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ORIGINAL RESEARCH

Optimizing Tildrakizumab Dosing in Psoriasis: A 52-Week Multicenter Retrospective Study Comparing 100 mg and 200 mg—IL PSO (Italian Landscape Psoriasis)

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ABSTRACT

***Introduction*:** Tildrakizumab is a monoclonal antibody targeting interleukin (IL)-23 approved for the treatment of moderate-to-severe plaque psoriasis across two different dosages (100 mg and 200 mg). The higher dosage is recommended for patients with a body weight ≥ 90 kg or a high disease burden (Psoriasis Area and Severity Index [PASI] ≥ 16 or the involvement of difficult-to-treat areas). We conducted a 52-week multicenter retrospective study to compare the effectiveness and safety of both dosages and assess their impact on specific patient subgroups.

***Methods*:** We enrolled a total of 540 patients with high disease burden or body weight ≥ 90 kg; 177 and 363 were treated with tildrakizumab 200 mg and 100 mg, respectively. The effectiveness was evaluated in terms of PASI 90, PASI 100, and PASI ≤ 2 at weeks 16, 28, and 52. We also performed subanalyses according to the body weight (≥ 90 kg), PASI ≥ 16, prior biologic exposure, involvement of difficult-to-treat areas, and the presence of at least one cardiometabolic comorbidity.

***Results*:** After 16 weeks of treatment, a higher proportion of patients in the 200-mg group achieved PASI 90 and PASI 100 compared to those in the 100-mg group (43.5% vs. 34.3% and 36.4% vs. 24.2%, respectively). These results were sustained at 1 year, with PASI 90 and PASI 100 reached by 68.6% and 52.9% of patients in the 200-mg group, respectively, versus 57.3% and 35% in the 100-mg group. All subgroup analyses consistently indicated a trend toward greater effectiveness with tildrakizumab 200 mg, particularly in terms of PASI 90 and PASI 100 achievement at weeks 16 and 52. No differences in the safety profile were observed throughout the study period.

***Conclusion*:** Our findings confirm the superior effectiveness of tildrakizumab 200 mg over 100 mg in specific subgroups of patients with a comparable safety profile across the study period.

Keywords: Anti-IL-23; Biologics; Psoriasis; Real-Life; Tildrakizumab

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Key Summary Points

Why carry out this study?

Psoriasis is a chronic immune-mediated skin disease affecting 2–3% of the global population. Biological therapies have significantly improved the management of moderate-to-severe plaque psoriasis.

Tildrakizumab, an IL-23 inhibitor, is available in two dosages (100 mg and 200 mg), with higher doses suggested for patients with a high disease burden (PASI [Psoriasis Area and Severity Index] ≥ 16 or involvement of difficult-to-treat areas) or body weight ≥ 90 kg. However, real-world evidence on the long-term effectiveness and safety of the 200-mg dose is limited.

Our study aimed to compare the effectiveness and safety of tildrakizumab 100 mg versus 200 mg in a real-world setting.

What was learned from this study?

Patients treated with tildrakizumab 200 mg were more likely to achieve PASI 90 and PASI 100 after 16 weeks (PASI 90: 43.5% vs. 34.3%, $p = 0.041$; PASI 100: 36.4% vs. 24.2%, $p = 0.004$) and 52 weeks (PASI 90: 68.6% vs. 57.3%, $p = 0.028$; PASI 100: 52.9% vs. 35%, $p < 0.001$) compared to those treated with tildrakizumab 100 mg.

Our findings suggest that higher doses of tildrakizumab (200 mg) are beneficial for patients with high disease burden and high body weight, supporting a more personalized dosing approach.

Future research should explore additional predictive factors for dose optimization and long-term outcomes in different patient subgroups.

INTRODUCTION

Psoriasis is a chronic immune-mediated skin disease affecting approximately 2–3% of the global population [1]. Biological therapies have revolutionized the treatment landscape of moderate-to-severe plaque psoriasis, leading to substantial advancements in patient care and improvement in quality of life [2, 3]. These therapies provide targeted interventions that modulate pro-inflammatory cytokines, which represent key drivers of the inflammatory pathways responsible for disease onset, persistence, and relapse [1, 2]. Among these cytokines, interleukin (IL)-17 and IL-23 hold a key role in the pathogenesis of psoriasis [1, 2]. In particular, tildrakizumab is a humanized IgG1 monoclonal antibody selectively targeting the p19 subunit of IL-23. Specifically, it is the only IL-23 inhibitor available in two different dosages (100 mg or 200 mg) for the treatment of moderate to severe plaque psoriasis [4]. This allows physicians to tailor the dose to each patient's profile, ensuring a personalized treatment approach [4–7]. According to the Summary of Product Characteristics, dose selection remains flexible, with the 200-mg dose being a recommended option for patients weighing more than 90 kg or presenting with a high disease burden, defined by a Psoriasis Area and Severity Index (PASI) score ≥16 or the involvement of at least one difficult-to-treat area (including scalp/face, nails, genitalia, and palms/soles) [4]. The two phase 3 clinical trials, reSURFACE 1 and 2, showed greater efficacy in patients treated with tildrakizumab 200 mg compared to tildrakizumab 100 mg in cases of weight ≥90 kg or PASI ≥20 [8]. However, this difference was not statistically significant, but the authors suggested that the higher dose may provide greater clinical benefit [8]. This finding was further supported by a 5-year pooled analysis of reSURFACE studies, which demonstrated that the 200-mg dose had higher efficacy in patients with a body weight ≥120 kg [9]. Cardiometabolic comorbidities, including high body weight, are commonly associated with psoriasis and are well-recognized factors influencing psoriasis severity, progression, and therapeutic response to therapy [10–13]. Recent real-world studies have shown the effectiveness and safety of tildrakizumab 200 mg, particularly in patients with high body weight and/or high disease burden [5, 6, 14]. However, the

therapeutic implications of the 200-mg dose, especially regarding long-term outcomes, require further investigation.

This 52-week multicenter retrospective study aims to compare the effectiveness and safety of tildrakizumab 200 mg with tildrakizumab 100 mg in patients with moderate-to-severe plaque psoriasis. We considered body weight ≥ 90 kg and the high disease burden (PASI ≥ 16 or the involvement of difficult-to-treat areas) as variables predictive of a better response to the 200-mg dosage. By providing real-world insights, the study also seeks to optimize tildrakizumab dosing strategies for improved clinical outcomes and personalized psoriasis management.

METHODS

We conducted this multicentric retrospective by collecting data from databases of 23 Italian Dermatology Units from September 2023 to February 2025.

We enrolled 177 patients treated with tildrakizumab 200 mg for at least 16 weeks who had a body weight ≥ 90 kg or high disease burden, including those with a PASI score at baseline ≥ 16 or the involvement of difficult-to-treat areas (scalp/face, nails, genitalia, and palms/soles) [15]. We compared this group with 363 patients treated with tildrakizumab 100 mg who had the same characteristics at baseline (high disease burden or high body weight).

Patients' eligibility for tildrakizumab treatment was assessed according to the Italian Adaptation of EuroGuiDerm Guideline on the systemic treatment of chronic plaque psoriasis [16]. All patients received tildrakizumab 100 mg or 200 mg in accordance with the Summary of Product Characteristics [4].

Patients' clinical and demographic characteristics, including gender, age, weight, body mass index (BMI), cardiometabolic comorbidities, concomitant psoriatic arthritis (PsA), previous exposure to other biological agents, involvement of difficult-to-treat areas, and PASI score were obtained from the electronic medical records.

As a result of the retrospective design of the study, missing data could not be recovered or retrieved.

The effectiveness of tildrakizumab was evaluated at weeks 16, 28, and 52 in terms of the percentage of patients who achieved PASI 90 (reduction of at least 90% in PASI score from baseline) and PASI 100 (complete skin clearance). In accordance with the Italian Adaptation of EuroGuiDerm Guideline, we also evaluated the percentage of patients who achieved an absolute PASI score ≤ 2 at the same time points. Additionally, we performed subgroup analyses to compare the effectiveness of the two dosages in patients with a baseline weight ≥ 90 kg, those with a baseline PASI score greater or equal to 16, those with the involvement of difficult-to-treat areas, individuals with at least one cardiometabolic comorbidity, and patients who have failed at least another biological treatment. Safety was assessed by analyzing all adverse events (AEs) reported in the medical records at each follow-up visit.

Continuous variables were expressed as mean and standard deviation (SD), while categorical variables were reported as absolute numbers and percentages.

We evaluated the statistical differences between tildrakizumab 100 mg and 200 mg in terms of baseline characteristics and effectiveness outcomes at weeks 16, 28, and 52. We used a chi-squared test for categorical variables and Student's t test for continuous variables. A p value of ≤ 0.05 was considered statistically significant.

Statistical analysis was conducted using an "as observed" basis and was performed using Stata/SE 18.0. Tables and figures were generated using Microsoft Excel and GraphPad Prism 10.2.3, respectively.

Institutional review board approval was exempted as the study protocol did not deviate from standard clinical practice. All patients received tildrakizumab as in good clinical practice, in accordance with Italian guidelines. All included patients had provided written consent for retrospective study of data collected during routine clinical practice (demographics,

clinical scores). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy.

RESULTS

A total of 540 patients were enrolled in this study, with 363 receiving tildrakizumab 100 mg and 177 receiving tildrakizumab 200 mg. All patients in the 100-mg group completed at least 52 weeks of treatment, whereas 153 and 121 patients in the 200-mg group reached 28 and 52 weeks, respectively.

Regarding the tildrakizumab 100 mg cohort, 241 patients were male (66.4%), and 49 (13.5%) had a concomitant PsA. Similarly, among those receiving tildrakizumab 200 mg, 113 patients were male (63.8%), while 17 received a previous diagnosis of PsA (9.6%). Patients treated with tildrakizumab 100 mg had a higher mean age (55.44 years, SD 15.17) than those receiving tildrakizumab 200 mg (52.36 years, SD 14.10). Regarding prior exposure to other biologics, more patients in the 200-mg group were bio-experienced compared to the 100-mg group (49.7% vs. 36.1%). Other significant differences at baseline were observed in the body weight and BMI between the two groups. In particular, the mean body weight at baseline was 79.79 kg (SD 16.97) in the 100-mg group and 90.53 kg (SD 18.88) in the 200-mg group. Correspondingly, BMI was 26.90 kg/m^2 (SD 5.37) in the 100-mg cohort and 30.31 kg/m^2 (SD 6.15) in the 200-mg cohort. Patients receiving tildrakizumab 200 mg were more likely to have the involvement of at least one difficult-to-treat area, including nails, palms/soles, scalp, and genitalia, compared to those receiving 100 mg (71.8% vs. 33.1%). Furthermore, at least one cardiometabolic comorbidity (CMD), including type 2 diabetes mellitus, obesity, arterial hypertension, hypercholesterolemia, or cardiovascular disease, was observed in 92 patients (25.3%) in the 100-mg group and 119 patients (67.2%) in the 200-mg group. Additional characteristics at baseline of both groups are shown in Table 1.

Regarding the effectiveness, after 16 weeks of treatment, PASI 90 was reached by 34.3% of patients treated with tildrakizumab 100 mg compared with 43.5% of those receiving tildrakizumab 200 mg ($p = 0.041$). At the same time point, 24.2% of patients in the 100-mg group achieved a complete skin clearance (PASI 100) compared to 36.4% of those in the 200-mg group ($p = 0.004$). At 28 weeks of follow-up, the clinical outcomes were comparable without any statistically significant differences between the two cohorts. Specifically, PASI 90 and PASI 100 were achieved by 54.8% and 34.7% of patients receiving tildrakizumab 100 mg and by 54.9% and 38.6% of those receiving tildrakizumab 200 mg, respectively. After 1 year, PASI 90 was achieved by 57.3% of patients treated with tildrakizumab 100 mg compared to 68.6% of patients treated with tildrakizumab 200 mg ($p = 0.028$). At the same time point, complete skin clearance was observed in 35% and 52.9% of patients receiving tildrakizumab 100 mg and 200 mg, respectively ($p < 0.001$).

There were no statistically significant differences between the two cohorts in terms of absolute PASI throughout the study period. In particular, an absolute PASI ≤ 2 was reached by 53.3%, 73.3%, and 77.1% of patients treated with tildrakizumab 100 mg at 16, 28, and 52 weeks of follow-up, respectively. For the 200-mg group, the corresponding percentages were 54.8%, 72.6%, and 81.8% at each of the same time points during follow-up. Additional data regarding the effectiveness of tildrakizumab 100 mg and 200 mg in terms of PASI 90, PASI 100, and PASI ≤ 2 are shown in Fig. 1.

Furthermore, patients treated with tildrakizumab 200 mg consistently showed better treatment outcomes across multiple subgroups.

One hundred and six patients treated with tildrakizumab 100 mg weighed ≥ 90 kg at baseline, compared to 88 patients receiving tildrakizumab 200 mg. After 16 weeks, patients treated with tildrakizumab 200 mg were more likely to achieve complete skin clearance compared to those treated with 100 mg (43.2% vs. 23.6%, $p = 0.004$). After 1 year of treatment, these results

Table 1 Baseline demographic and clinical characteristics of patients treated with tildrakizumab 100 mg and those treated with tildrakizumab 200 mg

	100 mg (*n* = 363)	**200 mg (*n* = 177)**	***p* value**
	N (%)		
Male	241 (66.4)	113 (63.8)	0.558
Female	122 (33.6)	64 (36.2)	0.558
PsA	49 (13.5)	17 (9.6)	0.195
At least one difficult-to-treat area	120 (33.1)	127 (71.8)	< 0.001*
Bio-experienced	131 (36.1)	88 (49.7)	0.002*
At least one cardiometabolic comorbidity	92 (25.3)	119 (67.2)	< 0.001*
Weight ≥ 90 kg	106 (29.2)	88 (49.7)	< 0.001*
PASI ≥ 16	145 (39.9)	63 (35.6)	0.329
	Mean (SD)		
Age, years	55.44 (15.17)	52.36 (14.10)	0.024*
BMI, kg/m^2	26.90 (5.37)	30.31 (6.15)	< 0.001*
Body weight, kg	79.79 (16.97)	90.53 (18.88)	< 0.001*
PASI at baseline	14.34 (5.53)	13.37 (7.22)	0.086

PsA psoriatic arthritis, *BMI* body mass index, *SD* standard deviation, *PASI* Psoriasis Area and Severity Index

*Statistically significant (as $p \leq 0.05$)

were confirmed with the patients in the 200-mg group showing better performance in terms of PASI 90, PASI 100, and PASI ≤2 (83.1% vs 50%, $p < 0.001$; 67.8% vs. 31.1%, $p < 0.001$; 89.8% vs. 75.5%, $p = 0.025$, respectively) (Fig. 2).

At baseline, severe psoriasis (PASI ≥16) was recorded in 145 patients receiving tildrakizumab 100 mg versus 63 treated with tildrakizumab 200 mg. Those treated with tildrakizumab 200 mg were more likely to achieve PASI 100 at weeks 16 (34.9% vs. 20.7%, $p = 0.029$) and 52 (62.3% vs. 31%, $p < 0.001$) and PASI 90 at week 52 (77.4% vs. 57.9%, $p = 0.012$) (Fig. 3).

Among 120 and 127 patients with at least one difficult-to-treat area in the 100-mg and 200-mg groups, respectively, the higher-dose group showed better PASI 90 (43.1% vs. 27.5%, $p = 0.01$) and PASI 100 (37% vs. 20.8%, $p = 0.005$) at week 16. These differences remained statistically significant at 1 year of follow-up (PASI 90: 70.2% vs. 53.3%, $p = 0.015$; PASI 100: 56% vs. 30.8%, $p < 0.001$) (Fig. 4).

We also performed a subgroup analysis based on previous exposure to other biologics. One hundred and thirty-one patients treated with tildrakizumab 100 mg and 80 treated with tildrakizumab 200 mg were bio-experienced. Patients receiving the 200 mg had a higher rate of PASI 100 at week 16 (38.6% vs. 22.9%, $p = 0.012$) and PASI 90 (75.4% vs. 53.4%, $p = 0.003$) and PASI 100 (63.1% vs. 31.3%, $p < 0.001$) at week 52 compared to those treated with the lowest dosage (Fig. 5).

Regarding the presence of cardiometabolic comorbidities, patients in the 200-mg group achieved better PASI 100 responses at week 16 (42% vs. 26.1%, $p = 0.016$). At week 52, PASI 90 was achieved by 76.5% of patients treated with 200 mg, versus 56.5% of those receiving tildrakizumab 100 mg ($p = 0.006$), while complete skin

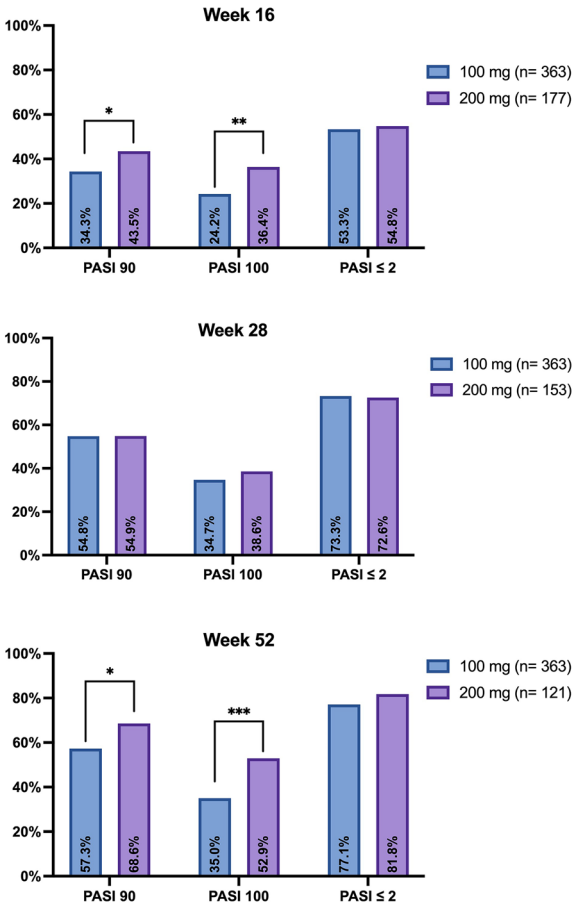

Fig. 1 Effectiveness of tildrakizumab 100 and 200 mg in terms of PASI 90, PASI 100, and PASI ≤ 2 throughout the study period. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

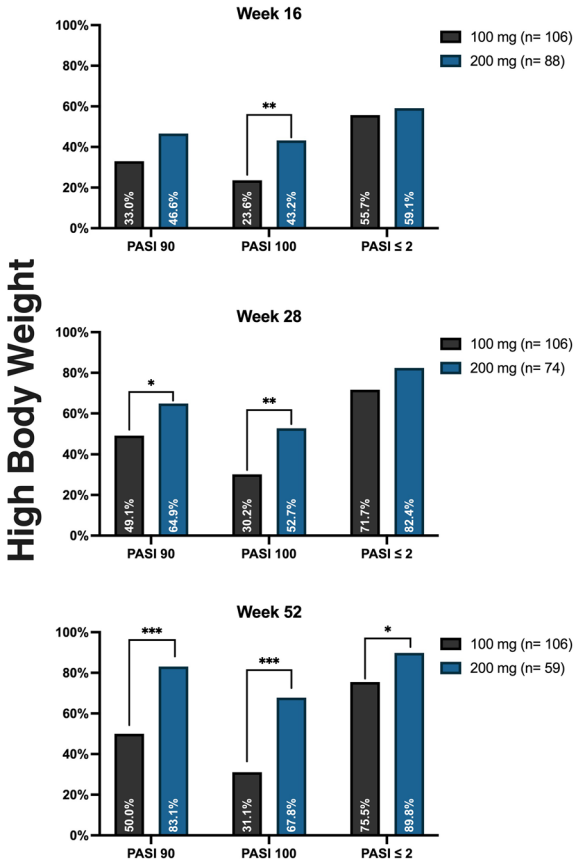

Fig. 2 Percentage of patients achieving PASI 90, PASI 100, and PASI ≤ 2 throughout the study period according to body weight ≥ 90 kg. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

clearance (PASI 100) was reached by 64.2% of them versus 32.6% ($p < 0.001$) (Fig. 6).

Regarding safety, no severe AEs or AEs that led to discontinuation were observed (Table 2). There were no statistically significant differences between the two groups. The most frequently reported AE was upper respiratory tract infection, affecting 17 patients, followed by headache in 3 patients. Three patients tested positive for TB QuantiFERON. However, no signs of reactivation were detected during annual thoracic radiography and pulmonology visits. Similarly, although eight patients showed serological evidence of chronic viral hepatitis (six with hepatitis B and two with hepatitis C), follow-up laboratory assessments and periodic hepatology visits revealed no signs of viral reactivation throughout the course of tildrakizumab treatment.

DISCUSSION

Tildrakizumab was assessed in the phase 3 clinical trials reSURFACE 1 and reSURFACE 2 at two different dosages (100 mg and 200 mg), showing comparable efficacy and safety throughout the study period [3, 8]. However,

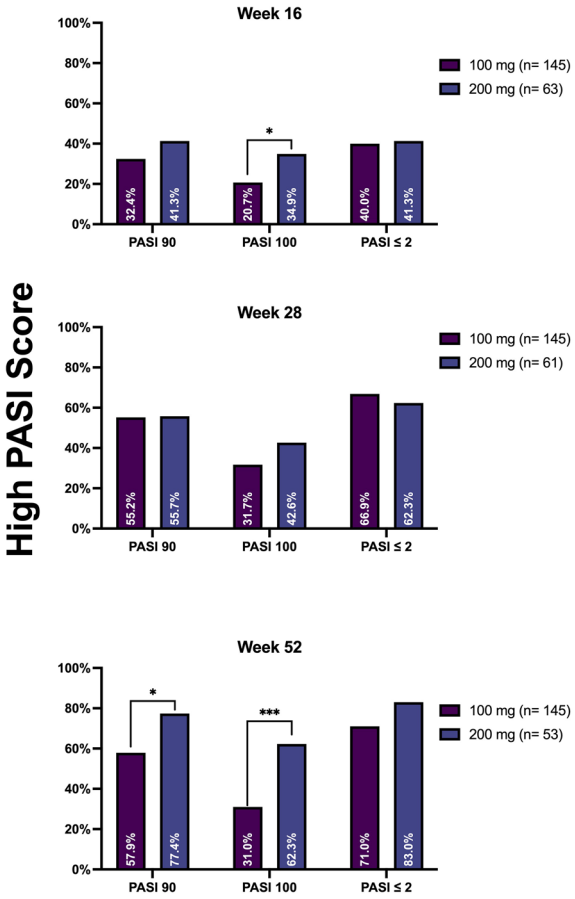

Fig. 3 Percentage of patients achieving PASI 90, PASI 100, and PASI ≤ 2 throughout the study period according to PASI ≥ 16. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

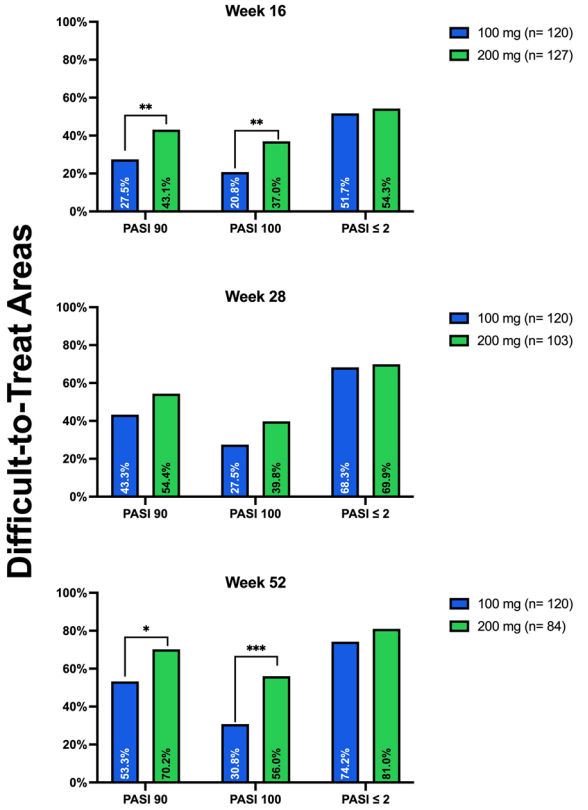

Fig. 4 Percentage of patients achieving PASI 90, PASI 100, and PASI ≤ 2 throughout the study period according to the involvement of difficult-to-treat areas. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

evidence resulting from post hoc analyses and real-world studies suggests that specific patient characteristics, such as body weight, baseline PASI score, and involvement of difficult-to-treat areas, may influence treatment response and could guide clinical dosage management [5–7, 9]. In particular, in the post hoc analysis, Thaçi et al. examined the impact of body weight on treatment outcomes, highlighting that patients weighing more than 120 kg had better clinical responses to the 200-mg dose. In addition, although no statistically significant differences in PASI < 3 and PASI < 1 response rates were observed between those above or below 90 kg over the study period, the analysis showed better PASI < 3 responses in patients with a body weight ≥ 90 kg treated with tildrakizumab 200 mg compared to those treated with tildrakizumab 100 mg at 28 weeks [9]. In our study, we observed slightly higher effectiveness in patients with a body weight of 90 kg or more treated with tildrakizumab 200 mg. Specifically, after 28 weeks of follow-up, 82.4% of our patients achieved a PASI ≤ 2, while PASI < 3 was reached by 66.3% of patients in the pooled analyses. After 1 year, 89.8% of our patients achieved a PASI ≤ 2, while 84.5% of patients in the pooled analyses achieved a PASI < 3 [9].

Obesity influences the pharmacokinetics and pharmacodynamics of biological therapies, potentially requiring dosage adjustments to achieve optimal therapeutic outcomes [12, 13, 17]. Since biologics are primarily distributed within the vascular compartment, excess

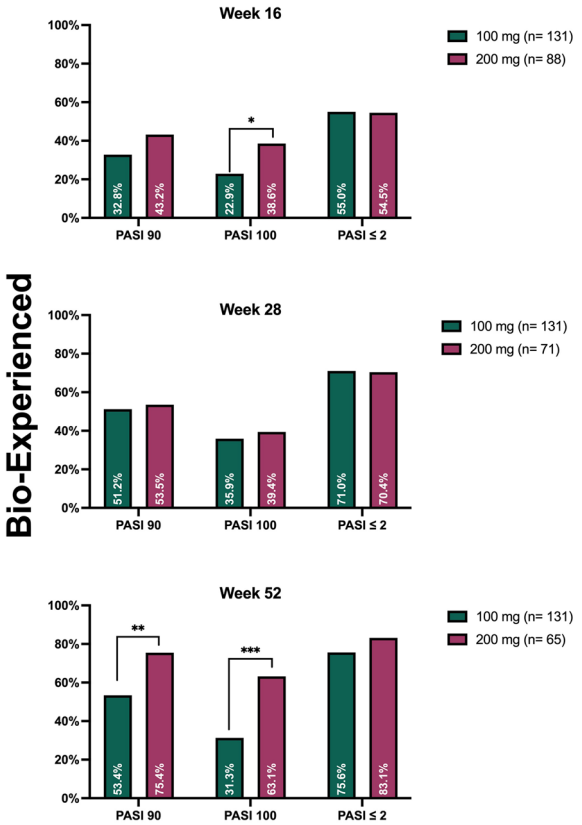

Fig. 5 Percentage of patients achieving PASI 90, PASI 100, and PASI ≤ 2 throughout the study period according to the previous exposure to other biological treatments. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

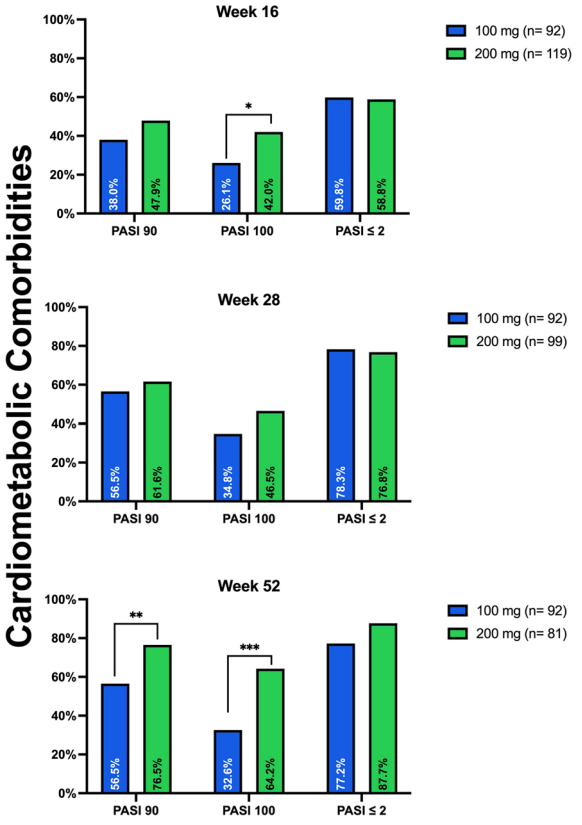

Fig. 6 Percentage of patients achieving PASI 90, PASI 100, and PASI ≤ 2 throughout the study period according to the presence of cardiometabolic comorbidities. *PASI* Psoriasis Area and Severity Index; $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

adipose tissue may alter drug distribution and clearance, reducing efficacy at standard doses [18, 19]. This effect may be of particular relevance when considering the pharmacokinetics of monoclonal antibodies, given the established association between obesity and altered drug clearance and distribution. Consequently, higher dosages may be required to achieve optimal therapeutic outcomes [18, 19].

Moreover, a pooled analysis by Papp et al. showed higher efficacy rates in patients with a higher body weight treated with the 200-mg dosage [18].

These results highlight the necessity of identifying baseline cutoff values for weight and PASI at baseline based on real-world clinical practice data that can drive clinicians to optimize dose selection and enhance patient outcomes. Data

Table 2 Safety profile of tildrakizumab 100 mg and tildrakizumab 200 mg during the whole study follow-up period

AE	Total	100 mg	200 mg	*p* value
URTIs	17 (3.1%)	11 (3%)	6 (3.4%)	0.447
Headache	3 (0.6%)	2 (0.6%)	1 (0.6%)	0.874
Total	20 (3.7%)	13 (3.6%)	7 (4%)	0.326
Severe AEs	0	0	0	N/A
AEs leading to discontinuation	0	0	0	N/A

AE adverse event, *URTI* upper respiratory tract infection, *N/A* not applicable

from real-world studies suggest that patients with a higher disease burden (PASI ≥ 16 and/or involvement of difficult-to-treat areas) or a body weight ≥ 90 kg could benefit significantly from the 200-mg dosage [5–7]. Our study reinforces these findings and provides valuable real-world insights into the long-term comparative effectiveness and safety of tildrakizumab 100 mg and 200 mg in the treatment of moderate-to-severe psoriasis.

Our study demonstrated that the clinical response to tildrakizumab 200 mg is particularly marked in patients with a high disease burden and a body weight of ≥ 90 kg, especially at weeks 16 and 52. These findings suggest that higher dosing may be a necessary strategy for optimizing treatment outcomes in these subgroups. The improved outcomes at week 52 reinforce the importance of long-term follow-up in psoriasis management and suggest that the full therapeutic benefit of tildrakizumab may manifest over time. These findings are consistent with those from clinical trials and real-world evidence, emphasizing the importance of baseline characteristics, such as body weight and disease severity, in predicting biological treatment response [19–21]. The clinical management of moderate-to-severe psoriasis should consider each patient's characteristics and potential risk factors, ensuring a personalized treatment approach. Notably, in our study, patients with the involvement of difficult-to-treat areas and those who have previously failed another biologic demonstrated a greater benefit from the 200-mg dosage, suggesting that these subgroups of patients may particularly benefit from a higher dosage regimen. The impact of cardiometabolic comorbidities on treatment response should also be considered. Several studies have suggested that insulin resistance, obesity, and other cardiometabolic disorders may contribute to a chronic pro-inflammatory state that contributes to the persistence, worsening, and relapse of psoriasis [10–13]. As a result, increasing attention has been given to the concurrent management of these comorbidities to enhance the effectiveness of biological therapies. Our findings showed that patients with at least one cardiometabolic comorbidity exhibited enhanced responses to tildrakizumab 200 mg. However, a recent real-world study by Ibba et al. has shown no statistically significant differences between patients with and without cardiometabolic comorbidities treated with risankizumab, confirming the effectiveness of IL-23 inhibitors also in this subgroup of patients [11]. Obesity represents a cardiometabolic comorbidity more prevalent in patients with psoriasis than in the general population [17, 22]. However, its bidirectional relationship with psoriasis remains an active area of research and is not yet fully understood. Recent studies indicate that adipokines, pro-inflammatory molecules secreted by adipocytes, may play a role in psoriasis pathogenesis by amplifying systemic inflammation [12, 22]. Di Vincenzo et al. recently demonstrated that insulin can stimulate IL-23 expression in human adipocytes, providing a mechanistic insight into the link between obesity and psoriasis [12]. Furthermore, Cacciapuoti et al. found that treatment with tildrakizumab significantly reduced adipokine levels (resistin and leptin), with a more pronounced decrease observed in fast responders compared to slow responders, suggesting a potential connection between adipokine modulation and clinical outcomes [23].

Real-world studies have suggested that obesity may be a potential predictor of improved clinical response to tildrakizumab 200 mg. Notably, De Brizzi et al. reported a higher rate of patients achieving PASI ≤ 5 at week 16 among those with a BMI greater than 30, suggesting that tildrakizumab 200 mg was particularly effective in patients with obesity [5].

Our study did not identify any significant safety findings, and there were no differences in the frequency or type of common AEs between the two dosing regimens. The most commonly reported AEs were mild and did not lead to treatment discontinuation. No reactivation of latent tuberculosis or viral hepatitis was observed throughout the study period, confirming previous research on IL-23 inhibitors [24]. These findings confirm the favorable risk–benefit

profile of tildrakizumab 200 mg, even in patients with different comorbidities.

Our study's real-world design allows for a broader patient population than clinical trials. Unlike randomized controlled trials, which often impose strict inclusion and exclusion criteria, our study included patients with multiple comorbidities, prior biological failures, and heterogeneous baseline PASI scores. This enhances the generalizability of our findings to everyday clinical practice.

Our study has a few limitations, the first being its retrospective design. The second limitation is that patients in the two groups were enrolled during different time frames as a result of the later approval of the 200-mg dosage in Italy. An additional limitation is the presence of baseline demographic differences in body weight, prior biological exposure, and the presence of difficult-to-treat areas between the two treatment groups, which may have influenced treatment response. Lastly, as this was a multicenter study, patients were assessed by different clinicians, which may have led to heterogeneous clinical outcomes assessments.

CONCLUSION

This real-world study highlights the superior effectiveness of tildrakizumab 200 mg compared to the 100-mg dose in patients with higher disease burden or body weight ≥90 kg, particularly at weeks 16 and 52. Importantly, the comparable safety profiles of both regimens reinforce the clinical utility of the 200-mg dose in selected patient populations who may benefit from higher dosage while confirming the effectiveness of the 100-mg dose in achieving satisfactory responses in other subsets. These findings support a more personalized approach to biological therapy in psoriasis, where baseline characteristics can help guide optimal dosing decisions. Further prospective studies are needed to validate these observations and to better define predictive factors for enhanced treatment response.

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Author Contributions. All authors contributed to the conception and design of the study. Material preparation and data analysis were conducted by Luciano Ibba, Mario Valenti, Sara Di Giulio and Luigi Gargiulo. Data collection was performed by Piergiorgio Malagoli, Anna Balato, Federico Bardazzi, Martina Burlando, Anna E. Cagni, Norma Cameli, Francesco Loconsole, Carlo G. Carrera, Andrea Carugno, Aldo Cuccia, Paolo Dapavo, Eugenia V. Di Brizzi, Valentina Dini, Maria Concetta Fargnoli, Francesca M. Gaiani, Claudio Guarneri, Claudia Lasagni, Gaetano Licata, Angelo V. Marzano, Matteo Megna, Santo R. Mercuri, Alessandra Michelucci, Maria L. Musumeci, Diego Orsini, Romina Ortega, Luca Potestio, Luca Rapparini, Simone Ribero, Francesca Satolli, Davide Strippoli, Emanuele Trovato, Marina Venturini, and Leonardo Zichichi. The first draft of the manuscript was written by Luciano Ibba, Sara Di Giulio, and Mario Valenti, and all authors commented on previous versions of the manuscript. Alessandra Narcisi and Mario Valenti performed the review and the editing of the final draft of the manuscript. Alessandra Narcisi and Antonio Costanzo supervised the study. All authors read and approved the final manuscript.

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

Declarations

Conflict of Interest. Mario Valenti has been a consultant and/or speaker for Sanofi, Leo Pharma, Eli Lilly, Novartis, Janssen, AbbVie, and Boehringer Ingelheim. Mario Valenti is an Editorial Board member of *Dermatology and Therapy*.

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Ethical Approval. Institutional review board approval was exempted as the study protocol did not deviate from standard clinical practice. All patients received tildrakizumab as in good clinical practice, in accordance with European guidelines. All included patients had provided written consent for retrospective study

of data collected during routine clinical practice (demographics, clinical scores). The study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy.

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