Early and maintained response levels in psoriasis patients treated with tildrakizumab

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INTRODUCTION

- Tildrakizumab is an IgG1/κ monoclonal antibody that selectively inhibits the p19 subunit of interleukin-23 and is approved in the US, Europe, and Australia to treat adult patients with moderate to severe plaque psoriasis[1]
- The efficacy and safety of tildrakizumab has been demonstrated in two phase 3, double-blind, randomized, controlled trials (reSURFACE 1, NCT01722331; and reSURFACE 2, NCT01729754)[2,3]
- This post hoc analysis examined the long-term efficacy of tildrakizumab 100 mg up to week 148 among patients achieving various Psoriasis Area and Severity Index (PASI) responses at week 28 in reSURFACE 1 and 2

METHODS

- Both reSURFACE 1 and reSURFACE 2 used a three-part design:[3]
  - Part 1 (0–12 weeks): Patients were randomized (1:2:2) to blinded subcutaneous placebo or tildrakizumab 100 or 200 mg at weeks 0 and 4
  - Part 2 (12–28 weeks): Patients previously receiving placebo were rerandomized to tildrakizumab 100 or 200 mg at weeks 12 and 16 and every 12 weeks (Q12W) thereafter. Patients continuing tildrakizumab from Part 1 received a placebo injection at week 12 to maintain the blind and a dose of tildrakizumab at weeks 16 and 28. At week 28, tildrakizumab nonresponders (PASI <50) discontinued
  - Part 3 (reSURFACE 1: 28–64 weeks; reSURFACE 2: 28–52 weeks): Tildrakizumab responders (PASI ≥75) were rerandomized to receive placebo every 2 weeks (reSURFACE 1) or tildrakizumab 100 or 200 mg Q12W (reSURFACE 1 and 2). Responders who were rerandomized to placebo were retreated with the same tildrakizumab dose upon relapse (defined as reduction in maximum PASI response by 50%)
- Patients who received tildrakizumab in Part 1 and achieved PASI ≥50 at the end of Part 3 were eligible to enter the long-term extension (LTE) study[3]
- Patients treated with tildrakizumab 100 mg in parts 1–3 (at weeks 0, 4, and every 12 weeks after) and who received ≥1 dose during the LTE were included in this analysis
- Percent PASI improvement from baseline to week 148 was examined for patients achieving PASI 50–74, 75–89, 90–99, and 100 responses at week 28 using both observed data and imputed data with last observation carried forward (LOCF)

RESULTS

- A total of 335 patients were included in the analysis

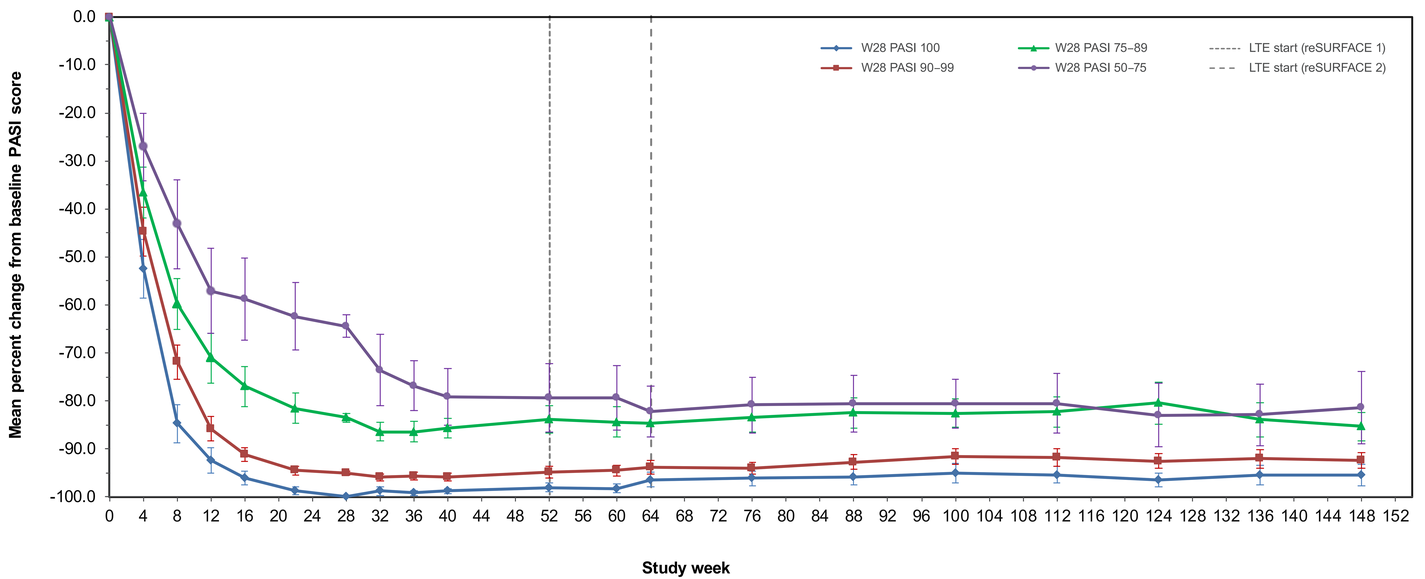
Table. Baseline demographics and clinical characteristics by % PASI improvement from baseline to week 28

	PASI 50–74 (n = 34)	PASI 75–89 (n = 79)	PASI 90–99 (n = 131)	PASI 100 (n = 91)
Age, years	46.9 (14.36)	45.9 (12.78)	45.2 (13.06)	42.4 (14.07)
Male, n (%)	26 (76.5)	53 (67.1)	94 (71.8)	62 (68.1)
Body surface area, %	34.5 (20.11)	31.1 (16.43)	33.7 (18.79)	29.0 (16.06)
Disease duration, years	13.9 (10.44)	18.0 (12.42)	16.9 (11.18)	14.5 (10.83)
PASI score	20.24 (8.80)	19.46 (6.44)	20.99 (8.03)	18.49 (5.82)
Comorbidities, n (%)				
PsA	7 (20.6)	11 (13.9)	22 (16.8)	16 (17.6)
Diabetes	4 (11.8)	7 (8.9)	9 (6.9)	8 (8.8)
CVD	9 (26.5)	21 (26.6)	25 (19.1)	22 (24.2)
Prior biologics, n (%)	4 (11.8)	10 (12.7)	2 (19.8)	11 (12.1)

Data are mean (standard deviation) unless otherwise specified.
CVD, cardiovascular disease; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.

- Patients had longstanding psoriasis (mean 16.1 years), but 85.2% had not previously been treated with a biologic (**Table**)
- Mean PASI improvements at week 4 were 27.1%, 36.6%, 44.7%, and 52.5% for week 28 PASI 50–74, 75–89, 90–99, and 100 groups, respectively

Figure. Mean percent change from baseline PASI score (95% CI) by study week and week 28 PASI status category



Number of patients:

W28 PASI 100	91	91	91	91	91	91	91	89	90	91	90	91	89	86	86	83	84	85	82	81
W28 PASI 90–99	131	131	131	131	130	131	131	128	129	131	131	130	130	129	125	127	127	122	121	117
W28 PASI 75–89	79	79	79	79	79	79	79	75	78	79	78	78	79	78	76	75	70	70	63	63
W28 PASI 50–74	34	34	34	34	34	34	34	33	34	34	34	34	34	34	33	33	33	27	26	22

Data are as observed; sample size at each study week is based on patients with non-missing data.
CI, confidence interval; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; W28, week 28.

- A greater mean PASI response at week 8 was indicative of a greater mean PASI response at week 28 (**Figure**)
- Responses were sustained through week 148 in patients achieving a week 28 mean PASI 75 response or higher
  - Responses were 85.3%, 92.4%, and 95.4% for PASI 50–74, 75–89, 90–99, and 100, respectively
- Patients achieving week 28 PASI 50–74 had continuous mean PASI improvement from week 28 (64.4%) to week 52 (79.4%) and week 64 (82.2%); responses were further sustained through 148 weeks (81.4%)
- Results were similar when using either data as observed or imputed using LOCF

DISCUSSION

- Patients who received tildrakizumab and achieved PASI ≥90 at week 28 had rapid improvements as early as week 4
- Among patients achieving PASI ≥50 at week 28, PASI improvements were improved or sustained through 148 weeks

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