Systematic review and indirect treatment comparison of the efficacy of tildrakizumab vs guselkumab or risankizumab for the treatment of moderate-to-severe plaque psoriasis

Mohannad Abu-Hilal[1], Paul Serafini[2], Gopika Balasubramanian[2], Pak Chan[3], Thomas Ferro[4]

[1]Division of Dermatology, McMaster University, Hamilton, ON, Canada; [2]Evidinno Outcomes Research Inc., Vancouver, BC, Canada; [3]Sun Pharma Canada Inc., Brampton, ON, Canada; [4]Sun Pharmaceutical Industries, Inc., Princeton, NJ, USA

LEARNING OBJECTIVES

1. To describe the methodology and findings from an indirect treatment comparison (ITC) of the efficacy of tildrakizumab vs guselkumab and risankizumab for the treatment of moderate-to-severe plaque psoriasis
2. To compare the Psoriasis Area and Severity Index (PASI) response rates for tildrakizumab and guselkumab in an ITC
3. To compare the PASI response rates for tildrakizumab and risankizumab in an ITC

TAKEAWAY MESSAGE

- Tildrakizumab was not significantly different from or statistically noninferior to guselkumab or risankizumab in terms of efficacy. No inferences can be made based on the results of this ITC regarding the efficacy of tildrakizumab compared with guselkumab or risankizumab

INTRODUCTION

- The interleukin (IL)-23 inhibitors tildrakizumab, guselkumab, and risankizumab are approved in Canada for the treatment of adults with moderate-to-severe plaque psoriasis[1-3]
- Previous meta-analyses did not compare the efficacy of tildrakizumab with other IL-23 inhibitors for psoriasis treatment past Week 12/16; combined data from disparate time points, which may bias the results in favor of the treatments with later time points; and utilized network meta-analyses with large networks of treatments as opposed to the simpler and easier-to-interpret Bucher ITC[4,5]
- To address these limitations, we conducted a systematic literature review and ITC of the efficacy of tildrakizumab after Weeks 24 to 28 compared with guselkumab and with risankizumab for the treatment for moderate-to-severe plaque psoriasis

METHODS

Study design

- A systematic literature review was performed using the following sources to identify randomized clinical trials that assessed the efficacy of tildrakizumab, guselkumab, or risankizumab with placebo in adults with moderate-to-severe plaque psoriasis:
  - MEDLINE®, Embase, and CENTRAL databases up to August 2022
  - The American Academy of Dermatology and the European Academy of Dermatology and Venereology conference proceedings from 2020 to 2022
  - The US and European clinical trial registries to identify randomized controlled trials that reported results but were not published in peer-reviewed journals
- Duplicate studies were removed from the search results. Two independent reviewers screened the results using the Population, Intervention, Comparison, Outcomes, and Study design criteria (**Table 1**). Discrepancies were resolved by consensus or a third reviewer

Table 1. PICOS eligibility criteria

PICOS item	Inclusion criteria	Exclusion criteria
Population	Adults with moderate-to-severe plaque psoriasis	Patients with mild plaque psoriasis or any other condition
Intervention	Tildrakizumab, guselkumab, and risankizumab	Anti-TNF therapies (etanercept, adalimumab, infliximab, and certolizumab pegol), and other approved and investigational therapies
Comparison	Placebo	N/A
Outcomes	PASI 75/90/100 response	N/A
Study design	Randomized clinical trials	Single-arm clinical trials, observational studies, narrative reviews, case reports/series, books, letters, notes, comments, and editorials

N/A, not applicable; PASI 75/90/100, ≥75%/≥90%/100% improvement from baseline Psoriasis Area Severity Index score; PICOS, Population, Intervention, Comparison, Outcomes, and Study design; TNF, tumor necrosis factor.

- Identified studies were included in separate pairwise ITCs performed using the Bucher method to compare the efficacy of tildrakizumab vs guselkumab or risankizumab using the last available pre-crossover placebo responses carried forward.[6] Both analyses were repeated with fixed-effects and random-effects models

Effectiveness assessment

- Effectiveness was evaluated at Weeks 24 to 28 based on the percentages of patients achieving ≥75%/≥90%/100% improvement from baseline PASI score (PASI 75/90/100)

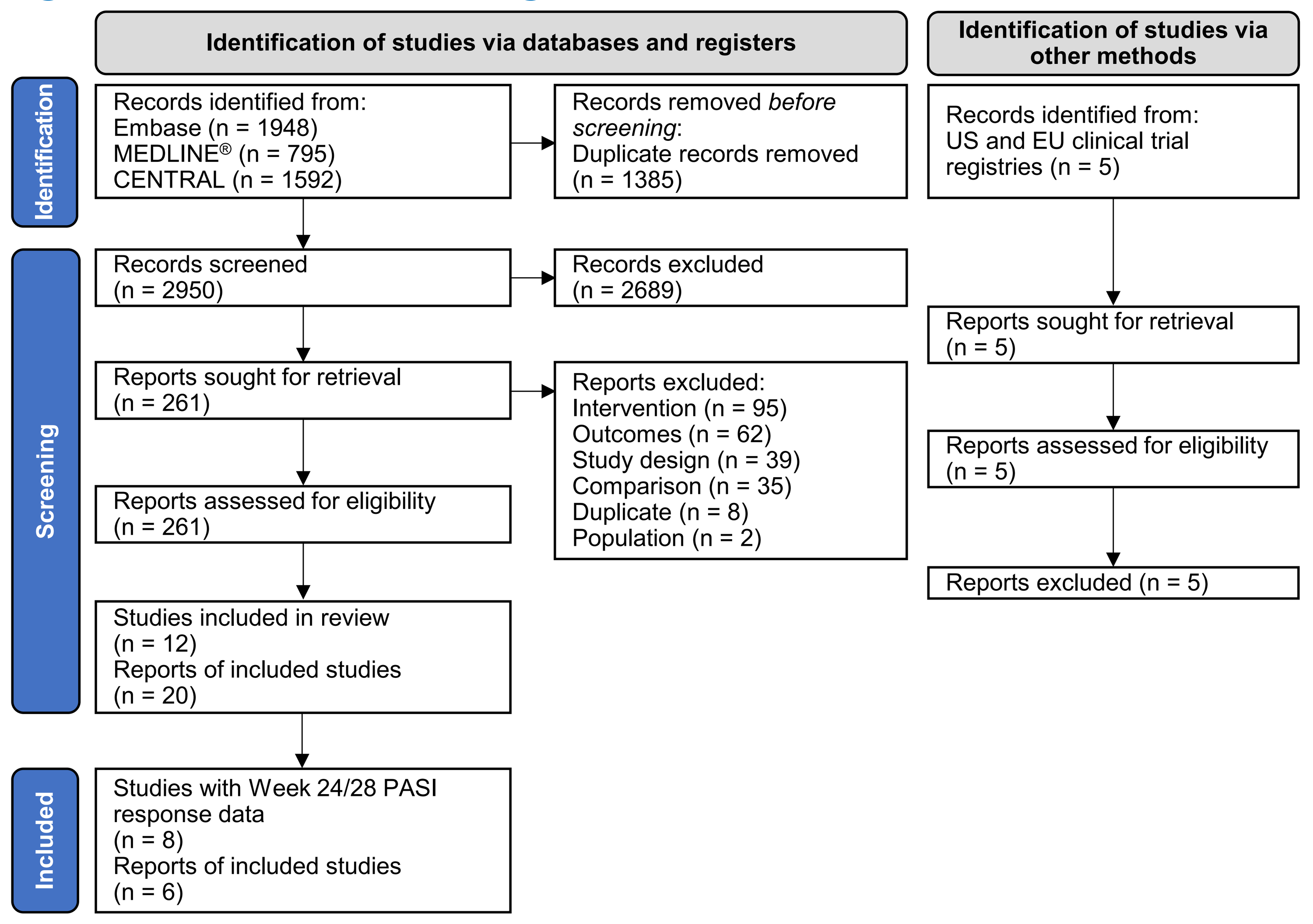
Statistical analysis

- Risk ratios (RRs) and 95% confidence intervals for PASI 75/90/100 response rates at Weeks 24 to 28 were reported
- Noninferiority was evaluated post hoc using a margin of 25%, which corresponds to an RR of at least 0.8. The generic threshold of 25% based on the Grading of Recommendations, Assessment, Development, and Evaluations criteria for dichotomous outcomes[7] was used as there is no published minimal clinically important difference or noninferiority margin for PASI 75/90/100 response rates
- Significance was evaluated at an alpha level of 0.05

RESULTS

- Of 1385 identified unique studies, eight Phase 3 randomized controlled trials with Week 24 to 28 data were included in the ITC (**Figure 1**), including 2 for tildrakizumab (reSURFACE 1 and reSURFACE 2)[8], 3 for guselkumab (VOYAGE-1, VOYAGE-2, and Ohtsuki M, et al. 2018)[9-11], and 3 for risankizumab (IMMhance, UltIMMa-1, and UltIMMa-2)[12,13]

Figure 1. PRISMA flow diagram



PASI, Psoriasis Area and Severity Index; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

- Patients were predominantly female (range, 66.2%–79.5%), with a mean age of 43.7 to 50.4 years (**Table 2**)
- Mean ± standard deviation baseline PASI scores were reported by 7 studies and ranged from 17.5 ± 4.7 to 26.3 ± 8.7 (**Table 2**)

Table 2. Demographics and baseline characteristics of included studies with Week 24 to 28 data

Characteristic	Tildrakizumab		Guselkumab			Risankizumab		
	reSURFACE 1 (NCT01722331)	reSURFACE 2 (NCT01729754)	VOYAGE-1 (NCT02207231)	VOYAGE-2 (NCT02207244)	Ohtsuki M, et al. 2018	IMMHance (NCT02672852)	UltIMMAa-1 (NCT02684370)	UltIMMAa-2 (NCT02684357)
Female, %	66.2	71.7	72.6	68.5	79.5	70.2	71.3	68.4
Age, years, mean ± SD	46.9 ± 9.8	45.2 ± 9.9	43.7 ± 12.7	43.7 ± 8.8	48.1 ± 7.7	50.4 ± 12.3	48.2 ± 8.9	46.7 ± 9.1
BMI, kg/m^2, mean ± SD	NR	NR	29.6 ± 6.5	29.3 ± 4.5	25.9 ± 3.5	30.2 ± 5.7	29.8 ± 4.6	31.0 ± 4.6
Body weight, kg, mean ± SD	88.2 ± 18.1	88.9 ± 16.2	NR	88.0 ± 14.5	72.9 ± 10.6	89.4 ± 17.0	88.2 ± 15.0	92.1 ± 14.3
BSA, %, mean ± SD	29.7 ± 13.0	33.1 ± 12.1	28.0 ± 16.7	28.3 ± 12.2	35.7 ± 14.1	19.8 ± 11.2	26.4 ± 10.3	24.7 ± 10.3
DLQI, mean ± SD	13.7 ± 5.1	13.9 ± 5.3	14.0 ± 7.3	14.8 ± 5.2	10.5 ± 5.3	NR	13.0 ± 4.6	13.0 ± 4.8
PASI, mean ± SD	19.8 ± 5.7	20.3 ± 5.5	21.9 ± 9.2	21.8 ± 6.4	26.3 ± 8.7	17.5 ± 4.7	20.5 ± 5.0	19.7 ± 5.0
Prior biologic exposure, %	22.8	NR	NR	20.8	1.6	55.4	34.4	41.3

BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; NR, not reported; PASI, Psoriasis Area and Severity Index; SD, standard deviation.

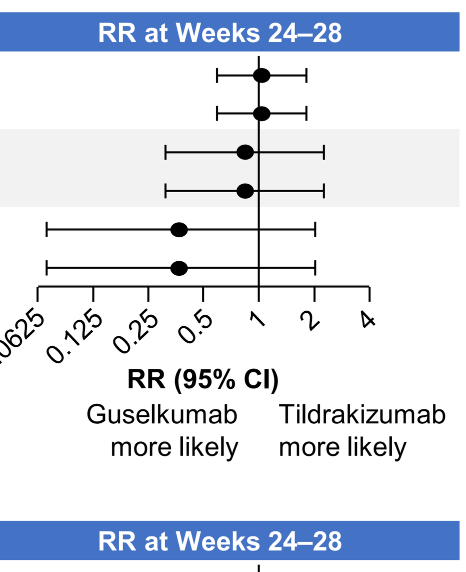
Effectiveness

- In the ITCs, the PASI 75/90/100 response rates for tildrakizumab at Weeks 24 to 28 were not significantly different from those for guselkumab (**Figure 2A**) or risankizumab (**Figure 2B**) using either the random-effects or fixed-effects models
- Tildrakizumab did not achieve statistical noninferiority to guselkumab or risankizumab based on the noninferiority margin of 25%

Figure 2. Forest plots of the log$_2$ risk ratios for indirect treatment comparison at 24 to 28 weeks

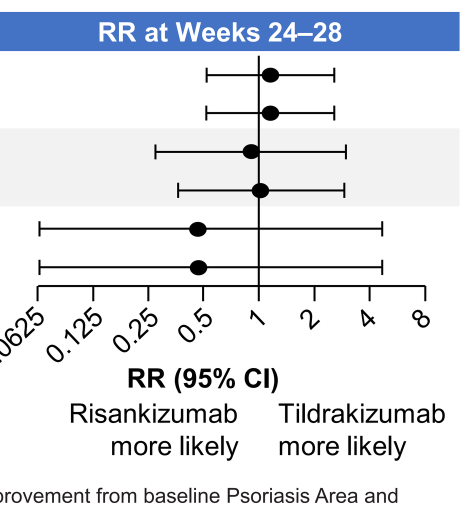
(A) Tildrakizumab vs guselkumab

Endpoint	N	Fixed/Random	RR (95% CI)
PASI 75	4	RE	1.04 (0.59, 1.83)
		FE	1.04 (0.59, 1.83)
PASI 90	4	RE	0.84 (0.31, 2.25)
		FE	0.84 (0.31, 2.25)
PASI 100	4	RE	0.37 (0.07, 0.21)
		FE	0.37 (0.07, 0.21)



(B) Tildrakizumab vs risankizumab

Endpoint	N	Fixed/Random	RR (95% CI)
PASI 75	3	RE	1.14 (0.51, 2.55)
		FE	1.14 (0.51, 2.55)
PASI 90	5	RE	0.90 (0.27, 2.94)
		FE	1.01 (0.36, 2.89)
PASI 100	3	RE	0.46 (0.05, 4.68)
		FE	0.46 (0.05, 4.68)



CI, confidence interval; FE, fixed effects; N, number of included studies; PASI 75/90/100, ≥75%/≥90%/100% improvement from baseline Psoriasis Area and Severity Index score; RE, random effects; RR, risk ratio.

CONCLUSIONS

- The efficacy of tildrakizumab was not significantly different from guselkumab or risankizumab after 24 to 28 weeks of treatment based on model assumptions

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CONFLICTS OF INTEREST

The authors declare the following real or perceived conflicts of interest in relation to this poster presentation: **MAH** received advisory board honoraria and consulting fees from AbbVie, Eli Lilly, Galderma, Hikma Pharmaceuticals, Janssen, LEO Pharma, L'Oréal, Medexus Pharma, Novartis, Pfizer, Sanofi, and Sun Pharma. **PS** and **GB** are employees of Evidinno Outcomes Research Inc. **PC** is an employee of Sun Pharma Canada Inc. **TF** is an employee of Sun Pharma