Etanercept: a soluble TNF-α receptor in the treatment of psoriasis

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Among tumor necrosis factor (TNF)-α neutralizing drugs, etanercept is unique in as much as it is a recombinant, fully human, soluble form of the TNF-α receptor. Previously licensed for the treatment of adult and juvenile rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, recent double-blind, placebo-controlled, randomized trials have provided large and consistent evidence that etanercept induces a major clinical benefit in psoriasis. Etanercept rapidly and substantially improves psoriatic skin symptoms and leads to significant gain in quality of life. It allows safe and effective long-term control of psoriasis. Therefore, evidence-based treatment guidelines recommend the use of etanercept in moderate-to-severe plaque-type psoriasis.

Psoriasis is a common inflammatory skin disease characterized by a chronic-recurrent course and affecting approximately 2% of the total population [1]. It is diagnosed in patients of all ages, while the median age of onset is 29.1 years [2].

Plaque-type psoriasis is by far the most common manifestation, occurring in more than 80% of the cases. Clinical features include sharply demarginated, erythematous plaques with nonadherent, silvery scales. Pain, itching and cracking of the skin may be prominent as well. These lesions most typically affect elbows, knees, scalp, lumbar and umbilical areas. Guttate psoriasis is often a form that begins in childhood or early adulthood; it appears as eruption of scattered 0.1–1 cm 'drop' shaped, erythematous, scaly papules. Inverse psoriasis is typically localized to the axilla, submammary folds, genitocrural area and neck. These lesions usually have no scale and appear as well-demarcated, salmon-red plaques that can fissure. Palmoplantar psoriasis affects the palms and soles, presenting as discrete, erythematous, scaling patches and plaques. These lesions are usually bilateral, and involvement of the palms typically stops at the wrist–palm junction. The potential of psoriasis to principally affect every site of the body is reflected by the so-called erythrodermic psoriasis, presenting as generalized indurated erythema with diffuse exfoliation of fine scales. The patients may also present with fever, chills, rigors, arthralgias and trouble maintaining core body temperature. More rarely, pustular types of psoriasis may occur. Additionally, scalp and nails may also be affected. Finally, some 20–30% of patients develop joint involvement. In most patients, this so-called psoriatic arthritis occurs up to 10 years after the first skin symptoms.

Unmet needs in the treatment of psoriasis

Although a wide spectrum of antipsoriatic therapies is currently available, their application is often limited by numerous factors, particularly insufficient practicability (topical and phototherapies), lack of long-term safety (photo and systemic therapies); some are either not sufficiently effective as a monotherapy (retinoids) or are frequently not tolerated (fumarates). These shortcomings of established antipsoriatic therapies are reflected in part by poor satisfaction among patients: in a recent survey, only some 25% stated they were satisfied with the treatment successes encountered [3]. Besides, noncompliance is high among psoriatic patients [4]. Reasons for dissatisfaction and/or non-compliance comprise poor tolerability and/or efficacy, impracticability and lack of information on adverse drug reactions.

The impact of psoriasis on physical and mental aspects of life is still widely underestimated, even though numerous studies have documented a high burden of disease comparable to other major entities such as cancer or rheumatoid arthritis [5]. Consequently, improvement of health-related quality of life is an integral part of managing psoriasis.

Psoriasis is associated with several comorbidities, such as obesity, hypertension and diabetes [6]. These interfere with effective treatment because they represent contraindications

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for numerous therapies, which themselves could cause comorbidities. Incorporation of these comorbidities into patient management is particularly important given the substantially increased risk for cardiovascular disease and mortality among psoriatic patients [7,8].

Finally, a substantial percentage of patients need treatment of both psoriasis as well as psoriatic arthritis. Numerous drugs effective on the joints may either have no effect on the skin or could even worsen it, whereas others may be effective on the skin but not the joints [9,10].

Biologics in the treatment of psoriasis

Biologics, defined as molecular species generated in cell-based systems, have the potential to meet some of the aforementioned needs [11]. Major trials evaluating biologics in psoriasis have focused on moderate-to-severe plaque-type psoriasis. Measures currently used to document therapeutic efficacy include determination of the affected body surface area (BSA), Psoriasis Area and Severity Index (PASI), and the Dermatology Life Quality Index (DLQI) [11]. In the absence of a precise definition, moderate-to-severe psoriasis is considered to be characterized by scores greater than ten in any of these instruments [12]. Treatment success is defined by a reduction of the respective scores. Typically, the percentage of patients achieving at least a 75% reduction in the PASI (PASI-75) is considered a good clinical response.

Currently, four biologics are approved for the treatment of plaque-type psoriasis [9]. Whereas alefacept (approved only by the US FDA) and efalizumab both interfere with T-cell function, infliximab and etanercept block the proinflammatory cytokine TNF-α; the latter three are approved by the FDA as well as the European Agency for the Evaluation of Medicinal Products (EMEA). Both agencies are expected to approve the use of adalimumab, another TNF-α blocker, in the near future. All biologics mentioned have proven safety and efficacy as well as practicability and improvement of quality of life in double-blind, placebo-controlled, randomized trials; however, only the TNF-α antagonists have consistently demonstrated efficacy in psoriatic arthritis.

Structure

Etanercept is a recombinant, fully human, soluble, dimeric fusion protein that consists of two copies of the extracellular ligand-binding domain of the human 75 kDa TNF-α receptor linked to the Fc portion of human immunoglobulin (Ig) G1 (**Table 1**). It is produced by recombinant DNA technology in a Chinese hamster ovary mammalian cell expression system. The structure of etanercept makes it a 50–100-fold more potent binder of TNF-α than the endogenous unconjugated soluble TNF-α receptor [13]. Given its dimeric structure, each etanercept molecule can bind up to two TNF-α molecules. Linkage of the receptor to the Fc portion of IgG1 also substantially prolongs the half-life of etanercept relative to the endogenous soluble TNF p75 receptors.

Pharmacokinetics

The pharmacokinetic parameters for etanercept are similar regardless of age, sex or disease state of the patient [14]. Whereas a weight-based dosing schedule is warranted for pediatric patients, no dosage adjustment is required in the elderly. The presence of renal or hepatic impairment should not require a change in dosage of etanercept, as suggested by limited data in patients with acute renal failure or acute hepatic failure.

Etanercept is administered by subcutaneous injection once- or twice-weekly. Its rate of absorption is slower than that observed with agents administered intravenously. Peak serum concentrations are achieved 50–70 h after single-dose administration [15]. Studies have consistently indicated that the absolute bioavailability is approximately 60%. Administering a single 25-mg dose subcutaneously to healthy individuals resulted in a mean peak concentration of 1.5 mg/l at 51 h compared with 1.1 mg/l at 69 h in patients with rheumatoid arthritis. With multiple weekly dosing, etanercept achieves a smooth and uniform steady-state concentration–time profile that is linearly proportional to the weekly dosage administered. The absorption profile of etanercept is similar in patients with rheumatoid arthritis and psoriasis. At the end of 24 weeks' treatment with etanercept 25 mg subcutaneously twice weekly, patients with rheumatoid arthritis achieved a mean peak concentration of 2.4 mg/l at 32 h after the last dose. Steady-state pharmacokinetic profiles of etanercept 50 mg once weekly and etanercept 25 mg twice weekly are similar in terms of peak concentration (2.4 vs 2.6 mg/l), trough concentration (1.2 vs 1.4 mg/l), and partial area under the concentration-time curve (297 vs 316 mg•h/l) (**Table 1**).

The apparent volume of distribution of etanercept is about 12 l after single-dose administration. This is larger than the plasma volume, but less than that of extracellular water. Despite its molecular size, data suggest that etanercept penetrates into synovial fluid [16].

Table 1. Pharmacology of etanercept.

Structure	Soluble TNF receptor fusion protein (ligand-binding portion of TNF p75 receptor linked to the Fc region of IgG1)	
Mechanism of action	Binds to soluble or membrane-bound TNF-α	
Pharmacodynamics	Modulates biological responses mediated by TNF-α, including expression of adhesion molecules important for leukocyte migration, and serum levels of other cytokines and matrix metalloproteinase	
Pharmacokinetics	***Healthy individuals***	***Patients with rheumatoid arthritis****
Single dose (25 mg)		
– C_{max} (mean ± SD)	1.5 ± 0.72 mg/l	1.1 ± 0.6 mg/l
– t_{max} (mean ± SD)	51 ± 14 h	69 ± 34 h
Multiple dosing (25 mg twice weekly)		
– C_{max} (mean ± SD)		2.6 ± 1.2 mg/l
– t_{max} (mean ± SD)		62 ± 29 h
Multiple dosing (50 mg once weekly)		
– C_{max} (mean ± SD)		2.4 ± 1.5 mg/l
Mean absolute bioavailability	58.0%	62.6%
Half-life	2.8 ± 0.8 days (single 25-mg dose)	4.3 ± 1.3 days (25 mg twice weekly)
Indication in dermatology (dosage)‡	Moderate-to-severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant of other systemic therapy, including methotrexate, cyclosporine, or psoralen plus ultraviolet A phototherapy (25 mg twice weekly for up to 24 weeks. 50 mg twice weekly may be used for up to 12 weeks followed, if necessary, by 25 mg twice weekly, for up to 24 weeks total)	

**The pharmacokinetic parameters for etanercept are similar regardless of age, sex, or disease state of the patient.*

‡European Medicines Agency (EMEA).

C_{max}: Peak concentration; Ig: Immunoglobin; SD: Standard deviation; t_{max}: Time to peak concentration; TNF: Tumor necrosis factor.

Modified from [37].

A single subcutaneous administration of etanercept 25 mg in patients with rheumatoid arthritis resulted in a mean half-life of 102 h (approximately 4 days) and a clearance rate of 160 ml/h, with no significant change in these pharmacokinetic parameters observed with repeated dosing (**Table 1**). Although not confirmed, it is thought that the elimination of etanercept occurs after it binds to TNF, and metabolism of the complex could occur through either peptide or amino acid degradation pathways. Amino acids could then be recycled or eliminated through the bile or urine. The metabolites of etanercept are not bioactive.

Limited studies have evaluated drug–drug interactions for etanercept. Importantly, concomitant treatment with methotrexate, which is often given concomitantly with etanercept in patients with rheumatoid arthritis, does not significantly affect the pharmacokinetic profile of etanercept.

Pharmacodynamics

The proinflammatory cytokine TNF-α plays an important role in the pathogenesis of a number of chronic inflammatory disorders, including psoriasis and psoriatic arthritis. Etanercept modulates biological responses that are initiated or controlled by TNF-α through competitive binding, thus preventing TNF from binding to endogenous receptors. Etanercept also binds to TNF expressed on cell surface membranes (cell-bound TNF). TNF-α, which circulates in its soluble form, is primarily produced by macrophages and to a lesser extent by T cells. There are two types of TNF-α cell-surface receptors, a 55-kDa protein (p55) and a 75-kd protein (p75), and interaction with these receptors triggers the effects of TNF-α. The etanercept TNF-α p75 receptor binds to and inactivates TNF-α. Unlike monoclonal antibodies, the soluble fusion protein etanercept does not induce complement-mediated cell lysis. Overall, etanercept results in little impairment of general immune function in patients with rheumatoid arthritis, as shown by the lack of a significant effect on delayed-type hypersensitivity reactions, serum Ig levels, T-cell proliferative response, neutrophil function and incidence of infection.

In psoriasis, etanercept competitively binds to TNF-α and prevents interactions with its cell surface receptors on keratinocytes and

Table 2. Efficacy of etanercept in the treatment of psoriasis.

Study	Agent	Study type	n	Dosing	Results*	Comments	Ref.
Mease (2000)	Etanercept	RDBPC	38	2 × 25 mg weekly s.c.	PASI-75 after 12 weeks: 26%	PsA/PsO study: 38/60 patients evaluated by the PASI	[20]
Mease (2004)	Etanercept	RDBPC	128	2 × 25 mg weekly s.c.	PASI-75 after 24 weeks: 23%	PsA/PsO study: 128 patients evaluated by the PASI	[21]
Gottlieb (2003)	Etanercept	RDBPC	112	2 × 25 mg weekly s.c.	PASI-75 after 12 weeks: 30%		[22]
Leonardi (2003)	Etanercept	RDBPC	672	1 × 25 mg vs 2 × 25 mg vs 2 × 50 mg weekly s.c.	PASI-75 after 12 weeks: 14 vs 34 vs 49%	Dose-finding study	[23]
Papp (2001)	Etanercept	RDBPC	145	2 × 25 mg for 24 weeks vs 2 × 50 mg for 12 weeks, followed by 2 × 25 mg	PASI-75 after 12 weeks: 34 vs 49%; PASI-75 after 24 weeks: 45 vs 54%	Evaluation of optimal initiation dose	[24]

**Percentage of patients achieving a PASI-75 response.*

PASI: Psoriasis Area and Severity Index; PsA: Psoriatic arthritis; PsO: Psoriasis; RDBPC: Randomized, double-blind, placebo-controlled; s.c.: Subcutaneous.

Adapted from [9].

endothelial as well as inflammatory cells. In patients with psoriasis, etanercept significantly reduced keratinocyte adhesion molecule expression, epidermal T-cell infiltration, and markers of keratinocyte activation and proliferation, with resulting reduced epidermal thickness (**Table 1**) [17,18]. Recently, Malaviya *et al.* demonstrated that etanercept selectively induces apoptosis of pathogenic dermal dendritic cells in responding patients early in the course of treatment [19]. These important actions on psoriasis skin lesions are thought to be the result of down-regulation of proinflammatory and proproliferative gene expression induced in keratinocytes as a result of local TNF-α synthesis.

Clinical efficacy

The efficacy of etanercept for the treatment of plaque psoriasis has been evaluated in five placebo-controlled studies, two of which evaluated psoriasis in the setting of psoriatic arthritis (**Table 2**). The first of these studies by Mease and colleagues also examined a subset of 38 patients who had more than 3% of their BSA covered with plaque psoriasis [20]. Of the 38 patients, 19 received etanercept 25 mg subcutaneously twice weekly, while the remaining 19 received placebo. After 12 weeks of therapy, 26% of those subjects receiving etanercept achieved PASI-75 compared with 0% of those receiving placebo. These results were later confirmed in a comparable, but larger trial including 128 patients suffering from psoriasis and psoriatic arthritis [21].

A larger, Phase II, randomized, double-blind and placebo controlled study examined the efficacy and safety of etanercept 25 mg subcutaneously twice weekly compared with placebo, as monotherapy for moderate-to-severe plaque psoriasis [22]. After 12 weeks of therapy, 30% of patients achieved a PASI-75 compared with 2% in the placebo group. After 24 weeks of continuous therapy, 56% of patients receiving etanercept achieved PASI-75 compared with 5% in the control group.

Leonardi and colleagues later conducted a Phase III, placebo-controlled, double blind study that evaluated etanercept for psoriasis [23]. Patients with moderate-to-severe psoriasis that were not receiving any other therapies including systemic, phototherapy or topical treatments, were enrolled. A total of 672 patients underwent randomization and 652 received either placebo or etanercept subcutaneously at low dose (25 mg once weekly), medium dose (25 mg twice weekly), or high dose (50 mg twice weekly). After 12 weeks, patients who were in the placebo group began twice weekly treatment with 25 mg of etanercept. After 12 weeks of therapy, patients achieving a PASI-75 on placebo, 25 mg once weekly, 25 mg twice weekly, and 50 mg twice weekly were 4, 14, 32, and 47%, respectively. After 24 weeks of continuous therapy, the

PASI-75 score in the low-dose group was 21% compared with 41% in those receiving 25 mg twice weekly and 54% in those receiving the high dose of 50 mg twice weekly.

A second large, Phase III, double-blind study evaluating etanercept for moderate-to-severe plaque psoriasis was conducted in the US, Europe and Canada [24]. The study involved three groups of patients, each receiving placebo twice weekly, etanercept 25 mg twice weekly, or etanercept 50 mg twice weekly, for the first 12 weeks. After 12 weeks, all three groups were continued on etanercept 25 mg twice weekly for 12 weeks. After the first 12 weeks of therapy, 3, 34 and 49% of patients receiving placebo, 25 mg twice weekly, and 50 mg twice weekly, achieved PASI-75, respectively; these findings are consistent with those results seen in the US studies. During the second 12-week period during which all patients received 25 mg, those patients who were previously receiving 25 mg twice weekly continued to improve, with 45% achieving PASI-75 at week 24. The high-dose group (50 mg twice weekly) who were then placed on 25 mg twice weekly maintained their previous improvements, with 54% achieving PASI-75 at week 24, and those patients who were previously received placebo, 28% achieved a PASI-75. These findings suggested that induction with high-dose etanercept can then be maintained with a lower dose and still preserve PASI-75 scores.

Safety

In psoriasis clinical trial experience, etanercept has been well tolerated (**Table 3**). The most common adverse event in patients receiving placebo or any dose of etanercept was injection site reaction, where rates in the previously mentioned two Phase III trials ranged from 6–18%. These reactions typically occur 2–3 weeks into treatment and consist of erythema, pain, itching and/or swelling [25], and typically resolve in 3–5 days.

Table 3. Frequency of adverse events associated with etanercept based on clinical trials and postmarketing experience.

Frequency*	Adverse event
Very common (>1/10)	Injection site reactions
	Infections
Common (>1/100, <1/10)	Fever
	Pruritus
	Allergic reactions
	Autoantibody formation
Uncommon (>1/1000, <1/100)	Serious infections
	Rash
	Angioedema
	Urticaria
	Thrombocytopenia

**Number of adult patients expected to experience the reaction. Adapted from [37].*

In placebo-controlled trials for all uses of etanercept, the most common type of adverse event was an upper respiratory tract infection, which occurred in 12–20% of patients, but not at an increased frequency when compared with placebo groups [26]. In rheumatoid arthritis patients in whom there is more long-term data, it appears that etanercept may increase the risk of serious infection. In clinical trials, the rates of infection that required hospitalization or parental antibiotic therapy were 0.04 per patient-year in etanercept-treated groups, which is very similar to the total population. In postmarketing data on the use of etanercept, serious infections and sepsis were reported in patients using etanercept, but most of these cases were in patients receiving concomitant immunosuppressive therapies. Rare cases of reactivation of tuberculosis have been noted in patients receiving etanercept [27].

The rates of malignancy in patients with psoriasis do not appear to be increased in those receiving etanercept [26]. In placebo-controlled, randomized studies, eight of 933 etanercept treated patients were diagnosed with malignancy whereas one in 414 patients receiving placebo were diagnosed with malignancy. The rate of lymphoma was threefold greater in patients receiving etanercept than in the general population. A cohort study by Gelfand, however, found that psoriasis patients are at a threefold increased risk of developing lymphoma [28]. Taking this into account, analysis of the effects of etanercept or any other immunosuppressive therapy must consider the inherit risk of lymphoma to that specific disease population.

Postmarketing surveillance has reported rare incidences of demyelinating disorders or exacerbations of pre-existing multiple sclerosis [29] in patients receiving etanercept.

Approximately 6% of patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis or plaque psoriasis developed non-neutralizing antibodies to the TNF receptor [26]. Antinuclear antibodies develop in some patients receiving etanercept, but in the majority of cases, this finding has no clinical significance. There are rare cases of systemic and cutaneous lupus associated with etanercept use [30,31].

Etanercept was evaluated for its use in patients with congestive heart failure (CHF) [32], but the studies were terminated early owing to lack of efficacy. One of the studies actually suggested a higher mortality rate in patients with CHF who received treatment with etanercept [31]. In addition, there have been case reports describing new onset of CHF in patients receiving etanercept [33] who had no previous symptoms and were aged under 50 years.

Clinical use & treatment guidelines

Based on the aforementioned trials, both the FDA as well as the EMEA have approved etanercept for the treatment of moderate-to-severe plaque psoriasis in adult patients. Whereas etanercept can be considered alongside other systemic or phototherapy in the USA, the more restrictive European label demands that patients must have failed to respond to, have a contraindication to, or are intolerant to other systemic therapy. Two evidence-based European guidelines recommend the use of etanercept in patients fulfilling the aforementioned criteria defined by the European label, particularly in patients with simultaneous relevant psoriatic arthritis [34,35]. Expert comments on these criteria as well as recommendations for the clinical use of etanercept have been recently summarized elsewhere [12].

In brief, measures currently used to document disease severity include determination of the affected BSA, the PASI and the DLQI. In the absence of a precise definition, moderate to severe psoriasis is considered to be characterized by scores over 10 in any of these instruments, but other criteria such as involvement of the face or joints may also be used. The current standard dose is either 2 × 25 or 1 × 50 mg/week, in particularly severe cases 2 × 50 mg should be used because of its faster mode of onset. Etanercept treatment should not be initiated in patients with active infections, decompensated heart insufficiency (NYHA III–IV), and pregnant or breast-feeding women.

Treatment should be continued as needed. Monitoring should include white blood cell counts, alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), tuberculin skin test plus chest x-ray, and pregnancy test in women of child-bearing potential. Criteria for permanent discontinuation include lack of efficacy (PASI-50 response not achieved after 12 weeks despite 2 × 50 mg/week), severe drug-related toxicity, and severe intercurrent diseases such as chronic infections (tuberculosis), malignancies other than non-metastatic/non-melanoma skin cancer, signs of demyelination, or development of severe chronic heart failure. Temporary interruptions are validated because of acute infections, surgery, pregnancy, immunizations, or upon achievement of the treatment goal.

Although not approved for treating psoriasis in children, etanercept is most experts' first choice in such patients, given its label for juvenile rheumatoid arthritis.

Expert commentary

Etanercept has reproducibly proven to allow rapid and effective control of moderate-to-severe plaque psoriasis along with substantial improvement of health-related quality of life in several well-designed clinical studies. Simple self-administration and minimal monitoring requirements add to its practicability from the patients' and physicians' perspective. Etanercept was generally well tolerated, with comparable rates and types of adverse events in the active and placebo groups. Additionally, etanercept frequently caused mild injection site reactions. Infections, mainly of the upper respiratory tract, also occurred. Dropout rates in the studies were approximately 10%, but were not due to adverse effects. Long-term safety data are available from patients treated for other indications, particularly rheumatoid arthritis. A slight increase in tuberculosis has been observed in these patients. No increased incidence of malignancies was observed in several studies in rheumatoid arthritis or psoriasis.

Two evidence-based European guidelines recommend the use of etanercept in adult patients with moderate-to-severe plaque psoriasis, particularly in cases with simultaneous significant psoriatic arthritis. Moreover, expert opinion also recommends the use of etanercept in high-need pediatric patients.

Future perspective

A prominent feature of etanercept as well as all other biologics approved for the treatment of psoriasis is its high direct costs. Given the limited resources of healthcare systems around the world, appropriate patient selection will become an increasingly challenging issue. Interestingly, three European pharmacoeconomic studies [36,37,101] show that the use of etanercept is cost-effective in patients with severe psoriasis. Since the average PASI of patients included in the aforementioned clinical studies was approximately 18, etanercept

as well as the other biologics may be placed as first-line therapy for severe psoriasis, rather than second- or even last-line therapy for moderate-to-severe psoriasis, in future treatment guidelines.

TNF-α does not only play a central role in the pathogenesis of psoriasis, but acts as a so-called adipokine, mediating insulin resistance, a mechanism linking together obesity, inflammation and diabetes [38]. A hotspot of clinical research will therefore be the investigation of continuous TNF-α blockade on the development of the comorbidities associated with psoriasis, particularly atherosclerosis and its consequences. Along this line, the option to possibly prevent the onset of psoriatic arthritis will also be evaluated.

Finally, now that biologics in general have highlighted suitable targets for treating psoriasis, innovative strategies will be developed to target these structures, but using less costly technologies. The mid-term future may well belong to orally applicable smart small molecules interfering with already established key steps in the pathogenesis of psoriasis.

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Executive summary

- Psoriasis is a common chronic-recurrent inflammatory skin disease that is frequently associated with psoriatic arthritis and substantially reduces the patients´ quality of life.
- The use of current established therapies is limited by lack of practicability, insufficient long-term safety, and contra-indications because of comorbidities associated with psoriasis.
- The pro-inflammatory cytokine tumor necrosis factor (TNF)-α plays a central pathogenetic role in psoriasis and psoriatic arthritis.
- Etanercept is a soluble TNF-α receptor, capable of neutralizing this cytokine without substantial alterations of the function of the immune system.
- The use of etanercept for the treatment of moderate-to-severe plaque psoriasis is highly evidence-based (level 1B, grade A). Several well-designed clinical studies reproducibly confirmed a rapid and dose-dependent mode of onset (75% reduction in Psoriasis Area and Severity Index after 12 weeks in some 35% of patients receiving 2 × 25 mg per week and 50% in those receiving 2 × 50 mg per week), paralleled by a substantial improvement of the patients´ quality of life.
- Continuation of etanercept treatment and/or re-treatement allows effective long-term control of the disease. Self-administration and minimal monitoring requirements add to its practicability.
- Etanercept treatment is generally well tolerated. Injection-site reactions are common. Tuberculosis may occur more frequently, but there is currently no indication of a higher risk of developing malignancies.
- Evidence-based guidelines recommend the use of etanercept in patients with moderate-to-severe psoriasis, particularly in patients with simultaneous significant psoriatic arthritis. Expert opinion also recommends its use in high-need pediatric patients with psoriasis.

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