions		
		Methotrexate	Hepatotoxicity, teratogenic, bone-marrow suppression, nausea, fatigue, insomnia; contraindicated in patients with alcoholism or liver disease
		Cyclosporine	Renal dysfunction, hypertension, skin cancer risk
		Acitretin	Hyperlipidemia, retinoid mucocutaneous side effects, alopecia, teratogenic, alcohol consumption is contraindicated in women due to the prolongation of potential teratogenic effects

SOURCE: Lebwohl 2001b, Lebwohl 2001c

ing, a common and often difficult-to-treat symptom of psoriasis, and reduced both the frequency and severity of cutaneous psoriasis-related symptoms (Data on file, Genentech). When therapy was extended from 12 to 24 weeks, PASI responses were often maintained or improved with continuous therapy (Lebwohl, submitted).

An ongoing open-label, long-term study is assessing the efficacy and safety of continuous therapy, up to 3 years. Preliminary data from this study were announced at the Ameri-

can Academy of Dermatology Academy meeting (Aug. 2002). Overall, 79 percent of the patient cohort completing 1 year of efalizumab therapy (n=215) maintained 50 percent or greater improvement in PASI scores (PASI-50). Sixty-one percent of this cohort had 75 percent or greater PASI improvement (PASI-75) after 1 year of therapy (Data on file, Genentech). Pooled safety data of greater than 1,000 patients demonstrated that efalizumab is generally safe and well tolerated (Koo 2002). Efalizumab is often associated with mild to moderate, transient, flu-like symptoms at weeks 1 and 2. By week 3, the incidence of acute adverse events is comparable to that for subjects who received placebo. Efalizumab is not known to cause hepatotoxicity or nephrotoxicity, and there is no expected need for laboratory monitoring. The advantages of efalizumab therapy are the rapid onset of clinical benefit and the ease of administration with a once-weekly SC injection. This affords patients the option to self-administer therapy, which eliminates the need for an office visit to receive treatment. Efalizumab dosing is weight-based, allowing individualized treatment and reducing the potential of overdosing or underdosing certain individuals. Based on ongoing long-term studies, it appears that efalizumab provides continuous control of symptoms with continued treatment. Efalizumab has a favorable safety profile with no known end-organ toxicity. Given that the effects of efalizumab are reversible, disease returns on cessation of efalizumab therapy. Because there is no cure for this disease, disease recurrence is observed with efalizumab as with other psoriasis therapies.

Managing psoriasis by targeting cytokines

Another strategy to manage psoriasis involves targeting postsecretory cytokines, preventing their pro-inflammatory effects on keratinocytes and the subsequent formation of plaques. Two agents under evaluation that alter the effects of TNF-alpha: infliximab (Remicade, Centocor) and etanercept (Enbrel, Amgen), both of which are approved by the FDA for indications other than psoriasis. Given that the TNF inhibitors have been available since 1998, there is more extensive safety experience captured in postmarketing adverse-event surveillance. Although it remains to be seen how some of these adverse events pertain to patients with psoriasis, they are important to consider, nonetheless.

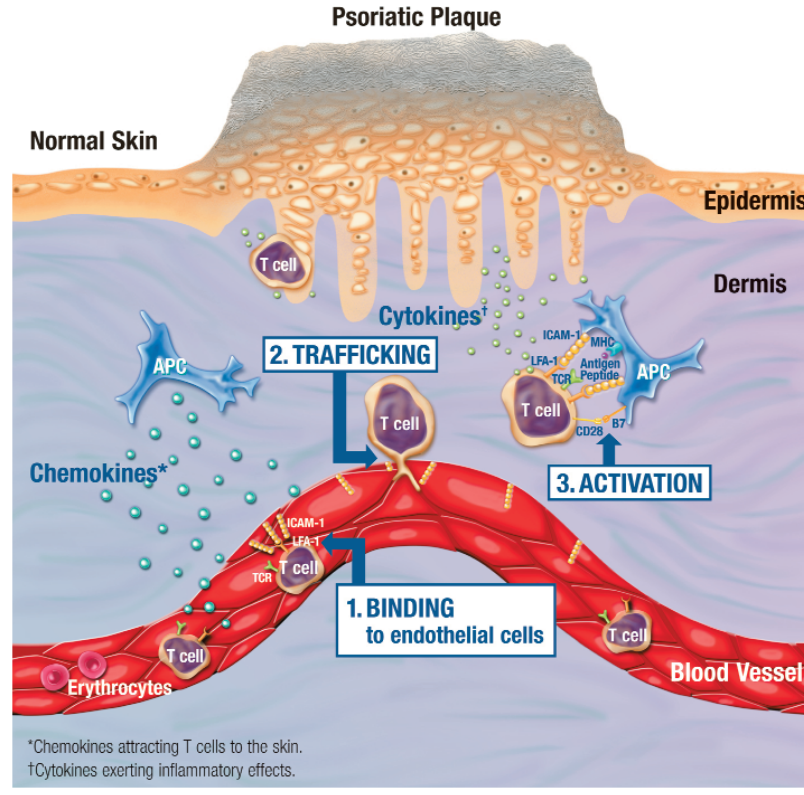

FIGURE 2 Efalizumab modulates various T-cell processes

Infliximab, a chimeric monoclonal antibody of murine origin, currently is approved for treatment of rheumatoid arthritis (RA) and Crohn's disease. Chimeric antibodies retain more than 5 percent of their parent DNA sequences, thus having the potential to induce formation of antibodies directed against a therapeutic agent. Infliximab inhibits newly bound surface and soluble circulating TNF. In a phase 2 evaluation, 33 patients with psoriasis received 5 or 10 mg/kg slow IV infusion during 2 to 3 hours at weeks 0, 2, and 6 (Gottlieb 2002c). At week 10, 73 percent and 82 percent of patients who received 10 mg/kg and 5 mg/kg, respectively, achieved ≥75 percent PASI improvement. At 6 months, 48 percent of patients had maintained their PASI response. The median time to response was 4 weeks. Because infliximab is a chimeric antibody, patients may develop anti-infliximab antibodies, which can diminish the response, necessitating a dose increase to maintain response (Baert 2003). Infliximab has been used in many patients for indications other than psoriasis, thus providing safety experience for a large cohort of patients. There is a risk of intravenous infusion-related reactions (22 percent vs 9 percent

with placebo), and cases of anaphylaxis have been reported (Remicade 2002). Serious infections, including sepsis and fatal sepsis, have been reported. The package insert carries a "black box" warning about the risk of infection and the recommendation of a tuberculin skin test to rule out latent tuberculosis (TB) infection. Patients with active infection should not be treated, and patients with congestive heart failure (CHF) should not receive doses exceeding 5 mg/kg. Approximately 10 percent of patients develop neutralizing antibodies, and there is the potential for serum sickness. Recently, the FDA reviewed eight cases of lymphoproliferative disorders reported in the postmarketing adverse-event surveillance (Brown 2002). At this time, a clear causal relationship has not been established; this is cause for concern, however.

Phase 2 multicenter studies are ongoing and will further characterize the efficacy and safety of infliximab in patients with psoriasis. Infliximab has a rapid onset of response with durable responses. It requires infrequent administration, and there has been no evidence of end-organ toxicity. Drawbacks include the 120-minute infusion that must be administered in an office or infusion center, the risk of infusion-related reactions, the requirement for tuberculin skin testing, the potential need for dose escalation ("dose creep"), and the necessity to discontinue therapy in the event of severe infection.

Etanercept, another TNF-alpha antagonist, is now FDA-approved for RA, juvenile RA, and psoriatic arthritis. This is a fusion protein derived from the high affinity p75 TNF-alpha receptor that binds surface-bound TNF-alpha and blocks its interaction with cell-surface TNF receptors (Singri 2002). In a phase 2 multicenter evaluation, 112 psoriasis patients received etanercept 25 mg SC twice weekly. At 12 and 24 weeks, 30 percent and 56 percent of patients, respectively, achieved ≥75 percent PASI improvement (compared with 2 percent and 5 percent, respectively, for placebo) (Gottlieb 2002d). Etanercept has been administered in patients for indications other than psoriasis and has an established 5-year safety profile. The incidence of injection-site reactions is 37 percent (compared with 10 percent for placebo) and infection of any kind has been reported in 53 percent of patients (compared with 36 percent for placebo). Rarely, cases of TB and demyelinating disorders have been reported. Etanercept is contraindicated in patients with active infection and should be used cautiously in patients with CHF. As with infliximab, cases of lymphoproliferative disorders have been identified (18); causality is being explored (Brown 2002). Ongoing phase 3 trials will shed more light on the safety of etanercept in patients with psoriasis.

Etanercept can be conveniently administered at home; it must be injected twice weekly, however. It does not require laboratory monitoring and has dual efficacy in psoriasis and psoriatic arthritis. As with the other biologics, no end-organ damage has been documented. While joint disease improves rapidly during etanercept therapy, cutaneous symptoms resolve more slowly.

Biologic agent approved by the FDA

Alefacept (Amevive, LFA-3TIP, Biogen) exerts its therapeutic effects via elimination of pathologic T cells. Alefacept received FDA approval in January 2003 for the treatment of moderate to severe psoriasis. Alefacept is a fusion protein that contains the binding site of lymphocyte function-associated antigen-3 (LFA-3). LFA-3 is expressed on APCs, and its costimulatory ligand, CD2, is expressed on T cells and natural killer (NK) cells (Krueger 2002b). Alefacept binds to T cells that express CD2 and blocks the costimulatory pathway, which inhibits T-cell activation and proliferation. In addition, it depletes memory-effector T cells

TABLE 2 Biologic therapies for psoriasis (approved or in late-stage clinical evaluation)

Generic name	Class	Target	Therapeutic strategy	Administration	Phase
Infliximab* (Remicade, Centocor)	Chimeric monoclonal antibody	TNF-alpha	Bind the postsecretory cytokine, TNF-alpha	IV infusion over 2 hours, weeks 0, 2, and 6	2
Etanercept* (Enbrel, Amgen)	Receptor-antibody fusion protein	TNF-alpha (also binds TNF-alpha)	Bind the postsecretory cytokine, TNF-alpha	SC, twice weekly	3
Efalizumab (Raptiva, Genentech)	Humanized monoclonal antibody	Anti-CD11a	Block T-cell activation or migration	SC, once weekly	Filed
Alefacept (Amevive, Biogen)	Receptor-antibody fusion protein	LFA-3	Eliminate pathologic T cells	IV push/IM, once weekly	Approved

*FDA-approved for indications other than psoriasis.

(Singri 2002, Krueger 2002b). In one phase 3 study, patients received 12 weekly doses of alefacept (n=367) administered as 7.5 mg IV push or placebo (n=186) (Amevive 2003). After the first 12-week course, patients entered a treatment-free period for 12 weeks and subsequently received a second 12-week treatment course. PASI assessments were made 2 weeks following the last dose. Following the first 12-week course, 14 percent of alefacept-treated patients achieved PASI-75 and 38 percent achieved PASI-50 (vs 4 percent and 10 percent for placebo, respectively). Following the second 12-week treatment course, 23 percent of patients achieved PASI-75. In another phase 3 trial with a similar design, patients received two 12-week courses of weekly 15 mg alefacept (n=166) via IM injection or placebo (n=168). Following the first course, 21 percent of alefacept-treated patients achieved PASI-75 and 42 percent achieved a PASI-50 response (compared with 5 percent and 18 percent for placebo, respectively).

The true response rates of alefacept-treated patients have been difficult to characterize, because significant reductions in PASI occurred well after those seen at the primary endpoints. Consistent with its mechanism of action, alefacept results in dose-dependent T-cell depletion. The most frequently reported adverse events are pharyngitis, dizziness, increased cough, nausea, pruritus, myalgia, and chills. In the IM study, 16 percent of alefacept-treated patients experienced injection-site reactions that were typically mild and occurred on a single occasion.

The approved regimen of alefacept is 7.5 mg IV bolus once weekly or 15 mg IM once weekly for 12 weeks, under the guidance and supervision of a physician (Amevive 2003). T-cell counts should be monitored weekly, and the dose should be withheld in the event that CD4+ T lymphocyte counts fall below 250 cells/μL. If the counts remain depressed below 250 cells/μL for 1 month, therapy should be discontinued. Patients can receive a second 12-week course of alefacept retreatment only if CD4+ lymphocytes are within normal limits and a minimum of 12 weeks has passed since the prior alefacept course. At present, no data support greater than two cycles of treatment. An apparent absence of end-organ damage is an advantage of alefacept therapy; disadvantages include the need for weekly office visits to receive an IM or IV injection, a slow onset of response (mean maximal response is not observed until 8 weeks), and weekly monitoring of CD4+ lymphocytes.

CONCLUSIONS

Biologic therapies are targeted treatments that have been shown to be efficacious for managing moderate to severe plaque psoriasis. Given the chronicity of this disease, long-term safety is of considerable importance. Thus far, biologic therapies have not been associated with end-organ toxicity, bone-marrow toxicity, evidence of teratogenicity, or drug-drug interactions. While the long-term safety of biologic agents is yet to be determined, more than 275,000 patients have received biologic therapy (for psoriasis and for other indications), and the overall safety profile of this class appears to be excellent.

Biologic therapies are regarded as first-line treatment for psoriasis in a consensus statement proposed by the AAD. This statement would advise physicians to consider numerous factors when selecting the optimal treatment for psoriasis, including disease location, extent, and severity; predominant symptoms; patient age; concomitant conditions or illnesses (including childbearing potential or desire to become pregnant for women); response to previous treatment(s); quality of life; access to their physician, hospital, or ultraviolet light facilities; and economic factors.

Although the drug acquisition costs of biologic therapies will be greater than traditional therapies, other factors must be considered when determining the true cost differential between traditional and biologic treatments. For example, those patients who receive methotrexate therapy must undergo liver biopsies, and the renal function of patients receiving cyclosporine must be assessed regularly. Furthermore, the potential costs to the health care system of iatrogenic hepatotoxicity or nephrotoxicity cannot be dismissed. Patients receiving alefacept therapy will require weekly T-cell monitoring; however, routine laboratory monitoring is not expected to be necessary for efalizumab, etanercept, or infliximab.

Not unexpectedly, the costs associated with treating psoriasis are greatest in patients with severe disease (Feldman 1997). Because the overall percentage of the psoriasis population that is afflicted with moderate to severe disease is small, treating this subgroup of patients with biologic therapy is not expected to have a profound economic impact overall. The favorable efficacy and safety of biologic therapies may translate into improved outcomes in some patients, thus avoiding the costs associated with disease- and treatment-related complications (e.g., hospitalization). The economic impact of treatment on the quality of life of psoriasis subjects has not been established; the importance of improved quality of life and an enhanced level of functioning cannot be underestimated, however.

With alefacept approved, efalizumab filed with the FDA, and etanercept and infliximab in late stages of clinical testing, there are and will be additional new agents available offering many psoriasis patients renewed hope for improved management of their disease.

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