Received: 13 December 2022 | Accepted: 20 April 2023

DOI: 10.1111/jdv.19229

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

ORIGINAL ARTICLE

Tildrakizumab improves high burden skin symptoms, impaired sleep and quality of life of moderate-to-severe plaque psoriasis patients in conditions close to clinical practice

Antonio Costanzo[1,2] | Mar Llamas-Velasco[3] | Gabriella Fabbrocini[4] | Aldo Cuccia[5] | Raquel Rivera-Diaz[6] | Kristian Gaarn Du Jardin[7] | Ismail Kasujee[7] | Lluís Puig[8] | José Manuel Carrascosa[9]

[1]Section of Dermatology, Department of Biomedical Sciences, Humanitas University, Milan, Italy

[2]Dermatology Unit, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy

[3]Department of Dermatology, Hospital Universitario de la Princesa, Madrid, Spain

[4]Section of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy

[5]Unit of Dermatology, San Donato Hospital, Arezzo, Italy

[6]Department of Dermatology, Hospital Universitario 12 de Octubre, Universidad Complutense, Madrid, Spain

[7]Almirall R&D, Barcelona, Spain

[8]Department of Dermatology, IIB SANTPAU, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[9]Department of Dermatology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain

Correspondence
Antonio Costanzo, Section of Dermatology, Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy.
Email: antonio.costanzo@hunimed.eu

Funding information
Almirall R&D

Abstract

Background: Tildrakizumab (TIL) is an interleukin (IL)-23p19 inhibitor for the treatment of moderate-to-severe plaque psoriasis with long-term efficacy and safety demonstrated in Phase III trials. Studies conducted in conditions closer to clinical practice are needed.

Objectives: The TRIBUTE study (open-label, Phase IV) assessed the efficacy and impact on health-related quality of life (HRQoL) of TIL 100 mg in adult moderate-to-severe psoriasis patients (naïve to IL-23/Th17 pathway inhibitors) in conditions similar to clinical practice.

Methods: Key efficacy measure was Psoriasis Area Severity Index (PASI). HRQoL was evaluated using the Dermatology Life Quality Index (DLQI) and Skindex-16. Additional patient-reported outcomes included Pain-, Pruritus- and Scaling-Numerical Rating Scale (NRS), Medical Outcome Study (MOS)-Sleep, Work Productivity and Activity Impairment (WPAI), Patient Benefit Index (PBI) and Treatment Satisfaction Questionnaire for Medication (TSQM).

Results: One hundred and seventy-seven patients were enrolled (six patients did not complete the study). After 24 weeks, the proportion of patients achieving PASI scores ≤ 3, PASI 75, PASI 90 and DLQI 0/1 was 88.4%, 92.5%, 74.0% and 70.4%, respectively. Skindex-16 overall score improved (mean absolute change from baseline, MACB [95%CI]: −53.3 [−58.1, −48.5]). Significant benefits (MACB [95%CI]) were found on pruritus-, pain- and scaling-NRS scores (−5.7 [−6.1, −5.2], −3.5 [−4.1, −3.0] and −5.7 [−6.2, −5.2], respectively), MOS-Sleep (−10.4 [−13.3, −7.4] Sleep problems Index II) and WPAI (−36.4 [−42.6, −30.2] activity impairment, −28.2 [−34.7, −21.7] productivity loss, −27.0 [−32.9, −21.1] presenteeism and −6.8 [−12.1, −1.5] absenteeism). 82.7% of patients reported PBI ≥ 3 and the mean (SD) global TSQM score was high (80.5 [18.5]). Only one serious treatment-emergent adverse event was reported (not-related to TIL).

Conclusions: TIL 100 mg treatment after 24 weeks in conditions close to real clinical practice showed a quick and high improvement in psoriasis signs and HRQoL. Patient reported improvements in sleep outcomes and work productivity, relevant benefits and high treatment satisfaction. The safety profile was favourable and consistent with Phase III trials.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease that has substantial negative impact on both physical and psychological health.[1] Chronic plaque psoriasis is the most common form of psoriasis and affects 2%–4% of the population in Western countries.[2] Although the mechanisms underlying the pathogenesis of chronic plaque psoriasis are not entirely defined, therapeutics targeting the interleukin (IL)-23/IL-17 axis have shown high efficacy.[3] Among these, the humanized monoclonal antibody tildrakizumab (TIL), targeting the IL-23p19 subunit, is a systemic treatment approved for adult patients with moderate-to-severe plaque psoriasis.[4] Tildrakizumab has demonstrated efficacy and favourable safety profile in treating psoriasis in large scale randomized controlled Phase III trials (reSURFACE 1 and reSURFACE 2) for up to 5 years.[5,6] However, regulatory randomized controlled trials (RCTs) often impose stringent inclusion and exclusion criteria. Consequently, RCT patient populations often display higher baseline disease severity and fewer comorbidities, such as cardiovascular disease, compared to patients in real life clinical practice, and concerns have been raised about the external validity of these trials. In fact, recent large registry studies have demonstrated that 78.4% of patients receiving systemic treatment for psoriasis in clinical practice would not be eligible for regulatory RCTs.[7-9] Thus, the collection of data closer to the everyday clinical practice becomes essential in order to properly characterize the benefits of modern therapy to psoriasis patients.

Besides high burden physical symptoms such as pruritus and skin pain, psoriasis negatively impacts multiple aspects of patients' lives including sleep, work, leisure, as well as health-related quality of life (HRQoL) and people suffering from this disease often experience poor functional and emotional well-being.[10-15] Thus, in order to accurately determine the holistic value and benefits of modern treatments, psoriasis studies should assess multiple aspects of not only physical symptoms of psoriasis, but also patients' daily life such as sleep, work and key HRQoL domains.[16]

TRIBUTE is a 24-week international, multicentre, open label Phase IV clinical study enrolling patients with moderate-to-severe chronic plaque psoriasis and aiming to assess efficacy of TIL 100 mg and impact on HRQoL in conditions similar to real-world clinical practice. Moreover, TRIBUTE evaluated the effect of TIL on a variety of key PROs including pruritus, skin pain, scaling, sleep and work and activity impairment, patient benefit and overall treatment satisfaction.

MATERIALS AND METHODS

Study design

The study was an international (Spain and Italy), multicentre, open label phase IV clinical study in patients with moderate-to-severe chronic plaque psoriasis naïve to IL-23/Th17 pathway inhibitors (including IL-12/23p40, IL-17, and/or IL-23p19 inhibitors). The eligibility criteria used in this study resemble clinical practice in Spain and Italy and patients were treated according to the Summary of Product Characteristics (SmPC) of TIL (the selection criteria are described in Table S1).

Tildrakizumab was administered at the approved dose of 100 mg via subcutaneous injection at Week 0 (Day 1), and 4 and every 12 weeks thereafter (corresponding to Week 16).[6]

The study was registered at The European Union Clinical Trials Register (Eudract No. 2019-002804-42) and the study protocol was approved by the independent ethics committees of the participating medical centres.

Patients

Patients ($n = 177$) were enrolled across 40 study centres in Europe (20 centres in Spain and 20 in Italy). Adult patients aged 18 years or older, were eligible to participate in the study if they had diagnosis of chronic plaque psoriasis for at least 6 months. Patients had to have at least moderate plaque psoriasis at the screening visit.[17,18] Non-treatment-naïve patients had to follow the corresponding wash-out period according to the current or last treatment for psoriasis. All patients gave written informed consent before any study-related tests was done. The full list of inclusion and exclusion criteria are described in detail in Table S1.

Procedures

The efficacy and impact of TIL 100 mg on HRQoL was assessed by PASI and DLQI (co-primary endpoints) at Week 24 after three doses. The secondary efficacy endpoints included assessment of DLQI and DLQI-R, PASI, Physician's Global Assessment (PGA), body surface area (BSA) scores and pruritus-numerical rating scale (NRS), pain-NRS, and scaling-NRS, Skindex-16, Medical Outcomes Study [MOS]-Sleep, Work Productivity and Activity Impairment (WPAI), Patient Benefit Index (PBI) and Treatment Satisfaction Questionnaire for Medication (TSQM). The safety and tolerability endpoints included: vital signs, physical examination, vital signs, safety laboratory and Treatment-Emergent Adverse Events (TEAEs).

The PASI instrument assesses three severity parameters (erythema, induration and scaling) for each body region. The sum of the three severity scores is multiplied by the area score for each body region; the scores for each body region are then summed to produce a total score ranging from 0 to 72.[19]

The DLQI questionnaire is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired.[20] DLQI-R scoring is the traditional DLQI score multiplied by a conversion factor that eliminates the not relevant responses (NRRs) items of the DLQI, and thereby adjusts the total score to the relevant items.[21]

The BSA assessment measures the total area of the body affected by psoriasis.

The PGA is the assessment by the Investigator of the overall disease severity. The PGA is a 6-point scale ranging from 0 (clear) to 5 (severe).[19]

The pruritus-NRS, pain-NRS, and scaling-NRS scores range from 0 to 10. The cut-off point NRS <3 was applied to identify patients with mild itch or pain.[23]

The Skindex-16 measures the quality of life of patients with skin diseases. It includes three domains (emotion, functioning and symptom) and an overall score ranging from 0 (best quality of life) to 100 (worst quality of life).[23]

The MOS-Sleep questionnaire consists of 12 items leading to six domains (sleep disturbance, sleep adequacy, daytime sleepiness, snoring, being awakened by shortness of breath or by a headache, and quantity of sleep), ranging from zero to 100 (with the exception of sleep quantity, that was scored continuously from 0 to 24 h). Higher scores on the MOS-Sleep reflects more of the attribute indicated by the subscale name. The MOS-Sleep Index II is an aggregate measure of four sleep domains (sleep disturbance, awakening short of breath or with headache, sleep adequacy and somnolence). The score ranges from 0 to 100, with higher scores indicating worse sleep problems. The minimal clinically important difference (MCID) is a change of ≥5.1 and a population norm has been estimated at 25.8.[25,26]

The WPAI questionnaire consists of six questions and four scores are derived from the questions: percent absenteeism (work time missed), percent presenteeism (impairment at work), percent work productivity loss (overall work impairment due to absenteeism and presenteeism), and percent activity impairment (activities performed outside of work). Higher scores indicate a higher level of impairment. The MCIDs for both (work productivity loss and the activity impairment domains) has been estimated to be 20% in patients with psoriasis.[28]

The PBI questionnaire assesses patient-relevant treatment needs and benefits. The first part of the PBI corresponds to the Patient Needs Questionnaire (PNQ), where the patients rate the importance of each treatment goal on a Likert scale ranging from 0 = 'not at all [important]' to 4 = 'very [important]'. The second part corresponds to the patient benefit questionnaire (PBQ) and it consists of the same items as the PNQ, but the instructions differ. Here, the patients rate the extent to which the treatment needs have been achieved by therapy using a Likert scale ranging from 0 = 'treatment did not help at all' to 4 = 'treatment helped a lot'. In addition, the Likert scale contains the option 'does not apply to me' in the PNQ and the option 'did not apply to me' in the PBQ. The PBI score ranges from 0 (no benefit) to 4 (maximal benefit) and a PBI ≥ 1 is considered as relevant benefit from treatment.[29,30]

The TSQM is designed to measure patients' satisfaction with medication. It contains four subscales ranging from 0 to 100, with higher scores representing higher satisfaction on that domain.

Statistical analysis

The analyses were performed in a total of 177 patients, corresponding to the safety analyses set (SAF) population and the Intention-to-treat (ITT) population.

All parameters were either nominally or ordinally scaled, tabulated by absolute frequencies and percentages were calculated as observed. Presented analysis was based on observed cases (OC). Sensitivity analyses using the non-responder imputation (NRI) for absolute PASI, DLQI 0/1 and DLQI-R 0/1 scores were also performed.

RESULTS

Subject disposition and baseline characteristics

A total of 198 patients were assessed for eligibility in the TRIBUTE study (21 were screening failures and were not included in the analysis population). The remaining 177 patients were included in the safety and ITT populations.

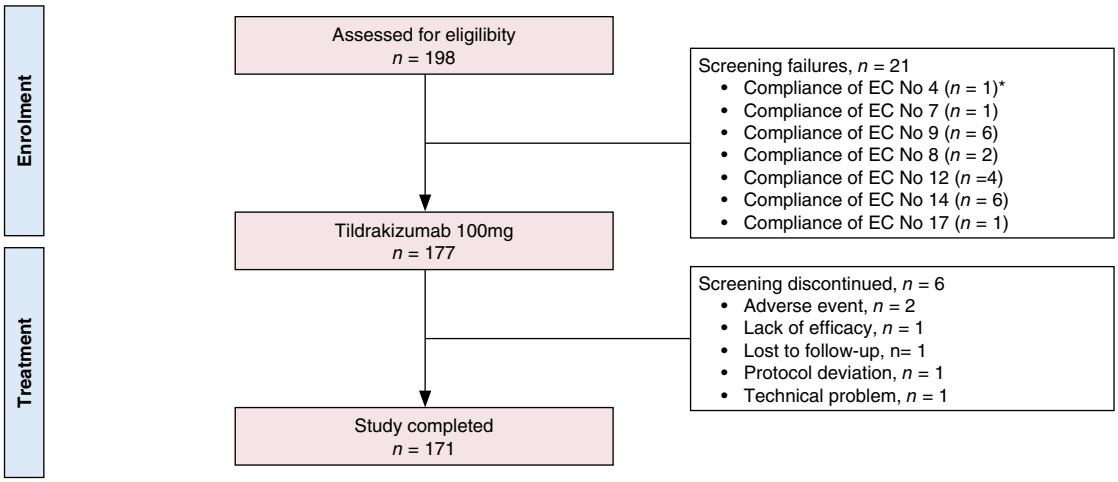

FIGURE 1 Patient disposition flow chart. *IC No.4 of the Spanish protocol. EC, exclusion criteria; IC, inclusion criteria; No, number.

The patients' disposition is shown in Figure 1. Most patients (96.6%) continued TIL treatment at 24 weeks. Demographics and baseline characteristics are shown in Table 1. Out of 177 patients, 113 patients (63.8%) had experienced a past medical condition at screening visit or suffered from comorbidities with hypertension being the most prevalent (32 patients, 18.1%), followed by depression (10 patients, 5.6%) and asthma (nine patients, 5.1%).

Clinical response

Psoriasis area and severity index (PASI)

The mean (SD) PASI (co-primary endpoint) score decreased from 16.2 (8.5) at baseline to 1.0 (1.7) at Week 24 (Figure 2a), with a mean (95% CI) absolute change from baseline of −15.1 (−16.3, −13.8). The proportion of patients achieving absolute PASI scores of ≤5, ≤3 and ≤1 increased from baseline to Week 24 (96.0%, 88.4% and 66.5%, respectively; Figure 2b). The percentage of patients achieving PASI 75 and PASI 90 at Week 24 were 92.5% and 74.0%, respectively. Absolute PASI scores of ≤5, ≤3 and ≤1 by NRI imputation are described in Table S2.

Body surface area (BSA)

The mean (SD) absolute BSA score decreased from 21.7 (13.8) at baseline to 1.8 (3.4) at Week 24, with a mean (95% CI) absolute change from baseline of −19.9 (−22.0, −17.8).

Physician's global assessment (PGA)

The mean (SD) PGA score decreased from 2.9 (0.8) at baseline to 0.6 (0.7) at Week 24 (Figure 2c), with an overall mean (95% CI) absolute change from baseline of −2.3 (−2.5, −2.2). The proportion of patients achieving PGA scores of 0 or 1 with at least a 2-grade reduction from baseline was 78.0% at Week 24 (Figure 2d). At Week 24, the absolute PGA score ranging from 0 (clear) to 5 (severe) was achieved by 54.9%, 37.6%, 5.2%, 1.7%, 0.6% and 0% of patients, respectively.

Heath-related quality of life

Dermatology life quality index (DLQI) and DLQI-relevant (DLQI-R)

Both DLQI and DLQI-R mean (SD) absolute scores decreased from 14.1 (7.4) and 14.9 (7.5) at baseline to 2.0 (3.6) and 2.3 (4.0) at Week 24, respectively, with a mean (95% CI) absolute change from baseline of −12.1 (−13.3, −10.8) score in DLQI (co-primary endpoint) and −12.6 (−13.9, −11.3) score in DLQI-R (Figure 3a). The percentage of patients achieving DLQI 0/1 scores (DLQI and DLQI-R) at Week 24 was 70.4% and 59.1%, respectively (Figure 3b). When imputing missing values using NRI, these percentages were 63.3% and 53.1%, respectively (Tables S3 and S4).

TABLE 1 Demographic and other baseline characteristics (SAF population).

Characteristics	*N*	Mean (SD)/*n* (%)
Age (years)	177	44.6 (12.4)
<65 years		167 (94.4%)
Sex (male)	177	123 (69.5%)
BMI (kg/m^2)	177	27.5 (5.7)
Time since psoriasis diagnosis (years)	177	15.6 (12.4)
Prior exposure to biologic systemic therapy for psoriasis, *n* (%)	176	37 (20.9%)
PASI	177	16.24 (8.5)
BSA	177	21.7 (13.8)
PGA	177	2.9 (0.8)
DLQI	168	14.1 (7.4)
DLQI-R	168	14.9 (7.5)
Pruritus-NRS	174	7.4 (2.0)
Pain-NRS	174	4.6 (3.1)
Scaling-NRS	173	7.4 (2.0)
Work productivity and activity impairment		
% Work time missed (absenteeism)	107	11.1 (22.6)
% Impairment while working (presenteeism)	113	35.0 (30.1)
% Total work impairment	107	40.2 (32.5)
% Total activity impairment	146	45.5 (32.1)
Medical outcomes study sleep scale		
Adequacy	173	52.5 (25.7)
Disturbance	173	44.7 (24.4)
Quantity (h)	167	6.5 (1.1)
Shortness of breath/headache	173	18.4 (21.9)
Snoring	173	43.4 (32.2)
Somnolence	173	34.3 (20.2)
Sleep Problems Index II	173	39.8 (20.3)
Skindex-16, overall	168	68.5 (25.0)
Emotion subscale	168	74.2 (25.4)
Functioning subscale	167	57.0 (32.5)
Symptom subscale	168	73.0 (24.1)

Abbreviations: BSA, body surface area; DLQI, Dermatology Life Quality Index; DLQI-R, DLQI-Relevant; NRS, numerical rating scale; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; PNQ, Patient Needs Questionnaire; SAF, safety analyses set; SD, standard deviation. [Correction added on 21 July 2023 after first online publication: The author has revised the data in Medical outcomes study sleep scale.]

Skindex-16

The mean (SD) scores decreased from baseline to Week 24: overall score (68.5 [25.0] to 14.9 [21.8]), emotions (74.2 [25.4] to 17.2 [23.9]), symptoms (73.0 [24.1] to 16.0 [22.8]), and

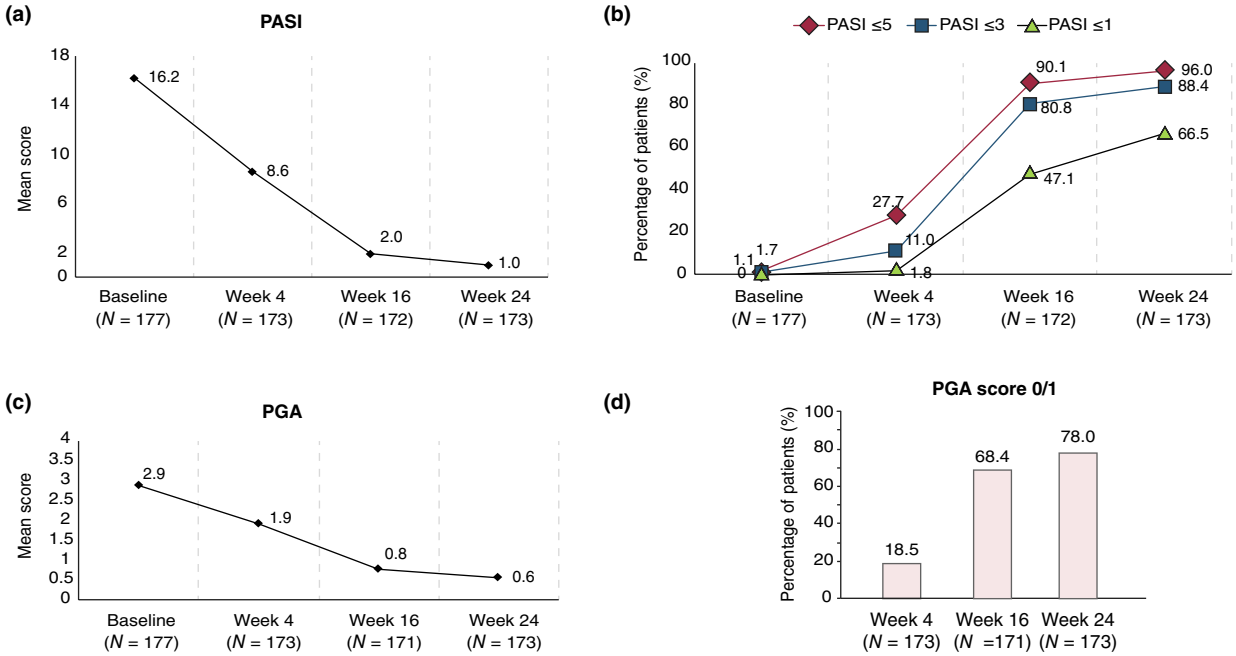

FIGURE 2 (a) Absolute total mean PASI score from baseline to Week 24; (b) PASI ≤ 5, PASI ≤ 3 and PASI ≤ 1 from baseline to Week 24; (c) Absolute total mean PGA score from baseline to Week 24; (d) Percentage of patients achieving PGA score 0/1 and at least a 2-grade reduction from baseline; ITT population. ITT, intention-to-treat; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; SD, standard deviation.

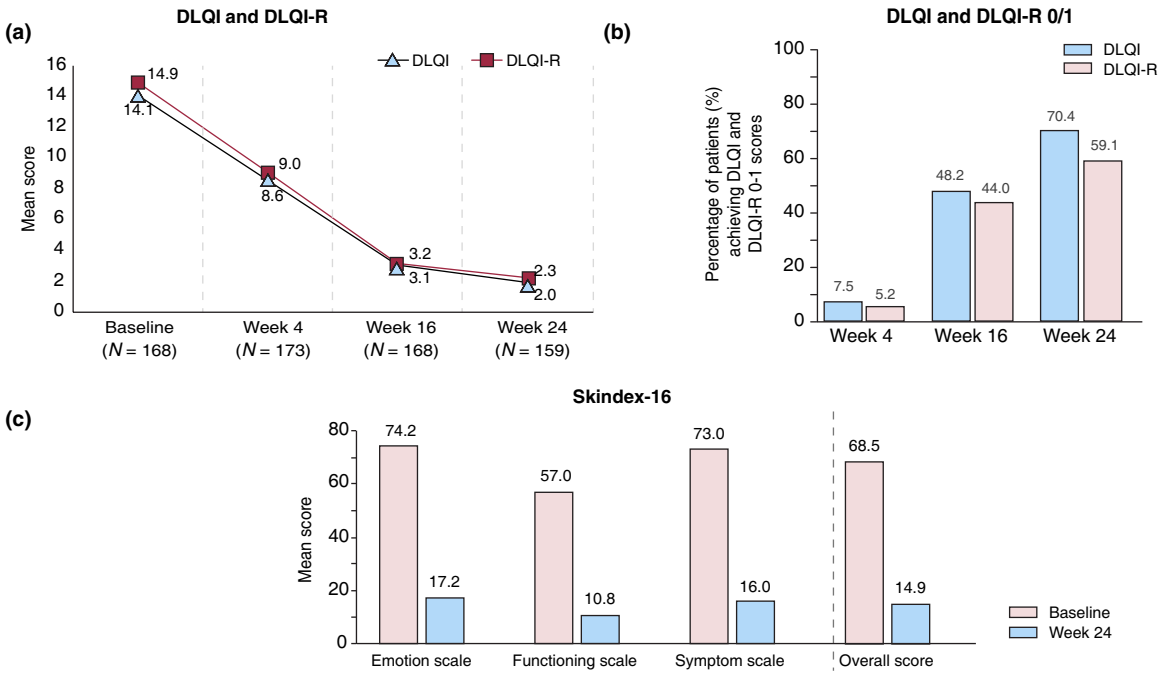

FIGURE 3 (a) Absolute total mean DLQI and DLQI-R scores from baseline to Week 24; (b) Proportion of patients achieving absolute DLQI and DLQI-R scores between 0/1 from Week 4 to 24; (c) Absolute mean scores in the Skindex-16 questionnaire at baseline and Week 24; ITT population. DLQI, Dermatology Life Quality Index; DLQI-R, DLQI-Relevant; ITT: intention-to-treat.

functioning domains (57.0 [32.5] to 10.8 [21.6]; see Figure 3c). The mean (95% CI) Skindex-16 absolute changes from baseline to Week 24 in the overall score, emotions, symptoms, and functioning domains were −53.3 (−58.1, −48.5), −56.5 (−61.6, −51.5), −57.7 (−62.7, −52.7), and −45.6 (−51.1, −40.0), respectively.

Additional patient-reported outcomes

Pruritus-NRS, Pain-NRS and Scaling-NRS

The proportion of patients achieving pruritus-NRS <3 and pain-NRS <3 increased from 27 (15.7%) and 75 (43.9%) at Week 4 to 124 (76.5%) and 135 (84.9%) at Week 24, respectively (Figure 4a). The pruritus-NRS, pain-NRS and scaling-NRS scores decreased from baseline to Week 24 (mean [SD]: 7.4 [2.0] to 1.7 [2.3] pruritus-NRS score, 4.6 [3.1] to 1.1 [2.1] pain-NRS score, and 7.4 [2.0] to 1.8 [2.9] scaling-NRS score; Figure 4b). After 24 weeks of treatment, patients reported an absolute mean (95% CI) change from baseline of −5.7 (−6.1, −5.2), −3.5 (−4.1, −3.0), −5.7 (−6.2, −5.2) in pruritus-NRS, pain-NRS and scaling-NRS scores, respectively.

MOS-Sleep

Results from the MOS-Sleep questionnaire showed a decrease after 24 weeks of treatment with TIL in the domain of disturbance, adequacy and somnolence (according to change from baseline 95% CI; Figure 5). The mean (SD) Sleep Problems Index II at baseline was 39.8 (20.3) and decreased to 28.5 (15.6) at Week 24 with an absolute mean (95% CI) change from baseline of −10.4 (−13.3, −7.4).

Work productivity and activity impairment (WPAI)

The work productivity and activity impairment improved after 24 weeks of treatment with TIL (mean (SD) from baseline to Week 24: 11.1 [22.6] to 3.1 [15.6] percent work time missed [absenteeism], 35.0 [30.1] to 5.8 [14.9] percent impairment while working [presenteeism], 40.2 [32.5] to 8.1 [19.7] percent overall work impairment and 45.5 [32.1] to 8.3 [16.2] percent activity impairment; Figure 6). The largest improvement was observed on the patient's regular daily activities impairment, with a mean (95% CI) absolute change from baseline of −36.4 (−42.6, −30.2). A mean (95% CI) absolute change from baseline of −28.2 (−34.7, −21.7) in the overall work impairment, −27.0 (−32.9, −21.1) in the impairment while working (presenteeism) and −6.8 (−12.1, −1.5) in work time missed (absenteeism) was observed.

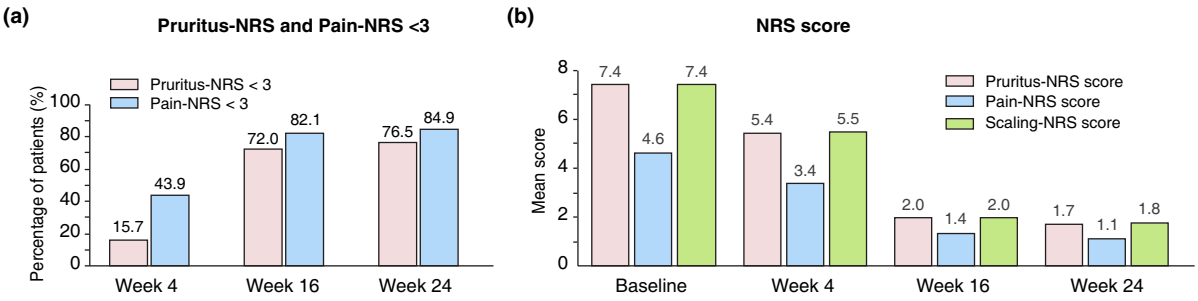

FIGURE 4 (a) Proportion of patients achieving absolute pruritus-NRS < 3 and pain-NRS < 3 at all study visits; (b) Absolute NRS score from baseline to Week 24 in the pruritus-NRS, pain-NRS and scaling-NRS scores; ITT population. ITT, intention-to-treat; NRS, numerical rating scale.

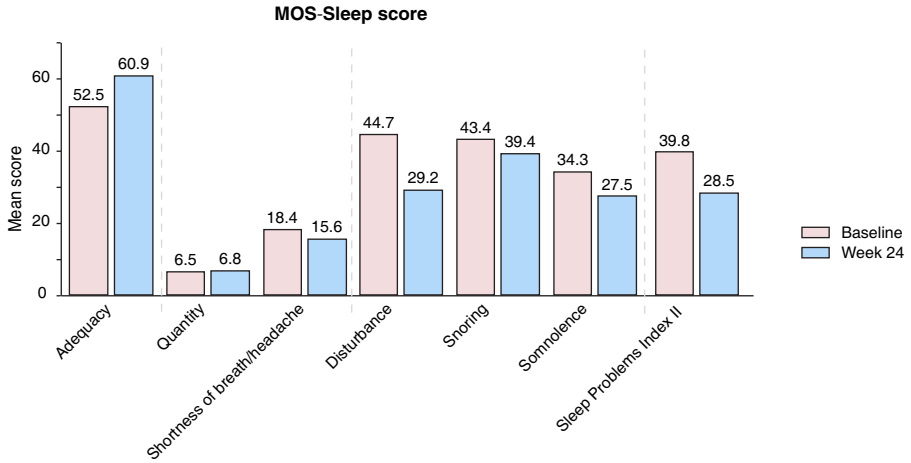

FIGURE 5 Absolute mean values in the MOS-Sleep score by domains and Sleep problems Index II at baseline and Week 24; ITT population. ITT, intention-to-treat; MOS, medical outcomes study.

Patient benefit index (PBI)

The therapy goals are described in the PNQ, the mean scores by each item of the questionnaire are shown in Table S5. The top three treatment goals with the highest mean (SD) score were 'to be healed of all skin defects' (3.9 [0.4]), 'to be free of itching' (3.8 [0.5]) and 'to regain control of the disease' (3.8 [0.6]). All the top three treatment goals were considered important/very important as graded by more than 95% of the population.

The PBQ scores are summarized in Figure 7. The highest agreements were achieved in 'to be confident in the therapy', 'to be able to lead a normal day life' and 'to regain control do the disease'.

At Week 24, the mean (SD) PBI total score was 3.4 (0.6). A total of 98.7% of patients (148 out of 150 patients) achieved PBI total score ≥ 1, whereas 82.7% of patients (124 patients) achieved a total score of ≥3.

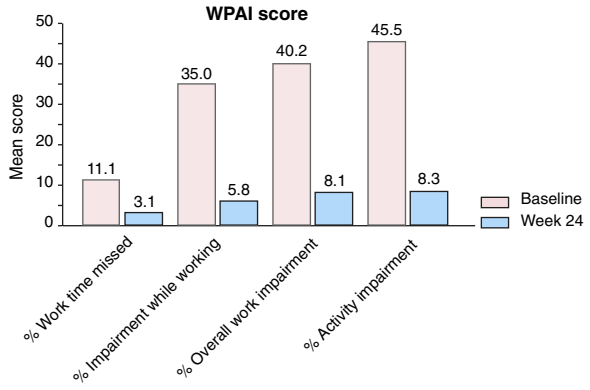

FIGURE 6 Absolute mean values in the WPAI score at baseline and Week 24; ITT population. ITT, intention-to-treat; WPAI, work productivity and activity impairment.

Patient's treatment satisfaction (TSQM)

At Week 24, patients reported the highest satisfaction in the side-effect's subscale (mean [SD] score of 96.8 [12.5]), followed by global satisfaction (mean [SD] score of 80.5 [18.5]), convenience (mean [SD] score of 79.6 [16.2]) and effectiveness (mean [SD] score of 77.6 [23.3]; Figure 8).

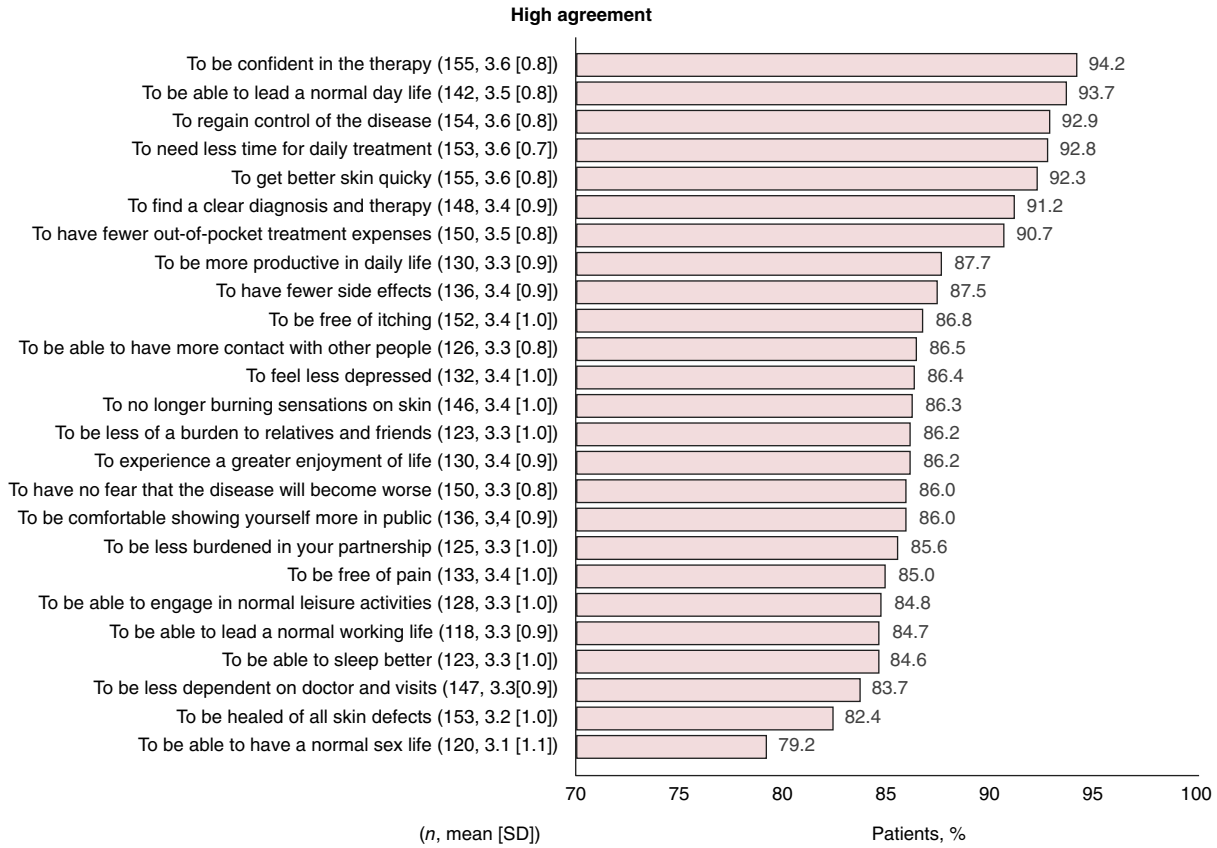

FIGURE 7 Percentage of patients with high agreement (PBQ, by all items) at Week 24, sorted from higher to lower treatment needs achieved; ITT population. ITT, intention-to-treat; *n*, number of patients who completed this item; PBQ, Patient Benefit Questionnaire; SD, standard deviation. Percentage calculation excluded missing and 'does not apply to me' answers. Possible answers include 0 = not at all/does not apply to me, 1 = somewhat, 2 = moderately, 3 = quite, and 4 = very. High agreement is defined as positive responses including answers of 'quite' or 'very'.

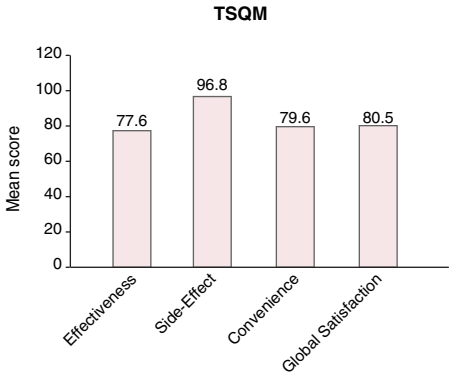

FIGURE 8 Absolute mean values in the TSQM score at Week 24; ITT population. ITT, intention-to-treat; TSQM, patient's treatment satisfaction.

Safety assessments

A total of 177 patients received at least one dose of TIL 100 mg and were included in the safety population. The exposure to study medication ranged from 1 day to 134 days, with a mean (SD) treatment duration of 104.8 (15.2) days. Up to Week 24, 52 out of 177 patients (29.4%) had at least one TEAE. The most frequent TEAEs were headache (6.2%), coronavirus infection (2.3%) and back pain (2.3%; see Table 2). All TEAEs occurred during the study are displayed in Table S6. Among the four patients with coronavirus events, three of them were resolved. Two patients (1.1%) reported a TEAE that led to study discontinuation. One patient (0.6%) had a serious TEAE of coronavirus infection that led to death although it was considered not related to the study drug. The other patient discontinued the study because of an erythrodermic psoriasis event that was considered possibly related to TIL.

Table 3 shows TEAE of special interest. No malignancy or major adverse cardiovascular events (MACE) occurred in this study.

TABLE 2 Most common TEAEs (>1%; SAF population).

System organ class term, Preferred term	Total events/*n* (%) (*N* = 177)
Gastrointestinal disorders	
Nausea	2/2 (1.1%)
Vomiting	3/2 (1.1%)
General disorders and administration conditions	
Asthenia	2/2 (1.1%)
Infections and infestations	
Corona virus infection	4/4 (2.3%)
Musculoskeletal and connective tissue disorders	
Back pain	5/4 (2.3%)
Nervous system disorders	
Dizziness	3/2 (1.1%)
Headache	14/11 (6.2%)
Migraine	3/2 (1.1%)
Skin and subcutaneous tissue disorders	
Pruritus	3/3 (1.7%)

Abbreviations: SAF, safety analyses set; TEAE, treatment-emergent adverse event.

TABLE 3 TEAEs of special interest (SAF population).

TEAEs of special interest (preferred term)	Number of TEAEs	Number of patients with TEAE	% of patients with TEAE
Drug hypersensitivity	1	1	0.6%
Injection site hypersensitivity	1	1	0.6%
Corona virus infection	4	4	2.3%

Abbreviations: SAF, safety analyses set; TEAE, treatment-emergent adverse event.

DISCUSSION

Here, we present the results of the Phase IV clinical TRIBUTE study to assess the efficacy, safety and impact on HRQoL of TIL 100 mg in patients with moderate-to-severe chronic plaque psoriasis and without previous biological treatment with an IL-23/Th17 pathway inhibitor at Week 24, in conditions close to the clinical practice. The eligibility criteria used in this study resemble clinical practice in Spain and Italy and patients were treated according to the SmPC of TIL. Baseline PASI and DLQI values were lower than those reported in RCT, and comparable to real-world evidence (RWE) cohorts. Moreover, included patients have a broad variety of comorbidities and medical history.

Under these circumstances, treatment with TIL 100 mg displayed high PASI response rates. Almost nine out of 10 patients achieved a clinically meaningful target of PASI < 3 and two thirds achieved PASI < 1, meaning that most of patients achieved a highly relevant treatment goal after 24 weeks of treatment.[31] Additionally, patients experienced a significant improvement in burden of disease; at Week 24 DLQI score was 0/1, indicating no impairment of HRQoL, in 70% of patients.

A limitation of the DLQI is that items marked as 'not relevant' are scored as 0 = 'no impairment', which may occur in up to 40% of psoriasis patients.[31,32] Large surveys indicate that patients who declare an item as 'not relevant' in many instances have a higher disease-related burden and may in fact be too impaired by the skin disease to take part in certain areas of life. Thus, for patients with 'not relevant' responses, it might be more difficult to fulfil the DLQI > 10 required by clinical guidelines to become candidates for systemic treatment. To avoid the bias associated with the NRR option, the DLQI-R score that adjusts the total score to the relevant items has been assessed.[23,31] Using this more conservative and perhaps less biased score, most patients (59%) still did not appear to have HRQoL impairment (DLQI-R score 0/1) at Week 24.

The PASI 90 and DLQI 0/1 response rates at Week 24 (74% and 70.4%, respectively) appeared higher in the present

study than in the phase III, reSURFACE trials (52%/56% with PASI 90 response and 52%/54% of patients with DLQI score 0/1 and at Week 28 in reSURFACE 1 and 2, respectively).[33] Unlike the reSURFACE trials, the response rates in the TRIBUTE study seem similar to the effectiveness found in some RWE studies.[34-36] Reasons for these differences in response rates might be different time period (2012 vs. 2020), different standard of care and increased knowledge of psoriasis. However, standard measurements in clinical trials would make clinical research more reproducible and comparable than RWE studies. It should be mentioned that the higher baseline disease severity and more homogeneous patient population often seen in regulatory Phase III trials speak against lower response rates in the reSURFACE trials.

The PASI 75 and PASI 90 response rates reported for the other IL-23p19 inhibitors, guselkumab and risankizumab, in real-life settings appear consistent with those observed in this study with TIL.[37-42] Likewise, recent real world evidence studies reporting PASI response rates for all three IL-23p19 inhibitors from the same cohort have found very similar effectiveness.[35,43]

In addition to the DLQI questionnaire, the Skindex-16 measure was utilized in the TRIBUTE study to comprehensively assess the impact on HRQoL. Compared to DLQI, the Skindex questionnaire may better capture emotional impact of psoriasis and treatment according to patients' criteria.[44] Moreover, comparisons of the measurement properties of the DLQI, DLQI-R and Skindex-16 outcomes for patients with mild symptoms showed that DLQI and DLQI-R seemed to be insensitive to small impairments in HRQoL.[45] Evidence for the benefits of modern biological treatment, particularly Il-23p19 inhibition, on HRQoL using the Skindex questionnaire is extremely limited in psoriasis. Thus, for the first time, the results of this study showed a clear benefit on several Skindex-16 domains, including emotion, for patients treated with an IL-23p19 inhibitor.

Although surprisingly under-recognized until recent years, pruritus is a frequent symptom in psoriasis (up to 96% of patients with moderate-to-severe psoriasis reported pruritus[46]). However, despite this prevalence, there is a paucity of clinically relevant data regarding pruritus in psoriasis as well as its response to treatment, and it has been pointed out that physicians may not routinely query their psoriasis patients about it.[15,24,46-49] Pruritus has a multidimensional nature, being a predictor of depressive symptoms and anxiety, negatively impacting daily activities (e.g. concentration, sleep, attend work or school), and leading to a deterioration in quality of life. Skin pain is a prominent symptom of psoriasis observed in 70%–96% of patients,[24,50] and together with other psoriasis-related sensory skin symptoms has a negative impact on functions such as sleep, mood, and enjoyment of life.[10] In this study, treatment with TIL showed a prominent, early reduction in pruritus, pain, and scaling (after only two doses), and more than seven out of 10 patients reported mild pruritus and more than eight out of 10 patients reported skin pain-NRS <3 at Week 24.[22]

Pruritus, pain and burning sensations associated with psoriatic lesions may have a direct effect on the development of sleep disturbances causing difficulties with falling asleep and awakening,[51,52] and these symptoms are thought to be the main predictors of impaired sleep together with chronic obstructive pulmonary disease and sleep apnoea.[51-54] Some reports indicate that sleep disorders are not correlated with psoriasis severity, suggesting that PASI alone cannot be used for the prognosis of sleep disorders.[55] In general, patients with moderate-to-severe psoriasis have substantial sleep impairment, and unsurprisingly, sleep impairment is strongly linked with decreased quality of life.[56] The present study assessed patient-reported sleep problems using the MOS-Sleep scale, and after 24 weeks of TIL treatment, significant improvements in the sleep domain of disturbance and somnolence and an increase in adequacy were determined. The mean at baseline of the composite score MOS sleep problem Index II was 39.8, significantly worse than a general population norm (25.8), suggesting impaired sleep of psoriasis patients in line with previous reports.[11,12,52,54] At Week 24, TIL treatment significantly improved the score to 28.5, approaching the general population norm (25.8).[25] The mean improvement was significantly higher than 5.1 (mean change of −10.4 [95% CI: −13.3, −7.4]), which is described as the MCID.[26] The effect of biological therapy on sleep impairment in psoriasis has been scarcely studied, with only a few reports available concerning TNF inhibition.[11,56] Thus, to our knowledge, this is the first time that significant and clinically relevant benefits of Il-23p19 inhibition on sleep impairment in psoriasis has been demonstrated.

The physical and emotional deterioration associated with psoriasis, including sleep difficulties, frequently impact patients' ability to perform in the workplace, with affected individuals reporting impairment during work time and increased absenteeism.[57-60] Our results indicate that psoriasis has high negative effects on work productivity and activity, as described previously.[12] After 24 weeks of treatment with TIL, significant improvements were reported for presenteeism, work productivity (overall work impairment), activity impairment and absenteeism. Recently, MCID for work productivity and activity impairment for psoriasis has been established as a 20% change in both domains, and the benefits found here for TIL clearly surpass this threshold[27] (mean change [95% CI] from baseline of −28.2 [−34.7, −21.7] and −36.4 [−42.6, −30.2], respectively). Such improvement in work productivity and activity is expected to confer a reduction in the productivity-related cost burden to the patient and the patient's family.

Using PBI, the TRIBUTE study provides valuable assessments of treatment benefits that are important for patients' lives. Our findings on the PNQ and PBQ items revealed that seven out of the top 10 patient-reported key treatment needs were also identified among the top 10 treatment benefit items at Week 24, which may indicate alignment between patient needs and benefits of TIL

in this study. Notably, the means of all PBQ items were higher than 3, which is considered the threshold for high treatment benefit.[33] Overall, 99% of patients had a PBI total score equal or higher than 1 after 24 weeks of TIL treatment, which confirms a significant clinical benefit, and 82.7% of patients reported a high treatment benefit (PBI ≥ 3).[32,33]

In line with findings on HRQoL and patient benefits, patients treated with TIL 100 mg reported high treatment satisfaction (mean global satisfaction score of 80.5), especially in the side-effect's subscale of the TSQM questionnaire, followed by convenience and effectiveness subscales (mean scores of 96.8, 79.6, 77.6, respectively).

Finally, TIL showed no safety concerns. The only death occurred during the study, due to a TEAE of coronavirus infection, was considered not related to the study drug as the patient had high risk factors for progression of a pulmonary infection (elderly patient, hypertension and overweight). No other serious TEAEs were reported, in accordance with the well-established favourable safety profile of tildrakizumab.[6,9,35,36,43]

One important limitation of this study is the open-label design, which could have induced bias in the reporting outcomes.

By contrast, this study has some strengths as to obtain data closer to the clinical practice as well as to provide the absolute PASI score that has been suggested as a better measure of therapeutic success than the relative reduction in PASI score (according to the Psoriasis Group of the Spanish Academy of Dermatology and Venereology).[61,62]

In conditions close to real clinical practice, TIL improved physical signs of psoriasis, including burdensome symptoms such as pruritus and skin pain after 24 weeks of treatment. Moreover, clinically relevant benefits were reported to key aspects of patients' daily life such as sleep, work and HRQoL impairment. These findings were accompanied by significant patient treatment benefits and satisfaction as well as a favourable safety profile of TIL.

ACKNOWLEDGEMENTS

This manuscript is dedicated to the memory of Prof. Gabriella Fabbrocini, who passed away while this manuscript was being peer-reviewed. She will be deeply missed. Medical writing support was provided by Stefania Ippati, PhD, TFS HealthScience and Eva Mateu, PhD, TFS HealthScience in accordance with Good Publication Practice (GPP3) guidelines. Open access funding provided by BIBLIOSAN.

FUNDING INFORMATION

Almirall R&D, Barcelona, Spain.

CONFLICT OF INTEREST STATEMENT

ACo has received honoraria from Abbvie, Almirall, Amgen, Eli Lilly, Galderma Novartis and UCB; ML-V has received speaker's honoraria and/or received grants and/or participated in clinical trials of AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer and UCB; GF has received honoraria from Abbvie, Almirall, Alfasigma, Amgen, Biogen, Janssen, Leo Pharma, Eli Lilly, Novartis, Pfizer, Sandoz and UCB; ACu has been an advisor board member and/or consultant and/or received speakers' honoraria and/or received grants and/or received research support and/or participated in clinical trials with the following pharmaceutical companies: Almirall, Celgene, Eli Lilly, Janssen-Cilag, Novartis and Pierre Fabre; RR acted as a consultant and/or speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie/Abbott, Almirall, Amgen, Celgene, Janssen-Cilag, Leo Pharma, Lilly, MSD-Schering-Plough, Novartis, Pfizer and UCB; KGdJ and IK are employees of Almirall; LP has received grants/research support or participated in clinical trials (paid to institution) from Abbvie, Almirall, Amgen, Boehringer Ingelheim, Janssen, Leo-Pharma, Lilly, Novartis, and UCB; received honoraria or consultation fees from Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, JS BIOCAD, Leo-Pharma, Lilly, Novartis, Pfizer, Sandoz, Samsung-Bioepis and UCB; and participated in company-sponsored speaker's bureau for Janssen, Lilly, Novartis and UCB; JMC has participated as PI/SI and/or member of steering committees and/or advisor and/or invited speaker for Celgene, Amgen, AbbVie, Almirall, Novartis, Leo-Pharma, Lilly, Sandoz, Mylan and Janssen.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The patients in this manuscript have given written informed consent for publication of their non-identifiable health information.

ORCID

Antonio Costanzo https://orcid.org/0000-0001-9697-2557
Mar Llamas-Velasco https://orcid.org/0000-0002-1187-1341
Raquel Rivera-Diaz https://orcid.org/0000-0002-4604-0724
Lluís Puig https://orcid.org/0000-0001-6083-0952
José Manuel Carrascosa https://orcid.org/0000-0003-4266-0771

REFERENCES

1. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015;386(9997):983–94.
2. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013;133(2):377–85.
3. Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. Lancet. 2021;397(10275):754–66.
4. European medicines agency. Ilumetri [Internet]. 2018 [cited 2021 Dec 16]. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/ilumetri

5. Reich K, Papp KA, Blauvelt A, Tyring SK, Sinclair R, Thaçi D, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet. 2017;390(10091):276–88.
6. Thaci D, Piaserico S, Warren R b, Gupta A k, Cantrell W, Draelos Z, et al. Five-year efficacy and safety of tildrakizumab in patients with moderate-to-severe psoriasis who respond at week 28: pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2). Br J Dermatol. 2021;185(2):323–34.
7. Mason KJ, Barker JNWN, Smith CH, Hampton PJ, Lunt M, McElhone K, et al. Comparison of drug discontinuation, effectiveness, and safety between clinical trial eligible and ineligible patients in BADBIR. JAMA Dermatol. 2018;154(5):581–8.
8. Masson Regnault M, Castañeda-Sanabria J, Diep Tran MHT, Beylot-Barry M, Bachelez H, Beneton N, et al. Users of biologics in clinical practice: would they be eligible for phase III clinical studies? Cohort study in the French psoriasis registry PSOBIOTEQ. J Eur Acad Dermatol Venereol. 2020;34(2):293–300.
9. Drerup KA, Seemann C, Gerdes S, Mrowietz U. Effective and safe treatment of psoriatic disease with the anti-IL-23p19 biologic Tildrakizumab: results of a real-world prospective cohort study in nonselected patients. Dermatology. 2022;238(4):615–9.
10. Ljosaa TM, Mork C, Stubhaug A, Moum T, Wahl AK. Skin pain and skin discomfort is associated with quality of life in patients with psoriasis. J Eur Acad Dermatol Venereol. 2012;26(1):29–35.
11. Strober BE, Sobell JM, Duffin KC, Bao Y, Guérin A, Yang H, et al. Sleep quality and other patient-reported outcomes improve after patients with psoriasis with suboptimal response to other systemic therapies are switched to adalimumab: results from PROGRESS, an open-label phase IIIB trial. Br J Dermatol. 2012;167(6):1374–81.
12. Kimball AB, Edson-Heredia E, Zhu B, Guo J, Maeda-Chubachi T, Shen W, et al. Understanding the relationship between pruritus severity and work productivity in patients with moderate-to-severe psoriasis: sleep problems are a mediating factor. J Drugs Dermatol. 2016;15(2):183–8.
13. Prignano F, Ricceri F, Pescitelli L, Lotti T. Itch in psoriasis: epidemiology, clinical aspects and treatment options. Clin Cosmet Investig Dermatol. 2009;2:9–13.
14. Tyring S, Gottlieb A, Papp K, Gordon K, Leonardi C, Wang A, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomised phase III trial. Lancet. 2006;367(9504):29–35.
15. Zhu B, Edson-Heredia E, Guo J, Maeda-Chubachi T, Shen W, Kimball AB. Itching is a significant problem and a mediator between disease severity and quality of life for patients with psoriasis: results from a randomized controlled trial. Br J Dermatol. 2014;171(5):1215–9.
16. Taliercio VL, Snyder AM, Webber LB, Langner AU, Rich BE, Beshay AP, et al. The disruptiveness of itchiness from psoriasis: a qualitative study of the impact of a single symptom on quality of life. J Clin Aesthet Dermatol. 2021;14(6):42–8.
17. Llamas-Velasco M, de la Cueva P, Notario J, Martínez-Pilar L, Martorell A, Moreno-Ramírez D. Moderate psoriasis: a proposed definition. Actas Dermosifiliogr. 2017;108(10):911–7.
18. Gisondi P, Altomare G, Ayala F, Bardazzi F, Bianchi L, Chiricozzi A, et al. Italian guidelines on the systemic treatments of moderate-to-severe plaque psoriasis. J Eur Acad Dermatol Venereol. 2017;31(5):774–90.
19. Langley RG, Ellis CN. Evaluating psoriasis with psoriasis area and severity index, psoriasis global assessment, and lattice system Physician's global assessment. J Am Acad Dermatol. 2004;51(4):563–9.
20. Basra MKA, Fenech R, Gatt RM, Salek MS, Finlay AY. The dermatology life quality index 1994–2007: a comprehensive review of validation data and clinical results. Br J Dermatol. 2008;159(5):997–1035.
21. Rencz F, Gulácsi L, Péntek M, Szegedi A, Remenyik É, Bata-Csörgő Z, et al. DLQI-R scoring improves the discriminatory power of the dermatology life quality index in patients with psoriasis, pemphigus and morphea. Br J Dermatol. 2020;182(5):1167–75.
22. Reich A, Chatzigeorkidis E, Zeidler C, Osada N, Furue M, Takamori K, et al. Tailoring the cut-off values of the visual analogue scale and numeric rating scale in itch assessment. Acta Derm Venereol. 2017;97(6):759–60.
23. Chren MM. The Skindex instruments to measure the effects of skin disease on quality of life. Dermatol Clin. 2012;30(2):231–6.
24. Mrowietz U, Chouela EN, Mallbris L, Stefanidis D, Marino V, Pedersen R, et al. Pruritus and quality of life in moderate-to-severe plaque psoriasis: post hoc explorative analysis from the PRISTINE study. J Eur Acad Dermatol Venereol. 2015;29(6):1114–20.
25. Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the medical outcomes study sleep measure. Sleep Med. 2005;6(1):41–4.
26. Rejas J, Ribera MV, Ruiz M, Masrramón X. Psychometric properties of the MOS (medical outcomes study) sleep scale in patients with neuropathic pain. Eur J Pain. 2007;11(3):329–40.
27. Wu JJ, Lin C, Sun L, Goldblum O, Zbrozek A, Burge R, et al. Minimal clinically important difference (MCID) for work productivity and activity impairment (WPAI) questionnaire in psoriasis patients. J Eur Acad Dermatol Venereol. 2019;33(2):318–24.
28. Feuerhahn J, Blome C, Radtke M, Augustin M. Validation of the patient benefit index for the assessment of patient-relevant benefit in the treatment of psoriasis. Arch Dermatol Res. 2012;304(6):433–41.
29. Augustin M, Kleyn CE, Conrad C, Sator PG, Ståhle M, Eyerich K, et al. Characteristics and outcomes of patients treated with apremilast in the real world: results from the APPRECIATE study. J Eur Acad Dermatol Venereol. 2021;35(1):123–34.
30. Gisondi P, Talamonti M, Chiricozzi A, Piaserico S, Amerio P, Balato A, et al. Treat-to-target approach for the Management of Patients with moderate-to-severe plaque psoriasis: consensus recommendations. Dermatol Ther (Heidelb). 2021;11(1):235–52.
31. Rencz F, Poór A, Péntek M, Holló P, Kárpáti S, Gulácsi L, et al. A detailed analysis of 'not relevant' responses on the DLQI in psoriasis: potential biases in treatment decisions. J Eur Acad Dermatol Venereol. 2018;32(5):783–90.
32. Langenbruch A, Radtke MA, Gutknecht M, Augustin M. Does the dermatology life quality index (DLQI) underestimate the disease-specific burden of psoriasis patients? J Eur Acad Dermatol Venereol. 2019;33(1):123–7.
33. Gordon KB, Reich K, Crowley JJ, Korman NJ, Murphy FT, Poulin Y, et al. Disease activity and treatment efficacy using patient-level psoriasis area and severity index scores from tildrakizumab phase 3 clinical trials. J Dermatolog Treat. 2022;33(1):219–28.
34. Caldarola G, Zangrilli A, Bernardini N, Bavetta M, De Simone C, Graceffa D, et al. Risankizumab for the treatment of moderate-to-severe psoriasis: a multicenter, retrospective, 1 year real-life study. Dermatol Ther. 2022;35(6):e15489.
35. Megna M, Tommasino N, Potestio L, Battista T, Ruggiero A, Noto M, et al. Real-world practice indirect comparison between guselkumab, risankizumab, and tildrakizumab: results from an Italian 28-week retrospective study. J Dermatolog Treat. 2022;33(6):2813–20.
36. Burlando M, Castelli R, Cozzani E, Parodi A. Treatment of moderate-to-severe plaque psoriasis with tildrakizumab in the real-life setting. Drugs Context. 2021;10:1–4.
37. Galluzzo M, Tofani L, Lombardo P, Petruzzellis A, Silvaggio D, Egan CG, et al. Use of Guselkumab for the treatment of moderate-to-severe plaque psoriasis: a 1 year real-life study. J Clin Med. 2020;9(7):2170.
38. Malara G, Trifirò C, Bartolotta A, Giofré C, D'Arrigo G, Testa A, et al. Real-world effectiveness and safety of Guselkumab for the treatment of psoriasis: a 6-month prospective study in a series of psoriatic patients. Eur Rev Med Pharmacol Sci. 2021;25(1):406–12.
39. Gerdes S, Asadullah K, Hoffmann M, Korge B, Mortazawi D, Wegner S, et al. Real-world evidence from the non-interventional, prospective, German multicentre PERSIST study of patients with psoriasis after 1 year of treatment with guselkumab. J Eur Acad Dermatol Venereol. 2022;36(9):1568–77.
40. Gkalpakiotis S, Cetkovska P, Arenberger P, Dolezal T, Arenbergerova M, Velackova B, et al. Risankizumab for the treatment of

moderate-to-severe psoriasis: real-life multicenter experience from The Czech Republic. Dermatol Ther (Heidelb). 2021;11(4):1345–55.
41. Gerdes S, Bräu B, Hoffmann M, Korge B, Mortazawi D, Wiemers F, et al. Real-world effectiveness of guselkumab in patients with psoriasis: health-related quality of life and efficacy data from the non-interventional, prospective, German Multicenter PERSIST Trial. J Dermatol. 2021;48(12):1854–62.
42. del Alcázar E, López-Ferrer A, Martínez-Doménech Á, Ruiz-Villaverde R, del Llamas-Velasco M, Rocamora V, et al. Effectiveness and safety of guselkumab for the treatment of psoriasis in real-world settings at 24 weeks: a retrospective, observational, multicentre study by the Spanish psoriasis group. Dermatol Ther. 2022;35(2):e15231.
43. Ruggiero A, Picone V, Martora F, Fabbrocini G, Megna M. Guselkumab, risankizumab, and tildrakizumab in the management of psoriasis: a review of the real-world evidence. Clin Cosmet Investig Dermatol. 2022;15:1649–58.
44. Paudyal P, Apfelbacher C, Jones C, Siddiqui S, El-Turki A, DeGiovanni C, et al. 'DLQI seems to be "action", and Skindex-29 seems to be "emotion"': qualitative study of the perceptions of patients with psoriasis or eczema on two common dermatology-specific quality of life measures. Acta Derm Venereol. 2020;100(8):adv00105, adv00106.
45. Szabó Á, Brodszky V, Rencz F. A comparative study on the measurement properties of dermatology life quality index (DLQI), DLQI-relevant and Skindex-16. Br J Dermatol. 2022;186(3):485–95.
46. Zachariae R, Lei U, Haedersdal M, Zachariae C. Itch severity and quality of life in patients with pruritus: preliminary validity of a Danish adaptation of the itch severity scale. Acta Derm Venereol. 2012;92(5):508–14.
47. Globe D, Bayliss MS, Harrison DJ. The impact of itch symptoms in psoriasis: results from physician interviews and patient focus groups. Health Qual Life Outcomes. 2009;7:62.
48. Elewski B, Alexis AF, Lebwohl M, Stein Gold L, Pariser D, Del Rosso J, et al. Itch: an under-recognized problem in psoriasis. J Eur Acad Dermatol Venereol. 2019;33(8):1465–76.
49. Pärna E, Aluoja A, Kingo K. Quality of life and emotional state in chronic skin disease. Acta Derm Venereol. 2015;95(3):312–6.
50. Gowda S, Goldblum OM, McCall WV, Feldman SR. Factors affecting sleep quality in patients with psoriasis. J Am Acad Dermatol. 2010;63(1):114–23.
51. Nowowiejska J, Baran A, Flisiak I. Mutual relationship between sleep disorders, quality of life and psychosocial aspects in patients with psoriasis. Front Psych. 2021;12:674460.
52. Jensen P, Zachariae C, Skov L, Zachariae R. Sleep disturbance in psoriasis: a case-controlled study. Br J Dermatol. 2018;179(6):1376–84.
53. Halioua B, Misery L, Seite S, Delvigne V, Chelli C, Taieb J, et al. Influence of skin subjective symptoms on sleep quality in patients with cutaneous disorders: a study of 2871 subjects. Clin Cosmet Investig Dermatol. 2021;14:143–52.
54. Gupta MA, Simpson FC, Gupta AK. Psoriasis and sleep disorders: a systematic review. Sleep Med Rev. 2016;29:63–75.
55. Nowowiejska J, Baran A, Lewoc M, Grabowska P, Kaminski TW, Flisiak I. The assessment of risk and predictors of sleep disorders in patients with psoriasis-a questionnaire-based cross-sectional analysis. J Clin Med. 2021;10(4):664.
56. Thaçi D, Galimberti R, Amaya-Guerra M, Rosenbach T, Robertson D, Pedersen R, et al. Improvement in aspects of sleep with etanercept and optional adjunctive topical therapy in patients with moderate-to-severe psoriasis: results from the PRISTINE trial. J Eur Acad Dermatol Venereol. 2014;28(7):900–6.
57. Kimball AB, Naegeli AN, Edson-Heredia E, Lin CY, Gaich C, Nikaï E, et al. Psychometric properties of the itch numeric rating scale in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2016;175(1):157–62.
58. Schaefer CP, Cappelleri JC, Cheng R, Cole JC, Guenthner S, Fowler J, et al. Health care resource use, productivity, and costs among patients with moderate to severe plaque psoriasis in the United States. J Am Acad Dermatol. 2015;73(4):585–93.e3.
59. Finlay AY, Coles EC. The effect of severe psoriasis on the quality of life of 369 patients. Br J Dermatol. 1995;132(2):236–44.
60. Horn EJ, Fox KM, Patel V, Chiou CF, Dann F, Lebwohl M. Association of patient-reported psoriasis severity with income and employment. J Am Acad Dermatol. 2007;57(6):963–71.
61. Del Alcázar VE, Lamas Doménech N, Salleras RM. Absolute versus relative psoriasis area and severity index in clinical practice. Actas Dermosifiliogr (Engl Ed). 2019;110(7):606–10.
62. Carrascosa JM, Puig L, Romero IB, Salgado-Boquete L, Del Alcázar E, Lencina JJA, et al. Practical update of the guidelines published by the psoriasis Group of the Spanish Academy of dermatology and venereology (GPs) on the treatment of psoriasis with biologic agents: part 2 – Management of Special Populations, patients with comorbid conditions, and risk. Actas Dermosifiliogr. 2022;113(6):583–609.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Costanzo A, Llamas-Velasco M, Fabbrocini G, Cuccia A, Rivera-Diaz R, Gaarn Du Jardin K, et al. Tildrakizumab improves high burden skin symptoms, impaired sleep and quality of life of moderate-to-severe plaque psoriasis patients in conditions close to clinical practice. J Eur Acad Dermatol Venereol. 2023;37:2004–2015. https://doi.org/10.1111/jdv.19229