Journal of Dermatological Treatment

ISSN: 0954-6634 (Print) 1471-1753 (Online) Journal homepage: www.tandfonline.com/journals/ijdt20

Effectiveness of tildrakizumab 200 mg: an Italian multicenter study

Annunziata Dattola, Nicoletta Bernardini, Francesca Svara, Anna Balato, Giacomo Caldarola, Domenico D'Amico, Clara De Simone, Eugenia Veronica Di Brizzi, Maria Esposito, Claudia Giofrè, Domenico Giordano, Claudio Guarneri, Francesco Loconsole, Viviana Lora, Gaia Moretta, Diego Orsini, Severino Persechino, Concetta Potenza, Simone Ragonesi, Giovanni Pellacani, Ketty Peris, Maria Concetta Fargnoli & Antonio Giovanni Richetta

To cite this article: Annunziata Dattola, Nicoletta Bernardini, Francesca Svara, Anna Balato, Giacomo Caldarola, Domenico D'Amico, Clara De Simone, Eugenia Veronica Di Brizzi, Maria Esposito, Claudia Giofrè, Domenico Giordano, Claudio Guarneri, Francesco Loconsole, Viviana Lora, Gaia Moretta, Diego Orsini, Severino Persechino, Concetta Potenza, Simone Ragonesi, Giovanni Pellacani, Ketty Peris, Maria Concetta Fargnoli & Antonio Giovanni Richetta (2024) Effectiveness of tildrakizumab 200 mg: an Italian multicenter study, Journal of Dermatological Treatment, 35:1, 2420825, DOI: 10.1080/09546634.2024.2420825

To link to this article: https://doi.org/10.1080/09546634.2024.2420825

Published online: 27 Oct 2024.

JOURNAL OF DERMATOLOGICAL TREATMENT
2024, VOL. 35, NO. 1, 2420825
https://doi.org/10.1080/09546634.2024.2420825

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Effectiveness of tildrakizumab 200 mg: an Italian multicenter study

Annunziata Dattola[a], Nicoletta Bernardini[b], Francesca Svara[a], Anna Balato[c], Giacomo Caldarola[d,e], Domenico D'Amico[f], Clara De Simone[d,e], Eugenia Veronica Di Brizzi[c], Maria Esposito[g], Claudia Giofrè[h], Domenico Giordano[i], Claudio Guarneri[j], Francesco Loconsole[k], Viviana Lora[l], Gaia Moretta[m], Diego Orsini[l], Severino Persechino[i], Concetta Potenza[b], Simone Ragonesi[a], Giovanni Pellacani[a], Ketty Peris[d,e], Maria Concetta Fargnoli[g] and Antonio Giovanni Richetta[a]

[a]Dermatology Unit, Department of Clinical Internal, Anesthesiological and Cardiovascular Science, University of La Sapienza, Rome, Italy; [b]Department of Medical-Surgical Sciences and Biotechnologies, Dermatology Unit "Daniele Innocenzi", Sapienza University of Rome, Polo Pontino, Italy; [c]Department of Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy; [d]Institute of Dermatology, Università Cattolica del Sacro Cuore, Rome, Italy; [e]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [f]Dermatology unit in Hospital Facility "A. Pugliese" and UOC "R.Dulbecco", Catanzaro, Italy; [g]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [h]Dermatology UOC "Papardo" Hospital, Messina, Italy; [i]Sant'Andrea Hospital University of Rome, Rome, Italy; [j]Department of Biomedical, Dental Sciences and Morphofunctional Imaging, Section of Dermatology, University of Messina, Messina, Italy; [k]Division of Dermatology, University Hospital Consorziale, Bari, Italy; [l]Division of Dermatology, San Gallicano Dermatological Institute, IRCCS, Rome, Italy; [m]Department of Dermatology, Istituto Dermopatico dell'Immacolata IRCCSRome, Italy

ABSTRACT

Introduction: Psoriasis is a chronic immune-mediated disease that can be challenging to treat, especially in patients with severe disease or high body weight. Tildrakizumab is a monoclonal antibody which inhibits IL-23, approved for moderate-to-severe psoriasis with a standard 100 mg dose. A 200 mg dose may provide greater efficacy for patients over 90 kg or with high disease burden.

Methods: This multicenter, prospective study evaluated the effectiveness and safety of tildrakizumab 200 mg in patients with moderate-to-severe psoriasis, focusing on those with specific challenges: body weight over 90 kg, baseline PASI ≥20, and difficult-to-treat areas. The study also compared bio-naive versus bio-experienced and male versus female patients. Adults received tildrakizumab 200 mg subcutaneously at weeks 0 and 4, then every 12 weeks.

Results: Clinical improvements were assessed using PASI, DLQI, genital PASI, and NAPSI scores. After 24 weeks, the mean PASI score dropped from 14.6 to 0.4, with PASI 90 and PASI 100 scores exceeding 80% (100.0% and 80.3%, respectively). DLQI scores improved from 14.2 to 1.8, and significant improvements were seen in genital PASI and NAPSI scores. No significant adverse events occurred.

Conclusions: Tildrakizumab 200 has been shown to be an effective therapeutic option, particularly for patients with high body weight, significant disease burden, and involvement of sensitive areas with no new safety signals.

ARTICLE HISTORY
Received 16 September 2024
Accepted 14 October 2024

KEYWORDS
Effectiveness; psoriasis; tildrakizumab; tildrakizumab 200 mg; anti-IL23

Introduction

Psoriasis is a chronic immune-mediated inflammatory skin disorder with a global estimated prevalence of 2-3% (1). A variety of treatments are available for patients with psoriasis, including phototherapy, as well as topical and systemic therapies (2). Variability in drug response is influenced by factors such as disease severity, comorbidities, genetic profile, and overall clinical condition. Emerging evidence underscores the correlation between disease severity and excess weight, as well as its impact on the efficacy of various treatments (3–5). Biological therapies have revolutionized the management of psoriasis by targeting specific immune pathways like Interleukin (IL)-23 and IL-17, which play pivotal roles in the inflammatory process (6). Recent studies emphasize the importance of personalized therapy to enhance therapeutic outcomes, reduce side effects, and optimize treatment efficacy (7). Tildrakizumab is a monoclonal antibody approved for the treatment of moderate to severe psoriasis. It selectively targets the p19 subunit of IL-23, blocking its interaction with its receptor and thereby inhibiting the IL17-TH17 pathway (8). It is approved with a standard dose of 100 mg at weeks 0, 4, and subsequently every 12 weeks. However, an increased dose of 200 mg may be considered for patients with specific characteristics, such as a high disease burden or body weight over 90 kg (9). Pharmacokinetic studies reveal reduced drug exposure with increasing body weight, with a typical 30% reduction in exposure among adult patients weighing over 90 kg compared to their counterparts (4). Notably, dosage adjustments during therapy afford significant flexibility (10,11). The aim of our study was to evaluate the effectiveness of tildrakizumab 200 mg in patients with moderate-to-severe psoriasis with a focus on patients with a body weight over 90 kg and/or presenting PASI ≥ 20 or involvement of difficult to treat areas, bio-naive versus bio-experienced patients and male vs female patients.

CONTACT Francesca Svara francescasvara@gmail.com Dermatology Unit, Department of Clinical Internal, Anesthesiological and Cardiovascular Science, University of La Sapienza, Rome, Italy

Materials and methods

Study design

This is an observational, prospective, multicenter, real-world study, performed in 12 sites in central and southern Italy. A total of 89 patients were enrolled between October 2023 and January 2024, with an observation period lasting 24 weeks; additional data will be collected for up to one year. All patients included in our study had a body weight above 90 kg and/or a high disease burden (PASI ≥ 20 or the involvement of difficult-to-treat areas). Patients' eligibility for tildrakizumab treatment was assessed according to the Italian Adaptation of euroGuiDerm guideline on the systemic treatment of chronic plaque psoriasis (12). Tildrakizumab was administered in line with standard clinical practice, adhering to AIFA appropriateness criteria and the product's summary of characteristics. The dosing regimen consisted of one subcutaneous injection of 200 mg tildrakizumab at Weeks 0 and 4, followed by subsequent injections every 12 weeks. All patients enrolled have signed the informed consensus. All patients enrolled have signed the informed written consensus to take part in the research prior to the commencement of the study. The study has been conducted accordingly to the Declaration of Helsinki.

Primary end point

The primary endpoint consisted in assessing the effectiveness of tildrakizumab 200 mg over time evaluating the improvement in psoriasis severity using the Psoriasis Area and Severity Index (PASI) scores. The evaluation was carried out at different time points (baseline, week 4, week 16, week 24) and the percentage of patients achieving significant reductions in PASI scores from baseline was assessed (e.g. PASI90 and PASI100).

Secondary end points

Secondary end points consisted in assenting the clinical improvement for patients suffering from genital, palmoplantar and/or nail psoriasis. GPASI (Genital PASI) and NAPSI score (Nail Psoriasis Severity Index) as well as DLQI (Dermatology Life Quality Index) have been also evaluated.

Statistical analysis

The sample has been described in its clinical and demographic characteristics applying descriptive statistics techniques. Qualitative variables have been described with absolute frequencies and percentage; quantitative variables have been summarized with mean and standard deviation. Normality test has been performed applying the Wilcoxon signed rank test. To evaluate the efficacy of tildrakizumab 200 mg, PASI and DLQI have been considered. Results from PASI score, NAPSI, G-PASI and DLQI have been, for each time points, described applying the already mentioned descriptive statistics techniques. To evaluate the efficacy of tildrakizumab 200 mg, changes over times of PASI score, DLQI score, G-PASI and NAPSI have been investigated. A Friedman test has been performed on PASI, G-PASI and NAPSI score (given the violation of normality) with Bonferroni correction for multiple comparisons. To evaluate the changes over time of DLQI score the Wilcoxon Signed Rank Test has been performed. Four subgroup analyses were performed comparing the therapeutic response, in terms of PASI and DLQI improvement, in patients with a body weight over 90 kilograms, in patients presenting a high disease burden (PASI score at baseline over 20), bio-naïve patients vs bio-experienced and males vs females; an ANOVA mixed model for repeated measures has been applied. Tildrakizumab 200 mg safety was evaluated investigating the frequency and the severity of adverse events. A p-value < 0.05 was considered as significant. Analyses were performed using R version 4.1.2 (2021-11-01).

Results

A total of 89 patients, 70.8% males and 29.2% females, with mean age of 50 years (SD = 13.7) have been included in the study. The diagnosis was psoriasis (PsO) for all the 89 patients. Concerning the affected body areas, 12 patients (13.5%) presented genital psoriasis, 11 patients (12.4%) nail psoriasis and 11 patients (12.4%) palmoplantar psoriasis. Two patients (2.2%) presented all of the three areas as affected. A total of 8 patients (8.9%) presented a combination of two affected areas. The mean age of disease onset was 34.1 years (SD = 13.6) and the mean disease duration was 16.1 years (SD= 11.9). The mean BMI was 30.1 (SD= 5.1) and 84.3% of patients presented a BMI higher than 25. Concerning therapies, 75.3% of patients underwent a traditional systemic therapy and 43.8% were bio-naïve. The majority of sampled patients (66.3%) presented comorbidities. Patients classified as having a high disease burden (PASI score at baseline ≥20) were 27 (30.3%). Table 1 describes

Table 1. Clinical and demographic characteristics of the sample ($N = 89$).

Sex (n; %)		
M	63	70.8
F	26	29.2
Diagnosis (n; %)		
PsO	89	100.0
Details about psoriasis affecting genital, ungual or palmoplantar area (n; %)		
No difficult-to-treat areas	45	50.6
Genital	12	13.5
Palmoplantar	11	12.4
Ungual	11	12.4
Palmoplantar and Ungual	5	5.6
Genital and Ungual	2	2.2
Palmoplantar and Genital and Ungual	2	2.2
Palmoplantar and Genital	1	1.1
Age (mean; SD)	50.1	13.7
BMI (mean; SD)	30.1	5.1
Disease onset age (years) (mean; SD)	34.1	13.6
Disease duration (years) (mean; SD)	16.1	11.9
Traditional therapy (n; %)		
Yes	67	75.3
No	22	24.7
Bio-Naive (n; %)		
No	50	56.2
Yes	39	43.8
Comorbidities (n; %)		
Yes	59	66.3
No	30	33.7
Comorbidities [(1)] (n; %)		
Dismetabolic	44	
Dislipidemia	42	
Cardiometabolics	20	
CVD	8	
Cancer	5	
COPD	1	
Depression	1	
other	6	
Weight (cutoff = 90 kg)		
≥90	50	56.2
<90	39	43.8
BMI (cutoff = 25)		
≥25	75	84.3
<25	14	15.7
Baseline PASI (cutoff = 20)		
<20	62	69.7
≥20	27	30.3

PsO: Psoriasis; SD: Standard Deviation; BMI: Body Mass Index; (1)=Number of times a certain group of pathologies has been mentioned; each patient could indicate more than one disease.

clinical and demographic details about the sample and Table 2 for details about administered therapies prior to tildrakizumab.

PASI score

At baseline the mean **PASI** score was 14.6 (SD = 7.7), with a minimum of 2 and a maximum of 38 points. After 4 weeks of treatment, PASI scores reduced reaching a mean value of 6.0 (SD = 4.7), with a minimum of 0 and a maximum score of 19 points. After 16 weeks of treatment the mean PASI score was 1.1 (SD = 1.7) and during the last follow-up (24 weeks) the mean PASI score reached the mean value of 0.4 (SD = 1.0). A Friedman test highlighted that there were differences in PASI score between the timepoints ($p < 0.0001$). Pairwise comparisons were performed with a Bonferroni correction for multiple comparisons and only the comparison between week 16 and week 24 PASI score was not statistically significantly different ($p = 0.106$). Concerning PASI-90 and PASI-100, after 4 weeks of treatment 98.7% of patients achieved PASI-90 and 9.7% achieved PASI-100. By the end of the follow-up 100.0% of patients achieved PASI-90 and 80.3% achieved PASI-100 (see Table 3 and Figures 1 and 2).

DLQI score

DLQI score decreased significantly from baseline to week 24. The median value at baseline was 14.0 and at week 24 was 0.0 (Table 4). The Wilcoxon signed rank test highlighted a significant difference between the two considered time points, $p < 0.001$.

Table 2. Distribution of traditional systemic therapy and distribution of biologics therapy administered prior to tildrakizumab.

A: Distribution of traditional systemic therapy ($N = 67$)		
	n	%
Methotrexate	20	29.9
Cyclosporin	17	25.4
Methotrexate Cyclosporin	11	16.4
Acitretin	6	9.0
Acitretin Methotrexate	2	3.0
Cyclosporin Steroids	2	3.0
Dimethyl fumarate	2	3.0
Acitretin Apremilast	1	1.5
Cyclosporin Acitretin	1	1.5
Cyclosporin Steroids Methotrexate	1	1.5
Phototherapy	1	1.5
Methotrexate Steroids	1	1.5
Methotrexate Steroids Topic calcipotriol	1	1.5
Steroids	1	1.5
Total	67	100.0
B: Distribution of biologics therapy ($N = 50$)		
	n	%
ADALIMUMAB	18	36.0
ETANERCEPT	7	14.0
TILDRAKIZUMAB 100	5	10.0
BRODALUMAB	3	6.0
ADALIMUMAB - INFLIXIMAB - USTEKINUMAB	2	4.0
ADALIMUMAB - SECUKINUMAB	2	4.0
RISANKIZUMB - TILDRAKIZUMAB 100	2	4.0
SECUKINUMAB	2	4.0
USTEKINUMAB	2	4.0
ADALIMUMAB - BRODALUMAB	1	2.0
ANTI TNF-α	1	2.0
ETANERCEPT - SECUKINUMAB	1	2.0
ETANERCEPT - TILDRAKIZUMAB 100	1	2.0
IXEKIZUMAB	1	2.0
RISANKIZUMAB	1	2.0
SECUKINUMAB - TILDRAKIZUMAB 100	1	2.0
TOTAL	50	100.0

G-PASI score

Concerning the **G-PASI** (17 patients affected; 19.1%), at baseline the mean G-PASI score was 6.71 (SD = 3.46), with a minimum of 2 and a maximum of 14 points. After 4 weeks of treatment, G-PASI scores had reduced reaching a mean value of 1.87 (SD = 1.55). After 16 weeks of treatment the mean G-PASI score was 0.18 (SD = 0.5) and these results remained stable until the end of the study; see Table 5. A Friedman test highlighted that there were differences in G-PASI score between the timepoints ($p < 0.001$). Pairwise comparisons highlighted that the comparisons between baseline and all the other timepoints were

Table 3. Descriptive statistics for PASI score at each timepoint.

	PASI_BL	PASI_WEEK_4	PASI_WEEK_16	PASI_WEEK_24
N	89	82	82	71
Mean	14.6	6.0	1.1	0.4
Std.dev.	7.7	4.7	1.7	1.0
Median	13.0	4.9	0	0
Min	2	0	0	0
Max	38	19	10	5
PASI 90		81/82 (98.7%)	82/82 (100.0%)	71/71 (100.0%)
PASI 100		8/82 (9.7%)	42/82 (51.2%)	57/71 (80.3%)

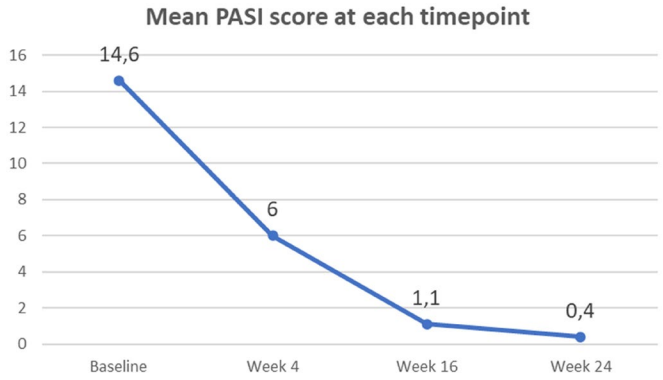

Figure 1. Mean PASI score for the whole sample at each timepoint.

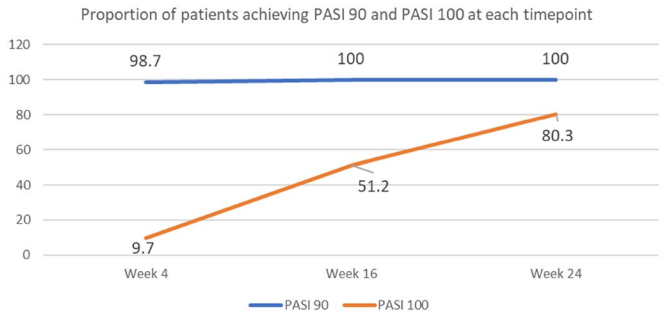

Figure 2. Proportion of patients in the sample achieving PASI 90 and PSI 100 at each timepoint.

Table 4. Descriptive statistics for DLQI score at each timepoint.

	Baseline	Week 24
N	88	72
Mean	14.2	1.8
Std.dev.	6.4	2.7
Median	14.0	0
Min	1	0
Max	30	12

statistically significantly different (baseline vs wk-4: $p = 0.038$; baseline vs wk-16: $p < 0.001$; baseline vs wk-24: $p < 0.001$) and moreover wk-4 vs wk-24: $p = 0.046$.

Concerning G-PASI-90 and G-PASI-100, already at week 4 93.3% of patients achieved G-PASI-90 and 20.0% achieved G-PASI-100. G-PASI-90 achieved 100% of patients in week 16 and maintained the result until the end of the study. G-PASI-100 reached 87.5% in week16 and the decreased to 81.8% in week 24. This is due to the fact that 5 patients who achieved G-PASI-100 in week 16 were missed at 24 weeks follow-up (Table 5).

NAPSI score

NAPSI has been evaluated at baseline and at each time point of the follow-up. At baseline the mean NAPSI score was 16.1 (SD = 18.3) and by the end of the study it reached a mean value of 3.0 (SD = 6.7). A Friedman test highlighted that there were differences in NAPSI score between the timepoints ($p < 0.001$). Pairwise comparisons highlighted that only two comparisons between timepoints were not statistically significantly different: baseline vs week 4 ($p = 0.053$) and week 16 vs week 24 ($p = 0.302$). See Table 6 for details and Figure 3.

Table 5. Descriptive statistics for G-PASI score at each timepoint.

	G-PASI_BL	G-PASI_WEEK_4	G-PASI_WEEK_16	G-PASI_WEEK_24
N	17	15	16	11
Mean	6.71	1.87	0.188	0.182
Std.dev.	3.46	1.55	0.544	0.405
Median	7	2	0	0
Min	2	0.0	0.0	0.0
Max	14.0	5.0	2.0	1.0
G-PASI 90		14/15 (93.3%)	16/16 (100.0%)	11/11 (100.0%)
G-PASI 100		3/15 (20%)	14/16 (87.5%)	9/11 (81.8%)

Table 6. Descriptive statistics for NAPSI score at each timepoint.

	Baseline	Week 4	Week 16	Week 24
N	20	20	19	18
Mean	16.1	10.3	5.5	3.0
Std.dev.	18.3	10.0	11.6	6.7
Median	10.0	8.0	0	0
Min	2	0	0	0
Max	70	40	46	22

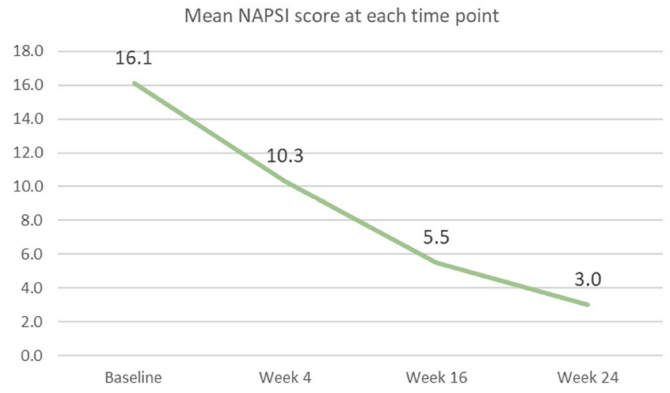

Figure 3. Mean NAPSI score at each timepoint for patients affected by nail psoriasis.

Subgroups analyses

PASI

Results highlighted a statistically significant main effect of time ($p < 0.0001$) for all the considered subgroups with all the pairwise comparisons significant: the sample, regardless of the subgroups, has significantly different PASI levels across the timepoints. **There was not** a statistically significant difference in mean PASI score between **males and females** ($p = 0.771$), between **weight <90 Kg or weight ≥90 Kg** ($p = 0.175$) and between **Bio Naive and Bio Experienced** ($p = 0.635$). However, grouping patients by burden of disease (**Baseline PASI < 20 vs Baseline PASI ≥20**) the highlighted result is that both the groups experienced a significant reduction of PASI score with time ($p < 0.0001$) and, in more details, PASI score were statistically significantly different in the two groups at baseline ($p < 0.0001$) and at 4 weeks ($p < 0.0001$) but no statistically significant difference was highlighted at week 16 ($p = 0.129$) and week 24 ($p = 0.869$); see Table 7 and Figure 4.

DLQI

Results highlighted a statistically significant main effect of time ($p < 0.0001$) for all the considered subgroups with the two pairwise comparisons significant: the sample, regardless of the subgroups, has significantly different DLQI levels across the two timepoints. Results highlighted that **there was not** a statistically significant difference in mean DLQI score between **males and females** ($p = 0.457$), between **weight <90 Kg or weight ≥90 Kg** ($p = 0.132$) and between **Bio Naive and Bio Experienced** ($p = 0.217$). Grouping patients by burden of disease (**Baseline PASI < 20 vs Baseline PASI ≥20**) the highlighted result is that both the groups experienced a significant reduction of DLQI score with time ($p < 0.0001$) and, in more details, the two groups of patients presented a statistically significantly different DLQI score at baseline ($p < 0.0001$) and at week 24 ($p = 0.035$) (Table 8).

Adverse events and safety

During the observation period, one mild adverse event related to the drug, itching at the injection site, and two mild events unrelated to the treatment, thoracic herpes zoster and headache, were recorded.

Discussion

Effective long-term management of chronic plaque psoriasis often requires ongoing treatment and medication adjustments, which may involve treatment interruption and re-administration, dosage modifications, or switching from one biologic to a newer one with a different mechanism of action (4). Patient weight and disease severity are important factors that can influence the response of psoriasis to systemic medications (13–15). Studies have shown that higher body weight may reduce the efficacy of these drugs, potentially due to altered pharmacokinetics and pharmacodynamics (16). Additionally, the severity of psoriasis can impact treatment outcomes, as more severe cases may require higher doses or combination therapies to achieve the same level of efficacy. Understanding these variables is crucial for optimizing treatment strategies and improving patient outcomes. In the European Union, biologics for psoriasis are generally administered in fixed dosages.

Table 7. PASI score subgroup analysis.

		Baseline	Week 4	Week 16	Week 24
F	N	26	25	24	19
	mean	14.8	6.5	0.7	0.2
	Std.dev.	8.7	4.7	1.1	0.6
M	N	63	57	58	52
	mean	14.6	5.8	1.3	0.5
	Std.dev.	7.3	4.7	1.9	1.1
		Baseline	Week 4	Week 16	Week 24
Weight < 90Kg	N	39	38	37	35
	mean	14.8	5.6	0.7	0.2
	Std.dev.	7.9	4.4	1.3	0.5
Weight ≥ 90Kg	N	50	44	45	36
	mean	14.4	6.3	1.4	0.7
	Std.dev.	7.7	4.9	1.9	1.3
		Baseline	Week 4	Week 16	Week 24
Baseline PASI < 20	N	62	56	56	45
	mean	10.4	4.2	0.9	0.5
	Std.dev.	4.4	3.3	1.2	1
Baseline PASI ≥ 20	N	27	26	26	26
	mean	24.2	9.7	1.6	0.4
	Std.dev.	4.5	5.1	2.5	1
		Baseline	Week 4	Week 16	Week 24
Bio experienced	N	50	49	47	41
	mean	14.1	6.7	1.4	0.5
	Std.dev.	7.1	5.1	1.9	1.2
Bio naïve	N	39	33	35	30
	mean	15.2	4.9	0.7	0.3
	Std.dev.	8.5	3.7	1.4	0.7

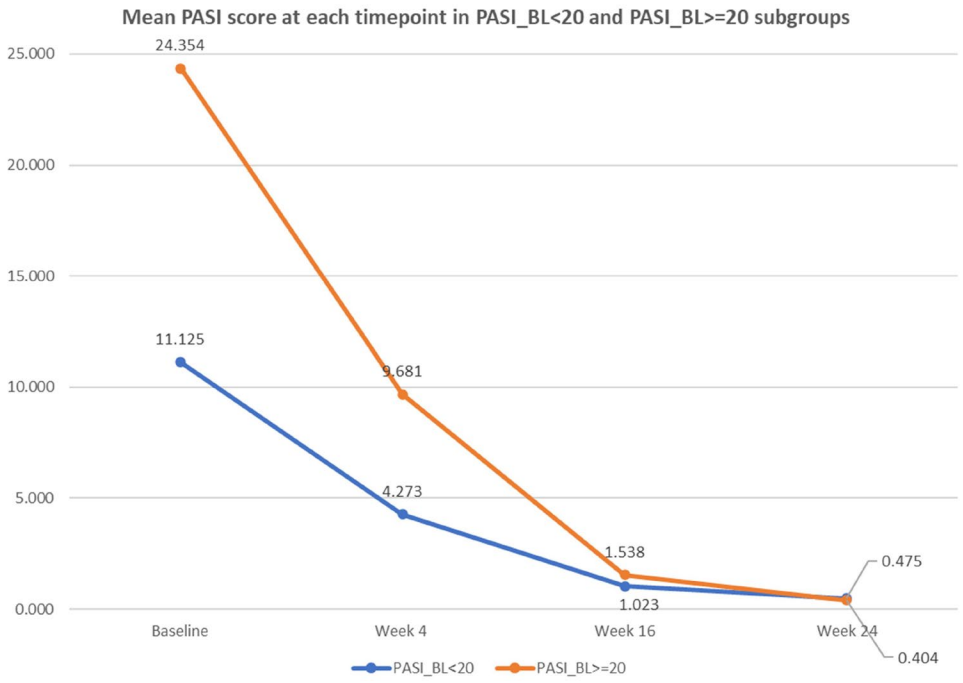

Figure 4. Mean PASI score at each timepoint in PASI_BL < 20 and PASI_BL ≥ 20 subgroups.

However, certain biologics allow for different dosages based on patient weight and response. For instance, ustekinumab offers two distinct fixed dosages depending on the patient's body weight. Bimekizumab's treatment frequency can be increased to enhance response in patients weighing ≥120 kg who do not achieve complete skin clearance by week 16 (16,17). Additionally, secukinumab can be administered every two weeks to provide additional benefits for patients weighing ≥90 kg (18). In this context, it can be stated that dosing flexibility is a peculiarity of tildrakizumab as it is the only biologic for the treatment of moderate to severe plaque psoriasis that leaves the physician the choice of the optimal dosage for each patient. Indeed, as reported in the tildrakizumab's Summary of Product Characteristic (SmPC), the recommended dose is 100 mg by subcutaneous injection at weeks 0, and 4 and every 12 weeks thereafter but at the physician's discretion, in patients with high disease burden or in patients above 90 kg of body weight a dose of 200 mg may provide greater efficacy. The effectiveness and safety of tildrakizumab in treating plaque psoriasis were established through two phase III, double-blind, randomized studies: reSURFACE 1 and reSURFACE 2 (11,19). These studies enrolled adult patients with moderate-to-severe plaque psoriasis and participants were assigned to receive either tildrakizumab

Table 8. DLQI score subgroup analysis.

		Baseline	Week 24
F	N	26	19
	mean	14.8	1.6
	Std.dev.	6.1	2.5
M	N	62	53
	mean	14.0	1.9
	Std.dev.	6.5	2.8
		Baseline	Week 24
Weight < 90Kg	N	39.0	35.0
	mean	15.7	1.8
	Std.dev.	6.8	2.4
Weight ≥ 90Kg	N	49.0	37.0
	mean	13.1	1.7
	Std.dev.	5.8	3.1
		Baseline	Week 24
Baseline PASI < 20	N	61	46
	mean	12.5	2.3
	Std.dev.	5.8	3.1
Baseline PASI ≥ 20	N	27.0	26.0
	mean	18.1	0.9
	Std.dev.	6.1	1.7
		Baseline	Week 24
Bio experienced	N	49.0	41.0
	mean	13.4	1.5
	Std.dev.	6.3	2.1
Bio naïve	N	39.0	31.0
	mean	15.2	2.2
	Std.dev.	6.5	3.3

200 mg, tildrakizumab 100 mg, or placebo in reSURFACE1, including an additional group receiving etanercept 50 mg in reSURFACE2. Both studies demonstrated that tildrakizumab 200 mg and 100 mg were significantly more effective than placebo and Etanercept, with good tolerance observed for both doses and long-term control of psoriasis maintained for up to five years. Tildrakizumab, administered at both dosages, also demonstrated improved efficacy during therapy and good response following drug interruption with subsequent re-adminitration (20). Further pooled post-hoc analysis from both reSURFACE studies showed that body weight had minimal impact on PASI and DLQI changes at week 28. Patients weighing more than 90 kg responded similarly to both doses of tildrakizumab, with no significant differences at weeks 28, 52, or 244. However, stratifying patients based on weight, a trend indicated that those over 90 kg had a slightly better response to tildrakizumab 200 mg compared to 100 mg and this data became statistically significant in patients weighing 120 kg or more, suggesting a clinical advantage for this subgroup (19). The treatment remained effective and had a favorable safety profile even in patients with metabolic syndrome (11). Notably, stratifying patients based on baseline PASI, it was observed that patients with PASI ≥ 20 responded better to tildrakizumab 200 mg (59.4%) compared to tildrakizumab 100 mg (48.6%), at week 28, suggesting greater efficacy of the higher dose in patients with a high disease burden (4). Although there is ample evidence regarding the efficacy of tildrakizumab 100 mg in clinical practice, real-world data on the efficacy of tildrakizumab 200 mg are limited (21–24). Becher et al. conducted a real-life study assessing the efficacy and tolerability of the drug at both doses in 122 patients. They found a 75% effectiveness rate overall, with patients weighing >120 kg responding better to the higher dosage, consistent with findings from reSURFACE 1 and 2 (9). Gargiulio et al. conducted a 16-week multicenter retrospective study to compare the efficacy and safety of tildrakizumab 200 mg versus tildrakizumab 100 mg in 498 patients suffering from moderate-to-severe plaque psoriasis with significant disease burden or high body weight. Tildrakizumab 200 mg demonstrated superior efficacy compared to 100 mg in patients with a body weight ≥ 90 kg and substantial disease burden. Specifically, tildrakizumab 200 mg exhibited better performance after 16 weeks in individuals with severe plaque psoriasis affecting challenging-to-treat areas (25). In our real-world study, at week 16, PASI 90 and PASI 100 were achieved by 100.0% and 51.2% of patients. PASI 100 reached 80.3% at week 24 with a mean PASI value of 0.4. DLQI score decreased significantly from baseline to week 24. The median value at baseline was 14.0 and at week 24 was 0.0. GPASI 90 and GPASI 100 were already achieved by, respectively, 100.0% and 87.5% of patients by the 16th week with a mean score of 0.18 which remained stable until the end of the study. NAPSI also showed excellent nail component response, starting from a mean value of 16.1 at baseline to reach 3.0 after 24 weeks. Weight did not appear to influence therapy response when patients were stratified into ≥90 kg and <90 kg groups. Similarly, sex did not influence the response to therapy. Patients with a high disease burden (Baseline PASI ≥ 20) presented a statistically significant higher PASI score, compared to Baseline PASI < 20 patients, at the beginning of the treatment; this difference was not statistically significant in week 16 and week 24. Moreover tildrakizumab 200 mg produced a reduction in mean PASI from baseline to week 4 of 60% in both subgroups, indicating its effectiveness also in high burden patients. Therefore, despite patients with a high disease burden requireing more time to achieve an optimal response, tildrakizumab 200 mg has proven effective in this group of patients, confirming findings from reSURFACE I and II. Comparing response curves of biologically naive and experienced patients, these are overlapping as early as the fourth week of therapy. Therefore, efficacy of tildrakizumab 200 mg is not influenced by prior biological therapies. In our study, tildrakizumab demonstrated a favorable safety profile, with no significant adverse effects reported up to week 24 among all patients receiving the treatment, consistent with findings from phase III studies. Unfortunately, it was not possible to perform subgroup analyses for patients presenting psoriasis in difficult-to-treat areas due to the small amount of such a patients. However, even patients with up to 3 difficult-to-treat areas affected, at the end of follow-up achieved results comparable to those of patients with no difficult-to-treat areas affected.

Conclusions

In conclusion, our study represents the first prospective real-world analysis about the effectiveness of tildrakizumab 200 mg in patients with moderate-to-severe psoriasis. Consistent with findings from the phase III studies reSURFACE 1 and 2, our work confirms tildrakizumab 200 mg as an effective therapeutic option, particularly for patients with high body weight, significant disease burden, and involvement of sensitive areas. It has demonstrated safety despite the multiple comorbidities of the patients examined and has maintained efficacy in subjects previously treated with other biologic therapies. Moreover, the possibility to adjust the dosage and potentially maintain tildrakizumab's effect upon treatment discontinuation and re-administration suggests the potential for personalized therapy. Further studies are needed to differentiate between patients who have received only one biologic drug and those who have failed multiple biologic therapies. Additionally, more real-world studies are necessary to assess the long-term safety and effectiveness of tildrakizumab 200 mg.

Ethical approval

The study has been conducted accordingly to the Declaration of Helsinki.

Disclosure statement

AD and GP has served as speaker/consultant for Abbvie, Amgen, Almirall, Eli Lilly, Janssen, Leopharma, Novartis, UCB outside the submitted work. ME has served as speaker/consultant for Abbvie, Amgen, Almirall, Eli Lilly, Janssen, Leopharma, Novartis, Pfizer, Sanofi, UCB. CG has received consultation fees and/or grants for research projects, advisory panels and giving educational lectures from Pfizer, Abbvie, Janssen, Novartis, LEO-Pharma, LEO-Pharma Denmark, Ely-Lilly, Celgene, Merck-Serono, UCB Pharma, Sanofi-Aventis, Amgen, Bristol-Myers, Boheringer-Ingelheim and Almirall. CG acted as speaker and/or consultant for AbbVie, Janssen-Cilag, Novartis, Leo-Pharma, Amgen, Lilly, UCB. GM: speaker and/or consultant for AbbVie and Leo Pharma. Other authors reported no conflict of interest.

Funding

This research received no external funding.

ORCID

Giacomo Caldarola http://orcid.org/0000-0002-8837-9232

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Damiani G, Bragazzi NL, Karimkhani Aksut C, et al. The global, regional, and national burden of psoriasis: results and insights from the global burden of disease 2019 study. Front Med (Lausanne). 2021;8:743180. doi: 10.3389/fmed.2021.743180.
2. Dattola A, Del Duca E, Saraceno R, et al. Safety evaluation of apremilast for the treatment of psoriasis. Expert Opin Drug Saf. 2017;16(3):381–385. doi: 10.1080/14740338.2017.1288714.
3. Vata D, et al. Update on obesity in psoriasis patients. Life Basel Switz. 2023;13:1947.
4. Kerbusch T, Li H, Wada R, et al. Exposure-response characterisation of tildrakizumab in chronic plaque psoriasis: pooled analysis of 3 randomised controlled trials. Br J Clin Pharmacol. 2020;86(9):1795–1806. doi: 10.1111/bcp.14280.
5. Xu C, Ji J, Su T, et al. The association of psoriasis and obesity: focusing on IL-17A-related immunological mechanisms. Int J Dermatol Venereol. 2021;4(2):116–121. doi: 10.1097/JD9.0000000000000155.
6. Lee H-J, Kim M. Challenges and future trends in the treatment of psoriasis. Int J Mol Sci. 2023;24(17):13313. doi: 10.3390/ijms241713313.
7. Schwarz CW, Loft N, Rasmussen MK, et al. Predictors of response to biologics in patients with moderate-to-severe psoriasis: a danish nationwide cohort study. Acta Derm Venereol. 2021;101(10):adv00579. doi: 10.2340/actadv.v101.351.
8. Näslund-Koch C, Zachariae C, Skov L, et al. Tildrakizumab: an evidence-based review of its use in the treatment of moderate-to-severe chronic plaque psoriasis. Ther Clin Risk Manag. 2020;16:903–916. doi: 10.2147/TCRM.S227880.
9. Becher G, Conner S, Ingram JA, et al. A retrospective real-world study of the effectiveness and tolerability of Tildrakizumab in UK adults with moderate-to-severe chronic plaque psoriasis. Dermatol Ther (Heidelb). 2022;12(10):2343–2354. doi: 10.1007/s13555-022-00800-3.
10. Fernandez AP, Dauden E, Gerdes S, et al. Tildrakizumab efficacy and safety in patients with psoriasis and concomitant metabolic syndrome: *post hoc* analysis of 5-year data from reSURFACE 1 and reSURFACE 2. J Eur Acad Dermatol Venereol. 2022;36(10):1774–1783. doi: 10.1111/jdv.18167.
11. Dapavo P, Burlando M, Guarneri C, et al. Tildrakizumab: the value of a personalized and flexible approach for treating moderate-to-severe plaque psoriasis in patients with high body weight or high disease burden. Expert Opin Biol Ther. 2024;24(3):133–138. doi: 10.1080/14712598.2024.2325547.
12. Gisondi P, Fargnoli MC, Amerio P, et al. Italian adaptation of EuroGuiDerm guideline on the systemic treatment of chronic plaque psoriasis. Ital J Dermatol Venerol. 2022;157(Suppl. 1 to No. 1):1–78. doi: 10.23736/S2784-8671.21.07132-2.
13. Lebwohl MG, Leonardi CL, Mehta NN, et al. Tildrakizumab efficacy, drug survival, and safety are comparable in patients with psoriasis with and without metabolic syndrome: long-term results from 2 phase 3 randomized controlled studies (reSURFACE 1 and reSURFACE 2). J Am Acad Dermatol. 2021;84(2):398–407. doi: 10.1016/j.jaad.2020.09.047.
14. Chiricozzi A, Pavlidis A, Dattola A, et al. Efficacy and safety of infliximab in psoriatic patients over the age of 65. Expert Opin Drug Saf. 2016;15(11):1459–1462. doi: 10.1080/14740338.2016.1226279.
15. Bellinato F, Gisondi P, Balato A, et al. Awareness of obesity among patients with psoriasis. J Eur Acad Dermatol Venereol. 2024;38(5):e391–e393. doi: 10.1111/jdv.19617.
16. Burlando M, Maul J-T, Salvi I, et al. Psoriasis patients' characteristics associated with high PASI response to tildrakizumab: an international dual center study. Eur Rev Med Pharmacol Sci. 2022;26(18):6772–6776. doi: 10.26355/eurrev_202209_29777.
17. Gargiulo L, Narcisi A, Ibba L, et al. Effectiveness and safety of bimekizumab for the treatment of plaque psoriasis: a real-life multicenter study-IL PSO (Italian landscape psoriasis). Front Med (Lausanne). 2023;10:1243843. doi: 10.3389/fmed.2023.1243843.
18. Augustin M, Reich K, Yamauchi P, et al. Secukinumab dosing every 2 weeks demonstrated superior efficacy compared with dosing every 4 weeks in patients with psoriasis weighing 90 kg or more: results of a randomized controlled trial. Br J Dermatol. 2022;186(6):942–954. doi: 10.1111/bjd.20971.
19. Egeberg A, et al. Five-year safety of tildrakizumab in patients with moderate-to-severe psoriasis from two phase 3 trials (reSURFACE 1 and reSURFACE 2): number needed to harm for occurrence of adverse events of special interest. J. Dermatol. Treat. 2023;34:2220447.
20. Kimball AB, Papp KA, Reich K, et al. Efficacy and safety of tildrakizumab for plaque psoriasis with continuous dosing, treatment interruption, dose adjustments and switching from etanercept: results from phase III studies. Br J Dermatol. 2020;182(6):1359–1368. doi: 10.1111/bjd.18484.
21. Bhatia N, et al. Quality of life and patient-reported symptoms in a Phase 4, real-world study of tildrakizumab in patients with moderate-to-severe psoriasis: week 28 interim analysis. J. Dermatol. Treat. 2023;34:2200872.
22. Campione E, Lambiase S, Gaeta Shumak R, et al. A real-life study on the use of tildrakizumab in psoriatic patients. Pharmaceuticals. 2023;16(4):526. doi: 10.3390/ph16040526.
23. Narcisi A, Valenti M, Gargiulo L, et al. Real-life effectiveness of tildrakizumab in chronic plaque psoriasis: A 52-week

multicentre retrospective study—IL PSO (ITALIAN LANDSCAPE PSORIASIS). J Eur Acad Dermatol Venereol. 2023;37(1):93–103. doi: 10.1111/jdv.18594.

24. Orsini D, Caldarola G, Dattola A, et al. Efficacy and safety of tildrakizumab in elderly patients: real-world multicenter study (ESTER - study). J Dermatolog Treat. 2024;35(1):2319304. doi: 10.1080/09546634.2024.2319304.
25. Gargiulo L, Ibba L, Cascio Ingurgio R, et al. Comparative effectiveness of tildrakizumab 200 mg versus tildrakizumab 100 mg in psoriatic patients with high disease burden or above 90 kg of body weight: a 16-week multicenter retrospective study – IL PSO (Italian landscape psoriasis). J Dermatolog Treat. 2024;35(1):2350760. doi: 10.1080/09546634.2024.2350760.