

The switch from etanercept originator to SB4: data from a real-life experience on tolerability and persistence on treatment in joint inflammatory diseases

Cosimo Bruni^{ID}, Stefano Gentileschi, Giovanni Pacini, Caterina Baldi, Marco Capassoni, Lorenzo Tofani, Marco Bardelli, Laura Cometi, Luca Cantarini, Francesca Nacci, Michele Vietri, Francesca Bartoli, Ginevra Fiori, Bruno Frediani and Marco Matucci-Cerinic

Abstract

Aims: Switching from originator to biosimilar is part of current practice in inflammatory rheumatic musculoskeletal diseases (iRMDs) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondylarthritis (axSpA), with evidences derived from both etanercept (ETN) to SB4-switching randomized controlled trials and real-life registries. We investigated the safety and treatment persistence of ETN/SB4 in a multi-iRMD cohort derived from two rheumatology departments in our region.

Methods: Adult patients with iRMDs, treated with ETN for at least 6 months and switched to SB4 in stable clinical condition, were eligible for this retrospective evaluation. Retrospective data on adverse events, loss of efficacy and persistence on treatment were collected until latest available follow-up.

Results: A total of 220 patients (85 RA, 81 PsA, 33 axSpA, 14 juvenile idiopathic arthritis and seven other conditions; 142 females, mean age 58 ± 7 years, disease duration 12 ± 4 years, ETN duration 7 ± 4 years) were enrolled, with median follow-up of 12.1 (9.7–15.8) months. A total of 50 patients (22.7%) presented with at least one adverse event, with 36 (16.4%) disease flares and 30 (13.6%: 11 for safety and 19 loss of efficacy) SB4 withdrawals. Cumulative SB4 treatment persistence was 99.1%, 88.6% and 64.6% at 6, 12 and 18 months respectively. Back-switch to ETN was performed in 17/30 cases, the remaining cases were managed with change of biologic disease modifying or conventional synthetic anti-rheumatic drug. Age was the only significant predictor of SB4 interruption at 6 months.

Conclusion: Our real-life data confirm the safety profile of switching from ETN to SB4, with slightly higher treatment persistence rates compared with other real-life registries.

Keywords: etanercept, persistence, rheumatic diseases, safety, SB4, switch

Received: 9 May 2020; revised manuscript accepted: 9 September 2020.

Introduction

Inflammatory rheumatic musculoskeletal diseases (iRMDs) are a wide, heterogeneous group of chronic disorders. Biologic disease modifying anti-rheumatic drugs (bDMARDs) marked a turning point in the treatment of iRMDs, allowing a reduction of non-steroidal anti-inflammatory

drug (NSAID) and corticosteroid (CCS) employment, while also providing additional efficacy when synergizing with conventional synthetic DMARDs (csDMARDs) or used as monotherapy.^{1–3} Among bDMARDs, anti-tumour necrosis factor (TNF) alpha was the first to obtain the goal of a long-term remission and to significantly

Ther Adv Musculoskel Dis

2020, Vol. 12: 1–9

DOI: 10.1177/
1759720X20964031

© The Author(s), 2020.
Article reuse guidelines:
sagepub.com/journals-
permissions

Correspondence to:

Cosimo Bruni
Department of
Experimental and Clinical
Medicine, Division of
Rheumatology, University
of Firenze, Via delle Oblate
4, 50141, Firenze, Italy
cosimobruni85@gmail.com

Stefano Gentileschi
Caterina Baldi
Marco Bardelli
Luca Cantarini
Bruno Frediani
Department of Medical
Sciences, Surgery
and Neurosciences,
Rheumatology Unit,
University of Siena, Siena,
Italy

Giovanni Pacini
Marco Capassoni
Lorenzo Tofani
Laura Cometi
Francesca Nacci
Department Experimental
and Clinical Medicine,
Division of Rheumatology,
University of Florence,
Florence, Italy

Michele Vietri
Department Experimental
and Clinical Medicine,
University of Florence,
Florence, Italy

Ethical Committee of
Central Tuscany Region,
Florence, Italy

Francesca Bartoli
Ginevra Fiori
Department Geriatric
Medicine, Division of
Rheumatology, Azienda
Ospedaliero Universitaria
Careggi, Firenze, Italy

Marco Matucci-Cerinic
Department Experimental
and Clinical Medicine,
Division of Rheumatology,
University of Florence,
Florence, Italy

Department Geriatric
Medicine, Division of
Rheumatology, Azienda
Ospedaliero Universitaria
Careggi, Firenze, Italy

improve patients' quality of life.⁴ Etanercept (ETN) is a recombinant human TNF receptor p75Fc fusion protein, licensed for rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA; including radiographic and non-radiographic spondylarthritis and ankylosing spondylitis), polyarticular juvenile idiopathic arthritis (JIA), and adult and paediatric psoriasis.⁵ Biosimilars are biologic products (drugs) that share the amino-acid sequence and tridimensional structure of an already authorized reference biologic agent, with confirmed evaluation in terms of physical-chemical characteristics, biological activity, efficacy and safety.^{6,7} Recently, SB4 was developed as a biosimilar to the reference product ETN,^{8,9} with equivalent clinical efficacy demonstrated through phase III randomized clinical trials in RA patients.¹⁰⁻¹² When compared with non-switched groups of patients treated with SB4 or ETN, patients switched from ETN to SB4 (ETN/SB4) were not significantly different in terms of efficacy and safety up to 100 weeks of follow-up.¹² In another phase III clinical trial, SB4 was proven to be less associated with injection site reactions and also to have less immunogenic power than ETN in RA patients.¹³ With this background, switching from originator bDMARD to biosimilar has become part of clinical practice, despite geographical differences: in fact, while common in European countries, the practice of switching from originator to biosimilar product is confined to a very small minority of cases in other regions, such as the USA, possibly due to the differences in healthcare systems.¹⁴ This is particularly true for the non-medical switching (NMS), performed for non-medical reasons (mostly economic), which has raised several concerns from both physicians and patients.¹⁵ A recent systematic literature review on NMS showed this practice being rarely associated with positive endpoints, including both clinical and economic ones.¹⁶ In fact, NMS was perceived as having a negative impact on quality of work and patient care, with increase in time spent on administrative work, as shown by a recent survey on over 1000 US physicians.¹⁷

Despite these considerations, the large real-life DANBIO cohort showed positive data regarding NMS in iRMD patients, with the ETN/SB4 retention rate being higher than ETN non-switched patients but lower than the historical ETN cohort. Moreover, the analysis of this registry identified patient-related but not drug-related factors as predictors for SB4 interruption.¹⁸

Neutral data were derived regarding the medical economic burden, which was unchanged when comparing the year before and after ETN/SB4 switching in the same cohort.¹⁸ Similar results were repeated in other real-life cohorts, where SB4 and ETN originator showed similar effectiveness in maintaining low disease activity in PsA patients, as well as in plaque psoriasis patients without arthritis.¹⁹⁻²¹

The aim of the present study was to report our real-life experience in assessing tolerability and persistence on treatment with SB4 in a cohort of ETN/SB4 medical and non-medical switching patients during up to 24 months of follow-up.

Materials and methods

The data concerning adult patients diagnosed with RA, PsA, axSpA, JIA and other rheumatologic diseases who switched from ETN to SB4 while in stable clinical condition, concerning the iRMD, were retrospectively evaluated for study inclusion. Patients were switched from ETN to SB4 by the treating physician during regular clinic appointments, following detailed discussion and information regarding both medical and non-medical features of this practice, based on both literature data and personal experience. Patients' acceptance and reactions were not recorded and are not part of the aims of this study. Patients were enrolled if aged ≥ 18 years old and treated with ETN for at least 6 months before the switch and with at least one follow-up clinical visit available, otherwise excluded. All enrolled patients signed an informed consent; the study was approved by the local IRB (CAEVC 15659) and conducted in accordance with the Declaration of Helsinki.

We created a dedicated Excel database to retrospectively collect data about the specific iRMD, age, gender, disease duration, previous and concomitant iRMD targeted treatments [bDMARDs (in particular whether ETN was the first bDMARD used in naïve patients or a second-line treatment in previous bDMARDs failure patients), csDMARDs (new initiation or increase in dosage or interruption), prescription and dose of CCS, prescription of cyclic NSAIDs], adverse events (AEs; local and systemic, serious and non-serious – with specific details regarding management of SB4 secondary to their occurrence) from date of switch to last available follow-up. Data about persistence on treatment (defined as continued prescription

or temporary interruption with plan for restart of SB4 treatment on latest available follow-up), reason for SB4 discontinuation and subsequent treatment protocols were also collected at last available follow-up assessment.

For each continuous variable, mean and standard deviation are reported, while for categorical variables absolute frequencies and percentage for each category are provided. We used logistic regression and Student *t* test to evaluate the change of categorical and continuous variables, respectively. The potential predictive factors for treatment discontinuation (such as iRMD, ETN/SB4 as first *versus* subsequent bDMARD treatment line, concomitant therapy with a csDMARD, gender, age, disease duration and previous ETN therapy duration) were also analysed at 6, 12 and 18 month follow-up. The association between survival and possible baseline categorical risk factor was evaluated using log-rank test and Kaplan–Meier curve. Furthermore, hazard ratio (HR) and its 95% confidence interval (CI) were estimated using Cox model regression, to quantify the risk over time. Still, logistic regression was used to test the global probability of treatment persistence at 6, 12 and 18 months.

Results

In two academic rheumatology divisions (Florence and Siena university hospitals), 220 patients (142 females, 64.5%, average age 58 ± 14 years, disease duration 14 ± 8 years) were enrolled. The patients included in the study had received ETN for an average duration of 7 ± 4 years, representing the first bDMARD treatment in 169 patients (76.8%), the second in 39 (17.7%), the third in seven (3.2%) and the fourth in five (2.3%) cases respectively. The study population was composed of 85 RA (38.6%), 81 PsA (36.8%), 33 axSpA (15.0%), 14 JIA (6.4%) and seven (3.2%) patients affected by other iRMDs (five systemic sclerosis, one synovitis, acne, pustulosis, hyperostosis and osteitis syndrome and one TNF receptor-associated periodic syndrome).

At baseline, patients received different regimens of concomitant medications: 33 patients (15.0%) were treated with cyclic NSAIDs, 32 (14.5%) with chronic CCS and 86 (39.1%) patients with csDMARDs. No statistically significant differences in terms of prevalence of concomitant medications were found at last available follow-up, although a trend for reduction of NSAIDs and

CCS use was observed (see Table 1). Follow-up data were available for all patients, with an average duration of 12 ± 4 months.

Safety

During the follow-up period, 50 patients (22.73%) presented at least one AE. Among these cases, four (two RA, two PsA) complained of local injection site reactions and 46 (18 RA, 17 PsA, eight axSpA, two JIA, two other) of non-severe systemic AEs; only one patient experienced both.

In detail, systemic AE were represented by different features of clinically defined disease flares (33 joint, two cutaneous and one ocular relapses) among 35/47 (74.5%) patients, with one patient experiencing both articular and cutaneous relapses. In this subgroup, four patients were treated with a brief CCS cycle, four were temporarily given NSAIDs and four were treated with a new concomitant csDMARD prescription; no increase in the dosage of a pre-existing csDMARD was recorded. These approaches led to the achievement of disease control (12/12, 100%). Among the other 23 patients, 13 cases were back-switched to ETN originator, six were switched/swapped to another bDMARD, one patient reduced the dosing interval (from once biweekly to once weekly) and one increased SB4 dosage from 25 mg weekly to 50 mg weekly; a wait-and-see approach was adopted for two patients.

The non-disease-flaring patients with AEs ($n=12$) experienced infections (four RA, two PsA, one axSpA) and constitutional symptoms, mainly fatigue or malaise (one RA, three PsA, two axSpA, one JIA), with two patients presenting both. In this subgroup, five patients were back-switched to ETN, five patients were switched/swapped to another bDMARD and one patient discontinued SB4 treatment while continuing with the csDMARD. One patient continued with SB4 treatment.

A summary flow-chart of patient outcome regarding SB4 treatment persistence/discontinuation and further details of the patients back-switched to ETN are showed in Figure 1 and Table 2, respectively.

Treatment persistence

During the first 6 months, SB4 treatment was stopped for safety issues in 2/212 patients (one RA and one PsA). From the sixth to the 12th

Table 1. Number of patients with ongoing concomitant medications at baseline and at last available follow-up.

	Baseline	Follow-up
Females, <i>n</i> (%)	142 (64.5)	N/A
Age, years, mean ± SD	58 ± 14	N/A
Disease duration, years, mean ± SD	14 ± 8	N/A
Duration of treatment with originator etanercept, years, mean ± SD	7 ± 4	N/A
Cyclic non-steroidal anti-inflammatory drugs, <i>n</i> (%)	33 (15.0%)	24 (10.9%)
Conventional synthetic DMARD, <i>n</i> (%)	86 (39.1%)	85 (38.6%)
Methotrexate, <i>n</i> (%)	50 (22.7%)	47 (21.5%)
Leflunomide, <i>n</i> (%)	14 (6.4%)	14 (6.4%)
Sulphasalazine, <i>n</i> (%)	11 (5.1%)	11 (5.1%)
Hydroxychloroquine, <i>n</i> (%)	16 (7.3%)	14 (6.4%)
Chronic CCS, <i>n</i> (%)	32 (14.5%)	22 (10.0%)
Prednisone equivalents, mg, in the chronic CCS patients, mean ± SD	2.5 ± 2.8	1.8 ± 2.9

CCS, corticosteroid; N/A, not applicable.

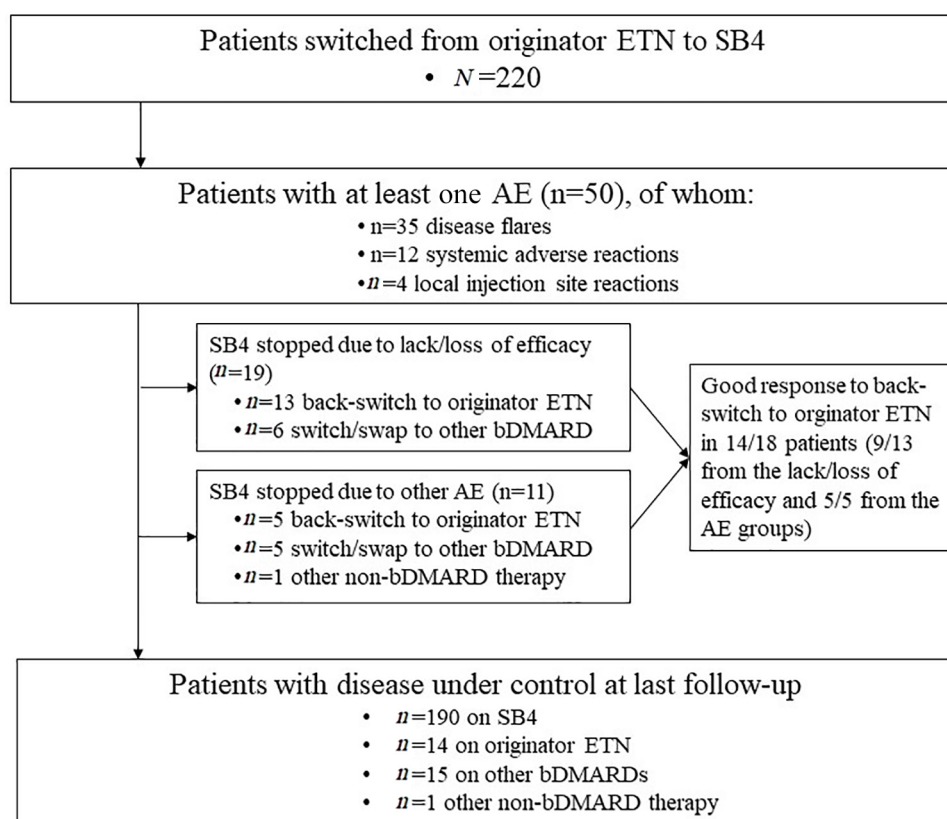


Figure 1. Flow-chart of treatment outcome in the study population. AE, adverse event; bDMARD, biologic disease modifying anti-rheumatic drug; ETN, etanercept.

Table 2. Characteristics of patients who interrupted SB4 and back-switched to originator etanercept and their clinical outcomes.

Gender	Disease	Switch age (years)	SB4 duration (months)	Reason for SB4 interruption	Management	Outcome (last follow-up available)
F	axSpA	65	11	Loss of efficacy	Back-switch plus sulphasalazine	Disease under control after 7 months of ETN plus sulphasalazine
F	RA	67	5	Injection site reaction	Back-switch	Disease under control after 7 months of ETN therapy
M	PsA	56	3	Loss of efficacy	Back-switch	8 months after back-switch, PsA was still not controlled. Successfully swapped to adalimumab biosimilar
F	RA	67	6	Loss of efficacy	Back-switch	Disease under control after 9 months of ETN therapy
F	RA	60	17	Loss of efficacy	Back-switch	Disease under control after 8 months of ETN therapy
F	RA	69	12	Loss of efficacy	Back-switch, then swap	6 months after back-switch, RA was still not controlled. Successfully swapped to abatacept
F	axSpA	65	16	Loss of efficacy	Back-switch, then swap	Adverse reaction to originator after back-switch, now disease under control with adalimumab biosimilar
F	PsA	59	2	Injection site reaction	Back-switch	Disease under control after 15 months of ETN therapy
F	RA	46	4	Lack of efficacy	Back-switch	Adverse reaction to originator after back-switch, now disease under control with adalimumab biosimilar
M	axSpA	62	11	Loss of efficacy	Back-switch	Disease under control after 9 months of ETN therapy
F	RA	69	3	Systemic AE	Back-switch	Disease under control after 15 months of ETN therapy
F	RA	70	4	Injection site reaction	Back-switch	Disease under control after 15 months of ETN therapy
F	PsA	65	4	Loss of efficacy	Back-switch	Disease under control after 12 months of ETN therapy
F	axSpA	45	2	Lack of efficacy	Back-switch	Disease under control after 20 months of ETN therapy
F	RA	60	1	Systemic AE	Back-switch	Disease under control after 20 months of ETN therapy
F	axSpA	61	6	Loss of efficacy	Back-switch	Disease under control after 13 months of ETN therapy
F	PsA	72	11	Loss of efficacy	Back-switch	Disease under control after 12 months of ETN therapy
F	PsA	65	10	Loss of efficacy	Back-switch	Disease under control after 11 months of ETN therapy

AE, adverse event; axSpA, axial spondylarthritis; ETN, etanercept originator; F, female; M, male; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

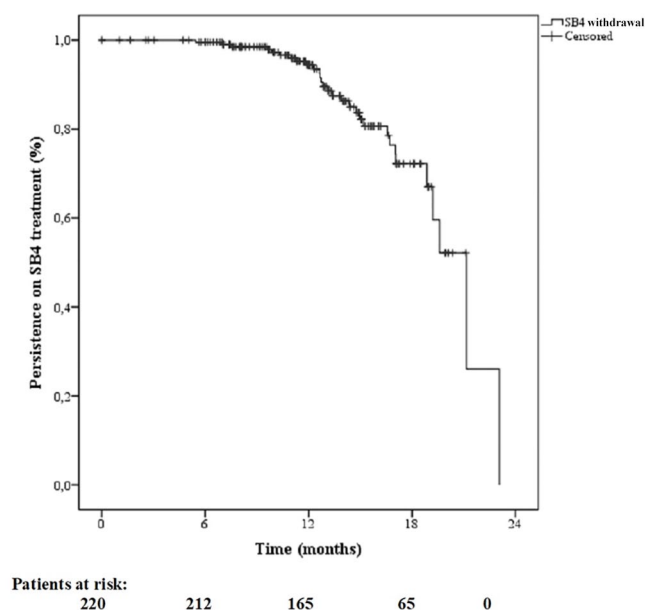


Figure 2. Survival curve of persistence on treatment with SB4.

month of follow-up, 15/165 patients (five RA, eight PsA, one axSpA, one JIA) interrupted SB4 treatment: among them, 10 stopped SB4 due to loss of efficacy and five for safety concerns. During the third semester (12th to 18th month), 12/65 patients discontinued SB4 treatment, four for safety issues (one PsA, one axSpA, one JIA and one other) and eight for loss of efficacy (two RA, four PsA, one axSpA and one JIA). After the 18 month follow-up visit, one patient stopped the treatment for loss of efficacy. Cumulatively, the probability of persistence on treatment at 6, 12 and 18 months was 99.1%, 88.6% and 64.6% respectively (Figure 2).

At 6 months, age was the only significant factor to predict discontinuation (HR 1.058, 95% CI 1.007–1.112, $p=0.026$), which was not confirmed at 12 and 18 months. All other analysed variables did not represent a predictive factor for treatment interruption (data not presented).

Discussion

Our clinical data show that patients with iRMD switching from the originator ETN to the biosimilar SB4 presented a high persistence on treatment at 6, 12 and 18 months. Loss of efficacy represented the most frequent reason for discontinuation while 22.3% of patients experienced AEs. Most frequently, these patients had disease flares, lower extent of infectious events or constitutional symptoms.

Our data are in line with the studies previously assessing SB4 treatment discontinuation after switching from ETN. In particular, the DANBIO registry included over 1600 RA, axSpA and PsA patients switching from ETN to SB4, showing an 82% crude persistence on treatment at one-year follow-up, compared with 88% in an ETN historic cohort and 70% in the non-switched population.¹⁸ Among the 299 (18.4%) SB4 discontinuations, the DANBIO registry found that these were due to lack of efficacy in 46% (137 patients – equivalent to 8.4% of the whole population) and 26% (77 patients – equivalent to 4.8% of the study population) to adverse events. From our cohort study, the 30 (13.6%) cases of SB4 withdrawal were due to loss of efficacy or AEs in 19 (60%) and 11 (40%) patients respectively. Similarly, the BIO-SPAN study reached discontinuation rates of 10% in ETN/SB4 switched patients at 6 months,²² while the cumulative persistence was around 75% at 12 months in a recent systematic review on 11053 ETN/SB4 switching patients.²³ When compared with those significantly larger populations, our patients showed a higher treatment persistence at 6- and 12-month evaluations and first results at 18 months, despite the fact that a direct comparison cannot be made.

Similarly, our rate of adverse events was comparable to the data available in the literature. In fact, data from the registrative trials found at least one treatment-related emerging AE in 48.7% of RA ETN/SB4 switched patients, mostly upper respiratory tract infections (7.9%). Furthermore, no ETN/SB4 switched patients reported injection site reactions.¹² In a Romanian national cohort study, Codreanu *et al.* showed that 12/119 ETN/SB4 switching RA patients developed AEs at 6 month follow up.²⁴ Finally, a recent systematic review also addressed the issue of safety and found an incidence of AE around 34.2% in psoriatic ETN/SB4 patients, with 17.1% being infectious events. Comparable results were also reported by Ebberts *et al.*²³ When considering AEs in detail, still the DANBIO registry reports that, in particular, a prevalence of joint disease flares after 3 months from switching ranged from 5% to 24% of patients, according to different disease specific definitions.¹⁷ These data regarding disease flares are in line with our population, in which any extent of clinically defined disease flare (including joint, but also cutaneous, ocular and intestinal) was recorded in 35 (15.9%) over a longer

follow-up, based on both physician and patient evaluation.

Interesting results were also seen for the sub-population that was back-switched to ETN. In fact, 14/18 back-switched patients (5/5 due to AEs and 9/13 due to lack or loss of efficacy) returned to a clinically stable disease control which was present at baseline, before the switch. In contrast to Scherlinger *et al.*,²⁵ our population did not present cases of isolated, patient-reported but physician non-detectable disease flares and a high prevalence of return to disease control was reached. Despite the difference in the route of administration (intravenous infliximab for Scherlinger *et al.* versus subcutaneous ETN for our population), we think that the experience derived from previous switching to biosimilars for other intravenous and subcutaneous bDMARDs might have increased physician perception of switch feasibility^{26,27} and, therefore, determined better informed, data- and real-life driven confident information at the time of switch proposal to each patient.

Our real-life study has some strengths, such as the medium-large sample size including different rheumatologic conditions and the considerable follow-up duration. On the other side, our study presents relevant limitations: first of all the lack of standardized efficacy assessments, such as patient-reported outcomes (including acceptance rates²⁸) and activity indexes, may limit the robustness of our data; as we were aware of this, we did not perform any efficacy analysis and solely reported the status of our population after switching in terms of treatment persistence and safety. Similarly, standardized definition of disease flares was not pre-set when starting this retrospective observational data collecting: this was arbitrarily decided in order to reduce the number of non-eligible patients due to lack of data at baseline and follow-up and to increase the inclusiveness of our population, making our results more representative of a real-life scenario than a clinical research protocol. Finally, dosages of concomitant DMARDs, serological status, immunogenicity and radiological progression data were also not recorded. These, together with the observational retrospective nature of the study, are indeed limitations of our study.

In conclusion, our retrospective real-life results confirmed the safety profile derived from randomized trials and from other prospective and retrospective cohorts, in particular regarding disease

flares and related discontinuation rates. Likely, the most interesting result was the overall good persistence on treatment observed in our patients undergoing medical and non-medical switching from ETN to SB4 for the treatment of iRMD beyond the first year.

Author contributions

All authors contributed to the study conception, design, results interpretation. Material preparation, data collection and analysis were performed by CB, SG, GP, MC, LT. The first draft of the manuscript was written by GP and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of interest statement

LuC reports advisory board honoraria with Biogen. MMC reports speaker's and advisory board honoraria from Biogen Italia. All other authors declare no conflict of interest with the scientific content of the manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Cosimo Bruni  <https://orcid.org/0000-0003-2813-2083>

References

1. Smolen JS, Landewé RBM, Bijlsma JWJ, *et al.* EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*. Epub ahead of print 22 January 2020. DOI: 10.1136/annrheumdis-2019-216655.
2. Gossec L, Smolen JS, Ramiro S, *et al.* European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis* 2016; 75: 499–510.
3. Ward MM, Deodhar A, Gensler LS, *et al.* 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis research and treatment network recommendations for the treatment of Ankylosing Spondylitis and nonradiographic axial Spondyloarthritis. *Arthritis Rheumatol* 2019; 71: 1599–1613.

4. Monaco C, Nanchahal J, Taylor P, *et al.* Anti-TNF therapy: past, present and future. *Int Immunol* 2015; 27: 55–62.
5. European Medicines Agency. Enbrel, summary of product characteristics, www.ema.europa.eu/en/documents/product-information/enbrel-epar-product-information_en.pdf (2019, accessed 12 March 2020).
6. Weise M, Bielsky MC, De Smet K, *et al.* Biosimilars-why terminology matters. *Nat Biotechnol* 2011; 29: 690–693.
7. European Medicines Agency. Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues, www.ema.europa.eu/en/documents/scientific-guideline/guideline-similar-biological-medicinal-products-containing-biotechnology-derived-proteins-active_en-2.pdf (2020, accessed 12 March 2020).
8. European Medicines Agency. Benepali, summary of product characteristics, https://www.ema.europa.eu/en/documents/product-information/benepali-epar-product-information_en.pdf (2020, accessed 12 March 2020).
9. Lee YJ, Shin D, Kim Y, *et al.* A randomized phase I pharmacokinetic study comparing SB4 and etanercept reference product (Enbrel®) in healthy subjects. *Br J Clin Pharmacol* 2016; 82: 64–73.
10. Emery P, Vencovský J, Sylwestrzak A, *et al.* A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy. *Ann Rheum Dis* 2017; 76: 51–57.
11. Emery P, Vencovský J, Sylwestrzak A, *et al.* 52-week results of the phase 3 randomized study comparing SB4 with reference etanercept in patients with active rheumatoid arthritis. *Rheumatology (Oxford)* 2017; 56: 2093–2101.
12. Emery P, Vencovský J, Sylwestrzak A, *et al.* Long-term efficacy and safety in patients with rheumatoid arthritis continuing on SB4 or switching from reference etanercept to SB4. *Ann Rheum Dis*. Epub ahead of print 9 August 2017. DOI: 10.1136/annrheumdis-2017-211591.
13. Girolomoni G, Feldman SR, Emery P, *et al.* Comparison of injection-site reactions between the etanercept biosimilar SB4 and the reference etanercept in patients with rheumatoid arthritis from a phase III study. *Br J Dermatol* 2018; 178: e215–e216.
14. Yazdany J. Failure to launch: biosimilar sales continue to fall flat in the United States. *Arthritis Rheumatol* 2020; 72: 870–873.
15. Benucci M and Cantini F. Non-medical switching: save today and pay tomorrow. *J Med Econ* 2019; 22: 1160–1161.
16. Weeda ER, Nguyen E, Martin S, *et al.* The impact of non-medical switching among ambulatory patients: an updated systematic literature review. *J Mark Access Health Policy* 2019; 7: 1678563.
17. Salam T, Duhig A, Patel AA, *et al.* Physicians' perspectives regarding non-medical switching of prescription medications: results of an internet e-survey. *PLoS One* 2020; 15: e0225867.
18. Glintborg B, Loft AG, Omerovic E, *et al.* To switch or not to switch: results of a nationwide guideline of mandatory switching from originator to biosimilar etanercept. One-year treatment outcomes in 2061 patients with inflammatory arthritis from the DANBIO registry. *Ann Rheum Dis* 2019; 78: 192–200.
19. Bonifati C, De Felice C, Lora V, *et al.* Effectiveness of etanercept biosimilar SB4 in maintaining low disease activity in patients with psoriatic arthritis switched from etanercept originator: an open-label one-year study. *J Dermatolog Treat*. Epub ahead of print 15 April 2019. DOI: 10.1080/09546634.2019.1606886.
20. Pescitelli L, Lazzeri L, Di Cesare A, *et al.* Clinical experience with the etanercept biosimilar SB4 in psoriatic patients. *Int J Clin Pharm* 2019; 41: 9–12.
21. Giunta A, Manfreda V, Esposito M, *et al.* Etanercept biosimilar SB4 in the treatment of plaque-type psoriasis and psoriatic arthritis: a single-centre, observational, retrospective, real-life study. *Br J Dermatol* 2019; 181: 1078–1079.
22. Tweehuysen L, Huiskes VJB, van den Bemt BJB, *et al.* Open-label, non-mandatory transitioning from originator etanercept to biosimilar SB4: six-month results from a controlled cohort study. *Arthritis Rheumatol* 2018; 70: 1408–1418.
23. Ebberts HC, Pieper B, Issa A, *et al.* Real-world evidence on etanercept biosimilar SB4 in etanercept-naïve or switching patients: a systematic review. *Rheumatol Ther* 2019; 6: 317–338.
24. Codreanu C, Popescu CC, Mogoşan C, *et al.* Efficacy and safety of original and biosimilar etanercept (SB4) in active rheumatoid arthritis - a comparison in a real-world national cohort. *Biologicals* 2019; 62: 27–32.
25. Scherlinger M, Germain V, Labadie C, *et al.* Switching from originator infliximab to biosimilar CT-P13 in real-life: the weight of patient acceptance. *Joint Bone Spine* 2018; 85: 561–567.

26. Bruni C, Bitti R, Nacci F, *et al.* Efficacy and safety of switching from reference adalimumab to SB5 in a real-life cohort of inflammatory rheumatic joint diseases. *Clin Rheumatol*. Epub ahead of print 8 June 2020. DOI: 10.1007/s10067-020-05199-w.
27. Gentileschi S, Barreca C, Bellisai F, *et al.* Switch from infliximab to infliximab biosimilar: efficacy and safety in a cohort of patients with different rheumatic diseases; response to: Nikiphorou E, Kautiainen H, Hannonen P, *et al.* Clinical effectiveness of CT-P13 (Infliximab biosimilar) used as a switch from Remicade (infliximab) in patients with established rheumatic disease. Report of clinical experience based on prospective observational data. *Expert Opin Biol Ther*. 2015;15:1677–1683. *Expert Opin Biol Ther* 2016; 1: 1311–1312.
28. Scherlinger M, Langlois E, Germain V, *et al.* Acceptance rate and sociological factors involved in the switch from originator to biosimilar etanercept (SB4). *Semin Arthritis Rheum* 2019; 48: 927–932.

Visit SAGE journals online
[journals.sagepub.com/
home/tab](https://journals.sagepub.com/home/tab)

 SAGE journals