Psoriasis: Targets and Therapy

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ORIGINAL RESEARCH

Patient-Reported Well-Being in Value-Based Routine Care Using Tildrakizumab: 52-week Interim Data of the Phase IV Positive Study

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Purpose: Psoriasis profoundly impairs patients' social, emotional, and physical condition, impacting on their overall well-being. Tildrakizumab is an interleukin-23p19 inhibitor labelled for the treatment of moderate-to-severe plaque psoriasis. The main objective of this study was to assess the effect of tildrakizumab on the overall well-being of people with psoriasis. Effectiveness, quality of life (QoL), symptomatology, treatment satisfaction, and the impact of psoriasis on the patients' partners were also evaluated.

Patients and Methods: POSITIVE is a 24-month observational study in adults with moderate-to-severe psoriasis treated with tildrakizumab in a real-world setting (ClinicalTrials.gov ID: NCT04823247). Outcome measurements included the 5-item WHO Well-being Index (WHO-5), Psoriasis Area and Severity Index (PASI), Dermatology Life Quality Index-Relevant (DLQI-R), Treatment Satisfaction Questionnaire for Medication (TSQM-9), and FamilyPso. We report 52-week (W52) interim data (N = 400; observed cases).

Results: Mean ± 95% CI WHO-5 score increased from 53.8 ± 2.2 at baseline to 66.0 ± 2.3/65.7 ± 2.7 at W28/W52 ($p < 0.0001$, both). Mean ± 95% CI PASI decreased from 13.1 ± 0.8 at baseline to 1.7 ± 0.3/1.5 ± 0.3 at W28/W52 ($p < 0.0001$, both). At W28 and W52, 85.8%/54.8% and 88.4%/56.8% of patients achieved PASI ≤ 3/≤ 1. Mean ± 95% CI DLQI-R score decreased from 12.6 ± 0.8 at baseline to 3.3 ± 0.6/3.1 ± 0.6 at W28/W52 ($p < 0.0001$, both). At W52, mean ± 95% CI TSQM-9 domain scores were 77.4 ± 3.2 for effectiveness, 81.5 ± 2.6 convenience, and 81.1 ± 2.6 global satisfaction. Mean ± 95% CI total FamilyPso decreased from 1.3 ± 0.1 at baseline to 0.7 ± 0.2 at W52 ($p < 0.0001$). At the point of this analysis, 24.0% of patients had ≥1 adverse event (AE). Only one patient discontinued due to a treatment-related AE.

Conclusion: Tildrakizumab successfully contributes to value-based long-term health care for moderate-to-severe psoriasis by increasing patient wellbeing, QoL and clinical outcomes while showing very good safety and tolerability.

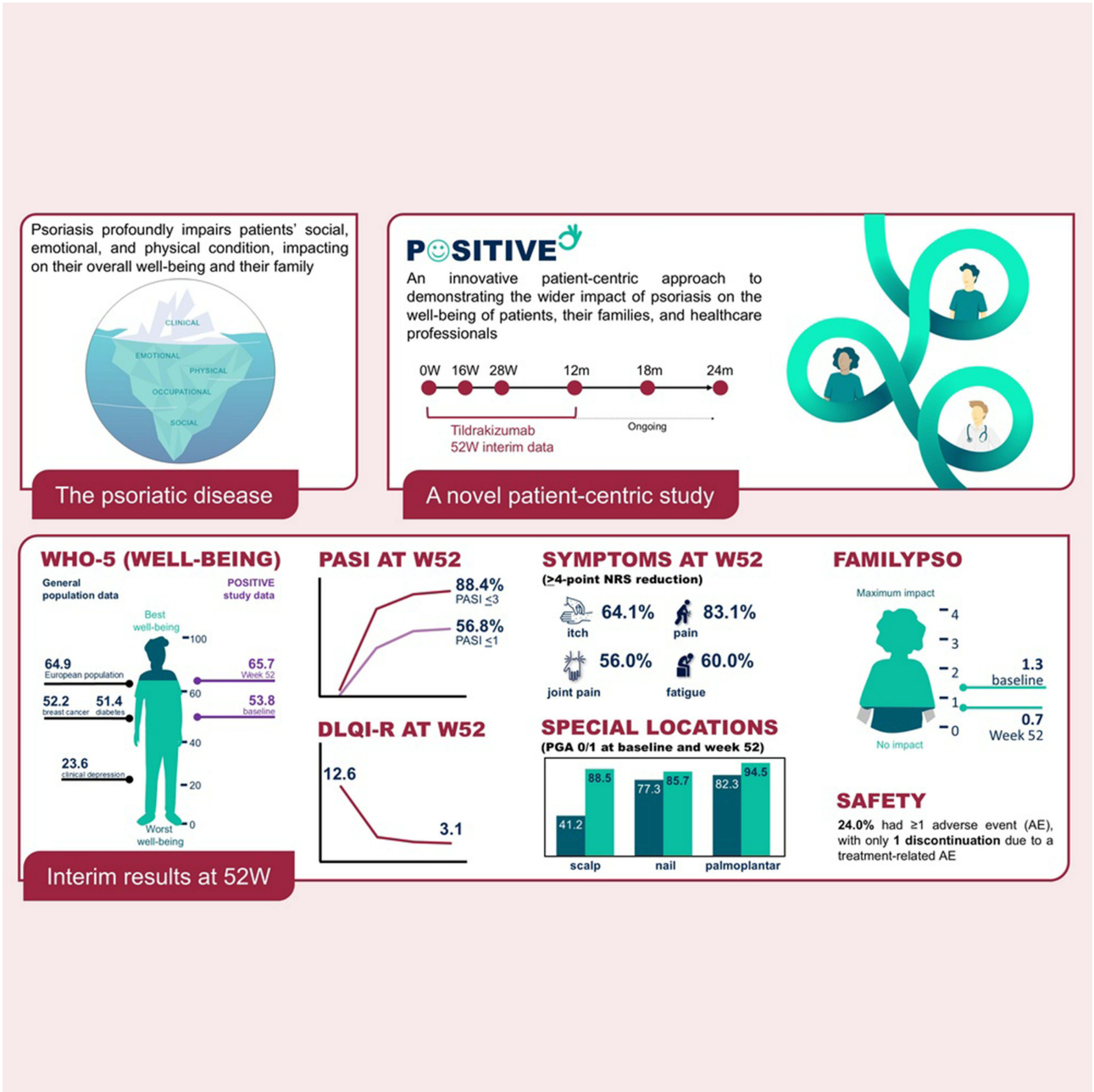
Keywords: effectiveness, psoriasis, real-world evidence, RWE, tildrakizumab, well-being, WHO-5 Well-being Index

Introduction

Psoriatic disease is a chronic inflammatory condition, with a complex pathophysiology, affecting over 60 million people worldwide.[1–3] Beyond its physical impact on the skin, plaque psoriasis can profoundly affect patients' psychological and

Received: 6 March 2025
Accepted: 22 May 2025
Published: 28 June 2025

Graphical Abstract



social well-being.[4–10] Thus, the disease has been associated with an increased risk of numerous medical and psychiatric comorbidities,[11,12] including anxiety and depression,[13] or even suicidality.[14]

Traditionally, the assessment of plaque psoriasis has primarily focused on skin clearance (eg, Psoriasis Area and Severity Index [PASI] and health-related quality of life [HRQoL] improvement (eg, Dermatology Life Quality Index [DLQI]).[15–18] However, this approach likely overlooks the holistic impact of plaque psoriasis on patients.[19,20] Recent studies highlight that plaque psoriasis affects the overall well-being of patients, their families, as well as their personal, social and occupational life.[8] Unfortunately, these crucial dimensions are often absent from commonly used decision-making tools.[21,22]

The term "well-being" was incorporated to the definition of health at the World Health Organization (WHO) constitution in 1948. According to the WHO, health is "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".[23,24] Hence, despite being one of the main goals of a treatment, PASI improvement does not necessarily mean having a good well-being or being healthy.[17,18,25,26] Recently, a series of recommendations for implementing well-being in the management of psoriasis in clinical practice has been proposed.[26] Among these recommendations is the need to listen to the patient and evaluate the physical and also the emotional impact of the disease (well-being). However, robust evidence on how plaque psoriasis and treatments influence both the well-being of patients and their families is lacking.

Tildrakizumab is an interleukin (IL)-23p19 inhibitor approved for the treatment of adults with moderate-to-severe plaque psoriasis with demonstrated long-term disease control both in clinical trials and in the real-life setting.[27–32] Tildrakizumab has also recently showed an improvement on disease-related symptoms such as itch, skin pain and scaling, which is also associated with better sleep quality, work productivity, and quality of life.[31,32]

For the first time in psoriasis research, the POSITIVE study uses patient-reported well-being as the primary endpoint with therapeutic intervention to holistically evaluate the impact of plaque psoriasis and a biologic therapy, tildrakizumab, on patient lives in a real-world setting.[33] To assess patient well-being, this study applies the 5-item WHO Well-being Index (WHO-5), a widely used questionnaire assessing psychological health-related well-being across a wide range of chronic diseases such as diabetes mellitus, cancer or mental disorders.[34] In addition, traditional endpoints such as PASI and DLQI are also included to assess the effectiveness of tildrakizumab and its impact on the quality of life of the patients. The POSITIVE study also encompasses the entire environment of the patient (assessing the long-term benefit of tildrakizumab reported by patients in terms of treatment satisfaction [TSQM-9], and treatment-related patient benefits [PBI-S-10], work impairment due to psoriasis [WPAI:PSO] and extent of the skin manifestations on the entire body using a "heat map"), as well as the impact on partners (FamilyPsO) as well as treating physicians. Here, we present the interim analysis up to week 52 of the POSITIVE study.[33]

Materials and Methods

Study Design

POSITIVE is an ongoing 24-month, multinational, observational phase IV study in adult patients with moderate-to-severe plaque psoriasis who require systemic biologic therapy and qualify for treatment with tildrakizumab in real-world clinical practice (ClinicalTrials.gov ID: NCT04823247).[33] All participant inclusion and exclusion criteria, participating countries as well as details of the study design and ethics committees that approved the study, have been previously reported.[33]

The study assessments for this interim analysis (up to week 52) encompassed outcomes reported by patients, their partners, and the physicians.

Primary Outcome

Well-being was assessed using the WHO-5,[34] a global rating scale measuring subjective well-being by positive assertions. The respondent is asked to rate the extent to which each of the five items applies to him/her in the last 2 weeks from 5 (all the time) to 0 (none of the time). The standardized score ranges from 0 to 100, where 0 = "absence of well-being" and 100 = "maximal well-being". In order to monitor possible changes in well-being, an increase of 10 points after treatment versus baseline in a continuous score change from baseline (in a range from 0 to 100 points) is considered a clinically meaningful change.[34]

The WHO-5 questionnaire is provided in the Supplementary Material.

Secondary Outcomes

Full details on the secondary assessments can be found elsewhere.[33] Briefly, routine clinical documentation records included medical charts; physician assessments: PASI (0–72),[35] Physicians Global Assessment (PGA) global, scalp, nails and palmoplantar; skin manifestations distribution (heat map/patient's) according to location and total percentage of area affected; and Patient Reported Outcomes (PROs): HRQoL (DLQI; 0–30,[36] which was rated using the DLQI-Relevant

[DLQI-R] scoring system), treatment satisfaction (TSQM-9 and physicians' satisfaction questionnaire),[33,37] treatment related patient benefits (PBI-S-10), work productivity (WPAI:PSO),[38,39] and symptomatology (Numeric Rating Scale [NRS] for itch, pain, joint pain and fatigue). In addition, the impact on partner's life was assessed using the FamilyPso questionnaire.[40]

DLQI includes 10 items to assess patient's HRQoL during the previous week on a 4-point scale, indicating "not at all", "a little", "a lot" and "very much", respectively. For each patient, the DLQI- R score is estimated as a sum score of the original DLQI score replacing items rated "not relevant" by the mean of the other items.[36] TSQM-9 consists of nine statements distributed in three domains: efficacy (three items), convenience (three items) and global satisfaction (three items). Each domain is computed by summing the individual TSQM items and then transforming the composite score into a value ranging from 0 to 100.[37]

DLQI, TSQM-9, PBI-S-10, and FamilyPso questionnaires are provided in the Supplementary Material.

Safety

The number of withdrawals and discontinuations, adverse events (AEs), and treatment-related AEs, with their degree of severity, were collected. All AE terms were coded by system organ class and preferred term using the Medical Dictionary for Regulatory Activities.

Statistical Analysis

This analysis was based on the data cut-off date of 23rd October 2023, and represents the full analysis set for all the endpoints and the safety analysis set for all safety outcomes until week 52.

All data analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). Interim data through week 52 are presented here using observed cases (OC), last observation carried forward (LOCF) and multiple imputation (MI) approaches. Descriptive analyses were performed to describe the change from baseline in the different questionnaires at weeks 16, 28 and 52. Tests for whether the change from baseline was significant were conducted using paired t-tests (or Wilcoxon signed-rank test).

Results

Baseline Characteristics

A total of 400 moderate-to-severe patients with plaque psoriasis reaching week 52 as per protocol interim analysis were analyzed. Demographic and baseline characteristics are shown in Table 1.

Psychological Well-Being

Overall, the mean total (95% CI) WHO-5 score at the baseline was 53.8 (2.3), significantly lower than the general population of the European countries participating in the POSITIVE study (mean of 64.9).[41] In comparison with the general population, the overall score and percent change from baseline were 11.3 and 46.0%, above the minimal clinically important difference (MCID) of the questionnaire,[34] confirming that moderate-to-severe patients with plaque psoriasis in Europe, have a clinically meaningful impact on their well-being.

As early as 16 weeks of treatment, the WHO-5 score increased from 53.8 to 65.2 (2.2) [$p < 0.0001$], returning the psychological well-being levels back to the general population (Figure 1 and Table S1). This improvement was maintained over time, with scores of 66.0 (2.3) and 65.7 (2.7) after 28 and 52 weeks, respectively ($p < 0.0001$ for both timepoints).

Clinical Response

The mean (95% CI) PASI significantly decreased from 13.1 (0.8) at baseline to 2.4 (0.3), 1.7 (0.3) and 1.5 (0.3) at weeks 16, 28 and 52 ($p < 0.0001$), with a mean (SD) change from baseline of −10.4 (7.9), −11.3 (8.0) and −11.7 (8.2), respectively (Figure 2a). MI and LOCF sensitive analysis are shown in Table S1.

Table 1 Demographic and Other Baseline Characteristics

Variable	
Gender, N (%) (female)	147 (36.8%)
Age (years), mean (SD)	46.5 (15.1)
Weight (kg), mean (SD)	85.4 (20.1)
BMI (kg/m^2), mean (SD)	28.4 (5.8)
Smoking habit, N (%)	
Non-smoker	165 (41.3%)
Ex-smoker	72 (18.0%)
Current smoker	147 (36.8%)
Unknown	16 (4.0%)
Marital status, N (%)	
Married	184 (46.0%)
Consensual union	64 (16.0%)
Single	98 (24.5%)
Divorced	31 (7.8%)
Widowed	6 (1.5%)
Unknown	17 (4.3%)
Time since diagnosis (years), mean (SD)	15.1 (13.0)
Location of plaque psoriasis at diagnosis, N (%)	
Scalp	264 (66.0%)
Nails	138 (34.5%)
Flexures	114 (28.5%)
Genitalia	113 (28.3%)
Palms	67 (16.8%)
Soles	45 (11.3%)
Psoriatic arthritis at inclusion date, N (%)	48 (12.0%)
Co-morbidities at inclusion date, N (%)	180 (45.0%)
High blood pressure	84 (21.0%)
Depression	36 (9.0%)
Dyslipidemia	30 (7.5%)
Diabetes Mellitus	25 (6.3%)
Fatty liver disease	20 (5.0%)
Cardiovascular disease	17 (4.3%)
Metabolic syndrome	12 (3.0%)
Neoplasm	8 (2.0%)
Kidney disease	5 (1.3%)
Inflammatory bowel disease	2 (0.5%)
Psoriasis drug therapy history, N (%)	
Topicals	213 (53.3%)
Phototherapy	127 (31.8%)
Systemic non-biologic	184 (46.0%)
Biologic	110 (27.5%)
Tildrakizumab dose at baseline, N (%)	
100 mg	381 (95.5%)
200 mg	18 (4.5%)

Abbreviations: BMI, body mass index; SD, standard deviation.

The proportion of patients achieving PASI ≤ 3 responses at weeks 16, 28 and 52 was 73.4%, 85.8% and 88.4%, respectively; while 40.7%, 54.8% and 56.8% of patients achieved a PASI ≤ 1, respectively (Figure 2b).

A total of 298 patients (75.3%) had a PGA score of 3/4 at baseline. Overall, 70.3%, 84.4% and 83.4% reached the treatment goal of PGA 0/1 (clear or almost clear signs) after 16 weeks, 28 weeks and 52 weeks, respectively.

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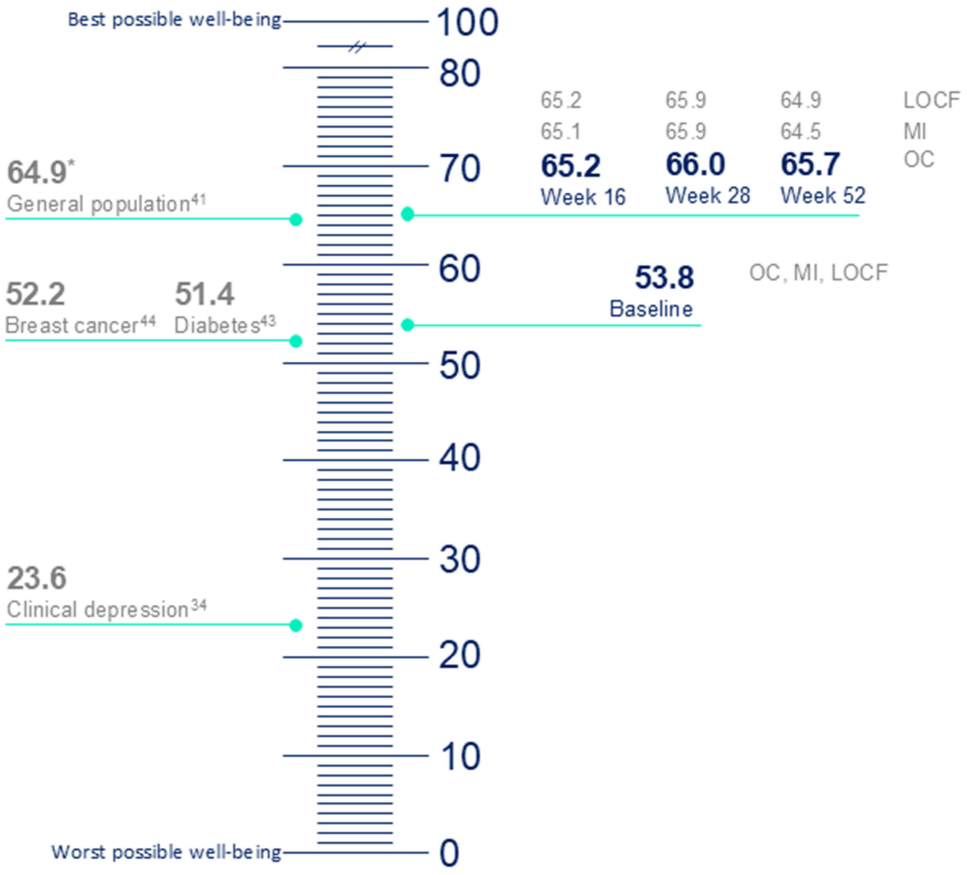

Figure 1 Mean WHO-5 scores up to Week 52. Left side, score in the general population and other representative diseases. Right side, scores from the POSITIVE study. *Mean WHO-5 score in the general population of the countries participating in the POSITIVE study. Baseline: n = 359, Week 16: n = 317, Week 28: n = 284, Week 52: n = 218.
Abbreviations: n, valid sample size; LOCF, last observation carried forward; MI, multiple imputation; OC, observed cases; WHO-5, World Health Organization-Five Well-Being Index.

Heath-Related Quality of Life

HRQoL was evaluated using the well-established DLQI questionnaire, however, here we used a recently developed scoring that adjusts the total score of the questionnaire for the number of "not relevant" responses indicated by a patient (DLQI-R).[42]

The mean (95% CI) DLQI-R significantly decreased from 12.6 (0.8) to 4.1 (0.6), 3.3 (0.6) and 3.1 (0.6) at weeks 16, 28 and 52 ($p < 0.0001$ for all) (Figure 3a) (See Table S1 for MI and LOCF data).

At weeks 16, 28 and 52, 38.4%, 46.5% and 47.3% of patients reported no effect on their HRQoL (DLQI-R between 0 and 1.99), respectively (Figure 3b).

Patients and Physician's Satisfaction with Tildrakizumab

In general, patients reported high levels of satisfaction with tildrakizumab in all three domains of the TSQM-9 questionnaire: effectiveness, convenience, and overall satisfaction with the treatment (Figure 4).

Physician's satisfaction was high throughout the study. The "satisfaction with treatment score" scale (0 to 5 range) showed a mean score of 4.2, 4.2 and 4.3 at weeks 16, 28 and 52 (p-values: 0.3500, 0.0002 and <0.0001, respectively). For the "compassionate scale" (0 to 5 range), physicians' satisfaction was remarkably high at baseline (4.3) and remained stable over time.

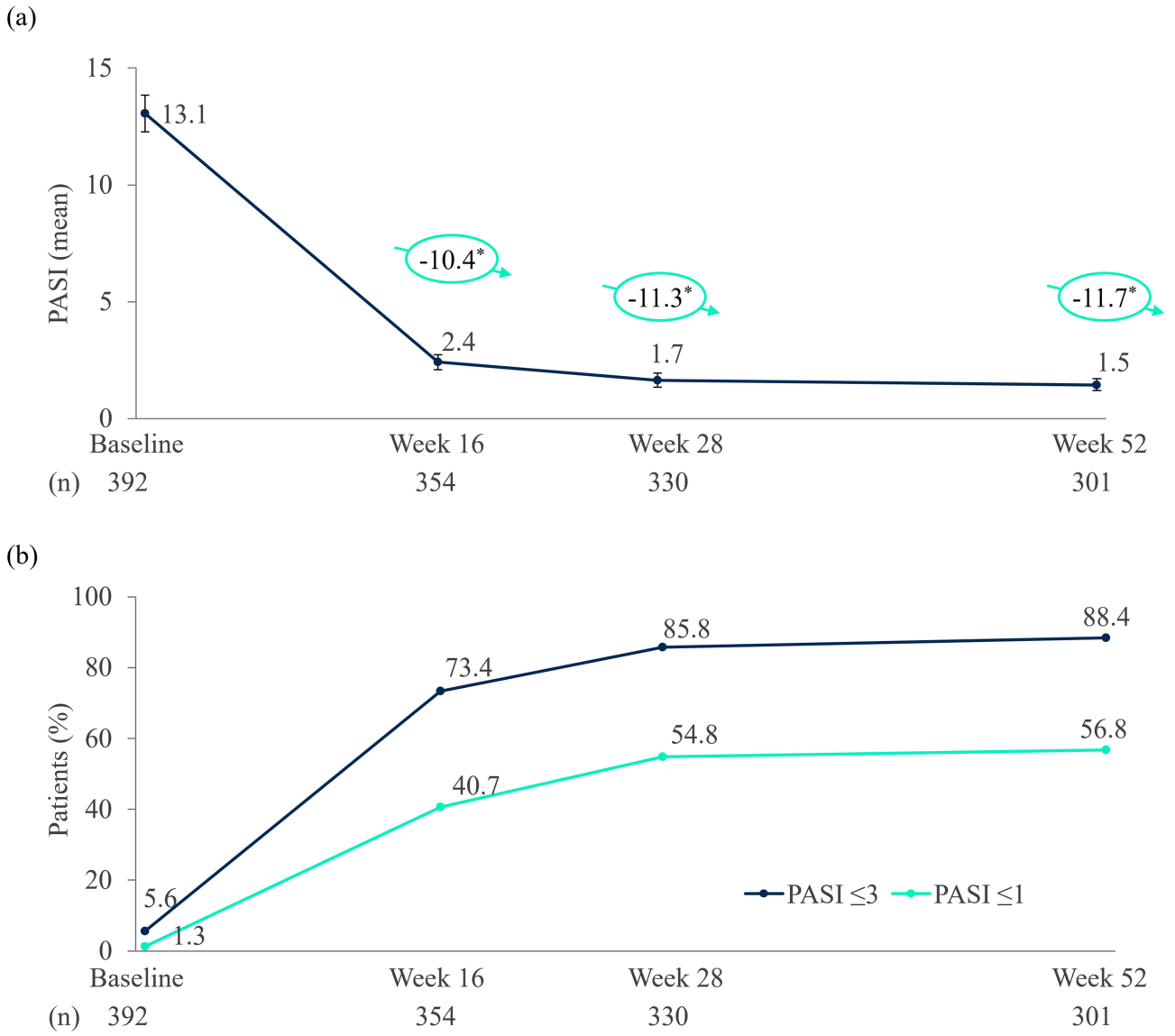

Figure 2 Mean absolute PASI scores up to Week 52 **(a)** and percentage of patients achieving PASI ≤ 3 and PASI ≤ 1 **(b)** (OC). *Mean change from baseline ($p < 0.0001$). Error bars represent 95% confidence intervals.
Abbreviations: n, valid sample size. OC, observed cases; PASI, Psoriasis Area and Severity Index.

Well-Being of the Partners: The FamilyPso

We used the FamilyPso questionnaire to assess the burden in the partners of the patients. The mean (95% CI) FamilyPso score at baseline was 1.3 (0.1) points, which significantly decreased to 0.9 (0.2), 0.8 (0.2) and 0.7 (0.2) at weeks 16, 28 and 52 ($p < 0.0001$) (Figure 5a) (See Table S1 for MI and LOCF data). The FamilyPso is composed of 5 factors, all of them showing a significant decrease throughout the study (Figure 5b).

Work Productivity: WPAI:PSO

The work productivity and activity impairment improved throughout the study, with a decrease in all four domains of the questionnaire: the percent work time missed (absenteeism) was changed from 8.4 at baseline to 1.3, 1.8 and 4.2 at weeks 16, 28 and 52 ($p < 0.0001$, 0.0002 and 0.3063), respectively; the percent impairment while working (presenteeism) was changed from 22.3 to 8.7, 6.2 and 4.7 ($p < 0.0001$); the percent overall work impairment was changed from 25.2 at baseline to 9.2, 7.0 and 7.3; and the percent activity impairment was changed from 32.8 to 16.1, 11.4 and 11.0 at weeks 16, 28 and 52 ($p < 0.0001$), respectively (Figure 6).

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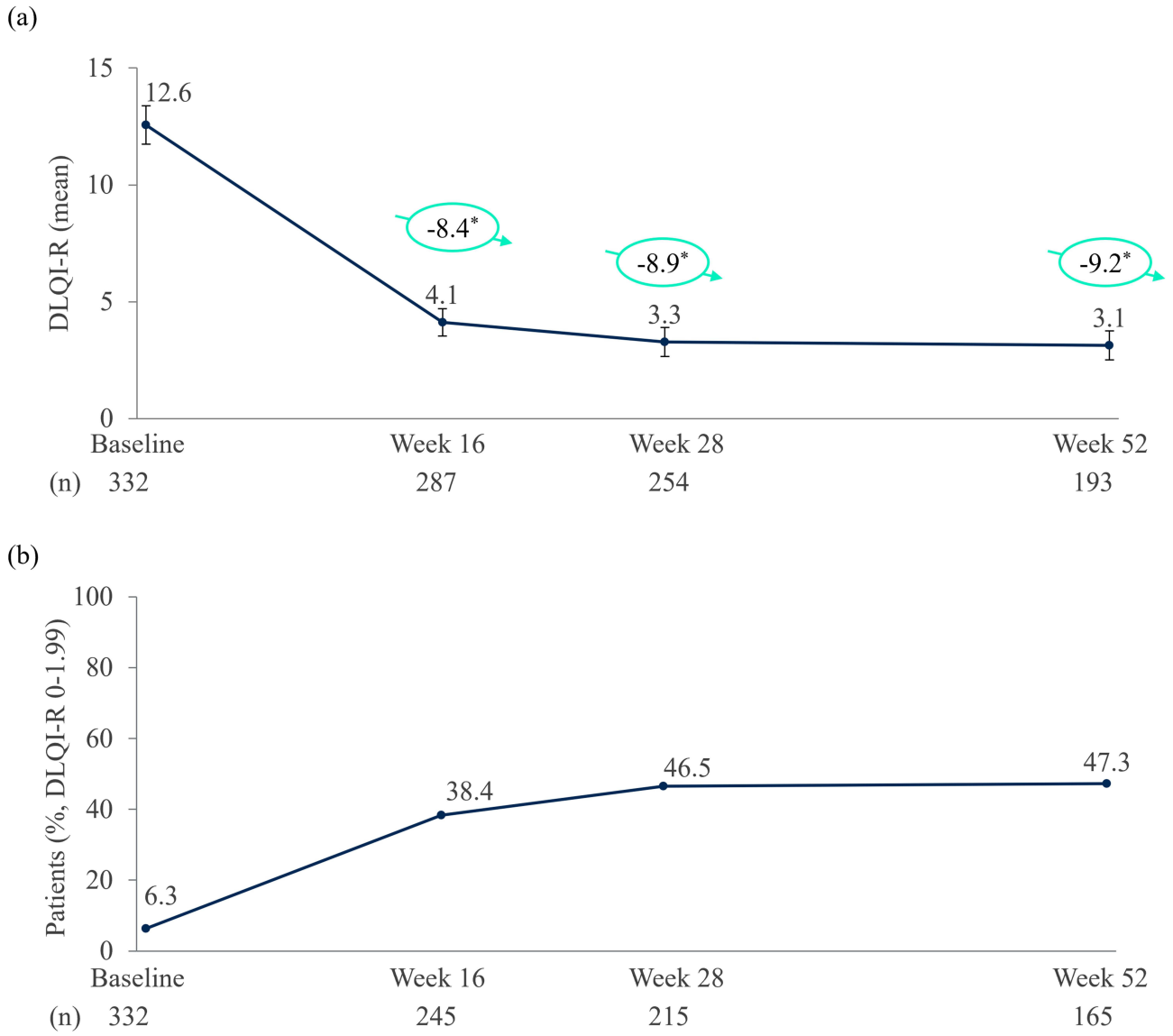

Figure 3 Mean DLQI-R scores up to Week 52 **(a)** and percentage of patients achieving DLQI-R 0–1.99 **(b)** (OC). *Mean change from baseline ($p < 0.0001$). Error bars represent 95% confidence intervals.
Abbreviations: n, valid sample size. DLQI-R, Dermatology Life Quality Index-Relevant; OC, observed cases.

Patient Benefit Index (PBI)-10-S

The goals and the mean scores as described in the Patient Needs Questionnaire were assessed at baseline (Figure 7a). The top three treatment goals were regaining control of the disease (94.5), get better skin quickly (93.3%) and be healed of all skin defects (92.4%), with more than 75% of the patients reaching their top three goals after treatment.

A total of 89.8%, 93.6% and 97.2% of patients achieved a PBI total score ≥1 at weeks 16, 28 and 52, respectively, considered a minimum clinically meaningful improvement (Figure 7b).

Symptoms of Plaque Psoriasis: Pruritus-, Pain-, Joint Pain-, and Fatigue-NRS

Tildrakizumab showed a remarkable effectiveness in reducing the main symptoms associated with plaque psoriasis, as summarized in Figure 8.

The proportion of patients achieving a clinical meaningful reduction of >4 points was 68.3%, 69.3% and 64.1% for pruritus-NRS (Figure 8a); 69.6%, 74.0% and 83.1% for pain-NRS (Figure 8b); 52.9%, 52.1% and 56% for joint pain-NRS (Figure 8c);and 59.0%, 65.6% and 60% for fatigue-NRS at weeks 16, 28 and 52 (Figure 8d), respectively.

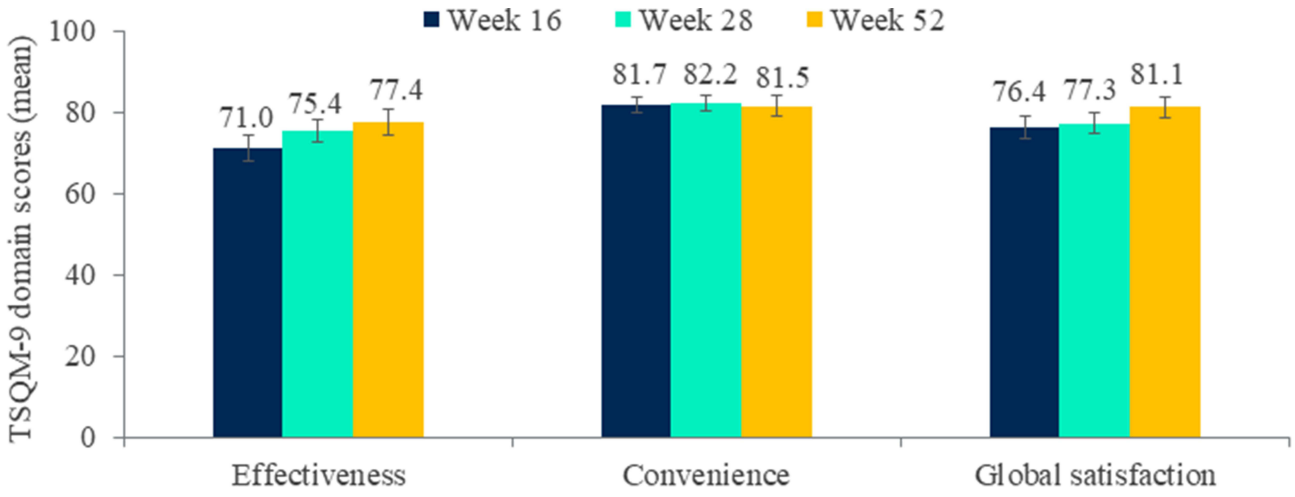

Figure 4 Mean TSQM-9 domain scores at weeks 16, 28, and 52 (OC) Week 16: n = 280, Week 28: n = 255, Week: n = 198. Error bars represent 95% confidence intervals.
Abbreviations: n, valid sample size. OC, observed cases; TSQM-9, Treatment Satisfaction Questionnaire for Medication.

Skin Manifestations Distribution

The PGA was also evaluated in patients suffering from plaque psoriasis in special locations: scalp (sPGA; n = 233 patients), nails (nPGA; 90 patients) and/or palmoplantar (ppPGA; 70 patients) affectation. Tildrakizumab improved all three scores throughout the study, with the following proportion of patients reaching a PGA 0/1: 82.3%, 87% and 88.5% for sPGA; 84.8%, 90.5% and 94.5% for ppPGA; and 63.4%, 77.9% and 85.7% for nPGA, at weeks 16, 28 and 52, respectively.

The most frequently mentioned affected body areas (body map grid) were the lower legs (70.4%), elbows (58%) and lower arms (52.4%) (Figure 9).

Safety

During the first 52 weeks of the study, 24.0% of patients had ≥1 AE, with infections and infestations (12.3%), mostly COVID-19 (4.0%) and nasopharyngitis (3.0%), being the most common system organ class and preferred terms, respectively, and 4.0% of patients had ≥1 related AE.

The percentage of patients who dropped out of the study for any reason up to week 52 was 15.8% (N = 63); 9.3% were due to lack or loss of efficacy, 0.8% due to an AE, and the rest due to loss of follow-up (2.3%), poor compliance to protocol (1.8%) or other reasons (1.8%).

Discussion

Modern people-centered health care (PCHC) for psoriatic disease as promoted by WHO includes changing perspectives on the outcomes of treatment between physician, patient, and patients' relatives. To achieve this, WHO demands the use of patient-relevant outcomes instruments including a measure for health-related well-being. Overall, this concept of PCHC resonates with value-based care as positioned in health economics. To our knowledge, the POSITVE study presented in this publication is the first study, which encompasses a broad set of outcomes instruments reflecting different levels of values. In particular, the choice of WHO-5 as the primary endpoint is a novel concept that emphasizes the patient's perspective in measuring the value of treatment.

For the first time, the POSITIVE study demonstrated that people with moderate-to-severe psoriasis had a significant impact of their psychological well-being (mean 53.8), with numbers significantly lower than in the general European population (mean 64.9), and similar to other chronic diseases such as type 2 diabetes with distress (51.4) or breast cancer (52.2).[43,44]

The results of the study showed that within 16 weeks of treatment, tildrakizumab quickly improved the psychological well-being of the people with psoriasis to similar levels of the general population (mean 65.2)[41] (Figure 1). This

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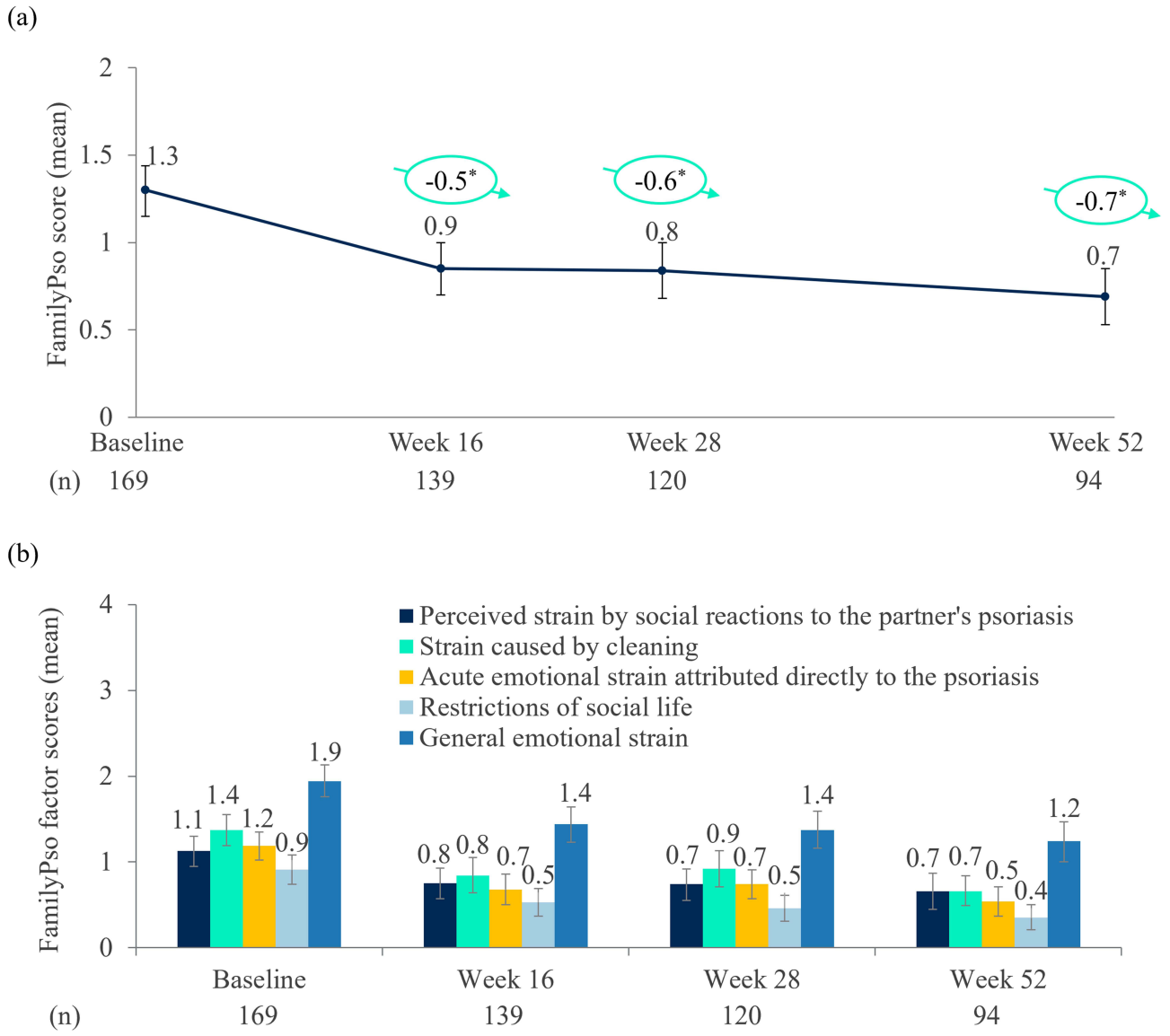

Figure 5 Mean total FamilyPso scores up to Week 52 **(a)** and mean scores by FamilyPso factor **(b)** (OC). *Mean change from baseline ($p < 0.0001$). Error bars represent 95% confidence intervals.
Abbreviation: OC, observed cases.

improvement was maintained over the 52 weeks of this interim analysis (mean 65.7). These results confirm that adding well-being (WHO-5 – less than 1 minute to complete) as a complementary treatment goal, together with PASI and DLQI, contributes to an improved health of people with psoriasis within the framework of the WHO initiative of people-centered health care.[45]

Importantly, we showed that tildrakizumab significantly reduced absolute PASI, with almost 9 out of 10 patients (85.8%) reaching the clinically meaningful target of PASI ≤ 3 at week 28,[46] and maintained over the 52 weeks. Of whom, 64% achieved clear skin (PASI < 1). Similar proportion of patients reached clear or almost clear signs (PGA 0/1). Furthermore, tildrakizumab was effective in improving plaques at different body parts (Figure 9) of special clinical interest (nail, genital and palmoplantar), often associated with a major impact on the HRQoL of the patients.[47] Despite the correlation between improvement and well-being or HRQoL was not assessed in this interim analysis, nearly 9 out of 10 patients reached clear or almost clear symptoms in these three areas in 28 weeks, which was maintained at week 52. Our findings further support the effectiveness of tildrakizumab and quality of life improvements in patients with

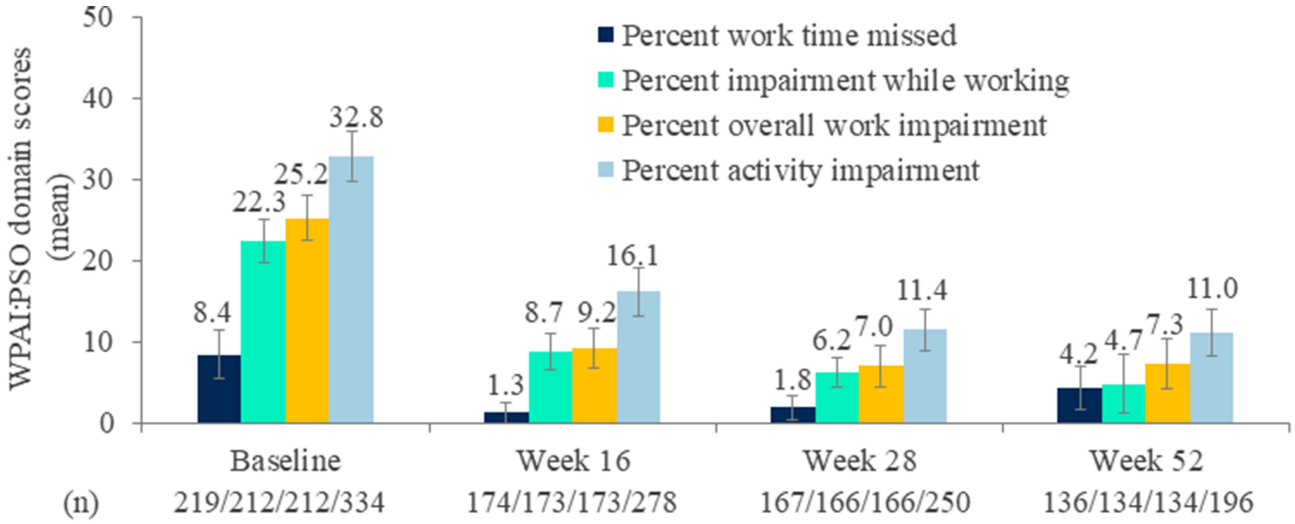

Figure 6 Mean WPAI:PSO domain scores up to Week 52 (OC) Error bars represent 95% confidence intervals.
Abbreviations: n, valid sample size. OC, observed cases; WPAI:PSO, Work Productivity and Activity Impairment Questionnaire: Psoriasis.

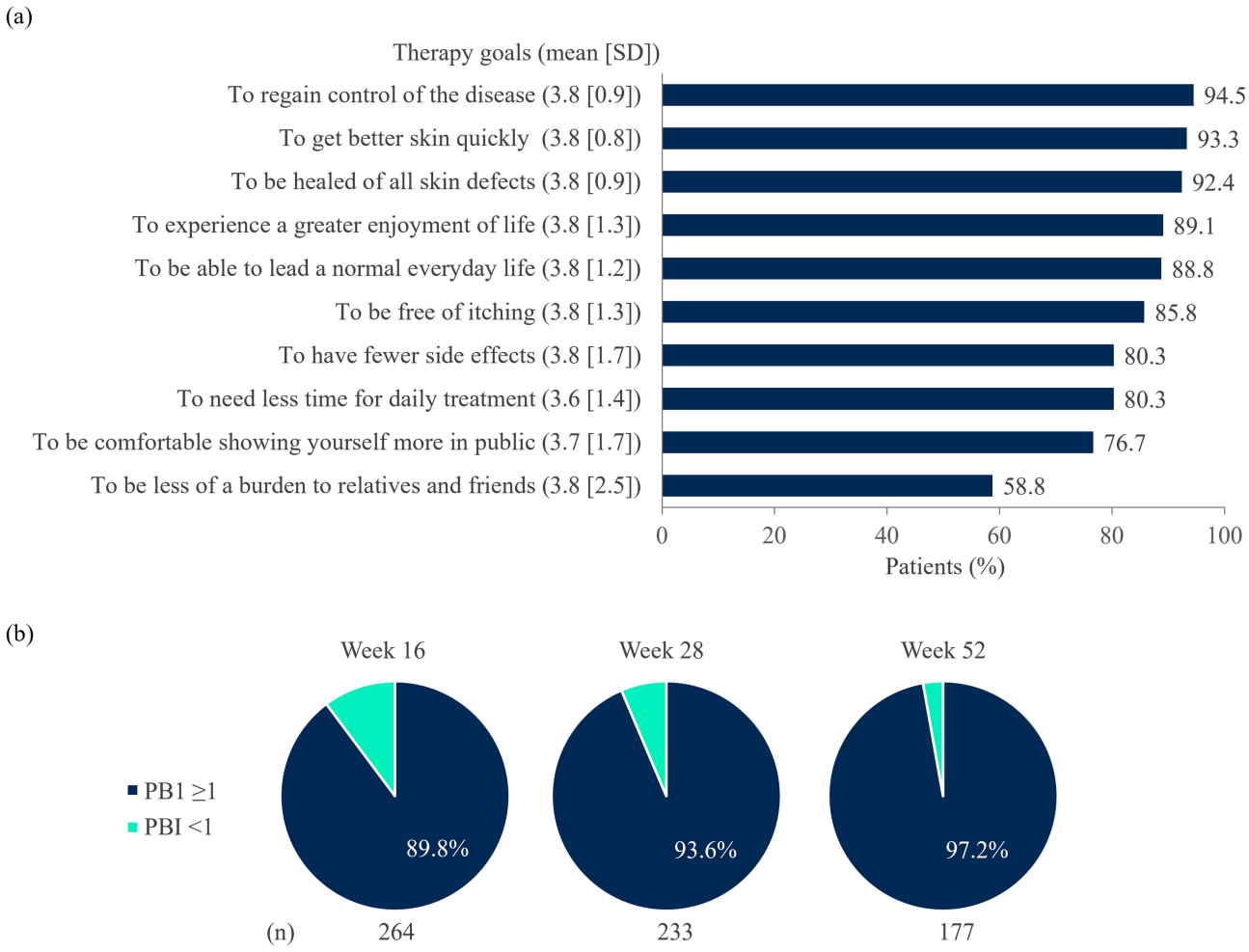

Figure 7 Therapy goals at baseline (n = 330; percentage of patients answering "quite" or "very much") **(a)** and percentage of patients achieving PBI ≥1 at weeks 16, 28 and 52 **(b)** (OC).
Abbreviations: n, valid sample size. OC, observed cases; PBI, Patient Benefit Index; SD, standard deviation.

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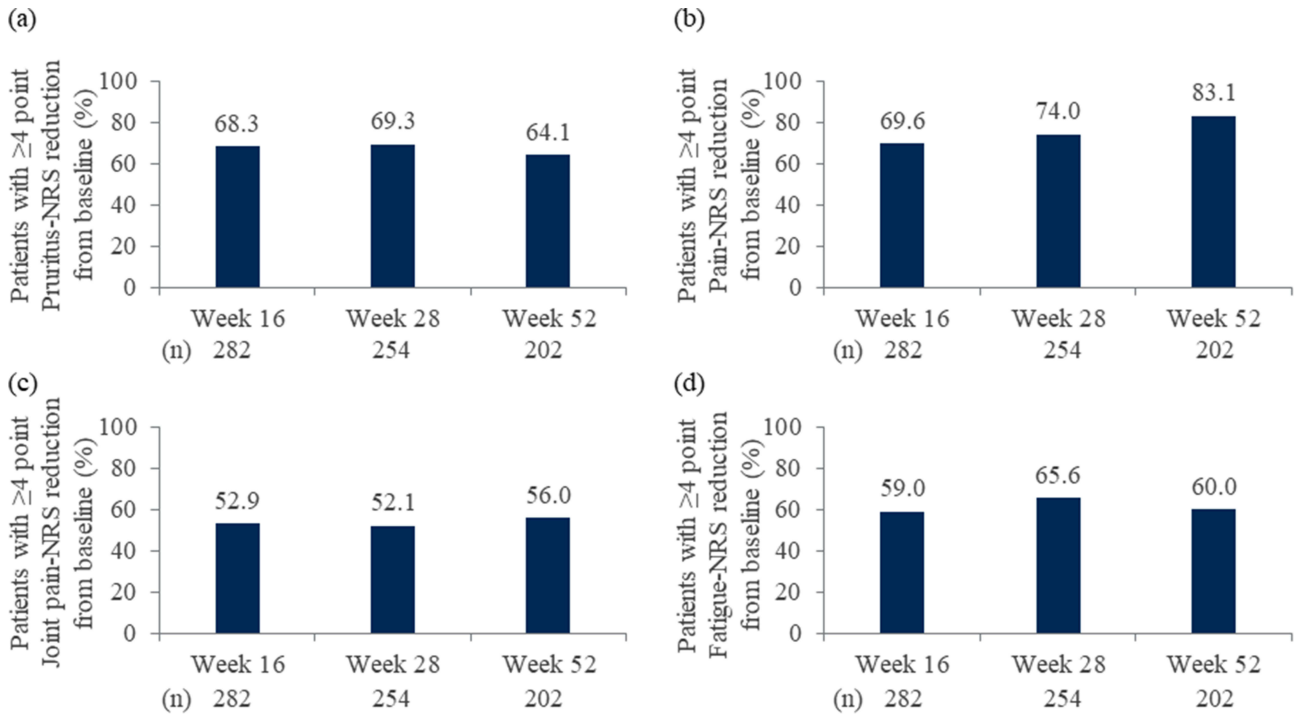

Figure 8 Percentage of patients (OC) achieving a reduction of ≥4 points for pruritus- **(a)**, pain- **(b)**, joint pain- **(c)**, and fatigue-NRS **(d)**.
Abbreviations: n, valid sample size. NRS, Numeric Rating Scale; OC, observed cases.

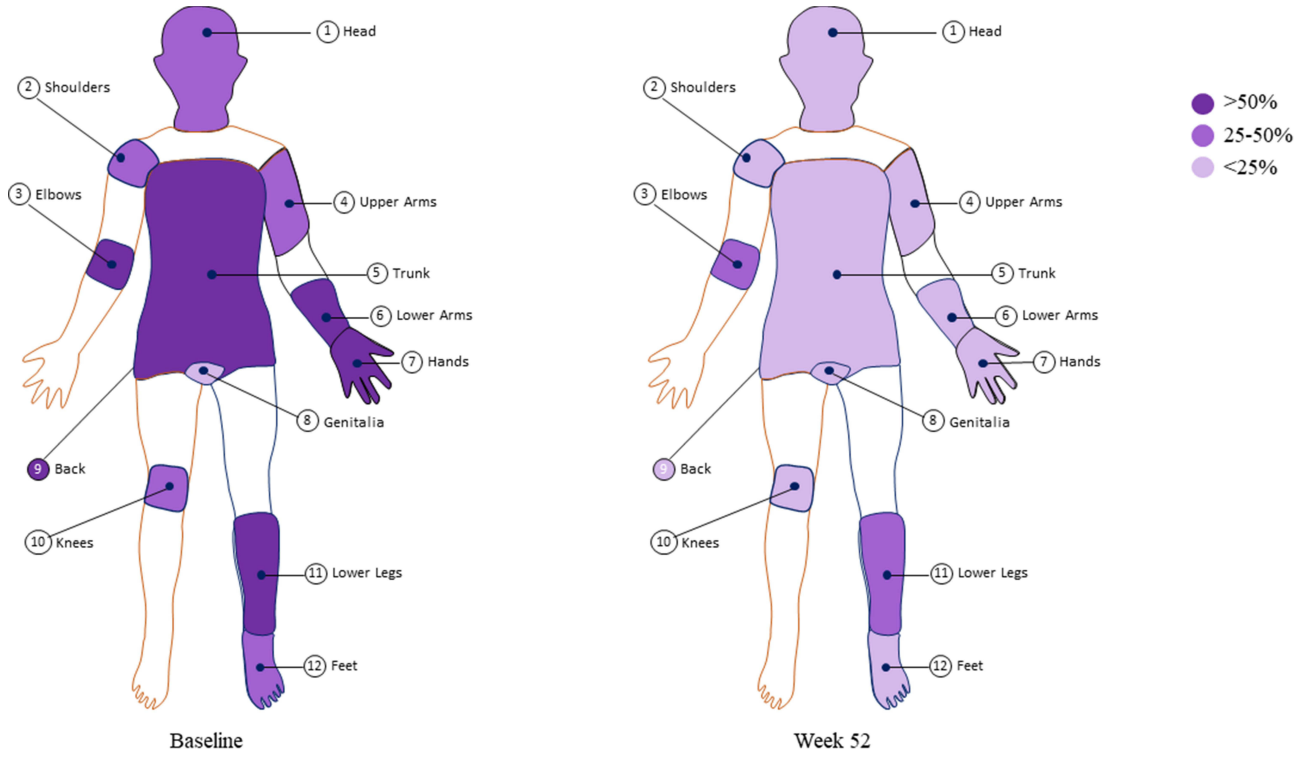

Figure 9 Skin manifestations distribution according to location and total percentage of area affected.

moderate-to-severe plaque psoriasis, and the response rates align closely with those observed in previously reported RWE studies of tildrakizumab[30,48] and the other IL-23p19 inhibitors.[49–54]

In the POSITIVE study, it was shown for the first time that a biologic treatment for plaque psoriasis benefits the life of partners living together with people with psoriasis. Apart from the reduction of the global FamilyPso score, its five domains showed similar improvement.[40,55] Reducing the burden of partners is an important element in the patient's daily life and is adding to their well-being.[26] Interestingly, the impact on the partners improved significantly in only 16 weeks after starting tildrakizumab treatment, and there was a continued improvement over time, with a statistically significant change from week 28 to week 52 ($p < 0.005$).

In order to provide a holistic picture of the impact of psoriatic disease and its treatment, the POSITIVE study also investigated key symptoms and PROs that are likely to be associated with a patient's well-being. Pruritus is a frequent and debilitating symptom of plaque psoriasis, and nearly 90% of patients in this study reported that being free of itching was quite or very much important for them (PBI-10-S; Figure 7).[29,32,56,57] Here, we showed a prominent reduction in pruritus, with nearly 70% of patients reaching >4 points reduction from baseline, and scoring itch intensity as absent or mild. Likewise, burdensome but often underreported symptoms of plaque psoriasis, such as pain and joint pain decreased throughout the study. Interestingly, only half of the patients reporting joint pain at baseline were diagnosed with psoriatic arthritis.

Intense itch and pain can result in sleep deprivation due to night scratching, thereby increasing fatigue.[58] However, to our knowledge, this is the first time that fatigue intensity has been assessed in a prospective study in patients with moderate to severe plaque psoriasis. Although fatigue is more prominent in psoriatic arthritis rather than in plaque psoriasis alone,[59] in our study half of the patients reported a moderate to severe fatigue at baseline, which improved in more than 60% after 52 weeks of tildrakizumab treatment.

Our results confirm that psoriatic disease has a high negative effect on work productivity, and that tildrakizumab is able to improve all four domains, above the MCID score (20% change from baseline).[39] Future correlation analyses may unveil which aspects of the disease are responsible for this negative impact on work productivity.

The positive holistic effect of tildrakizumab, along with other treatment characteristics such as patient friendly dosing regimen are likely responsible for the high treatment satisfaction in the short and long-term (≥70% in all three domains at each time-point).[27,32]

Our findings on the PNQ and PBQ items from the PB-10-S index confirmed that tildrakizumab helped patients to reach their treatment goals that are important for their lives, with more than 70% reporting quite or very much in nine out of the 10 items.

During tildrakizumab treatment, no new or unexpected safety signals were seen. Only one treatment-related AE led to discontinuation of treatment. These findings are in accordance with the well-established favorable safety profile of this drug.[27–32,48]

One important limitation of this study is the open-label design, which could have induced bias in the reporting outcomes. Moreover, no data about MCID for the Physicians' satisfaction and the FamilyPso questionnaires are available to date. Another potential limitation is the number of missing data due to the nature of an interim analysis; however, both LOCF and MI sensitive analysis confirm the results presented based on the observed cases.

Conclusion

This prospective study demonstrated that 52 weeks treatment of tildrakizumab had a significant impact on well-being (WHO-5), skin (PASI), HRQoL (DLQI-R), psoriasis symptoms and burden on the partners (FamilyPsO). Both patients and physicians rated treatment satisfaction highly with a reassuring safety profile.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Statement of Ethics

This study was approved by ethics committees at each participating country and is being conducted in accordance with the ethical principles of the latest version of the Declaration of Helsinki that are consistent with Good Pharmacoepidemiology Practices and local applicable laws and regulations. Written informed consent must be given by patients prior to data collection.

Acknowledgments

We would like to thank Mónica Giménez, PhD, and Eva Mateu, PhD, of TFS HealthScience for editorial assistance and writing support.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This publication was funded by Almirall S.A., Barcelona, Spain.

Disclosure

UM has been an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Aditxt, Almirall, Amgen, Aristea, Boehringer-Ingelheim, Bristol-Myers Squibb, Celgene, Dr. Reddy's, Eli Lilly, Formycon, Immunic, Janssen-Cilag, LEO Pharma, Merck, Sharp & Dohme, MetrioPharm, Novartis, Phi-Stone, Sanofi-Aventis, UCB Pharma, UNION therapeutics. *RS* has been an advisor and/or received speaker honoraria and/or received grants from AbbVie, Almirall, Beiersdorf, Janssen, Leo Pharma, Novartis and UCB. SG has been an advisor and/or received speakers' honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Affibody AB, Akari Therapeutics Plc, Almirall-Hermal, Amgen, Anaptys Bio, Argenx BV, AstraZeneca AB, Biogen Idec, Bioskin, Boehringer-Ingelheim, Celgene, Dermira, Eli Lilly, Forward Pharma, Galderma, Hexal AG, Incyte Inc., Janssen-Cilag, Johnson & Johnson, Kymab, Leo Pharma, Medac, MSD, Neubourg Skin Care GmbH, Novartis, Pfizer, Principia Biopharma, Regeneron Pharmaceutical, Sandoz Biopharmaceuticals, Sanofi-Aventis, Trevi Therapeutics, and UCB Pharma. ZR has been an advisor, investigator, and/or speaker for AbbVie, Alumis, Amgen, Almirall, Avene, Boehringer-Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Eli Lilly, Janssen-Cilag, Leo-Pharma, MEDAC, MSD, Novartis, Pierre Fabre Dermatologie, Pfizer, Sanofi, Takeda and UCB. WW has received speaker and/or consulting honoraria and/or travel refunds from AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, and Sandoz. ED has the following conflict of interests: Advisory Board member, consultant, grants, research support, participation in clinical trials, honorarium for speaking, research support, with the following pharmaceutical companies: AbbVie/Abbott, Almirall, Amgen, Boehringer-Ingelheim, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, MSD-Schering-Plough, Celgene, Lilly, and UCB. J-TM has served as advisor and/or received speaking fees and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Pierre Fabre, Roche, Sanofi, and UCB. P-DG has received speaker and investigator fees or grants from AbbVie, Almirall, Amgen, BMS, Eli Lilly, Flen, Galderma, Janssen, LEO Pharma, Maruho, Meda, Menarini, MSD, Novartis, PellePharm, Pfizer, Serono, UCB and Viatris.

PL received honoraria and/or grants as an investigator, speaker, and/or advisory board member for AbbVie, Almirall, Actelion, Celgene, Janssen, Galderma, Lilly, Sanofi, Leo, UCB, Novartis, Pfizer. LN received consultation fees from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, IBSA, Menarini, Janssen, Novartis, and Sanofi. EdJ has received research grants for the independent research fund of the department of dermatology of the Radboud University

Medical Center Nijmegen, The Netherlands from AbbVie, Leo Pharma, Janssen Pharmaceuticals, Novartis, Pfizer, and UCB and has acted as consultant and/or paid speaker for and/or participated in research sponsored by companies that manufacture drugs used for the treatment of psoriasis including AbbVie, Almirall, Celgene, Galapagos, Janssen Pharmaceutica, Leo Pharma, Lilly, Novartis, Sanofi, and UCB. All funding is not personal but goes to the independent research fund of the department of dermatology of Radboud University Medical Center Nijmegen (Radboudumc), The Netherlands. SM is employed as a scientific officer at the International Federation of Psoriasis Associations (IFPA), receiving no individual compensation. In this role, IFPA has engaged in consultancy services for pharmaceutical companies, including Boehringer Ingelheim, Novartis, Almirall, and UCB. Over the past 12 months, IFPA has received grants and funding from AbbVie, Almirall, Amgen, Bristol Myers Squibb, Boehringer Ingelheim, Janssen, Leo Pharma, Eli Lilly, Novartis, Pfizer, UCB, and Takeda. VK, EM, AD, KGdJ, and IK are employees of Almirall. MA has received consulting fees and/or speaker honoraries and/or institutional research support from the following pharmaceutical companies manufacturing drugs for psoriasis: AbbVie, Almirall, Amgen, Biogen, Boehringer, Bristol Myers Squibb, Celgene, Celltrion, Centocor, Eli Lilly, Fresenius, GSK, Hexal, Janssen, Klinge, LEO, MC2, Medac, Merck, MSD, Novartis, Pfizer, Sandoz, Sun, UCB and Viatris. The authors report no other conflicts of interest in this work.

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