Real-world effectiveness and quality of life outcomes of tildrakizumab for moderate-to-severe plaque psoriasis in the United States: A systematic literature review and meta-analysis

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INTRODUCTION

- Psoriasis affects approximately 2% of adults in the US, with plaque psoriasis being the most prevalent form, representing up to 90% of cases[1]
- Plaque psoriasis is characterized by red, scaly plaques, often located on the elbows, knees, and scalp, although these plaques may also appear more extensively[2]
- The condition significantly impairs quality of life, causing physical discomfort such as itching and pain, psychological stress including depression and suicidal thoughts, and social difficulties like stigmatization[3-5]
- While psoriasis is not curable, various treatment options are available to manage symptoms, including topical treatments, phototherapy, systemic therapies, and biologics
  - Treatment selection often depends on the characteristics of the lesions and patient preferences[6-8]
- Tildrakizumab, a monoclonal antibody targeting interleukin-23 p19, is a therapeutic option for patients who qualify for systemic therapy or phototherapy

OBJECTIVE

- This systematic literature review and meta-analysis evaluated the real-world effectiveness of tildrakizumab and quality of life in patients with moderate-to-severe plaque psoriasis in the US with comparison to the ex-US population

METHODS

Systematic literature review

- MEDLINE® and Embase® were comprehensively searched on November 16, 2023
  - Key dermatology and rheumatology conferences (2021–2023), as well as bibliographies of previous literature reviews, were also searched
- Eligible studies were real-world evidence (RWE) studies, published in English, examining the effectiveness or quality of life associated with tildrakizumab in adults (aged ≥18 years) with chronic moderate-to-severe plaque psoriasis
  - Included RWE study designs were cohort studies, single-arm trials, Phase IV trials, pragmatic trials, case-control studies, and case series
  - Outcomes of interest were effectiveness (Psoriasis Area and Severity Index [PASI] score, Physician Global Assessment [PGA], affected Body Surface Area % [%BSA]), and quality of life (Dermatology Life Quality Index [DLQI] score)
- Quality of the included studies was assessed using the Newcastle-Ottawa Scale for non-randomized studies[9] and the Joanna Briggs Institute tool for case series[10]

Meta-analysis

- Meta-analyses were determined to be feasible for effectiveness and quality of life outcomes at grouped time points (12–16 weeks, 24–28 weeks, and 36–52 weeks)
  - Either random effects (DerSimonian and Laird inverse variance method) or fixed effects meta-analyses were used based on the degree of observed statistical heterogeneity[11]
  - Analyses were stratified by geographic setting (ie, US vs ex-US)
  - Estimates were reported as mean and 95% confidence interval (CI)

RESULTS

Study selection

- Of 9865 records identified, 43 unique studies pertaining to 62 publications were included in the review (**Figure 1**)
  - 37 of these unique studies, pertaining to 45 publications, were determined eligible for meta-analysis

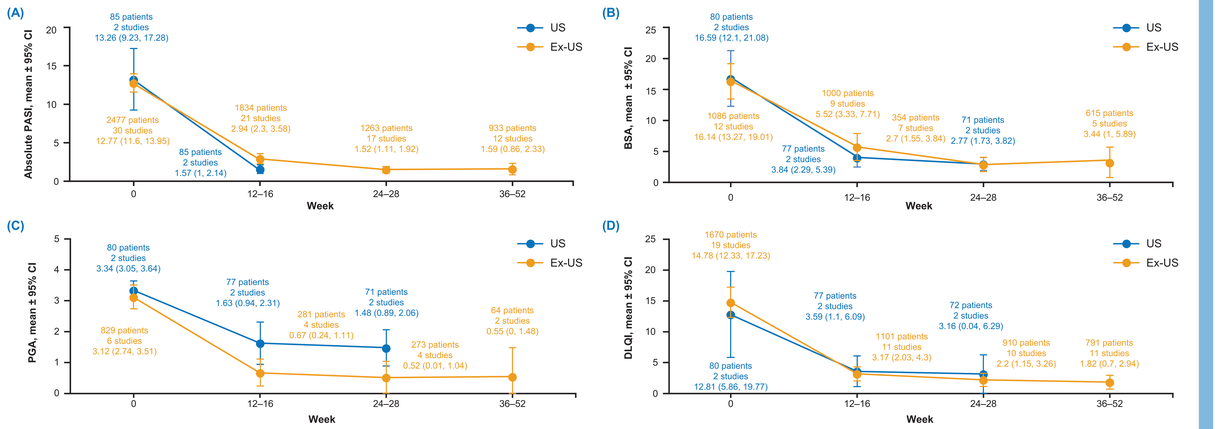
Characteristics of studies included for meta-analysis

- Three US studies were included: 2 prospective cohorts and 1 retrospective cohort
  - The remaining 34 studies were conducted in Europe; designs included 4 prospective and 29 retrospective cohorts, and 1 case series
- Studies were conducted between 2018 and 2021 for US studies, and from 2019 to 2023 for ex-US studies
- Study sample size ranged from 25 to 30 patients in US studies (110 patients total)
  - Sample size of ex-US studies ranged from 8 to 1981 participants (5199 patients total)
- Data sources of US studies included dermatology outpatient clinics in two studies; the third study did not report a data source
  - Data sources in ex-US studies also typically encompassed hospitals or clinics

Tildrakizumab-treated patients in the US experienced between 56% and 88% improvement across all four clinical outcomes at 12–16 and 24–28 weeks

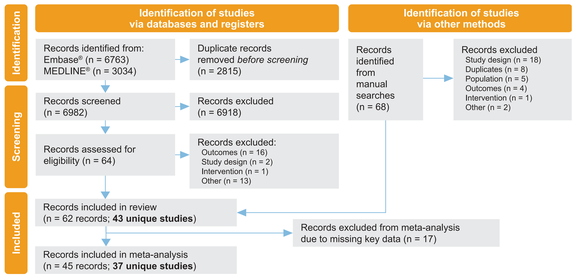
(88% improvement in mean absolute PASI scores at 12–16 weeks, 83% improvement in %BSA at 24–28 weeks, 56% improvement in PGA scores at 24–28 weeks, and 75% improvement in DLQI at 24–28 weeks)

Figure 2. Meta-analysis results for (A) absolute PASI score, (B) %BSA, (C) PGA, and (D) DLQI across different time points (95% CI) for US vs ex-US studies



For absolute PASI score, values range from 0 to 72 and values closer to 1 denote less severe disease; PASI score <5 indicates mild disease. For %BSA, values range from 0 to 100; values <5% denote mild disease, while values >10% denote severe disease. For PGA, scores range from 0 to 5 and values closer to 0 denote less severe symptoms; score of 2 indicate mild disease. For DLQI, scores range from 0 to 30 and scores closer to 0 denote less severe disease; scores of 0 to 1 indicate no effect of the disease on patients' quality of life. BSA, body surface area; CI, confidence interval; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

Figure 1. PRISMA flow diagram



n, number of records.

Patient characteristics and quality of studies included for meta-analysis

- Studies conducted in the US vs ex-US were generally homogeneous in terms of age and sex (**Table 1**)
- Diabetes mellitus, hypertension, and psoriatic arthritis were prevalent comorbidities
- Study quality was generally moderate to high due to reliable sample representation and data collection methods

Meta-analysis of US studies

- Single-arm meta-analyses of absolute PASI scores showed a reduction in mean score from 13.26 (95% CI: 9.23, 17.28) at baseline to 1.57 (95% CI: 1.00, 2.14) at 12–16 weeks (**Figure 2A**)
- %BSA decreased from 16.59% (95% CI: 12.10, 21.08) to 2.77% (95% CI: 1.73, 3.82) at 24–28 weeks (**Figure 2B**)
- PGA showed improvement from 3.34 (95% CI: 3.05, 3.64) to 1.48 (95% CI: 0.89, 2.06) at 24–28 weeks (**Figure 2C**)
- DLQI decreased from 12.81 (95% CI: 5.86, 19.77) to 3.16 (95% CI: 0.04, 6.29) at 24–28 weeks (**Figure 2D**)

Table 1. Summary of patient characteristics

Setting	Mean age, years	Males, %	Diabetes mellitus, %	Hypertension, %	Psoriatic arthritis, %
United States	48.6 – 60.6 Median: 52.6	50.9 – 68.0 Median: 56.7	23.3	40.0	–
Ex-United States	41.7 – 70.5 Median: 47.9	36.4 – 90.0 Median: 60.9	5.5 – 37.5 Median: 15.7	17.9 – 75.0 Median: 33.7	6.7 – 62.5 Median: 20.5

Meta-analysis of ex-US studies

- Outside of the US, results were similar at comparable time points (**Table 2**). Absolute PASI decreased from 12.77 at baseline (95% CI: 11.60, 13.95) to 2.94 (95% CI: 2.30, 3.58) at 12–16 weeks (**Figure 2A**)
- %BSA decreased from 16.14% (95% CI: 13.27, 19.01) to 2.70% (95% CI: 1.55, 3.84) at 24–28 weeks (**Figure 2B**)
- PGA showed reduction from 3.12 (95% CI: 2.74, 3.51) to 0.52 (95% CI: 0.01, 1.04) at 24–28 weeks (**Figure 2C**)
- DLQI decreased from 14.78 (95% CI: 12.33, 17.23) to 2.20 (95% CI: 1.15, 3.26) at 24–28 weeks (**Figure 2D**)

Table 2. Percent improvement in clinical outcomes from baseline to latest comparable time point for United States vs ex-United States studies

Outcome (latest comparable time point)	Improvement from baseline	
	United States	Ex-United States
Absolute PASI (12–16 weeks)	88%	77%
BSA (24–28 weeks)	83%	83%
PGA (24–28 weeks)	56%	83%
DLQI (24–28 weeks)	75%	85%

BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment.

DISCUSSION

- This comprehensive meta-analysis is the first to exclusively examine real-world studies of patients with plaque psoriasis treated with tildrakizumab; findings showed sustained improvements in symptoms over time
  - US patients treated with tildrakizumab showed improvements consistent with those from ex-US studies
  - Findings for both US and ex-US studies aligned with those from randomized controlled trials[12]
- While rigorous statistical methods were applied to aggregate the published data,[11] results should be interpreted with caution due to the inherent biases within real-world studies

CONCLUSIONS

- This systematic review and meta-analysis of RWE demonstrates that tildrakizumab is consistently associated with sustained, long-term effectiveness and improved quality of life, and is well tolerated in US patients with moderate-to-severe plaque psoriasis
- In patients with moderate-to-severe plaque psoriasis who were treated with tildrakizumab, improvement in the first 3 months of treatment was observed for PASI, BSA, PGA, and DLQI
  - These improvements were sustained for up to 6 months in US patients
  - Pooled estimates of outcomes indicated characteristics of moderate-to-severe disease at baseline and mild disease after 6 months of tildrakizumab treatment
  - Results were consistent with data from ex-US studies
- Tildrakizumab showed consistency in improvements across all four clinical outcomes (PASI, BSA, PGA, and DLQI)

REFERENCES

1. Weigle N, et al. *Am Fam Physician.* 2013;87(9):626–33.
2. Lowes MA, et al. *Nature.* 2007;445(7130):866–73.
3. Zhong H, et al. *Health Qual Life Outcomes.* 2021;19(1):271.
4. Colombo D, et al. Quality of Life in Psoriasis. In: Hermenio L, ed. *Psoriasis - Types, Causes and Medication.* Rijeka: IntechOpen; 2013:Ch. 7.
5. Bhosle MJ, et al. *Health Qual Life Outcomes.* 2006;4(1):35.
6. Reid C, et al. *Acta Derm Venereol.* 2020;100(3):adv00032.
7. Anderson KL, et al. *J Am Acad Dermatol.* 2015;72(5):868–878.e861.
8. Menter A, et al. *J Am Acad Dermatol.* 2011;65(1):137–74.
9. Wells GA, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analyses. 2001.
10. Munn Z, et al. *JBI Evidence Synthesis.* 2020;18(10):2127-33.
11. Deeks JJ, et al. Chapter 10: Analysing data and undertaking meta-analyses. In: *Cochrane Handbook for Systematic Reviews of Interventions.* Cochrane Statistical Methods Group; 2023.
12. Reich K, et al. *Lancet.* 2017;390(10091):276–88.

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