Sustained and Improved Efficacy of Tildrakizumab from Week 28 to Week 52 in Treating Moderate-to-Severe Plaque Psoriasis

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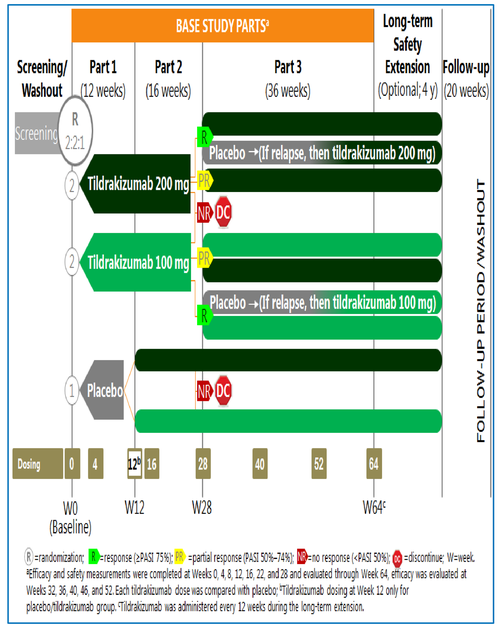
INTRODUCTION

- Psoriasis is a common, chronic, and immune-mediated skin disease, affecting 3.2% of the US population. Approximately 7.4 million people in the US have psoriasis[1].
- Psoriasis is characterized by painful, pruritic, well-demarcated, erythematous plaques with silver scale[1,2], and often negatively impacts patients' overall health, quality of life, productivity, and interpersonal relationship[2-4].
- Tildrakizumab is a high-affinity, humanized, IgG1 κ, anti-interleukin–23 monoclonal antibody designed to block interleukin-23 p19[5]. It is administered subcutaneously once every 12 weeks, after two initial doses administered 4 weeks apart[5].
- Two phase-3, double-blind, randomized controlled trials (reSURFACE 1: NCT01722331; reSURFACE 2: NCT01729754) demonstrated efficacy and safety of tildrakizumab in the treatment of adult patients with moderate-to-severe plaque psoriasis over the first 28 weeks[5].
- This analysis evaluated longer-term data from these two trials to examine whether the efficacy is sustained or improved from week 28 through week 52.

METHODS

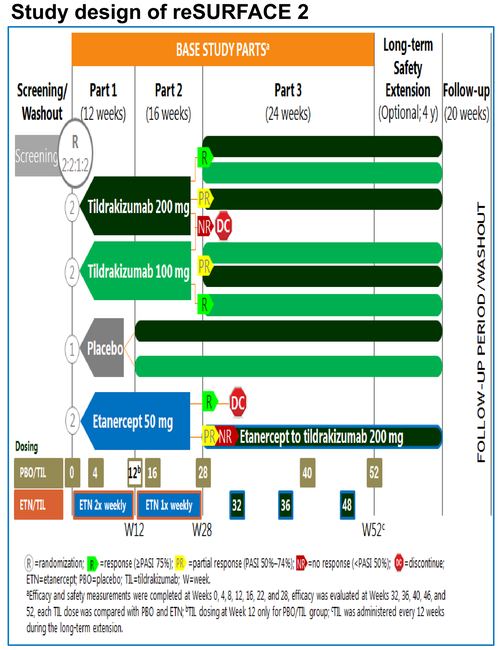
- Both phase-3 trials randomized adult patients with moderate-to-severe plaque psoriasis to receive tildrakizumab 100 mg or tildrakizumab 200 mg at weeks 0, 4, then every 12 weeks, and used three-part study design
  - Part 1 (week 0-12) randomized patients to: tildrakizumab 100 mg, tildrakizumab 200 mg, placebo, or etanercept 50mg (in reSURFACE 2)
  - Part 2 (week 12-28) re-randomized placebo patients to tildrakizumab;
  - Part 3 (week 28-64, reSURFACE 1; week 28-52, reSURFACE 2) re-randomized patients with Psoriasis Area and Severity Index (PASI) response ≥50% to the same, a higher or a lower dose of tildrakizumab, or placebo based on their week-28 PASI responses
- This analysis included only patients treated with the same dose of tildrakizumab (100 mg or 200 mg) throughout the first 52 weeks.
- Four mutually exclusive groups were created based on patients' week-28 PASI response: PASI 100, PASI 90-99, PASI 75-89 and PASI 50-74.
- Baseline characteristics and PASI responses at week 52 (observed data) were analyzed for each week-28 PASI-response group.

Study design of reSURFACE 1



R=randomization; R=response (≥PASI 75%); PR=partial response (PASI 50%–74%); NR=no response (<PASI 50%); DC=discontinue; W=week. [a]Efficacy and safety measurements were completed at Weeks 0, 4, 8, 12, 16, 22, and 28 and evaluated through Week 64; efficacy was evaluated at Weeks 32, 36, 40, 46, and 52. Each tildrakizumab dose was compared with placebo; [b]Tildrakizumab dosing at Week 12 only for placebo/tildrakizumab group. [c]Tildrakizumab was administered every 12 weeks during the long-term extension.

Study design of reSURFACE 2



R=randomization; R=response (≥PASI 75%); PR=partial response (PASI 50%–74%); NR=no response (<PASI 50%); DC=discontinue; ETN=etanercept; PBO=placebo; TIL=tildrakizumab; W=week. [a]Efficacy and safety measurements were completed at Weeks 0, 4, 8, 12, 16, 22, and 28, efficacy was evaluated at Weeks 32, 36, 40, 46, and 52, each TIL dose was compared with PBO and ETN; [b]TIL dosing at Week 12 only for PBO/TIL group; [c]TIL was administered every 12 weeks during the long-term extension.

RESULTS

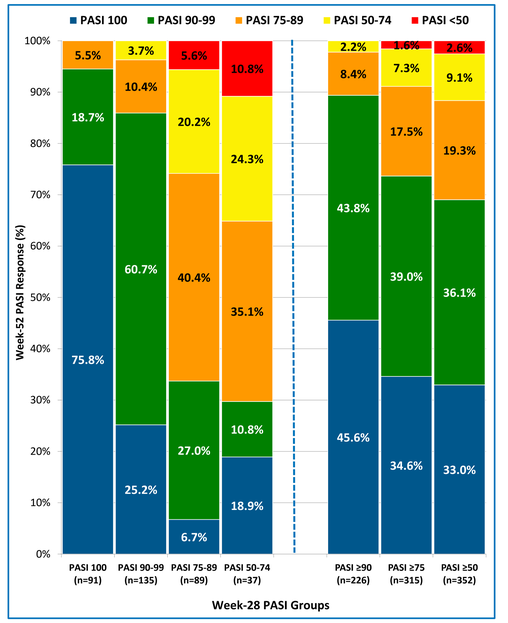
- Overall, 352 patients on tildrakizumab 100 mg (male: 69.9%; mean baseline age: 44.9 years) and 313 on tildrakizumab 200 mg (male: 67.1%; mean baseline age: 46.4 years) were included.
- The proportions of patients achieving PASI 100, PASI 90-99, PASI 75-89 and PASI 50-74 at week 28 were 25.9%, 38.4%, 25.3%, and 10.5% respectively for those on the 100 mg dose, and 24.6%, 24.3%, 19.5%, and 31.6% respectively for those on the 200 mg dose.
- Week-52 PASI responses for patients treated with tildrakizumab 100 mg:
  - Among patients achieving week-28 PASI 100 (n=91), 75.8% maintained PASI 100, 18.7% had PASI 90-99, 94.5% had PASI≥90, and all had PASI≥75 at week 52
  - Among patients achieving week-28 PASI 90-99 (n=135), 25.2% improved to PASI 100, 60.7% maintained PASI 90-99, and 10.4% had PASI 75-89 at week 52
  - Among patients achieving week-28 PASI 75-89 (n=89), 6.7% improved to PASI 100, 27.0% improved to PASI 90-99, and 40.4% maintained PASI 75-89 at week 52
  - Among patients achieving week-28 PASI 50-74 (n=37), 18.9% improved to PASI 100, 10.8% improved to PASI 90-99, 35.1% improved to PASI 75-89, and 24.3% maintained PASI 50-74 at week 52
- Week-52 PASI responses for patients treated with tildrakizumab 200 mg:
  - Among patients achieving week-28 PASI 100 (n=77), 84.4% maintained PASI 100, 11.7% had PASI 90-99, 96.1% had PASI≥90, and all had PASI≥75 at week 52
  - Among patients achieving week-28 PASI 90-99 (n=76), 32.9% improved to PASI 100, 48.7% maintained PASI 90-99, and 17.1% had PASI 75-89 at week 52
  - Among patients achieving week-28 PASI 75-89 (n=61), 8.2% improved to PASI 100, 32.8% improved to PASI 90-99, and 39.3% maintained PASI 75-89 at week 52
  - Among patients achieving week-28 PASI 50-74 (n=99), 6.1% improved to PASI 100, 14.1% improved to PASI 90-99, 32.3% improved to PASI 75-89, and 41.4% maintained PASI 50-74 at week 52
- Among patients who achieved week-28 PASI≥90 with either dose of tildrakizumab, 88.9-89.4% maintained PASI≥90 at week 52.
- Overall, 91.1% patients on the 100 mg dose and 93.9% on the 200 mg dose with week-28 PASI≥75 maintained PASI≥75 at week 52.
- In addition, 33.7%-41.0% of patients with week-28 PASI 75-89 improved to PASI≥90.
- Among patients with week-28 PASI 50-74, 20.2-29.7% achieved PASI≥90 and 52.5-64.9% achieved PASI≥75 at week 52.
- Overall, 2.6% of patients on the 100 mg (9 out of 352) or 200 mg (8 out of 313) dose had week-52 PASI<50.

Baseline Characteristics

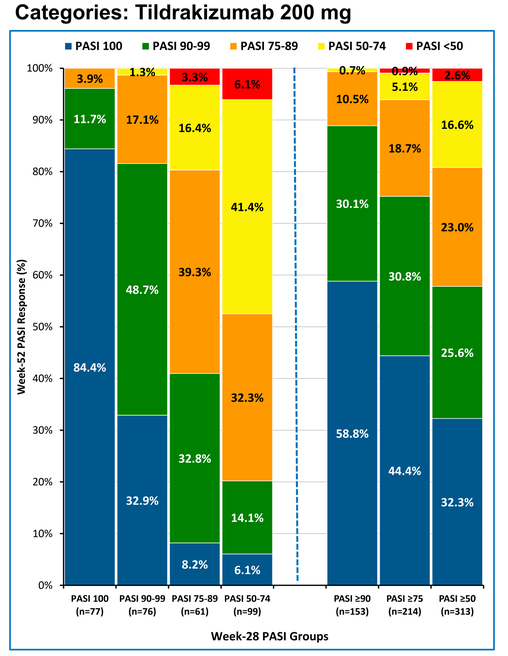
	Week-28 PASI Categories				
	100	90-99	75-89	50-74	≥50
Tildrakizumab 100 mg Cohort					
Number of Patients	91	135	89	37	352
Mean Age (year, SD)	42.6 (14.1)	45.0 (13.1)	46.1 (13.1)	47.2 (13.8)	44.9 (13.5)
Proportion of males (%)	69.2%	70.4%	66.3%	78.4%	69.9%
Race (%)					
White	80.2%	86.7%	85.4%	70.3%	83.0%
Black	3.3%	1.5%	3.4%	0.0%	2.3%
Asian	6.6%	9.6%	9.0%	27.0%	10.5%
Others	9.9%	2.2%	2.2%	2.7%	4.2%
Weight (Kg): mean (SD)	83.0 (18.8)	87.4 (21.6)	94.5 (23.6)	83.4 (22.4)	87.6 (21.9)
BMI3 (kg/m^2): mean (SD)	28.1 (5.7)	29.2 (6.7)	31.9 (7.7)	28.4 (7.1)	29.5 (6.9)
Body Surface Area: % (SD)	28.9 (16.1)	33.5 (18.6)	32.0 (16.6)	35.7 (19.9)	32.2 (17.7)
Disease Duration: years (SD)	14.3 (10.9)	16.8 (11.1)	17.8 (12.8)	14.3 (10.4)	16.2 (11.5)
PASI: mean (SD)	18.5 (5.8)	20.9 (7.9)	19.6 (6.6)	20.6 (8.5)	19.9 (7.2)
Previous medical conditions (%)					
Psoriatic arthritis	17.6%	16.3%	15.7%	18.9%	16.8%
Cardiovascular diseases	25.3%	18.5%	29.2%	29.7%	24.1%
Diabetes	8.8%	6.7%	7.9%	10.8%	8.0%
Hypercholesterolemia	7.7%	5.2%	4.5%	8.1%	6.0%
Hyperlipidemia	12.1%	4.4%	3.4%	8.1%	6.5%
Hypertension	24.2%	18.5%	29.2%	27.0%	23.6%
Obesity	1.1%	6.7%	7.9%	10.8%	6.0%
Previously treated with biologics	12.1%	19.3%	13.5%	10.8%	15.1%
Tildrakizumab 200 mg Cohort					
Number of Patients	77	76	61	99	313
Mean Age (year, SD)	45.8 (13.5)	45.4 (14.1)	47.8 (12.7)	46.9 (13.0)	46.4 (13.3)
Proportion of males (%)	74.0%	69.7%	54.1%	67.7%	67.1%
Race (%)					
White	81.8%	85.5%	68.9%	76.8%	78.6%
Black	0.0%	2.6%	4.9%	2.0%	2.2%
Asian	14.3%	10.5%	19.7%	21.2%	16.6%
Others	3.9%	1.4%	6.5%	0.0%	2.6%
Weight (Kg): mean (SD)	86.1 (24.5)	89.5 (22.5)	87.3 (19.0)	90.2 (24.4)	88.4 (23.0)
BMI3 (kg/m^2): mean (SD)	28.7 (7.5)	30.7 (8.9)	31.1 (7.5)	30.1 (6.7)	30.1 (7.6)
Body Surface Area: % (SD)	30.8 (17.5)	29.6 (15.3)	31.7 (17.5)	33.2 (19.6)	31.4 (17.6)
Disease Duration: years (SD)	16.8 (13.1)	17.9 (13.5)	18.7 (13.3)	17.6 (11.6)	17.7 (12.8)
PASI: mean (SD)	20.7 (9.3)	19.7 (6.5)	20.1 (7.2)	20.1 (8.8)	20.1 (8.1)
Previous medical conditions (%)					
Psoriatic arthritis	14.3%	17.1%	9.8%	22.2%	16.6%
Cardiovascular diseases	24.7%	30.3%	32.8%	30.3%	29.4%
Diabetes	9.1%	13.2%	11.5%	14.1%	12.1%
Hypercholesterolemia	5.2%	5.3%	6.6%	5.1%	5.4%
Hyperlipidemia	3.9%	6.6%	4.9%	8.1%	6.1%
Hypertension	24.7%	29.0%	32.8%	30.3%	29.1%
Obesity	2.6%	7.9%	9.8%	8.1%	7.0%
Previously treated with biologics	18.2%	17.1%	19.7%	17.2%	17.9%

Notes: PASI= Psoriasis Area and Severity Index; SD=standard deviation; BMI=body mass index

Week-52 PASI Responses by Week-28 PASI Categories: Tildrakizumab 100 mg



Week-52 PASI Responses by Week-28 PASI Categories: Tildrakizumab 200 mg



CONCLUSIONS

- Among patients with moderate-to-severe psoriasis treated with tildrakizumab 100 or 200 mg at weeks 0, 4, then every 12 weeks, those who achieved week-28 PASI≥50 and continued on the same dose had sustained or improved efficacy from week 28 through week 52.
- The majority patients who achieved week-28 PASI≥75 or PASI≥90 maintained PASI≥75 or PASI≥90 at week 52.
- More than half of partial responders (PASI 50-74) at week 28 eventually achieved PASI≥75 and at least 1 in 5 achieved PASI≥90 at week 52.

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DISCLOSURES

Drs. Elewski, Menter, Crowley, Tyring and Gordon were investigators of the two phase-3 clinical trials for tildrakizumab (reSURFACE 1 and reSURFACE 2). Drs. Zhao, Lowry, Rozzo and Mendelsohn and Mr. Parno are employees of Sun Pharmaceutical Industries.