Efficacy and safety of tildrakizumab for the treatment of moderate-to-severe plaque psoriasis of the scalp: Week 52 results from a Phase 3b, randomized, double-blind, placebo-controlled trial

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INTRODUCTION

- Tildrakizumab is an anti–interleukin-23 p19 monoclonal antibody approved for the treatment of adults with moderate-to-severe plaque psoriasis[1]
- The efficacy and safety of tildrakizumab for the treatment of scalp psoriasis were investigated in a Phase 3b, randomized, double-blind, placebo-controlled study (NCT03897088)[2]
  - The primary efficacy endpoint, Investigator Global Assessment modified 2011 of the scalp (IGA mod 2011 [scalp]) response—defined as clear (0) or almost clear (1) with a ≥2-point reduction from baseline at Week 16—was met[2]

OBJECTIVE

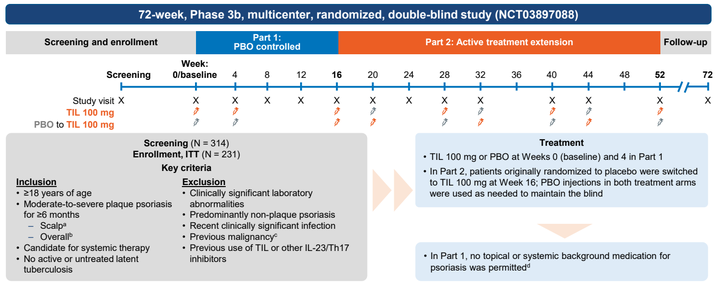
- To assess the efficacy and safety of tildrakizumab in patients with moderate-to-severe plaque psoriasis of the scalp after 52 weeks of treatment with tildrakizumab[2]

METHODS

Study design and population

- Patients ≥18 years of age with moderate-to-severe plaque psoriasis of the scalp (IGA mod 2011 [scalp] ≥3, Psoriasis Scalp Severity Index [PSSI] ≥12, and ≥30% scalp surface area affected) were eligible
- During Part 1, patients were randomized 1:1 to receive tildrakizumab 100 mg or placebo at Week 0 and Week 4 (**Figure 1**)
- During Part 2, patients originally randomized to tildrakizumab 100 mg continued to receive tildrakizumab at Week 16 and every 12 weeks thereafter through Week 52; patients originally randomized to placebo were switched to tildrakizumab 100 mg at Weeks 16, 20, 32, and 44 (**Figure 1**)
- After Week 52, all patients entered a 20-week, observational, treatment-free, safety follow-up period to monitor safety and tolerability of tildrakizumab through Week 72 (Part 3; **Figure 1**)

Figure 1. Study design



[a]Moderate-to-severe plaque psoriasis of the scalp was defined as IGA mod 2011 (scalp) ≥3, PSSI score of ≥12, and ≥30% of SSA affected. [b]Moderate-to-severe plaque psoriasis overall was defined as IGA mod 2011 (whole body) of at least moderate severity (≥3 on a 5-point scale), PASI score of ≥12, and BSA involvement of >10%. [c]Excluding successfully treated basal cell carcinoma, squamous cell carcinoma of the skin in situ, squamous cell carcinoma of the skin with no evidence of recurrence within 5 years, or carcinoma in situ of the cervix that was adequately treated. [d]During Part 2, Class VI or VII low-potency topical corticosteroids (such as prednicarbate 0.05%, triamcinolone acetonide 0.025%, fluocinolone acetonide 0.01%, desonide 0.05%, hydrocortisone 2.5%, or hydrocortisone 1%) were allowed.
BSA, body surface area; IGA mod 2011, Investigator Global Assessment modified 2011; IL, interleukin; ITT, intention-to-treat; PASI, Psoriasis Area and Severity Index; PBO, placebo; PSSI, Psoriasis Scalp Severity Index; SSA, scalp surface area; Th17, T-helper 17 cell; TIL, tildrakizumab.

Efficacy assessments

- The IGA mod 2011 (scalp)[3] and PSSI were assessed at screening and at each visit during the study (baseline and Weeks 1, 4, 8, 12, 16, 20, 24, 28, 32, 40, 44, and 52)
  - The IGA mod 2011 (scalp) is a 5-point rating scale (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe)
- The proportions of Week 16 IGA mod 2011 (scalp) and PSSI 90 responders who maintained responses were assessed at Week 52
  - IGA mod 2011 (scalp) response was defined as an IGA score of clear (0) or almost clear (1) with a ≥2-point reduction from baseline
  - PSSI 90 response was defined as a ≥90% reduction from baseline in PSSI score

Safety assessments

- Safety was assessed from treatment-emergent adverse events (TEAEs) through Week 72

Statistical analysis

- The proportions of patients achieving IGA mod 2011 (scalp) and PSSI 90 responses through Week 16 were analyzed using a Cochran-Mantel-Haenszel test stratified by body weight (≤90 kg vs >90 kg) and prior exposure to tumor necrosis factor (TNF)-α inhibitors through Week 16; all other statistics are reported descriptively
- The modified intention-to-treat (mITT) population included all patients with a baseline IGA mod 2011 (scalp) assessment who were dispensed study treatment
- Missing data were handled using nonresponder imputation
- Safety analyses were performed in all randomized patients who received at least 1 dose of study treatment (safety population)

RESULTS

- All of the 231 patients enrolled received treatment (safety population), and 171 were included in the mITT population **(Table 1)**
- Patients in the mITT population were predominantly male (60.2%) and White (78.9%), with a mean age of 44.8 years **(Table 1)**
- The majority of mITT patients had moderate disease burden at baseline based on the IGA mod 2011 scale **(Table 1)**

Table 1. Baseline demographics and clinical characteristics

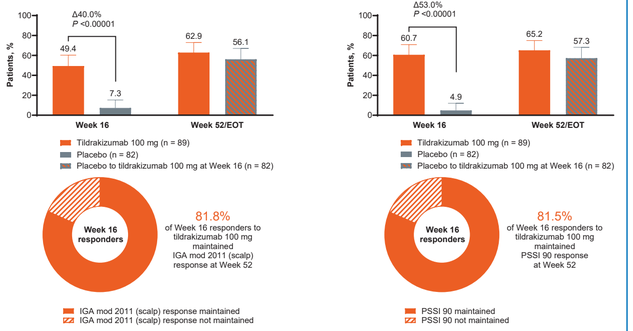
	mITT population		Safety population[a]	
	TIL 100 mg (n = 89)	PBO (n = 82)	TIL 100 mg (n = 117)	PBO (n = 114)
Age, years, mean ± SD	44.2 ± 15.1	45.4 ± 12.9	45.6 ± 15.3	44.8 ± 13.0
Sex, male, n (%)	59 (66.3)	44 (53.7)	71 (60.7)	63 (55.3)
Race, n (%)				
White	71 (79.8)	64 (78.0)	92 (78.6)	90 (78.9)
Black or African American	9 (10.1)	5 (6.1)	10 (8.5)	9 (7.9)
Asian	4 (4.5)	7 (8.5)	8 (6.8)	9 (7.9)
Native Hawaiian or Other Pacific Islander	3 (3.4)	2 (2.4)	3 (2.6)	2 (1.8)
American Indian or Alaskan Native	2 (2.2)	1 (1.2)	4 (3.4)	1 (0.9)
Other	0	3 (3.7)	0	3 (2.6)
Ethnicity, not Hispanic or Latino, n (%)	58 (65.2)	53 (64.6)	75 (64.1)	69 (60.5)
Weight, kg, mean ± SD	88.3 ± 20.9	90.1 ± 21.7	88.4 ± 21.4	89.6 ± 22.5
BMI, kg/m², mean ± SD	30.3 ± 6.2	31.4 ± 6.9	30.8 ± 6.9	31.4 ± 7.0
Prior use of TNF-α inhibitors, yes, n (%)	9 (10.1)	7 (8.5)	15 (12.8)	15 (13.2)
IGA mod 2011 (scalp), n (%)				
3	75 (84.3)	64 (78.0)	NA	NA
4	13 (14.6)	15 (18.3)	NA	NA
Missing	1 (1.1)	3 (3.7)	NA	NA
PSSI, mean ± SD	33.8 ± 15.1	31.7 ± 15.8	34.5 ± 15.2	32.9 ± 15.5
SSA, mean ± SD	58.8 ± 24.7	55.5 ± 22.9	60.3 ± 24.9	56.5 ± 22.7
IGA mod 2011 (whole body), n (%)				
3	77 (86.5)	69 (84.1)	NA	NA
4	11 (12.4)	10 (12.2)	NA	NA
Missing	1 (1.1)	3 (3.7)	NA	NA
PASI, mean ± SD	19.3 ± 6.7	18.3 ± 7.9	18.9 ± 6.5	18.5 ± 7.6
BSA, mean ± SD	24.3 ± 13.8	22.8 ± 14.5	23.3 ± 14.0	22.5 ± 13.7

[a]IGA mod 2011 (scalp) and IGA mod 2011 (whole body) were only assessed in the mITT population.
BMI, body mass index; BSA, body surface area; IGA mod 2011, Investigator Global Assessment modified 2011; mITT, modified intention-to-treat; NA, not available; PASI, Psoriasis Area and Severity Index; PBO, placebo; PSSI, Psoriasis Scalp Severity Index; SD, standard deviation; SSA, scalp surface area; TIL, tildrakizumab; TNF, tumor necrosis factor.

Efficacy

- The proportions of IGA mod 2011 (scalp) responders to tildrakizumab continued to increase from 49.4% at Week 16 to 62.9% at Week 52; 81.8% of Week 16 responders (36/44) maintained responses at Week 52 (**Figure 2A**)
- The proportions of PSSI 90 responders to tildrakizumab continued to increase from 60.7% at Week 16 to 65.2% at Week 52; 81.5% of Week 16 responders (44/54) maintained responses at Week 52 (**Figure 2B**)

Figure 2. (A) Maintenance of IGA mod 2011 (scalp) and (B) PSSI 90 responses from Week 16 to Week 52

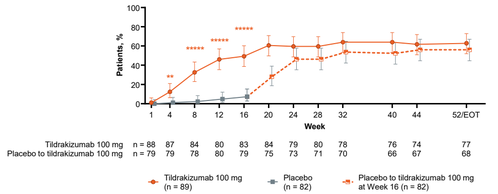


IGA mod 2011 (scalp) response and PSSI 90 response were analyzed in the mITT analysis set with NRI. Treatment difference is shown only at Week 16. The percentage of Week 16 responders who maintained response at Week 52 is calculated using N as the denominator, where N is the number of IGA mod 2011 (scalp) or PSSI 90 responders to tildrakizumab at Week 16 in the mITT.
EOT, end of treatment; IGA mod 2011 (scalp) response, Investigator Global Assessment modified 2011 score of 0 or 1 with a ≥2-point reduction from baseline for the scalp; mITT, modified intention-to-treat; NRI, nonresponder imputation; PSSI 90 response, ≥90% improvement from baseline in Psoriasis Scalp Severity Index score.

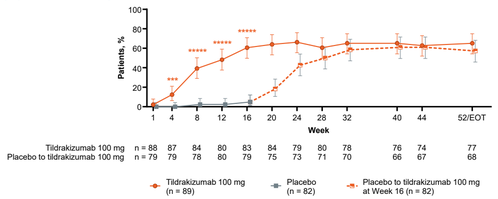
- IGA mod 2011 (scalp) response and PSSI 90 response rates by visit through Week 52 are shown in **Figure 3A** and **3B**

Figure 3. (A) Proportion of IGA mod 2011 (scalp) and (B) PSSI 90 responders by visit through Week 52

(A) IGA mod 2011 (scalp) response



(B) PSSI 90 response



**P <0.005. ***P <0.001. ****P <0.00001.
IGA mod 2011 (scalp) and PSSI 90 responses were analyzed in the mITT analysis set with NRI. 95% confidence intervals are shown. The number of patients assessed at each visit is shown below each graph.
EOT, end of treatment; IGA mod 2011 (scalp) response, Investigator Global Assessment modified 2011 score of 0 or 1 with a ≥2-point reduction from baseline for the scalp; mITT, modified intention-to-treat; NRI, nonresponder imputation; PSSI 90 response, ≥90% improvement from baseline in Psoriasis Scalp Severity Index score.

Safety

- Overall, the proportion of patients with at least 1 TEAE was comparable between treatment arms; most TEAEs were mild-to-moderate in severity (**Table 2**)
- During Parts 2 and 3, a total of 5 patients experienced AEs of special interest, comprising 4 patients with relevant medical history who had cardiac events that were not considered related to study treatment and 1 patient with a macular rash
- Six patients experienced serious AEs during Parts 2 and 3; none were considered related to study treatment
- During Parts 2 and 3, 6 (2.6%) patients experienced TEAEs considered potentially related to tildrakizumab treatment: 2 (1.7%) patients in the tildrakizumab arm (upper respiratory tract infection and low-density lipoprotein increased) and 4 (3.5%) patients in the placebo-to-tildrakizumab arm (fungal skin infection, viral rhinitis, impaired fasting glucose, vulvovaginal candidiasis, hand dermatitis, and macular rash)
- No prespecified AEs of clinical interest, treatment-related serious AEs, or deaths occurred during the study

Table 2. Summary of AEs through Week 72

	Part 1 (Weeks 0 to 16)		Parts 2 and 3 (Weeks 16 to 72)		Overall (Weeks 0 to 72)	
	TIL 100 mg (n = 117)	PBO (n = 114)	TIL 100 mg (n = 117)	PBO to TIL (n = 114)	TIL 100 mg (n = 117)	PBO to TIL (n = 114)
Any TEAE	41 (35.0)	24 (21.1)	41 (35.0)	41 (36.0)	62 (53.0)	59 (51.8)
Treatment-related TEAEs	4 (3.4)	7 (6.1)	2 (1.7)	4 (3.5)	6 (5.1)	11 (9.6)
Deaths	0	0	0	0	0	0
SAEs	1 (0.9)	0	2 (1.7)	4 (3.5)	3 (2.6)	4 (3.5)
Treatment-related SAEs	0	0	0	0	0	0
TEAEs leading to discontinuation	0	0	0	1 (0.9)	0	1 (0.9)
AEs of special interest	3 (2.6)	2 (1.8)	2 (1.7)	3 (2.6)	4 (3.4)	5 (4.4)
Injection site reaction	0	1 (0.9)	0	0	0	1 (0.9)
NMSC	2 (1.7)	0	0	0	2 (1.7)	0
MACE	0	0	2 (1.7)	2 (1.8)	2 (1.7)	2 (1.8)
Treatment-related hypersensitivity reactions	1 (0.9)	1(0.9)	0	1 (0.9)	1 (0.9)	2 (1.8)
AEs of clinical interest[a]	0	0	0	0	0	0
COVID-19–related TEAEs	2 (1.7)	0	4 (3.4)	5 (4.4)	6 (5.1)	5 (4.4)
Most frequent AEs[b]						
Preferred term						
Headache	1 (0.9)	4 (3.5)	2 (1.7)	2 (1.8)	3 (2.6)	6 (5.3)
Hypertension	3 (2.6)	1 (0.9)	3 (2.6)	2 (1.8)	6 (5.1)	3 (2.6)
Nasopharyngitis	3 (2.6)	1 (0.9)	2 (1.7)	5 (4.4)	5 (4.3)	5 (4.4)
COVID-19	1 (0.9)	0	3 (2.6)	4 (3.5)	4 (3.4)	4 (3.5)
Viral URTI	3 (2.6)	1 (0.9)	1 (0.9)	1 (0.9)	4 (3.4)	1 (0.9)
URTI	1 (0.9)	1 (0.9)	2 (1.7)	2 (1.8)	3 (2.6)	3 (2.6)
Diarrhea	2 (1.7)	3 (2.6)	0	0	2 (1.7)	3 (2.6)
Pruritus	1 (0.9)	2 (1.8)	0	1 (0.9)	1 (0.9)	3 (2.6)
Sinusitis	2 (1.7)	0	1 (0.9)	1 (0.9)	3 (2.6)	1 (0.9)
Cough	0	2 (1.8)	0	1 (0.9)	0	3 (2.6)
Influenza	0	1 (0.9)	0	2 (1.8)	0	3 (2.6)
Ligament sprain	1 (0.9)	0	2 (1.7)	0	3 (2.6)	0
SARS-CoV-2 test positive	1 (0.9)	0	1 (0.9)	2 (1.8)	2 (1.7)	2 (1.8)
Acute kidney injury	0	1 (0.9)	1 (0.9)	1 (0.9)	1 (0.9)	2 (1.8)
ALT increased	1 (0.9)	1 (0.9)	0	1 (0.9)	1 (0.9)	2 (1.8)
Arthralgia	0	1 (0.9)	2 (1.7)	0	2 (1.7)	1 (0.9)
Hyperlipidemia	1 (0.9)	1 (0.9)	1 (0.9)	0	2 (1.7)	1 (0.9)
Seasonal allergy	2 (1.7)	1 (0.9)	0	0	2 (1.7)	1 (0.9)
UTI	0	1 (0.9)	2 (1.7)	0	2 (1.7)	1 (0.9)
Basal cell carcinoma	2 (1.7)	0	0	0	2 (1.7)	0
Blood triglycerides increased	0	2 (1.8)	0	0	0	2 (1.8)
Bronchitis	2 (1.7)	0	0	0	2 (1.7)	0
Gout	0	0	2 (1.7)	0	2 (1.7)	0
Hypercholesterolemia	0	0	0	2 (1.8)	0	2 (1.8)
Rheumatoid arthritis	0	0	2 (1.7)	0	2 (1.7)	0
Sciatica	1 (0.9)	0	1 (0.9)	0	2 (1.7)	0
Seborrheic dermatitis	2 (1.7)	0	1 (0.9)	0	2 (1.7)	0
Tendonitis	0	1 (0.9)	0	1 (0.9)	0	2 (1.8)
Urticaria	1 (0.9)	0	1 (0.9)	0	2 (1.7)	0
Vulvovaginal candidiasis	0	1 (0.9)	0	1 (0.9)	0	2 (1.8)
Weight increased	0	0	2 (1.7)	0	2 (1.7)	0

Data are presented as n (%). [a]Defined as an overdose of study treatment; an elevated AST or ALT laboratory value that is ≥3x the ULN and an elevated total bilirubin laboratory value that is ≥2x the ULN and, at the same time, an alkaline phosphatase laboratory value that is <2x the ULN as determined by protocol-specified laboratory testing or unscheduled laboratory testing; infections that require intravenous or intramuscular antibiotics but do not meet the definition of an SAE; or depression, suicidal ideation, and other behavior events. [b]Preferred terms in ≥1% of patients in either treatment arm.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PBO, placebo; SAE, serious AE; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TEAE, treatment-emergent AE; TIL, tildrakizumab; URTI, upper respiratory tract infection; ULN, upper limit of normal; UTI, urinary tract infection.

CONCLUSIONS

- The efficacy of tildrakizumab in patients with moderate-to-severe scalp psoriasis was maintained through Week 52
- There were no new safety signals observed through Week 72

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