Tildrakizumab efficacy by metabolic syndrome status in psoriasis: Post hoc analysis of 3-year data from the phase 3 reSURFACE 1 and reSURFACE 2 studies

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BACKGROUND

- Metabolic syndrome (MetS) is a combination of common cardiometabolic abnormalities associated with an increased risk of cardiovascular disease and diabetes[1] and has higher prevalence in patients with moderate to severe psoriasis compared with the overall population[2-4]
- In patients with psoriasis treated with anti-tumor necrosis factor or anti–interleukin (IL)-17 agents, MetS may reduce the absolute Psoriasis Area and Severity Index (PASI) response and long-term drug survival[5-7]
- Tildrakizumab—a high-affinity, humanized, immunoglobulin G1κ, anti–IL-23p19 monoclonal antibody—is approved in the US, Europe, Australia, and Japan for treatment of plaque psoriasis
  - The efficacy of tildrakizumab was demonstrated in 2 phase 3 clinical studies, reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754)[8]
  - Treatment with tildrakizumab significantly increased the proportion of patients with ≥75%, ≥90%, and 100% improvement in PASI scores (PASI 75, PASI 90, and PASI 100, respectively) and Physician's Global Assessment 0/1 response rates compared with placebo[8]
- Previously, we evaluated tildrakizumab efficacy in patients meeting National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) criteria[9] for MetS (including diminished high-density lipoprotein cholesterol and elevated blood pressure, body mass index [BMI], triglycerides, and glucose) after 1 year of treatment
  - MetS has a minimal effect on tildrakizumab efficacy[10] and safety[11] and there are no increases in cardiac events or worsening of diabetes in patients with MetS following 1 year of tildrakizumab treatment[12]

OBJECTIVE

- To update the efficacy of tildrakizumab in psoriasis patients with vs without MetS with up to 3 years (148 weeks) of follow-up in reSURFACE 1 and reSURFACE 2

METHODS

Study design

- This post hoc analysis of the reSURFACE 1 and reSURFACE 2 phase 3, double-blind, randomized controlled studies included patients aged ≥18 years with moderate to severe chronic plaque psoriasis; full trial designs were published previously[8]
- Tildrakizumab 100 or 200 mg was administered at week 0, week 4, and every 12 weeks thereafter up to week 220/244 (reSURFACE 1/2)
  - Additional patients in reSURFACE 2 received etanercept twice weekly to week 12 and once weekly to week 28

Table 1. Clinical definition of metabolic syndrome at baseline

Risk factor	Defining level
BMI[a]	>30 kg/m^2
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥110 mg/dL

[a]Diagnosis of metabolic syndrome was made when ≥3 risk factors were present. BMI was used as a surrogate for waist circumference.
BMI, body mass index; HDL, high-density lipoprotein.

Evaluations and assessments

- At baseline, metabolic syndrome was defined as the presence of ≥3 risk factors per the NCEP-ATP III criteria (**Table 1**)[9]
- Data were collected from patients who continuously received tildrakizumab 100 or 200 mg
- Efficacy of tildrakizumab, stratified by MetS status, was determined by the proportion of patients achieving PASI 75/90/100 in each visit, and absolute and percent changes in median PASI scores from baseline to week 148
- Missing data were imputed as nonresponse for PASI response rates and using last observation carried forward methodology for PASI scores

RESULTS

- Of patients who continuously received tildrakizumab 100 (n = 124) and 200 mg (n = 147), 26 (21%) and 34 (23%), respectively had MetS in reSURFACE 1
- In reSURFACE 2, 44 (21%) and 30 (19%) patients continuously receiving tildrakizumab 100 (n = 214) and 200 mg (n = 160), respectively, had MetS
- Baseline demographic and disease characteristics were similar between groups; patients with MetS had numerically higher mean baseline weight, BMI, and prevalence of cardiovascular disease and diabetes mellitus vs patients with no MetS (**Table 2**)

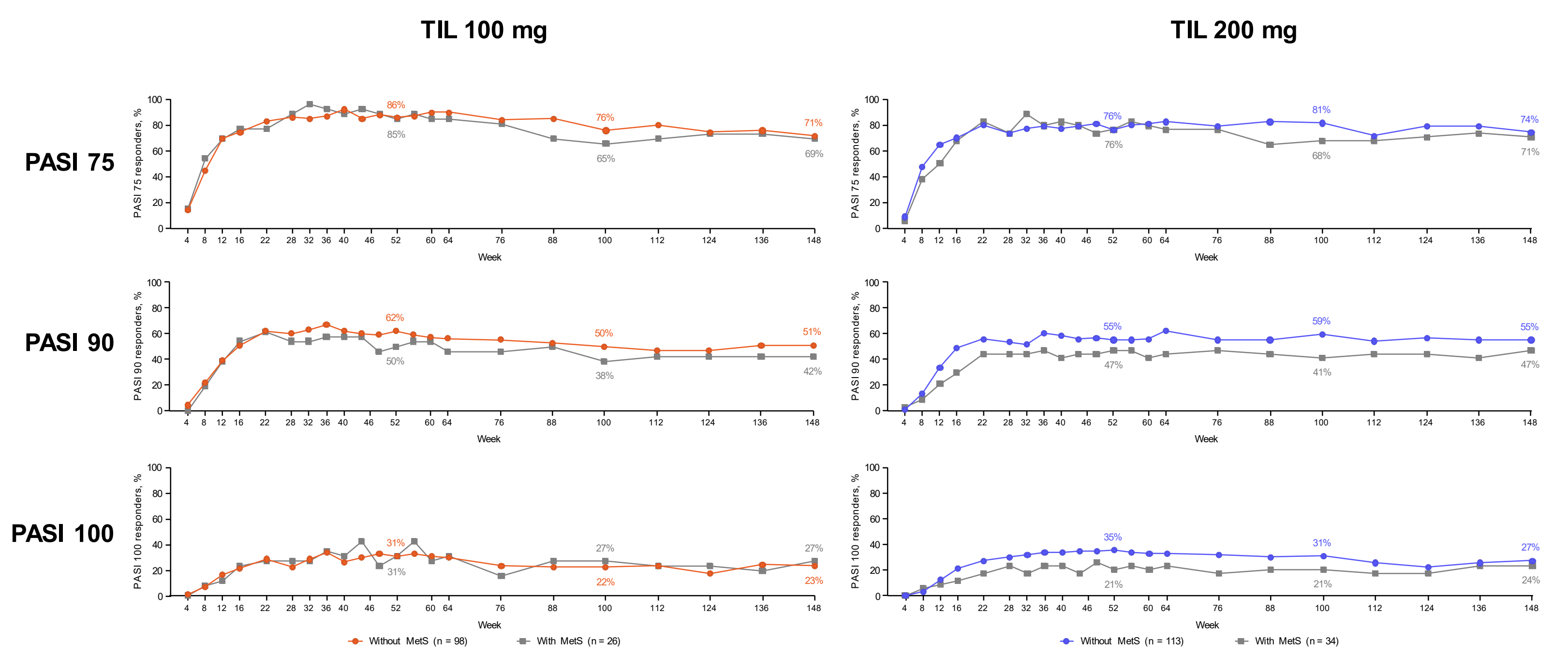
Table 2. Patient demographics and disease characteristics by trial, treatment group and metabolic syndrome status

	reSURFACE 1				reSURFACE 2			
	TIL 100 mg		TIL 200 mg		TIL 100 mg		TIL 200 mg	
	Without MetS (n = 98)	With MetS (n = 26)	Without MetS (n = 113)	With MetS (n = 34)	Without MetS (n = 170)	With MetS (n = 44)	Without MetS (n = 130)	With MetS (n = 30)
Age, y	46.1 ± 14.0	49.1 ± 12.7	46.2 ± 13.5	50.7 ± 11.0	43.2 ± 13.2	45.9 ± 12.7	44.6 ± 13.2	48.7 ± 12.4
Sex, male, n (%)	65 (66.3)	18 (69.2)	80 (70.8)	19 (55.9)	120 (70.6)	34 (77.3)	82 (63.1)	23 (76.7)
Race, White, n (%)	64 (65.3)	21 (80.8)	67 (59.3)	27 (79.4)	156 (91.8)	41 (93.2)	118 (90.8)	29 (96.7)
Weight at baseline, kg	80.8 ± 18.1	106.0 ± 29.6	81.7 ± 17.5	112.0 ± 32.2	82.6 ± 17.0	106.9 ± 21.7	82.0 ± 17.8	108.2 ± 17.6
BMI, kg/m^2	27.9 ± 6.0	35.6 ± 8.5	28.3 ± 5.8	38.5 ± 8.3	27.5 ± 5.3[a]	35.6 ± 6.1	27.3 ± 5.3	37.6 ± 9.8
Body surface area, %	29.4 ± 16.7	32.2 ± 16.6	32.6 ± 19.5	30.1 ± 19.4	34.1 ± 18.4	30.3 ± 18.9	31.4 ± 17.2	27.6 ± 12.9
Disease duration, y	17.2 ± 12.6	16.2 ± 12.3	16.6 ± 11.5	16.7 ± 12.9	16.1 ± 10.6	15.2 ± 11.2	18.0 ± 13.5	20.1 ± 14.8
Baseline PASI score	19.9 ± 7.1	20.5 ± 7.1	21.5 ± 9.3	20.6 ± 9.7	19.6 ± 6.9	20.8 ± 8.8	19.5 ± 7.2	19.2 ± 6.3
Baseline PGA score	3.3 ± 0.6	3.4 ± 0.6	3.4 ± 0.6	3.5 ± 0.6	3.3 ± 0.5	3.4 ± 0.6	3.3 ± 0.6[b]	3.4 ± 0.6
CV disorders, n (%)	14 (14.3)	17 (65.4)	31 (27.4)	16 (47.1)	29 (17.1)	17 (38.6)	27 (20.8)	16 (53.3)
Diabetes, n (%)	8 (8.2)	8 (30.8)	11 (9.7)	8 (23.5)	5 (2.9)	7 (15.9)	11 (8.5)	7 (23.3)
Psoriatic arthritis, n (%)	16 (16.3)	5 (19.2)	19 (16.8)	9 (26.5)	24 (14.1)	11 (25.0)	17 (13.1)	4 (13.3)
Response to ≥1 traditional systemic medicine, n (%)[c]	22 (44.9)	5 (71.4)	40 (65.6)	8 (57.1)	111 (65.3)	24 (54.6)	80 (61.5)	17 (56.7)
Prior exposure to biologic therapy for psoriasis, n (%)	16 (16.3)	8 (30.8)	20 (17.7)	7 (20.6)	23 (13.5)	5 (11.4)	17 (13.1)	7 (23.3)

Data provided as mean ± standard deviation unless otherwise indicated.
[a]n = 169; [b]n = 129; [c]Data not available for the missing patients in each group.
BMI, body mass index; CV, cardiovascular; MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; TIL, tildrakizumab.

- In reSURFACE 1, a total of 2 patients with MetS (both receiving tildrakizumab 100 mg [7.7%]) and 17 patients without MetS (n = 11 [11.2%] receiving tildrakizumab 100 mg and n = 6 [5.4%] receiving tildrakizumab 200 mg) did not complete the study through week 148
- In reSURFACE 2, 12 patients with MetS (n = 7 [15.9%] receiving tildrakizumab 100 and n = 5 [16.6%] receiving tildrakizumab 200 mg) and 37 patients without MetS (n = 21 [12.6%] receiving tildrakizumab 100 mg and n = 16 [12.4%] receiving tildrakizumab 200 mg) did not complete the study through week 148
  - The most frequent reason for discontinuation was withdrawal by patient
  - Two patients with MetS receiving tildrakizumab 200 mg withdrew due to an adverse event in reSURFACE 2
- In reSURFACE 1, the proportion of patients receiving tildrakizumab 100 mg and 200 mg who achieved PASI 75/90/100 were comparable between patients with vs without MetS at week 52 and remained comparable at weeks 100 and 148 (**Figure 1**)

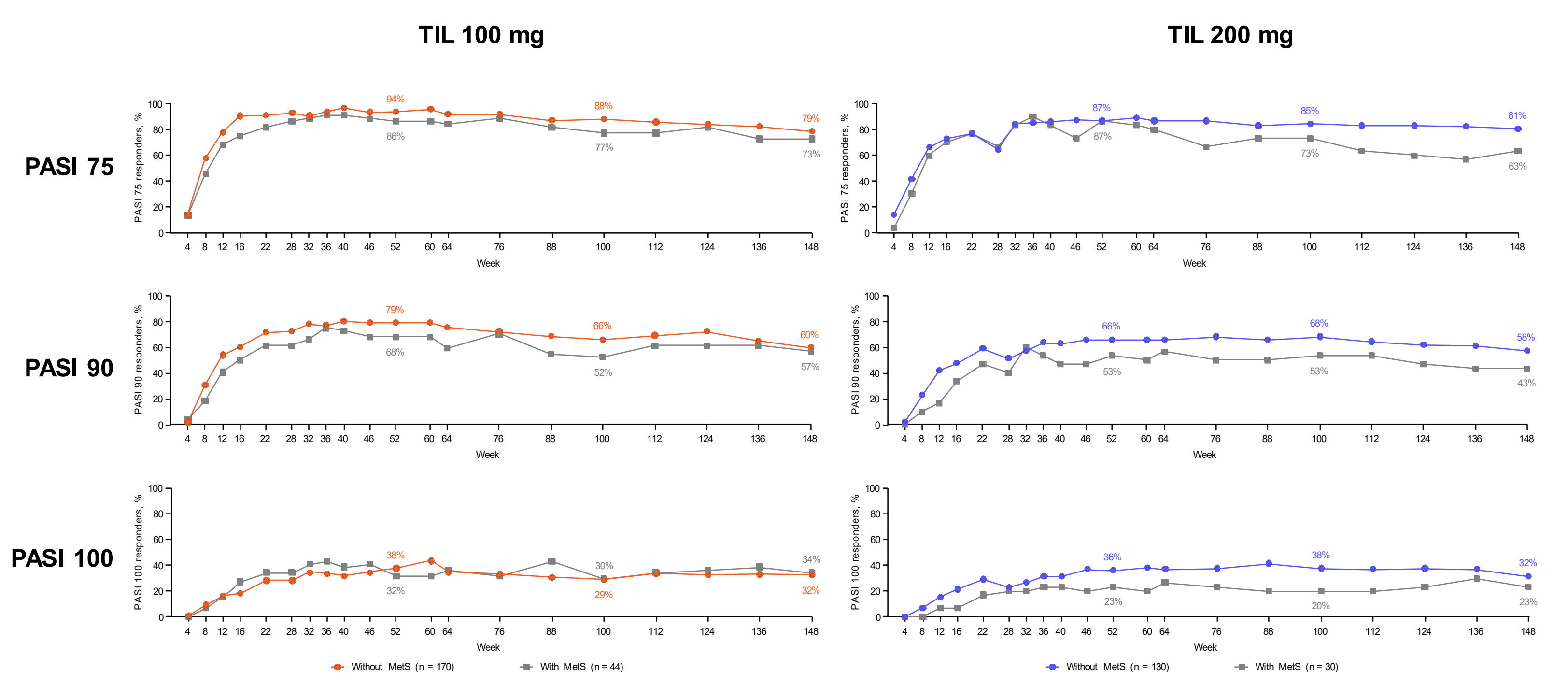
Figure 1. Percentage of PASI 75, PASI 90, and PASI 100 responders receiving continuous tildrakizumab 100 mg (left) and 200 mg (right) over time by baseline metabolic syndrome status in reSURFACE 1



MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

- In reSURFACE 2, the proportion of patients receiving tildrakizumab 100 mg who achieved PASI 75/90/100 were comparable between patients with vs without MetS at week 52 and remained comparable at weeks 100 and 148 (**Figure 2**)

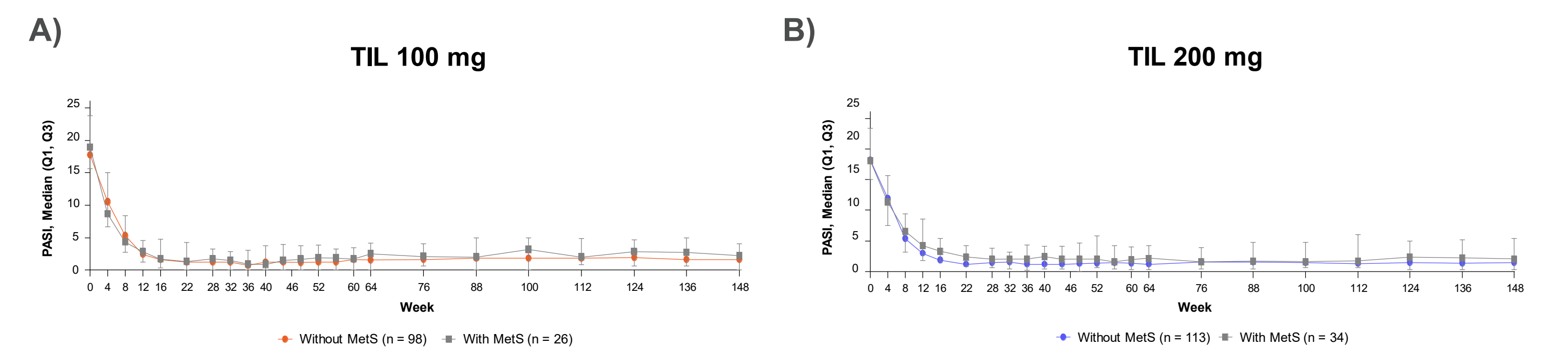
Figure 2. Percentage of PASI 75, PASI 90 and PASI 100 responders receiving continuous tildrakizumab 100 mg (left) and 200 mg (right) over time by baseline metabolic syndrome status in reSURFACE 2



MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

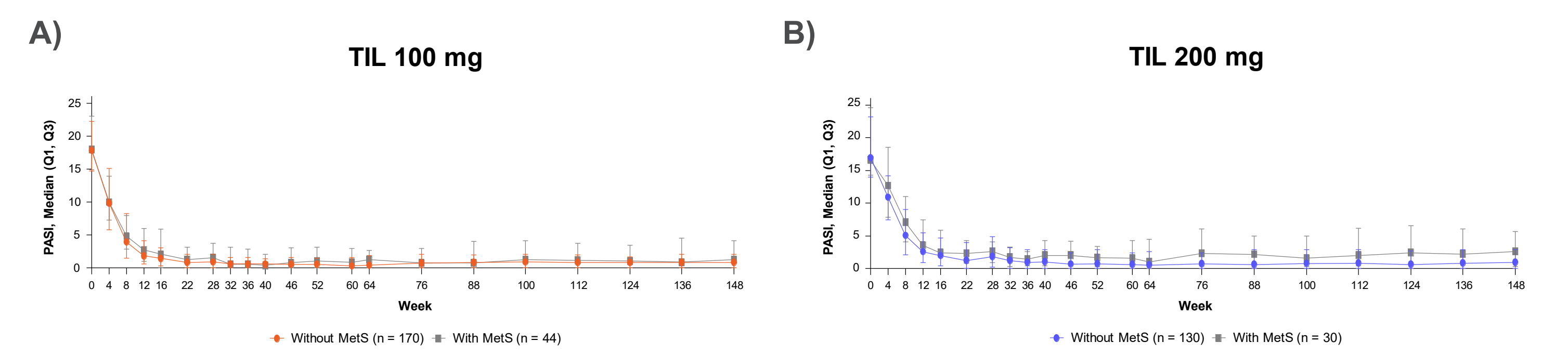
- In patients receiving tildrakizumab 200 mg in reSURFACE 2, those with MetS had numerically lower PASI 75 response rates at week 100 and week 148 relative to patients without MetS; PASI 90 and PASI 100 response rates at weeks 52, 100, and 148 were also lower in patients with MetS vs without MetS (**Figure 2**)
- At week 148, in both reSURFACE 1 (**Figure 3**) and reSURFACE 2 (**Figure 4**), overall PASI scores decreased from baseline
  - In reSURFACE 1, the percentage decrease in median PASI scores in patients with vs without MetS was 89% vs 92% (tildrakizumab 100 mg) and 88% vs 91% (tildrakizumab 200 mg), respectively
  - In reSURFACE 2, the percentage decrease in median PASI scores in patients with vs without MetS was 93% vs 96% (tildrakizumab 100 mg) and 84% vs 94% (tildrakizumab 200 mg), respectively

Figure 3. Median absolute PASI scores over time in patients receiving **A)** tildrakizumab 100 mg and **B)** tildrakizumab 200 mg, stratified by metabolic syndrome status in reSURFACE 1



MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

Figure 4. Median absolute PASI scores over time in patients receiving **A)** tildrakizumab 100 mg and **B)** tildrakizumab 200 mg, stratified by metabolic syndrome status in reSURFACE 2



MetS, metabolic syndrome; PASI, Psoriasis Area and Severity Index; TIL, tildrakizumab.

CONCLUSIONS

- The efficacy of both tildrakizumab 100- and 200-mg doses was maintained over 148 weeks of the reSURFACE 1 and 2 studies without evidence of reduced drug survival in patients with MetS and was comparable to that of patients without MetS

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