International Journal of Clinical Pharmacy (2019) 41:9–12
https://doi.org/10.1007/s11096-018-0769-7

SHORT RESEARCH REPORT

Clinical experience with the etanercept biosimilar SB4 in psoriatic patients

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Received: 20 October 2018 / Accepted: 14 December 2018 / Published online: 4 January 2019

Abstract

Background After the expiry of the patent of reference etanercept, several biosimilars have been developed, including SB4. *Objective* To study safety and efficacy of SB4 in psoriatic patients previously treated with etanercept and in the etanercept naive ones. *Method* Patients affected by moderate to severe psoriasis and/or psoriatic arthritis attending the Psoriasis Center of Florence University, treated with SB4 were enrolled in the study. Patients were divided in two cohorts. Cohort 1 included 32 patients who were switched from previous etanercept, cohort 2 included 12 patients who were naive to etanercept. *Results* Evaluation of the efficacy of SB4 in cohort 1 patients revealed rates of clinical remission (defined as both PASI and/or DAS28 increase < 10%) of 92% and 64% for psoriasis and psoriatic arthritis respectively. In cohort 2 at week 24 PASI 75 was observed in 75% of patients. *Conclusion* In our experience switching from originator to SB4 in psoriatic patients seems not to influence efficacy, especially cutaneous manifestations, over a median observational period of 24 weeks.

Keywords Biologics · Biosimilars · Etanercept · Psoriasis

Impacts on practice

- The biosimilar SB4 shows no difference in terms of efficacy and safety to etanercept.
- Because the costs of biological therapy in the treatment of psoriasis is increasing, the use of the biosimilar SB4 instead of etanercept should be considered.

Introduction

Etanercept (Enbrel®, Amgen/Pfizer) (ETN) was among the first anti-TNF-α agent to be approved for use in rheumatic diseases more than 15 years ago. It is licensed for treatment of different inflammatory diseases including plaque psoriasis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and juvenile idiopathic arthritis [1]. The efficacy of etanercept in patients with moderate-to-severe psoriasis and psoriatic arthritis is supported by good clinical data with a well-established safety and tolerability profile [2]. The patent of ETN expired in Europe in 2015. This has led to the development of several ETN biosimilars, copy versions of an already authorized biological medicinal product "with demonstrated similarity in physicochemical characteristics, efficacy and safety, based on a comprehensive comparability exercise" [3].

SB4 (Benepali©, Samsung Bioepis/Biogen) is a p75 recombinant human TNF- receptor etanercept biosimilar that binds TNF-α with high affinity and specificity [1]. SB4 was developed as a biosimilar of etanercept, in accordance with ICH guidelines and the current Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines on the development of biosimilar products and it is already approved for the same indications as the reference drug in Europe [4].

In Italy, healthcare policies can be included in regional regulations. As happened to infliximab biosimilar, Tuscany was among the first regions in Italy to impose use of etanercept biosimilars as the first choice treatment of both naive and not-naive psoriatic patients in 2017.

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Aim of the study

To describe our experience with the use of the etanercept biosimilar Benepali© (SB4) in the treatment of patients with moderate to severe plaque psoriasis.

Ethics approval

This study was approved by our local ethics committee.

Methods

Patients affected by moderate to severe psoriasis (Pso) and/or psoriatic arthritis (PsA), attending the Psoriasis Center of Florence University Dermatological Unit, and treated with SB4 were included in the study. Patients were divided in 2 cohorts. Cohort 1 included patients who were switched from previous ETN therapy to SB4. Patients in cohort 2 were naïve to ETN, and started on SB4.

Results

Overall the study included 44 patients (mean age 54.7 years; 32 M, 12 F) with moderate-severe psoriasis, with a mean duration of disease of 24.7 years. All patients had been previously treated with at least two conventional systemic treatments (methotrexate, cyclosporine, acitretin), which were withdrawn due to lack of efficacy. Seven patients had been previously treated with biologics other than ETN (3 with infliximab, 1 with adalimumab, 3 with efalizumab). Articular involvement was present in 17 patients (10 M, 7F; mean duration 11.9 years). Baseline demographic characteristics are presented in Table 1 whereas skin and joint disease activity (PASI and DAS 28) at the beginning of SB4 treatment and after 12 and 24 weeks are presented in Table 2.

Table 2 PASI and DAS28 scores at the beginning of SB4 treatment, after 12 and 24 weeks

	Switch (n = 32)	Naive (n = 12)
PASI score t0, mean + SD	2.15 + 1.88	13.09 + 2.25
PASI score t12, mean + SD	1.51 + 1.35	5.24 + 2.11
PASI score t24, mean + SD	1.20 + 1.15	3.98 + 2.42
DAS 28 t0, mean + SD	1.91 + 0.90	
DAS 28 t12, mean + SD	1.90 + 0.91	
DAS 28 t24, mean + SD	1.74 + 1.07	

PASI psoriasis area and severity index, *DAS28* disease activity score in 28 joints

Cohort 1: patients with Pso and/or PsA who switched from ETN to SB4

Thirty-two patients (mean age 54.1 years, 25 M, 7F) had ongoing ETN treatment at study initiation (May 2, 2017). Thirteen patients also had a diagnosis of PsA (mean age 54.7 years, 9 M, 4F). The median time on ETN was 265 weeks (range 48–492). After switching to SB4, treatment was continued on the same schedule and dosage as ETN (50 mg weekly). Evaluation of the efficacy of SB4 in all patients revealed rates of clinical remission (defined as both PASI and/or DAS 28 increase < 10%) of 92% and 64% for psoriasis and psoriatic arthritis patients, respectively. Analysis of variance (repeated measures ANOVA) revealed absence of statistically significant differences in terms of DAS 28 before and after switch, whereas PASI improved significantly ($P < 0.001$). With regard to safety, injection site-reaction to SB4 was observed in 4 patients.

Table 1 Patients' characteristics at baseline

	Switch (n = 32)	Naive (n = 12)	Total (n = 34)
Male sex (%)	78.12	58.33	72.72
PsA (%)	40.62	33.33	36.95
Age (years), mean + SD	54.16 + 14.82	56.33 + 14.28	54.75 + 14.54
Duration of plaque psoriasis (years), mean + SD	27.34 + 12.13	17.83 + 11.80	24.75 + 12.65
Duration of psoriatic arthritis (years), mean + SD	12.61 + 4.31	9.75 + 6.99	11.94 + 4.96
BMI (kg/m^2)	27.14 + 4.97	28.66 +7.09	27.56 + 5.59
Smoking habit (%)	21.87	41.66	26.08
Prior biological treatment (other than ETN), n	13	8	21
Duration of ETN treatment (months), mean + SD	67.15 + 26.41	–	–

PASI psoriasis area and severity index, *DAS28* disease activity score in 28 joints

Cohort 2: ETN-naıve patients who started treatment with SB4

Cohort 2 included 12 patients (mean age 56.3 years, 7 M, 5F) who had not been previously treated with ETN. Four patients had been treated with biological other than ETN (3 with infliximab and 1 with adalimumab), which were withdrawn due to lack of efficacy. The mean PASI score at the beginning of the treatment was 13.9. Two patients had an associated PsA. All cohort 2 patients received SB4 with a starting dose of 50 mg twice weekly for 3 months, followed by maintenance dose of 50 mg weekly in patients who were considered responders. Two patients discontinued treatment at week 16 because of PsA reactivation and psoriasis worsening, and therefore were switched to other biologics. Improvement > 50% in PASI score was observed as soon as week 12 in 8 out of 12 patients, with further amelioration at week 24 (PASI 75 observed in 9 out of 10 patients).

Three patients complained diffuse pruritus after the first injection and 2 patients reported mild fatigue during SB4 treatment.

Discussion

Due to the high costs of biological therapy and the expiration of patents of some biologics in the last few years, the development and approval of new biosimilars has recently gained much attention. Both FDA and EMA have already approved different biosimilars and considering the high number of applications that are currently under investigation by these agencies, it can be expected that the number of approved biosimilars will greatly increase in the future. The approval of SB4 was based on the results of stringent comparability exercises, demonstrating its similarity, in terms of safety and efficacy but also biological activity, to the originator [4].

As part of the EU recommendation process for biosimilars, it was considered justifiable to extrapolate clinical data (pharmacokinetic properties, efficacy and safety) for SB4 from key clinical trials to other approved therapeutic indications for reference ETN, since they share a common mechanism of action [5]. The principal comparability studies between ETN and SB4 were performed on patients with Rheumatoid Arthritis [6]. To the best of our knowledge no studies have been published on the efficacy and safety of SB4 in Pso and PsA [7].

Real-world experience on transitioning from ETN to SB4 is very limited. The Danish registry DERMBIO, involving patients with moderate-to-severe psoriasis treated with biologics [8], demonstrated no difference in terms of treatment discontinuation between patients who continued ETN and those who switched from ETN to SB4 over a 6-month period. Of 621 patients treated with etanercept only 55 were treated with SB4. More recently, data from the Italian Psobiosimilar registry were reported. In that registry, 158 patients who were switched from ETN to SB4 experienced meaningful change in PASI or new severe adverse events with a 6 months follow-up [9]. These results are in line with our study.

The EGALITY study was designed to evaluate the safety and efficacy of ETN and another ETN biosimilar (GP2015, Erelzi®) in patients with moderate-to-severe psoriasis, using a switching protocol. Patients were initially randomized to treatment with either ETN or GP2015 for 12 weeks and then re-randomized to either stick to their treatment or to undergo three switches between treatments at 6-week intervals to week 30. Study results were similar in terms of efficacy, safety and immunogenicity between the two treatments group indicating that repeated switching not affect clinical data [10].

Biologic therapies are important for the treatment of a wide range of immune-inflammatory diseases, including psoriasis. However, they are also expensive and their cost can lead to restricted access for many patients. Biosimilars represent an opportunity to reduce healthcare costs also taking into account similarity in terms of efficacy and safety compared with their original products. The extrapolation of clinical data as part of the biosimilar approval process is valid but requires stringent analysis on a case-by-case basis.

Conclusion

Switching from originator to SB4 in psoriatic patients seems to not influence efficacy, expecially for cutaneous manifestations over a median observational period of 6 months. Regarding the efficacy on articular symptoms we found a mild decrease in efficacy.

The incidence of sporadic mild adverse events before and after switching did not differ and consistent with the safety profile of the ETN molecule. All cutaneous events were mild to moderate in severity and easily manageable with emollients and antihistamines. No severe infections were reported.

Funding None.

Conflicts of interest The authors declare that they have no conflict of interest.

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