ORIGINAL RESEARCH

Real-Life Effectiveness of Adalimumab Biosimilars in Patients with Chronic Plaque Psoriasis

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ABSTRACT

Introduction: The real-life effectiveness of adalimumab biosimilars in patients with psoriasis has rarely been investigated.

Objective: To investigate drug survival of adalimumab biosimilars in patients with chronic plaque psoriasis and factors associated with its discontinuation.

Methods: We carried out a retrospective observational study including all consecutive patients with chronic plaque psoriasis who initiated adalimumab biosimilar MSB11022 (Idacio), ABP501 (Amgevita), or SB5 (Imraldi) between 1 January 2018 and 1 January 2021. The 1-year drug survival of adalimumab biosimilar and independent factors associated with its discontinuation were investigated. Cox regression models were fit to estimate adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs) for the risk of adalimumab discontinuation. A propensity score matching (PSM) model was adopted as sensitivity analysis.

Results: The study involved a total of 410 patients with follow-up of 549.84 person-years, 271 (66.1%) men, a mean (SD) age of 51.8 (14.5) years, and a baseline PASI of 14.54 (5.02). Among adalimumab biosimilars, 250 (61%) patients received MSB11022, 98 (24%) received ABP501, and 62 (15%) received SB5. Drug survival of adalimumab biosimilars at 1 year was 81.5% in the overall study population. Obesity was associated with increased risk of adalimumab discontinuation (HR = 2.01; 95% CI 1.33–3.03), whereas psoriatic arthritis (aHR = 0.32; 95% CI 0.16–0.64) and receiving adalimumab as first systemic treatment (aHR = 0.44; 95% CI 0.27–0.70) were associated with lower risk.

Conclusion: The real-life effectiveness of adalimumab biosimilars in patients with psoriasis is consistent with that previously reported for the originator.

Keywords: Psoriasis; Adalimumab; Biosimilar; Drug survival; Early intervention

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Key Summary Points

Why carry out this study?

High-quality biosimilars of anti-tumor necrosis factor α inhibitors have been providing a cheaper, yet effective option for the treatment of moderate to severe chronic plaque psoriasis.

The real-life effectiveness of adalimumab biosimilars in patients with psoriasis has rarely been investigated.

What was learned from the study?

Drug survival of adalimumab biosimilars at 1 year was approximately 80%, which is consistent with that of the originator, previously reported.

Drug survival of adalimumab biosimilars in patients with chronic plaque psoriasis is longer when used as first systemic treatment than after failure of other conventional systemics such as methotrexate, acitretin, or cyclosporine.

INTRODUCTION

Adalimumab is a fully human anti-tumor necrosis factor α (TNF-α) monoclonal antibody indicated for the treatment of moderate to severe plaque psoriasis in adults and pediatric patients (aged > 4 years) [1]. Patients with concomitant psoriatic arthritis (PsA), inflammatory bowel disease, hidradenitis suppurativa, and/or uveitis could be good candidates for adalimumab since it is effective also in these disorders [2]. High-quality TNF-α inhibitor biosimilars have been providing a cheaper, yet effective option, therefore being suitable for prescription early in the patient care path [3, 4]. The biological properties of biosimilars in terms of pharmacokinetic and pharmacodynamic features and immunogenicity are comparable to the originator [5]. The US Food and Drug Administration and/or the European Medicines Agency have so far approved several adalimumab biosimilars, including MSB11022 (Idacio), ABP501 (Amgevita), SB5 (Imraldi), BI695501 (Cyltezo), GP2017 (Hyrimoz), FKB327 (Hulio), PF06410293 (Amsparity/Abrilada), and CTP17 (Celltrion) [6]. The real-life effectiveness of adalimumab biosimilars in patients with psoriasis has rarely been investigated [7]. Drug survival, which is the probability of continuing to receive a selected therapy over a certain period, is deemed an indirect predictor of effectiveness [8]. The objective of this study is to investigate the drug survival of adalimumab biosimilars in patients with chronic plaque psoriasis and the factors associated with discontinuation.

METHODS

A retrospective observational study including all consecutive adult patients with moderate-to-severe chronic plaque psoriasis attending the Dermatology Unit of the University Hospital of Verona was undertaken. Eligible patients were considered those who met the following inclusion criteria: age > 18 years; clinically confirmed diagnosis of moderate-to-severe chronic plaque psoriasis; those who initiated adalimumab biosimilar MSB11022, ABP501, or SB5 between 1 January 2018 and 1 January 2021. Exclusion criteria were history of any previous treatment with other biological drugs and concomitant treatment with any conventional systemic including methotrexate and/or phototherapy. Clinical data of the patients were retrieved from the electronic medical records and retrospectively analyzed up to 1 February 2022. The following clinical parameters were collected at enrollment: age, gender, body mass index (BMI), diagnosis of psoriatic arthritis (PsA), diabetes mellitus, arterial hypertension, severity (PASI) and duration of psoriasis, history of any previous systemic treatment for psoriasis, and disease localization in sensitive areas including palmoplantar, nails, and skin folds. Treatment cycle was defined as time from initiation of adalimumab biosimilar to its discontinuation, switching, swapping, or last

observation. The primary endpoint was to investigate the drug survival of adalimumab biosimilars at 1 year. The secondary end point was to investigate the independent factors (age, gender, obesity, psoriatic arthritis, and receiving adalimumab biosimilar as first systemic treatment) associated with its discontinuation. MSB11022, ABP501, and SB5 were selected because they are the only biosimilars that we are allowed to prescribe based on the current framework agreement of the Veneto region [9–11]. Adalimumab biosimilars were prescribed according to the label and reimbursement national criteria [9–11]. Adalimumab is approved for the treatment of moderate to severe plaque psoriasis (PASI > 10, body surface area > 10, Dermatology Life Quality Index > 10, and/or involvement of sensitive areas) and is reimbursed in case of contraindication, failure, and/or intolerance to at least one conventional systemic including methotrexate, cyclosporine, and phototherapy [12]. Adalimumab biosimilars have occasionally been prescribed as first systemic treatment because of contraindications to conventional drugs according to the EuroGuiDerm guideline [13] and/or patient refusal of conventional systemic for personal beliefs related to their risk of toxicity. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The ethics committee exempted the study from the informed consent requirement because we only retrospectively accessed a deidentified database for the purpose of data analysis.

Statistical Analysis

The cumulative incidence of drug discontinuation over time was estimated by the Kaplan--Meier method, and Cox regression models were fit to estimate adjusted hazard ratios (aHRs) with 95% CIs for risk of adalimumab discontinuation. Log-rank test was applied to compare patients receiving adalimumab biosimilar as first systemic treatment versus those who had experienced other conventional systemics before. Propensity score matching (PSM) analysis was performed by fitting a regression model

in which disease duration was used as the predictor matching variable and receiving adalimumab biosimilar as first treatment was the dependent variable. After fitting the logistic regression model, the logit transformation of PSM for all patients was collected for subsequent use in the matched groups. By the PSM procedure, patients treated with adalimumab biosimilar as first systemic treatment were matched with those who had been treated with other conventional systemic drugs before using a 1:1 nearest-neighbor algorithm without replacement and with a caliper width of 0.50 standard deviation. The analysis was conducted using the STATA software (version 13; Stata-Corp, Collage Station, TX, USA).

Table 1 Descriptive characteristics of the study population

Number of patients	410
Age, mean $\pm$ SD, years	51.76 $\pm$ 14.54
Gender, male, n (%)	271 (66.1)
BMI, mean $\pm$ SD, kg/m^2	26.81 $\pm$ 4.11
PASI, mean $\pm$ SD	14.54 $\pm$ 5.02
Psoriasis duration, years	16.38 $\pm$ 16.29
Body areas affected by psoriasis	
Palmoplantar, n (%)	57 (13.9)
Nails, n (%)	74 (18.1)
Folds, n (%)	55 (13.4)
Comorbidities	
Diabetes, n (%)	32 (7.8)
Arterial hypertension, n (%)	98 (23.9)
PsA, n (%)	67 (16.3)

Continuous and categorical variables presented as mean $\pm$ standard deviation (SD) and proportion, respectively

BMI, body mass index; PASI, psoriasis area and severity index; PsA, psoriatic arthritis

RESULTS

Descriptive characteristics of the study population are presented in Table 1. The study included 410 patients, 271 (66.1%) men, with a mean (SD) age of 51.8 (14.5) years, and PASI of 14.5 (5.0). A total of 150 (36.6%) patients received adalimumab biosimilar as first systemic, and 260 (63.4%) had been treated before with conventional systemic, including methotrexate (181, 70%), cyclosporine (64, 25%), acitretin (12, 5%), and fumarates (3, 1%)

(Supplementary Fig. 1). Two hundred fifty (61%) patients received MSB11022, 98 (24%) received ABP501, and 62 (15%) received SB5. The overall cohort of patients had follow-up of 549.81 person-years, with an incident rate of drug discontinuation of 0.20 (95% CI 0.16–0.24). A total of 109 drug discontinuations were found. Treatment failure was the most common reason for drug discontinuation occurring, in 87 (80%) of patients. In the other 22 patients (20%), adalimumab was withdrawn due to safety issues, remission of psoriasis, or
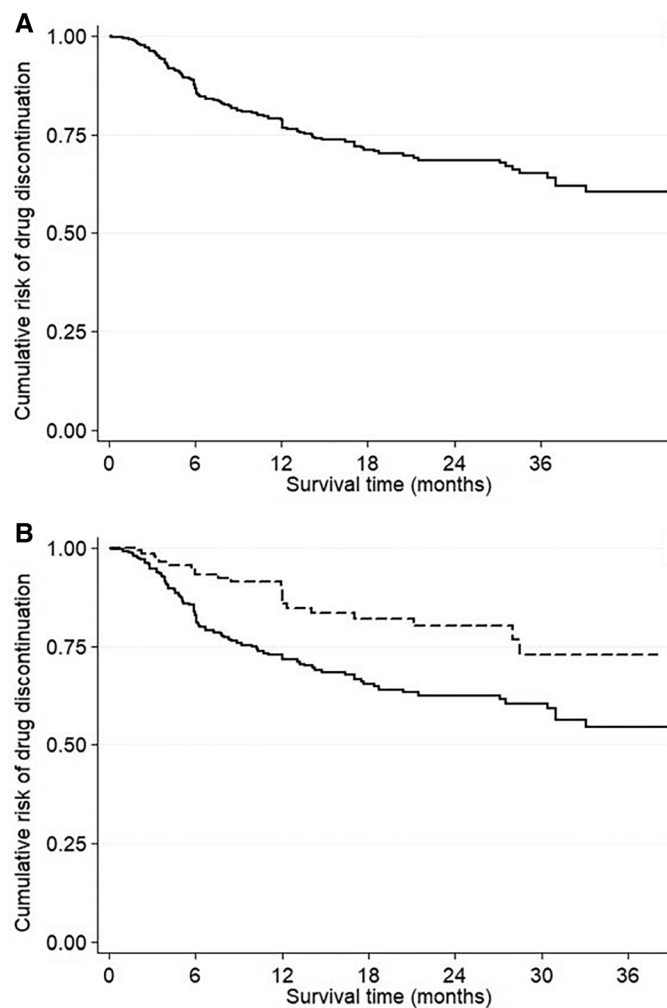

Fig. 1 Drug survival of adalimumab biosimilars in the overall study population of patients with moderate to severe plaque psoriasis (A). Drug survival in patients receiving adalimumab biosimilars as first systemic treatment (dashed line) versus after failure of conventional systemic drugs (continue line) (B). Log-rank test for equality of survivor functions $p < 0.001$

Table 2 Multivariate Cox regression model assessing risk of adalimumab biosimilar discontinuation

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	aHR (95% CI)	p
Gender, male	0.97 (0.65–1.46)	0.890	1.05 (0.69–1.57)	0.832
Age (years)	1.01 (0.99–1.02)	0.768	1.00 (0.99–1.01)	0.865
BMI $\geq$ 30 kg/m^2	2.01 (1.34–3.02)	< 0.001	2.01 (1.33–3.03)	< 0.001
PsA	0.37 (0.18–0.72)	0.004	0.32 (0.16–0.64)	< 0.001
Adalimumab as first systemic treatment	0.45 (0.28–0.72)	< 0.001	0.44 (0.27–0.70)	< 0.001

$N = 410$

BMI, body mass index; PsA, psoriatic arthritis

upon patient request (Supplementary Fig. 1). Drug survival of adalimumab biosimilars at 1 year was 81.5% (Fig. 1A). No differences in drug survival among the three adalimumab biosimilars were found. According to univariate and multivariate time-dependent analysis, obesity was associated with increased risk of adalimumab discontinuation (aHR = 2.01; 95% CI 1.33–3.03), whereas psoriatic arthritis and receiving adalimumab as first systemic were associated with lower risk (aHR = 0.32; 95% CI 0.16–0.64; aHR = 0.44; 95% CI 0.27–0.70, respectively), as reported in Table 2.

We compared the retention rate of patients receiving adalimumab as first systemic versus those who received it after conventional systemic. No differences in terms of clinical characteristics including psoriasis severity and disease localization in sensitive areas were found between the two groups except for a longer disease duration in patients who have already received conventional systemic treatments (Supplementary Table 1). The cumulative incidence of drug discontinuation in the two groups is shown in Fig. 1B (log-rank test for equality of survivor functions, $p < 0.001$). Stratified analyses yielded drug survival at 6, 12, and 24 months of 95.0%, 92.0%, and 86.7% versus 84.2%, 75.4%, and 68.9% for those who received adalimumab as first systemic versus those already treated with conventional drugs, respectively. After PSM adjustment based on disease duration, being naïve to conventional drugs was still associated with lower risk of adalimumab discontinuation (aHR = 0.55; 95% CI 0.31–0.96) (Supplementary Fig. 2; Supplementary Tables 2, 3).

DISCUSSION

In this study, we investigated the real-word effectiveness of adalimumab biosimilars in patients with moderate to severe plaque psoriasis. In our population, drug survival of adalimumab biosimilars at 1 year was 81.5%, consistent with previous findings [14–18]. The long-term efficacy and safety profile is emerging from different national registries, such as the Italian PsoBiosimilars, British BADBIR, and Danish DERMBIO registries [3], but real-world data for adalimumab biosimilars in patients with psoriasis are needed.

Drug survival of biologics is useful to evaluate long-term drug performance in daily practice and can be affected by different clinical and metabolic variables [15, 16]. A recent meta-analysis of 16 cohort studies found that female sex and obesity were associated with reduced biological drug survival, while PsA were associated with prolonged persistence [17, 18]. Obesity is another well-known predictor for biologic discontinuation. Higher body surface area, lower blood drug levels, or an increase in proinflammatory cytokines and adipokines deeply linked to obesity have been hypothesized to explain this phenomenon [19]. In our population, BMI higher than 30 kg/m^2 was

associated with poor drug survival, whereas PsA predicted longer drug survival. Mourad et al. [20] speculated that the greater combined therapeutic benefit, the increased motivation of healthcare providers, and/or increased awareness of the importance of treatment persistence could explain this observation. Adalimumab is known to more likely induce antidrug antibody when given without concomitant methotrexate, and shows longer drug survival when used in combination therapy [21]. However, adalimumab is approved and is almost exclusively in real life used as monotherapy for plaque psoriasis, as recommended by European and national guidelines [22].

Of significance, in this study, a substantial proportion of patients receiving adalimumab biosimilar as first systemic showed longer drug survival compared with those with failure of previous conventional drugs (92% versus 75.4% at 1 year, respectively). This is consistent with the finding that patients treated with a second-line biologic have already failed one or more treatments and will therefore be at increased risk of failing another drug [23]. A recent cost-effectiveness analysis conducted in the UK showed that adalimumab biosimilars may represent an ideal first-line biologic treatment [24]. Given the longer drug survival, staring early with adalimumab biosimilar might prevent or delay switching to other, more expensive drugs, with marked pharmacoeconomic advantages. Biosimilars have reduced cost compared with their biologic originator, but pharmacoeconomic studies comparing them with conventional drugs are lacking.

Moreover, whether early intervention with biologics, including adalimumab, could impact on the psoriasis course in terms of prevention of PsA and/or cumulative life course impairment (CLCI) is currently under investigation [25–29]. Two recent studies by Acosta Felquer et al. [27] and Gisondi et al. [26] found that earlier treatment with biologics may delay or reduce the risk of incident PsA compared with skin-directed therapies such as phototherapy or topical therapies. The persistence of the disease burden over time leads to a nonreversible impact on patient life that could potentially be prevented by early introduction of biologics [30, 31].

We acknowledge the limitations of our study, including the retrospective, nonrandomized, real-life design, and monocentric sampling. The major limitation of the study is confounding by indication; i.e., patients treated with adalimumab biosimilars as first-line therapy may be selected because of medical contraindications, personal beliefs related to toxicity, or pharmacoeconomic reasons. Another limitation is negative selection; i.e., patients treated with adalimumab who have already failed one treatment are at increased risk of failing another drug. We cannot exclude that use of conventional disease-modifying antirheumatic drugs (DMARDs) might have selected out some more recalcitrant patients and that some other patients can be easily controlled with conventional DMARDs. Drug survival is not a perfect predictor of drug efficacy, as it also reflects safety. Reasons for drug discontinuation are difficult to confirm, particularly since an assessment of PASI and BSA variations was not provided. In addition, dose tapering may not be intercepted by drug survival, although we rarely use this practice in our real life. In this study, we considered three different biosimilars, because we are required to prescribe the biosimilar with lowest cost, which can vary depending on contingent calls of tenders. Nonetheless, this study also has strengths, including the periodical follow-up allowing the completeness of the database and the adjustment for potential bias such as disease duration based on propensity score matching.

CONCLUSIONS

The real-life effectiveness of adalimumab biosimilars in patients with psoriasis is consistent with that previously reported for the originator. The favorable cost-effective profile of biosimilars is expected not only to allow wider access to biologics but also to redefine the standard of care of psoriasis [3, 32]. Given increasing healthcare costs and cost-cutting initiatives, starting patients with biosimilars can lower the cost of therapy while still allowing maintenance of high-quality care [3].

ACKNOWLEDGEMENTS

Compliance with Ethics Guidelines. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The ethics committee exempted the study from the informed consent requirement because we only accessed retrospectively a de-identified database for the purpose of data analysis.

Data Availability. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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