

Original

Real-World 52-Week Effectiveness of Tildrakizumab for Psoriasis: Analysis Stratified by Age, Disease Duration, and Body Mass Index

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Background: Age, disease duration, and body mass index (BMI) influence the real-world effectiveness of tildrakizumab for psoriasis. We evaluated the 52-week real-world effectiveness of tildrakizumab for psoriasis patients stratified by age (<65 versus ≥65 years), disease duration (≤2 vs >2 years), and BMI (<25 versus ≥25 kg/m²).

Methods: This study included 55 patients with psoriasis who were treated with tildrakizumab 100 mg. Clinical outcomes and laboratory indices were assessed during the 52-week treatment period.

Results: Psoriasis area and severity index (PASI) decreased throughout the 52-week treatment period in all patients. At week 52, PASI 90 and PASI 100 rates were higher in patients aged <65 years, those with a disease duration of ≤2 years, and those with a BMI of <25 kg/m² than in their respective comparison groups. PASI 90 rates were 62.5% versus 35.7%, 100% versus 36.8%, and 60.0% versus 33.3%, respectively. At week 52, the rate of an absolute PASI ≤1 was higher in patients aged <65 years, those with a disease duration ≤2 years, and those with a BMI ≥25 kg/m². The systemic immune-inflammation index, calculated as neutrophil × platelet/lymphocyte count, was significantly lower at week 52 than at baseline. Metabolic laboratory indices did not change significantly during the 52-week treatment period.

Conclusions: Tildrakizumab showed sustained real-world effectiveness for psoriasis for 52 weeks across patient subgroups stratified by age, disease duration, and BMI.

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Introduction

Psoriasis is a chronic inflammatory skin disease that affects patient quality of life^{1–3}. The interleukin (IL)-23/IL-17 axis is central to its pathogenesis, and biological agents that target this axis are important options for long-term treatment⁴. Tildrakizumab is a humanized IgG 1κ monoclonal antibody that selectively binds IL-23p19^{5,6}. Previous clinical trials reported that tildrakizumab was effective and well tolerated in patients with moderate-to-severe plaque psoriasis⁵. Real-world studies have further supported its effectiveness and safety throughout 52 weeks in routine clinical practice^{7,8}.

However, several clinically important questions remain. Psoriasis is a heterogeneous disease, and treatment outcomes vary according to patient background. Unfortunately, few long-term real-world studies have examined the effects of age, disease duration, and body mass index (BMI). Furthermore, changes in laboratory indices during tildrakizumab treatment have not been investigated in detail in Japanese patients with psoriasis.

This study evaluated the 52-week real-world effectiveness of tildrakizumab for psoriasis patients stratified by age (≥65 versus <65 years), disease duration (≤2 versus >2 years), and BMI (≥25 versus <25 kg/m²). We also ex-

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amined changes in inflammatory and metabolic indices during the 52-week tildrakizumab treatment.

Materials and Methods

Study Design and Data Collection

This retrospective single-center study was conducted in Japan between September 2021 and March 2026. Patients were eligible if they were at least 15 years old and had moderate-to-severe psoriasis diagnosed based on clinical findings. All patients received tildrakizumab 100 mg by subcutaneous injection at weeks 0 and 4, and every 12 weeks thereafter. The Institutional Review Board of Nippon Medical School Chiba Hokusoh Hospital approved the study (ethics approval number: 937). All procedures complied with the principles of the 2004 Declaration of Helsinki. Informed consent was obtained from all the patients involved in the study.

The baseline variables comprised age, BMI, sex recorded as male or female, psoriasis duration, and arthritis status. We additionally documented diabetes, cardiovascular disease, current smoking, and prior systemic treatment with apremilast, deucravacitinib, or biologic agents.

Clinical and laboratory assessments included psoriasis area and severity index (PASI) and static physician's global assessment (sPGA) scores. Metabolic laboratory indices, including hemoglobin A1c (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), and uric acid (UA), were recorded at weeks 0, 16, and 52, when available in routine clinical practice. Additionally, C-reactive protein (CRP) level, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) were calculated. Inflammatory markers, such as systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI), were also evaluated. SII was calculated as (platelet count $\times$ neutrophil count) / lymphocyte count, and SIRI was calculated as (neutrophil count $\times$ monocyte count) / lymphocyte count⁹⁻¹³.

Inclusion and Exclusion Criteria

The study sample comprised patients with moderate-to-severe plaque psoriasis, psoriatic arthritis, or erythrodermic psoriasis. Clinical scores obtained before earlier systemic therapy were unavailable in some cases. To prevent duplicate observations, we omitted data from patients who discontinued and later restarted tildrakizumab. Additional exclusion criteria were severe cardiovascular disease (myocardial infarction, stroke, or heart failure), seri-

ous infection including tuberculosis, previous hypersensitivity to tildrakizumab, and pregnancy or breastfeeding.

Assessment of Treatment Effectiveness

PASI and sPGA were recorded at baseline and at weeks 4, 16, 28, 40, and 52. At each follow-up, we calculated percentage change in PASI relative to baseline and determined the proportions of patients achieving PASI 75, PASI 90, and PASI 100, defined as improvements of $\geq 75\%$, $\geq 90\%$, and 100% , respectively. We also determined the proportions with absolute PASI values of ≤ 3 , ≤ 2 , and ≤ 1 . Among patients with a baseline sPGA of ≥ 2 , sPGA 0/1 required a score of 0 or 1 together with an improvement of ≥ 2 points. Outcomes were summarized separately in relation to BMI (<25 versus ≥ 25 kg/m²), age (<65 versus ≥ 65 years), and disease duration, namely, short disease duration (SDD, ≤ 2 years) vs long disease duration (LDD, >2 years). Disease duration was defined as the period from psoriasis onset to the start of tildrakizumab. The LDD group was not defined as a delayed-intervention group because patients with LDD could have received prior systemic therapies, including biologics, before tildrakizumab.

Statistical Methods

Normally distributed variables are summarized as means with standard deviations and nonparametric variables are reported as medians with interquartile ranges. Differences between individual time points were analyzed using Friedman's test and Bonferroni's post-hoc test. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical School, Saitama, Japan).

Results

Baseline Characteristics

Of the 55 patients, 21 were younger than 65 years and 34 were 65 years or older. Among those with available BMI data, BMI was <25 kg/m² in 24 patients and ≥ 25 kg/m² in 26 patients (Table 1).

PASI Changes through Week 52, by Age

The younger group entered treatment with a higher mean PASI than the older group (Figure 1). In both groups, the mean PASI score decreased from week 0 to 52.

Percentage Reduction in PASI through Week 52, by Age

PASI improved over time in both age groups, although

Table 1 Baseline characteristics of psoriasis patients stratified by age, disease duration, and BMI

Characteristic	Age < 65 years (<i>n</i> = 21)	Age ≥ 65 years (<i>n</i> = 34)	Disease duration ≤ 2 years (<i>n</i> = 8)	Disease duration > 2 years (<i>n</i> = 45)	BMI < 25 kg/m ² (<i>n</i> = 24)	BMI ≥ 25 kg/m ² (<i>n</i> = 26)	Total patients (<i>n</i> = 55)
Male sex	17 (81.0)	20 (58.8)	6 (75.0)	30 (66.7)	13 (54.2)	21 (80.8)	37 (67.3)
Age (years), median [IQR]	49.0 [38.0-59.0]	75.5 [72.0-79.8]	62.5 [49.5-77.5]	69.0 [54.0-77.0]	72.0 [58.5-77.3]	66.0 [49.3-75.8]	69.0 [53.0-77.5]
BMI (kg/m ²), median [IQR]	25.9 [23.8-29.2]	24.6 [20.9-25.7]	24.4 [21.9-30.5]	25.1 [22.5-27.8]	21.5 [19.5-23.0]	28.0 [25.4-29.6]	25.1 [22.5-28.1]
Disease duration (years), median [IQR]	7.0 [3.0-15.0]	9.0 [4.0-20.5]	1.0 [1.0-2.0]	10.0 [5.0-21.0]	10.0 [4.8-19.0]	6.5 [3.0-10.8]	8.0 [3.0-20.0]
Type of psoriasis							
Plaque psoriasis	20 (95.2)	31 (91.2)	8 (100.0)	41 (91.1)	21 (87.5)	26 (100.0)	51 (92.7)
Psoriatic arthritis	0 (0.0)	1 (2.9)	0 (0.0)	1 (2.2)	1 (4.2)	0 (0.0)	1 (1.8)
Erythrodermic psoriasis	0 (0.0)	1 (2.9)	0 (0.0)	1 (2.2)	1 (4.2)	0 (0.0)	1 (1.8)
Current smoker	8 (38.1)	10 (29.4)	1 (12.5)	16 (35.6)	10 (41.7)	7 (26.9)	18 (32.7)
Diabetes mellitus	3 (14.3)	8 (23.5)	1 (12.5)	9 (20.0)	4 (16.7)	5 (19.2)	11 (20.0)
Pretreatment							
Topical corticosteroid and/or vitamin D3 alone	11 (52.4)	12 (35.3)	5 (62.5)	16 (35.6)	13 (54.2)	6 (23.1)	23 (41.8)
Apremilast	5 (23.8)	8 (23.5)	3 (37.5)	10 (22.2)	4 (16.7)	8 (30.8)	13 (23.6)
Deucravacitinib	9 (42.9)	11 (32.6)	2 (25.0)	18 (40.0)	5 (20.8)	15 (47.7)	20 (36.4)
Adalimumab	1 (4.8)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	1 (3.8)	1 (1.8)
Bimekizumab	4 (19.0)	0 (0.0)	1 (12.5)	3 (6.7)	1 (4.2)	3 (11.5)	4 (7.3)
Brodalumab	0 (0.0)	1 (2.9)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	1 (1.8)
Infliximab	0 (0.0)	1 (2.9)	0 (0.0)	1 (2.2)	1 (4.2)	0 (0.0)	1 (1.8)
Ixekizumab	3 (14.3)	1 (2.9)	0 (0.0)	4 (8.9)	3 (12.5)	1 (3.8)	4 (7.3)
Guselkumab	0 (0.0)	4 (11.8)	0 (0.0)	4 (8.9)	1 (4.2)	3 (11.5)	4 (7.3)
Risankizumab	0 (0.0)	4 (11.8)	0 (0.0)	4 (8.9)	1 (4.2)	2 (7.7)	4 (7.3)
Secukinumab	0 (0.0)	2 (5.9)	0 (0.0)	2 (4.4)	0 (0.0)	2 (7.7)	2 (3.6)
Ustekinumab	0 (0.0)	3 (8.8)	0 (0.0)	3 (6.7)	2 (8.3)	1 (3.8)	3 (5.5)
Clinical indices							
sPGA							
Mild (score of 2)	1 (4.8)	7 (20.6)	0 (0.0)	6 (13.3)	2 (8.3)	4 (15.4)	8 (14.5)
Moderate (score of 3)	13 (61.9)	21 (61.8)	5 (62.5)	29 (64.4)	14 (58.3)	17 (65.4)	34 (61.8)
Severe (score of 4)	7 (33.3)	6 (17.6)	3 (37.5)	10 (22.2)	8 (33.3)	5 (19.2)	13 (23.6)
PASI, mean ± SD	15.5 ± 11.7	10.9 ± 8.2	17.0 ± 10.4	12.4 ± 9.7	15.1 ± 9.9	11.7 ± 10.0	12.7 ± 9.9

Data are presented as *n* (%) unless otherwise indicated. Counts in the SDD/LDD or BMI-stratified columns may not sum to the total because disease duration or BMI data were missing in some patients. BMI, body mass index; IQR, interquartile range; SD, standard deviation; PASI, psoriasis area and severity index; sPGA, static physician's global assessment.

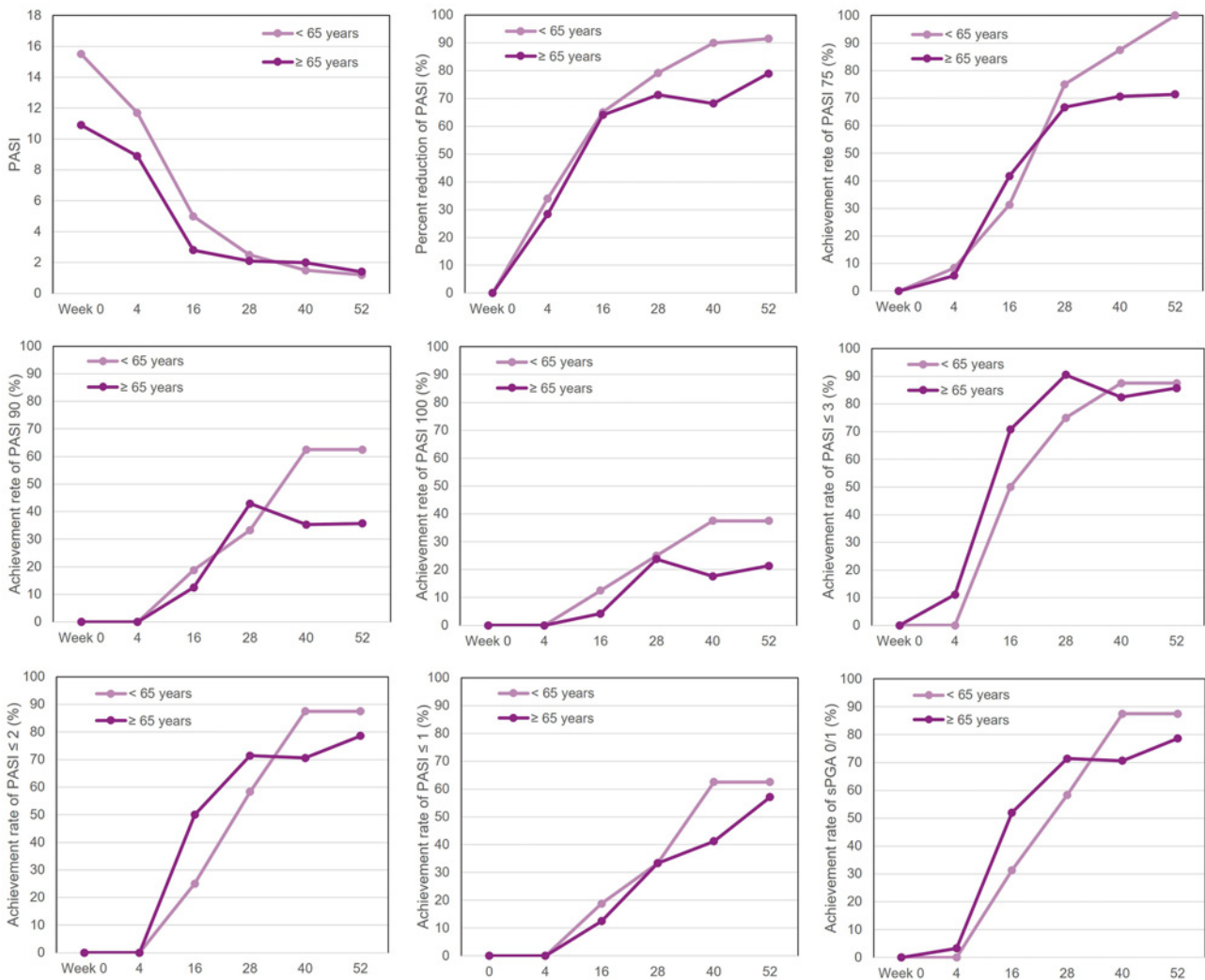


Figure 1 Change in psoriasis area and severity index (PASI), percent reduction of PASI, and rates of PASI 75, PASI 90, PASI 100, absolute PASI ≤ 3 , absolute PASI ≤ 2 , absolute PASI ≤ 1 , and static physician's global assessment (sPGA) 0/1 in psoriasis patients stratified by age during 52 weeks of tildrakizumab treatment

The graphs show means for PASI, percent reduction of PASI, and achievement rates for individual endpoints in patients aged <65 years and ≥ 65 years.

improvement slowed after week 28 among patients aged ≥ 65 years. Mean reductions at weeks 16, 28, and 52 were 65.1%, 79.2%, and 91.5% in patients aged <65 years and 64.1%, 71.3%, and 79.0% in those aged ≥ 65 years, respectively (**Figure 1**).

PASI Response, Absolute PASI, and sPGA Outcomes, by Age

Among patients aged <65 years, PASI 75 rose through week 52. In those aged ≥ 65 years, it increased through week 28 and then changed little; from week 28 onward, rates were higher in the younger group (**Figure 1**). PASI 90 and PASI 100 increased through week 40 and then remained stable in the younger group, whereas both reached their highest rates at week 28 and declined slightly thereafter in the older group. From week 40,

PASI 90 and PASI 100 were more frequent in patients aged <65 years.

Absolute PASI ≤ 3 , absolute PASI ≤ 2 , and sPGA 0/1 were more frequent in the older group through week 28, after which the younger group had higher rates. At week 52, rates in patients aged <65 versus ≥ 65 years were 100% versus 71.4% for PASI 75, 62.5% versus 35.7% for PASI 90, 37.5% versus 21.4% for PASI 100, 87.5% versus 85.7% for absolute PASI ≤ 3 , 87.5% versus 78.6% for absolute PASI ≤ 2 , 62.5% versus 57.1% for absolute PASI ≤ 1 , and 87.5% versus 78.6% for sPGA 0/1.

PASI Changes through Week 52, by Disease Duration

Mean PASI at baseline was higher in the SDD group than in the LDD group (**Figure 2**). In both groups, the mean PASI score decreased from week 0 to 52.

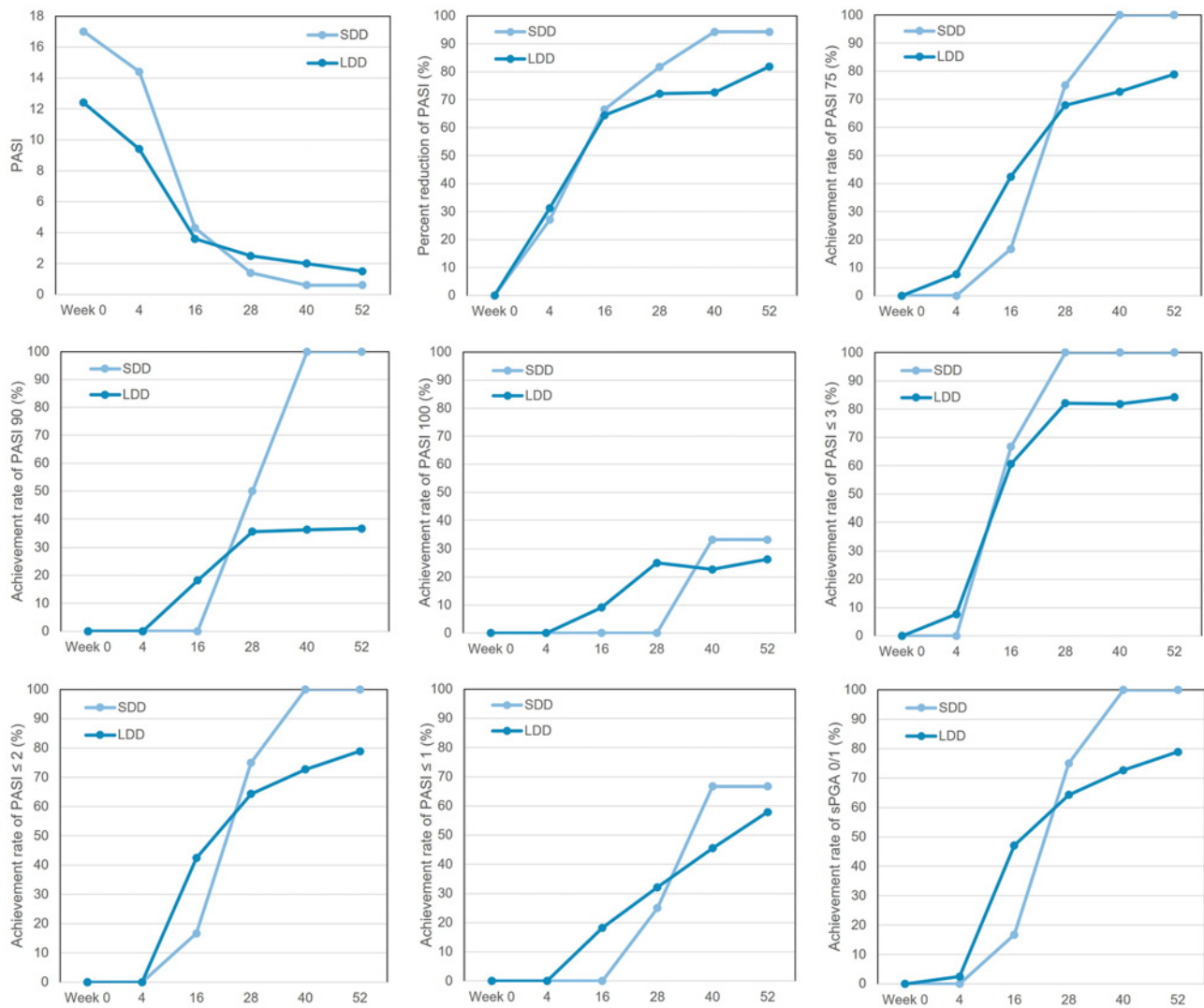


Figure 2 Change in psoriasis area and severity index (PASI), percent reduction of PASI, and rates of PASI 75, PASI 90, PASI 100, absolute PASI ≤ 3 , absolute PASI ≤ 2 , absolute PASI ≤ 1 , and static physician's global assessment (sPGA) 0/1 in psoriasis patients stratified by disease duration during 52 weeks of tildrakizumab treatment

The graphs show means for PASI, percent reduction of PASI, and achievement rates for individual endpoints in patients with short disease duration (SDD [≤ 2 years]) and long disease duration (LDD [> 2 years]).

Percentage Reduction in PASI through Week 52, by Disease Duration

Mean percentage reduction in PASI continued to increase until week 52 in the SDD group but slowed after week 28 in those with LDD. The values were 66.6%, 81.7%, and 94.3% in patients with SDD and 64.5%, 72.2%, and 81.9% in patients with LDD at weeks 16, 28, and 52, respectively (Figure 2).

PASI Response, Absolute PASI, and sPGA Outcomes, by Disease Duration

In the SDD group, PASI 75 and PASI 90 reached 100% at week 40, and absolute PASI ≤ 3 reached 100% by week 28; all 3 endpoints remained at these levels thereafter (Figure 2). In the LDD group, PASI 75, PASI 90, and ab-

solute PASI ≤ 3 continued to rise through week 52, but their rates after week 28 remained below those in the SDD group.

Patterns for PASI 100 and absolute PASI ≤ 1 differed between the groups. No patient with SDD achieved PASI 100 through week 28. The rate rose until week 40 and then remained unchanged. In the LDD group, PASI 100 increased until week 28 and subsequently stabilized; rates were lower than those for the SDD group after week 40. Absolute PASI ≤ 1 was not observed in the SDD group through week 16, but the rate increased to a maximum at week 40 and then remained stable. In the LDD group, this endpoint rose through week 52, although rates after week 40 remained below those in SDD.

At week 52, SDD versus LDD rates were 100% versus

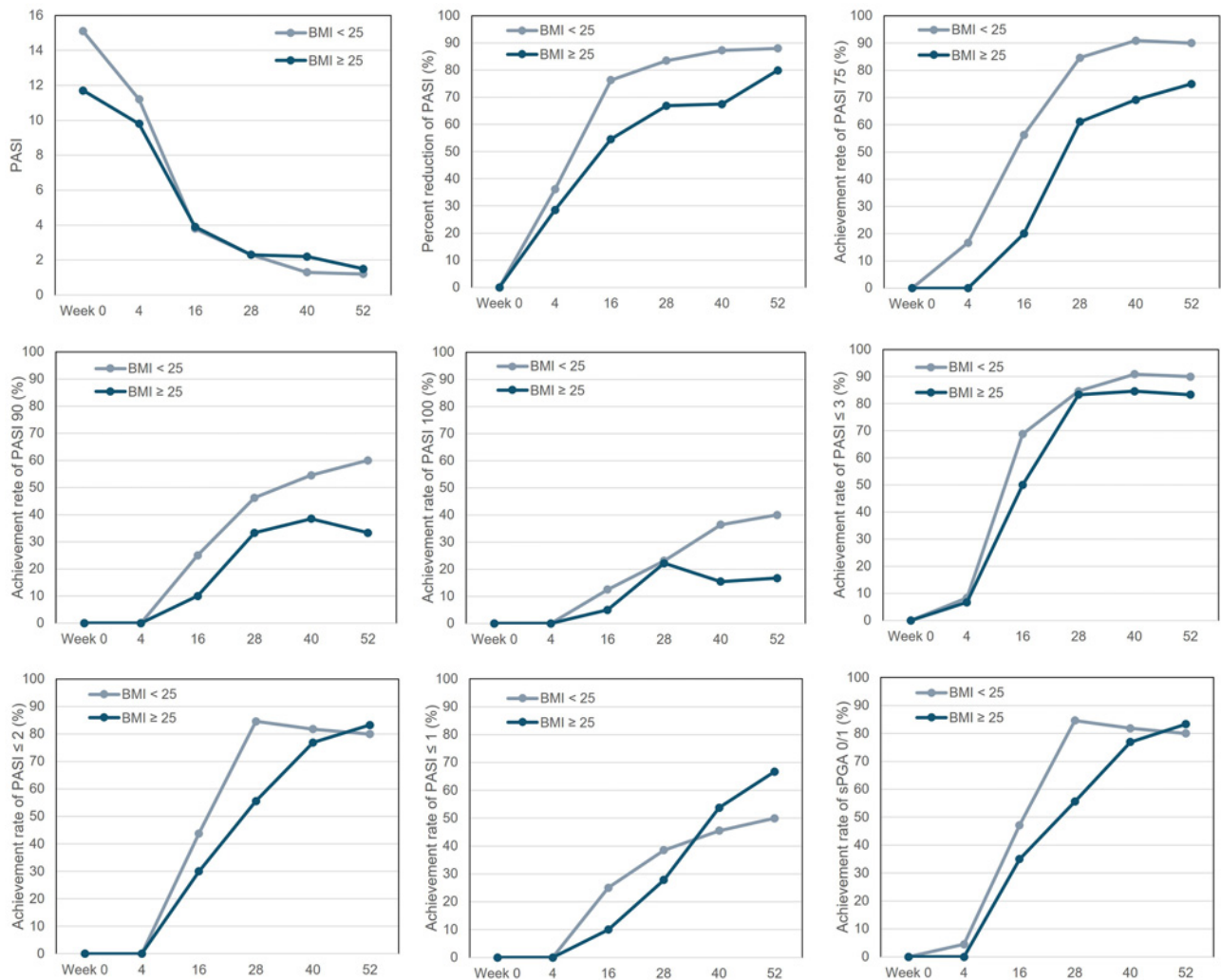


Figure 3 Change in psoriasis area and severity index (PASI), percent reduction of PASI, and rates of PASI 75, PASI 90, PASI 100, absolute PASI ≤3, absolute PASI ≤2, absolute PASI ≤1, and static physician's global assessment (sPGA) 0/1 in psoriasis patients stratified by body mass index (BMI) during 52 weeks of tildrakizumab treatment

The graphs show PASI, percent reduction of PASI, and achievement rates for individual endpoints in patients with BMI values of <25 and ≥25 kg/m².

78.9% for PASI 75, 100% versus 36.8% for PASI 90, 33.3% versus 26.3% for PASI 100, 100% versus 84.2% for absolute PASI ≤3, 100% versus 78.9% for absolute PASI ≤2, 66.7% versus 57.9% for absolute PASI ≤1, and 100% versus 78.9% for sPGA 0/1.

PASI Changes through Week 52, by BMI

The BMI <25 kg/m² group had a higher mean PASI at baseline than did the BMI ≥25 kg/m² group (Figure 3). In both groups, the mean PASI score decreased from week 0 to 52.

Percentage Reduction in PASI through Week 52, by BMI

PASI improvement increased in both BMI groups and was generally greater with BMI <25 kg/m² (Figure 3).

Mean reductions at weeks 16, 28, and 52 were 76.3%, 83.5%, and 88.0% for a BMI <25 kg/m² and 54.6%, 66.9%, and 79.9% for a BMI ≥25 kg/m², respectively.

PASI Response, Absolute PASI, and sPGA Outcomes, by BMI

Among patients with a BMI <25 kg/m², PASI 75, PASI 90, and absolute PASI ≤3 continued to rise through week 40 or 52 (Figure 3). Among those with a BMI ≥25 kg/m², PASI 75 increased through week 52, whereas PASI 90 and absolute PASI ≤3 changed little after week 28; these rates were generally lower than those in the BMI <25 kg/m² group.

At week 52, rates in the BMI <25 versus BMI ≥25 kg/m² groups were 90.0% versus 75.0% for PASI 75, 60.0% versus 33.3% for PASI 90, 90.0% versus 83.3% for abso-

Table 2 Inflammatory and metabolic laboratory indexes during 52-week treatment with tildrakizumab

Parameter	n (week 0/week 16/week 52)	Week 0, median [IQR]	Week 16, median [IQR]	Week 52, median [IQR]	Significance
Inflammatory laboratory indexes					
NLR	50/37/18	2.12 [1.43–3.28]	1.94 [1.52–2.44]	2.02 [1.33–2.67]	None
MLR	50/38/18	0.23 [0.16–0.30]	0.22 [0.17–0.29]	0.23 [0.19–0.38]	None
PLR	46/38/18	136.59 [102.81–176.28]	128.47 [108.05–159.82]	114.70 [68.06–142.67]	None
CRP	50/37/16	0.10 [0.06–0.27]	0.08 [0.04–0.23]	0.13 [0.06–0.32]	None
SII	50/37/18	493.23 [323.11–818.53]	424.67 [316.92–627.76]	326.02 [98.67–515.18]	Week 0 vs week 52, $p = 0.014$
SIRI	49/37/18	0.86 [0.54–1.42]	0.66 [0.58–0.89]	0.86 [0.43–1.44]	None
Metabolic laboratory indexes					
HbA1c	32/23/9	5.90 [5.60–6.23]	5.80 [5.65–6.15]	5.80 [5.60–6.10]	None
TC	37/26/11	205.0 [164.0–228.0]	211.5 [153.5–231.5]	213.0 [204.0–234.5]	None
LDL-C	35/25/10	120.0 [91.5–142.0]	124.0 [85.0–142.0]	134.5 [100.0–154.0]	None
TG	37/27/11	123.0 [95.0–153.0]	140.0 [112.5–222.0]	118.0 [94.0–139.5]	None
UA	36/26/11	6.00 [5.08–6.85]	6.30 [5.50–6.75]	5.40 [4.60–6.70]	None

Data are presented as median [IQR]. Differences across timepoints were assessed by the Friedman test with Bonferroni's post-hoc test. NLR was calculated as neutrophil count/lymphocyte count. MLR was calculated as monocyte count/lymphocyte count. PLR was calculated as platelet count/lymphocyte count. SII was calculated as (platelet count $\times$ neutrophil count) /lymphocyte count. SIRI was calculated as (neutrophil count $\times$ monocyte count) /lymphocyte count.

CRP, C-reactive protein; HbA1c, hemoglobin A1c; IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; TC, total cholesterol; TG, triglycerides; UA, uric acid.

lute PASI ≤ 3 , 80.0% versus 83.3% for absolute PASI ≤ 2 , and 80.0% versus 83.3% for sPGA 0/1.

PASI 100 rose through week 52 in the BMI < 25 kg/m² group. In the BMI ≥ 25 kg/m² group, it reached its highest rate at week 28 and then declined slightly, remaining below the rate in the lower-BMI group. Absolute PASI ≤ 1 increased in both groups; it was more common with BMI < 25 kg/m² at weeks 16 and 28 but more common with BMI ≥ 25 kg/m² thereafter. At week 52, PASI 100 and absolute PASI ≤ 1 rates were 40.0% and 50.0%, respectively, for a BMI < 25 kg/m² and 16.7% and 66.7% for a BMI ≥ 25 kg/m².

Change in Inflammatory Laboratory Indices during 52-Week Treatment with Tildrakizumab

Among inflammatory laboratory indices, only SII was significantly lower at week 52 than at week 0 ($p = 0.014$, Friedman test with Bonferroni's post-hoc test). No significant differences between individual time points were observed for NLR, MLR, PLR, CRP, or SIRI (Table 2).

Change in Metabolic Laboratory Indices during 52-Week Treatment with Tildrakizumab

The metabolic laboratory indices did not significantly change during the 52-week treatment with tildrakizumab

(Table 2).

Discussion

The response to tildrakizumab was favorable in both age groups. Through week 28, absolute PASI ≤ 3 , absolute PASI ≤ 2 , and sPGA 0/1 tended to be more frequent among patients aged ≥ 65 years; however, PASI 90, PASI 100, and absolute PASI ≤ 1 were generally more frequent among those aged < 65 years over the 52-week period. The greater late reduction in PASI and the higher rates of several endpoints in younger patients may partly reflect their higher baseline PASI and, therefore, greater potential for numerical improvement. In the pooled analysis of reSURFACE 1 and 2, treatment responses in older patients were generally similar to those in younger patients¹⁴. A recent multicenter real-world study that included only elderly patients suggested that tildrakizumab is a valuable option for this group¹⁵. The present older patients may have already received systemic or biologic treatment before starting tildrakizumab, and their baseline PASI was lower than that of younger patients. This background may partly reflect Japanese clinical practice, in which psoriasis is often recognized and treated before patients develop very severe disease. The present real-world results support the usefulness of til-

drakizumab in older patients, although they indicate that complete or almost completely clear skin may be more difficult to obtain.

Regarding disease duration, both the SDD and LDD groups responded favorably to tildrakizumab; however, there were differences in response patterns. The LDD group had higher response rates in the early phase, before week 28, whereas the SDD group showed a higher percentage reduction in PASI and higher response rates in the later phase. This difference may be partially due to higher baseline PASI levels in the SDD group, indicating more room for improvement in the later phase in the SDD group and earlier cessation of improvement in the LDD group. Furthermore, the rate of prior systemic treatment was higher in the LDD group than in the SDD group (Table 1), indicating that responsiveness may have been affected by prior systemic treatment in the former. Thus, the LDD group should not be interpreted simply as patients receiving delayed systemic intervention. To date, conflicting results have been reported regarding the influence of disease duration on response to systemic treatment. A recent study indicated that disease duration did not affect the outcomes of systemic treatments, including biologics, methotrexate, or acitretin¹⁶. However, a prospective real-life study reported that longer disease duration correlated with better outcomes in achieving PASI ≤ 5 at week 16 of tildrakizumab 200 mg treatment¹⁷. Thus, the influence of disease duration on the response to tildrakizumab is not clear and needs to be further clarified in larger cohort studies using systemic treatment-naïve patients with SDD and LDD with similar backgrounds.

Regarding BMI, patients with a BMI < 25 showed earlier and higher PASI reduction and generally higher response rates (PASI 75, 90, 100) than did those with a BMI ≥ 25 . However, from weeks 40 to 52, absolute PASI ≤ 3 , absolute PASI ≤ 2 , absolute PASI ≤ 1 , and sPGA 0/1 rates in the BMI ≥ 25 kg/m² group were comparable to, or marginally higher than, corresponding rates in the BMI < 25 kg/m² group. The lower PASI reduction and lower response rates (PASI 75, 90, 100) in patients with a BMI ≥ 25 may be partially due to their lower baseline PASI levels, indicating less room for improvement, and indicate the difficulty in achieving complete or almost complete skin clearance. However, late-phase improvement of responses (absolute PASI ≤ 3 , PASI ≤ 2 , PASI ≤ 1 , and sPGA 0/1) in the higher BMI group indicates potential response catch-up at later phases. Obese and overweight patients may receive substantially lower doses of tildrakizumab

per unit weight, resulting in lower treatment responsiveness. A previous analysis suggested that patients with a body weight > 90 kg may benefit from a higher dose of tildrakizumab (200 mg)¹⁸. A real-world study suggested favorable results in obese patients treated with tildrakizumab 200 mg¹⁷. Another real-world study reported that the effectiveness of tildrakizumab 100 mg, including achievement rates of PASI 75 and PASI 90, was not affected by BMI¹⁹. Our results indicate that BMI may impair the speed and completeness of the response to tildrakizumab; however, patients with a higher BMI can still have a favorable reduction in PASI in response to tildrakizumab. Since the present study used tildrakizumab 100 mg, the findings for 200 mg treatment should be interpreted with caution. Moreover, Japanese patients generally have lower BMI values than Western cohorts, and the present cohort included few patients with a BMI ≥ 30 kg/m². Therefore, direct comparison with overseas cohorts and conclusions about severe obesity require caution.

Regarding laboratory data, only SII significantly decreased during treatment; the values of other inflammatory and metabolic markers did not significantly change. At the cohort level, the decrease in SII was observed together with clinical improvement in PASI, but this study did not test a patient-level correlation between changes in SII and PASI. Thus, the SII result should be interpreted as an exploratory finding. Previous studies suggested that SII and SIRI reflect psoriasis severity and may decrease during biological treatment^{11,20}. SII includes platelet count as well as neutrophil and lymphocyte counts, whereas SIRI uses monocyte count instead of platelet count. This difference may partly explain why SII but not SIRI decreased significantly in the present cohort. Thus, SII may be more sensitive to treatment-related changes in systemic inflammation, whereas SIRI may be less sensitive in this cohort. Therefore, SII may act as a biomarker for monitoring systemic inflammatory changes during tildrakizumab treatment. This should be examined in future studies with larger cohorts and longer observation periods.

This study had several limitations. First, it was conducted at a single institution. Second, the sample size was small, particularly in the SDD group. The SDD group included only 8 patients, whereas the LDD group included 45 patients; therefore, response rates in the SDD group, including rates achieving 100%, should be interpreted with caution. Third, the study was limited to Japanese patients. Because Japanese patients generally

have lower BMI values than Western patients, direct comparison of BMI results with overseas studies requires caution. Few patients had a BMI ≥ 30 kg/m², and the present results may not apply to patients with severe obesity. Fourth, laboratory data were collected retrospectively in real-world clinical practice. Inflammatory indices can be affected by upper respiratory infections, general physical condition, and subclinical viral infection, and these external factors could not be completely excluded. We did not perform a post-hoc sensitivity analysis that excluded outliers, because no outlier rule was predefined, the number of patients with week-52 laboratory data was limited, and such exclusion could introduce bias. Finally, we did not perform an additional topical-therapy-only subgroup analysis because further stratification by disease duration would have yielded very small subgroups and unstable estimates.

Conclusion

In conclusion, tildrakizumab sustainably reduced PASI over 52 weeks in a real-world cohort study. Younger age, shorter disease duration, and lower BMI were associated with higher and sustained rates, achieving stricter responses, including PASI 90 and PASI 100. In addition, SII significantly decreased during treatment.

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