# A systematic literature review and meta-analysis of the real-world effectiveness, quality of life, and safety of tildrakizumab for moderate-to-severe plaque psoriasis

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## BACKGROUND

- Psoriasis affects roughly 2% of adults in the United States (US); plaque psoriasis is the most common variant, accounting for up to 90% of cases[1,2]
- Plaque psoriasis is characterized by red, scaly plaques typically found on elbows, knees, and the scalp; however, plaques may also become more widespread[3]
- Impacts on quality of life are significant and debilitating and include physical discomfort (itching, pain), psychological stress (depression, suicidal ideation), and social challenges (stigmatization)[4-6]
- Although incurable, treatment options for symptoms include topical treatments, phototherapy, systemic therapies, and biologics
  - — Treatments are often chosen based on lesion characteristics and patient preferences[7-9]
- Tildrakizumab, an anti-IL-23 p19 monoclonal antibody, offers a treatment option for patients eligible for systemic therapy or phototherapy

## OBJECTIVE

- This systematic literature review and meta-analysis evaluated the real-world effectiveness, quality of life, and safety of tildrakizumab for treatment of patients with moderate-to-severe plaque psoriasis

## METHODS

### Study selection

- 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, quality of life, and safety associated with tildrakizumab in adults (aged ≥18 years) with chronic moderate-to-severe 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's Global Assessment [PGA], affected Body Surface Area % [%BSA]), quality of life (Dermatology Life Quality Index [DLQI] score), or safety (serious adverse events [SAE], treatment-related AEs [TRAE], or withdrawals due to AEs [WDAE])
- Quality of the included studies was assessed using the Newcastle-Ottawa Scale for non-randomized studies[10] and the Johanna Briggs Institute tool for case series[11]

### Meta-analysis

- Meta-analyses were determined to be feasible for outcomes on effectiveness, quality of life, and safety 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[12]
  - — Subgroup analyses (geographic setting, prior biologic exposure, and presence of comorbidities) were explored

## RESULTS

### Study selection

- Of 9,865 records identified, 43 unique studies pertaining to 62 publications were included in the qualitative analysis (**Figure 1**)
  - — 37 of these unique studies, pertaining to 45 publications, were determined to be eligible for the meta-analysis

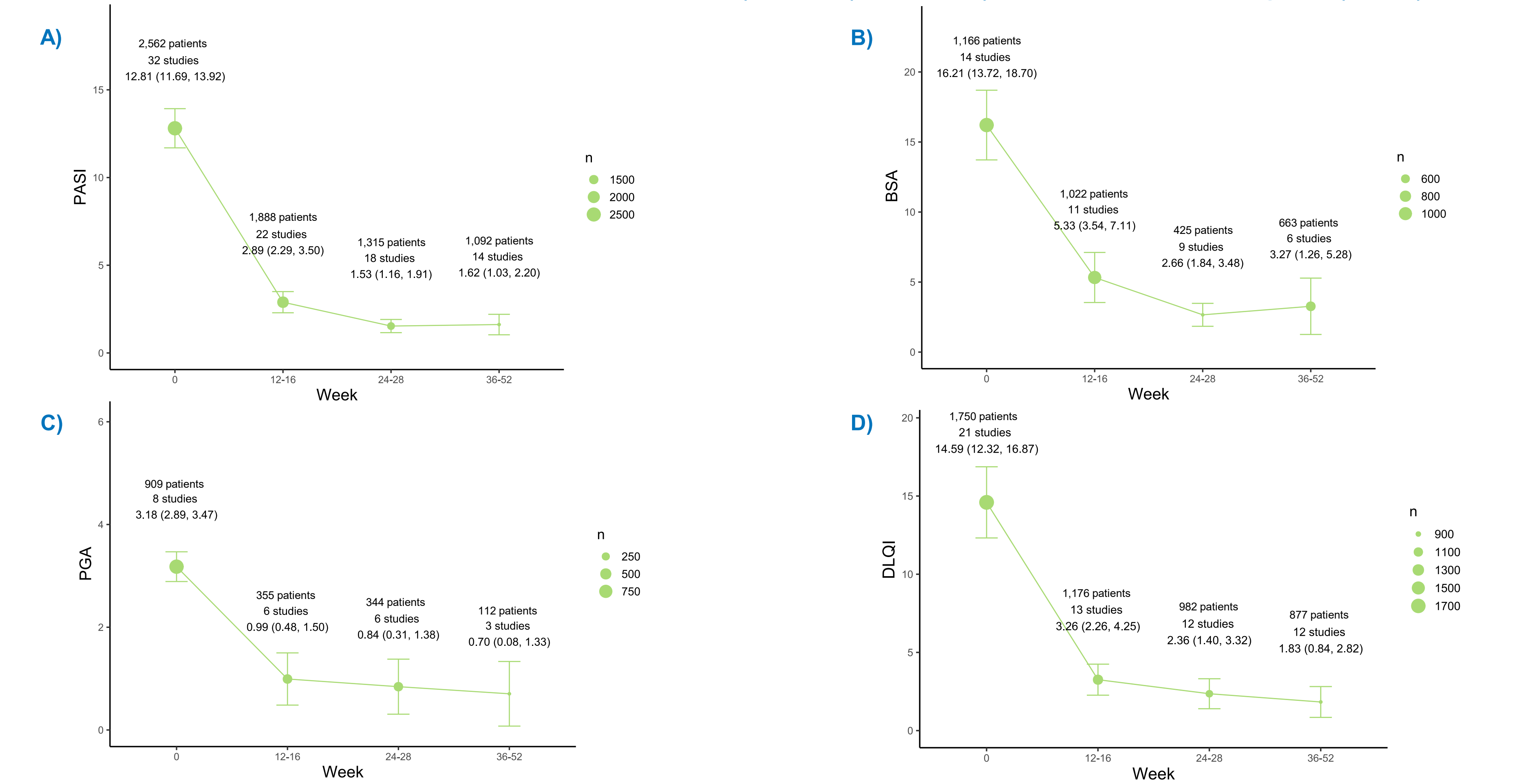
### Study characteristics

- Studies were conducted between 2018 and 2023
- Designs included 34 retrospective cohorts, 5 prospective cohorts, 3 Phase IV observational studies, and 1 case series
  - — Data sources encompassed 31 studies from hospitals or clinics and 4 from databases or registries; 8 studies did not report a data source
- Studies were generally conducted in the US and Europe; majority were conducted in Europe
- Study sample size ranged from 8 to 4,178 participants (median: 81)
- Majority were single-arm studies that measured outcomes for tildrakizumab only
  - — 6 studies compared tildrakizumab directly with guselkumab and 5 compared with risankizumab

## Tildrakizumab-treated patients experienced between 78% and 87% improvement across all four clinical outcomes at 36 to 52 weeks

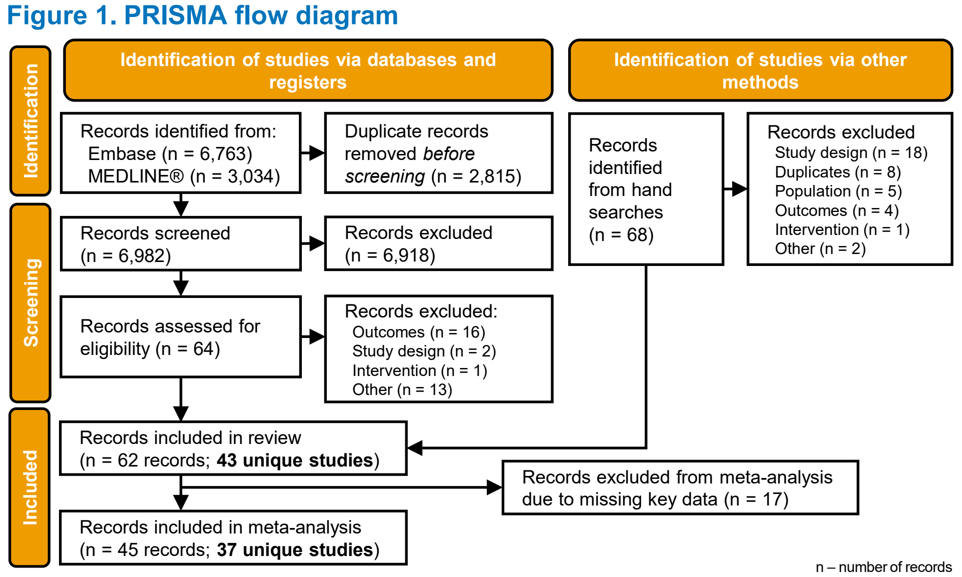
## (87% improvement in mean absolute PASI scores, 80% improvement in %BSA, 78% improvement in PGA scores, and 87% improvement in DLQI)

**Figure 2. Meta-analysis results for A) absolute PASI score, B) %BSA, C) PGA, and D) DLQI across different timepoints (95% CI)**




Findings from meta-analyses of effectiveness and quality-of-life data from real-world evidence studies of tildrakizumab are presented. Larger point estimates represent a larger number of data points contributing to the pooled estimate. 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 0/1, scores range from 0 to 4 and values closer to 0 denote less severe symptoms; scores 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; n – number of patients; PASI – Psoriasis Area and Severity Index; PGA – Physician's Global Assessment.

**Figure 1. PRISMA flow diagram**




### Patient characteristics and study quality

- Studies were generally considered homogeneous in terms of age and sex (**Table 1**)
- Prevalent comorbidities were diabetes mellitus, hypertension, and psoriatic arthritis
- The quality of included studies was generally moderate to high, indicating reliable sample representation and outcome data collection methods

### Meta-analysis

- Single-arm meta-analyses of absolute PASI scores for tildrakizumab demonstrated a reduction in mean score from 12.81 at baseline (95% confidence interval [CI] 11.69, 13.92) to 1.62 (95% CI 1.03, 2.20) after 36-52 weeks (**Figure 2A**)
- %BSA showed an improvement from 16.21% at baseline (95% CI 13.72, 18.70) to 3.27% (95% CI 1.26, 5.28) at 36-52 weeks (**Figure 2B**)

**Table 1. Summary table of frequently reported patient characteristics**

| | Mean Age, Years | Males, % | Diabetes Mellitus, % | Hypertension, % | Psoriatic Arthritis, % |
|---|---|---|---|---|---|
| **Range** | 41.9 - 70.5 | 36.4 - 76.5 | 5.5 - 32.4 | 18.0 - 70.6 | 6.7 - 52.9 |
| **n** | 37 | 38 | 23 | 21 | 18 |

n – number of studies reporting

- Clinically important reductions were also identified at 36-52 weeks for PGA 0/1 (**Figure 2C**) and DLQI (**Figure 2D**)
- Comparative meta-analyses found no significant differences at 12-16 or 24-28 weeks for PASI score and %BSA for tildrakizumab vs. guselkumab or risankizumab (data not shown)
- Single-arm meta-analyses (**Table 2**) and comparative meta-analyses (data not shown) of safety outcomes showed that SAEs, TRAEs, and WDAEs were rare and similar in frequency for tildrakizumab compared with guselkumab and risankizumab
- Subgroup analyses corroborated the findings from the primary analyses (data not shown)

**Table 2. Summary of safety findings from single-arm meta-analyses of real-world evidence studies of tildrakizumab**

| Pooled percentage (95% CI) of patients with adverse event from meta-analysis for tildrakizumab | | | | |
|---|---|---|---|---|
| **Time** | **% with any AE (n = 13; N = 1,043)** | **% with SAE (n = 15; N = 941)** | **% with TRAE (n = 4; N = 843)** | **% with WDAE (n = 16; N = 1,227)** |
| **Weeks 24-28** | 4.79 (0.31, 12.56); n = 8; N = 626 | 0 (0 to 0.12); n = 9; N = 475 | 3.30 (0, 10.95); n = 2; N = 288 | 0 (0, 0.12); n = 9; N = 606 |
| **Weeks 48-52** | 1.77 (0.01, 5.33); n = 5; N = 417 | 0.25 (0, 2.26); n = 6; N = 466 | 10.13 (2.54, 21.76); n = 2; N = 555 | 0.31 (0, 1.56); n = 7; N = 621 |

Findings from meta-analyses of real-world evidence studies of tildrakizumab are presented. AE – adverse event; n – number of studies included in meta-analysis; N – number of patients included in meta-analysis; SAE – serious adverse event; TRAE – treatment-related adverse event; WDAE – withdrawal due to adverse event

## DISCUSSION

- This is the first comprehensive meta-analysis to focus solely on real-world studies of patients with plaque psoriasis who received tildrakizumab; results demonstrated sustained improvements in patients' symptoms over time
  - — Although standard and robust statistical methods were used to synthesize published data,[12] real-world studies have inherent biases, and data should be interpreted with caution
- Findings were consistent with those from randomized controlled trials[13]

## 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 patients with moderate-to-severe plaque psoriasis
- In patients with moderate-to-severe plaque psoriasis who were treated with tildrakizumab, a considerable improvement in the first 3 months of treatment was observed for PASI, BSA, PGA, and DLQI
  - — Improvements in these outcomes were sustained for up to one year
  - — Pooled estimates of outcomes indicated characteristics of moderate-to-severe disease at baseline and mild disease after one year of tildrakizumab treatment
- Tildrakizumab showed consistency in improvements across all four clinical outcomes (PASI, BSA, PGA, and DLQI)
- Findings are consistent with those from randomized controlled trials

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## DISCLOSURES

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