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Long-Term Efficacy of Etanercept for Plaque-Type Psoriasis and Estimated Cost in Daily Clinical Practice

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ABSTRACT

Background: There are numerous clinical trials proving efficacy and safety profiles of etanercept. Newer studies, however, include patients with significant comorbidities, unstable psoriasis, or concomitant treatments. **Objective:** The objective of this study was to provide data on long-term response to etanercept and estimate the cost in daily practice. **Methods:** This is an observational retrospective study including patients with plaque-type psoriasis receiving etanercept 50 mg/wk for more than 6 months at the Dermatology Department of the University Hospital of La Coruña (Spain). Psoriasis severity was determined using the Psoriasis Area and Severity Index (PASI) at baseline and then at 12 weeks, 24 weeks, and annually until treatment discontinuation. **Results:** A total of 102 patients aged 24 to 78 years were included. Response rates of 58.8% and 66.3% for PASI 75 score (reduction of at least 75% in PASI score compared with baseline) were achieved after 12 and 24 weeks of treatment, respectively. Among patients who continued treatment, the PASI 75 score was maintained by 75.3% at 1 year, 82.5% at 2 years, and 88.2% at 3 years. The percentage of patients receiving other systemic treatments was 38.2%. Adverse effects were reported in 13.7%, all of them mild, except one case of urinary sepsis. The average cost per patient was €244.68 ± €45.27 per week and €34.95 ± €6.46 per day. **Conclusions:** We provide data on long-term response to etanercept and its costs in a real-world setting. Response rates were higher than in some clinical trials, with progressive efficacy and not related to body mass index. Etanercept cost was comparable with that estimated in other studies. Combination with a conventional systemic agent can enhance efficacy without additional adverse events.

Keywords: cost, daily clinical practice, efficacy, etanercept, aque-type psoriasis.

Introduction

Etanercept is a tumor necrosis factor alpha antagonist whose efficacy and safety profiles have been proved in numerous clinical trials. Nevertheless, these studies usually enroll only patients with stable disease, without significant comorbidities, who undergo a washout period of previous systemic treatments [1–4].

The aim of this study was to provide data on long-term response to etanercept and estimate the cost for the treatment of patients with moderate to severe plaque-type psoriasis in daily clinical practice.

Methods

This is an observational retrospective follow-up study including patients with moderate to severe plaque-type psoriasis receiving 50 mg/wk of etanercept for more than 6 months at the Psoriasis Unit of the Dermatology Department of the University Hospital of La Coruña in Spain. We included patients treated with etanercept between January 1, 2005 (the year in which the treatment was authorized in our hospital), and December 31, 2012. Patients with intermittent therapy were not excluded. Data were obtained from chart review and patient interview. All patients signed an informed consent form to be included in the study.

Baseline demographic and disease status data were collected: age, sex, body mass index (BMI), psoriasis duration, previous psoriasis treatments, history of psoriatic arthritis, date of etanercept initiation and dose, duration of treatment, and date and reason for treatment discontinuation.

Psoriasis severity was determined using the Psoriasis Area and Severity Index (PASI) at baseline and then at 12 weeks, 24 weeks, and annually until treatment discontinuation. Psoriasis was considered moderate to severe in patients with a PASI score of 10 or greater or those receiving systemic treatment for their psoriasis at study inclusion. Treatment efficacy was assessed in all patients enrolled in the study at these time points by PASI 75 score (reduction of at least 75% in PASI score compared with baseline), taking into account the BMI and the dose of etanercept (50 mg/wk or 50 mg twice weekly).

Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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We registered changes in the administration schedule of etanercept, addition of concomitant treatments for psoriasis, the causes for etanercept discontinuation, the occurrence of adverse events, their severity, and the relationship with etanercept therapy. Furthermore, we assessed the average cost of etanercept treatment per patient according to the official selling price in Spain at the end of the study (€227.806 per 50 mg prefilled syringe), taking into account registered changes in the administration schedule and doses.

Statistical Analysis

All statistical analysis was performed using the Statistical Package for Social Science, version 18.0, for Windows. Descriptive statistics such as mean, median, and SDs were computed for continuous variables, and percentages (%) were used for categorical variables. The chi-square test was used for studying the relationship between PASI 75 score and BMI. Statistical significance was set at $P < 0.05$.

Results

A total of 102 patients aged 24 to 78 years were included. Their mean age was 52.3 ± 12.4 years; 74.5% were men and 25.5% were women. The mean duration of psoriasis was 22.0 ± 10.6 years (range 5–49 years).

Family history of psoriasis was present in 52.6% of the patients and psoriatic arthropathy in 27.7% of the patients at the start of etanercept treatment.

Body weight was within normal limits in 20.2% of the patients (BMI 18.5–24.9 kg/m^2). There was overweight in 41.5% (BMI 25–29.9 kg/m^2), obesity in 36.2% (BMI 30–39.9 kg/m^2), and morbid obesity in 2.1% of the patients (BMI of >40 kg/m^2).

The mean PASI score at the start of etanercept treatment was 10.6 ± 9.1. The mean duration of etanercept treatment was 124.8 ± 71.3 weeks in all patients and 91.5 ± 51.8 weeks in patients in whom treatment discontinuation was necessary because of loss of efficacy or adverse events (46.0%). The mean duration of treatment was 166.2 ± 64.9 weeks in patients maintaining treatment at the end of the study.

Five patients (4.9%) received intermittent therapy with etanercept, whereas the remaining patients received continuous treatment. The usual dose of 50 mg/wk was increased to twice a week in 19.6% of the patients who failed to respond to the lower dose, for a mean of 24.1 ± 11.6 weeks, after which the 50 mg/wk dose was re-established.

The percentage of patients receiving other systemic treatments during the study was 38.2% (9.8% acitretin, 21.6% cyclosporine, 5.9% methotrexate, and 1% phototherapy). The mean duration of concomitant therapy was 57.7 ± 58.0 weeks with acitretin, 26.0 ± 14.1 weeks with cyclosporine, 23.0 ± 20.6 weeks with methotrexate, and 18 weeks in the case of phototherapy. Concomitant systemic treatment had been started before etanercept in 66.7% of the patients and was continued for a mean of 33.3 ± 39.4 weeks until withdrawal and maintenance of etanercept monotherapy. In the remaining 33.3% of the patients, concomitant therapy was subsequently added to improve etanercept efficacy and was maintained for a mean of 33.9 ± 15.6 weeks. Concomitant topical treatment was prescribed in all patients at some point during the study.

Demographic data and psoriasis characteristics are summarized in Table 1. The PASI 75 score was achieved by 58.8% of the patients at 12 weeks of treatment (60 of 102) and by 66.3% (65 of 102) at 24 weeks. Among patients who continued etanercept treatment, the PASI 75 score was maintained by 75.3% at 1 year (61 of 81), 82.5% at 2 years (47 of 57), and 88.2% at 3 years (30 of 34). All patients who are still being treated at 4 and 5 years maintained the PASI 75 score (9 of 9 and 5 of 5 patients, respectively) (Fig. 1). Treatment efficacy (PASI 75 score at 12 and 24 weeks) was not related to BMI ($P = 0.61$ and 0.33, respectively).

The reasons for etanercept discontinuation were loss of efficacy and switch to another treatment in 43.10% and other reasons in 6.9% (adverse events or loss of patient follow-up) of the cases. Fifty percent of the patients maintained etanercept treatment at the time of study completion. Adverse effects were reported in 13.7% of the patients, all of them mild, except in one case on etanercept monotherapy, in which treatment withdrawal was necessary due to urinary sepsis. This was considered as a serious adverse event that might have been influenced by etanercept.

The average cost per patient treated with etanercept was €244.6 ± €45.2 per week and €34.9 ± €6.4 per day. Additional cost of concomitant systemic and topical therapies was not included in this calculation.

Discussion

Efficacy and safety profiles of etanercept have been proved in numerous controlled clinical trials [1–4]. However, because most of them exclude patients with significant comorbidities, unstable types of psoriasis, or concomitant treatments, results in daily practice may be quite different to these trials.

Treatment efficacy (PASI 75 score) at 12 and 24 weeks in our patients was higher than that observed in some clinical trials, with response rates of 14% to 49% and 25% to 59% for the PASI 75 score after 12 and 24 weeks of treatment, respectively [2–4]. Some reports on the use of etanercept in daily practice found that the efficacy at 12 and 24 weeks was lower than that found in placebo-controlled trials [5–7]. Because eligibility criteria for biologic therapy in daily practice require ineffectiveness, intolerance, or contraindications to classic systemic therapies, the selection of a more therapy-resistant group of patients compared with clinical trials could explain these differences.

As in our case, however, other studies in daily practice have demonstrated similar or even better results than clinical trials [8–10]. These differences may be due to the use of different dosage schedules or the addition of concomitant antipsoriatic medication in daily practice, which might introduce a bias toward more favorable efficacy outcomes.

In our study, etanercept efficacy was not evaluated as monotherapy. Therefore, it is possible that our results about its efficacy were better than they would have been under controlled clinical trial conditions. However, we included a high percentage of obese patients, resistant to classical systemic therapies or with other comorbidities (hypertension, diabetes mellitus, and dyslipidemia), which might negatively influence etanercept efficacy. Although the prevalence of metabolic syndrome and cardiovascular risk scores were not calculated in this study, we found a prevalence of 24.6% of metabolic syndrome and a significant proportion of patients at intermediate and high risk of suffering a major cardiovascular event in the next 10 years (30.5% and 11.4%, respectively, based on Framingham risk score) in a population of 395 patients with plaque-type psoriasis [11,12].

Treatment efficacy seems to improve at 24 weeks and at 1 year of treatment, as was observed in other studies [5,9,10,13,14]. Arcese et al. [13] observed that among patients who responded to etanercept treatment, response (PASI 50 score, defined as ≥50% improvement from baseline in the PASI score, and a PASI score of <10) was achieved in a higher percentage of patients in more than 24 weeks of treatment (67.1%) compared with shorter treatment times (25.3%, 5.1%, and 2.5% of the patients achieved

Table 1 – Baseline demographic data, clinical disease characteristics, and treatment costs.

Characteristic	n (%)	Mean ± SD	Median	Range
Sex				
Male	76 (74.5)			
Female	26 (25.5)			
Age (y)		52.3 ± 12.4	52.0	24–78
Time since diagnosis (y)		22.0 ± 10.6	21.0	5–49
Psoriatic arthropathy	28 (27.7)			
Family history of psoriasis	51 (52.6)			
Body mass index (kg/m^2)				
Normal (18.5–24.9)	19 (20.2)			
Overweight (25–29.9)	39 (41.5)			
Obesity (30–39.9)	34 (36.2)			
Morbid obesity (>40)	2 (2.1)			
PASI score at baseline		10.6 ± 9.1	7.7	0–46.7
Treatment duration (wk)		124.8 ± 71.3	119.0	
Intermittent therapy	5 (4.9)			
Continuous therapy	97 (95.1)			
Concomitant systemic treatment				
Acitretin	10 (9.8)			
Cyclosporine	22 (21.6)			
Methotrexate	6 (5.9)			
Phototherapy	1 (1.0)			
Treatment cost per day (€)		34.9 ± 6.4	32.5	23.0–60.2
Treatment cost per week (€)		244.6 ± 45.2	227.8	161.4–421.8

PASI, Psoriasis Area and Severity Index.

response in 19–24 weeks, 13–18 weeks, and ≤12 weeks, respectively) [13]. In their study, 80% of the patients achieved the PASI 75 score, which is higher than rates observed in controlled clinical trials.

Similarly, Puig et al. [14] in a multicentric prospective study at 12-month follow-up observed a PASI 75 response of 64% at week 12, reaching a maximum at week 24 (76.1%) and maintaining to the end of the study. Van Lümig et al. [5] described the long-term efficacy of etanercept in real-world practice and although response rates were lower than in randomized controlled trials, the percentage of patients achieving the PASI 75 score progressively increased from week 12 (23.6%) to week 24 (38.1%) until the end of the study at week 24 (60%). As in our case, these results from European studies suggest that the onset of etanercept activity may be delayed in some patients and that 12 weeks may be too short a period to assess efficacy in these cases.

It is well known that obesity, in addition to playing a role in the pathogenesis of psoriasis, has important implications in the treatment, such as a greater risk of adverse effects with conventional systemic drugs and reduced efficacy and/or increased cost with biologic agents; therefore, dosage adjustment should be considered according to patients' weight [15]. Although we found a high percentage of overweight and obese patients, BMI does not seem to be associated with treatment efficacy, unlike other studies performed in daily practice. The PASI 75 score was achieved by a higher percentage of patients with a body weight of 65 kg or less (87.5%) than those with a body weight of 66 to 80 kg (80.5%) or more than 80 kg (74.1%) [13].

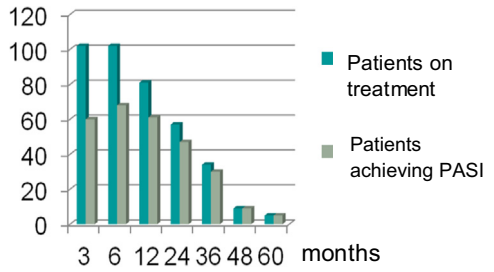

Fig. 1 – Etanercept efficacy over time. PASI, Psoriasis Area and Severity Index. (Color version of figure available online).

There are some studies about the concomitant use of etanercept and other systemic therapies, most of them with methotrexate in patients with rheumatic diseases [14–17]. Use of concomitant antipsoriatic therapy was relatively frequent in our study, especially during the initial phase of etanercept treatment because the washout period was not performed before starting biologic therapy to prevent the progression or relapse of the disease, which also explains the relatively low PASI scores at baseline. For one-third of the patients, systemic therapy was added to achieve a higher response, improving etanercept efficacy without any significant adverse event. Our data support that etanercept in combination with a conventional systemic agent can enhance efficacy without significant additional toxicity and permit safe transitioning from another systemic therapy. Although biologic therapy is a safe and effective option in the treatment of psoriasis, it is much more expensive than conventional systemic therapy. Few studies estimate the cost of these treatments in daily clinical practice [18].

In another Spanish study, the average cost in the maintenance phase of etanercept treatment (>24 weeks since the start of treatment) at standard doses was approximately €35/d with little variation among patients [19]. We obtained similar results. We estimate, however, the average cost from the start of treatment, including those patients treated with 50 mg twice weekly.

Conclusions

We provide data on long-term response to etanercept therapy and its costs in a real-world setting in La Coruña (Spain). Response rates were higher than those reported in some clinical trials, with gradual and progressive efficacy over time and not

related to patients' BMI. Combination with a conventional systemic agent can enhance efficacy without additional adverse events. Etanercept cost was comparable with that estimated in other studies.

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