Adv Ther (2025) 42:1994–2002
https://doi.org/10.1007/s12325-025-03122-w

BRIEF REPORT

Biologic Treatment Adherence and Persistence in Patients with Palmoplantar Pustulosis: A Real-World, Claims-Based Study

Steven R. Feldman · Ran Gao · Rhonda L. Bohn · Stephani Gray · Anouk Déruaz-Luyet · Jashin J. Wu

Received: December 5, 2024 / Accepted: January 20, 2025 / Published online: March 3, 2025

ABSTRACT

Introduction: Palmoplantar pustulosis (PPP) is a debilitating skin condition characterized by pustules, erythema, and scales on the palms and soles. Treatment adherence in psoriatic diseases is suboptimal.

Methods: A retrospective cohort study, using healthcare claims data from patients aged ≥ 18 years with newly diagnosed PPP (selected between October 1, 2016 and March 31, 2020 from IBM® MarketScan® Commercial and the Optum® Clinformatics® Data Mart databases), was conducted to investigate adherence to and persistence with biologics in patients with PPP.

Results: Biologics were dispensed to 114/840 (13.6%) MarketScan and 76/750 (10.1%) Optum patients. Mean proportion of days covered (PDC; range) for biologics was similar between databases (MarketScan, 66% [8–100%]; Optum, 61% [8–99%]), and good adherence (≥ 80% PDC) was infrequent (MarketScan, 42.1%; Optum, 34.2%). Mean (standard deviation) persistence was slightly longer in MarketScan (283 [121] days) versus Optum (275 [133] days). Mean (range) adherence was similar between ages, although persistence was longer in patients aged 18–64 versus ≥ 65 years (279 [132] vs 258 [140] days).

Conclusion: In patients with PPP, adherence to biologics was poor and persistence was variable; understanding and addressing the reasons behind these observations may improve treatment outcomes.

Ran Gao is now an employee of Gilead Sciences.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12325-025-03122-w.

S. R. Feldman
Department of Dermatology, Wake Forest University School of Medicine, Winston-Salem, NC, USA

R. Gao
Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA

R. L. Bohn · S. Gray
Bohn Epidemiology, Boston, MA, USA

A. Déruaz-Luyet
Boehringer Ingelheim International GmbH, Ingelheim, Germany

J. J. Wu (✉)
Department of Dermatology, University of Miami Miller School of Medicine, 1600 NW 10th Ave #1140, Miami, FL 33136, USA
e-mail: jashinwu@gmail.com

PLAIN LANGUAGE SUMMARY

Palmoplantar pustulosis (PPP) is a painful skin condition that causes pus-filled blisters, redness, and scaling on the palms of the hands and soles of the feet. These symptoms can seriously affect a person's quality of life.

Treatments for PPP are usually creams or ointments applied directly to the skin. However, they often do not work well because of the thickness of the skin in the affected areas. This means that many patients may need more advanced treatments. Biologics are one type of advanced treatment. Biologics work by targeting the immune system to try and reduce inflammation and ease symptoms.

Using data from two healthcare databases in the USA, this study examined how well patients with PPP followed medical advice (known as adherence and persistence) when taking their prescribed biologic medications. The study included newly diagnosed patients with PPP between 2016 and 2020. All patient data were anonymized in this study. In this study, only a small percentage of patients were prescribed biologics (14% in one database and 10% in the other).

Across the two databases, patients took their biologic medication between 61% and 66% of the time. On average, patients continued their treatment for around 9 months, with younger patients (aged 18–64 years) staying on treatment a bit longer than those aged 65 years and older.

Overall, low treatment adherence and persistence with biologics suggests a need for more patient-friendly treatments. Targeting these factors could lead to better treatment outcomes for people living with PPP.

Keywords: Adherence; Biologics; Claims data; Palmoplantar pustulosis; Persistence

Key Summary Points

Why carry out this study?

This study assessed the adherence and persistence of patients with palmoplantar pustulosis (PPP) to their biologic therapies using data from two US healthcare claims databases.

What was learned from the study?

Across the two databases, adherence to biologics amongst patients with PPP was generally poor, with only 34–42% of patients achieving good adherence (≥80% proportion of days covered) across two large US healthcare databases.

Tumor necrosis factor alpha (TNF-α) inhibitors and interleukin (IL) inhibitors were the most used biologics, with patients on IL inhibitors continuing their therapies longer than those on TNF-α or T-cell inhibitors.

Adherence and persistence varied by age and biologic class, with younger patients showing slightly better persistence than older patients, though overall adherence remained suboptimal.

There is a need for tailored PPP treatments that improve both adherence and long-term disease control, along with a better understanding of factors contributing to treatment discontinuation.

INTRODUCTION

Palmoplantar pustulosis (PPP) is a painful, debilitating, chronic skin condition characterized by pustules, erythema, and scales on the palms and soles [1, 2]. PPP disrupts daily functioning, impacting patients' quality of life (QoL), often to a greater extent than common plaque psoriasis [3]. Typically, PPP follows a chronic path, so patients experience long periods of reduced QoL, creating a need for well-tolerated, effective treatments [1, 4]

As topical therapies have limited penetration on acral skin regions, most patients require systemic intervention to realize disease improvements [2, 4]. Current systemic treatment options for PPP, including biologics, are primarily adopted from

medications approved to treat plaque psoriasis [5]. Good treatment adherence and persistence are important for achieving disease control; however, despite the impact of PPP on patients' QoL, suboptimal adherence (38–65%) has been observed in patients with psoriatic conditions [6, 7]. Recent evidence suggests that no systemic drug has demonstrated clear superiority over placebo for disease clearance or improvement, underscoring the challenges in managing PPP effectively [8]. We previously evaluated treatment patterns in patients with newly diagnosed PPP, and found that the use of biologics was low versus other treatments [9]. Here, we describe adherence to and persistence with biologics among US patients with PPP.

METHODS

Methods for this retrospective cohort study have been previously described [9]. Healthcare claims data from the IBM® MarketScan® Commercial (MarketScan) and the Optum® Clinformatics® Data Mart (Optum) databases were used to describe adherence to and persistence with biologics in patients with newly diagnosed PPP. The MarketScan and Optum databases contain commercially and non-commercially insured populations in the USA. All patient data were anonymized; therefore, informed consent was not necessary. Institutional review board approval is not required for publications citing Optum data. Optum data only contains de-identified health information as described by the Health Insurance Portability and Accountability Act (HIPPA) Privacy Rule. No direct identifiers of individuals, employers, households, or providers are included; as such, the study is exempt from patient consent requirements. Restrictions apply to the availability of these data because of a contract between Optum/MarketScan and Boehringer Ingelheim, and data are therefore unavailable to the public. For inquiries on the data set analyzed in this study, please contact Optum (https://www.optum.com) and/or MarketScan (https://www.ibm.com/products/marketscan-research-databases). The

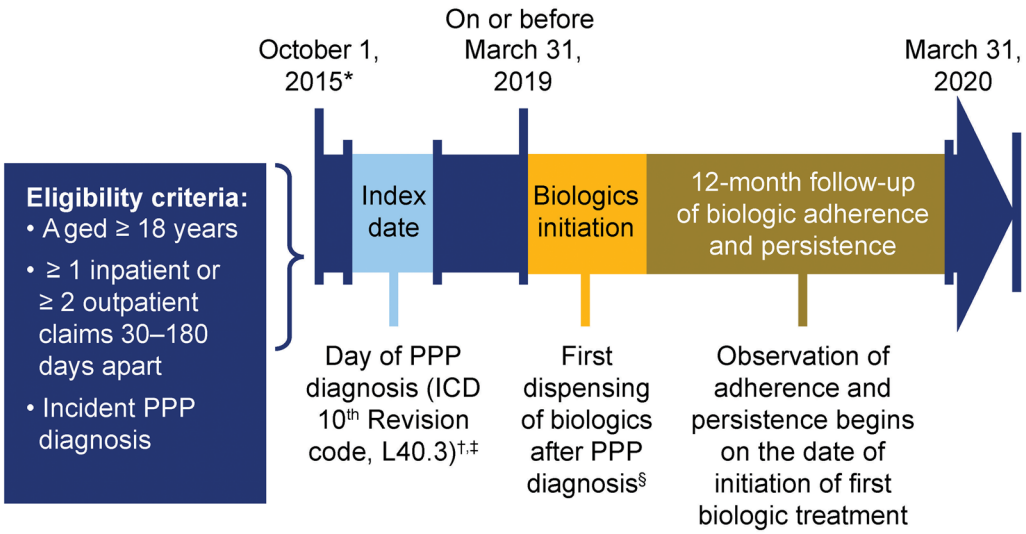

Fig. 1 Study design. *October 1, 2016 was chosen to permit 12 months of baseline evaluation of claims following the ICD 10th Revision in 2015, which introduced a unique code for PPP. †Patient index dates could occur at any point during the study period, and the earliest date was October 1, 2016. ‡A period of 12 months prior to the index date was used to check eligibility and ensure that no claims for PPP had been made prior to this date. §The date of dispensing for initial biologic treatment was also the onset of the 12-month follow-up observation of biologic adherence and persistence. Adult patients with newly diagnosed PPP and at least one inpatient or two outpatient claims data from the IBM® MarketScan® Commercial and the Optum® Clinformatics® Data Mart health databases were retrospectively identified. This study assessed adherence to and persistence with biologics from October 2015 to March 2020. ICD, International Classification of Diseases; PPP, palmoplantar pustulosis

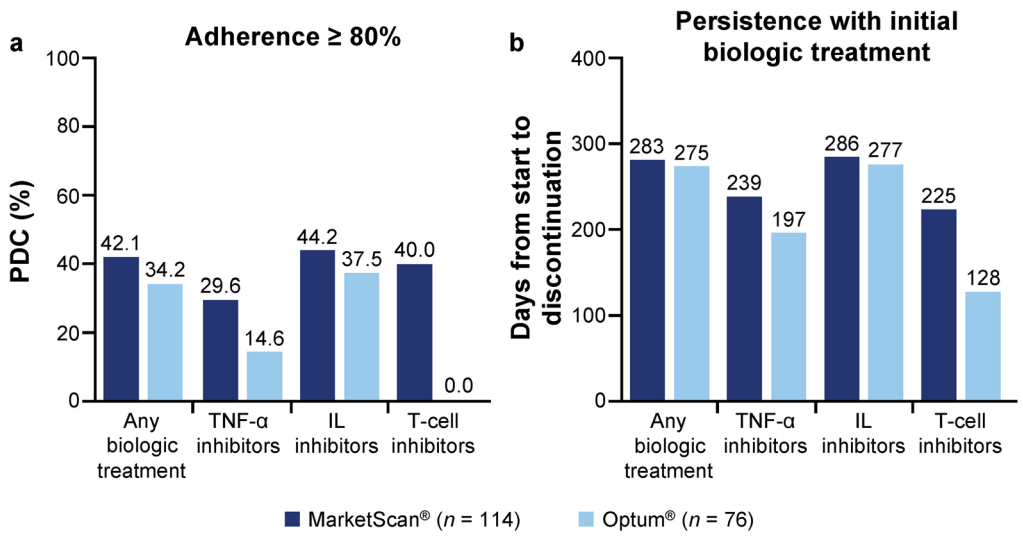

Fig. 2 Biologic treatment adherence (**a**) and persistence (**b**) for MarketScan® and Optum® databases. Patients may have received more than one biologic treatment during the 12-month follow-up period. IL, interleukin; PDC, proportion of days covered; TNF-α, tumor necrosis factor alpha

study spanned from October 1, 2015 to March 31, 2020 (Fig. 1).

Adherence measures how accurately patients take medications as prescribed by healthcare professionals; persistence is defined as the number of days to treatment discontinuation from first dose [7]. Adherence was measured over a 12-month follow-up period and calculated as the proportion of days covered (PDC)—the number of days with filled prescriptions for biologics divided by the total days of follow-up. Good adherence was defined as ≥ 80% PDC. As biologics are prescribed infrequently [9], a dispensing gap of 84 days was permitted and considered continuous use. Patients in the Optum database were reported by age (18–64 and ≥ 65 years); data were limited for patients aged ≥ 65 years in the MarketScan database. All analyses were descriptive; no formal comparisons were made.

RESULTS

Of the 840 (MarketScan) and 750 (Optum) patients with PPP, 114 (13.6%) and 76 (10.1%) patients, respectively, were dispensed biologics and had at least 12 months of follow-up after initiation. Of these, most were treated with tumor necrosis factor alpha (TNF-α) inhibitors (MarketScan, *n* = 81 [71.1%]; Optum, *n* = 49 [64.5%]), and a high proportion were treated with interleukin (IL) inhibitors (MarketScan, *n* = 52 [45.5%]; Optum, *n* = 40 [52.6%]). Few patients (MarketScan, *n* = 5 [4.4%]; Optum, *n* = 3 [3.9%]) were treated with T-cell inhibitors (Table S1).

Mean PDC (range) was similar between databases (MarketScan, 66% [8–100%]; Optum, 61% [8–99%]), with few achieving good adherence (MarketScan, *n* = 48 [42.1%]; Optum, *n* = 26 [34.2%]). Good adherence varied by biologic class but was generally poor (Fig. 2a). Mean (standard deviation [SD]) persistence with biologics was slightly longer in MarketScan versus Optum (283 [121] vs 275 [133] days). Although persistence varied between biologic classes, patients in both databases persisted with IL inhibitors for longer than other biologic classes (Fig. 2b): MarketScan versus Optum (286 [127] vs 277 [135] days), versus TNF-α inhibitors (239 [129] vs 197 [134] days), and T-cell inhibitors (225 [152] vs 128 [114] days).

A sub-analysis of adherence by age group included 76 Optum patients: 61 aged 18–64 years and 15 aged ≥ 65 years. Mean (range) PDC was similar between cohorts (18–64 years, 62% [8–99%]; ≥ 65 years, 57% [8–96%]). Few

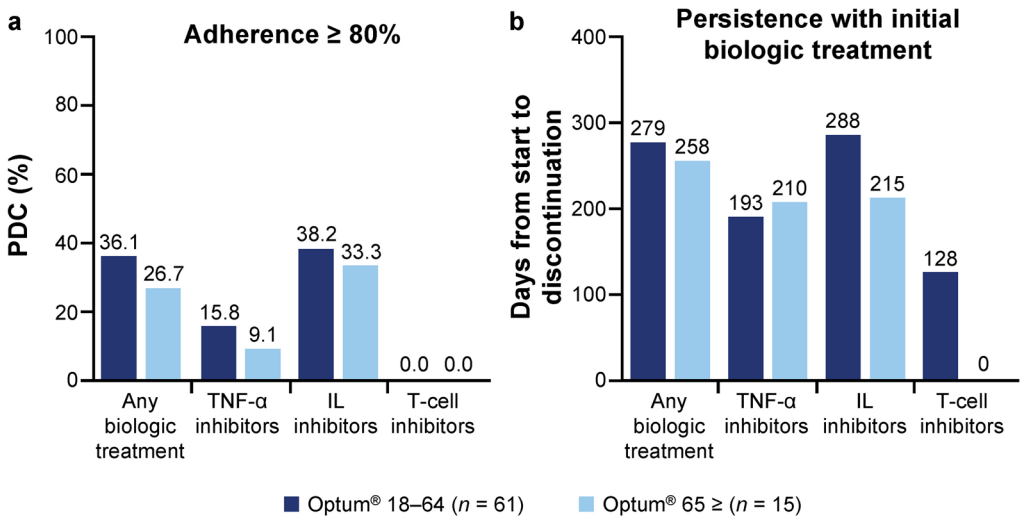

Fig. 3 Biologic treatment adherence (**a**) and persistence (**b**) for Optum® age groups (aged 18–64 and ≥ 65 years). Patients may have received more than one biologic treatment during the 12-month follow-up period. IL, interleukin; PDC, proportion of days covered; TNF-α, tumor necrosis factor alpha

patients in either age group reached good adherence (18–64 years, $n=22$ [36.1%]; ≥ 65 years, $n=4$ [26.7%]). Adherence was generally poor for IL inhibitors (18–64 years, $n=13/34$ [38.2%] and ≥ 65 years, $n=2/6$ [33.3%]) and TNF-α inhibitors ($n=6/38$ [15.8%] and $n=1/11$ [9.1%]). No patients aged 18–64 years reached good adherence to T-cell inhibitors, and no patients aged ≥ 65 years were treated with this biologic class (Fig. 3a). The mean (SD) persistence with biologics was longer in patients aged 18–64 versus ≥ 65 years (279 [132] vs (258 [140] days). Although persistence varied by biologic class (mean [SD]) (Fig. 3b), both cohorts persisted with IL inhibitors (18–64 years, 288 [129] days vs ≥ 65 years, 215 [167] days) for longer versus TNF-α inhibitors (193 [133] vs 210 [140] days) and T-cell inhibitors (128 [114] days vs not applicable).

DISCUSSION

This retrospective cohort study used data from two large US claims databases to describe adherence to and persistence with biologics in patients with PPP. The MarketScan and Optum databases contain claims data for enough patients (approx. 150 million and 65 million, respectively) to be considered largely representative of the population of commercially insured patients in the USA. Adherence was generally low regardless of database, age group, or biologic class, with few patients reaching good adherence. These data align with previous observations of suboptimal biologic adherence in patients with psoriasis [6, 7]. While German and US patients with PPP treated with biologics had higher levels of adherence compared with patients treated with other treatment options, the adherence levels were still not optimal [10]. In the current study, overall persistence was generally acceptable in both databases and age groups, but varied by biologic class. Broadly, patients persisted with IL inhibitors for longer than T-cell inhibitors or TNF-α inhibitors, suggesting that IL inhibitors may provide better disease control.

There are several potential explanations for the observed adherence and persistence. One possibility for the discontinuation of treatment is a lack of efficacy. This aligns with findings from a study by Bertelsen et al., which identified lack of efficacy as the most common cause of biologics discontinuation in PPP, accounting for 54.3% of cases [11]. Recent evidence from

the first ever genome-wide association study in PPP points to a pathogenic role of deregulated Th2 inflammatory responses [12]. Dupilumab, an anti-IL-4Ra monoclonal antibody that inhibits IL-4 and IL-13—key cytokines in Th2 inflammatory pathways—has demonstrated efficacy in a small case series of patients with PPP [13], supporting the role of Th2 inflammation in PPP. However, only a small percentage of patients in this study received biologics targeting Th2 signaling, and notably, none received dupilumab (Table S1). Further evidence from RNA sequencing of skin biopsy samples and peripheral blood from patients with PPP have shown complex T-cell activation patterns, involving Th17 to Th2 plasticity, providing a potential explanation for why biologic drugs that target individual T-helper-cell populations have shown limited therapeutic efficacy [14]. Together, these studies raise the possibility that the low adherence observed in our study may be attributed to the use of biologics that either do not target the key inflammatory processes underlying PPP or target only one of several complex inflammatory processes. These findings underscore the importance of identifying and developing therapies that align more closely with the pathophysiologic mechanisms of PPP to improve treatment outcomes.

As there are currently no standardized treatment guidelines for PPP [5], low adherence may reflect trial and error as healthcare professionals attempt to find an efficacious and tolerable treatment for their patients. Another possible explanation is that, paradoxically, biologics sometimes trigger or exacerbate PPP [15] and have associated adverse events (AEs) [16]. Therefore, treatment may have been discontinued because of AEs or biologic-induced symptomatic worsening. The relapsing–remitting cyclic nature of PPP may also be a factor impacting adherence and persistence [5]; following an initial improvement with a fast-acting monotherapy, a transition to a combined treatment may occur [17]. Adherence and persistence rates may be influenced by a patient's lack of habit of taking medication consistently [18].

The primary limitation of this study is that treatment data for patients with less than 12 months of follow-up after initial biologics dispensing were omitted. Although this likely led to the inclusion of fewer patients, these data could have skewed mean adherence and persistence, thus their exclusion may provide a reliable depiction of long-term real-world treatment adherence and persistence. Additionally, the reliability of accurately identifying patients with PPP using the International Classification of Diseases, 10th Revision code (L40.3) is not established; therefore, PPP cases may have been missed. It is possible that medications dispensed for PPP were coded under the general psoriasis code for insurance purposes, resulting in some patients who would otherwise have qualified for the study being missed. In these databases, it is not possible to confirm that medications were dispensed specifically to treat PPP. Furthermore, while prescription fills serve as a commonly used proxy for medication adherence, they do not confirm that medications were actually taken as prescribed. Claims databases, such as Optum or MarketScan, record only prescriptions filled and cannot capture true adherence without supplementary data, such as patient diaries or electronic monitoring. A further limitation is the small sample size, which, despite the use of the stringent inclusion criteria to increase the reliability of the results, may have affected the precision of the results. Finally, the methodologies in this study have not been validated; however, we have adhered to current best practices [19].

Further research is needed to understand the most common reasons for discontinuation of biologics in PPP. Bertelsen et al. analyzed 85 patients with PPP who underwent 194 biologic treatment courses from a Danish nationwide registry. Of these, 151 courses (77.8%) were discontinued, with lack of efficacy accounting for 54.3%, other causes for 27.2%, and AEs for 18.5% [11]. In our analysis, reasons for discontinuation were not captured in the databases. Establishing the reasons underlying poor adherence and implementing strategies to increase adherence may improve treatment outcomes for patients with PPP.

CONCLUSION

Our analyses describe the poor adherence to and variable persistence with biologics in patients with PPP. To improve adherence and persistence, rapidly active, PPP-directed treatments are needed to provide long-term disease control, including flare prevention.

ACKNOWLEDGEMENTS

We thank the participants of the study.

Medical Writing, Editorial and Other Assistance. In the preparation of this manuscript, Shivani Singh, PhD of Nucleus Global, and Alex Morrison, MSc and Clare Bellward, MRes of Hyperion, OPEN Health Communications, provided medical writing, editorial support, and formatting support, which was contracted and funded by Boehringer Ingelheim.

Author Contributions. Conceptualization: All authors. Methodology: All authors. Formal analysis and investigation: All authors. Study design: Steven R. Feldman, Rhonda L. Bohn, Ran Gao. Study investigator: Anouk Déruaz-Luyet. Enrolled patients: Not applicable. Collection and assembly of data: Ran Gao. Data analysis: Ran Gao, Rhonda L. Bohn, Anouk Déruaz-Luyet. Data interpretation: All authors. Manuscript preparation: All authors. Writing—review and editing: All authors. Manuscript review and revisions: All authors. Final approval of manuscript: All authors. Funding acquisition: Anouk Déruaz-luyet. Supervision: Ran Gao, Jashin J. Wu.

Funding. The study was supported and funded by Boehringer Ingelheim including the Rapid Service fee.

Data Availability. We conducted an observational study using claims data from the Optum® Clinformatics® data mart and IBM® MarketScan® commercial research databases, which are databases of commercially and non-commercially insured populations in the USA. All patient data were anonymized; therefore, informed consent was not necessary. Restrictions apply to the availability of these data because of a contract between Optum/MarketScan and Boehringer Ingelheim, and data are therefore unavailable to the public. For inquiries on the data set analyzed in this study, please contact Optum (https://www.optum.com) and/or MarketScan (https://www.ibm.com/products/marketscan-research-databases).

Declarations

Conflict of Interest. Steven R. Feldman declares receiving research, speaking, and/or consulting support from AbbVie, Accordant, Advance Medical, Almirall, Alvotech, Amgen, Arcutis, Arena Pharmaceuticals, Argenx, Biocon, Boehringer Ingelheim, Bristol Myers Squibb, Caremark, Celgene, Dermavant, Eli Lilly, Galderma, GSK/Stiefel, Helsinn, Informa, Janssen, Leo Pharma, Menlo, Merck, Mylan, National Biological Corporation, National Psoriasis Foundation, Novan, Novartis, Pfizer, Qurient, Regeneron, Samsung, Sanofi, Sun Pharmaceutical Industries, Suncare Research Laboratories, UCB, UpToDate, Valeant, and vTv Therapeutics. He is also the founder and majority owner of http://www.DrScore.com and has stock in Sensal. Ran Gao is a former employee of Boehringer Ingelheim. Rhonda L. Bohn is the founder of Bohn Epidemiology, LLC, and has served as a consultant to Boehringer Ingelheim. Stephani Gray declares being a consultant to Boehringer Ingelheim and Bohn Epidemiology, LLC. Anouk Déruaz-Luyet is an employee of Boehringer Ingelheim. Jashin J. Wu declares being an investigator, consultant, or speaker for AbbVie, Almirall, Amgen, Arcutis, Aristea Therapeutics, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, DermTech, Dr. Reddy's Laboratories, Eli Lilly, EPI Health, Galderma, Janssen, Leo Pharma, Mindera, Novartis, Pfizer, Regeneron, Samsung Bioepis, Sanofi Genzyme, Solius, Sun Pharmaceutical Industries, UCB, and Zerigo Health.

Ethical Approval. The MarketScan and Optum databases contain commercially and non-commercially insured populations in the

USA. All patient data were anonymized; therefore, informed consent was not necessary. Institutional review board approval is not required for publications citing Optum data. Optum data only contains de-identified health information as described by the HIPPA Privacy Rule. No direct identifiers of individuals, employers, households, or providers are included; as such, the study is exempt from patient consent requirements.

REFERENCES

1. Murakami M, Terui T. Palmoplantar pustulosis: current understanding of disease definition and pathomechanism. J Dermatol Sci. 2020;98(1):13–9.

2. Raposo I, Torres T. Palmoplantar psoriasis and palmoplantar pustulosis: current treatment and future prospects. Am J Clin Dermatol. 2016;17(4):349–58.

3. Lebwohl MG, Medeiros RA, Mackey RH, et al. Palmoplantar pustulosis has a greater disease burden than plaque psoriasis: real-world evidence from the CorEvitas Psoriasis Registry. J Psoriasis Psoriatic Arthritis. 2023;8(2):56–65.

4. Miceli A, Schmieder GJ. Palmoplantar psoriasis. StatPearls [Internet] 2022. https://www.ncbi.nlm.nih.gov/books/NBK448142/?report=classic. Accessed 26 Nov 2024.

5. Menter A, Van Voorhees AS, Hsu S. Pustular psoriasis: a narrative review of recent developments in pathophysiology and therapeutic options. Dermatol Ther (Heidelb). 2021;11(6):1917–29.

6. Doshi JA, Takeshita J, Pinto L, et al. Biologic therapy adherence, discontinuation, switching, and restarting among patients with psoriasis in the US Medicare population. J Am Acad Dermatol. 2016;74(6):1057–1065.e4.

7. Piragine E, Petri D, Martelli A, et al. Adherence and persistence to biological drugs for psoriasis: systematic review with meta-analysis. J Clin Med. 2022;11(6):1506.

8. Spencer RK, Jin JQ, Elhage KG, et al. Comparative efficacy of biologics and oral agents in palmoplantar psoriasis and palmoplantar pustulosis: a systematic review and network meta-analysis of randomized clinical trials. J Am Acad Dermatol. 2023;89(2):423–5.

9. Wu JJ, Gao R, Bohn RL, et al. Varied treatment patterns among patients with palmoplantar pustulosis (PPP): a claims-based cohort study using data from two large US databases. JAAD Int. 2024;15:192–4.

10. Cheng A, Ding X, Yang F, et al. Treatment patterns and negative health outcomes in palmoplantar pustulosis patients in Germany and the US. Dermatol Ther (Heidelb). 2024;14(3):627–41.

11. Bertelsen T, Egeberg A, Skov L, et al. Drug survival of biologic therapies for palmoplantar pustulosis: a nationwide study. J Eur Acad Dermatol Venereol. 2024;38(2):332–9.

12. Hernandez-Cordero A, Thomas L, Smail A, et al. A genome-wide meta-analysis of palmoplantar pustulosis implicates T(H)2 responses and cigarette smoking in disease pathogenesis. J Allergy Clin Immunol. 2024;154(3):657-665.e9.

13. Zheng YX, Chen XB, Wang ZY, et al. Efficacy of dupilumab in palmoplantar pustulosis treatment highlights the role of Th2 inflammation. Allergy. 2024;79(5):1361–4.

14. McCluskey D, Benzian-Olsson N, Mahil SK, et al. Single-cell analysis implicates T(H)17-to-T(H)2 cell plasticity in the pathogenesis of palmoplantar pustulosis. J Allergy Clin Immunol. 2022;150(4):882–93.

15. Li QY, Wang G. Successful treatment of adalimumab-resistant palmoplantar pustulosis with secukinumab: a case report. Chin Med J (Engl). 2020;133(24):3013–4.

16. Kishimoto M, Komine M, Kamiya K, Sugai J, Mieno M, Ohtsuki M. Drug survival of biologic agents for psoriatic patients in a real-world setting in Japan. J Dermatol. 2020;47(1):33–40.

17. Lebwohl M, Menter A, Koo J, Feldman SR. Combination therapy to treat moderate to severe psoriasis. J Am Acad Dermatol. 2004;50(3):416–30.

18. Thorneloe RJ, Griffiths CEM, Emsley R, et al. Intentional and unintentional medication non-adherence in psoriasis: the role of patients' medication beliefs and habit strength. J Investig Dermatol. 2018;138(4):785–94.

19. Sobell JM, Gao R, Golembesky AK, et al. Healthcare resource utilization and baseline characteristics of patients with generalized pustular psoriasis: real-world results from a large US database of multiple commercial medical insurers. J Psoriasis Psoriatic Arthritis. 2021;6(3):143–50.