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Real-world outcomes following switching from anti-TNF reference products to biosimilars for the treatment of psoriasis

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ABSTRACT

Tumor necrosis factor (TNF) inhibitors improved clinical outcomes for patients with psoriasis but are limited by their high cost. There are several biosimilar options approved for the treatment of psoriasis which provides a lower-cost alternative and the potential to increase treatment availability for both biologically naïve and bioexperienced patients. Numerous phase III randomized controlled trials (RCTs) have investigated the effects of switching from biologics to biosimilars; biosimilars had comparable safety and efficacy to their reference products. Real-world evidence may provide complementary information on the expected performance of biosimilars. In this literature review, we analyzed data from real-world studies on switching from biologics for psoriasis to their biosimilars. Effectiveness and safety profiles were comparable when switching from biologics to biosimilars of adalimumab, etanercept, and infliximab. These studies are limited by their sample sizes, duration of follow-up, and single-arm designs without control groups. Based on available real-world evidence, patients may safely and effectively undergo switching to biosimilar therapies for the treatment of psoriasis.

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Psoriasis; TNF-inhibitor; biosimilar; biological agents

Introduction

Biologic medications, including monoclonal antibodies and receptor fusion proteins targeting tumor necrosis factor (TNF), have dramatically improved clinical outcomes for patients with psoriasis (1). Current FDA-approved anti-TNF alpha agents for the treatment of psoriasis include adalimumab, etanercept, infliximab, and certolizumab (2). Despite being more effective than oral retinoids or methotrexate for the treatment of psoriasis, biologics are limited in clinical practice by their cost. Biosimilars have the potential to offer a lower-cost, yet equally effective alternative (3).

Biosimilars are biologic medical products that are highly similar to their reference products without clinically meaningful differences in safety or effectiveness (4). As a result of the large molecular size and complexity of biological therapies, variability exists between each batch of biologics, both for reference products and biosimilars. While biosimilars are not exact duplicates of reference products, different batches of the reference product are also not exact matches of previous batches (5). The development and approval of biosimilars require rigorous standards of quality, safety, and efficacy. However, in comparison to the approval process for biologics, the approval for biosimilars places greater emphasis on pre-clinical physicochemical and functional characterization at the earlier stages of development and less on clinical trials (6). These equivalence studies typically require smaller sample sizes than those for studies on the approval of novel biologics and do not need to be repeated for every indication of the reference product leading to a reduced cost of development (7).

As of September 2022, there are currently 13 biosimilar versions of TNF inhibitors approved in the United States for use in patients with psoriasis: six adalimumab (Amjevita, Cytezlo, Hadlima, Hyrimoz, Abrilada, Hulio, and Yusimry), two etanercept (Erelzi, Eticovo) and four infliximab (Inflectra, Renflexis, Ixifi, and Avsola) (Table 1) (2).

Switching refers to medication changes with the same therapeutic intent. Switching can refer to a change between two different biologic therapies, a change between a reference product and its biosimilar version, or between biosimilars of the same reference product. Non-medical switching is initiated for non-medical concerns including economic incentives or treatment availability (8). Since biosimilars were first approved, multiple phase III randomized controlled trials (RCTs) have evaluated outcomes after switching from reference products to biosimilars in the treatment of psoriasis, and biosimilars had similar safety and efficacy (9–12). Real-world data following switching to biosimilars in patients with psoriasis complement data from clinical trials. The purpose of this study is to assess whether biosimilars perform similarly to reference products based on real-world studies on switching from biologics to their respective biosimilars for the treatment of psoriasis.

Methods

A PubMed and Google Scholar search included the key words *switching between biosimilars in psoriasis, anti-TNF inhibitor*

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Table 1. FDA-approved biosimilars for psoriasis.

Reference product	Biosimilar	Suffix	Proprietary name
Adalimumab (Humira)	ABP 501	-atto	Amjevita
	BI 695501	-abdm	Cyltezo
	SB5	-bwwd	Hadlima
	GP2017	-adaz	Hyrimoz
	PF-06410293	-afzb	Abrilada
	FKB327	-fkjp	Hulio
	CHS-1420	-aqvh	Yusimry
Etanercept (Enbrel)	GP2015	-szzs	Erelzi
	SB4	-ykro	Eticovo
Infliximab (Remicade)	CT-P13	-dyyb	Inflectra
	SB2	-abda	Renflexis
	GP1111	-qbtx	Ixifi
	ABP 710	-axxq	Avsola

biosimilars in psoriasis, switching from adalimumab originator to biosimilar in psoriasis, switching from etanercept originator to biosimilar in psoriasis, switching from infliximab originator to biosimilar in psoriasis, adalimumab biosimilar, etanercept biosimilar, and *infliximab biosimilar.*

Articles were considered if they included effectiveness or safety data related to a switch from a reference therapy to a biosimilar. Articles were limited to studies with full text available in the English language and those discussing observational studies with real-world evidence. Results included five articles on adalimumab biosimilars, six articles on etanercept biosimilars, and seven articles on infliximab biosimilars which were prescreened by reviewing the abstracts. Additional articles were identified by reviewing reference lists in the key articles.

Results

Adalimumab

Five observational studies were identified examining effectiveness and safety following a single switch from adalimumab originator to biosimilar medication in patients with psoriasis (Table 2).

In a retrospective single-center study of 43 patients with psoriasis who switched from adalimumab to GP2017, no difference was seen in the mean overall Psoriasis Area and Severity Index (PASI) score ($p = .42$) or Dermatology Life Quality Index (DLQI) score ($p = .16$) from prior (13). There was an increase in adverse effects (AEs) from 0% to 39.5% ($n = 17$) after switching, although it is unclear if AEs were assessed in a consistent manner before and after the switch. The most frequently reported AEs were pruritus, flares, and headache. AEs were not correlated to patient-reported effectiveness of treatment or change in PASI or DLQI scores.

In a retrospective single-center study of 46 patients with psoriasis and psoriatic arthritis who underwent non-medical switching from adalimumab to ABP 501, there was no significant difference in mean PASI or Disease Activity Score in 28 joints (DAS28) seen after the switch through 6 months follow-up ($p > .05$) (14). This study also included 48 originator-naïve patients who initiated therapy with the biosimilar. Among these adalimumab-naïve patients, mean PASI improved significantly from 10.66 at baseline to 1.80 at 6 months ($p < .0001$) in both patients with psoriasis and psoriatic arthritis. Mean DAS28 improved as well from 3.95 to 2.5 but not to a significant degree ($p > .05$). There were no reported AEs in the group who underwent switching. Five originator-naïve patients (5.32%) experienced mild AEs, four with injection-site reactions, and one with an upper respiratory tract infection requiring antibiotic therapy.

In a 6-month prospective single-center study of 73 patients with psoriasis switched from adalimumab to an unnamed biosimilar, no difference in PASI score was seen between the time of the switch to follow up at 3–6 months ($p > .05$) (15). Articular symptoms were also evaluated using the Visual Analog pain Scale for joint pain (VAS). There was no difference in VAS following the switch to biosimilar medication, including after stratification by a concurrent diagnosis of psoriatic arthritis (PsA) or baseline joint pain. However, when stratifying by Body Mass Index (BMI), VAS at 3-month follow-up was higher in patients with BMI >25 following the switch ($p = .04$) without a change in PASI. AEs were only recorded following the switch and were noted to occur in 10% of patients. These included candida cheilitis, asthmatic-like symptoms, asthenia after injection, gastrointestinal symptoms, and injection site reactions.

In a small single-center study with 20 patients who underwent non-medical switching from adalimumab to SB5, there was no change in mean PASI following the switch to a biosimilar (16). Among the five patients enrolled with axial PsA, there was an increase in Bath Ankylosing Spondylitis Disease Activity Index (BADSI) after the switch, suggesting a possible loss of response to therapy in patients with axial disease. As there was no control group maintained on the reference product, the study was not informative of whether a similar loss of response would have occurred without the switch.

One study evaluated 348 patients in a Danish Dermatology (DERMBIO) registry with moderate to severe psoriasis who switched from adalimumab to either GP2017 or SB5 (17). This study included a comparator cohort of 378 patients who remained on the reference product. Effectiveness was evaluated using PASI, DLQI, and 1-year drug retention. This study corroborated the findings of the three single-center studies, concluding that the switch and control cohorts had similar effectiveness. More AEs occurred following the switch compared to the control cohort (9.1% vs 5.0%, $p = .04$), the most common being infection.

Overall, there was similar effectiveness for the control of cutaneous disease following the switch from adalimumab to biosimilar therapy in patients with psoriasis. Among the three studies evaluating articular disease, two found no loss of disease control following the switch to a biosimilar; the third study found a possible loss of response in patients with the axial disease however the sample size of this cohort was small ($n = 5$). There was an increased rate of mild AEs following the switch in two of the five studies, although only one of these included a control cohort.

Etanercept

Six observational studies were identified that evaluated clinical outcomes following a switch from an etanercept to a biosimilar or between biosimilars in patients with psoriasis (Table 2).

In a retrospective, single-center study of 32 patients with psoriasis and PsA switched from etanercept to SB4, there was no loss of effectiveness or difference in safety when followed for up to 6 months after the switch (18). In this study, effectiveness was evaluated by rates of clinical remission, defined as both PASI and/or DAS28 increase <10%). By these criteria, 92% of patients achieved remission of cutaneous symptoms, and PASI improved from $2.2 + 1.9$ to $1.2 + 1.2$ ($p < .001$) following

Table 2. Published real-world studies on switching to approved anti-TNF biosimilars for the treatment of psoriasis.

Study	Switch	Design	N patients	Follow-up	Effectiveness	Safety	Conclusions
Adalimumab RP							
Nielsen et al. (13)	Adalimumab to GP2017	Retrospective, single center, single arm	43	NR	The overall mean score in PASI and DLQI increased with 0.21 points (CI: −0.32 to 0.76; p = .42) and 1.09 points (CI: −0.46 to 2.63; p = .16).	The fraction of patients with AEs increased from 0% to 39.5% after switching, most commonly pruritus, flares and headache.	Switch was not associated with a change in PsO disease severity or quality of life, but did show increased rate of AEs.
Giunta et al. (14)	Adalimumab to ABP 501	Retrospective, single center, single switch	46 patients switched from originator 48 adalimumab-naïve patients	6 months	No difference in mean PASI or DAS28 seen following switch. Mean PASI improved from 10.66 at baseline to 1.80 at 6 months (p < .0001) and mean DAS28 improved from 3.95 to 2.5 (p > 0.05) in adalimumab-naïve patients.	No AEs after switch. Five adalimumab-naïve patients experienced mild AEs (4 injection-site reactions, 1 upper respiratory tract injection).	No loss of effectiveness or increase in safety concerns following switch for treatment of PsO or PsA. Treatment with ABP 501 in originator-naïve patients is effective and safe.
Gallo et al. (15)	Adalimumab to unnamed biosimilar	Prospective, single center, single switch	73	6 months	No difference in PASI or VAS between time of switch and 3- or 6-month follow up (p > .05). VAS at 3 months from the switch was higher compared to the switch in subgroup of patients with BMI > 25 (p = .04) without change in PASI.	9.6% of patients experienced mild AEs after switch (recurrent candida cheilitis, asthmatic-like symptoms, asthenia after injection, gastrointestinal symptoms, injection site reaction).	Switch was not associated with a change in effectiveness or safety but with trend toward increased AEs.
Di Cesare et al. (16)	Adalimumab to SB5	Single center, single switch	20	6 months	No relevant change in PASI score in 90% of patients; two patients demonstrated loss of effect LOE for cutaneous symptoms. Among the five patients with axial PsA, there was an increase in BADSI score from 1.1 ± 1.23 (0–2.9) to 3.66 ± 3.68 (0–7.6) after switch.	No safety issues were addressed.	Switch to B5 is well tolerated, safe and effective in the treatment of PsO and PsA although with trend toward progressive loss of response in patients with axial disease.
Loft et al. (17)	Adalimumab to GP2017 or SB5	Prospective, DERMBIO registry, single switch with comparator cohort of patients continued on originator	348 patients switched from originator 378 patients continued on adalimumab	12 mo	One-year drug retention rates were 92.0% (95% CI, 89.0–94.9%) for the adalimumab biosimilar cohort and 92.1% (95% CI, 89.4–94.8%) for the adalimumab originator cohort. Mean change in PASI and DLQI after switch was 0.0 (−0.3 to 0.2; p = .63) and 0.0 (−1.0 to 0.0; p = .75).	More AEs were seen in the biosimilar cohort compared to originator cohort (9.1% vs 5.0%, p = .04), the most common being infection.	Similar effectiveness between cohorts, but with increased rate of AEs after switch.
Etanercept RP							
Pescitelli et al. (18)	Etanercept to SB4	Retrospective, single center, single switch	32	6 months	Clinical remission (defined as both PASI and/or DAS28 increase < 10%) of 92% and 64% for PsO and PsA respectively in	No serious AEs; injection site-reaction to SB4 was observed in four patients after switch.	No change in effectiveness for treatment of cutaneous symptoms or AEs after switch, but

(*continued*)

Table 2. Continued.

Adalimumab RP

Study	Switch	Design	N patients	Follow-up	Effectiveness	Safety	Conclusions
					patients after switch. No significant differences in DAS28 after switch, whereas PASI improved significantly ($p < .001$).		with mild decrease in effectiveness for treatment of articular symptoms.
Lund et al. (19)	Etanercept to SB4	Retrospective, single center, single switch	24	NR	52.4% of PASI and 69.2% DLQI scores were the same or improved after switch. The rate of congruence between the self-reported measured change was 69.2%.	The fraction of patients with AEs increased after switch from 0% to 16.7% (fatigue, gastrointestinal complaints and pruritus).	40% of patients reported a worse effect after switch, although the absolute mean change in PASI score was small and not different among patients who reported the same/ better effect compared to those reporting a worse effect.
Giunta et al. (20)	Etanercept to SB4	Retrospective, single center, single switch with comparator cohort of etanercept-naïve patients	10 patients switched from originator 30 etanercept-naïve patients	6 months	PASI scores improved from 6.45 to 1.22 ($p < .001$) and DAS28 score improved from 5.45 to 3.27 ($p < .001$). No change in PASI or DAS28 between patients switched from etanercept to SB4 and etanercept naïve patients.	No serious AEs were observed or reported.	No change in effectiveness or AEs in patients switched compared to originator-naïve patients on biosimilar.
Egeberg et al. (21)	Etanercept to SB4	Prospective, DERMBIO registry, single switch with comparator cohort of patients continued on originator	55 patients switched from originator 566 patients continued on etanercept	6 months	No difference in treatment discontinuation between patients who continued etanercept and those who switched from etanercept to SB4 (crude HR 0.46, 95% CI: 0.11–1.98; $p = .3$).	Incidence of AEs was not higher for biosimilars than originators.	Switch had no impact on drug survival or increased AEs.
Gisondi et al. (22)	Etanercept to SB4	Psobiosimilars Registry, single switch with comparator cohort of etanercept-naïve patients	158 patients switched from originator 39 etanercept-naïve patients	6 months	Mean PASI was unchanged in the switch group from 3.1 ± 3.3 at baseline to 1.8 ± 1.9 at month 6 ($p > .05$). Mean PASI was reduced in the naïve group from 12.5 ± 6.2 at baseline to 6.7 ± 2.2 at month 6 ($p = .03$).	No difference in AEs between switch and naïve groups.	Patients with chronic plaque psoriasis who responded to etanercept and switched to SB4 did not experience a meaningful change in effectiveness or safety.
Piaserico et al. (23)	Etanercept to SB4 to GP2015	Prospective, multi-center, cross switch	76	12 months	Median PASI remained stable, from 1 (0–2) after 3 months to 0.5 (0–1) after 12 months.	No treatment emergent serious AEs were reported. After the cross-switch from SB4 to GP2015, two patients developed a flare-up of symptoms.	Switching between two etanercept biosimilars (from SB4 to GP2015) is both safe and effective.

(*continued*)

Table 2. Continued.

Study	Switch	Design	N patients	Follow-up	Effectiveness	Safety	Conclusions
Adalimumab RP							
Infliximab RP							
Lund et al. (19)	Infliximab to CT-P13	Retrospective, single center, single switch	45	NR	74.4% of PASI and 69.0% DLQI score were the same or improved after switch. The rate of congruence between the self-reported measured change was 66.7%.	The fraction of patients with AEs increased after switch 6.7% to 22.2% (fatigue, gastrointestinal complaints and pruritus).	25% of patients reported a worse effect after switch, although the absolute mean change in PASI score was small and not different among patients who reported the same/ better effect compared to those reporting a worse effect.
Dapavo et al. (24)	Infliximab to CT-P13	Prospective, single center, single switch with comparator cohort of infliximab-naïve patients	30 patients switched from originator 5 infliximab-naïve patients	33 weeks	PASI and VAS scores were not different after switch ($p > .05$). 4/5 infliximab-naïve achieved 75% improvement or better from baseline PASI to week 10.	No additional AEs reported after switch.	Patients with psoriasis and a long-lasting response to the infliximab originator can be switched to the infliximab biosimilar without experiencing a significant change in clinical response or additional AEs.
Ricceri et al. (25)	Infliximab to CT-P13	Prospective, single center, single switch	22	10 months	Rates of clinical remission (defined as both PASI and/or Ritchie index not increasing by $>$ 10%) of 86% and 77% for patients with PsO and PsA, respectively.	No change in AEs after switch.	Switching from the originator to biosimilar in patients with PsO has similar safety and effectiveness for control of cutaneous symptoms but with mild decrease in effectiveness for control of articular symptoms.
Egeberg et al. (21)	Infliximab to CT-P13	Prospective, DERMBIO registry, single switch with comparator cohort of patients continued on originator	90 patients switched to CT-P13 266 patients continued on infliximab	24 months	No difference in treatment discontinuation between patients who continued infliximab and those who switched from infliximab to CT-P13 (crude HR 1.64, 95% CI: 0.69–3.89; $p = .3$).	Incidence of AEs was not higher for biosimilars than originators.	Switching from originator to biosimilar infliximab had no impact on drug survival.
Gisondi et al. (26)	Infliximab to CT-P13	Psobiosimilars registry, single switch with comparator cohort of infliximab-naïve patients	122 patients switched from originator 82 Infliximab-naïve patients	6 mo	PASI score remained unchanged in the switch group (2.05 ± 2.8 vs. 2.2 ± 3.2; $p = .3$). PASI score was reduced in the naïve group from baseline 20.8 ± 12.1 to 6-month 7.2 ± 7.1 ($p = .001$).	No difference in number of AEs between switch and naïve groups.	Patients with chronic plaque PsO who respond to the infliximab originator can be switched to the biosimilar CT-P13 without experiencing a significant change in

(*continued*)

Table 2. Continued.

Adalimumab RP							
Study	Switch	Design	N patients	Follow-up	Effectiveness	Safety	Conclusions
							clinical response or additional AEs.
Gisondi et al. (27)	CT-P13 to SB2	Prospective, single center, single switch	96	6 months	PASI remained stable at time of switch to 2, 4, and 6 month follow ups (0.9 ± 2; 0.9 ± 1.6; 1.1 ± 2.2; 0.7 ± 1.1).	Acute infusion reactions ($n = 3$), upper respiratory infections ($n = 6$) and herpes zoster infection ($n = 1$) were reported.	The switch from CT-P13 to SB2 was not associated with a change in disease severity although did show treatment withdrawal 10% of patients because of loss of response ($n = 7$) or acute infusion reactions ($n = 3$).

PsO: psoriasis; PsA: psoriatic arthritis; AEs: adverse events; LOE: loss of effect; BMI: body mass index; PASI: Psoriasis Area and Severity Index; DLQI: Dermatology Life Quality Index; VAS: Visual Analog pain Scale for joint pain; BADSI: Bath Ankylosing Spondylitis Disease Activity Index; DAS28: Disease Activity Score in 28 joints.

the switch. Treatment of articular symptoms was less efficacious than cutaneous, with 64% of patients achieving remission of articular symptoms although there was no significant change in DAS following the switch.

Another retrospective, single-center study of 24 patients who underwent a switch from etanercept to SB4 evaluated mean PASI and DLQI compared to patient-reported outcomes (19). After switching to the biosimilar, 40% of patients reported a worse effect, and 30% reported a worse quality of life. However, the absolute mean change in both PASI and DLQI was small and not different among patients who reported the same or a better effect compared to patients reporting a worse effect after switching. The authors determined the congruence between self-reported and measured PASI to be 69.2%, suggesting that patients subjectively tended to favor the reference product over the biosimilar. The fraction of patients with self-reported mild AEs increased after the switch from 0% to 16.7%, with complaints of fatigue, gastrointestinal issues, and pruritus.

In a retrospective, single-center study of 40 patients treated with SB4 for 24 weeks, PASI scores improved from 6.5 to 1.2 ($p < .001$), while DAS28 scores improved from 5.4 to 3.3 ($p < .001$) (20). Of the 40 patients, 10 were previously treated with etanercept and subsequently switched to the biosimilar. There was no significant difference in improvement in either PASI or DAS28 between the patients who switched to SB4 and the etanercept-naïve patients. No serious AEs were observed or reported.

In a prospective study evaluating drug survival for 6 months among patients enrolled in the DERMBIO registry, rates of treatment discontinuation were similar between 55 patients who switched to SB4 and 566 patients who continued on etanercept reference product (crude HR 0.46, 95% CI: 0.11–1.98; $p = .3$) (21). There was also no difference in the rate of AEs.

In a study of patients enrolled in the Italian Psobiosimilars registry, 158 patients who switched from etanercept to SB4 had similar effectiveness and safety compared to pre-switch (22). Mean PASI was unchanged following the switch with up to 6 months of follow-up ($p > .05$). This study further evaluated a cohort of 39 etanercept-naïve patients started on SB4, among which mean PASI improved from 12.5 ± 6.2 at baseline to 6.7 ± 2.2 at 6 months ($p = .03$). A limited number of AEs were seen following initiation of treatment of the biosimilar without a difference between the switch and naïve groups.

One study evaluated patients who underwent a cross-switch between different etanercept biosimilars following an initial switch from the etanercept reference product (23). In this prospective, multicenter study of 76 patients with psoriasis, switching from etanercept to SB4 and then to GP2015 was both safe and effective, with stable PASI scores up to 12 months following the switch between biosimilars therapies and without additional AEs.

Overall, effectiveness for the treatment of cutaneous and articular disease was comparable following the switch from etanercept to biosimilar therapy or between etanercept biosimilars in patients with psoriasis. In one study AEs were more common following the switch; however, there was no control cohort that continued on the reference product to compare. Furthermore, AEs were patient-reported and subject to bias from a lack of blinding.

Infliximab

Six observational studies and one case report were identified that evaluated clinical outcomes following a switch from

infliximab to a biosimilar or between biosimilars in patients with psoriasis (Table 2).

In a retrospective, single-center study of 45 patients switched to CT-P13, 75% of patients reported the same or improved control of cutaneous symptoms following the switch (19). The absolute mean change in both PASI and DLQI following the switch from infliximab was small and not different among patients who reported stable or better versus worse effects. The rate of congruence between the self-reported measured change was 66.7% indicating that patients inherently preferred the reference product over the biosimilar drug. The rate of mild AEs increased after the switch from 6.7% to 22.2%.

In a prospective, single-center study of 30 patients switched to CT-P13 compared to a control arm 5 infliximab-naïve patients, both effectiveness and safety were unchanged following the switch with up to 33 weeks of follow-up (24). In addition to evaluating cutaneous disease with PASI scores, this study also analyzed articular symptoms with VAS scores. Both PASI and VAS were not different after switching from reference product to biosimilar ($p > .05$). Among the infliximab-naïve patients, 80% of patients achieved 75% improvement or better from baseline to week 10. No additional AEs were reported following the switch to CT-P13.

In a prospective single-center study of 22 patients switched to CT-P13, 86% of patients achieved clinical remission of cutaneous disease (defined as PASI not increasing by >10%) over a follow-up of 10 months. Furthermore, PASI remained stable following the switch (25). The treatment effectiveness of articular symptoms in patients with previously diagnosed PsA was also assessed using the Ritchie scale and was stable following the switch to the biosimilar. However, the rates of clinical remission of PsA were lower (defined as Ritchie not increasing by >10%), with 77% of patients achieving remission of joint disease. The incidence of mild AEs prior to and after the switch did not differ.

In a registry study evaluating rates of treatment discontinuation by 6 months, there was no difference in rates of discontinuation between 90 patients from the DERMBIO registry switched from infliximab to biosimilar CT-P13 compared to 266 patients continued on infliximab (crude HR 1.64, 95% CI: 0.69–3.89; $p = .3$) (21). There was also no difference in AEs among patients switched to the biosimilar.

In an additional registry study of 122 patients switched to CT-P13 compared to 82 infliximab-naïve patients, there was no change in treatment effectiveness following the switch, with stable PASI score in the switch group (2.0 ± 2.8 vs. 2.2 ± 3.2; $p = .3$) (26). In the comparator cohort of infliximab-naïve patients, PASI improved from baseline (20.8 ± 12.1 to 6 months 7.2 ± 7.1; $p = .001$) with 80% of patients achieving PASI 75 by 6 months. A total of 16 AEs were observed, including infusion reactions and viral infections, without any difference between switch and naïve groups.

One prospective single-center study examined a cross-switch between different infliximab biosimilars in 96 patients previously treated with the reference product. In this study, there was no change in effectiveness following the switch, with stable PASI at 2-, 4-, and 6-month follow-ups (no value of significance provided) (27). Treatment withdrawal occurred in 10% of patients because of loss of response ($n = 7$) or acute infusion reactions ($n = 3$).

Overall, there was comparable effectiveness for the treatment of both cutaneous and articular disease following the switch from infliximab to biosimilar therapy or between infliximab biosimilars in patients with psoriasis. There was an increased number of mild AEs in one study, although no statistical analysis was performed.

Discussion

The effectiveness and safety profiles of adalimumab, etanercept, and infliximab biosimilars are similar to those of the reference products in real-world use, supporting the practice of switching patients from these biologics to approved biosimilars when possible. The real-world evidence is consistent with controlled trials and may be reassuring to patients and providers.

A barrier to the usage of biosimilars in clinical practice is a lack of confidence by physicians and patients. Both physicians and patients report preferences for reference products over biosimilars due to concerns for patient mental health, treatment efficacy, and patient safety (28,29). Provider hesitancy may stem from the concern that the development of biosimilars is not subject to the same scrutiny as that of novel biologics. However, due to the large and complex nature of biologics and their vulnerability to manufacturing process conditions, heterogeneity exists from batch to batch of these drugs and duplication is not feasible even by the innovator company. Hence, biosimilars may be subject to more scrutiny than the current batch of the reference product. Furthermore, while there is a greater emphasis placed on clinical evaluation for novel biologics than on biosimilars, more emphasis is placed on pre-clinical comparative assessments for biosimilars at earlier stages of development (30). Prioritizing analytical similarity early in development reduces the need for more extensive clinical testing later in the process. If analytical testing shows that a biosimilar is structurally similar to the reference product, has similar binding affinity for its target, and has a similar pharmacokinetic profile, the biosimilar is likely to perform similarly to the reference product; small clinical trials may be all that is needed to confirm the similar performance.

Negative patient attitudes about biosimilars may be a nocebo effect, which is defined by a worsening of symptoms induced by negative expectations toward a therapeutic intervention (31). The nocebo effect has been described in a variety of medical interventions in different fields of medicine including biosimilar therapies and adds an additional barrier to their usage. Inciting factors include a lack of knowledge of the new intervention and a breakdown in patient-physician communication (31). Educating physicians and patients on how each batch of a reference product varies and on real-life findings following a switch to biosimilars may provide reassurance about the utility of biosimilars and mitigate this barrier to usage. Nevertheless, drugs sometimes stop working, and sometimes AEs pop up. If either happens after a switch, the switch may get blamed, even if the event was unrelated to the switch.

The studies included in this review have several limitations including sample sizes, duration of follow-up, and single-arm designs without control groups. Furthermore, these studies did not directly examine immunogenicity following switching to a biosimilar from a reference product. In theory, switching between non-identical biologic drugs could lead to exposure to additional epitopes formation of anti-drug antibodies, and decreased efficacy (8). However, biologics are too complex even for innovator companies to duplicate. While there may be a theoretical risk of the formation of anti-drug antibodies when

switching to a biosimilar, that theoretical risk is also present when switching from one batch of an innovator to another. Patients vary in how adherent they are to treat and to how they handle biological drug products (32); those variations may cause far more changes in outcomes than the minor differences between a biosimilar and the current batch of the innovator product.

Conclusion

Biosimilar therapies can provide a lower-cost alternative to innovator biologics and possibly could offer improved access to treatment for patients with moderate to severe psoriasis (although there may be little improvement in accessibility if the biosimilar is not dramatically less costly than the innovator). The cost saving may also reduce the economic burden of healthcare.

Understanding that biologics cannot be duplicated (not even from batch to batch of the innovator) makes clear that patients are already switching from one biologic to another, even when they think they are taking the same product. Doing so appears to be safe and effective, and the available real-world evidence suggests that patients can also safely and effectively undergo (non-medical) switching to biosimilar therapies for the treatment of psoriasis.

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