

ORIGINAL RESEARCH

Treatment of moderate-to-severe plaque psoriasis with tildrakizumab in the real-life setting

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Abstract

Background: Tildrakizumab is a high-affinity, humanized IgG1k monoclonal antibody targeting the p19 subunit of IL-23, which is a key regulatory cytokine in psoriasis. Based on evidence from clinical trials, tildrakizumab is approved for the treatment of moderate-to-severe plaque psoriasis in patients eligible for systemic therapy.

Methods: We report our clinical experience with 26 patients followed up to 24 weeks.

Results: No adverse event was observed and no patient discontinued tildrakizumab. Whilst no patient had a Psoriasis Area and Severity Index (PASI) score of <5 at baseline, at week 4, 8 (32%) patients had a PASI score of <3 and 6 of these had a PASI score of 0. At week 12, 19 (79%) patients had a PASI score of <5 and, among these, 18 had a PASI score of <3 of whom

16 had a PASI score of 0. At week 24, 22 (96%) patients had a PASI score of <3 and 20 (87%) had a PASI score of 0. Quality of life was improved after 4 weeks and through the whole period of observation.

Conclusion: Our experience in the real-life setting confirms the efficacy and safety of tildrakizumab as demonstrated by clinical trials.

Keywords: plaque psoriasis, Psoriasis Area and Severity Index, real life, tildrakizumab.

Citation

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Background

Tildrakizumab is a high-affinity, humanized IgG1k monoclonal antibody targeting the p19 subunit of IL-23, which is a key regulatory cytokine in psoriasis and stimulates the differentiation, proliferation and survival of T helper 17 cells.^{1,2} Two phase III trials demonstrated that tildrakizumab 100 mg and 200 mg were more effective in terms of Physician's Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI) 75 at week 12 in comparison with placebo and etanercept and were well tolerated without an increased incidence of serious adverse events.³ The efficacy of tildrakizumab has been shown to be sustained at 28 weeks and at 52 weeks of treatment and more than half of week 28 partial responders (PASI 50–75) improved their PASI responses to a PASI score of ≥ 75 at week 52.^{3,4} The pooled analysis of data from the two phase III trials found that responders at week 28 maintained their response through treatment for 3 years. In the same analysis, improvement of PASI scores at week 148 was found in

partial responders and non-responders to etanercept switched to tildrakizumab 200 mg.⁵ Based on evidence from clinical trials, tildrakizumab is approved for the treatment of moderate-to-severe plaque psoriasis in patients eligible for systemic therapy.⁶ Since approval, little has been published about the clinical use of this drug, suggesting that the reporting of experiences may be helpful to dermatologists to maximize the efficiency of this therapy.

Methods

In total, 26 patients with moderate-to-severe plaque psoriasis (body surface area involvement $\geq 10\%$, PGA score ≥ 3 and PASI score ≥ 12) at baseline and eligible for systemic therapy, who were referred to our clinic between March 2020 and September 2020, were administered 100 mg tildrakizumab at weeks 0 and 4 and then every 12 weeks by subcutaneous injection. This treatment was performed as recommended according to current clinical practice.⁶

Patients were assessed at baseline and at weeks 4, 12 and 24 by a clinical visit and recordings of PASI, PGA and Dermatology Life Quality Index (DLQI). At the moment of data collection, 23 patients had been followed up to week 24.

All patients signed informed consent to the use of clinical data for publication.

Statistical analysis

Data were summarized by descriptive analysis. Means, median and standard deviations (SDs) were calculated for continuous variables, whilst absolute values and frequency (percentage) were calculated for categorical variables. Comparison of mean values was performed by a *t*-test. The Wilcoxon-signed rank test was used to compare repeated measurements in each group and the Mann–Witney test was used to compare mean data between groups. All analyses were performed with IBM SPSS Statistics for Windows, Version 26.0.

Results

Baseline characteristics

Baseline characteristics are reported in Table 1. Only 5/26 (19%) patients had concomitant psoriatic arthritis, and hypertension was the most frequent comorbidity (12/26, 46%). All patients had received previous systemic therapy and 21/26 (81%) had never been treated with biologic drugs. Two patients had received adalimumab, one had received etanercept, one had

received ixekizumab and one had received ustekinumab. At baseline, mean PASI was 12.5 ± 6.5 , mean PGA was 2.6 ± 1 and mean DLQI was 15.9 ± 4 .

One patient was lost to follow-up before 4 weeks of treatment and was excluded from the analysis of results.

Tolerability

No adverse event was reported during treatment with tildrakizumab, and no patients discontinued the treatment.

Treatment efficacy

The mean PASI score was reduced to 6.1 ± 5.2 after 4 weeks of treatment ($n=25$), to 1.8 ± 2.9 after 12 weeks ($n=24$), and to 0.6 ± 2.1 after 24 weeks ($n=23$). All these changes from baseline were significant ($p<0.001$).

Whilst no patient had a PASI score of <5 at baseline, at week 4, 8 (32%) patients had a PASI score of <3 and 6 of these had a score of PASI 0. At week 12, 19 (79%) patients had a PASI score of <5 and, among these, 18 had a PASI score of <3 and, of these, 16 had a PASI score of 0. At week 24, 22 (96%) patients had a PASI score of <3 and 20 (87%) had a PASI score of 0.

PASI 90 was reached by 6/25 (24%) patients at 4 weeks, by 17/24 (71%) patients after 12 weeks and by 21/23 (91%) patients after 24 weeks. PASI 100 was reached by 6/25 (24%) patients at 4 weeks, by 16/24 (67%) patients after 12 weeks and by 20/23 (87%) patients after 24 weeks (Figure 1). In addition, mean PGA and DLQI scores were significantly reduced at each time point in comparison with baseline values ($p<0.001$ for both scores; Table 2).

No significant difference was found between patients who had not previously been treated with biologic drugs *versus* those who were not naive to biologic drugs and in patients who were overweight *versus* those of normal weight; indeed, we

Table 1. Baseline characteristics of 26 patients treated with tildrakizumab.

Characteristics	n (%) / mean \pm SD
Men	14 (53.8)
Age (years)	56 ± 16
Bodyweight (kg)	75 ± 16
BMI (kg/m ²)	26.4 ± 5.9
Psoriasis duration (years)	11.9 ± 8.3
Psoriatic arthritis	5 (19.2)
Obesity	4 (15.4)
Diabetes	2 (7.7)
Hypercholesterolaemia	5 (19.2)
Hypertension	12 (46.2)
Previous systemic therapy	26 (100)
Previous biologic therapy	5 (19.2)
Psoriasis Area and Severity Index (PASI)	12.5 ± 6.5
Physician's Global Assessment (PGA)	2.6 ± 1
Dermatology Life Quality Index (DLQI)	15.9 ± 4

Figure 1. Proportion of patients with PASI90 and PASI100 by visit.

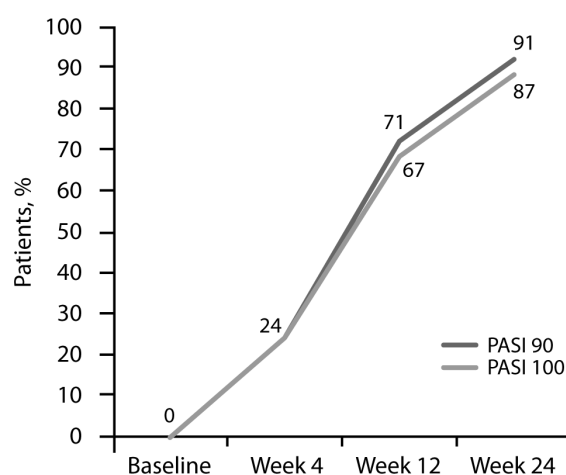


Table 2. Mean value \pm SD of PGA and DLQI at baseline and at visits.

<i>n</i>	Baseline	Visit value	<i>p</i> value
PGA			
25	2.6 \pm 1	Week 4 1.6 \pm 1.2	<0.001
24	2.6 \pm 1	Week 12 0.5 \pm 0.8	<0.001
23	2.6 \pm 1	Week 24 0.3 \pm 0.9	<0.001
DLQI			
26	15.9 \pm 4	Week 4 9.1 \pm 2	<0.001
24	15.8 \pm 4.0	Week 12 2.3 \pm 1.6	<0.001
23	15.7 \pm 4.1	Week 24 2.2 \pm 4.2	<0.001

DLQI, Dermatology Life Quality Index; PGA, Physician's Global Assessment.

acknowledge that the low number of patients may account for the impossibility to detect any role of previous treatments or body weight.

Psoriatic arthritis

The five patients with psoriatic arthritis had been diagnosed by a rheumatologist several years before our observation for plaque psoriasis. None of them had rheumatologic symptoms when tildrakizumab was initiated and no patient reported joint pain during treatment with tildrakizumab. They were all assessed up to week 24.

The mean PASI score was 15 \pm 9.3 at baseline, 8.4 \pm 6.9 at week 4, 2.8 \pm 3.9 at week 12 and 0.6 \pm 0.9 at week 24. Indeed, a PASI score of <3 (no patient had this score at baseline) was found in 1 patient at week 4, in 3 patients at week 12 and in all 5 patients at week 24. A PASI score of 0 was present in 3 patients at week 12 and was maintained in these 3 patients at week 24.

The mean PGA was 2.8 \pm 1.3 at baseline, 2.2 \pm 1.1 after 4 weeks, 0.8 \pm 1.1 after 12 weeks and 0.4 \pm 0.5 after 24 weeks. The DLQI score was 17.2 \pm 5.4 at baseline, 11 \pm 2.2 after 4 weeks, 2.2 \pm 1.5 after 12 weeks and 2 \pm 2 after 24 weeks.

Conclusion

Tildrakizumab 100 mg was well tolerated and no adverse event was reported by our patients during the whole 24-week follow-up period. No adverse event was reported and no patient discontinued the treatment. The therapy was as effective as expected based on data from clinical trials

Figure 2. Exemplary patients before (A and B) and after (C and D) treatment with tildrakizumab for 4 weeks.

(Figure 2). Although we cannot draw conclusions from a scant sample, we can observe that psoriasis improvement in our experience was relevant after only 4 weeks of treatment, suggesting that the time to response may be shorter than demonstrated by clinical trials. The improvement of plaque psoriasis progressed after 12 weeks of therapy up to 24 weeks and PASI 100 was obtained by a high proportion of patients at the end of this period. This observation is in agreement with evidence from the two randomized trials, where the maximal efficacy of tildrakizumab was reached between week 22 and week 28.³ Moreover, the overall efficacy was higher in our patients in comparison with results from trials.³ A significant benefit on quality of life was present after only 4 weeks of treatment and it was maintained up to the 24 weeks of follow-up. Tildrakizumab was as effective in overweight patients, who are often difficult to treat, as in non-overweight patients.^{7,8} Although the sample number is limited to draw conclusions, we observed that tildrakizumab efficacy and safety were similar in patients who had previously received systemic biologic treatment for psoriasis and in patients naïve to biologic drugs.

In conclusion, our experience confirms the efficacy and safety of tildrakizumab when used in real-life practice. Tildrakizumab represents an efficient strategy for subjects with moderate-to-severe disease, who need long-term persistent efficacy and safety of treatment.

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