Tildrakizumab Results in Significant and Sustained Improvements in Health-Related Quality of Life in Patients With Moderate to Severe Psoriasis in a Phase 3 trial (reSURFACE 1)

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BACKGROUND

- Tildrakizumab is a high-affinity, humanized, immunoglobulin G1κ, anti–interleukin-23p19 monoclonal antibody approved for the treatment of moderate to severe plaque psoriasis[1,2]
- Psoriasis has a significant impact on health-related quality of life (HRQoL). Although dermatology-specific instruments are the most sensitive, generic questionnaires, like the Short Form-36 (SF-36) and the European Quality of Life 5 Dimensions (EQ-5D), facilitate comparisons with other diseases
- In prior studies using the SF-36, patients with psoriasis reported an impact on physical and mental health comparable to other major medical diseases like cancer, arthritis, hypertension, heart disease, diabetes, and depression[3]

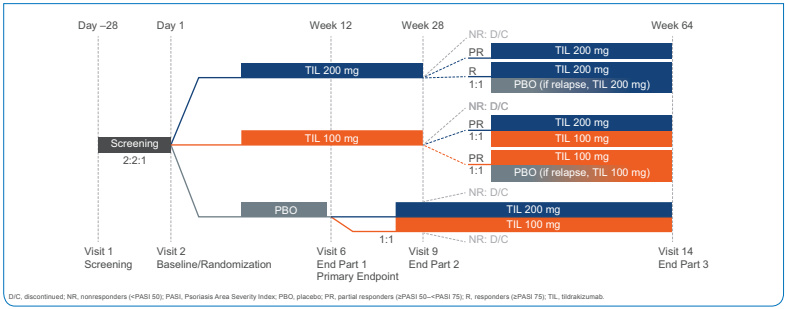
OBJECTIVE

- The objective was to evaluate the impact of tildrakizumab on generic HRQoL in patients with moderate to severe plaque psoriasis in the phase 3 clinical trial reSURFACE 1 (NCT01722331) (no generic measures were included in reSURFACE 2 [NCT01729754])

METHODS

- Exploratory analysis of the SF-36 and EQ-5D HRQoL scales in adult patients with moderate to severe chronic plaque psoriasis (≥10% body surface area involvement, Physician's Global Assessment score ≥3, Psoriasis Area Severity Index [PASI] score ≥12) who participated in a 3-part, 64-week, parallel-group, double-blinded, randomized controlled trial
- Part 1 (Weeks 0–12) was placebo-controlled; Part 2 (Weeks 12–28) rerandomized placebo-treated patients to tildrakizumab 100 or 200 mg; Part 3 (Weeks 28–64) rerandomized patients to receive the same, a higher or a lower tildrakizumab dose, or placebo, according to their PASI response at Week 28 (**Figure 1**)
- Placebo or tildrakizumab (as applicable) were administered at Weeks 0, 4, 16, 28, 40, and 52
- HRQoL was measured by the SF-36 and EQ-5D questionnaires at baseline and at Weeks 12, 28, 52, and 64
- The SF-36 measures 8 dimensions (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health), summarized in 2 scores: Physical Health (PH) and Mental Health (MH), ranging from 0 to 100 (**higher** scores correspond to **better** HRQoL)
- The EQ-5D provides a single index score value, which ranges from –0.59 (worse than death) to **1 (perfect health)**, based on 5 components (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression)
  - Each component has 3 levels, ranging from **1 (better) to 3 (worse)**: no problems (1), some problems (2), and extreme problems (3)
- We describe mean (95% confidence interval [CI]) change from baseline in PH, MH, EQ-5D index score, and EQ-5D components at Weeks 12, 28, and 64. Changes over time were compared with paired Student *t* tests. Data presented are based on observed cases

Figure 1. reSURFACE 1 Trial Design

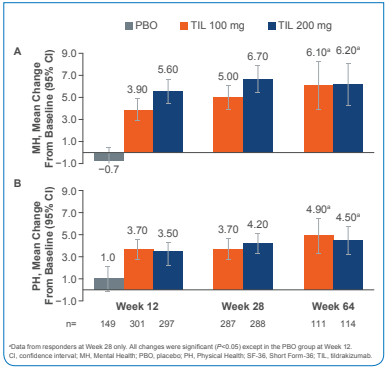


D/C, discontinued; NR, nonresponders (<PASI 50); PASI, Psoriasis Area Severity Index; PBO, placebo; PR, partial responders (≥PASI 50–<PASI 75); R, responders (≥PASI 75); TIL, tildrakizumab.

RESULTS

- Overall, 155 patients were randomized to receive placebo, 309 patients received tildrakizumab 100 mg, and 308 received tildrakizumab 200 mg. Mean (standard deviation) baseline HRQoL scores were similar between the placebo, tildrakizumab 100-mg, and tildrakizumab 200-mg groups: MH, 46.7 (11.2), 46.2 (11.2), and 45.1 (11.4); PH, 47.7 (9.2), 47.7 (9.1), and 46.9 (9.5); EQ-5D index score, 0.7 (0.2), 0.7 (0.2), and 0.7 (0.3), respectively
- Significant improvements in SF-36 MH and PH scores were observed at Week 12 (after 2 doses) and Week 28 (after 3 doses) in patients initially randomized to tildrakizumab 100 mg and 200 mg. In the placebo group, no changes were observed at Week 12, but significant increases were observed between Weeks 12 and 28, after switching to tildrakizumab 100 or 200 mg (**Figure 2**). During Part 3, the improvements in SF-36 scores were maintained up to Week 64, with no notable differences between the treatment groups (**Figure 2**)

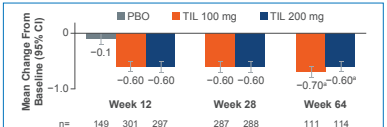
Figure 2. SF-36 MH and PH Scores Over Time



aData from responders at Week 28 only. All changes were significant (P<0.05) except in the PBO group at Week 12. CI, confidence interval; MH, Mental Health; PBO, placebo; PH, Physical Health; SF-36, Short Form-36; TIL, tildrakizumab.

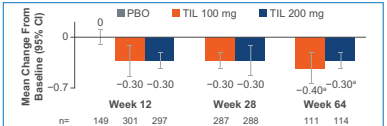
- The EQ-5D index score and the pain/discomfort and anxiety/depression components also improved significantly at Weeks 12 and 28 in the tildrakizumab 100-mg and 200-mg groups, while remaining stable in the placebo group up to Week 12. Significant improvements were observed in this group at Week 28, after the switch to tildrakizumab 100 mg or 200 mg. Improvements were maintained up to Week 64, with no notable differences observed between the treatment groups (**Figures 3** and **4**)

Figure 3. Pain/Discomfort Component of the EQ-5D Over Time



aData from responders at Week 28 only. All changes were significant (P<0.05) except in the PBO group at Week 12. CI, confidence interval; EQ-5D, European Quality of Life 5 Dimensions; PBO, placebo; TIL, tildrakizumab.

Figure 4. Anxiety/Depression Component of the EQ-5D Over Time



aData from responders at Week 28 only. All changes were significant (P<0.05) except in the PBO group at Week 12. CI, confidence interval; EQ-5D, European Quality of Life 5 Dimensions; PBO, placebo; TIL, tildrakizumab.

CONCLUSIONS

- Treatment with tildrakizumab resulted in clinically significant and sustained improvements in overall HRQoL as measured by the SF-36 and EQ-5D questionnaires in patients with moderate to severe chronic plaque psoriasis receiving continuous therapy through Week 64
- Of the previously mentioned HRQoL scales, pain, anxiety, and depression were the quality of life domains that showed the greatest improvements

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ACKNOWLEDGMENTS

We thank the patients for their participation. The study was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; analyses were funded by Almirall, Barcelona, Spain. Writing support was provided by TFS S.L. Additional editorial support was provided by JK Associates, Inc., part of the Fishawack Group of Companies, and was funded by Sun Pharmaceutical Industries, Inc.

DISCLOSURES

CEMG has received honoraria as a member of an advisory board and/or speaker from Almirall, AbbVie, Celgene, Janssen, Novartis, MSD, and LEO. **DT** has received honoraria as an advisor, speaker, and/or investigator from AbbVie, Almirall, Biogen-Idec, Boehringer Ingelheim, Celgene, Dermira, Dignity, Eli Lilly, Galapagos, GlaxoSmithKline, Leo, Janssen-Cilag, MSD, Mundipharma, Novartis, Pfizer, Regeneron-Sanofi, Roche-Posay, Sandoz, and UCB. **LI** has received honoraria as an advisor, investigator, and/or speaker from AbbVie, Almirall, Amgen, Celgene, Janssen-Cilag, Leo Pharma, Novartis, AstraZeneca, BMS, Boehringer Ingelheim, Centocor Kyowa, Pfizer, Samsung Bioips, and UCB. **AP** has nothing to disclose. **IP-C** has received honoraria and salary as an employee of Almirall R&D. **AB** has received research/grant support and served as Consultant for: AbbVie, Aclaris, Akros, Allergan, Almirall, Amgen, Arena, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira Inc., Eli Lilly and Company, Galderma, Genentech/Roche,GlaxoSmithKline, Janssen, Leo, Meiji, Merck Sharp & Dohme Corp., Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharmaceuticals, UCB Pharma, Valeant, Vidac and as paid speaker for Janssen, Regeneron, Sanofi Genzyme. **KR** has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Affibody, Almirall, Amgen, Biogen-Idec, Boehringer Ingelheim, Celgene, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Kyowa Kirin, Leo, Lilly, Medac, Merck Sharp & Dohme, Miltenyi, Novartis, Ocean Pharma, Pfizer, Samsung Bioepis, Sanofi, Takeda, UCB, Valeant, Xenoport. Analyses were presented at the 27th European Academy of Dermatology and Venereology (EADV) Congress, September 12–16, 2018, Paris, France.

Presented at the American Academy of Dermatology Annual Meeting, March 1–5, 2019, Washington, DC, USA