Efficacy and safety of tildrakizumab in Australian patients with chronic plaque psoriasis in a phase 3 clinical trial

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INTRODUCTION

- Psoriasis affects up to 6.6% of the Australian population[1]
- Tildrakizumab 100 mg is approved in the US, EU, Australia, and Japan for treatment of moderate to severe plaque psoriasis[2-4]
- This post hoc analysis presents tildrakizumab efficacy and safety in the subgroup of patients from Australia who participated in the pivotal phase 3 reSURFACE 1 trial (NCT01722331)[5]

METHODS

Study design and patients

- reSURFACE 1 was a 3-part, double-blind, randomised, placebo-controlled, 64-week study conducted at 118 study sites in 5 countries:[5] 7 sites in Australia, 16 in Canada, 45 in Japan, 3 in the UK, and 41 in the US
  - This post hoc analysis was conducted in the subgroup of Australian patients enrolled in reSURFACE 1
- Patients aged ≥18 years with moderate to severe chronic plaque psoriasis (body surface area involvement ≥10%, Physician's Global Assessment [PGA] score ≥3, and Psoriasis Area and Severity Index [PASI] score ≥12) were eligible[5]
- Patients were randomised 2:2:1 to receive tildrakizumab 100 mg, tildrakizumab 200 mg, or placebo by subcutaneous injection at weeks 0, 4, and every 12 weeks thereafter through week 64
  - Patients randomised to placebo treatment were rerandomised to receive tildrakizumab 100 or 200 mg at weeks 12 and 16, and every 12 weeks thereafter
  - At week 28, patients who achieved 75% improvement from baseline PASI (PASI 75) were rerandomised to continue receiving tildrakizumab at the same dose or to placebo treatment; patients rerandomised to placebo resumed tildrakizumab treatment at their previous dose upon relapse. All patients received placebo or tildrakizumab injections every 4 weeks to maintain the blind
  - Nonresponders (PASI <50) at week 28 discontinued the study; partial responders (PASI 50–<75) to tildrakizumab 200 mg at week 28 continued the same dose, while partial responders to tildrakizumab 100 mg were rerandomised to dose escalation (tildrakizumab 200 mg) or continued treatment with tildrakizumab 100 mg
- PASI and PGA were assessed at baseline and weeks 4, 8, 12, 16, 22, 28, 32, and every 4 weeks thereafter until week 64; adverse events (AEs) were monitored throughout the study and for up to 20 weeks after the last study visit
- The efficacy endpoints were proportion of patients with PASI 75 response at week 12 and proportion of patients with PGA score of "clear" or "minimal," with at least a 2-grade reduction from baseline (PGA 0/1), at week 12; and proportions of patients with PASI 75 or PGA 0/1 at weeks 28, 40, 52, and 64
- Safety was assessed from treatment-emergent AEs (TEAEs), serious TEAEs, and prespecified TEAEs of special interest (Tier 1)
  - Tier 1 AEs: serious infections, malignancies, nonmelanoma skin cancer, melanoma, confirmed extended major adverse cardiac events, and drug-related hypersensitivity reactions
- Proportions of patients achieving PASI 75 at week 12 were compared using nonresponder imputation; proportions of patients who achieved PGA 0/1 at week 12 were compared using last observation carried forward
  - Proportions of patients with PASI 75 and PGA 0/1 over time are shown with no imputation of missing data
- Efficacy data after week 28 include only patients who achieved PASI 75 response at week 28

RESULTS

Patients

- Of 772 patients in reSURFACE 1, 88 were Australian
- The majority of patients were male (72.7%) and White (84.1%); the median (range) age was 43 (18–70) years **(Table 1)**

Table 1. Patient demographics and baseline characteristics

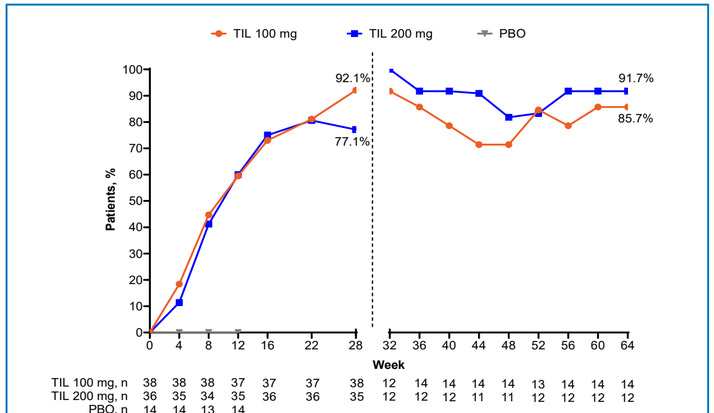
	TIL 100 mg (n = 38)	TIL 200 mg (n = 36)	Placebo (n = 14)	Total (N = 88)
Sex, male	35 (92.1)	24 (66.7)	11 (78.6)	64 (72.7)
Age, years, median (min, max)	42.5 (18.0, 70.0)	44.5 (19.0, 66.0)	54.5 (21.0, 63.0)	43.0 (18.0, 70.0)
Race				
White	35 (92.1)	30 (83.3)	9 (64.3)	74 (84.1)
Multiracial	3 (7.9)	1 (2.8)	3 (21.4)	7 (8.0)
Asian	0	4 (11.1)	1 (7.1)	5 (5.7)
Native Hawaiian or Other Pacific Islander	0	1 (2.8)	0	1 (1.1)
Missing	0	0	1 (7.1)	1 (1.1)
Weight, kg, mean ± SD	90.1 ± 15.5	87.6 ± 21.5	83.9 ± 20.0	88.1 ± 18.8
Height, cm, mean ± SD	175.9 ± 8.2	172.2 ± 9.8	170.6 ± 8.8	173.6 ± 9.2
Psoriatic arthritis present	10 (26.3)	4 (11.1)	2 (14.3)	16 (18.2)
Body surface area affected, %, mean ± SD	24.1 ± 16.1	29.0 ± 17.6	32.0 ± 21.1	27.4 ± 17.6
PASI score, mean ± SD	19.1 ± 7.6	19.5 ± 9.0	20.3 ± 7.3	19.5 ± 8.1
PGA score				
3	33 (86.8)	30 (83.3)	13 (92.9)	76 (86.4)
4	4 (10.5)	6 (16.7)	1 (7.1)	11 (12.5)
5	1 (2.6)	0	0	1 (1.1)
Previous medical conditions				
Hypertension	4 (10.5)	6 (16.7)	6 (42.9)	16 (18.2)
Hyperlipidaemia	1 (2.6)	5 (13.9)	2 (14.3)	8 (9.1)
Obesity	1 (2.6)	2 (5.6)	1 (7.1)	4 (4.5)
Type 2 diabetes mellitus	1 (2.6)	0	3 (21.4)	4 (4.5)
Hypercholesterolaemia	2 (5.3)	0	0	2 (2.3)

Data shown as n (%) unless otherwise indicated.
max, maximum; min, minimum; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; SD, standard deviation; TIL, tildrakizumab.

Efficacy

- At week 12, 23/38 patients receiving tildrakizumab 100 mg (60.5%) and 21/36 patients receiving tildrakizumab 200 mg (58.3%) achieved PASI 75; 0/14 patients receiving placebo achieved PASI 75 (both p <0.001) (**Figure 1**)
- At week 28, 35/38 (92.1%) and 27/35 (77.1%) patients continuously receiving tildrakizumab 100 and 200 mg, respectively, achieved PASI 75 (**Figure 1**)
  - The proportions of patients rerandomised from placebo to tildrakizumab at week 12 who achieved PASI 75 at week 28 were 62.5% (5/8) for tildrakizumab 100 mg and 80.0% (4/5) for tildrakizumab 200 mg
- Among PASI 75 responders at week 28 who continued receiving tildrakizumab 200 or 100 mg, 12/14 (85.7%) and 11/12 (91.7%), respectively, achieved PASI 75 at week 64 (**Figure 1**)
  - All patients who were rerandomised from tildrakizumab to placebo treatment, relapsed, and resumed tildrakizumab at their previous dose recaptured PASI 75 by week 64

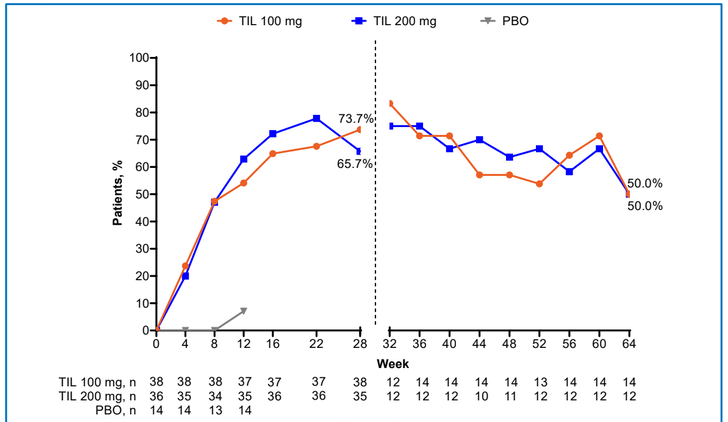
Figure 1. Proportions of patients achieving PASI 75 through week 64



Missing data were not imputed. Week 0 through week 12 includes the placebo, TIL 100 and 200 mg treatment arms. Week 12 through week 28 includes only patients receiving TIL 100 or 200 mg from baseline.
Week 32 through week 64 includes only patients who achieved PASI 75 at week 28 and continued receiving tildrakizumab.
PASI 75, 75% improvement from baseline Psoriasis Area and Severity Index score; PBO, placebo; TIL, tildrakizumab.

- The proportion of patients achieving PGA response at week 12 was significantly higher for patients receiving tildrakizumab 100 mg (20/38 [52.6%]; p = 0.005) or 200 mg (22/36 [61.1%]; p <0.001) vs placebo (1/14 [7.1%]) (**Figure 2**)
- At week 28, 28/38 (73.7%) and 23/35 (65.7%) patients receiving tildrakizumab 100 and 200 mg, respectively, achieved PGA 0/1 (**Figure 2**)

Figure 2. Proportions of patients achieving PGA minimal or clear with a ≥2-grade reduction from baseline through week 64



Missing data were not imputed. Week 0 through week 12 includes the placebo, TIL 100 and 200 mg treatment arms. Week 12 through week 28 includes only patients receiving TIL 100 or 200 mg from baseline.
Week 32 through week 64 includes only patients who achieved PASI 75 at week 28 and continued receiving tildrakizumab.
PGA, Physician's Global Assessment; PBO, placebo; TIL, tildrakizumab.

Safety

- Exposure-adjusted rates of AEs through week 64 were comparable across treatment arms; 70.1 patients per 100 person-years (PY) receiving tildrakizumab 100 mg, 69.9 patients/100 PY receiving tildrakizumab 200 mg, and 126.6 patients/100 PY receiving placebo experienced an AE (**Table 2**)
  - The most frequent AE in all treatment arms by exposure-adjusted rate was upper respiratory infection (**Table 2**)
- Serious AEs (SAEs) occurred in 14.0 patients/100 PY receiving tildrakizumab 100 mg, 17.5 patients/100 PY receiving tildrakizumab 200 mg, and 12.7 patients/100 PY receiving placebo (**Table 2**)
  - The most frequent SAEs by Medical Dictionary for Regulatory Activities System Organ Class were neoplasms benign, malignant, and unspecified (including cysts and polyps), occurring in 4.0 patients/100 PY receiving tildrakizumab 100 mg, 6.6 patients/100 PY receiving tildrakizumab 200 mg, and 8.4 patients/100 PY receiving placebo
- Prespecified AEs of special interest (Tier 1 AEs) occurred in <10.0 patients/100 PY each; the most frequent Tier 1 AE was nonmelanoma skin cancer at 4.0 patients/100 PY receiving tildrakizumab 100 mg, 4.4 patients/100 PY receiving tildrakizumab 200 mg, and 8.4 patients/100 PY receiving placebo

Table 2. Exposure-adjusted rates of adverse events through week 64

	TIL 100 mg[a] (n = 46; 2604 PW)	TIL 200 mg[a] (n = 42; 2388 PW)	Placebo[b] (n = 51; 1236 PW)
Any AE	70.1 (35)	69.9 (32)	126.6 (30)
Serious AE	14.0 (7)	17.5 (8)	12.7 (3)
AE leading to discontinuation	0	2.2 (1)	0
Death	0	0	0
Tier 1 AE			
Severe infections	2.0 (1)	2.2 (1)	0
Malignancies[c]	4.0 (2)	6.6 (3)	8.4 (2)
Nonmelanoma skin cancer	4.0 (2)	4.4 (2)	8.4 (2)
Melanoma	0	0	0
Confirmed extended MACE	0	0	0
Drug-related hypersensitivity reactions	0	0	0
AEs in ≥5% of patients in a treatment arm			
Upper respiratory tract infection	16.0 (8)	17.5 (8)	54.9 (13)
Nasopharyngitis	14.0 (7)	13.1 (6)	21.1 (5)
Psoriasis	0	2.2 (1)	12.7 (3)
Influenza	12.0 (6)	10.9 (5)	0
Pain in extremity	10.0 (5)	0	0
Lower respiratory tract infection	0	8.7 (4)	0
Back pain	6.0 (3)	6.6 (3)	4.2 (1)
Oropharyngeal pain	0	6.6 (3)	0
Urinary tract infection	2.0 (1)	6.6 (3)	4.2 (1)
Dizziness	6.0 (3)	2.2 (1)	4.2 (1)
Gamma-glutamyltransferase increase	6.0 (3)	0	0
Haematuria	6.0 (3)	2.2 (1)	0
Sinusitis	6.0 (3)	4.4 (2)	4.2 (1)

Data shown as exposure-adjusted rate in patients per 100 patient-years (n) analysed as-treated.
[a]Includes patients who received TIL 100 or 200 mg at any time during the study.
[b]Includes patients who received at least 1 dose of placebo in Part 1 or after rerandomisation to placebo in Part 3.
[c]Excluding carcinoma in situ of the cervix.
AE, adverse event; MACE, major adverse cardiac event; PW, person-weeks; TIL, tildrakizumab.

CONCLUSION

- Tildrakizumab treatment was effective, durable, and generally well tolerated in Australian patients

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