TILDRAKIZUMAB VERSUS GUSELKUMAB: A bucher indirect comparison

PDG4

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INTRODUCTION

Psoriasis is a chronic inflammatory skin condition that impacts quality of life (QoL) and requires long-term treatment and effective symptom management[1,2].

Interleukin-23 (IL-23) has emerged as a key player in the pathogenesis of psoriasis and tildrakizumab and guselkumab are both immunomodulatory agents that inhibit the p19 subunit of IL-23[3,4]. In its pivotal Phase III trial, tildrakizumab demonstrated greater efficacy than etanercept in moderate-to-severe psoriasis[5]. Results also demonstrated that tildrakizumab achieved greater efficacy compared with etanercept at week 28 vs. week 12[5] . Furthermore, long-term data have indicated sustained efficacy up to 148 weeks[6]. However, there are no head-to-head trials comparing IL-23 inhibitors.

OBJECTIVE

This study aimed to address the comparative effectiveness of IL-23p19 inhibitors ILUMETRI® (tildrakizumab) and TREMFYA® (guselkumab), indicated for the treatment of moderate-to-severe plaque psoriasis. We report results of an indirect comparison to compare tildrakizumab 100 mg (dosed per approved label on weeks 0, 4 and every 12 weeks thereafter) and guselkumab 100 mg (weeks 0, 4 and every 8 weeks thereafter).

METHODS

Identification of relevant trials: Literature review

- A literature search was conducted to identify trials of tildrakizumab and guselkumab in patients with moderate-to-severe psoriasis (Table 1).

Table 1. Details of literature review

Databases searched	Ovid SP MEDLINE MEDLINE In-Process MEDLINE(R) Daily Epub Ahead of Print Cochrane Central Register of Controlled Trials
Search period	Up to November 2018
Outcomes assessed	Severity of psoriasis: PASI 75 and PASI 90 Frequency of SAEs Treatment discontinuations for any cause

PASI: Psoriasis Area and Severity Index; SAEs: serious adverse events;

Indirect Comparison Methods: Bucher Indirect comparison

- A Bucher indirect comparison was conducted using placebo as a common comparator in three steps (Figure 1).

Figure 1. Steps for the development of Bucher indirect comparison.

STEP 1 Pairwise meta-analysis of placebo and tildrakizumab to estimate a risk ratio.

STEP 2 Pairwise meta-analysis of placebo and guselkumab to estimate a risk ratio.

STEP 3 Combination of these risk ratios to estimate a risk ratio of tildrakizumab and guselkumab.

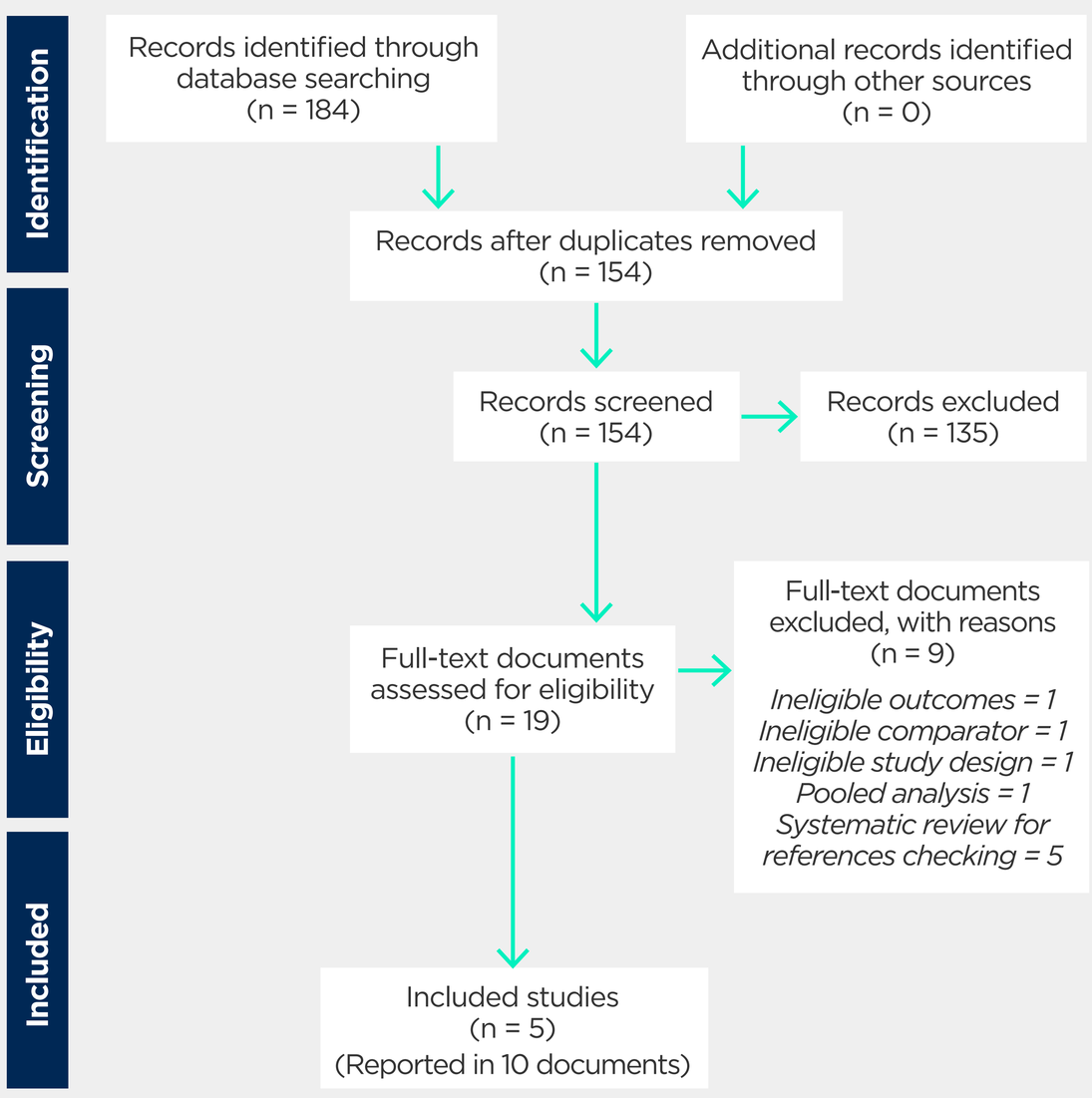
- Outcomes (PASI 75, PASI 90, frequency of SAEs and treatment discontinuations for any cause) were evaluated at Weeks 12–16 and 24–28.
- Analysis was based on the intent-to-treat (ITT) population and for all outcomes, the number of events reported were analysed as a proportion of the number of patients randomised to ensure consistency across trials.
- Pairwise meta-analysis were performed using random effects and fixed effect.
- Heterogeneity was quantified using the I^2 statistic.

RESULTS

Literature review

A literature search identified 154 unique records including five studies that met eligibility criteria and were included in the analysis (Figure 2): two were tildrakizumab trials (reSURFACE 1 and reSURFACE 2) and three guselkumab trials (VOYAGE 1, VOYAGE 2, and Ohtsuki et al.).

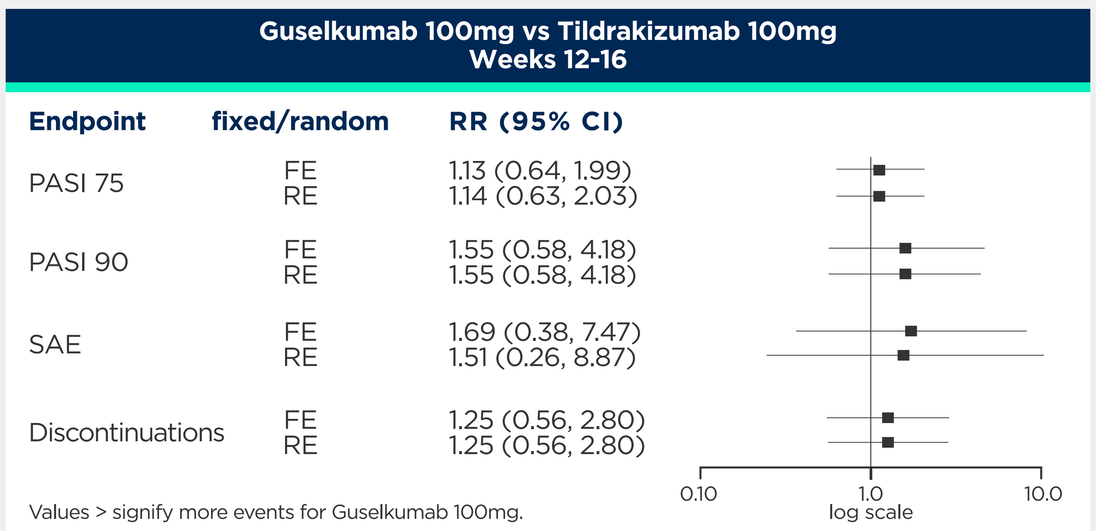
Figure 2. PRISMA Flow Diagram



Bucher Indirect comparison

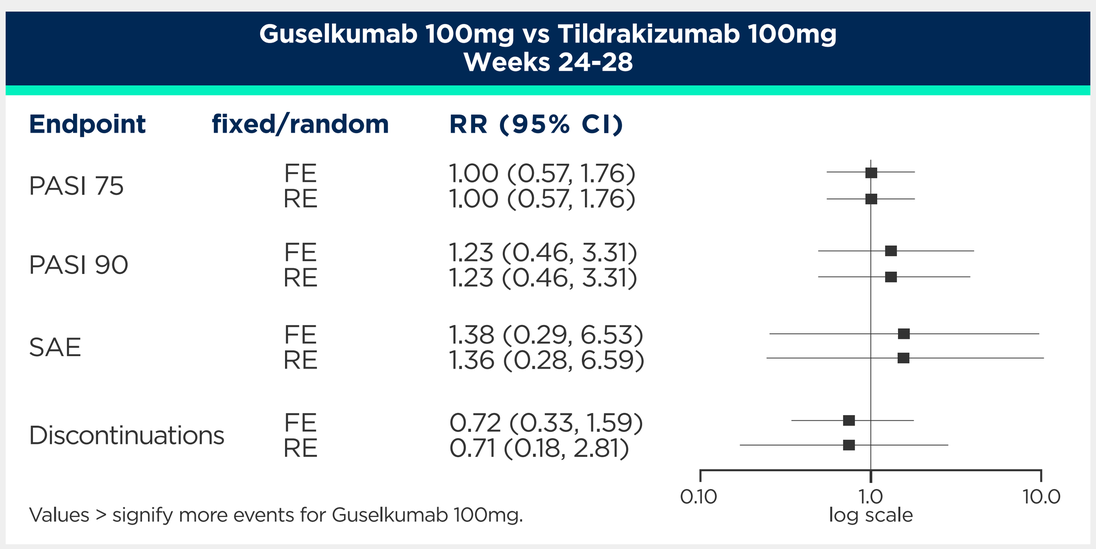
There was no statistically significant difference between guselkumab and tildrakizumab for PASI 75, PASI 90, SAE and rate of discontinuations at either timepoint at Weeks 12–16 (Figure 3) and Weeks 24–28 (Figure 4).

Figure 3. Comparisons of Endpoints: Guselkumab 100 mg vs. Tildrakizumab 100 mg (Weeks 12–16).



CI: Confidence Interval; FE: Fixed Effects; PASI: Psoriasis Area Sensitivity Index; RE: Random Effects; RR: Risk Ratio; SAE: Serious Adverse Event

Figure 4. Comparisons of Endpoints: Guselkumab 100 mg vs. Tildrakizumab 100 mg (Weeks 24–28).



CI: Confidence Interval; FE: Fixed Effects; PASI: Psoriasis Area Sensitivity Index; RE: Random Effects; RR: Risk Ratio; SAE: Serious Adverse Events

CONCLUSIONS

This indirect comparison does not provide evidence that one treatment is superior to the other.

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