Clinical Efficacy of Tildrakizumab in Patients With Chronic Plaque Psoriasis Over 2 Years of Treatment: Results From Long-term Extensions to 2 Phase 3 Clinical Studies

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BACKGROUND

- Tildrakizumab is a high-affinity, humanized, anti–IL-23p19 monoclonal antibody that has demonstrated efficacy in the treatment of chronic plaque psoriasis in 2 phase 3 studies: reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754)[1]
- Both of these studies have an optional long-term extension, each with an additional treatment period of up to 192 weeks

OBJECTIVE

- Preliminary evaluation of maintenance of response data in patients who were responders to tildrakizumab upon entering the extension periods and who maintained response a year into the extensions (a total of at least 2 years of treatment including base and extension periods)

METHODS

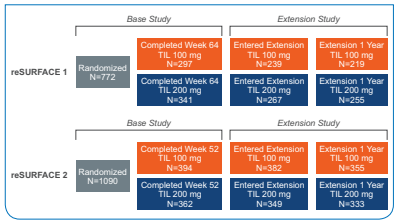
Base Studies

- The reSURFACE base studies are 3-part, double-blinded, randomized, placebo-controlled studies in patients with moderate to severe chronic plaque psoriasis
- Inclusion criteria included age ≥18 years, body surface area involvement ≥10%, Physician's Global Assessment (PGA) score ≥3, and Psoriasis Area and Severity Index (PASI) ≥12
- In the base studies, tildrakizumab 200 and 100 mg were evaluated for 64 weeks (reSURFACE 1) and 52 weeks (reSURFACE 2)
  - In Part 1 of the studies (Weeks 1–12), patients were randomized to subcutaneous tildrakizumab 200 mg, tildrakizumab 100 mg, or placebo, and treatment was administered at Weeks 0 and 4. In reSURFACE 2, there was an additional treatment arm of etanercept 50 mg administered twice weekly
  - In Part 2 (Weeks 12–28), patients previously receiving placebo were rerandomized to tildrakizumab 200 mg or 100 mg and received treatment at Weeks 12, 16, and 28. In reSURFACE 2, the dose in the etanercept arm was 50 mg once weekly

Extension Studies

- Eligibility criteria for the extension included:
  - Patients completed the base studies and chose to continue the optional long-term extensions
  - Patients achieved ≥50% improvement in PASI (PASI 50) at the end of the base studies
  - In reSURFACE 1 only, patients had to have received an active dose of tildrakizumab within 12 weeks of the end of the base study
- Patients received the same dose of tildrakizumab (200 or 100 mg every 12 weeks) as was received at the completion of the base studies; administration was open label after database lock for the base studies
- Efficacy objective for the extension period:
  - Evaluation of the maintenance of efficacy endpoints (ie, proportion of PASI 50, 75, 90, and 100 responders 1 year into the extension among PASI 50, 75, 90, and 100 responders at the start of the extension)
  - Prespecified to be based on observed data, with no statistical analyses planned for comparison between doses
  - The primary efficacy population was the full analysis set, defined as patients with at least 1 dose of extension treatment based on assigned treatment
- Safety objective for the extension period:
  - Evaluation of adverse events (AEs) for up to 5 years; prespecified AEs of interest were summarized by treatment over time
  - Yearly and cumulative (base and extension combined) incidence rates were calculated

Figure 1. Patient Flow



At Week 28 of each study, as specified in the trial designs, tildrakizumab nonresponders were discontinued and etanercept responders (reSURFACE 2) were discontinued; upon completion of base periods, subjects with at least PASI 50 were provided the option to enter the extensions. TIL, tildrakizumab.

- At the base study baseline, disease characteristics of patients who went on to enter the extension were similar between the 2 studies, and between the tildrakizumab 100-mg and 200-mg groups (**Table 1**)
  - The percentage of white patients was lower in reSURFACE 1 than 2 because reSURFACE 1 included sites in Japan, whereas reSURFACE 2 did not

RESULTS

- In reSURFACE 1, 772 patients entered the study, 638 patients completed the base period, and 506 patients entered the extension; in reSURFACE 2, 1090 patients entered the study, 756 patients completed the base period, and 731 patients entered the extension (**Figure 1**)

Efficacy

- PASI responses were maintained in most patients from the end of the base period through the extension period:
  - In reSURFACE 1, in patients entering the extension on tildrakizumab 200 mg, PASI 50/75/90/100 was maintained by 97%/91%/82%/63% (out of 255/208/135/70 patients with data at 1 year); in patients on tildrakizumab 100 mg, PASI 50/75/90/100 was maintained by 98%/90%/74%/53% (out of 219/195/121/70 patients with data at 1 year) (**Figure 2A**)
  - In reSURFACE 2, in patients entering the extension on tildrakizumab 200 mg, PASI 50/75/90/100 was maintained by 97%/88%/84%/70% (out of 330/293/191/97 patients with data at 1 year); for those on tildrakizumab 100 mg, PASI 50/75/90/100 was maintained by 99%/92%/84%/66% (out of 352/327/249/125 patients with data at 1 year) (**Figure 2B**)

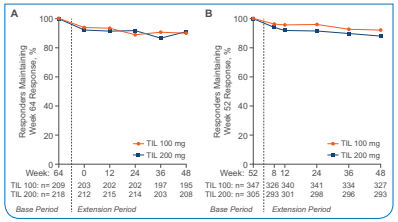
Table 1. Baseline Characteristics for Patients Entering Extension Period

	reSURFACE 1			reSURFACE 2		
	TIL 100 mg	TIL 200 mg	Total	TIL 100 mg	TIL 200 mg	Total
Subjects in population, n	239	267	506	382	349	731
Male	159 (66.5)	183 (68.5)	342 (67.6)	291 (76.2)	242 (69.3)	533 (72.9)
Age, mean (SD), y	46.9 (13.0)	47.1 (13.0)	47.0 (13.0)	44.2 (13.2)	45.6 (12.8)	44.9 (13.0)
Race, white	163 (68.2)	173 (64.8)	336 (66.4)	352 (92.1)	329 (94.3)	681 (93.2)
Baseline PASI score, mean (SD)	20 (7.6)	21.3 (9.6)	20.7 (8.7)	19.8 (7.6)	19.3 (6.9)	19.6 (7.3)
Weight, mean (SD), kg	87.1 (24.4)	87.8 (24.2)	87.5 (24.3)	88.4 (21.4)	89.0 (21.5)	88.7 (21.4)
Body surface area, mean (SD), %	30.2 (17.5)	31.7 (19.6)	31.0 (18.6)	32.6 (18.0)	30.1 (15.8)	31.4 (17.0)

Data in table are n (%) unless otherwise specified. PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

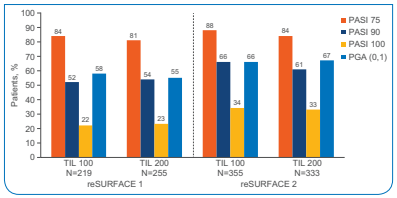
- After 2 years of treatment with tildrakizumab, including the base and extension periods, 84% and 88% of patients who received tildrakizumab 100 mg achieved PASI 75 in reSURFACE 1 and reSURFACE 2, respectively. Similarly, in the tildrakizumab 200-mg groups, 81% and 84% of patients achieved PASI 75 in reSURFACE 1 and reSURFACE 2, respectively (**Figure 3**)

Figure 2. Maintenance of PASI 75 Response From End of Base Period Through Extension Periods (A) reSURFACE 1 and (B) reSURFACE 2



FAS population; observed data. Patients entering the extension after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (ie, PASI ≥50). n=number of subjects with data. FAS, full analysis set; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

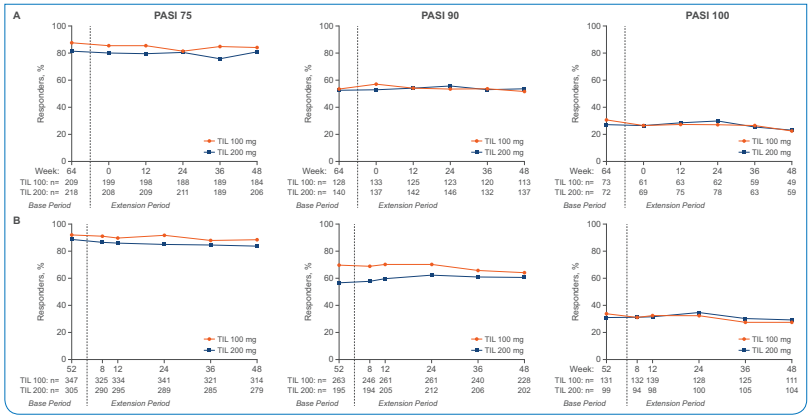
Figure 3. Overall Efficacy After 2 Years of Treatment With Tildrakizumab



FAS population; observed data. Patients entering the extension after 64 weeks (reSURFACE 1) or 52 weeks (reSURFACE 2) were at least partial responders (ie, PASI ≥50). FAS, full analysis set; PASI, Psoriasis Area and Severity Index; PGA, Physicians' Global Assessment; TIL, tildrakizumab.

- Overall, the proportions of patients achieving PASI 75/90/100 responses were stable during the extension period (**Figure 4**)

Figure 4. Overall Efficacy From End of Base Period Through Extension Periods (A) reSURFACE 1 and (B) reSURFACE 2



FAS population; observed data. n=number of responders. FAS, full analysis set; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

Safety

- After 2 years of treatment with tildrakizumab, the cumulative number of patients with prespecified AEs was low in both the 200-mg and 100-mg groups in both studies (**Table 2**)

Table 2. Two-Year Cumulative Number (Rate) of Patients With AEs of Interest

	reSURFACE 1		reSURFACE 2	
	TIL 100 mg n (Exposure-Adjusted Rate per 100 PY)	TIL 200 mg n (Exposure-Adjusted Rate per 100 PY)	TIL 100 mg n (Exposure-Adjusted Rate per 100 PY)	TIL 200 mg n (Exposure-Adjusted Rate per 100 PY)
Severe infections	5 (0.8)	6 (0.8)	7 (0.8)	9 (1.1)
Malignancies	6 (0.9)	2 (0.3)	4 (0.5)	7 (0.9)
Nonmelanoma skin cancer	2 (0.3)	2 (0.3)	3 (0.4)	4 (0.5)
Melanoma skin cancer	0	0	1 (0.1)[a]	0
Confirmed MACE	3 (0.5)	2 (0.3)	0	1 (0.1)
Deaths[b]	0	0	2 (0.2)	1 (0.1)
Drug-related hypersensitivity AEs	2 (0.3)	1 (0.1)	2 (0.2)	2 (0.2)

[a]The reported case of melanoma was melanoma in situ; [b]Not related to study medication. ASaT population. AE, adverse event; ASaT, all subjects as treated; MACE, major adverse cardiac event; PY, patient-years; TIL, tildrakizumab.

CONCLUSIONS

- Tildrakizumab 100 mg or 200 mg demonstrated maintenance of efficacy in the treatment of moderate to severe chronic plaque psoriasis for at least 2 years of treatment
- Over a cumulative 2-year treatment period in patients enrolled in reSURFACE 1 and reSURFACE 2, tildrakizumab 200 and 100 mg were well-tolerated with a low rate of AEs of interest

REFERENCES

1. Reich et al. *Lancet*. 2017;390(10091):276–288.

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DISCLOSURES

KP has served as an advisor, paid speaker and/or clinical study investigator for AbbVie, Akros, Allergan, Amgen, Anacor, Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol Myers Squib, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, GlaxoSmithKline, Janssen, Kyowa Hakko Kirin, Leo, Medimmune, Meiji Seika Pharma, Merck Sharp & Dohme, Merck Serono, Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant. **KR** has served as an advisor, paid speaker and/or clinical study investigator for AbbVie, Affibody, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Sanofi, Takeda, UCB Pharma, Xenoport. **AB** has served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Inc., Eli Lilly and Company, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac, and as a paid speaker for Eli Lilly and Company, Janssen, Regeneron, and Sanofi Genzyme. **DT** has served as an advisor, paid speaker and/or clinical study investigator for AbbVie, Almirall, Amgen, Astellas, Biogen-Idec, Boehringer-Ingelheim, Celgene, Dermira, Dignity, Eli Lilly, Forward-Pharma, Galapagos, GlaxoSmithKline, Leo, Janssen-Cilag, Maruho, MSD, Mitsubishi Pharma, Mundipharma, Novartis, Pfizer, Roche, Roche-Posay, Sandoz, XenoPort. **RS** has served as an advisor, 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. **SKT** is a clinical study investigator for Merck & Co. **NC, SG, QL**, and **CLR** are employees of Merck & Co, Inc.

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