Comparative Efficacy and Safety of Tildrakizumab for Moderate-to-Severe Plaque Psoriasis: A Systematic Literature Review (SLR) and Network Meta-Analysis (NMA)

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INTRODUCTION

- Moderate-to-severe plaque psoriasis is a chronic, immune-mediated condition that significantly impacts quality of life, but effective management is possible with biologic therapies.
- Comparisons of biologic therapies in previously published systematic literature reviews and network meta-analyses focused on the induction period or long-term follow-up.[1,2]
- Mid-range time points (such as week 28) are often omitted from analyses due to a lack of placebo data for network comparisons, leaving a significant gap in the literature. This is crucial as some biologics, such as tildrakizumab, do not reach full efficacy until well after the induction period.
- Therefore, comparison of biologics during the mid-range time point may assist healthcare providers in making informed decisions on patient care.

OBJECTIVE

Our aim was to compare the clinical efficacy of available biologics to treat moderate-to-severe plaque psoriasis at 28 weeks, and to explore changes in treatment efficacy over time.

METHODS

Systematic Literature Review

- An SLR was conducted following Cochrane guidelines, by searching MEDLINE®, Embase, CENTRAL, and grey literature sources from database inception to January 10, 2024.
- After exclusion of duplicates, two investigators reviewed all abstracts and proceedings identified through the searches and applied PICOS criteria to assess eligibility as follows:
  - **Population.** Studies that enrolled adults with moderate-to-severe plaque psoriasis were sought, while studies that enrolled patients with mild disease and other conditions were excluded.
  - **Interventions/Comparators.** Studies that compared groups receiving approved dosages of biologic treatments including tildrakizumab (TIL 100mg Q12W), secukinumab (SEC 150mg Q4W and SEC 300mg Q4W), risankizumab (RIS 150mg Q12W), ustekinumab (UST 45mg Q12W and UST 90mg Q12W), ixekizumab (IXE 80mg Q4W), guselkumab (GUS 100mg Q8W), brodalumab (BRO 210mg Q2W), adalimumab (ADA 40mg Q2W), certolizumab pegol (CER 400mg Q2W), etanercept (ETN 50mg BIW/QW), infliximab (INF 5mg/kg Q8W), bimekizumab (BIM 320mg Q4W) and placebo were included; studies of investigational or non-approved therapies were excluded.
  - **Outcomes.** Measures of PASI response (PASI 75, 90 and 100, respectively), PGA 0/1 response, and DLQI 0/1 response. The primary time point of interest for efficacy outcomes was mid-term follow-up at 28 weeks, while analyses of 12-week and 16-week data were also performed to explore changes in treatment efficacy over time. Safety outcomes of interest were measured at Week 16 and included the occurrence of any adverse event (AE) as well as serious adverse events (SAE).
  - **Study Design.** Randomized controlled trials.
- Study selection and extraction were performed by two independent reviewers then reconciled, with a third reviewer intervening when necessary to reach a consensus.

Network Meta-Analysis

- Bayesian NMAs adjusted for placebo group response were performed to assess the comparative efficacy via PASI (Psoriasis Area and Severity Index) 75/90/100, PGA (Physician's Global Assessment) 0/1, DLQI (Dermatology Life Quality Index) 0/1 at weeks 12, 16, and 28, safety (any AE, and discontinuation due to AE at week 12) of tildrakizumab against other biologics.
- When 12-, 16-, or 28-week data were not available, the nearest available data within two weeks were substituted in the 12- and 16-week analyses and within four weeks were used in the 28-week analysis. Since most psoriasis trials end placebo treatment after 12-16 weeks, missing placebo data were substituted with the latest available data (i.e., last observation carried forward).

METHODS (continued)

- Following the recommendations of the National Institute for Health and Care Excellence (NICE), we planned to use a fixed effects (FE) model when only one trial was available per treatment comparison. For all other cases, both the FE model and the RE model were applied, with the better-fitting model used for interpretation.
- Findings were expressed in terms of the number needed to treat (NNT) with 95% credible intervals (CrI), as well as risk differences (RD).
- NNTs nearest 1 and RDs nearest 100% were indicative of preferred treatments for efficacy outcomes.

RESULTS

Systematic Literature Review

- The search identified 10,683 publications. Following de-duplication, 7,418 unique publications were screened based on the title and abstract, of which 751 were screened based on their full-text articles.
- In total, 187 publications pertaining to 124 RCTs were included in the SLR, of which 103 RCTs formed the global network for the NMA (**Figure 1**).
- Studies were published from 2001 to 2022 with a median sample size of 250 participants (range 12 to 1,881). Most trials were inter-continental (56.3%) and double-blinded, multi-center studies.
- The median patient age was 45.2 years, with a median of 31.3% female participants. Median baseline values included a PASI score of 20.2, % BSA of 27.3%, DLQI of 12.6, and median proportion of patients with PGA severe or very severe was 29.2%.

Network Meta-Analysis

- NNTs vs. placebo for tildrakizumab from NMAs were comparable to those associated with other biologics for efficacy and quality of life endpoints at week 28 (**Figure 2** and **Figure 3**).
- Tildrakizumab demonstrated improved efficacy and quality of life over time:
  - **PASI 75**: Improved with tildrakizumab from week 12 (NNT 1.75, 95% CrI 1.56 to 1.99) to week 16 (NNT 1.42, 95% CrI 1.34 to 1.56) to week 28 (NNT 1.36, 95% CrI 1.32 to 1.46).
  - **PASI 90**: Improved with tildrakizumab from week 12 (NNT 2.51, 95% CrI 2.02 to 3.31) to week 16 (NNT 1.94, 95% CrI 1.60 to 2.44) to week 28 (NNT 1.56, 95% CrI 1.45 to 1.85).
  - **PASI 100**: Improved with tildrakizumab from week 12 (NNT 10.13, 95% CrI 6.88 to 16.77) to week 16 (NNT 6.08, 95% CrI 4.60 to 9.00) to week 28 (NNT 4.01, 95% CrI 3.26 to 5.35).
  - **PGA 0/1**: Improved with tildrakizumab from week 12 (NNT 2.18, 95% CrI 1.82 to 2.67) to week 16 (NNT 1.63, 95% CrI 1.43 to 1.89) to week 28 (NNT 1.51, 95% CrI 1.36 to 1.80).
  - **DLQI 0/1**: Improved with tildrakizumab from week 12 (NNT 3.17, 95% CrI 2.45 to 4.34) to week 16 (NNT 1.61, 95% CrI 1.39 to 2.78), then regressed slightly at week 28 (NNT 2.15, 95% CrI 1.67 to 2.96).
- Tildrakizumab had a similar safety profile to other active therapies:
  - For risk of any AE, tildrakizumab and every other therapy except infliximab 5mg/kg were not significantly different from placebo.
  - For risk of any SAE, no therapy was significantly different from placebo.

CONCLUSION

- This study provides the most up-to-date assessment of comparative efficacy and safety of biologics for moderate-to-severe plaque psoriasis.
- In multiple efficacy assessments, biologics were superior to placebo and demonstrated improvements in quality of life through 28 weeks of treatment.
- Tildrakizumab demonstrated a comparable efficacy profile at week 28 and safety profile at week 16 to those of other biologics.
  - Within the IL-23 inhibitor class, the efficacy differences at week 28 relative to placebo between tildrakizumab, risankizumab, and guselkumab were small with 95% CrIs around tildrakizumab capturing the other IL-23 inhibitors.
- These mid-term findings will assist healthcare providers in making informed treatment decisions when managing patients with moderate-to-severe plaque psoriasis.

Figure 1. Global Network

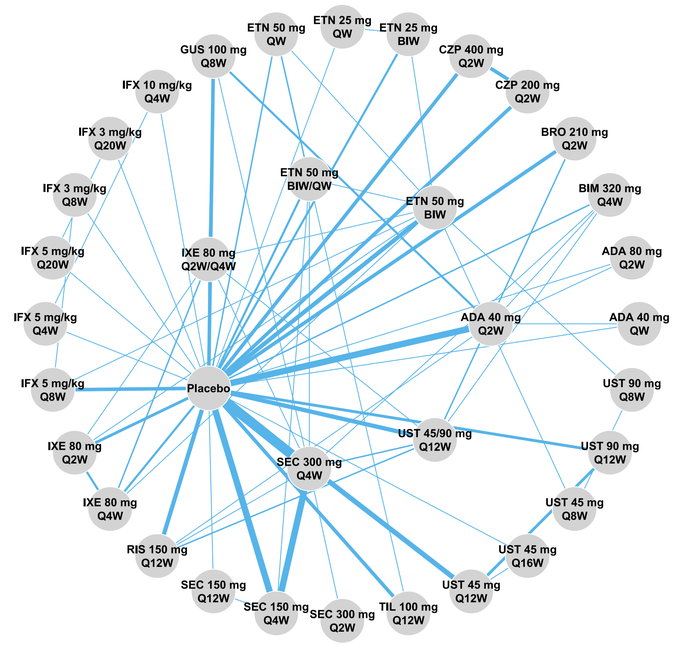
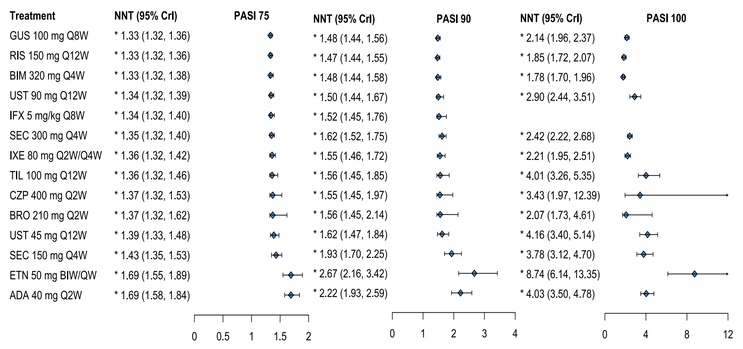
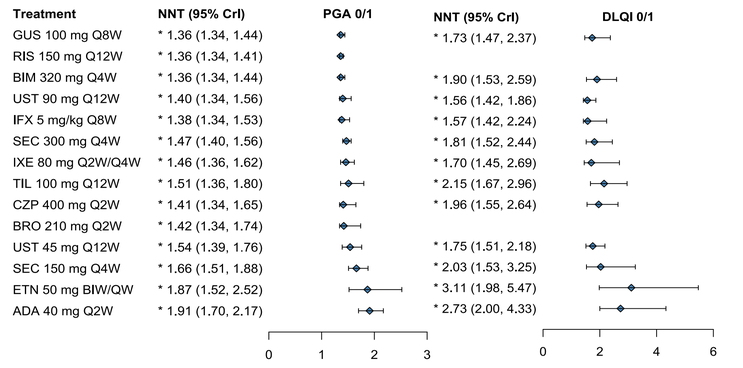


Figure 2. Forest plot of NNTs vs. placebo for PASI 75/90/100 at week 28.



Abbreviations: * – Statistically significant vs. placebo, ADA – Adalimumab, BIM – Bimekizumab, BIW – Twice Weekly, BRO – Brodalumab, CrI – Credible Interval, CZP – Certolizumab pegol, ETN – Etanercept, GUS – Guselkumab, IFX – Infliximab, IXE – Ixekizumab, NNT – Number Needed to Treat, PASI – Psoriasis Area and Severity Index, Q#W – Every # weeks, QW – Once Weekly, RIS – Risankizumab, SEC – Secukinumab, TIL – Tildrakizumab, UST – Ustekinumab

Figure 3. Forest plot of NNTs vs. placebo for PGA 0/1 and DLQI 0/1 at week 28.



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REFERENCES

1. Armstrong AW, Puig L, Joshi A, et al. Comparison of Biologics and Oral Treatments for Plaque Psoriasis: A Meta-analysis. JAMA Dermatology. 2020;156(3):258-269.
2. Leonardi CL, See K, Burge R, et al. Number Needed to Treat Network Meta-Analysis to Compare Biologic Drugs for Moderate-to-Severe Psoriasis. Advances in Therapy. 2022;39(5):2256-2269.

DISCLOSURES

- This study was funded by Sun Pharmaceutical Industries Limited and conducted by Evidinno Outcomes Research Inc.
- **Mark Lebwohl** is an employee of Mount Sinai; receives research funds from Abbvie, Arcutis, Avotres, Boehringer Ingelheim, Cara therapeutics, Clexio, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Janssen, Pfizer, Sanofi-Regeneron, and UCB; and is a consultant for Almirall, AltruBio Inc., Apogee, Arcutis, Inc., AstraZeneca, Atomwise, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celltrion, Corevitas, Dermavant Sciences, Dermsquared, Evommune, Inc., Facilitation of International Dermatology Education, Forte biosciences, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi-Regeneron, Seanergy, Strata, Takeda, Trevi, and Verrica. **André Carvalho** acted as a consultant and/or speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including Abbvie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Janssen Pharmaceuticals Inc., LEO Pharma, Novartis, Sun Pharma, and UCB. **Akihiko Asahina** has received honoraria and/or research grants from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eisai, Eli Lilly, Janssen, Kyowa Hakko Kirin, LEO Pharma, Maruho Co., Ltd., Mitsubishi Tanabe Pharma, Novartis, Pfizer, Sun Pharma, Taiho Pharma, Torii Pharmaceutical Co., Ltd., and UCB. **Jianzhong Zhang** reports nothing to disclose. **Mir Sohail Fazeli, Ellen Kasireddy,** and **Paul Serafini** report employment with Evidinno Outcomes Research Inc. **Thomas Ferro** and **Ranga Gogineni** report employment with Sun Pharmaceutical Industries Limited. **Diamant Thaçi** is an advisor, speaker, or consultant for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Galderma, Janssen, Kyowa Kirin, L'Oréal, LEO Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi/Genzyme, and UCB.