



Efalizumab in the treatment of psoriasis

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Efalizumab was approved by the US Food and Drug Administration in 2003 for the treatment of moderate-to-severe plaque psoriasis. In Phase I, II and III trials, efalizumab has shown significant improvement in the psoriasis area and severity index and quality of life measures in those patients treated with the drug. The most frequently reported side effects were acute adverse events that occurred within 48 h of the first two doses (predefined during the trials as headache, chills, nausea, fever, myalgia and vomiting).

Psoriasis is an incurable autoimmune disease that is mediated by T-lymphocytes [1–17]. It is a chronic skin disorder characterized by inflammation producing red, thickened areas with a flaky white build-up [2]. Normally, skin cells mature gradually and are shed approximately every 30 days. New skin cells replace the outer layers of the skin surface that are shed. In psoriasis, skin cells do not mature but instead move rapidly up to the surface of the skin and build up, forming the characteristic psoriasis plaque [101]. The areas range in size from small to large and typically occur on the knees, elbows, scalp, hands, feet or lower back. Psoriasis tends to be most prevalent in adults and those of the Caucasian race [3]. Plaque-type psoriasis is the most common form of the disease, occurring in approximately 80% of cases [3]. Guttate psoriasis occurs in about 10% of patients and erythrodermic and pustular psoriasis each occur in fewer than 3% [3].

Presently, there are several strategies of treatment for psoriasis; light, systemic, topical and biologic treatment. The unmet need for safe and effective therapies has generated the development of biologic therapies for psoriasis [1]. Efalizumab is a biologic therapy designed to target one possible step in the pathogenesis of psoriasis. It is a humanized monoclonal immunoglobulin (Ig)G1 antibody that inhibits T-cell activation and the binding of T-lymphocytes to endothelial cells and their subsequent migration [2]. Phase I and II studies demonstrated that efalizumab treatment results in histologic improvement and clinical benefit in patients with moderate-to-severe psoriasis [4].

Overview

Psoriasis is one of the most common diseases in dermatology. Most psoriasis patients are treated with topical treatments, but approximately 20%

of patients need phototherapy and/or systemic therapy [5]. All of these treatments do have the potential for serious side effects, such as hepatotoxicity and nephrotoxicity (methotrexate, cyclosporine), teratogenicity (oral retinoids and methotrexate) and skin cancer (long-wave ultraviolet radiation photochemotherapy [PUVA]), which limits their long-term use [6]. With the number of side effects and contraindications of existing treatments, new psoriasis therapies are in high demand. Several biologics interfering with key steps in the immunopathogenesis of the disease have the potential to treat moderate-to-severe psoriasis [5].

Well over 40 biologic compounds are being developed for psoriasis, some of which have already been approved by the US Food and Drug Administration (FDA). Along with efalizumab, two other biologic therapies have been approved by the FDA for the treatment of chronic plaque psoriasis: etanercept and alefacept. Etanercept is a fully human recombinant tumor necrosis factor (TNF)-receptor fusion protein [6,7]. Etanercept counteracts the effects of endogenous TNF by inhibiting its interaction with cell surface receptors [6,7]. It has been shown to be effective in patients with rheumatoid and psoriatic arthritis [7]. Etanercept has proven to be effective in clinical trials. In a 24-week, double-blind study, 672 patients were randomized. Of these, 652 patients received either placebo or etanercept subcutaneously at a low (25 mg once weekly), medium (25 mg twice weekly), or high dose (50 mg twice weekly) [7]. At week 24, there was at least 75% improvement in the psoriasis area and severity index (PASI) percent of the patients in the low-dose group, 44% in those in the medium-dose and 59% in the high-dose group [7]. The PASI assess the extent of psoriasis on four body

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surface areas (head, trunk and upper and lower limbs) and the degree of plaque erythema, scaling and thickness. The PASI scores account for both the extent of body surface area affected by the erythema, scaling and thickness and the severity of these measures. The score ranges from 0 (no disease) to 72 (maximal disease). The PASI improvements were similar in responses in the global assessments by physicians and the patients' quality of life measures [7].

Alefacept is a fully human fusion protein which has the extracellular domain of the lymphocyte function-associated antigen (LFA)3 fused to an IgG1 T-cell modulator. Alefacept interferes with the activation of T-lymphocytes by blocking the costimulator CD2 molecule and mediates T-cell elimination by inducing programmed cell death [6]. It is believed that these two processes contribute to the drug's clinical effectiveness. Alefacept has also proven to be effective in clinical trials. In a review of Phase II and III studies, a third of the patients studied achieved a reduction in PASI of either greater than or equal to 75% and of nearly two-thirds in PASI of either greater than or equal to 50% [8].

Introduction & chemistry of the compound

Biologic therapies are designed to target the mechanisms that cause diseases. In order for a biologic to target psoriasis, one of these four strategies are activated: reduction of pathogenic T-cells; inhibition of T-cell activation and migration; correction of cytokine deviation; or blocking proinflammatory cytokines [6]. Efalizumab employs inhibition of T-cell activation and migration. It is a humanized monoclonal antibody to CD11A, which in combination with CD18, forms the heterodimer integrin LFA-1 on the surface of T-cells [1–5]. CD11a is also expressed on the surface of B-lymphocytes, monocytes, neutrophils, natural killer cells and other leukocytes [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. The interaction between LFA-1 on T-cells and intracellular cell adhesion molecule (ICAM)-1 on antigen presenting cells is an important costimulatory signal resulting in T-cell activation [1]. ICAM-1 on endothelial cells also interacts with LFA-1 on circulating T-cells, a necessary step for migration of T-cells into inflamed skin [1]. Efalizumab can thus interfere with development of psoriasis by blocking T-cell migration into the skin and by preventing T-cell activation.

Pharmacodynamics, pharmacokinetics & metabolism

Various Phase I and II studies investigated the pharmacodynamic properties of efalizumab in intravenous studies. The studies were carried out either as a single intravenous dose of 0.01–30 mg/kg [9,10] or repeated weekly administrations of 0.01–1.0 mg/kg/week for up to 8 weeks [11,12]. Blood samples from treated patients were subjected to fluorescence-activated cell sorter analyses. These analyses reveal the relationship of CD11a and lymphocytes. In the single-dose study, treatment with efalizumab caused a rapid reduction in CD11a expression on T-cells and concentrations of efalizumab increased with dose [9–13]. CD11 levels on lymphocytes remained controlled as long as efalizumab remained in the circulation [9–12]. Doses above 0.3 mg/kg were required for the full pharmacodynamic effect [9–13]. After multiple weekly doses, circulating lymphocytes remained elevated but did not increase [9,10].

According to statistics provided by the manufacturer of efalizumab, at a dose of 1 mg/kg, efalizumab reduced expression of CD11 on circulating T-lymphocytes to approximately 12 to 55% of predose values and reduced free CD11a binding sites to a mean of either greater than or equal to 5% of predose values. These pharmacodynamic effects were observed 1 to 2 days after the first dose and were maintained between weekly 1 mg/kg doses. Following discontinuation of efalizumab CD11a expression returned to a mean of 74% of baseline at five weeks and remained at comparable levels at weeks 8 and 13. At complete discontinuation of efalizumab, free CD11a binding sites returned to a mean of 86% of baseline [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)].

Histological analyses of psoriasis lesions from patients in studies showed constant reductions in epidermal thickness after efalizumab administration [9,11–13]. The number of T-cells in the dermis and epidermis was reduced by greater than 50% on day 28 for patients who received repeated doses of the drug [11–13]. On day 28, the majority of patients showed no apparent CD11a binding sites in their skin [11,13]. The clinical, histological and pharmacodynamic data from these studies demonstrated that by reducing the available CD11a on circulating and cutaneous T-cells, efalizumab can block the inflammatory process that defines psoriasis [13].

In an early study, 39 patients with moderate-to-severe psoriasis were treated with intravenous doses of efalizumab for 7 weeks. In an open-label,

multiple-dose escalation, Phase I/II study. Subjects received the following levels of efalizumab in a dose-escalation design:

- Group A: 0.1 mg/kg every other week
- Group B: 0.1 mg/kg weekly
- Group C: 0.3 mg/kg weekly
- Group D: 0.3, 0.4, then 0.6 mg/kg for the remaining weeks
- Group E: 0.3, 0.4, 0.6, then 1.0 mg/kg for the remaining weeks and 0.3, 0.4, 0.6, then 1.0 mg/kg for the remaining weeks [14]

The subsets of efalizumab pharmacokinetics, CD11a downmodulation and CD11a saturation divide the five dosing groups into three categories. Category 1 (groups A and B) is defined by the inconsistency to maintain apparent efalizumab serum levels and T-cell surface CD11a downmodulation between doses. Category 2 (group C) is characterized by the presence of detectable efalizumab and T-cell CD11a downmodulation, but inconsistency to maintain CD11a saturation between doses. Category 3 (groups D and E) is characterized by T-cell CD11a downmodulation and absorption. Overall, the data indicate that a relationship exists among plasma level of efalizumab, CD11a saturation and downmodulation and histologic improvements [14]. Plasma levels were maintained between dosing in categories 2 and 3, but not in category 1 [14]. Category 2 trough levels were below the concentration needed to inhibit T-cell adhesion [14]. Category 3 trough levels were higher [14]. CD11a saturation was sustained only in category 3 and downmodulation was only shown in categories 2 and 3 [14].

Clinical efficacy (Phase I, II & III studies)

Phase I/II studies confirmed the biologic activity of efalizumab in patients with moderate-to-severe psoriasis. Efalizumab lessened epidermal thickness and doused CD11a on outlying T-lymphocytes [1,14]. These studies demonstrated that intravenous efalizumab administered as a single dose or as multiple weekly doses resulted in significant improvement in PASI scores, as well as significant clinical effects [14]. In the study referenced previously, significant disease improvement was observed in using multiple dose-escalations of efalizumab. During treatment, the PASI score changed little for subjects in category 1 but decreased for subjects in categories 2 and 3 [14]. Category 3 contained the largest change in PASI score. Some patients worsened after discontinuing therapy after

1 month. Patients in category 3 experienced a mean decrease in PASI score from baseline of 47% at day 56 compared with 45% in category 2 and 10% in category 1 ($p < 0.001$) [14].

A randomized, double-blind, placebo-controlled, multicenter Phase II trial studied patients receiving intravenous efalizumab at doses of 0.3 mg/kg per week or placebo. The study resulted in histologic improvement as observed in earlier studies [15]. Patients who received efalizumab demonstrated a significantly greater decrease in PASI score at day 56 compared with baseline than did patients who received placebo (-7.1 vs -1.8 , $p < 0.0001$) [4,15].

Various Phase III studies have been completed with patients receiving subcutaneous efalizumab. In a Phase III, multicenter, randomized, placebo-controlled, double-blind study, 597 subjects with psoriasis were assigned to receive efalizumab (1 or 2 mg/kg dependent on body weight) or placebo for 12 weeks. Depending on the response of the subject to efalizumab, subjects received an additional 12 weeks of treatment with efalizumab or placebo. Responses were assessed with the use of the PASI scale. There were no significant differences among the treatment groups with respect to demographics or the severity of the disease. There was a 75% or more improvement in the PASI score in 22% of the subjects who had received 1 mg/kg of efalizumab per week at week 12 ($p < 0.001$) [1]. Of those who had received 2 mg/kg per week, 28% had significant PASI improvement ($p < 0.001$) as compared with the 5% of the subjects in the placebo group [1]. Greater improvement in PASI scores were seen in efalizumab-treated than placebo-treated patients and these effects were seen as early as week 4 evaluations ($p < 0.001$). Among the efalizumab-treated subjects who had an improvement of 75% or more at week 12, improvement was maintained through week 24 in 77% of those who continued to receive the drug ($p < 0.001$) [1]. Efalizumab therapy resulted in significant improvements in plaque psoriasis. Extending efalizumab treatment from 12 to 24 weeks resulted in both continuance and improvement of responses [1].

In another Phase III trial, the effect of efalizumab on dermatology health-related quality of life measures in patients with moderate-to-severe psoriasis were examined. This randomized, double-blind, parallel-group, placebo-controlled multicenter trial was run for 12 weeks. All subjects were randomly assigned

to receive either subcutaneous efalizumab 1 mg/kg or placebo equivalent. Each subject received an initial dose of 0.7 mg/kg followed by 11 weekly doses of 1 mg/kg of study drug (placebo or efalizumab). Efalizumab-treated subjects experienced significantly greater improvements in all end points than those treated with placebo [16]. Efalizumab-treated subjects exhibited significantly greater mean percentage improvement than placebo-treated patients on the overall Dermatology Life Quality Index (47 vs 14%; $p < 0.001$), Itching Visual Analog Scale (38 vs -0.2%; $p < 0.001$), and Psoriasis Symptom Assessment frequency and severity subscales (48 vs 18% and 47 vs 17%, respectively; $p < 0.001$ for both) at the first assessment point [16].

A Phase III, randomized, double-blind, parallel-group, placebo-controlled study evaluated the efficacy and safety of 12 weekly doses of efalizumab 1.0 mg/kg/week and 2.0 mg/kg/week in 1095 subjects with moderate-to-severe psoriasis [17]. On day 84, 29.2% of patients who received efalizumab 1.0 mg/kg/wk and 27.6% who received 2.0 mg/kg/wk demonstrated a greater than or equal to 75% improvement in PASI relative to baseline compared with 3.4% of placebo-treated patients. 55.6% of patients treated with efalizumab 1.0 mg/kg/wk and 54.5% of those treated with 2.0 mg/kg/wk had a greater than or equal to 50% PASI improvement [17]. Only 15.1% of patients who received placebo had significant changes in PASI scores [17].

Safety & tolerability

Multiple Phase III studies conducted in approximately 1650 patients have determined the safety of efalizumab for the treatment of moderate-to-severe psoriasis [1,13,15,16]. Significantly more efalizumab-treated patients demonstrated improvement on all efficacy end points relative to the placebo [7–17].

Adverse events were generally mild-to-moderate amongst efalizumab-treated subjects. The most frequently reported events were acute adverse events (predefined during the trials as headache, chills, nausea, fever, myalgia and vomiting that occurred on the day of the dose or the following 48 h) after the first one or two injections of efalizumab [4–17]. By the third and all subsequent doses, the incidence was comparable between the efalizumab and placebo groups. The acute adverse events were generally mild-to-moderate in severity.

Infections

Efalizumab has the potential to increase the risk of infection and reactivate chronic infections [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. In the complete safety data from both controlled and uncontrolled studies, the overall incidence of hospitalization for infections was 1.6/100 patient years for efalizumab-treated patients compared with 1.2/100 patient years for placebo-treated patients [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. The infections reported were cellulitis, pneumonia, abscess, sepsis, sinusitis, bronchitis, gastroenteritis, aseptic meningitis, Legionnaire's disease, septic arthritis, and vertebral osteomyelitis [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)].

Malignancies

Efalizumab is an immunosuppressive agent and has the potential to increase the risk of malignancy [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. Among the 2762 psoriasis patients who received efalizumab at any dose, 31 were diagnosed with malignancies. Malignancies were observed in the efalizumab-treated patients namely non-melanoma skin cancer, noncutaneous solid tumors, Hodgkin's and non-Hodgkin's lymphoma and malignant melanoma [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. However, the majority of malignancies reported are non-melanoma and expected due to previous therapies such as phototherapy and methotrexate.

Thrombocytopenia

Platelet counts at or below 52,000 cell/ μ L were observed in eight (0.3%) efalizumab-treated patients during clinical trials compared with none among the placebo-treated patients [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)]. Of the eight patients, three were hospitalized for thrombocytopenia, including one with heavy uterine bleeding. Each case resulted in the discontinuation of efalizumab [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)].

Pregnancy

At this time, there are no adequate studies of efalizumab in pregnant women. It is unknown whether efalizumab can cause fetal harm when administered during pregnancy or can affect reproduction capacity [Genentech Inc.: Raptiva® (efalizumab) package insert (2003)].

Studies with extended treatment suggest the continuing efalizumab treatment therapy is more successful in maintaining and improving responses in the skin. Relapse of psoriasis (loss of

50% of PASI score) is usually seen within 60 to 70 days after discontinuation of therapy and rebound in less than 5% of patients [21]. The majority of patients who rebound never responded to efalizumab therapy.

Regulatory status

Efalizumab was FDA approved on October 27, 2003. Efalizumab is the only FDA-approved psoriasis therapy treatment that is a one-dose, once-a-week treatment that is self-injectable. Efalizumab is indicated for the treatment of adult patients (18 years or older) with chronic moderate-to-severe plaque psoriasis who are candidates for systemic or phototherapy. The drug is available from the manufacturer, Genentech Inc.

Conclusion & expert opinion

Efalizumab represents an important advance in the management and treatment of chronic plaque psoriasis. Efalizumab, which targets multiple stages in the psoriasis disease process, has proven through several Phase I, II and III studies to be effective [9–17]. Efalizumab targets psoriasis pathogenesis at multiple levels, inhibits T-cell activation and binds T-cells to endothelial cells, blocking trafficking of T-cells from the circulation into the skin and preventing reactivation of T-cells in the dermal and epidermal tissues [2–10].

Efalizumab has had a favorable impact on disease severity and patient reported outcomes, along with a rapid onset of clinical benefit. In some

studies, the PASI scores of patients had significant improvement by either the 2- or 4-week visits [1–9]. The convenience of self administered subcutaneous injection also adds to the ease of use for efalizumab.

Data to date indicates that it can be effectively and safely administered on a long-term basis (30 months of continuous data) [4]. Currently, the long-term efficacy of treatments available to manage moderate-to-severe psoriasis is limited by toxicity and poor tolerance [18]. Efalizumab can be seen as a major player in the dermatologic world due to its long-term treatment possibilities. Overall, efalizumab is an important addition in the management of moderate-to-severe psoriasis.

Outlook

The future of efalizumab in the treatment and maintenance of psoriasis appears bright. With the easy self-administration of the drug and the rapid clinical improvement after use, efalizumab will be in high demand amongst physicians and patients. There is also potential in the future for efalizumab to be part of combination therapy for chronic psoriasis due to its alternate mode of action. The potential for long-term toxicities is currently unknown, however, specific organ toxicities (e.g., renal or hepatic) that occur in patients taking other immunosuppressive drugs, such as cyclosporine or methotrexate have not been seen [19]. Topical has been used with systemic and phototherapy to reduce the amount of light treatment or systemic therapy needed [20]. This combination reduces the toxicity of these treatments and minimizes residual refractory plaques that have not responded. These combinations are still being researched but serve as a spotlight to future developments of efalizumab and other biologic therapies. The potential to integrate efalizumab more routinely into physician's private practices is another projection for the drug. Biologics are becoming more common in dermatology practices. The ease of self-injectable efalizumab will only encourage more patients to try a new therapy for their chronic psoriasis.

Highlights

- Efalizumab is a US Food and Drug Administration (FDA) -approved biologic therapy for the treatment of moderate-to-severe plaque psoriasis.
- Efalizumab is the only FDA-approved psoriasis therapy treatment that is a one-dose, once a week treatment that is self-injectable.
- Phase I, II and III clinical trials have shown significant improvements in psoriasis area and severity index (PASI) scores and quality of life measures for those patients treated with efalizumab.
- Efalizumab is projected to be a successful therapy due to the ease of self-administration and quick clinical response.

Bibliography

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. Lebwohl M, Tyring SK, Hamilton TK *et al.* •• for the Efalizumab Study Group. A novel targeted t-cell modulator, efalizumab, for plaque psoriasis. *N. Engl. J. Med.* 349, 2004–2013 (2003).
2. Doggrel A. Efalizumab for psoriasis? *Expert Opin. Invest. Drugs* 2(13), 551–554 (2004).
3. Lebwohl M. Psoriasis. *Lancet* 361(9364), 1197–1204 (2003).
4. Leonardi CL. Efalizumab: An overview. *J. Am. Acad. Dermatol.* 49, S98–S104 (2003).
5. Friedrich M, Philipp S, Sabat R, Asadullah K, Sterry W. Use of biologics in psoriasis. *Z. Rheumatol.* 62(5), 439–449 (2003).
6. Boehcke, WH. Immunomodulatory drugs for psoriasis. *Br. Med. J.* 327, 634–635 (2003).
7. Leonardi CL, Powers JL, Matheson RT *et al.* for the Etanercept Psoriasis Study Group. *N. Engl. J. Med.* 349, 1987–1990 (2003).
8. Krueger G, Callis K. Development and use of alefacept to treat psoriasis. *J. Am. Acad. Dermatol.* 49, 87–97 (2003).
9. Gottlieb A, Krueger JG, Bright R *et al.* •• Effects of administration of a single dose of a humanized monoclonal antibody to CD11a on the immunobiology and clinical activity of psoriasis. *J. Am. Acad. Dermatol.* 42, 428–435 (2000).

10. Bauer RJ, Dedrick RL, White ML, Murray MJ, Garovoy MR. Population pharmacokinetics and pharmacodynamics of the anti-CD11a antibody hu1124 in human subjects with psoriasis. *J. Pharmacokinet. Biopharm.* 27, 397–420 (1999).
11. Gottlieb AB, Krueger JG, Wittowski K, Dedrick R, Walicke PA, Garovoy M. Psoriasis as a model for T-cell mediated disease: Immunobiologic and clinical effects of treatment with multiple doses of efalizumab. *Arch. Dermatol.* 138, 591–600 (2002).
12. Papp K, Bissonnette R, Krueger JG *et al.*
 - The treatment of moderate to severe psoriasis with a new anti-CD11a monoclonal antibody. *J. Am. Acad. Dermatol.* 45, 665–674 (2001).
13. Jullien D, Prinz JC, Langley RGB *et al.* T-cell modulation for the treatment of chronic plaque psoriasis with efalizumab (Raptiva™): mechanisms of action. *J. Invest. Dermatol.* 208, 297–306 (2004).
14. Gottlieb AB, Krueger JG, Wittkowski K, Dedrick R, Walicke P, Garovoy M. Psoriasis as a model for T-cell-mediated disease: Immunobiologic and clinical effects of treatment with multiple doses of efalizumab, an anti-CD11a antibody. *Arch. Dermatol.* 138, 591–600 (2002).
15. Papp K, Bissonnette R, Krieger JG *et al.* The treatment of moderate to severe psoriasis with a new anti-CD11a monoclonal antibody. *J. Am. Acad. Dermatol.* 45, 665–674 (2001).
16. Gordon KB, Papp KA, Hamilton TK *et al.* for the Efalizumab Study Group. Efalizumab for patients with moderate-to-severe plaque psoriasis: *JAMA* 290, 3073–3080 (2003).
17. Menter A, Bissennette R, Gottlieb AB *et al.* Subcutaneous efalizumab (anti-CD11a) provides rapid clinical response in patients with moderate-to-severe plaque psoriasis. *Poster presentation at 60th Annual Meeting of the American Academy of Dermatology* New Orleans, LA USA (2000).
18. Tristani-Firouzi, Krueger GG. Efficacy and safety of treatment modalities for psoriasis. *Cutis* 61, 11–21 (1998).
19. Lebwohl M, Menter A, Koo J, Feldman SR. Combination therapy to treat moderate-to-severe psoriasis. *J. Am. Acad. Dermatol.* 50, 416–430 (2004).
20. Lebwohl M. Combining the new biologic agents with our current psoriasis armamentarium. *J. Am. Acad. Dermatol.* 49, 118–124 (2003).
21. Cather JC, Cather JC, Menter A. Modulating T cell responses for the treatment of psoriasis: a focus on efalizumab. *Expert Opin. Biol. Ther.* 3, 361–370 (2003).

Website

- 101 Raptiva website
www.raptiva.com/understanding/index.jsp
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