Real-world effectiveness and safety in a Phase 4 study of tildrakizumab in patients with moderate-to-severe plaque psoriasis

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INTRODUCTION

- Psoriasis is a chronic, systemic, inflammatory disorder characterized by scaly erythematous plaques on the skin[1]
- Tildrakizumab is an anti–interleukin-23 p19 monoclonal antibody approved for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy[2]
- Efficacy and safety of tildrakizumab in patients with moderate-to-severe plaque psoriasis were demonstrated in the Phase 3 reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754) trials,[3] but there is limited available real-world evidence regarding the effectiveness and safety of tildrakizumab in clinical practice

OBJECTIVE

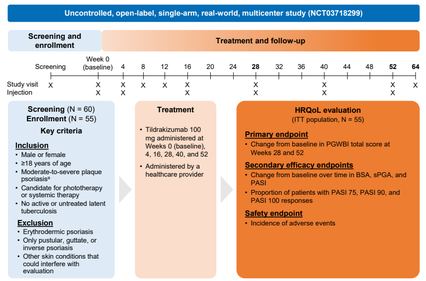
- To assess long-term effectiveness, as measured by clinical improvement and disease severity, and safety after 64 weeks of treatment with tildrakizumab under real-world conditions

METHODS

Study design and population

- In this Phase 4, 64-week, uncontrolled, open-label, single-arm real-world study (NCT03718299), patients ≥18 years of age with moderate-to-severe plaque psoriasis received tildrakizumab 100 mg at Week 0, Week 4, and every 12 weeks thereafter through Week 52 (**Figure 1**)
- The primary endpoint was improvement in health-related quality of life; secondary endpoints related to clinical effectiveness and safety are reported (**Figure 1**)

Figure 1. Study design



Time points (Weeks) shown in bold indicate when the primary efficacy endpoint was assessed (at Weeks 28 and 52) and the end of the study (at Week 64).
[a]BSA ≥3%.
BSA, body surface area; HRQoL, health-related quality of life; ITT, intention-to-treat; PASI, Psoriasis Area and Severity Index; PASI 75/90/100 response, ≥75%/≥90%/100% improvement from baseline in PASI score; PGWBI, Psychological General Well-Being Index; sPGA, static Physician Global Assessment.

Assessments

- Effectiveness was assessed from change from baseline in the percentage of body surface area (BSA) affected, static Physician Global Assessment (sPGA), and BSA x sPGA through Week 64 and Psoriasis Area and Severity Index (PASI) score through Week 52
  - Proportions of patients achieving ≥75%, ≥90%, and 100% improvement from baseline in PASI score (PASI 75, PASI 90, and PASI 100 responses) through Week 52 were also assessed
- Safety was assessed through Week 64 from the incidence (severity and causality) of adverse events (AEs)

Statistical analysis

- The intention-to-treat population was used for all efficacy analyses and included all patients who enrolled and were assigned to receive tildrakizumab
- The safety population was used for the safety analysis and included all enrolled patients who received at least 1 dose of tildrakizumab
- Changes from baseline in BSA, sPGA, BSA x sPGA, and PASI scores were analyzed using Student's t-tests
- The PASI response rates and AEs are reported descriptively
- Missing data were not imputed

RESULTS

Demographics and baseline characteristics

- Of 55 patients enrolled, 45 were assessed at Week 64 (end of study)
- The majority of patients were male (28/55; 50.9%) and White (52/55; 94.5%), with a mean ± standard deviation (SD) age of 48.6 ± 15.3 years (**Table 1**)

Table 1. Baseline demographics and clinical characteristics

Characteristic	Tildrakizumab (N = 55)
Sex, male	28 (50.9)
Race	
White	52 (94.5)
Black or African American	2 (3.6)
Asian	1 (1.8)
Ethnicity, not Hispanic or Latino	50 (90.9)
Age, years, mean ± SD	48.6 ± 15.3
BSA, mean ± SD	14.5 ± 11.5
sPGA	
0	0
1	0
2	4 (7.3)
3	36 (65.5)
4	15 (27.3)
5	0
PASI, mean ± SD	11.6 ± 7.1

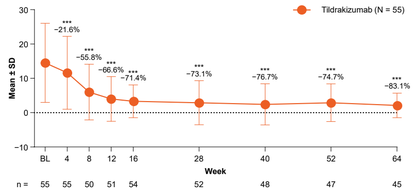
ITT population.
Data shown as n (%) unless otherwise noted.
BSA, body surface area; ITT, intention-to-treat; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

Effectiveness

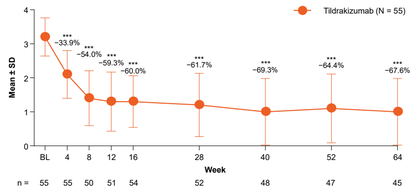
- Patients had significant improvements in multiple measures of disease severity through Week 64
  - Mean ± SD BSA decreased from 14.5 ± 11.5 at baseline to 2.1 ± 3.6 (P <0.001) at Week 64 (**Figure 2A**)
  - Mean ± SD sPGA decreased from 3.2 ± 0.6 at baseline to 1.0 ± 1.0 (P <0.001) at Week 64 (**Figure 2B**)
  - Mean ± SD BSA x sPGA decreased from 47.0 ± 41.5 at baseline to 4.6 ± 9.4 (P <0.001) at Week 64 (**Figure 2C**)

Figure 2. Mean change from baseline in disease activity measures over time through Week 64

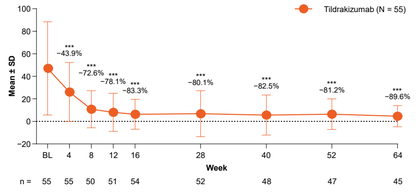
A. BSA



B. sPGA



C. BSA x sPGA

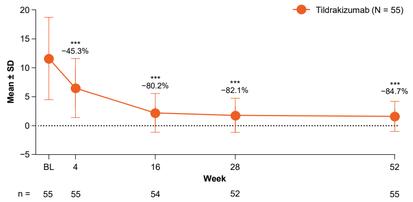


ITT population.
Data are graphed as the absolute score with the percent change from baseline shown over each time point.
***P <0.001.
BL, baseline; BSA, body surface area; ITT, intention-to-treat; SD, standard deviation; sPGA, static Physician Global Assessment.

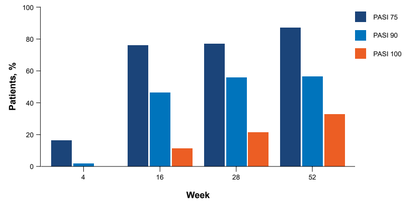
- Patients had statistically significant (P <0.001) mean changes from baseline in PASI score at Weeks 4, 16, 28, and 52, indicating clinical improvement of psoriasis over time (**Figure 3A**)
- At Week 52, 81.8%, 54.5%, and 30.9% of patients achieved PASI 75, PASI 90, and PASI 100 responses, respectively (**Figure 3B**)

Figure 3. Disease activity and clinical improvement based on PASI score through Week 52

A. Absolute PASI score



B. PASI 75, PASI 90, and PASI 100 response rates



ITT population.
***P <0.001.
BL, baseline; ITT, intention-to-treat; PASI, Psoriasis Area and Severity Index; PASI 75/90/100 response, ≥75%/≥90%/100% improvement from baseline in PASI score; SD, standard deviation.

Safety

- There were 34/55 (61.8%) patients who experienced a total of 85 treatment-emergent adverse events (TEAEs) through Week 64 (**Table 2**)
  - Of the 85 events, the majority (n = 63; 74.1%) were reported as mild in severity, 18 (21.2%) were moderate, and 4 (7.3%) were severe
  - The most common TEAEs were psoriasis (12.7%), hypertension (9.1%), and dermatitis (5.5%; **Table 2**)
  - Two (3.6%) patients experienced TEAEs, both serious, that led to treatment discontinuation, including transitional cell carcinoma and coronavirus disease 2019 pneumonia in 1 patient each
  - No TEAEs were considered by the investigators to be related to tildrakizumab treatment
  - There were no deaths during the study

Table 2. TEAEs through Week 64

Evaluation	Tildrakizumab (N = 55)
Number of TEAEs	85
Patients with ≥1 TEAE	34 (61.8)
Treatment-related TEAEs	0
Serious TEAEs	4 (7.3)
Ischemic stroke	1 (1.8)
Transitional cell carcinoma	1 (1.8)
IgA nephropathy	1 (1.8)
COVID-19 pneumonia	1 (1.8)
TEAEs leading to treatment discontinuation	2 (3.6)
Transitional cell carcinoma	1 (1.8)
COVID-19 pneumonia	1 (1.8)
Deaths	0
Most common TEAEs[a]	
Psoriasis	7 (12.7)
Hypertension	5 (9.1)
Dermatitis	3 (5.5)
Arthralgia	2 (3.6)
Eczema	2 (3.6)
Hematuria	2 (3.6)
Large intestine polyp	2 (3.6)
Nasopharyngitis	2 (3.6)
Skin papilloma	2 (3.6)
Upper respiratory tract infections	2 (3.6)

Data shown as n (%) of patients with event in the safety population reported according to MedDRA preferred term.
[a]TEAEs reported in ≥2 patients.
COVID-19, coronavirus disease 2019; IgA, immunoglobulin A; MedDRA, Medical Dictionary for Regulatory Activities; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Tildrakizumab treatment effectiveness was significant after 1 dose and through Week 64 across multiple measures of clinical improvement and disease severity in patients with moderate-to-severe plaque psoriasis in a real-world clinical setting
- Tildrakizumab maintained a favorable safety profile in patients with moderate-to-severe plaque psoriasis for up to 64 weeks in a real-world clinical setting

REFERENCES

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DISCLOSURES

NB is an advisor, consultant, and investigator for AbbVie, Almirall, Arcutis Biotherapeutics, Beiersdorf, Biofrontera, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant Sciences, Eli Lilly, EPI Health, Ferndale Pharma Group, Galderma, Incyte, ISDIN, Johnson & Johnson, La Roche-Posay, LEO Pharma, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Verrica Pharmaceuticals, Inc. **JGV** reports nothing to disclose. **BS** and **RG** are employees of Sun Pharmaceutical Industries, Inc. **JH** has been a speaker, advisor, and consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, and Novartis; an advisor for Galderma, Mayne Pharma, Regeneron, and Sanofi; an advisor and consultant for Ortho Dermatologics; and a speaker and advisor for Beiersdorf, Incyte, LEO Pharma, and Sun Pharma.