ORIGINAL REPORT

Tildrakizumab Treatment for Psoriasis in Real-world Practice: An Analysis from the Swiss Registry (SDNTT)

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Real-world data on the effectiveness and safety of tildrakizumab, an interleukin 23p19 inhibitor, in Switzerland is limited. The objectives of this analysis were to assess the effectiveness and safety of tildrakizumab in patients with moderate-to-severe plaque psoriasis in Switzerland. Twenty-eight adults from the Swiss Dermatology Network for Targeted Therapies registry (SDNTT), who were on tildrakizumab treatment and had at least 3 months' follow-up, were enrolled in this prospective, multicentre study. No missing data imputation was performed. The median Psoriasis Area and Severity Index (PASI) decreased from 9.5 at baseline to 2.1 and 0.3 (both $p < 0.001$) after 3 and 18 months, respectively, of tildrakizumab treatment. After 3 months, 76.9%/30.8% patients reached an absolute PASI < 3/ <1. These rates increased to 85.7%/57.1% after 18 months of treatment. The proportions of patients achieving PASI 90/100 responses were 47.8%/30.4% at month 6 and 42.9%/14.3% at month 18. A significant improvement in quality of life up to 18 months of follow-up was observed as measured by the Dermatology Life Quality Index. There were no treatment discontinuations due to adverse events. This real-world registry provides robust evidence supporting the long-term effectiveness and favourable safety profile of tildrakizumab in treating patients with moderate-to-severe psoriasis.

Key words: psoriasis; real-world; registry; tildrakizumab.

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SIGNIFICANCE

Based on data from patients participating in the Swiss Dermatology Network for Targeted Therapies registry, we assessed the long-term effectiveness and safety of tildrakizumab for the treatment of plaque psoriasis in clinical practice in Switzerland, a country with limited data available. After 3 months of treatment, tildrakizumab significantly improved both skin symptoms and quality of life of patients, maintaining these responses until month 18 and without safety concerns. Our study supports the long-term effectiveness and favourable safety profile of tildrakizumab for the treatment of moderate-to-severe plaque psoriasis.

Psoriasis is a common chronic inflammatory skin disease associated with multiple comorbidities, such as psoriatic arthritis, cardiometabolic diseases, or depression, with a significant impact on patients' quality of life (QoL) (1). In recent years, the interleukin (IL)-23/Th17 cell pathway has been identified as a therapeutic target in immune-driven diseases (2). For this reason, current therapeutic strategies that disrupt IL-23 or IL-17 cytokine signalling have become the gold standard in the treatment of moderate-to-severe psoriasis (3).

Interleukin-23 is a heterodimeric cytokine composed of 2 subunits: a p40 subunit shared with IL-12 and a unique p19 subunit. The most recent biologic agents targeting the p19 subunit of the IL-23 cytokine (guselkumab, risankizumab, and tildrakizumab) have demonstrated high levels of efficacy and favourable safety profiles for the treatment of moderate-to-severe psoriasis (4–7). Tildrakizumab is a humanized, immunoglobin G1κ monoclonal antibody that specifically binds to the IL-23 p19 subunit. The randomized, double-blind, placebo-controlled reSURFACE 1 and reSURFACE 2 trials demonstrated the long-term efficacy and safety of tildrakizumab for the treatment of adults with moderate-to-severe plaque psoriasis for up to 5 years (8–10).

Real-life studies have confirmed that tildrakizumab is an effective treatment for moderate-to-severe psoriasis, with a reassuring safety profile over 100 weeks (11–13). However, real-world data on the effectiveness and safety of tildrakizumab are limited and no data from Switzerland are available. So far, only real-world results on the use of tildrakizumab in Switzerland combined with data from an Italian cohort have been published (14). This study aims to examine the long-term effectiveness and safety of tildrakizumab for the treatment of plaque

psoriasis in clinical practice in Switzerland, based on data from the Swiss Dermatology Network for Targeted Therapies (SDNTT) registry.

MATERIALS AND METHODS

Patient selection

Male or female subjects aged ≥18 years with plaque psoriasis participating in the SDNTT registry (ClinicalTrials.gov Identifier: NCT01706692) (15–21) from 2 sites in Switzerland (University Hospital Basel and University Hospital Zürich) who initiated treatment with tildrakizumab as approved for plaque-type psoriasis at registry entry as first-line or subsequent therapy or during treatment in the registry and who had at least 3 months' follow-up were included. Written informed consent was obtained from all patients prior to inclusion in the registry and ethical approval was provided by all participating hospitals.

Data collection

The SDNTT registry collects data on the effectiveness, the quality of life, treatment satisfaction, comorbidities, and the safety of modern psoriasis therapies under everyday conditions from 8 study sites in Switzerland. Adult patients starting conventional systemic or biologic treatment are observed for up to 20 years after enrolment and regardless of subsequent therapy. Study data are collected at baseline, at 3 months, at 6 months, and thereafter at 6-month intervals, using case report forms for both patients and physicians.

This analysis includes the patients' baseline demographic data (sex, age, age at psoriasis diagnosis, bodyweight, body mass index, presence of comorbidities), the treatment effectiveness, which was assessed using the Psoriasis Area and Severity Index (PASI) response rates, Body Surface Area (BSA) affected, and static Physician Global Assessment (sPGA). Furthermore, the effect on quality of life (QoL) was measured using the Dermatology Life Quality Index (DLQI), and all reported adverse events (AEs) were analysed to evaluate the safety (22).

Outcomes

The effectiveness analysis included (a) the proportion of patients reaching absolute PASI scores <5, <3, and <1, (b) relative PASI 75, 90, and 100 response rates (i.e., patients achieving ≥75%, ≥90%, and 100% improvement from baseline PASI) at each visit, and (c) the evolution of PASI, BSA, and sPGA outcomes. Analogously, the QoL was assessed by analysing absolute DLQI scores and proportions of patients with a DLQI ≤5, ≤3, and 0/1 at respective study visits. The safety profile was based on the analysis of collected adverse events (AEs).

Statistical analysis

All baseline characteristics, as well as AEs, were analysed using standard descriptive statistics, including absolute and relative frequencies for categorical variables, and mean, standard deviation, median, minimum, and maximum for continuous variables based on observed cases.

For all effectiveness outcomes, the non-parametric Wilcoxon rank-sum test with continuity correction, considering the non-normality of the data confirmed by the Lilliefors test (Kolmogorov–Smirnov), was used to test for statistically significant changes in PASI, BSA, sPGA, or DLQI scores between follow-up and baseline visits. *P*-values of <0.05 were deemed statistically significant.

No imputation of missing data was performed. Recorded comorbidities and AEs were classified according to system organ classes and preferred terms from the Medical Dictionary for Regulatory Activities.

RESULTS

Demographics and disease characteristics at baseline

As per the cut-off date (1 July 2023), a total of 28 patients had started treatment with tildrakizumab either at the University Hospital Basel or University Hospital Zürich and have been included in this analysis. **Table I** presents the baseline data of the patients included in the present analysis. Hypertension was found to be one of the most frequent comorbidities (17.9%), while 25% of patients were smokers (Table I).

Effectiveness

At baseline, a median absolute PASI score of 9.5 was reported. Upon treatment initiation with tildrakizumab, this decreased significantly to 2.1 at month three, 0.9 at month 12, and 0.6 at month 18 ($p<0.001$, for all time points) (**Fig. 1**A). Correspondingly, the number of patients achieving absolute and relative PASI improvements increased. Overall, 92.3%, 76.9%, and 30.8% of patients achieved PASI <5, PASI <3, and PASI <1 at month 3. This increased to 94.7%, 94.7%, and 57.9% at month 12, and 92.9%, 85.7%, and 57.1%, at month 18, respectively (Fig. 1B). At month 6, 69.6% of patients achieved PASI 75, 47.8% a PASI 90, and 30.4% a PASI 100. At month 12, the rates were 79.0%, 47.4% and 10.5%, and after 18 months of tildrakizumab treatment, 71.4%, 43.0%, and 14.3% achieved PASI 75, PASI 90, and PASI 100, respectively (Fig. 1C).

In line with the PASI improvements, both the BSA and sPGA scores demonstrated significant improvements. The median affected BSA of patients at baseline was 10.5%. A significant reduction to 1.5% at month 3, 0.6% at month 12, and 0.5% at month 18 ($p<0.0001$, in all 3 cases) was observed (**Fig. 2**A). Lastly, the median sPGA at baseline was 2.0. This median decreased significantly to 1.0 at month 3 ($p<0.0001$), a reduction that was maintained until month 18 (Fig. 2B).

Quality of life

The quality of life of patients was assessed using the DLQI. At baseline patients reported a median DLQI of 13.0. Upon treatment initiation, the DLQI significantly decreased at each timepoint and a median DLQI of 1.0 was reported at month 6 ($p<0.0001$), 0.0 at month 12 ($p<0.001$), and 0.5 at month 18 ($p<0.0001$), respectively (**Fig. 3**A). Similarly, the number of patients achieving absolute DLQI values of ≤5, ≤3, and 0/1 increased over time. At month 6, 60.9%, 56.5%, and 26.1% of patients had a DLQI ≤5, ≤3, and 0/1, respectively. The DLQI

Table I. Demographics, disease characteristics, and comorbidities at baseline

Factor	*n*	*n* (%)	Mean (SD)	Median (min–max)
Gender* (male)	28	14 (50.0)		
Age (years)	28		47.4 (15.4)	46.5 (18.5-81.5)
Age at diagnosis (years)	20		30.1 (13.9)	27.5 (8.0-56.0)
Weight (kg)	28		75.0 (12.0)	75.0 (55.0-100.0)
BMI (kg/m^2)	28		25.9 (4.5)	25.1 (20.2-38.1)
<25	28	14 (50.0)		
25–29	28	4 (14.3)		
≥30	28	10 (35.7)		
PASI score	27		9.3 (5.8)	9.5 (0.0-29.4)
BSA affected (%)	27		13.1 (9.7)	10.5 (0.0-40.0)
sPGA	28		2.1 (1.0)	2.0 (0.0-4.0)
DLQI	23		11.7 (7.4)	13.0 (0.0-27.0)
Comorbidities** (yes)	28	20 (71.4)		
Social circumstances				
Tobacco user	28	7 (25.0)		
Ex-tobacco user	28	5 (17.9)		
Hepatobiliary disorders				
Hepatitis	28	4 (14.3)		
Hepatic steatosis	28	3 (10.7)		
Hepatic cirrhosis	28	2 (7.1)		
Hepatomegaly	28	1 (3.6)		
Vascular disorders				
Hypertension	28	5 (17.9)		
Peripheral arterial occlusive disease	28	3 (10.7)		
Peripheral venous disease	28	1 (3.6)		
Musculoskeletal and connective tissue disorders				
Osteoarthritis	28	2 (7.1)		
Metatarsalgia	28	1 (3.6)		
Periarthritis	28	1 (3.6)		
Psoriatic arthropathy	28	1 (3.6)		
Spondylitis	28	1 (3.6)		
Metabolism and nutrition disorders				
Type 2 diabetes mellitus	28	2 (7.1)		
Hyperuricaemia	28	1 (3.6)		
Iron deficiency	28	1 (3.6)		
Vitamin D deficiency	28	1 (3.6)		
Psychiatric disorders				
Alcohol abuse	28	2 (7.1)		
Depression	28	2 (7.1)		
Adjustment disorder	28	1 (3.6)		
Respiratory, thoracic, and mediastinal disorders				
Rhinitis allergic	28	3 (10.7)		
Asthma	28	1 (3.6)		
Sleep apnoea syndrome	28	1 (3.6)		
Nervous system disorders				
Drug withdrawal convulsions	28	1 (3.6)		
Migraine	28	1 (3.6)		
Parkinson's disease	28	1 (3.6)		
Polyneuropathy	28	1 (3.6)		
Blood and lymphatic system disorders				
Bicytopenia	28	1 (3.6)		
Hypersplenism	28	1 (3.6)		
Thrombocytopenia	28	1 (3.6)		
Cardiac disorders				
Cardiac failure	28	1 (3.6)		
Cardiomyopathy	28	1 (3.6)		
Coronary artery disease	28	1 (3.6)		
Neoplasms benign, malignant, and unspecified (including cysts and polyps)				
Clear cell renal cell carcinoma	28	1 (3.6)		
Myeloproliferative neoplasm	28	1 (3.6)		
Uterine leiomyoma	28	1 (3.6)		
Skin and subcutaneous tissue disorders				
Dermatitis atopic	28	1 (3.6)		
Granuloma annulare	28	1 (3.6)		
Congenital, familial, and genetic disorders				
Factor V Leiden mutation	28	1 (3.6)		
Endocrine disorders				
Hypothyroidism	28	1 (3.6)		
Eye disorders				
Neovascular age-related macular degeneration	28	1 (3.6)		
Gastrointestinal disorders				
Dysphagia	28	1 (3.6)		
General disorders and administration site conditions				
Pain	28	1 (3.6)		
Reproductive system and breast disorders				
Uterine polyp	28	1 (3.6)		
Surgical and medical procedures				
Hysterectomy	28	1 (3.6)		

*Age at the start of tildrakizumab treatment; **by system organ class and preferred term. Patients may have more than one comorbidity.
BMI: body mass index; BSA: body surface area; max: maximum; min: minimum; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area and Severity Index; SD: standard deviation; sPGA: static Physician Global Assessment.

0/1 response increased to 36.8% of patients at month 12, which was maintained until month 18, where 71.4% achieved a DLQI ≤3 and 35.7% a DLQI 0/1 (Fig. 3B).

Safety

The safety analysis included a follow-up time of 34.5 patient-years with a total of 17 AEs reported. No AEs led to treatment discontinuation. One serious AE (acute biventricular heart failure) was recorded that was assessed as not related to the treatment. Adverse events by system organ class and preferred term are listed in **Table II**. The most frequent AE was hypertension ($n=2$). Three patients reported gastrointestinal disorders and 3 reported nervous system disorders. Two patients reported infections (1 case of folliculitis and 1 case of an upper respiratory tract infection). One patient had a cardiac disorder (1 case of acute cardiac failure).

DISCUSSION

The present study is based on real-world data collected in the SDNTT registry at 2 hospital centres in Switzerland to assess the effectiveness, safety, and impact on QoL of tildrakizumab in the management of psoriasis. In line with previous results from Switzerland, this analysis showed high PASI response rates and a fast and lasting QoL improvement with tildrakizumab in a real-world setting (14).

Compared with the reSURFACE 1 and reSURFACE 2 clinical trials (8, 23), our cohort had lower baseline PASI, BSA, and sPGA scores, which was due to the stricter inclusion/exclusion criteria of the phase 3 trials as well as switches from other therapies (24), and a lower bodyweight that could be explained by the inclusion of a higher percentage of women in the current study. In addition, in the real-world setting, conventional systemic therapies are required prior to initiation of biologics and washout periods are uncommon, further facilitating lower absolute PASI values at baseline. Psoriasis is associated with an increased risk of several comorbidities, also known as the comorbidome, that may influence its progression and vice versa (25, 26). Examples of relevant comorbidities linked to psoriasis include cardiovascular, metabolic, or mental health diseases, as well as psoriatic

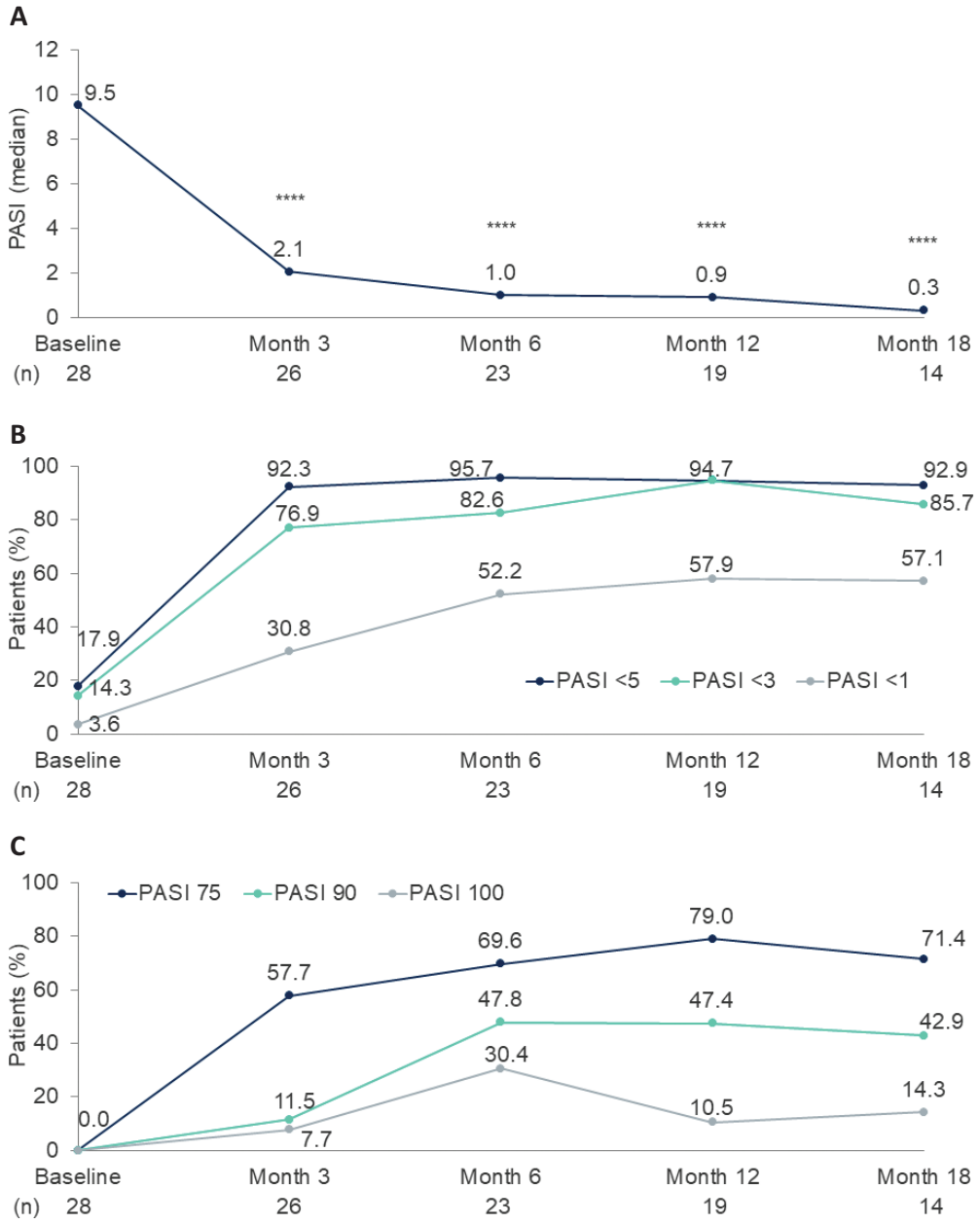

Fig. 1. (A) Absolute Psoriasis Area and Severity Index (PASI), (B) PASI < 5, < 3 and < 1 responses, and (C) PASI 75, 90, and 100 responses over time. ****p < 0.0001; Wilcoxon signed-rank test comparing baseline to follow-up.

arthritis (25, 26), which were well represented in our cohort (with 18% of patients reporting hypertension, 7% diabetes, 7% depression, and 3.6% psoriatic arthritis) and with frequencies in agreement with that of previous real-world studies (27, 28). Surprisingly, but in line with the lower bodyweight, hypertension was less frequent in this cohort than in the phase 3 reSURFACE trials (about 30%) (8).

In recent years, therapies have become more effective and, consequently, more ambitious treatment goals can be achieved and are being pursued. In addition, the focus has shifted from relative endpoints to an absolute outcome (e.g., PASI <3) (4, 5, 29–32). Overall, our study showed a significant improvement in PASI, BSA, and sPGA outcomes after 3 months of treatment with tildrakizumab, with approximately 80% of patients reaching an absolute PASI <3. This response increased through 1 year of follow-up, with 95% of patients achieving a PASI <3 at month 12, a higher percentage than observed in the pooled analyses of reSURFACE trials (82.0% and 85.3% among patients responding to tildrakizumab 100 and 200 mg, defined as PASI 75 response at week 28, respectively) (9). Similar effects (i.e., increased effectiveness compared with the efficacy observed in pivotal trials) have been reported not only in other real-world studies of tildrakizumab (24, 27) but also in real-world

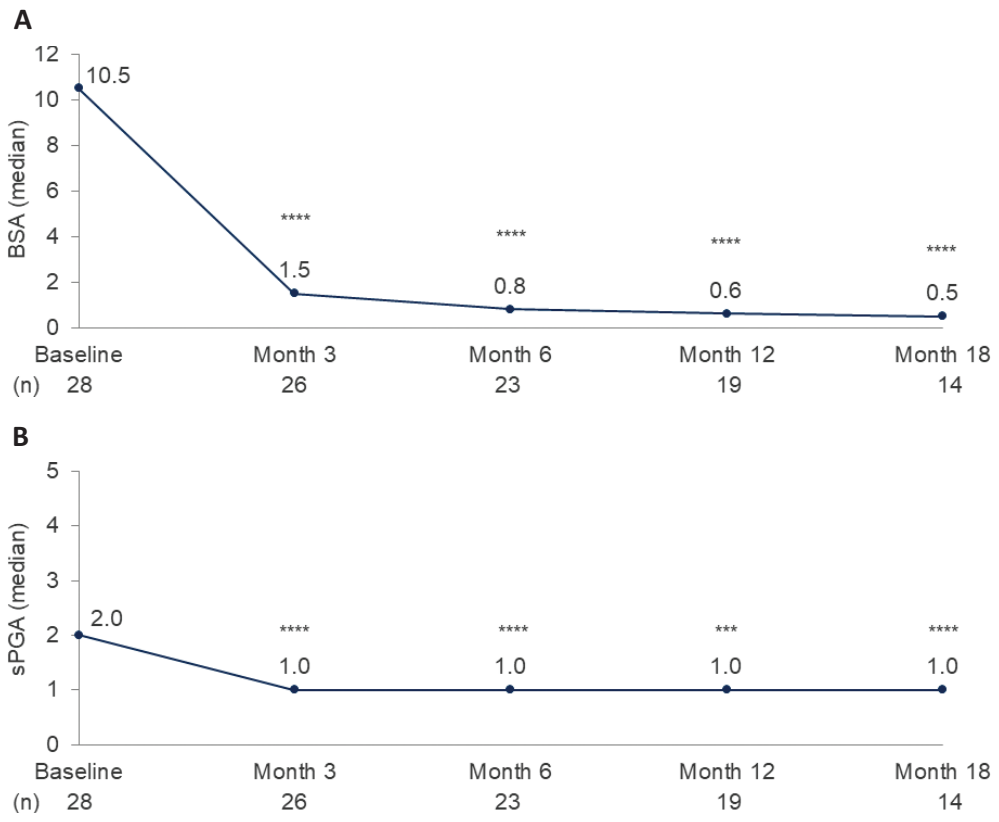

Fig. 2. (A) Body surface area (BSA) and (B) static Physician Global Assessment (sPGA) scores over time. ***$p < 0.001$, ****$p < 0.0001$; Wilcoxon signed-rank test.

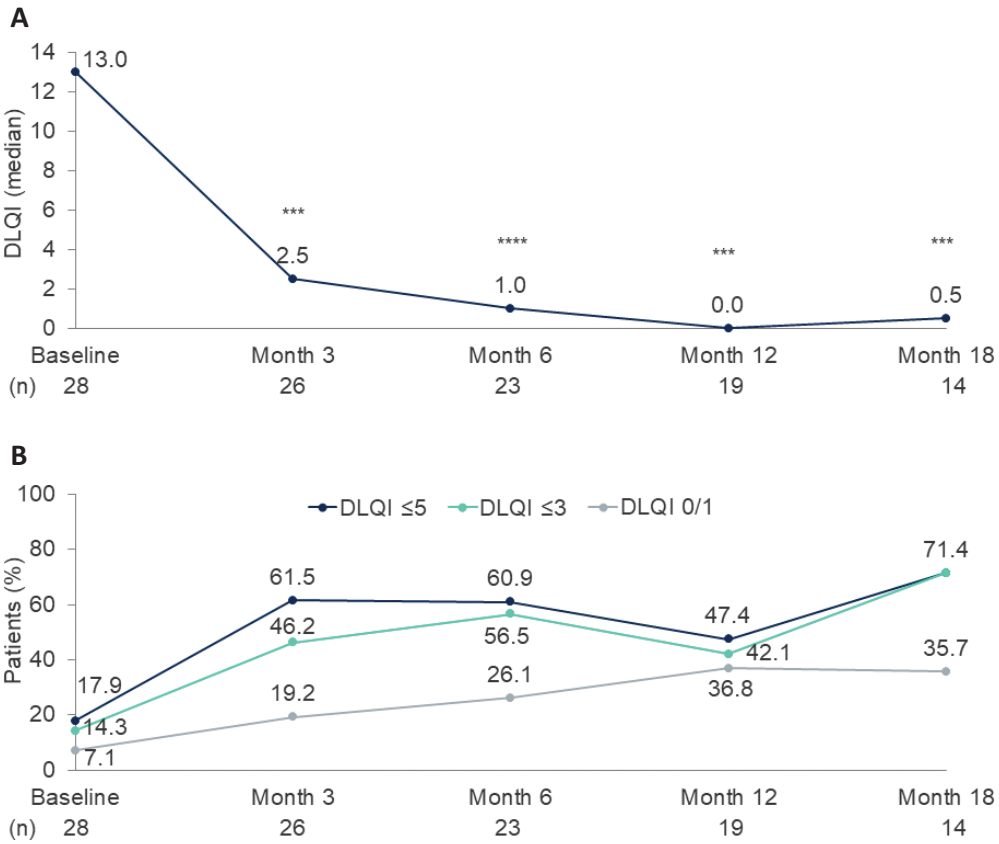

Fig. 3. (A) Dermatology Life Quality Index (DLQI) score and (B) proportions of patients with DLQI ≤5, ≤3, and 0/1 over time. ***$p < 0.001$, ****$p < 0.0001$; Wilcoxon signed-rank test.

Table II. Adverse events by system organ class and preferred term (*n* = 28)

System organ class	Preferred term	Patients, *n* (%)
Vascular disorders		
	Hypertension	2 (7.1)
Gastrointestinal disorders		
	Abdominal distension	1 (3.6)
	Diarrhoea	1 (3.6)
	Nausea	1 (3.6)
Nervous system disorders		
	Dizziness	1 (3.6)
	Headache	1 (3.6)
	Paraesthesia	1 (3.6)
Infections and infestations		
	Folliculitis	1 (3.6)
	Upper respiratory tract infection	1 (3.6)
Cardiac disorders		
	Cardiac failure acute	1 (3.6)
General disorders and administration site conditions		
	Fatigue	1 (3.6)
Hepatobiliary disorders		
	Liver disorder	1 (3.6)
Investigations		
	Weight increased	1 (3.6)
Musculoskeletal and connective tissue disorders		
	Arthralgia	1 (3.6)
Respiratory, thoracic, and mediastinal disorders		
	Cough	1 (3.6)
Skin and subcutaneous tissue disorders		
	Eczema	1 (3.6)

studies of guselkumab and risankizumab (33, 34). Although IL-23 inhibitors bind the IL-23 p19 subunit, each of them binds an epitope with a unique size, which may influence short- and long-term clinical efficacy *in vitro* (35). This is why real-world psoriasis data that account for patient complexity are so important.

Recent advances in biologic therapies for moderate-to-severe plaque psoriasis have facilitated the achievement of more ambitious endpoints such as PASI 90 or PASI 100 responses or absolute PASI scores of <3 or <1 in most patients. When comparing the relative PASI results obtained in this study with the phase 3 trials (baseline PASI of 9 vs 20, respectively), the observed PASI 90 and PASI 100 response rates at month 12 (47.4%/10.5%) were lower than those observed in the reSURFACE 1 and 2 trials (73.2%/34.4% and 75.6%/45.2% among patients responding to tildrakizumab 100 and 200 mg, respectively) (9). However, the absolute PASI response rates (i.e., PASI <3 and PASI <1) were higher compared with the reSURFACE trials. One contributing factor to this effect is certainly the relatively low baseline PASI observed in this cohort, highlighting the relevance of absolute PASI reporting for real-world effectiveness results (36).

In line with this, our study observed higher rates of patients obtaining a PASI of <3 and lower frequencies of PASI 90 responses at 12 months, when comparing PASI outcomes not only with phase 3 trials but also with other real-world investigations (11, 12, 14). These studies encompassed patients with moderate-to-severe plaque psoriasis treated with tildrakizumab in routine clinical settings. For example, the percentage of patients with PASI <3 and PASI 90 responses at month 12 was 74.6% and 57.7%, respectively, in the non-interventional TILOT study (11). However, the baseline PASI and BSA scores of the patients included in these studies were also higher than those of our cohort. Notably, patients in our study had a baseline PASI <10 but a baseline DLQI of 13, indicating that, despite effective symptom management in clinical practice, patients' QoL remained impaired.

There are few data on the long-term effects of tildrakizumab on patients' health-related QoL (HRQoL) in a real-world setting (11, 14). Although a high level of response for the HRQoL outcome was observed in our cohort, with 40% of patients achieving a DLQI of 0 or 1 at month 12, other real-world studies have found higher response rates. In the non-interventional TILOT study, the percentage of patients with a DLQI 0/1 was 48% at week 52 (11).

To date, most real-world evidence studies report a maximum follow-up period of 12 months (11, 12, 14). Here, we present data on the effectiveness of tildrakizumab over 18 months in a real-world setting. It is noteworthy that 86% of patients in this cohort maintained a PASI <3 response at month 18. These results are consistent with the 100-week data recently presented in the TILOT study, which showed that 84% of patients achieved an absolute PASI <3 after 100 weeks (13), further supporting the long-term effectiveness of tildrakizumab.

In terms of safety, few AEs were reported, and no patient discontinued the study drug due to an AE in this cohort. Tildrakizumab may increase the risk of infection. Adverse cardiovascular events and malignancies are also AEs of special interest among IL-23p19 inhibitors (6). At the time of this analysis, only 2 patients had reported infectious AEs and 1 patient had suffered a cardiac disorder. No malignancies were reported.

Limitations

Nonetheless, this study has several limitations. These include the small sample size and selection bias associated with real-world studies. In addition, only the 100 mg prefilled syringe of tildrakizumab was available during the study as the 200 mg prefilled syringe was not yet commercialized in Switzerland (the recommended dose is 100 mg, but a dose of 200 mg may be considered in patients with high disease burden or weighing more than 90 kg) (37).

Conclusion

This analysis of the effectiveness, safety, and impact on QoL of tildrakizumab for the treatment of psoriasis from the SDNTT registry demonstrated that, after 3 months of treatment, tildrakizumab significantly improved patients' skin symptoms and HRQoL, maintaining these responses until month 18. No new safety findings were recorded throughout the follow-up period. In conclusion, real-world data from the SDNTT registry support the

long-term effectiveness and favourable safety profile of tildrakizumab for the treatment of patients with moderate-to-severe plaque psoriasis. Overall, the results from Switzerland are consistent with those of real-world studies supporting the effectiveness and safety of long-term use of IL-23p19 inhibitors.

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Data availability statement: Datasets generated during and/or analysed during this study are available from the corresponding author upon reasonable request.

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