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BRIEF REPORT

Improvements in Psoriasis-Related Work Productivity with Tildrakizumab: Results from a Phase 4 Real-World Study in Patients with Moderate-to-Severe Plaque Psoriasis

Tina Bhutani · John Koo · Jayme Heim · Neal Bhatia · Jacob Mathew · Thomas Ferro · J. Gabriel Vasquez

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ABSTRACT

Introduction: Plaque psoriasis is a chronic condition that may impact patients' work productivity. Tildrakizumab, an interleukin-23 p19 inhibitor, is approved for treatment of moderate-to-severe plaque psoriasis in adults. However, the effect of tildrakizumab treatment on work productivity in patients with psoriasis is not well characterized.

Methods: In this multicenter, open-label, uncontrolled phase 4 study (NCT03718299), patients with moderate-to-severe plaque psoriasis received tildrakizumab 100 mg at week 0, week 4, and every 12 weeks thereafter through week 52. Patients completed the Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI:PSO) at baseline and every 12 weeks from week 16 through week 64. The following four domains of the WPAI:PSO were examined: absenteeism (percentage of time missed from work due to psoriasis), presenteeism (percentage reduction of productivity while at work due to psoriasis), total activity impairment (percentage impairment in activities other than work due to psoriasis), and total work productivity impairment (total percentage of work impairment from both absenteeism and presenteeism due to psoriasis). Missing data were not imputed.

Results: Of the 55 patients enrolled, 31 patients completed all domains of the WPAI:PSO at week 64. From baseline to week 64, respectively, mean ± standard deviation (SD) scores improved for presenteeism (20.5 ± 21.7 to 2.6 ± 5.8; $P < 0.001$), total activity impairment (29.5 ± 26.6 to 4.4 ± 9.4; $P < 0.001$), and total work productivity impairment (20.9 ± 22.2 to 2.6 ± 5.8; $P < 0.001$). The mean ± SD score for absenteeism decreased from 1.1 ± 5.7 at baseline to 0.0 ± 0.0 at week 64, but this change was not statistically significant.

Conclusion: Tildrakizumab treatment mitigated work productivity loss due to psoriasis as measured by the presenteeism, total activity impairment, and total work productivity impairment domains of the WPAI:PSO.

Trial Registration: ClinicalTrials.gov identifier, NCT03718299.

Keywords: Psoriasis; Tildrakizumab; Work productivity

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Key Summary Points

Why carry out this study?

- Patients with psoriasis often experience a loss of work productivity due to the disease. Treatment with biologics may mitigate this loss.
- Tildrakizumab is approved for the treatment of moderate-to-severe plaque psoriasis, but the effect of tildrakizumab on work productivity is not well established.
- This study evaluated the effect of tildrakizumab treatment on work productivity and activity impairment during 64 weeks of treatment.

What was learned from the study?

- Tildrakizumab significantly mitigated the work productivity loss and activity impairment associated with psoriasis as measured by the presenteeism, total activity impairment, and total work productivity impairment domains of the Work Productivity and Activity Impairment Questionnaire: Psoriasis.

INTRODUCTION

Psoriasis is a chronic inflammatory disorder with an overall prevalence of approximately 3% among US individuals 20 years of age and older, making it one of the most common immune-mediated diseases in the US [1, 2]. The overall economic burden of psoriasis includes substantial direct, indirect, and intangible costs for patients, insurance companies, and society [3]. Loss of work productivity is a significant part of this burden, contributing average indirect costs ranging from approximately US $3500 to $12,000 per patient with psoriasis [4]. Treatment of plaque psoriasis with biologics can mitigate the loss of work productivity associated with the disease [5–8].

Tildrakizumab is an anti-interleukin (IL)-23 p19 monoclonal antibody approved for the treatment of adults with moderate-to-severe plaque psoriasis [9]. The efficacy and safety of tildrakizumab for the treatment of moderate-to-severe plaque psoriasis were assessed in two pivotal phase 3 trials, reSURFACE 1 and reSURFACE 2 [10]. In the trials, the coprimary endpoints at week 12 were met: Significantly larger proportions of patients treated with tildrakizumab achieved a 75% improvement from baseline in Psoriasis Area and Severity Index (PASI) score compared with patients who received placebo or etanercept, and significantly more tildrakizumab-treated patients achieved a Physician Global Assessment score of "clear" or "minimal" with at least a two-grade reduction from baseline compared with patients who received placebo [10]. The number of reported serious adverse events was similar across treatment groups [10]. However, the effect of tildrakizumab treatment on work productivity was not reported in these studies [10].

In a phase 4 real-world study, treatment with tildrakizumab resulted in improvements in psychological general well-being, skin-related quality of life, and disease severity in patients with moderate-to-severe plaque psoriasis, with no new safety signals observed [11, 12]. This analysis describes improvement in psoriasis-related work productivity in the phase 4 study.

METHODS

Study Design, Patients, and Treatment

The study (ClinicalTrials.gov NCT03718299) was previously described in detail [11]. Briefly, adults with moderate-to-severe plaque psoriasis were treated with tildrakizumab 100 mg administered at week 0, week 4, and every 12 weeks thereafter through week 52 and followed through week 64 under real-world conditions.

Work Productivity Assessments

The Work Productivity and Activity Impairment Questionnaire: Psoriasis (WPAI:PSO) was administered at weeks 0, 16, 28, 40, 52, and 64. The WPAI:PSO is a validated self-reported assessment that determines the amount of absenteeism, presenteeism, and daily activity impairment attributed to a patient's psoriasis [13]. The following WPAI:PSO domains are reported: absenteeism, which measures the time missed from work due to psoriasis; presenteeism, which measures the reduction of productivity while at work due to psoriasis; total activity impairment, which measures impairment in nonwork activities due to psoriasis; and total work productivity impairment, which measures work impairment from both absenteeism and presenteeism due to psoriasis. Each WPAI:PSO domain score is expressed as percentage impairment (0–100%), with lower scores representing lesser impairment and higher scores representing greater impairment or worse outcome.

Statistical Analysis

Change from baseline and percent change from baseline in the WPAI:PSO domain scores were analyzed in the intention-to-treat population, which included all enrolled patients assigned to receive tildrakizumab. Differences between baseline and posttreatment values were analyzed using Student's paired *t* test. Missing data were not imputed.

Ethics Statement

The study protocol and all amendments were approved by the Western Institutional Review Board Copernicus Group (WCG) prior to study initiation. The study was conducted in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice guidelines, and local regulations. All patients provided written informed consent prior to commencing any study-related procedures.

Table 1 Baseline demographics and clinical characteristics

	Tildrakizumab (*N* = 55)
Sex	
Male	28 (50.9)
Female	27 (49.1)
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	
Not Hispanic or Latino	50 (90.9)
Hispanic or Latino	5 (9.1)
BSA, mean ± SD	14.5 ± 11.5
sPGA, mean ± SD	3.2 ± 0.6
PASI score, mean ± SD	11.6 ± 7.1
WPAI:PSO, mean ± SD	
Presenteeism domain	20.5 ± 21.7
Total activity impairment domain	29.5 ± 26.6
Total work productivity impairment domain	20.9 ± 22.2
Absenteeism domain	1.1 ± 5.7

All data are *n* (%) unless otherwise noted
BSA body surface area, *PASI* Psoriasis Area and Severity Index, *SD* standard deviation, *sPGA* static Physician Global Assessment, *WPAI:PSO* Work Productivity and Activity Impairment Questionnaire: Psoriasis

RESULTS

Of the 55 patients enrolled, 45 completed the total activity impairment domain and 31 completed the presenteeism, absenteeism, and total work productivity impairment domains of the WPAI:PSO at week 64. The majority of patients were male (28/55; 50.9%) and White (52/55, 94.5%), with a mean ± standard deviation (SD) age of 48.6 ± 15.3 years (Table 1).

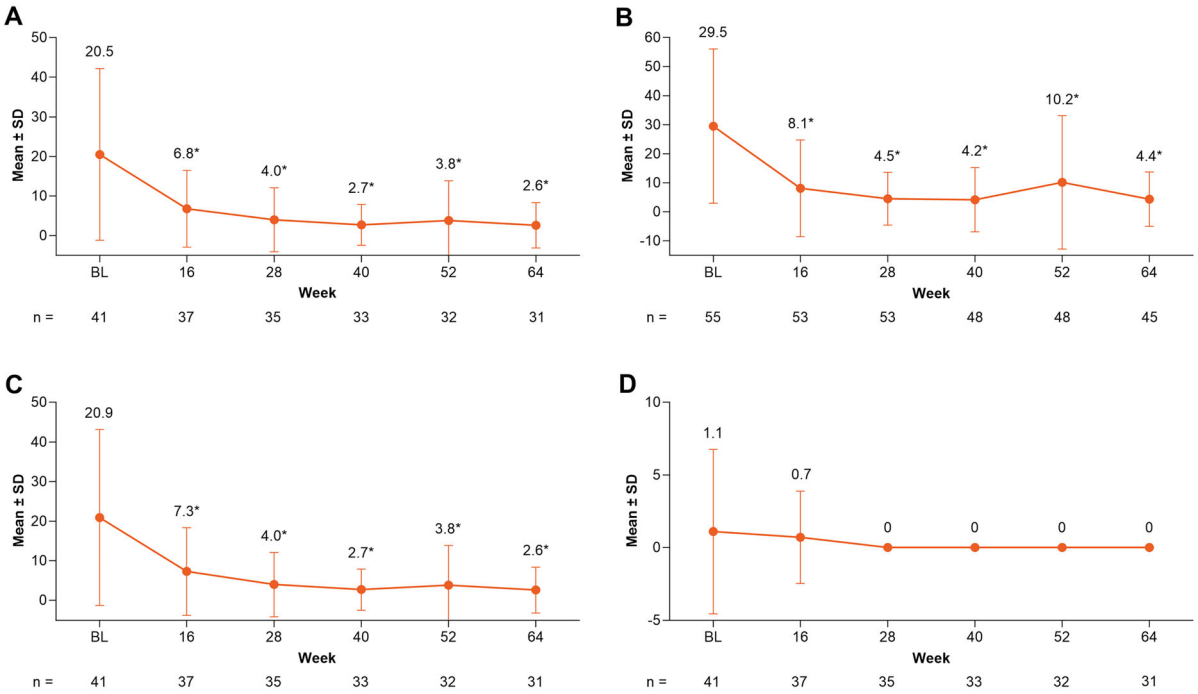

Fig. 1 Work Productivity and Activity Impairment Questionnaire: Psoriasis domain scores for the **a** presenteeism, **b** total activity impairment, **c** total work productivity impairment, and **d** absenteeism domains from baseline through week 64. Intention-to-treat population. Error bars represent the SD. *Statistically significant change from baseline based on Student's *t* test ($P < 0.001$). *BL* baseline, *SD* standard deviation

Patients treated with tildrakizumab had statistically significant improvements in work productivity relative to baseline for all WPAI:PSO domains except absenteeism, beginning at week 16 and continuing through week 64. Domain scores (mean ± SD) improved from baseline to week 64 for presenteeism (from 20.5 ± 21.7 to 2.6 ± 5.8; $P < 0.001$; change from baseline, − 89.7%; Fig. 1a), total activity impairment (from 29.5 ± 26.6 to 4.4 ± 9.4; $P < 0.001$; change from baseline, − 87.0%; Fig. 1b), and total work productivity impairment (from 20.9 ± 22.2 to 2.6 ± 5.8; $P < 0.001$; change from baseline, − 89.7%; Fig. 1c). The absenteeism domain score decreased from baseline to week 64 (from 1.1 ± 5.7 to 0.0 ± 0.0), but this change did not reach statistical significance (Fig. 1d).

DISCUSSION

This analysis demonstrated the benefit of tildrakizumab treatment on work productivity and activity across 64 weeks in patients with moderate-to-severe plaque psoriasis. Statistically significant improvements in tildrakizumab-treated patients were observed beginning at week 16 in the presenteeism, total activity impairment, and total work productivity impairment domains of the WPAI:PSO. This continued through the last visit at week 64. Total activity impairment decreased by 87.0%, and both presenteeism and total work productivity impairment decreased by 89.7% from baseline to week 64, exceeding the minimal clinically important difference of 20% reported by Wu et al. [14]. There was no significant effect of tildrakizumab treatment on absenteeism, likely due to the near-zero baseline value.

These results are consistent with those of TRIBUTE, a phase 4, multicenter, open-label

clinical study of tildrakizumab in moderate-to-severe plaque psoriasis that enrolled 177 patients in Spain and Italy [15]. Patients in TRIBUTE also experienced improvements in work productivity and activity impairment from baseline to week 24 of tildrakizumab treatment [15]. Mean scores for presenteeism decreased from 35.0 to 5.8, with a mean absolute change from baseline of − 27.0. Mean total work productivity impairment scores decreased from 40.2 to 8.1 (mean absolute change from baseline of − 28.2). The largest difference observed was in the total activity impairment domain, for which the mean score decreased from 45.5 to 8.3, with a mean absolute change from baseline of − 36.4. More substantial improvement in absenteeism (from a score of 11.1 to 3.1 with a mean absolute change from baseline of − 6.8) was observed in TRIBUTE relative to the current study, which may be due to the larger sample size and greater baseline value for absenteeism in TRIBUTE. Improvements in work productivity and activity during tildrakizumab treatment are also being evaluated in the phase 4, real-world, observational POSITIVE study, but results are not yet available [16].

Total work productivity loss associated with psoriasis is estimated to range from 10.1% to 29.4% of work hours depending on disease severity, with patients who report absenteeism losing an estimated 306 h of work annually [4, 17]. When these patients' other medical conditions are excluded, psoriasis alone is estimated to account for 38% of the total cost of lost productivity [17]. Treatment with biologics can mitigate the detrimental effects of psoriasis on work productivity and costs thereof, as increasing skin clearance during treatment leads to decreased rates of work impairment and reduces indirect costs related to psoriasis [18]. In the VOYAGE 1 trial, guselkumab, another IL-23 p19 inhibitor, significantly improved Dermatology Life Quality Index (DLQI) work/study domain scores compared with placebo at week 16. Of the 64 patients treated with guselkumab who reported an inability to work or study at baseline (DLQI work/study score = 3), 42 (65.6%; $P < 0.0001$ vs placebo) reported having no work/study problems at all (DLQI work/study score = 0) at week 16. This effect continued through week 48, with 52 patients (81.3%) achieving the same [19]. At baseline, the loss of work productivity in these patients translated to indirect costs of US $15,874. Treatment reduced these costs by week 16, an effect that continued to week 48 when costs decreased to approximately US $5452 [19]. Therefore, effective treatment of chronic plaque psoriasis can greatly reduce the costs associated with work productivity loss due to disease. The mitigation of work productivity loss due to psoriasis by tildrakizumab treatment in the current study could also decrease the overall economic burden of psoriasis.

Work productivity loss due to psoriasis is associated with alterations to patients' health-related quality of life (HRQoL) [4]. The DLQI is a measure of HRQoL, with lower scores representing better HRQoL. The TRIBUTE study, like the present study, also examined HRQoL as measured by the DLQI. In TRIBUTE at week 24, 70.4% of patients achieved a DLQI score of 0 or 1 (DLQI 0/1) [15]. Similar results were seen in this phase 4 study of tildrakizumab for the treatment of moderate-to-severe plaque psoriasis, with 62% of patients achieving DLQI 0/1 at week 64 [20]. Scores for DLQI and work productivity loss are correlated in patients with psoriasis, with a 1-unit increase on the DLQI increasing work productivity loss by 1.8% [4]. As shown here, tildrakizumab significantly mitigates work productivity loss due to disease, further supporting that improvement in work productivity may correlate with the overall improvement in quality of life in patients with psoriasis.

CONCLUSION

The data presented in this analysis further support improvement in work productivity and activity, as measured by the WPAI:PSO, in patients with moderate-to-severe plaque psoriasis treated with tildrakizumab. Tildrakizumab treatment resulted in significant improvement in three domains of the WPAI:PSO. One limitation of the study was the inability to assess the effect of tildrakizumab treatment on

absenteeism, due to the near-zero baseline value and the small number of patients. Altogether, the results indicate that tildrakizumab can mitigate work productivity loss in patients with moderate-to-severe plaque psoriasis treated in a real-world clinical setting.

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Data Availability. Data and other documents will be made available after publication, with no end date, to anyone who submits a reasonable request to the study sponsor.

Declarations

Conflict of Interest. Tina Bhutani has received research funding from AbbVie, Celgene, Galderma, Janssen, Lilly, Pfizer, Regeneron, and Sun Pharma and has served as an adviser for AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, LEO Pharma, and Novartis. John Koo has served as an adviser for AbbVie, Amgen, Celgene, EPI Health, Janssen, LEO Pharma, Lilly, Novartis, Ortho Dermatologics, Pfizer, Regeneron/Sanofi, Sun Pharma, and UCB. Jayme Heim has been a speaker, adviser, and consultant for Amgen, AbbVie, Celgene, Lilly, Janssen, and Novartis; an adviser for Galderma, Mayne, Regeneron, and Sanofi; an adviser and consultant for Ortho Dermatologics; and a speaker and adviser for Beiersdorf, InCyte, LEO Pharma, and Sun Pharma. Neal Bhatia is an adviser, consultant, and investigator for AbbVie, Almirall, Arcutis, Beiersdorf, Biofrontera, Boehringer Ingelheim, Bristol Myers Squibb, Cara, Dermavant, EPI Health, Ferndale, Galderma, InCyte, ISDIN, Johnson & Johnson, La Roche-Posay, LEO Pharma, Lilly, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and Verrica Pharmaceuticals, Inc. Jacob Mathew and Thomas Ferro are employees of Sun Pharmaceutical Industries, Inc. J Gabriel Vasquez reports nothing to disclose.

Ethical Approval. The study protocol and all amendments were approved by the Western Institutional Review Board Copernicus Group (WCG) prior to study initiation. The study was conducted in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice guidelines, and local regulations. All patients provided written informed consent prior to commencing any study-related procedures.

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REFERENCES

1. Armstrong AW, Mehta MD, Schupp CW, et al. Psoriasis prevalence in adults in the United States. JAMA Dermatol. 2021;157(8):940–6.
2. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029–72.
3. Brezinski EA, Dhillon JS, Armstrong AW. Economic burden of psoriasis in the United States: a systematic review. JAMA Dermatol. 2015;151(6):651–8.
4. Villacorta R, Teeple A, Lee S, et al. A multinational assessment of work-related productivity loss and indirect costs from a survey of patients with psoriasis. Br J Dermatol. 2020;183(3):548–58.
5. Armstrong AW, Lynde CW, McBride SR, et al. Effect of ixekizumab treatment on work productivity for patients with moderate-to-severe plaque psoriasis: analysis of results from 3 randomized phase 3 clinical trials. JAMA Dermatol. 2016;152(6):661–9.
6. Kimball AB, Yu AP, Signorovitch J, et al. The effects of adalimumab treatment and psoriasis severity on self-reported work productivity and activity impairment for patients with moderate to severe psoriasis. J Am Acad Dermatol. 2012;66(2):e67-76.
7. Beroukhim K, Danesh M, Nguyen C, et al. A prospective, interventional assessment of the impact of ustekinumab treatment on psoriasis-related work productivity and activity impairment. J Dermatolog Treat. 2016;27(6):552–5.
8. Saeki H, Kanai Y, Murotani K, et al. Work productivity in real-life employed patients with plaque psoriasis: results from the ProLOGUE study. J Dermatol. 2022;49(10):970–8.
9. ILUMYA® (tildrakizumab-asmn), injection for subcutaneous use. Full prescribing information. Sun Pharmaceutical Industries, Inc.; 2022.
10. Reich K, Papp KA, Blauvelt A, 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.
11. Bhatia N, Heim J, Schenkel B, Vasquez JG. Quality of life and patient-reported symptoms in a phase 4, real-world study of tildrakizumab in patients with moderate-to-severe psoriasis: week 28 interim analysis. J Dermatolog Treat. 2023;11:1–9.
12. Heim J, Vasquez JG, Schenkel B, Bhatia N. Real-world effectiveness and safety of tildrakizumab in patients with moderate-to-severe psoriasis: week 28 interim analysis of a phase 4 study. J Drugs Dermatol. 2023;22(8):754–60.
13. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993;4(5):353–65.
14. Wu JJ, Lin C, Sun L, 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.
15. Costanzo A, Llamas-Velasco M, Fabbrocini G, 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(10):2004–15.
16. Augustin M, Sommer R, Daudén E, et al. Patient-reported well-being in value-based care using tildrakizumab in a real-world setting: protocol of a multinational, phase IV, 1-cohort prospective observational study (the POSITIVE study). BMJ Open. 2023;13(2):e060536.
17. Mustonen A, Mattila K, Leino M, Koulu L, Tuominen R. How much of the productivity losses among psoriasis patients are due to psoriasis. BMC Health Serv Res. 2015;15:87.
18. Feldman SR, Zhao Y, Gilloteau I, et al. Higher psoriasis skin clearance is associated with lower annual indirect costs in the United States: a post hoc analysis from the CLEAR Study. J Manag Care Spec Pharm. 2018;24(7):617–22.
19. Li N, Teeple A, Muser E, et al. Work/study productivity gain and associated indirect cost savings with guselkumab compared with adalimumab in moderate-to-severe psoriasis: results from the VOYAGE 1 study. J Dermatolog Treat. 2022;33(1):278–83.
20. Bhatia N, Heim J, Vasquez JG, et al. Long-term quality of life outcomes from a phase 4 study of tildrakizumab in patients with moderate-to-severe plaque psoriasis in a real-world setting. J Dermatolog Treat. 2024 (in press).