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RESEARCH LETTER

Cross-Switch from Etanercept Originator to Biosimilar SB4 and to GP2015 in Patients with Chronic Plaque Psoriasis

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Dear Editor,

Biosimilars of anti-TNF-α inhibitors have become a valid and usually less expensive alternative to their originator drugs [1]. Therefore, switching from originator to biosimilar drugs is an increasingly widespread approach because of the potential cost savings. As more biosimilars become available, switching between biosimilars of the same originator will be likely.

To date, only a few studies have assessed the effectiveness and safety of switching between different biosimilar agents ('cross-switching'), mostly focusing on the anti-TNF-α inhibitor infliximab [2–4]. There are no studies investigating the efficacy and safety of cross-switching between different biosimilars of etanercept in psoriatic patients.

In this multi-center, prospective, observational cohort study, we examined the effectiveness and safety of cross-switching from etanercept originator to SB4 (Benepali) and subsequently to GP2015 (Erelzi) in 76 consecutive patients with moderate-to-severe psoriasis followed in the outpatient psoriasis clinic of the University Hospital of Padua, Modena and Verona.

Patients were included if they had plaque psoriasis treated with etanercept originator and were in stable remission (Psoriasis Area and Severity Index [PASI] score < 3) for at least 12 months before the first switch. No other inclusion or exclusion criteria were used.

Studied patients were asked to switch from etanercept originator to SB4 and subsequently to GP2015 after shared decision making. All the patients were switched because of non-medical reasons. The hospital pharmacy recommended the use of the least expensive drug available, which was initially SB4 and afterwards GP2015. We provided exhaustive information on biosimilars (with efficacy and safety data), including their lower price allowing savings for the health system and the possibility to switch back to originator or previous biosimilar upon request in case of lack of efficacy or intolerance.

Only one patient refused to switch to SB4, none refused the second switch to GP2015.

Demographic, clinical, and laboratory parameters were recorded at baseline and at 1, 3, 6 and 12 months after the second switch. In addition, all adverse events were also recorded.

Seventy-six patients (50 males and 26 females, mean age 62.9 ± 12.6 years) were included. Mean disease duration was 28.2 ± 12.5 years. Thirty-nine (51%) patients had psoriatic arthritis (PsA). Arterial hypertension, dyslipidemia and type 2 diabetes mellitus were diagnosed in 38 (50%), 22 (29%) and 9 (12%) patients, respectively.

The mean duration of treatments with etanercept originator and SB4 were 96.3 ± 42.3 and 16.5 ± 8.6 months, respectively (Fig. 1).

At the beginning of the treatment with the originator, median PASI was 10.5 (range 8–14.2), while at the time of the first switch it was 2 (1–3). During the treatment with SB4, three patients showed a loss of response and were switched to another biologic (two to secukinumab and one to ustekinumab).

During the 12-month period of observation after the second switch, median PASI remained stable, from 1 (0–2) after 3 months to 0.5 (0–1) after 12 months (Fig. 1). The mean duration of treatment with GP2015 was 17.7 ± 6.4 months.

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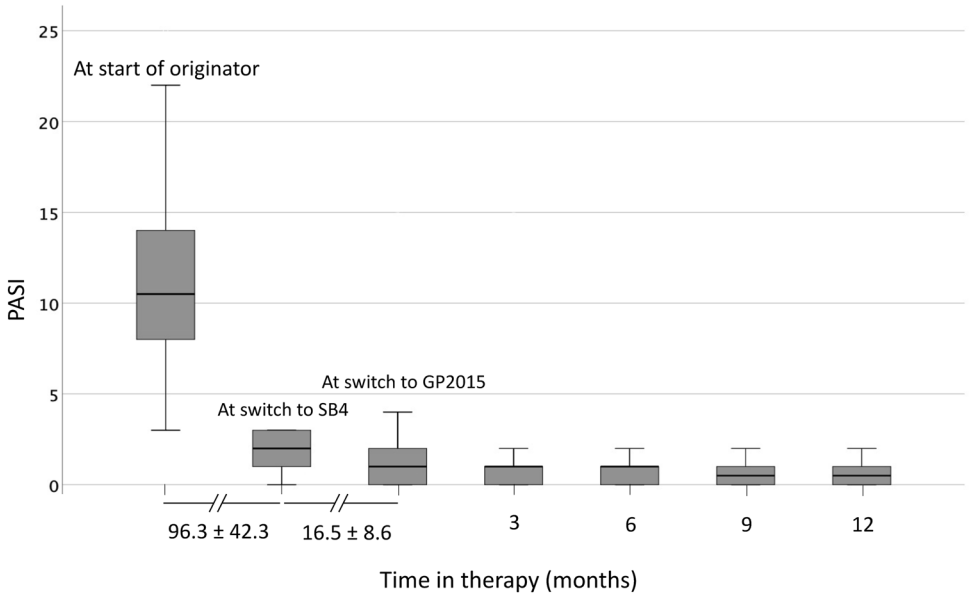

Fig. 1 Psoriasis Area and Severity Index (PASI) score median values in patients with psoriasis at initiation of treatment with etanercept originator, at time of the switch to SB4, at time of the cross-switch to GP2015 and at 3, 6, 9 and 12 months after this switch. The boxes include the PASI upper and lower quartiles; the whiskers represent the highest and lowest observations. Time is expressed in months (mean ± standard deviation)

After the cross-switch from SB4 to GP2015, two patients developed a flare-up. One patient's PASI increased from 1 to 8 at 3 months after the switch and he was therefore switched back to SB4, with a PASI decrease to 1 in 3 months. The other patient reported a relapse of psoriasis (PASI 15) and arthritis at 2 months after switching to GP2015. He was prescribed secukinumab with control of the disease.

No treatment-emergent serious adverse effects were reported. One patient interrupted the treatment after 9 months because of a pregnancy, whose outcome was positive.

This is the first study analyzing the consequences of switching between etanercept biosimilars in psoriatic patients. Two recent studies have assessed cross-switching between infliximab biosimilars (CT-P13 and SB2) [2, 3]. Gisondi et al. found that the switch from CT-P13 to SB2 was safe and effective [2]. However, the switch caused treatment withdrawal in 10 out of 96 (10%) patients because of loss of response ($n = 7$) or acute infusion reactions ($n = 3$).

Lauret et al. showed that the consecutive use of two infliximab biosimilars (CT-P13 and SB2) did not increase the risk of immunogenicity [3]. We did not measure antidrug antibodies (ADA) in our patients. However, etanercept, both originator and biosimilar, has shown to be associated with a low risk of immunogenicity and the very infrequent ADA to etanercept are non-neutralizing [5]. Therefore, we believe this will not represent a relevant issue when cross-switching with two etanercept biosimilars. Moreover, the EGALITY study on psoriatic patients showed that there are no effects on the production of ADA with multiple switches between GP2015 and Enbrel [6]. This will also likely apply to the case of cross-switching between etanercept biosimilars.

In our multicentric study we found that switching between two etanercept biosimilars (from SB4 to GP2015) is both safe and effective. Although we have not investigated PsA by applying formal outcome measures, only one patient has complained of a recurrence of joint pain.

Our results are in line with the few available real-life data that reported a high drug survival when switching from the etanercept originator to SB4 in psoriatic patients, while no such studies have been performed with GP2015 yet [7].

Recently, a study performed with rheumatologic patients showed no significant changes in disease activity when cross-switching the two etanercept biosimilars [4].

Switching from a biologic to a biosimilar or between two biosimilars has the obvious advantage of lowering costs, therefore allowing more people to access the same treatment. However, when it is mandated or the patients' choice is somehow limited, non-medical switch may induce a 'nocebo effect', which may reduce the effectiveness of the biosimilar in the real-life setting [8]. This nocebo effect can be reduced by informational and educational practices [8].

Our study has some limitations, which include its open design, the lack of a control group, the relatively small sample size and the lack of formal assessments for PsA. Nonetheless, our data showed that efficacy and safety are maintained after cross-switching between etanercept biosimilars.

In conclusion, biosimilars represent an important opportunity for earlier and equal access to biological treatment, reducing the growing pressure on health care budgets and being a viable treatment option for a larger number of patients. Further controlled studies with larger sample sizes are needed to provide data on the benefit/risk ratio of cross-switching between biosimilars.

Declarations

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Conflict of interest Stefano Piaserico has been a consultant and/or speaker for Abbvie, Almirall, Celgene, Janssen, Leo-pharma, Eli Lilly, Novartis, Sandoz, UCB; Andrea Conti has been a consultant and/or speaker for Abbvie, Janssen, Eli Lilly, Novartis, Pfizer and UCB; Francesco Messina has no conflict of interest; Alberto Meneguzzo has no conflict of interest; Giulia Odorici has no conflict of interest; Francesco Bellinato has no conflict of interest; Paolo Gisondi has been a consultant and/or speaker for Abbvie, Almirall, Celgene, Janssen, Leo-pharma, Eli Lilly, Novartis, Pfizer, Sandoz, UCB.

Authors' contributions SP, AC and PG designed the study, wrote the article and revised it critically; FM, AM, GO and FB collected the data and participated in the writing of the article and its revision.

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Consent to participate Not applicable.

Consent for publication Not applicable.

Availability of data and materials Not applicable.

Code availability Not applicable.

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