5-year efficacy of tildrakizumab 100 and 200 mg in achieving and maintaining PASI 75/90/100 and PGA 0/1 in reSURFACE 1 and 2

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INTRODUCTION

- Tildrakizumab is a high-affinity, humanized, anti–interleukin-23-19 monoclonal antibody approved for the treatment of moderate to severe plaque psoriasis in the US, Europe, Australia, and Japan[1-3]
- Approval of tildrakizumab was based on the results of 2 large phase 3, randomized, controlled clinical trials in patients with moderate to severe plaque psoriasis—reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754)[1–3]
  - Tildrakizumab was associated with significantly superior efficacy vs placebo as assessed by the Psoriasis Area and Severity Index (PASI 75, PASI 90, and PASI 100) and the Physician's Global Assessment (PGA) score by week 12 of treatment (primary endpoint)[1]
  - Patients who completed the base study with PASI ≥50 and received tildrakizumab within 12 weeks of base study completion were eligible for inclusion in a long-term open-label extension study[2]
- This analysis reports 5-year efficacy results for tildrakizumab 100 and 200 mg in the reSURFACE 1 and reSURFACE 2 extension studies

METHODS

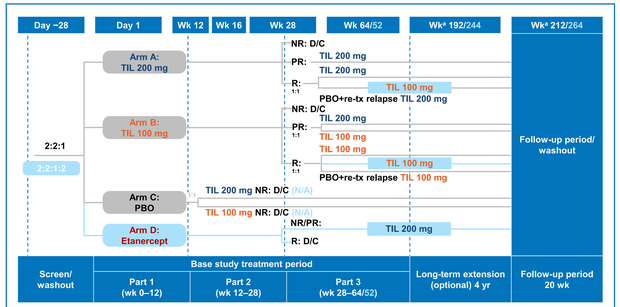
Patients

- Eligible patients were ≥18 years of age with moderate to severe chronic plaque psoriasis, defined as a body surface area involvement ≥10%, a PGA score ≥3, and a PASI score ≥12

Study Design

- Both reSURFACE 1 and reSURFACE 2 were 3-part, double-blind, randomized, placebo-controlled, parallel-group trials followed by a long-term extension phase (**Figure 1**)[1]

Figure 1. Design of the reSURFACE 1 and reSURFACE 2 trials with base and extension periods



Light blue color indicates differences between reSURFACE 1 and reSURFACE 2.
[a]Week 192 and week 212 start from extension week 0 of reSURFACE 1.
D/C, discontinued; N/A, not applicable; NR, nonresponder; PBO, placebo; PR, partial responder; R, responder; re-tx, retreatment; Screen, screening; TIL, tildrakizumab; tx, treatment; wk, week; yr, year.

Base Study

- The base study was 64 weeks in reSURFACE 1 and 52 weeks in reSURFACE 2
- In **Part 1** (**weeks 1–12**), patients were randomized (1:2:2) to placebo or tildrakizumab 100 or 200 mg administered subcutaneously at weeks 0 and 4. reSURFACE 2 also included an etanercept arm (50 mg twice weekly)
- In **Part 2** (**weeks 12–28**), patients previously receiving placebo were rerandomized to treatment with tildrakizumab 100 or 200 mg at weeks 12 and 16 and every 12 weeks (Q12W) thereafter. Patients continuing tildrakizumab received a placebo injection at week 12 to maintain the blind and a dose of tildrakizumab at weeks 16 and 28. Tildrakizumab patients who were nonresponders at week 28 (ie, PASI <50) were discontinued
- In **Part 3** (**weeks 28–64/52**), patients who responded to tildrakizumab (ie, PASI ≥75) were rerandomized to placebo (reSURFACE 1) or tildrakizumab 100 or 200 mg Q12W (reSURFACE 1 and 2). Responders who were rerandomized to placebo in reSURFACE 1 were treated with the same tildrakizumab dose upon relapse. Nonresponders or partial responders (PASI ≥50 and PASI <75) to etanercept in reSURFACE 2 transitioned to tildrakizumab 200 mg

Extension Study

- Patients who completed the base study with PASI ≥50 and received tildrakizumab within 12 weeks of base study completion (W64/52 of reSURFACE 1/2) were eligible to enter a long-term open-label study (reSURFACE 1: weeks 64–256; reSURFACE 2: weeks 52–244)
- Patients received the same dose of tildrakizumab as they were receiving at the completion of the base study

Efficacy Assessment

- All patients who received ≥1 dose of tildrakizumab during the extension studies were included in analyses (Full Analysis Set [FAS])
- Efficacy was assessed from proportions of patients who achieved PASI 75/90/100 and PGA of 0 or 1 with a Grade ≥2 improvement from baseline
- Missing data were not imputed

RESULTS

Patients

- In reSURFACE 1, 239 patients receiving tildrakizumab 100 mg and 267 patients receiving tildrakizumab 200 mg entered the extension study and received at least one dose (**Table 1**); of these, 171 (71.5%) and 208 (77.9%) patients receiving tildrakizumab 100 and 200 mg, respectively, completed the extension studies
- Of patients who entered the reSURFACE 2 extension study (**Table 1**), 290/381 (76.1%) receiving tildrakizumab 100 mg and 272/349 (77.9%) receiving tildrakizumab 200 mg completed the extension study

Table 1. Baseline demographics and clinical characteristics for patients in the extension studies

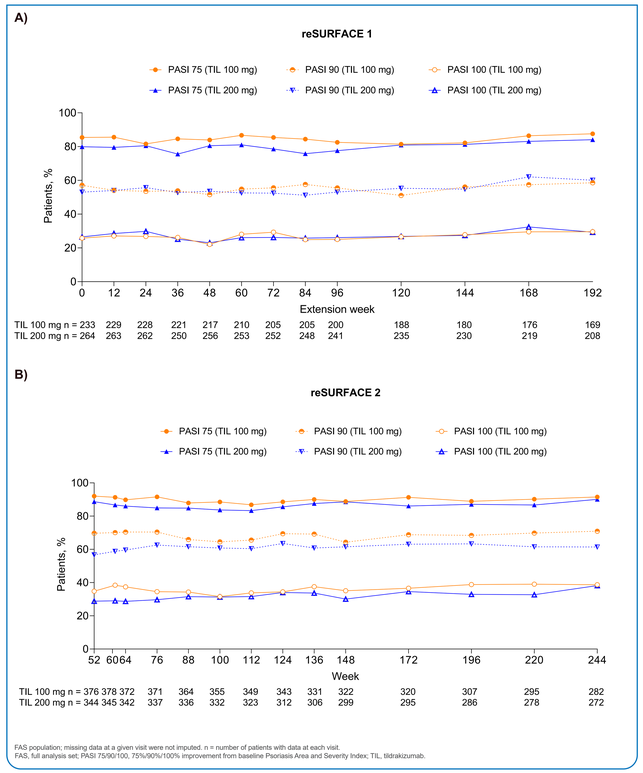
	reSURFACE 1		reSURFACE 2	
	TIL 100 mg (n = 239)	TIL 200 mg (n = 267)	TIL 100 mg (n = 381)	TIL 200 mg (n = 349)
Sex, male, n (%)	159 (66.5)	183 (68.5)	291 (76.4)	242 (69.3)
Age, years	46.9 ± 13.0	47.1 ± 13.0	44.2 ± 13.3	45.6 ± 12.8
Race, n (%)				
White	163 (68.2)	173 (64.8)	351 (92.1)	329 (94.3)
Asian	60 (25.1)	80 (30.0)	7 (1.8)	8 (2.3)
Weight, kg	87.1 ± 24.4	87.8 ± 24.2	88.4 ± 21.4	89.0 ± 21.5
Baseline PASI score	20.0 ± 7.6	21.3 ± 9.6	19.8 ± 7.7	19.3 ± 6.9
Body surface area, %	30.2 ± 17.5	31.7 ± 19.6	32.6 ± 18.0	30.1 ± 15.8
Duration of treatment, weeks, mean[a]	237.4	265.0	227.7	226.1

Values shown as mean ± SD unless otherwise noted.
[a]Duration of treatment during base and extension phases
PASI, Psoriasis Area and Severity Index; SD, standard deviation; TIL, tildrakizumab.

Efficacy

- PASI 75/90/100 responses were maintained over time during the extension phase (**Figure 2**)

Figure 2. PASI 75/90/100 responses during the extension study period by tildrakizumab dose in (A) reSURFACE1 and (B) reSURFACE2

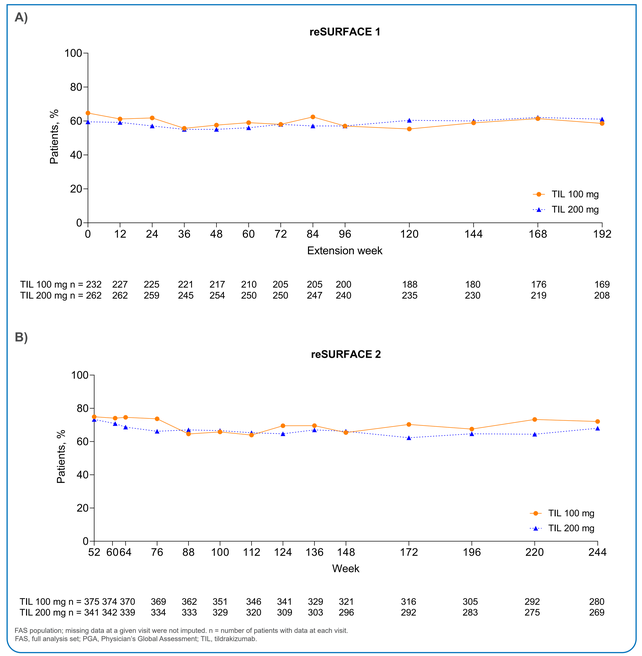


FAS population; missing data at a given visit were not imputed. n = number of patients with data at each visit.
FAS, full analysis set; PASI 75/90/100, 75%/90%/100% improvement from baseline Psoriasis Area and Severity Index; TIL, tildrakizumab.

- Of patients with available data, who achieved a PASI 50/75/90/100 response at the end of the reSURFACE 1 and reSURFACE 2 base studies, the majority maintained that response at the end of the extension phase
  - In reSURFACE 1, of patients receiving tildrakizumab 100 mg, 97% who achieved PASI 50 at week 64 maintained that response at the end of the extension study, as did 91% of patients achieving PASI 75, 77% achieving PASI 90, and 53% achieving PASI 100. Of patients receiving tildrakizumab 200 mg, 98%, 92%, 88%, and 57% maintained week 64 PASI 50, PASI 75, PASI 90, and PASI 100 response, respectively, at the end of the extension
  - In reSURFACE 2, of patients receiving tildrakizumab 100 mg who achieved each PASI response at week 52, 99% maintained PASI 50, 93% maintained PASI 75, 81% maintained PASI 90, and 66% maintained PASI 100 at the end of the extension study. Of patients receiving tildrakizumab 200 mg, 99%, 93%, 76%, and 62% maintained week 52 PASI 50, PASI 75, PASI 90, and PASI 100 response, respectively, at the end of the extension

- PGA responses over time during the extension phase are illustrated in **Figure 3**

Figure 3. Proportions of patients achieving PGA 0 or 1 with a grade ≥2 reduction from baseline during the extension study period by tildrakizumab dose in (A) reSURFACE1 and (B) reSURFACE2



FAS population; missing data at a given visit were not imputed. n = number of patients with data at each visit.
FAS, full analysis set; PGA, Physician's Global Assessment; TIL, tildrakizumab.

CONCLUSIONS

- In both reSURFACE 1 and reSURFACE 2, PASI and PGA response rates were high and durable over 5 years of treatment with tildrakizumab 100 and 200 mg

REFERENCES

1) Reich K, et al. *Lancet*. 2017;390:276–88. **2)** Reich K, et al. *Br J Dermatol*. 2020;182(3):605–17. **3)** Blauvelt A, et al. *Br J Dermatol*. 2018;179(3):615–22.

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DISCLOSURES

AB has served as a scientific adviser and/or clinical study investigator for AbbVie; Aclaris; Akros; Allergan; Almirall; Amgen; Arena; Athenex; Boehringer Ingelheim; Bristol-Myers Squibb; Celgene; Dermavant; Dermira, Inc.; Eli Lilly; FLX Bio; Galderma; Genentech/Roche; GlaxoSmithKline; Janssen; LEO Pharma; Meiji; Merck Sharp & Dohme; Novartis; Pfizer; Purdue Pharma; Regeneron; Revance; Sandoz; Sanofi Genzyme; Sienna Pharmaceuticals; Sun Pharmaceutical Industries, Inc.; UCB; Valeant; and Vidac; and as a paid speaker for AbbVie, Regeneron, and Sanofi Genzyme. **ASF** has received consulting fees or honorarium from Ortho-dermatologics; Sensus; and Sun Pharmaceutical Industries, Inc. **RS** has served as an advisor, and/or paid speaker and/or clinical study investigator for Amgen, Bayer, Boehringer Ingelheim, Celgene, Coherus Biosciences, Cutanea, Eli Lilly, GlaxoSmithKline, Janssen, LEO Pharma, MedImmune, Merck & Co., MSD, Novartis, Oncobiologics, Pfizer, Regeneron, Roche and Samson Clinical. **SH** has nothing to disclose. **AA** has received grants from Nobelpharma. **AI** has received honoraria as a member of an advisory board for AbbVie, Celgene K.K., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Maruho Co Ltd., Novartis Pharma K.K., and Sun Pharma Japan Ltd. **SG** has received grants and/or honoraria as an investigator and/or speaker from AbbVie; Amgen; Dermira; Eli Lilly; Encore Dermatology; Genentech; Janssen; LEO Pharma; LPfizer; Sun Pharmaceutical Industries, Inc.; UCB; and Vanda. **KE** has received honoraria as a speaker for Janssen. **HR** has served on advisory boards, clinical trials, speaker's bureaus, or acted as a consultant for Abbvie, Bayer, Celgene, Eli Lilly, Novartis, Pfizer, and Valeant. **SJR** is an employee of Sun Pharmaceutical Industries, Inc. **LG** has received honoraria andgrants as a speaker, consultant and investigator for AbbVie, Amgen, Celgene, Eli Lilly, Janssen; LEO Pharma, Merck, and Pfizer; received honoraria as a speaker and consultant for Tribute and Valeant; and received grants as an investigator for UCB.

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