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ORIGINAL RESEARCH ARTICLE

AVT04, a Biosimilar to Reference Product Ustekinumab, for the Treatment of Plaque Psoriasis: Insights from a Real-World Experience up to 28 Weeks

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ABSTRACT

Introduction: This study aims to evaluate the real-life efficacy and safety of a biosimilar to reference product (RP) ustekinumab for the treatment of plaque psoriasis in different patient scenarios. The cohort included ustekinumab-switched patients, who switched from the RP to the biosimilar, and ustekinumab-naïve patients, never treated with ustekinumab. Ustekinumab-naïve patients were subdivided into bio-naïve (no prior biologic therapy) and bio-experienced (previous non-ustekinumab biologic therapy).

Methods: Adult patients with chronic plaque psoriasis treated with AVT04 were followed up to 28 weeks. Efficacy of the biosimilar was assessed by improvement of the Psoriasis Area Severity Index (PASI) 75, 90, and 100 responses from baseline to weeks 16 and 28. A cost-minimisation analysis over a 1-year time horizon was performed to estimate costs and potential savings with AVT04 versus RP across the Italian National Health Service (NHS).

Results: Throughout the observation period, a sustained improvement in PASI was observed in the overall cohort of 183 patients, encompassing both the ustekinumab-switched and ustekinumab-naïve groups. Within the ustekinumab-naïve group, a trend toward more favourable PASI 75/90/100 responses was observed in bio-naïve patients compared to bio-experienced patients. By 28 weeks of treatment, a higher proportion of bio-naïve patients compared to the bio-experienced group achieved PASI 75 (72.7% vs. 56.2%), PASI 90 (72.7% vs. 50.0%), and PASI 100 (54.5% vs. 37.5%), respectively ($p > 0.05$). No adverse events were reported during the study. Furthermore, the cost-minimisation analysis suggested that compared to the RP, AVT04 has the potential to generate approximately €5200 in annual savings per patient for the Italian NHS, representing around €20 million in nationwide savings.

Conclusion: AVT04 biosimilar shows consistent efficacy results in both ustekinumab-switching and ustekinumab-naïve patients, supporting its integration into real-world practice as an effective and cost-saving therapeutic option. Further studies are warranted to confirm and expand these preliminary findings across a broader bio-naïve cohort.

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Key Summary Points

This 28-week real-world study of ustekinumab biosimilar showed sustained clinical efficacy in both ustekinumab-naïve and switched patients, corroborating the evidence for continued safety and efficacy during reference product (RP) transition.

In line with previous studies, switching from RP ustekinumab to AVT04 was effective and safe for ustekinumab-switched patients in real-world practice.

Within ustekinumab-naïve groups, treatment with ustekinumab biosimilar led to complete remission in 54.5% of bio-naïve patients and 37.5% of bio-experienced patients.

From the perspective of the Italian National Health Service, the adoption of the ustekinumab biosimilar is cost-saving, promoting more efficient healthcare resource use and increasing patient access to advanced biologic therapies.

INTRODUCTION

The advent of biological disease-modifying agents (biologics), has revolutionised the therapeutic landscape, substantially improving outcomes for a wide range of autoimmune disorders. Owing to their targeted action and high efficacy, demand for biologics has increased to meet the growing need for treating conditions with complex pathophysiology due to aberrant immune responses, including chronic and autoimmune inflammatory diseases [1].

Over the past decade, expenditure on biologics in Europe has increased by 10%, now representing 41% of total pharmaceutical spending, which led to an investment of €95 billion in 2024 [2]. However, reference biologics may not be cost-effective, and the loss of market exclusivity has opened opportunities for more affordable biosimilars to enter the healthcare space [3].

A biosimilar product shares a comparable efficacy, safety, pharmacokinetic and immunogenicity profile with the biological reference product (RP) [4]. Since 2006, when the first biosimilar was approved in Europe, the market penetration of biosimilars has steadily increased. Despite heterogeneous adoption across European countries, the surge in biosimilars generated significant savings of up to €56 billion in 2024 [2, 5]. Aside from generating considerable economic advantages that ease pressure on healthcare budgets globally, the impact of biosimilars has proven to be particularly beneficial in terms of wider and prompter access to treatments for patients, as well as mitigation of disease burden and improvement of patient care [6].

Psoriasis is one of the most common immune-mediated inflammatory skin diseases. Among various phenotypes, plaque psoriasis is a chronic, multisystemic condition affecting about 2–3% of the global population [7, 8]. However, these figures likely underestimate the actual disease burden because of underreporting and underdiagnosis [9]. The hallmark signs of psoriasis include red, scaly patches across multiple body areas, alongside emotional and psychological impacts on quality of life, systemic complications, and increased risk of comorbidities [10]. The severity of psoriasis depends on the extent of body involvement and associated comorbidities, with the disease progressing to psoriatic arthritis in 20–30% of cases.

Treatment with biologics has proven effective in the management of this lifelong condition after inadequate response with conventional systemic therapies, commonly based on cyclosporine and methotrexate. Among the current anti-psoriatic biologics, first-generation products include antagonists of tumour necrosis factor (TNF; infliximab, etanercept, adalimumab, and certolizumab pegol). Second-generation biologics refers to antagonists of interleukin (IL)-17 (secukinumab, ixekizumab, and bimekizumab), IL-12/23 (ustekinumab), and IL-23 (guselkumab and risankizumab).

To date, anti-TNF medications have been the preferred choice for patients with psoriasis,

primarily because of their cost-effectiveness and decades of clinical experience [11]. Switching to IL inhibitors is a common clinical practice in recovering clinical response after anti-TNF primary therapy as a result of inefficacy or side effects [12, 13]. Furthermore, the latest meta-analyses and updated consensus acknowledged the beneficial action of IL classes of biologics, also in severe psoriatic arthritis [13–16]. Despite a robust spectrum of established and emerging biologics, no single agent is unequivocally beneficial for all patients with psoriasis, but existing comorbidities and individual patient circumstances are to be considered [11]. In addition to international and nationwide recommendations, real-world clinical practice is confronted with complex psoriatic patient populations with differing disease severity and therapeutic histories [11, 15, 17, 18]. This reinforces the need for personalised treatment selection to ensure that each patient is likely to yield an optimal response.

Ustekinumab, an IL-12/23 antagonist, is a well-established treatment option approved in 2009 for moderate-to-severe plaque psoriasis in both adult and paediatric patients, particularly in those who have not responded to traditional systemic therapies [19, 20]. As of 2025, over ten biosimilars are available in Europe as alternatives to the RP and more are in development, showcasing a remarkable turnaround in savings, contributing to improving access to affordable psoriasis treatments[1] [21]. Supported by phase I and III trials demonstrating pharmacokinetic similarity and comparable efficacy to the RP biologic, respectively, AVT04 received approval in Europe in 2024 [22, 23].

The present study aims to assess the efficacy and safety of AVT04 in patients with plaque psoriasis across various real-life scenarios, including patients who switched from the RP ustekinumab (ustekinumab-switched) and ustekinumab-naïve patients, with no prior exposure to ustekinumab. Within the naïve cohort, patients were further stratified as bio-naïve (never treated with biologic drugs) and bio-experienced (previously treated with other biologic drugs). In addition, potential savings from AVT04 adoption compared to RP were determined from a nationwide perspective of the Italian National Health Service (NHS).

METHODS

Cohort and Clinical Endpoints

This monocentric, retrospective, observational study involved a cohort of patients with moderate-to-severe chronic plaque psoriasis referred to the Dermatology Unit at Tor Vergata University of Rome. All patients received AVT04 (Uzpruvo®), a biosimilar of RP ustekinumab (Stelara®; Janssen Biotech, Inc.). The cohort included ustekinumab-switched patients, who switched from ustekinumab RP to ustekinumab biosimilar, and ustekinumab-naïve patients, never treated with ustekinumab. Ustekinumab-naïve patients were further divided into bio-naïve, those with no prior biologic therapy, and bio-experienced, those with previous therapy with other biologic agents.

The analysis was conducted on an "as-treated" basis. As patients started therapy at different times during the study, the current data provide a real-world cross-sectional snapshot collected from January to October 2025.

According to the standard dosing regimen, ustekinumab-naïve patients received the biosimilar via subcutaneous (SC) injection (45 mg for patients ≤ 100 kg and 90 mg for patients > 100 kg) at weeks 0, 4, and then every 12 weeks (weeks 16 and 28). For ustekinumab-switching patients, the dosage and administration schedule already in place at 12-week intervals at the time of switching was maintained. As a result of body weight above 100 kg, five patients from the ustekinumab-naïve group and 21 patients from the ustekinumab-switched group received a 90-mg dose.

The improvement in psoriasis symptoms was evaluated through the Psoriasis Area and Severity Index (PASI). The assessment included mean PASI scores at different time points (baseline, week 16, and week 28) and the percentage of patients achieving reductions in PASI scores

[1] www.ema.europa.eu.

by 75% (PASI 75), 90% (PASI 90), and 100% (PASI 100). Data are presented as mean (SD) or percentage.

Safety was assessed by reporting adverse events related to the treatment, if any, as routinely carried out at the clinical centre.

Two representative clinical cases are shown from the bio-naïve study cohort to illustrate treatment response patterns with ustekinumab biosimilar observed in real-world practice. The clinical outcomes following biosimilar treatment were evaluated by comparing PASI and the Dermatology Life Quality Index (DLQI) from baseline to weeks 16 and 28.

Institutional review board approval was waived, as data were collected as part of routine clinical practice. All patients provided written informed consent for the collection of demographic and clinical data. The study was conducted in accordance with the principles of the Declaration of Helsinki and later amendments. Data collection and management complied with all applicable laws, regulations, and guidelines concerning patient protection and privacy.

Economic Analysis

A cost-minimisation analysis was conducted from the perspective of the Italian NHS. The analysis considered the hospital setting of the study cohort and nationwide data to estimate the potential savings with AVT04 versus the ustekinumab RP in the treatment of moderate-to-severe plaque psoriasis. Based on pharmacokinetic equivalence, efficacy and safety similarity, along with comparable costs for administration and for treating arising adverse events between the two products, only the differing drug acquisition cost was used for the estimation.

At the hospital level, costs were estimated by applying the ex-manufacturer acquisition prices for ustekinumab RP and biosimilar, as reported by the Italian Medicines Agency (AIFA),[2] to the treatment patterns observed in the study cohort (183 patients). The model reflected the proportions of biologic-naïve and switched patients (54 and 129, respectively) and their dosing regimens (4 doses per year for naïve and 6 doses per year for switched patients). The analysis adopted a 1-year time horizon and compared two alternative scenarios in which all patients were treated with either the RP or the biosimilar.

At the national level, a top-down approach was employed using official AIFA data. Ustekinumab consumption and baseline expenditure were obtained from the AIFA OsMed National Report 2023,[3] which provides information on per capita spending and consumption in defined daily doses (DDD) per 1000 inhabitants per day. Updated acquisition cost data were retrieved from the AIFA report "Biological and Biosimilar Drugs (information last updated: April 2025"[4]), which includes national mean prices per DDD and biosimilar market shares. These parameters were used to estimate national expenditure by combining DDD consumption data, mean cost per DDD, and national population figures, according to the following formula:

Annual expenditure (€) = DDD/1000 inhabitants/day × Population/1000 × 365 × Cost per DDD (€)

Given that biosimilar competition for ustekinumab only became possible after the expiry of the RP's supplementary protection certificate (SPC) in 2024, the 2023 OsMed data were used to represent a pre-biosimilar baseline scenario characterised by exclusive RP use. The 2025 AIFA data, by contrast, reflect a post-biosimilar market scenario, including both RP and biosimilar products with an estimated 25–30% biosimilar penetration at the national level. This allowed estimation of the potential cost impact associated with the transition from a pre-entry RP monopoly to a competitive environment.

Because AIFA data are not stratified by therapeutic indication, a dermatology-related share of 25–35% of total ustekinumab use was applied as assumption to represent the proportion attributable to psoriasis and psoriatic arthritis. At the national level, no distinction between biologic-naïve and switched patients was possible, as

[2] List of Class H medicinal products (last updated April 30, 2025).

[3] L'uso dei farmaci in Italia—Rapporto OsMed 2023.

[4] Monitoring of biosimilars consumption and expenditure report—April 2025.

AIFA data are aggregated by product rather than treatment line.

Statistical Analysis

Chi-square test was performed to assess differences in ustekinumab-naïve groups (bio-naïve versus bio-experienced). Significance was considered at p value ≤ 0.05 and all PASI analyses were performed using Stata version 11.2 (StataCorp LP Inc., College Station, TX, USA).

RESULTS

The cohort consisted of 183 patients, of whom 129 switched from RP ustekinumab to the AVT04, while 54 were naïve and receiving AVT04 biosimilar for the first time. The latter group comprised 33 (61.1%) bio-naïve patients, who had never been exposed to biologics before, and 21 (38.9%) bio-experienced patients who had been previously on a non-ustekinumab biologic therapy. The mean treatment duration with the ustekinumab RP was 565.6 ± 143.8 weeks in patients prior to switching to the biosimilar.

Table 1 displays the demographic characteristics and clinical features of the study cohort. Overall, the majority of patients were male across the three groups: 79 (61.2%) in the switched group, 22 (66.7%) in the bio-naïve group, and 12 (57.1%) in the bio-experienced group. The mean age ranged from 48.2 ± 13.1 to 59.2 ± 12.7 years, and the BMI was similar across all groups, ranging from 27 ± 4.3 to 27.1 ± 5.1 kg/m^2. Patients had a mean disease duration ranging from 21 to 30 years, with baseline PASI scores of 0.6 ± 2.8 for the switched group, 16.7 ± 7.8 for bio-naïve patients, and 7.1 ± 2.1 for bio-experienced patients. Bio-experienced patients previously treated with adalimumab (n = 12), secukinumab (n = 5), brodalumab (n = 1), guselkumab (n = 2), and deucravacitinib (n = 1) were switched to ustekinumab biosimilar because of a lack of efficacy of these previous biologics.

Regarding comorbidities, hypertension was the most common condition across the three groups, affecting 9 (27.2%) of bio-naïve, 4 (19.1%) of bio-experienced, and 41 (31.7%) of switched patients. Diabetes mellitus was the second most frequent comorbidity among 7 (21.2%) bio-naïve patients, whereas thyroid disease was more common, reported in 4 (19.1%) bio-experienced and 18 (13.9%) switched patients.

As expected, the mean PASI score at baseline showed differing response patterns between the ustekinumab-switched and bio-naïve groups throughout the observed period (Fig. 1). In the ustekinumab-naïve group (including both bio-naïve and bio-experienced patients), the mean PASI improved from 12.7 ± 7.9 at baseline, to 3.6 ± 2.8 at week 16. In the ustekinumab-switched group, the mean PASI remained stable over the same period from 0.6 ± 2.8 (baseline) to 0.4 ± 2.2 (week 16) and 0.4 ± 0.2 (week 28), indicating the maintenance of response after switching from ustekinumab RP.

Treatment responses to AVT04 in ustekinumab-naïve patients were assessed over time using PASI 75, 90, and 100 (Fig. 2). All PASI responses increased progressively up to week 28, where 65.7% of naïve patients achieved PASI 75, followed by 63.1% of patients reaching PASI 90, and 47.3% of patients reaching PASI 100.

PASI responses within the ustekinumab-naïve group were compared between bio-naïve and bio-experienced patients. At week 16, 56.5% of bio-naïve patients achieved PASI 75, which was significantly higher than 25.0% of bio-experienced patients (p = 0.05; Fig. 3a). By week 28, there was no significant difference between 72.7% of bio-naïve patients and 56.2% of bio-experienced patients reaching PASI 75 (p > 0.05).

A PASI 90 response was observed in 30.4% of bio-naive patients at week 16, compared to 12.5% of bio-experienced patients (p > 0.05; Fig. 3b). At week 28, PASI 90 response improved to 72.7% in bio-naïve patients and to 50% in bio-experienced patients (p > 0.05).

Complete patient remission, as assessed by PASI 100, was achieved by 21.7% at week 16, in the bio-naïve group, increasing to 54.5% at week 28 (p > 0.05; Fig. 3c). The bio-experienced group showed a lower but steady improvement, with PASI 100 rates rising from 12.5% at week 16 to 37.5% at week 28 (p > 0.05).

Table 1 Baseline characteristics of the population

Clinical characteristics	Ustekinumab-naïve (*N* = 54)		Ustekinumab-switched from RP (*N* = 129)
	Bio-naïve (*N* = 33)	Bio-experienced (*N* = 21)	
Patient features			
Male, *n* (%)	22 (66.7)	12 (57.1)	79 (61.2)
Female, *n* (%)	11 (33.3)	9 (42.9)	50 (38.8)
Age, mean (SD), years	56.3 (15.2)	48.2 (13.1)	59.2 (12.7)
BMI, mean (SD), kg/m^2	27 (4.3)	26.8 (5.2)	27.1 (5.1)
Current cigarette smoker, *n* (%)	12 (36.3)	12 (57.1)	67 (51.9)
Disease characteristics			
Age at disease onset, mean (SD)	29.4 (17.9)	22.9 (12.9)	28.9 (16.8)
Disease duration, mean (SD)	23.6 (15.8)	21.3 (17.1)	30.1 (13.6)
PASI at baseline, mean (SD)	16.7 (7.8)	7.1 (2.1)	0.6 (2.8)
Scalp involvement, *n* (%)	18 (54.5)	10 (47.6)	24 (18.6)
Nails involvement, *n* (%)	7 (21.2)	0 (0)	4 (3.1)
Palmoplantar involvement, *n* (%)	2 (6.1)	2 (9.5)	3 (2.3)
Genitalia involvement, *n* (%)	10 (30.3)	1 (4.7)	2 (1.5)
Biologic therapy, *n* (%)			
No previous biologic therapy	33 (61.1)		77 (59.6)[a]
Previous biologic therapy	_	21 (38.9)	52 (40.4)
1 biologic		18 (33.3)	34 (25.3)
2 biologics		3 (5.5)	15 (11.6)
≥ 3 biologics		0 (0)	3 (2.3)
Treatment duration with RP, mean (SD), weeks	_	_	565.5 (143.8)
Comorbidities, *n* (%)			
Hypertension	9 (27.2)	4 (19.1)	41 (31.7)
Dyslipidemia	5 (15.1)	3 (14.2)	14 (10.8)
Heart disease	4 (12.1)	2 (9.5)	2 (1.5)
Diabetes mellitus	7 (21.2)	1 (4.7)	12 (9.3)
Thyroid diseases	1 (3.1)	4(19.1)	18 (13.9)
Psychiatric illness	3 (9.1)	3 (14.2)	13 (10.1)
Previous or chronic HCV/HBV infection	5 (15.1)	0 (0)	8 (6.2)
Previous or current neoplasm	4 (12.1)	0 (0)	9 (6.9)

The cohort included: ustekinumab-switched patients, who switched from ustekinumab RP to AVT04 biosimilar, and ustekinumab-naïve patients, never treated with ustekinumab. Ustekinumab-naïve patients were further divided into bio-naïve patients, who have never been treated with biologics, and bio-experienced patients, who had previously been treated with non-ustekinumab biologic therapy. Data are presented as mean (SD) or number (percentage)

BMI body mass index, *HCV* hepatitis C virus, *HBV* hepatitis B virus, *PASI* Psoriasis Area and Severity Index, *RP* reference product, *SD* standard deviation

[a]Patients without prior biologic therapy at the start of treatment with ustekinumab originator

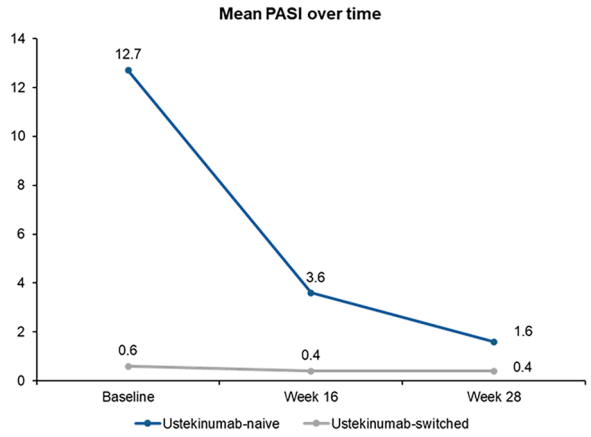

Fig. 1 Mean PASI over time in ustekinumab-switched and ustekinumab-naïve patients treated with AVT04 biosimilar. Ustekinumab-naïve patients (including bio-naïve and bio-experienced; $n = 54$ at baseline, 39 at week 16, 38 at week 28) are shown in blue, and ustekinumab-switched patients (previously treated with ustekinumab RP; $n = 129$ at baseline, 28 at week 16, 24 at week 28) are shown in grey. *PASI* Psoriasis Area and Severity Index, *RP* reference product

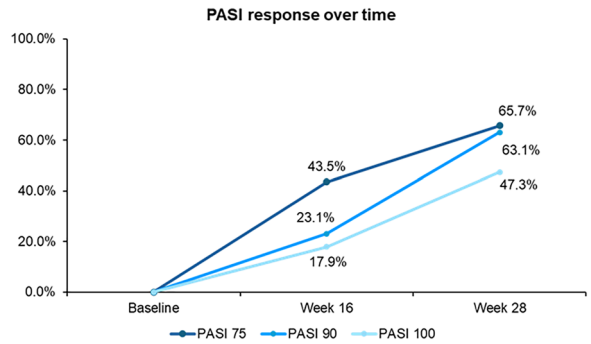

Fig. 2 PASI response over time in the ustekinumab-naïve cohort treated with AVT04 biosimilar. Proportion of patients achieving PASI 75, PASI 90, and PASI 100 at baseline, week 16, and week 28. Patients observed: $n = 54$ at baseline, $n = 39$ at week 16, $n = 38$ at week 28. PASI 75 is shown in dark blue, PASI 90 in light blue, and PASI 100 in turquoise. *PASI* Psoriasis Area and Severity Index

Overall, no significant adverse events related to the biosimilar were reported during the observation period.

CASE REPORTS

Case 1

A 32-year-old man, previously treated with methotrexate for 1 year and bio-naïve with no comorbidities, presented with plaque psoriasis with involvement of the genital region, back and upper and lower extremities (Table 2 and Fig. 4; case 1, T0). At baseline, a PASI score of 20 and a DLQI score of 14 were recorded. After 16 weeks of treatment with AVT04, complete resolution of skin lesions was observed along with improved quality of life (PASI = 0; DLQI = 0) (Table 2 and Fig. 4; case 1, T16).

Case 2

A 24-year-old man, previously treated with cyclosporine for 3 months and bio-naïve, with no comorbidities, presented with plaque psoriasis with involvement of the genital region, back, anterior trunk and lower extremities (Table 2 and Fig. 4; case 2, T0). At baseline, a PASI score of 20 and a DLQI score of 16 were recorded. After 28 weeks of treatment with AVT04, complete resolution of skin lesions was observed resulting in a positive impact on the quality of life (PASI = 0; DLQI = 0) (Table 2 and Fig. 4; case 2, T28).

Economic Analysis

Building on the observed comparable clinical efficacy and safety, an economic analysis was conducted to quantify the potential savings linked to biosimilar adoption.

At the hospital level, considering the study cohort, the total annual cost for treating 183 patients with ustekinumab RP was €2,388,019, compared to €1,432,813 if all 183 patients were treated using the biosimilar, leading to total yearly savings of €955,206. Among ustekinumab-naïve patients ($n = 54$), annual treatment costs dropped from €921,093 with the originator to €552,656 with the biosimilar, resulting in savings of €368,437. Among ustekinumab-switched patients ($n = 129$), total annual costs reduced from €1,466,926 with the RP to €880,156 with the biosimilar, corresponding to €586,769 in

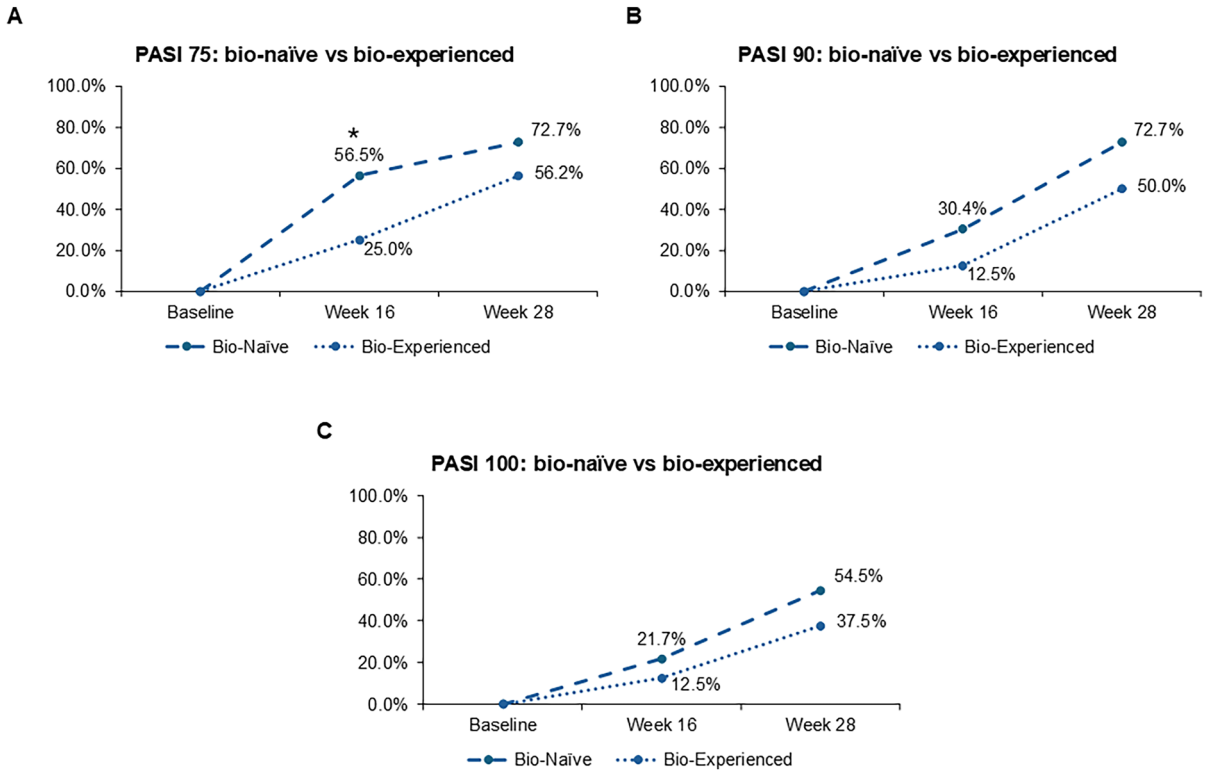

Fig. 3 **a** PASI 75, **b** PASI 95, **c** PASI 100 response in naïve patients treated with ustekinumab biosimilar. Comparison between bio-naïve (no prior biologic therapy) and bio-experienced (previous non-ustekinumab biologic therapy) patients. Bio-naïve patients are represented by a dashed line, and bio-experienced patients by a dotted line. Chi-square test showed no significant differences between groups ($p > 0.05$), except for PASI 75 at week 16 ($^*p = 0.050$). *PASI* Psoriasis Area and Severity Index

savings. The average yearly cost per patient under the RP scenario was €13,051, compared with €7829 for the biosimilar, resulting in mean savings of approximately €5222 per patient per year (Fig. 5).

At the national level, in 2023 RP ustekinumab showed a mean cost of €14.11 per DDD and a consumption of 0.5 DDD/1000 inhabitants/day, corresponding to an estimated total annual expenditure of €153.3 million (all indications combined). Following the introduction of biosimilars, in 2025 total ustekinumab had a weighted mean cost per DDD of €8.68 (RP + biosimilar mix, with 25–30% biosimilar penetration), corresponding to a total national expenditure of approximately €93.4 million under the same consumption assumption with a 40% reduction in ustekinumab expenditure overall.

Since ustekinumab is approved for multiple indications, including psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis, national expenditure cannot be directly attributed to dermatologic use. The AIFA datasets do not provide indication-specific disaggregation; therefore, the dermatologic share (including psoriasis and psoriatic arthritis) was estimated as assumption to account for roughly 25–35% of ustekinumab utilisation in Italy, while inflammatory bowel diseases represent the remaining majority.

Applying this adjustment range, the 2025 dermatology-related expenditure is estimated at €23–33 million (RP + biosimilar mix, with 25–30% biosimilar penetration), compared with €38–54 million in 2023 (RP only), corresponding to a 40% reduction in costs for dermatologic indications. Because national AIFA data

Table 2 Characteristics of clinical cases

Characteristics	Case 1	Case 2
Age (years)	32	24
Weight (kg)	68	66
Height (m)	1.78	1.71
BMI (kg/m^2)	21.5	22.5
Medical history	Psoriasis vulgaris (plaque type) onset at age 22	Psoriasis vulgaris (plaque type) onset at age 2
Genital involvement	Yes	Yes
Previous therapy	Methotrexate (10 mg/week for 1 year)	Cyclosporine (3 months)
Reason for discontinuation	Nausea	Lack of efficacy
Comorbidities	No	No
Concomitant therapies	No	No
PASI T0	20	20
DLQI T0	14	16
PASI Tx	0 (T16)	0 (T28)
DLQI Tx	0 (T16)	0 (T28)

BMI body mass index, *DLQI* Dermatology Life Quality Index, *PASI* Psoriasis Area and Severity Index, *T0* baseline, *T16* week 16, *T28* week 28

are aggregated by product and not by treatment line, this analysis does not distinguish between naïve and switched patients. The resulting figures reflect average acquisition costs across all procurement channels and should be interpreted as conservative.

Overall, the increasing use of ustekinumab biosimilar instead of the RP is expected to generate substantial economic benefits for the Italian NHS, both at the institutional and system-wide levels.

DISCUSSION

This study provides insights into the efficacy of 28-week exposure to AVT04, a biosimilar to ustekinumab RP, in a real-world setting, encompassing both switching and naïve to ustekinumab scenarios.

Regardless of ustekinumab-switching or ustekinumab-naïve status, this study shows that the response to ustekinumab biosimilar remained consistent with previous findings, corroborating the sustained clinical efficacy [22]. In particular, in the ustekinumab-switched group, treatment with the biosimilar was consistently maintained over time, with a mean PASI score ranging from 0.6 (baseline) to 0.4 (week 28). This indicates that switching from the RP to the biosimilar preserved remission and safety in patients [22, 24]. The findings of the present study provide robust evidence for the continued safety and efficacy of treatment after switching, along with a reassuring treatment persistence profile and minimal nocebo effects during the biosimilar transition. Meanwhile, treatment in the ustekinumab-naïve group resulted in a reduction of the mean PASI score from 12.7 to 3.6 after 16 weeks. Additionally, no adverse event was reported during the study period, in line with other reports [25].

This study further explored the treatment response with the biosimilar within the ustekinumab-naïve cohort, with a particular focus on both bio-naïve and bio-experienced subgroups.

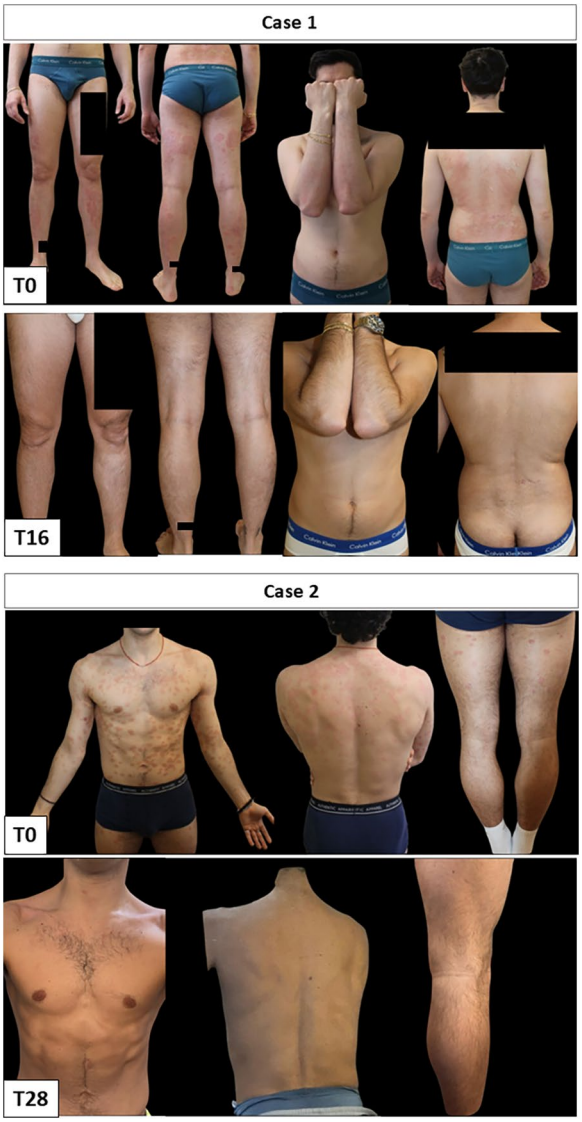

Fig. 4 Clinical cases of plaque psoriasis described in case 1 and case 2. Before treatment in case 1 (T0) and case 2 (T0); after treatment with AVT04 biosimilar for 16 weeks in case 1 (T16) and 28 weeks in case 2 (T28)

In light of the evolving treatment goals, the 2021 European Guideline for psoriasis management encouraged using PASI 90 and 100 scores over the conventional PASI 75, alongside DLQI as sensitive indicators of clinical outcomes and treatment success [11]. Based on these considerations, this real-world study shows that 28 weeks of treatment with the biosimilar led to remission in 47.3% of ustekinumab-naïve patients. This value is comparable to the results

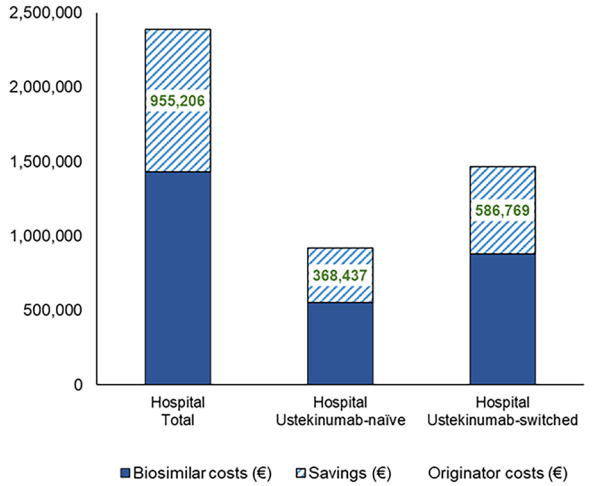

Fig. 5 Estimated annual cost savings associated with the use of biosimilar versus ustekinumab RP at hospital level. Bars represent yearly costs for the RP (outline) and AVT04 biosimilar (filled area), with the hatched segment indicating the annual savings. Results are shown for total, ustekinumab-naïve, and ustekinuamb-switched patient groups. *RP* reference product

of the registrative trial assessing the efficacy of AVT04 at week 28, in which approximately 40% of patients who either continued RP therapy or switched to AVT04 achieved PASI 100 [22]. Although the present study is limited by a smaller sample size, the alignment of PASI response across studies provides supportive evidence for the robustness of this real-world investigation on the treatment persistence and efficacy of AVT04 in routine clinical practice.

As shown by photographic records of two representative cases of bio-naïve patients, treatment with the biosimilar resulted in complete skin clearance and substantial improvement in quality of life, as indicated by PASI and DLQI outcomes. Moreover, while PASI 90 and PASI 100 scores steadily increased in all ustekinumab-naïve patients, a trend emerged showing greater improvement in PASI scores at the end of treatment among bio-naïve patients compared to those who were bio-experienced. Consistent with the trends of PASI 90 and 100, significantly more bio-naïve patients achieved PASI 75 by week 16 compared to bio-experienced patients. By week 28, no significant difference was observed, indicating similar treatment efficacy between the

groups. Therefore, even if superseded to some extent, the results obtained with the conventional PASI 75 score remain informative. It should be acknowledged, however, that the limited sample size of the ustekinumab-naïve group reduces the strength of the subgroup comparisons and should be treated with caution, with validation needed for larger, powered studies. Yet, bio-naïve patients may achieve a desirable outcome with this biologic when used as a primary therapeutic option. Supporting this observation, other studies have found that ustekinumab elicited a better response in naïve patients than those previously treated with biologic therapy [25]. Moreover, several retrospective studies with other anti-IL biologics suggest that bio-naïve patients tend to achieve a faster PASI response than bio-experienced patients [26, 27]. This finding aligns with another real-world European experience showing superior efficacy in terms of PASI 90 and 100 in bio-naïve patients treated with an anti-IL agent compared to those with prior experience of biologics [28].

Historically, anti-TNF inhibitors have been the first-line recommendation over anti-IL inhibitors largely because of the availability of marketed adalimumab biosimilars, with anti-IL inhibitors used as a second-line treatment after failure of initial therapy [11]. However, there is a growing consensus to redefine the role of anti-IL treatments for effective psoriasis management, considering both clinical evidence and financial pressures on healthcare systems [14, 15, 29, 30]. A real-life study has assessed whether previous exposure to biologic therapy might limit maximum clinical efficacy, whereas being biologically naïve could lead to substantial PASI improvements in patients receiving anti-IL treatments [30]. Taken together, ustekinumab biosimilars represent an affordable alternative and position this anti-IL as an essential biologic therapy [31].

Mounting evidence confirms the use of biosimilars as a strategic and affordable intervention with dual purposes: to facilitate patient care and improve the quality of life for people living with this condition, while also increasing healthcare market accessibility at a competitive price [17, 32, 33]. This view serves as a central tenet to ensure early and equitable access to treatment. With this in mind, ustekinumab and related biosimilars have been listed among the essential medicines for priority diseases by the World Health Organisation, owing to well-characterised safety and cost-effectiveness [31].

The results of the economic analysis further support optimal resource allocation, demonstrating that the use of biosimilar versus RP ustekinumab may generate substantial cost savings for the Italian NHS. Annual savings of nearly €1 million were estimated for the study cohort, corresponding to an average reduction of approximately €5200 per patient per year. These savings primarily derive from the lower cost of the biosimilar compared to the RP, assuming clinical outcome equivalence and comparable administration costs to those of the RP. Such findings emphasise the potential budgetary benefits of broader biosimilar adoption in psoriasis management, supporting more efficient healthcare resource allocation and wider patient access to advanced biologic therapies. Nevertheless, some limitations should be acknowledged. The cost-minimisation model relied on several simplifying assumptions, including the use of ex-manufacturer drug prices without accounting for confidential hospital discounts or regional procurement variations across Italian regions that may affect real-world costs. Because of regional autonomy in the management of healthcare services, such heterogeneity in procurement mechanisms may yield cost savings slightly lower than those modelled in this study. Furthermore, the analysis adopted a 1-year time horizon, which does not capture potential long-term effects such as treatment persistence, switching rates, or the impact of future price dynamics. Additionally, a 1-year time horizon cannot account for the potential risk of an immunogenic response arising from anti-drug antibody development that may emerge in the long-term and could affect safety and efficacy. Indirect costs and broader societal implications, such as productivity gains associated with improved disease control, were not considered. While indicative of substantial potential savings, these estimates should be viewed as conservative projections that require confirmation through longitudinal, real-world pharmacoeconomic studies.

In addition to being cost-saving, ustekinumab shows high patient adherence: in this study, ustekinumab-switching patients had

remained on treatment with the RP for over a decade before switching to the biosimilar. This reflects low discontinuation rates, in line with real-world evidence showing that favourable tolerability and convenient dosing makes ustekinumab a durable and patient-friendly option compared with other biologics [34, 35].

CONCLUSION

In the context of psoriasis management, clinical decision-making should aim to minimise the risk of therapeutic failure while enhancing adherence and long-lasting clinical outcomes in routine practice. Switching to ustekinumab biosimilar confirmed sustained clinical efficacy and safety comparable to RP treatment, underscoring its integration into real-world settings as a cost-saving therapeutic option. Although the small sample size and short observation period pose a limitation, the findings of this study encourage further investigation into the role of ustekinumab biosimilar in attaining a more beneficial response in patients who are naïve to biological therapies. Therefore, future studies are warranted to explore differences in therapeutic responses and rates of long-term remission across broader populations of bio-naïve and bio-experienced patients, to identify optimal responders who would most benefit from ustekinumab treatment.

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Data Availability. The datasets analysed in the present study are available upon reasonable request from the corresponding author, Marco Galluzzo.

Declarations

Conflict of Interest. Marco Galluzzo and Marina Talamonti have served as speakers and/or consultants for AbbVie, Almirall, Eli-Lilly, Johnson & Johnson, LeoPharma, Novartis, and Sanofi outside the submitted work. Luca Bianchi has served as a speaker and consultant for AbbVie, Novartis, Johnson & Johnson, Pfizer, UCB, and LeoPharma outside the submitted work. All other authors, Edoardo Mortato, Lorenzo Savastano, Lorenzo Marcelli, Lorenzo Tofani, Valerio Gneo, Domenico Marrapodi, Maria Rosa Ingrosso, have no relevant conflicts of interest to declare.

Ethical Approval. Institutional review board approval was waived, as data were collected as part of routine clinical practice. All patients provided written informed consent for the collection of demographic and clinical data. The study was conducted in accordance with the principles of the Declaration of Helsinki and later amendments. Data collection and management complied with all applicable laws, regulations, and guidelines concerning patient protection and privacy.

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