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ORIGINAL RESEARCH

Improvement in Patient-reported Symptoms and Satisfaction with Tildrakizumab in a Real-world Study in Patients with Moderate-to-severe Plaque Psoriasis

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OBJECTIVE: Tildrakizumab, an anti–interleukin-23 p19 monoclonal antibody, is approved for the treatment of adults with moderate-to-severe plaque psoriasis. Limited evidence is available regarding the effects of tildrakizumab on patient-reported symptoms and satisfaction. This report describes the secondary endpoints of patient-reported symptoms and treatment satisfaction over 64 weeks in patients with moderate-to-severe plaque psoriasis treated with tildrakizumab in a Phase IV, real-world study. **METHODS:** In this uncontrolled, open-label study (NCT03718299), patients received tildrakizumab 100 mg at baseline, Week (W)4, and every 12 weeks thereafter to W52, with the final assessment at W64. Patient-reported secondary endpoints included numerical rating scale (NRS) scores for itch, pain, and scaling, and treatment satisfaction measured by 3 rating scales (Treatment Satisfaction Questionnaire for Medication [TSQM], Tildrakizumab Overall Satisfaction, and Patient Happiness with Psoriasis Control instrument) through W64. **RESULTS:** Of the 55 patients enrolled, 45 were assessed at W64. Mean NRS scores for itch, pain, and scaling all decreased from baseline beginning as early as W4 with maintenance through W64 ($P \leq 0.001$). Treatment satisfaction was positive throughout treatment based on all 3 measures. Mean±SD TSQM domain scores increased from 59.5±17.0 at W4 to 79.5±20.1 at W64 for Effectiveness and from 72.7±18.6 to 81.9±20.5 for Global Satisfaction. **LIMITATIONS:** The study is small and lacks a comparator arm. **CONCLUSION:** Tildrakizumab treatment improved patient-reported symptoms in patients with moderate-to-severe plaque psoriasis in a real-world setting and was associated with high levels of treatment satisfaction over 64 weeks. **KEYWORDS:** patient-reported outcomes, patient satisfaction, Phase 4 clinical trial, psoriasis, tildrakizumab

Plaque psoriasis is a chronic, immune-mediated skin disease characterized by scaly, erythematous plaques.[1] Among psoriasis-related symptoms, itch and pain are some of the most important contributors to patients' diminished health-related quality of life (HRQoL).[2–5] Itch, in particular, often leads to scratch-induced bleeding and other physical damage and interferes with daily activities, social interactions, work productivity, and sleep.[4,5]

Understanding treatment priorities and the effectiveness of therapy from the patients' perspective may help facilitate shared decision-making between health care providers and patients with plaque psoriasis, which may ultimately contribute to better long-term outcomes and greater treatment satisfaction.[6,7] Almost 95 percent of patients with psoriasis consider it highly important for a treatment to achieve and maintain clear skin and provide overall relief from itch and pain.[7]

Tildrakizumab is an anti–interleukin-23 p19 monoclonal antibody approved for the treatment of moderate-to-severe plaque psoriasis in patients who are candidates for systemic therapy or phototherapy.[8] To date, limited real-world evidence is available regarding the effectiveness of tildrakizumab in reducing itch, pain, and scaling in patients with moderate-to-severe psoriasis or regarding patient satisfaction with this agent.[9,10] A Phase IV study was performed in the US to evaluate improvement in HRQoL and other patient-reported outcomes under real-world conditions in patients with moderate-to-severe plaque psoriasis. An interim analysis of data at 28 weeks has recently been published.[11,12] Here, we describe the completed results at 64 weeks for patient-reported relief from itch, pain, and scaling and overall patient satisfaction with treatment.

METHODS

Study design and patients. This Phase IV, 64-week, uncontrolled, open-label, real-world study was conducted at two sites in the US (NCT03718299). Detailed methods were previously published;[11] briefly,

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DISCLOSURES: Ms. Heim has been a speaker, adviser, and consultant for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, and Novartis; an adviser for Galderma, Mayne Pharma, Regeneron Pharmaceuticals, and Sanofi; an adviser and consultant for Ortho Dermatologics; and a speaker and adviser for Beiersdorf, Incyte, LEO Pharma, and Sun Pharma. Dr. Bhutani has received research funding from AbbVie, Celgene, Eli Lilly, Galderma, Janssen, Pfizer, Regeneron Pharmaceuticals, and Sun Pharma; and has served as an adviser for AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, LEO Pharma, and Novartis. Dr. Koo has served as an adviser for AbbVie, Amgen, Celgene, Eli Lilly, EPI Health, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron Pharmaceuticals, Sanofi, Sun Pharma, and UCB. Drs. Mathew and Ferro are employees of Sun Pharmaceutical Industries, Inc. Dr. Bhatia is an adviser, consultant, and investigator for AbbVie, Almirall, Arcutis Biotherapeutics, Advanced Derm Solutions, Amytrx, Beiersdorf, Biofrontera, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle, Dermavant Sciences, Eli Lilly, Ferndale, Foamix, Galderma, Incyte, ISDIN, Johnson & Johnson, La Roche-Posay, LEO Pharma, Mindera, Novartis, Ortho Dermatologics, Pfizer, Procter & Gamble, Regeneron Pharmaceuticals, Sanofi, Skinfix, Soligenix, Sun Pharma, Verrica Pharmaceuticals, and Zerigo Health. Dr. Vasquez reports no conflicts of interest relevant to the content of this article.

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TABLE 1. Demographics and baseline characteristics of the intention-to-treat population

CHARACTERISTIC	TILDRAKIZUMAB N=55
Sex	
Female	27 (49.1)
Male	28 (50.9)
Age, years, mean±SD	48.6±15.3
Race	
White	52 (94.5)
Black or African American	2 (3.6)
Asian	1 (1.8)
Ethnicity	
Hispanic or Latino	5 (9.1)
Not Hispanic or Latino	50 (90.9)
Itch-NRS, mean±SD	6.6±2.6
Pain-NRS, mean±SD	3.8±3.2
Scaling-NRS, mean±SD	7.0±2.3
Patient Happiness with Psoriasis Control, mean±SD	2.7±2.3

Data shown as n (%) unless otherwise noted.
NRS, numerical rating scale; SD, standard deviation.

immunocompetent patients 18 years of age or older were eligible if they had moderate-to-severe plaque psoriasis affecting three percent or more of total body surface area, had been diagnosed at least six months before study entry, and were candidates for phototherapy or systemic therapy. Patients with erythrodermic psoriasis or only pustular, guttate, or inverse psoriasis were excluded, as were patients with evidence of skin conditions other than psoriasis that would interfere with study-related evaluations. Patients were also excluded if they had received treatment with any biologic other than tildrakizumab within one week prior to baseline or any investigational agent or device within 12 weeks of baseline.

All patients received subcutaneous injections of tildrakizumab 100mg at Week 0, Week 4, and then every 12 weeks through Week 52, administered by qualified study personnel. Patients attended study visits at baseline and at Weeks 4, 8, 12, 16, 28, 40, 52, and 64. The study was conducted in compliance with Good Clinical Practice guidelines, the principles of the Declaration of Helsinki, and local regulations. The study protocol and all amendments were approved by a Central Institutional Review Board prior to study initiation, and all patients provided written informed consent before they received any treatment.

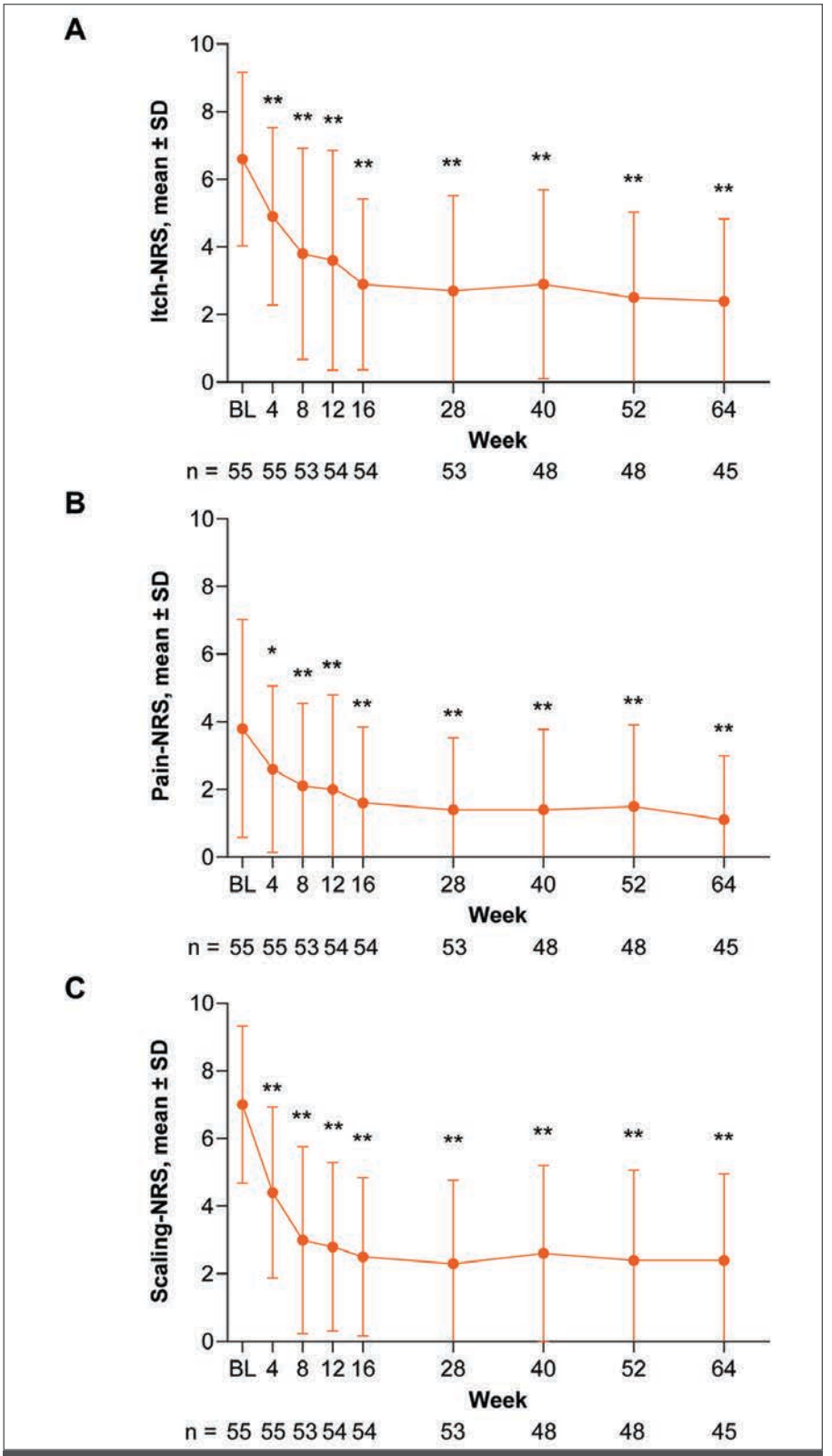

FIGURE 1. Patient-reported symptoms from baseline through Week 64.
Intention-to-treat population. Error bars represent the SD.
*P=0.001; **P<0.001; statistically significant change from BL based on Student's t-test.
BL: baseline; NRS: numerical rating scale; SD: standard deviation

Assessments. Patients rated the severity of itch, pain, and scaling at baseline and at each post baseline visit through Week 64 using an 11-point numerical rating scale (NRS) with scores ranging from 0 (no itch, pain, or scaling) to 10 (worst imaginable itch, pain, or scaling). Patient satisfaction with treatment was evaluated using three instruments: the 14-item Treatment Satisfaction Questionnaire for Medication (TSQM),[13] the Tildrakizumab Overall Satisfaction scale, and the Patient Happiness with Psoriasis Control instrument. The TSQM includes the Effectiveness, Side Effects, Convenience, and Global Satisfaction domains and generates a total score ranging from 0 to 100, with higher scores indicating greater satisfaction. The Tildrakizumab Overall Satisfaction scale includes the Improvement in Symptoms, Speed of Improvement, Frequency of Dosing, and Side Effects domains. Overall satisfaction and satisfaction in specific areas are rated on an 11-point scale from 0 (not satisfied) to 10 (extremely satisfied). The Patient Happiness with Psoriasis Control instrument asks patients to rate their overall happiness with psoriasis control on an 11-point scale from 0 (extremely unhappy) to 10 (extremely happy). All three assessments were administered at all post baseline visits; the Patient Happiness with Psoriasis Control instrument was also administered at baseline.

Endpoints. The primary endpoint of the study was change in HRQoL as measured by the change from baseline in the total Psychological General Well-Being Index score at Weeks 28 and 52;[11] the 52-week data for this endpoint will be reported elsewhere.[14] Secondary effectiveness endpoints reported included (1) changes from baseline to each post baseline study visit in mean itch-, pain-, and scaling-NRS scores; (2) the proportion of patients with an itch-, pain-, and scaling-NRS score of 0 at baseline and each post baseline study visit; (3) mean TSQM domain scores at post baseline visits through Week 64; (4) mean Tildrakizumab Overall Satisfaction domain scores at post baseline visits through Week 64; and (5) change in mean Patient Happiness with Psoriasis Control score from baseline through Week 64.

Statistical analysis. No formal sample size calculations were performed; the screened sample of 60 patients was considered sufficient to provide adequate estimates of changes from baseline in the population.

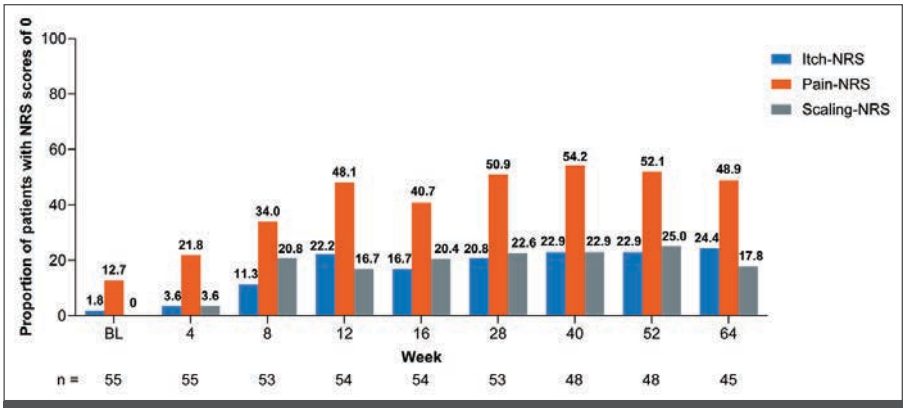

FIGURE 2. Proportion of patients with an itch-, pain-, or scaling-NRS score of 0 from baseline through Week 64. Intention-to-treat population.
BL: baseline; NRS: numerical rating scale; SD: standard deviation

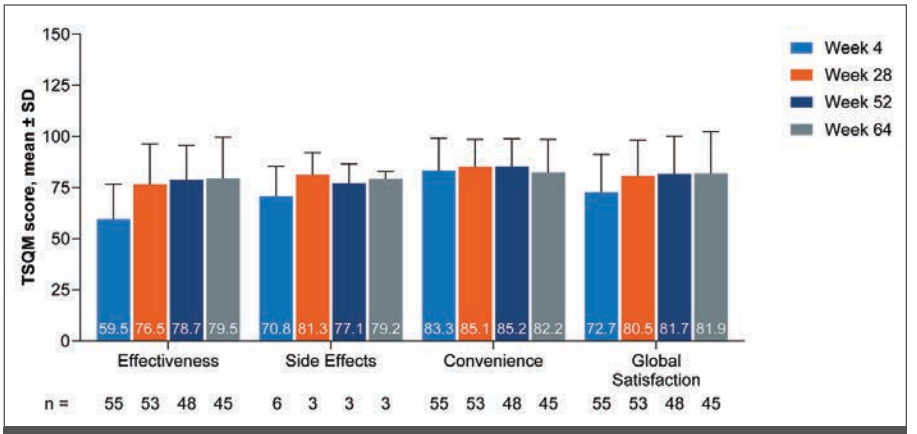

FIGURE 3. Mean TSQM domain scores from baseline through Week 64. Intention-to-treat population. Error bars represent the SD.
SD: standard deviation; TSQM: Treatment Satisfaction Questionnaire for Medication

The intention-to-treat population was used for analyses of patient-reported symptoms and patient satisfaction and included all patients who enrolled and were assigned to receive tildrakizumab. Data were summarized descriptively, and changes from baseline in itch-, pain-, and scaling-NRS scores and in Patient Happiness with Psoriasis Control were analyzed using Student's t-tests. Missing data were not imputed. All statistical analyses were performed using SAS® version 9.4 or higher.

RESULTS

Patients. Overall, 60 patients were screened, 55 were enrolled, and 45 (81.8%) were assessed at Week 64 (end of study). The reasons for early discontinuation were withdrawal by the patient (n=6), physician decision (n=2), loss to follow-up (n=1), and an adverse event (n=1).

Twenty-eight of 55 patients were male (50.9%), and most patients were White (52/55; 94.5%). Patients were 18 to 77 years of age (mean±standard deviation [SD], 48.6±15.3 years) at baseline (Table 1). All but two patients (96.4%) had received previous treatment for psoriasis.

Patient-reported symptoms. Patients receiving tildrakizumab had significant improvements from baseline in patient-reported symptoms beginning as early as Week 4; improvements were sustained through Week 64. The mean±SD itch-NRS score improved from 6.6±2.6 at baseline to 4.9±2.6 at Week 4 and 2.4±2.4 at Week 64 (both $P<0.001$ for change from baseline; Figure 1A). The mean±SD pain-NRS score decreased from 3.8±3.2 at baseline to 2.6±2.5 at Week 4 ($P=0.001$ for change from baseline) and 1.1±1.9 at Week 64 ($P<0.001$ for change from baseline; Figure 1B). The mean±SD scaling-NRS score improved from

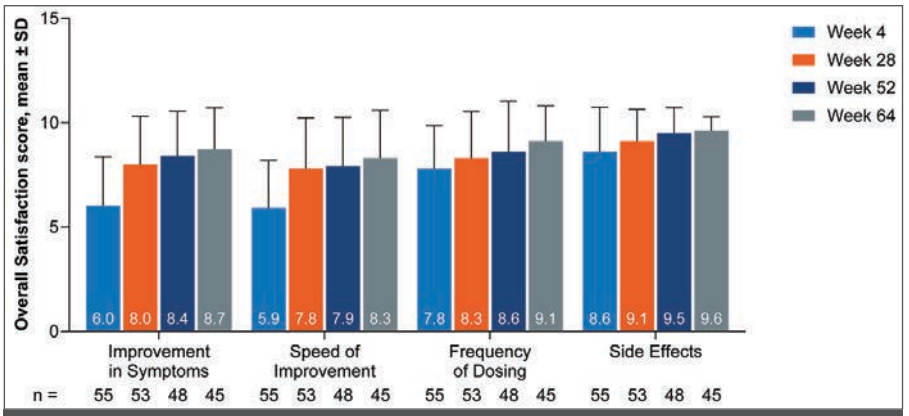

FIGURE 4. Mean Tildrakizumab Overall Satisfaction domain scores from baseline through Week 64. Intention-to-treat population. Error bars represent the SD.
SD: standard deviation

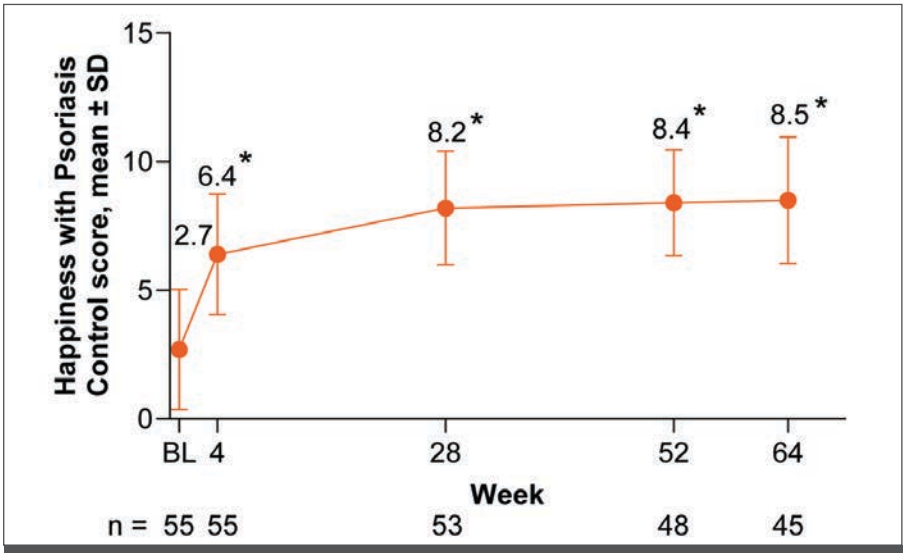

FIGURE 5. Mean Patient Happiness with Psoriasis Control score from BL through Week 64. Intention-to-treat population. Error bars represent the SD.
*$P<0.001$; statistically significant change from baseline based on Student's t-test.
BL: baseline; SD: standard deviation

7.0±2.3 at baseline to 4.4±2.5 at Week 4 and 2.4±2.6 at Week 64 (both $P<0.001$ for change from baseline; Figure 1C). The proportion of patients with an itch-, pain-, and scaling-NRS score of 0 (no itch, pain, or scaling) increased from baseline through Week 64. At Week 64, the percentage of patients with an NRS score of 0 was 24.4 percent for itch, 48.9 percent for pain, and 17.8 percent for scaling (Figure 2).

Patient satisfaction. From Week 4 to Week 64, the mean±SD TSQM domain scores increased from 59.5±17.0 to 79.5±20.1 for Effectiveness and from 72.7±18.6 to 81.9±20.5 for Global Satisfaction. The Convenience score remained stable from Week 4 to Week 64 (83.3±15.9 to 82.2±16.4, respectively), and 6 or fewer patients reported scores for Side Effects (Figure 3). From Week 4 to Week 64, the mean±SD Tildrakizumab Overall Satisfaction domain scores increased from 6.0±2.4 to 8.7±2.0 for Improvement in Symptoms, 5.9±2.4 to 8.3±2.3 for Speed of Improvement, 7.8±2.1 to 9.1±1.7 for Frequency of Dosing, and 8.6±2.1 to 9.6±0.7 for Side Effects (Figure 4). For the Patient Happiness with Psoriasis Control instrument, the mean±SD score increased from 2.7±2.3 at baseline to 8.5±2.5 at Week 64, corresponding to "extremely happy" ($P<0.001$ from Week 4 through Week 64; Figure 5).

DISCUSSION

Tildrakizumab rapidly and significantly improved patient-reported itch, pain, and scaling in patients with moderate-to-severe plaque psoriasis in a real-world setting. Patients also reported significant improvements in treatment satisfaction during the study. Statistically significant effects were observed after one dose and were maintained for up to 64 weeks. These results are consistent with the data from the Week 28 interim analysis.[11]

This Phase IV study showed both meaningful reductions in Psoriasis Area and Severity Index (PASI) score during up to one year of treatment with tildrakizumab—as have previous clinical trials and real-world studies—and significant reductions in patient-reported scales of sign and symptom severity during the 64 weeks following the start of treatment.[9,10,12,15–20] Our finding of a correlation between PASI and patient-reported outcomes in patients with psoriasis is consistent with the PSO-BIO-REAL study, a 12-month, multinational, prospective, observational study of adults with moderate-to-severe psoriasis receiving biologics. In PSO-BIO-REAL, patient-reported symptoms as assessed with the Psoriasis Symptom Inventory (PSI; measures itch, redness, scaling, burning, stinging, cracking, flaking, and pain) correlated with PASI scores. Among patients with complete skin clearance based on PASI (PASI 100), 64.8 percent had complete resolution of symptoms from the patient perspective (PSI score of 0) at Month 6,[21] with the rates of resolution of individual symptoms ranging from 78.9 percent of patients with complete relief from itch to 92.6 percent of patients with complete relief from pain.[21] Our results are also consistent with previous evidence from the real-world, multicenter, open-label, Phase IV study TRIBUTE, conducted in Spain and Italy. In TRIBUTE, a decrease in the mean PASI score from 16.2 at baseline to 1.0 at Week 24 was accompanied by decreases in the mean patient-reported symptom scores (on a scale of 0 to 10) from 7.4 to 1.7 for the pruritus-NRS, 4.6 to 1.1 for the pain-NRS, and 7.4 to 1.8 for the scaling-NRS.[9]

The high patient satisfaction observed in the current study is generally consistent with high rates of satisfaction reported at 24 weeks in the TRIBUTE study[9] and at 52 weeks in an interim analysis of the TILOT study, a three-year, prospective, multicenter study of

tildrakizumab for the treatment of moderate-to-severe psoriasis conducted in Germany.[10] In TRIBUTE, the mean TSQM subscale scores at Week 24 were 77.6 for Effectiveness, 79.6 for Convenience, 96.8 for Side Effects, and 80.5 for Global Satisfaction.[9] In TILOT, 91.4 percent of patients were satisfied or very satisfied with the effectiveness of tildrakizumab and 97.1 percent of patients were satisfied or very satisfied with the tolerability of tildrakizumab at Week 52.[10]

Limitations. Our study is not without limitations. The study was small in size and lacked any comparator arm. This may have introduced the possibility of response bias, a placebo effect, and regression to the mean. As it is unknown if some patients discontinued tildrakizumab treatment because of low treatment satisfaction, there may be an overestimation of the effect of treatment on this parameter.

CONCLUSION

Tildrakizumab treatment significantly reduced the severity of patient-reported itch, pain, and scaling and was associated with positive patient satisfaction that increased over time in patients with moderate-to-severe psoriasis in a real-world setting.

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