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ORIGINAL RESEARCH

Early Discontinuation of Apremilast in Patients with Psoriasis and Gastrointestinal Comorbidities: Rates and Associated Risk Factors

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ABSTRACT

Introduction: Apremilast, the first oral targeted treatment for moderate to severe psoriasis, is associated with diarrhea, nausea, and vomiting, which have contributed to treatment discontinuation. This study describes early apremilast discontinuation rates in patients with psoriasis, including a cohort with gastrointestinal (GI) comorbidities, and associated characteristics.

Methods: This retrospective cohort study used IBM® (now Merative™) MarketScan® commercial and Medicare claims data to identify adults with psoriasis who filled their first apremilast prescription between September 1, 2014 and March 31, 2020. Discontinuation was defined as a gap of > 30 days after exhausting the days' supply of a prescription fill. The GI comorbidity cohort included patients with ≥ 1 claim for inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), or other GI comorbidity during the study period.

Results: Discontinuation rates were high, regardless of previous biologic treatment or GI comorbidities. Among all patients, 25.5% discontinued within 60 days and 56.4% discontinued within 180 days. Patients who discontinued were more likely to be younger, female, and have IBD, Crohn's disease, or a mental health disorder. At 180 days, patients who used biologics previously were more likely to discontinue than biologic-naive patients. Patients with IBD discontinued at a greater rate than those without IBD at 60 days (30.3% vs 24.4%; $P = 0.018$) and 180 days (63.6% vs 57.2%; $P = 0.026$). Differences in discontinuation rates were minimal between GI comorbidity groups; patients with IBS discontinued at numerically higher rates than those without IBS.

Conclusions: High rates of early discontinuation were observed for patients with and without GI comorbidities. Early discontinuation, whether attributable to poor tolerability or effectiveness, suggests the need for additional oral treatment options.

Keywords: Claims analysis; Cohort study; Retrospective study; Treatment adherence

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PLAIN LANGUAGE SUMMARY

Patients with moderate to severe psoriasis, a chronic condition, often must take medication regularly. Effective treatments are available, but patients may be reluctant to use them because they are shots, are expensive, can lose effectiveness, or may cause side effects. Apremilast is a pill, so it eliminates the need for shots. However, it has been linked to gastrointestinal side effects, such as diarrhea, nausea, and vomiting, which cause some patients to stop taking apremilast. Because patients with psoriasis may also have a condition that increases their sensitivity to gastrointestinal side effects, the side effects of apremilast may be concerning, and these patients may stop apremilast treatment more often than those without such conditions. This study looked into that question by examining information from prescription claims from patients treated for psoriasis during a specific time frame. Patients were categorized as those with and those without gastrointestinal conditions (inflammatory bowel disease, irritable bowel syndrome, and other gastrointestinal conditions). Among all patients, the proportion who stopped apremilast treatment was high, regardless of whether they had a gastrointestinal condition. Two months after starting treatment, 25% had stopped, and by 6 months, 56% had stopped. More patients with inflammatory bowel disease stopped treatment than those without the condition, but differences between patients with and without other gastrointestinal conditions were slight. Because more than half of patients stopped taking apremilast within 6 months of starting treatment, regardless of why they stopped, there is a need for additional treatment options.

Graphical Abstract:

Early Discontinuation of Apremilast in Patients With Psoriasis and Gastrointestinal Comorbidities: Rates and Associated Risk Factors

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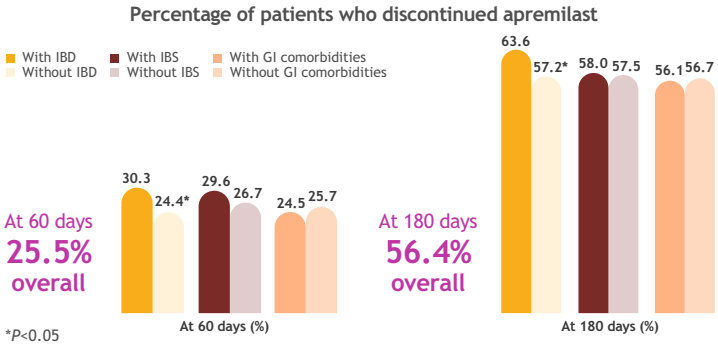
Key findings

Treatment discontinuation rates are high among patients with psoriasis who are treated with apremilast, regardless of their GI comorbidity status



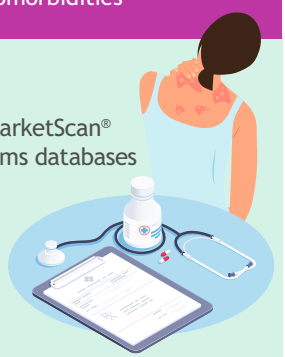
Early discontinuations signal the need for additional oral treatment options

Study objective

To determine real-world early discontinuation rates of apremilast in patients with psoriasis, with and without GI comorbidities

Study design

Retrospective claims analysis using the IBM® MarketScan® (now Merative) Commercial and Medicare claims databases



Patient population

Patients with psoriasis who filled a prescription for apremilast between September 1, 2014, and March 31, 2020 (**N=11,618**)

Patients were propensity score matched by the presence of >1 claim for IBS and/or IBD and/or other GI comorbidities to adjust for potential selection bias

GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

Adis OPEN ACCESS PEER-REVIEWED FEATURE

Key Summary Points

Apremilast for the treatment of moderate to severe plaque psoriasis is associated with adverse events that can include diarrhea, nausea, and vomiting, which may result in treatment discontinuation.

Many patients with psoriasis have a comorbidity that can increase their susceptibility to gastrointestinal (GI) adverse events.

Increased susceptibility to GI adverse events coupled with treatment-associated GI comorbidities may affect early discontinuation of apremilast among patients with moderate to severe plaque psoriasis.

Early discontinuation rates with apremilast were high, ranging from 24.4% to 63.6%, depending on the time point of the evaluation and on the comorbidities present.

High rates of early discontinuation may be a cause of concern for patients receiving apremilast, regardless of GI comorbidity status, and suggest the need for additional oral treatment options.

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.23585952.

INTRODUCTION

Patients with moderate to severe psoriasis often require systemic therapy, which may include traditional nonbiologic therapies as well as biologics, including antitumor necrosis factor agents, interleukin (IL)-23, IL-12/23, and IL-17 inhibitors, and the newest class, tyrosine kinase 2 (TYK2) inhibitors [1–3]. The use of biologics may be limited by their injectable route of administration, loss of effect, high costs, and potential adverse events [4, 5]. Apremilast, a phosphodiesterase 4 inhibitor, was the first oral targeted therapy approved by the US Food and Drug Administration for the treatment of patients with psoriasis who are candidates for systemic treatment [6, 7]. Tolerability of apremilast is a concern, as apremilast treatment is associated with adverse events that can include diarrhea, nausea, and vomiting. These may require dose reduction or suspension, as noted in the warnings and precautions section of the apremilast package insert [8].

Early discontinuation of apremilast because of these tolerability issues is common in patients with psoriasis [9] and was observed during randomized controlled trials of apremilast [10, 11]. Furthermore, many patients with psoriasis have comorbidities that can increase their susceptibility to gastrointestinal (GI) adverse events [12]. Real-world studies found that among patients who discontinued apremilast as a result of adverse events, diarrhea was the most commonly reported adverse event [13, 14]. Additionally, apremilast treatment duration decreased as patients' comorbidity burden increased [13], which raises the question of whether patients with psoriasis and GI comorbidities that predispose them to nausea, vomiting, and diarrhea may, in fact, discontinue treatment at a higher rate than patients without such comorbidities.

The objective of this study was to determine real-world early discontinuation rates of apremilast (at 60, 90, and 180 days after starting apremilast treatment) in patients with psoriasis with and without GI comorbidities. Patient characteristics associated with early discontinuation were also assessed to further explore factors associated with treatment discontinuation.

METHODS

Study Design

Data for this retrospective cohort study of patients with psoriasis newly initiated on

apremilast were obtained from the IBM® (now Merative™) MarketScan® Research Commercial Claims and Encounters and Medicare Supplemental and Coordination Benefits databases. The study period spanned from September 1, 2013, through March 31, 2021. The index period extended from September 1, 2014, to March 31, 2020, with the 12 months prior to the index date (first apremilast prescription fill) designated as the baseline period, and the 12 months post-index designated as the follow-up period (Fig. 1).

This retrospective cohort study using administrative claims data complied with the Helsinki Declaration of 1964. All patient data were de-identified, and no patients were directly involved in the study. Thus, institutional review board approval was waived.

Patient Selection

The study population included adults at least 18 years of age who had at least two medical claims with a psoriasis diagnostic code (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code 696.1; ICD-10-CM diagnosis codes L40.0–L40.4, L40.8, L40.9) (at least 1 day apart) during the study period and who newly initiated apremilast treatment. All patients were required to have a minimum of 12 months of continuous enrollment pre- and post-index.

The overall cohort contained both biologic-naive and biologic-experienced patients, with biologic-experienced patients having received biologic treatment during the baseline period. Specific cohorts were created for patients with and without irritable bowel syndrome (IBS), with and without inflammatory bowel disease (IBD), and with and without GI comorbidities. Gastrointestinal comorbidities included (1) IBD, which included Crohn's disease or ulcerative colitis; (2) IBS; and (3) other GI comorbidities, which included gastroenteritis, colitis, vascular disorder of the intestine, intestinal obstruction, diverticulitis, fissure/fistula, abscess, and hemorrhoids. Patients in the "with GI comorbidity" cohort had at least one claim recorded with a diagnosis code for a GI comorbidity at any time during the continuously enrolled pre- and post-index periods (ICD-9 diagnosis codes 555.0–555.2, 555.9, 556.0–556.6, 556.8, 556.9; ICD-10 diagnosis codes K50.00, K50.10, K50.80, K50.90, K51.00, K51.20–K51.40, K51.80, K51.90).

Outcome Measures

The primary outcome measures were the numbers and percentages of patients with and without GI comorbidities who discontinued treatment within the first 60, 90, and 180 days after the initiation of apremilast and the identification of patient characteristics associated with early treatment discontinuation. Patients were identified as discontinuers if they had a gap of more than 30 days following the exhaustion of days' supply of their index apremilast fill.

Statistical Analysis

Patient demographics and clinical characteristics were evaluated during the baseline and follow-up periods. Descriptive statistics were provided for patient characteristics and outcomes. Continuous variables were summarized using means, standard deviations (SDs), and medians. Categorical variables were assessed using counts and percentages. Descriptive baseline patient characteristics and outcomes among patients with and without selected comorbid conditions were compared using a χ^2 test for categorical variables and a Kruskal–Wallis test for continuous variables. A P value of 0.05 or less was considered statistically significant.

Patients were propensity score matched by the presence of IBS and/or IBD comorbidities as well as other GI comorbidities during the pre- and post-index periods to adjust for potential selection bias. A logistic regression was used to estimate the propensity score for individual patients controlling for the following covariates: age, sex, region, index year, Charlson Comorbidity Index (CCI) score, baseline comorbidities, and treatment history. Variable

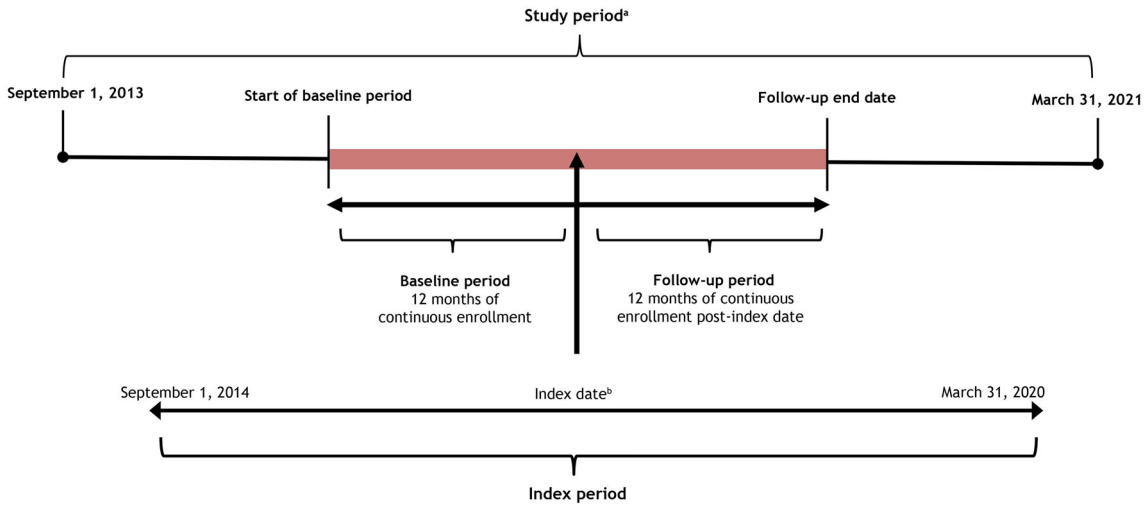


Fig. 1 Study design. [a]Patient data at any time during the continuously enrolled baseline and follow-up periods were used to identify comorbidities. [b]Index date is the date of the patient's first apremilast prescription filled during the index period (September 1, 2014–March 31, 2020)

ratio matching was performed in which each patient with an IBS or IBD comorbidity was matched with four comparison patients, and patients with GI comorbidities were matched 1:1 to patients without GI comorbidities.

RESULTS

A total of 11,618 patients were included in the study population, with 8591 in the biologic-naive cohort and 3027 in the biologic-experienced cohort (Table 1). The overall mean age was 50.6 years (SD, 12.6 years), and the majority of patients were female (57.1%). The overall mean CCI score was 0.85 (SD, 1.43). The most common baseline comorbidities included psoriatic arthritis, hypertension, hyperlipidemia, and obesity. At baseline, 57.2% of patients had a GI comorbidity, 3.2% had IBD, and 7.5% had IBS.

In the overall population, the apremilast discontinuation rates were high, regardless of previous biologic treatment experience and GI comorbidities (Fig. 2). Among all patients, 25.5% discontinued by 60 days and 56.4% discontinued by 180 days. At 60 days, discontinuation rates ranged from a low of 25.0% in patients with GI comorbidities to a high of 26.3% for those without GI comorbidities. At 180 days, discontinuation rates ranged from a low of 55.1% for biologic-naive patients to a high of 60.0% for those who were biologic experienced.

Patients who discontinued apremilast at 180 days were significantly younger than those who did not discontinue (49.4 vs 52.2 years; $P < 0.0001$). A greater proportion of patients who discontinued than those who did not discontinue had comorbid IBD (1.4% vs 0.8%, respectively; $P = 0.019$), Crohn's disease (0.6% vs 0.3%, respectively; $P = 0.008$), or mental health disease (20.7% vs 17.4%, respectively; $P < 0.0001$). Conversely, a smaller proportion of patients who discontinued versus those who did not discontinue had hyperlipidemia (35.8% vs 40.3%, respectively; $P < 0.0001$) or hypertension (37.8% vs 42.1%, respectively; $P < 0.0001$).

After propensity score matching patients with and without IBS, IBD, and other GI comorbidities, apremilast discontinuation rates remained high for patients with GI comorbidities in general, as well as for those with IBS and IBD specifically. A significantly greater proportion of patients with IBD discontinued compared with those without IBD at 60 days (30.3% vs 24.4%; $P = 0.018$) and 180 days (63.6% vs 57.2%; $P = 0.026$) (Fig. 3). A numerically greater proportion of patients with IBS discontinued compared with those without IBS, with

Table 1 Demographics and baseline clinical characteristics

Characteristic	Patients (N = 11,618)
Age at index, years	
Mean (SD)	50.6 (12.6)
Median (min, max)	52.0 (18.0, 100)
Sex, *n* (%)	
Female	6631 (57.1)
Male	4987 (42.9)
CCI score, mean (SD)	0.85 (1.43)
Comorbidities, *n* (%)	
Hypertension	4608 (39.7)
Hyperlipidemia	4389 (37.8)
Psoriatic arthritis	3512 (30.2)
Obesity	2550 (21.9)
Mental health disorder	2236 (19.3)
Diabetes	2069 (17.8)
GI comorbidities[a]	6643 (57.2)
IBS	868 (7.5)
IBD[b]	376 (3.2)

CCI Charlson Comorbidity Index, *GI* gastrointestinal, *IBD* inflammatory bowel disease, *IBS* irritable bowel syndrome, *SD* standard deviation

[a]GI comorbidities included gastroenteritis, colitis, vascular disorder of the intestine, intestinal obstruction, diverticulitis, fissure/fistula, abscess, and hemorrhoids

[b]IBD includes Crohn's disease and ulcerative colitis

discontinuation rates ranging from nearly 30% at 60 days to approximately 60% by 180 days. Conversely, a numerically smaller proportion of patients with GI comorbidities than those without discontinued, with discontinuation rates ranging from approximately 25% at 60 days to nearly 60% at 180 days (Figs. 4 and 5).

DISCUSSION

This real-world claims analysis demonstrated that early discontinuation rates with apremilast were high, ranging from 24.4% to 63.6%, depending on the time point of the evaluation and on the comorbidities present. These findings are consistent with previously published real-world studies. At 1-year follow-up, 43% of patients who initiated treatment with biologics either discontinued or switched to another therapy [15]. Among patients using apremilast, treatment discontinuation rates by 52 weeks ranged from 40.6% to 53.1% [16, 17], while other studies reported that 32.4% of patients discontinued by week 24 [14], and 45.1% of patients discontinued after an average of 39 weeks [13]. Additionally, our finding that patients who discontinued apremilast were significantly younger than those who did not discontinue is supported in the literature [17]. High early discontinuation rates may be a reflection of poor effectiveness or tolerability [10] and may lead to greater burden on clinical staff to process new treatment approvals and monitor tolerability issues. Previous research demonstrated that treatment duration is shorter among patients with a higher comorbidity burden [13], and that treatment side effects, including GI conditions, are one of the common reasons for early apremilast discontinuation [9–11, 16, 17]. High discontinuation rates, particularly within the first 90 to 180 days, are a concern because clinicians may be unaware when patients stop treatment, thus their symptoms will remain inadequately addressed, and patients who discontinue treatment incur higher healthcare utilization costs [15]. In addition, insurance preauthorization requirements for many psoriasis treatments take considerable time to process and patients may discontinue treatment before the prescription is approved.

A key strength of this retrospective study is its use of insurance claims data to provide a fuller understanding of real-world psoriasis treatment practice and patient adherence patterns compared with those observed under the controlled conditions of a clinical trial. Furthermore, retrospective claims analyses allow for the inclusion of patients who are often under-represented in clinical trials owing to exclusion criteria, such as those with specific

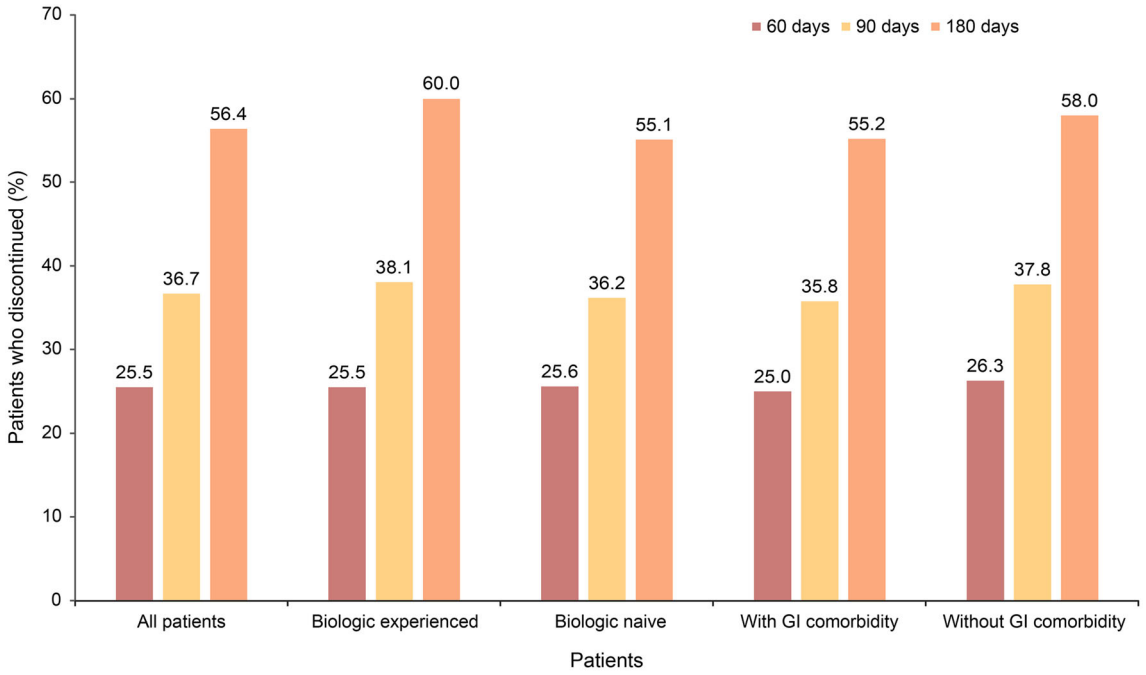


Fig. 2 Overall apremilast treatment discontinuation rates. *GI* gastrointestinal

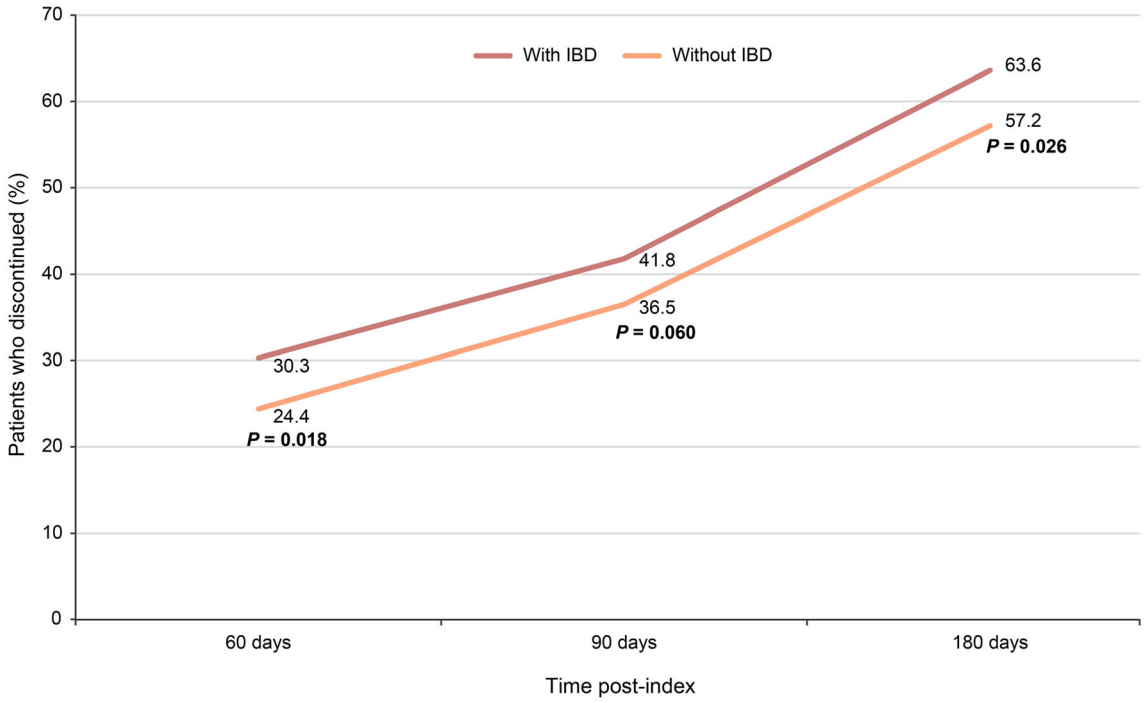


Fig. 3 Discontinuation rates for IBD cohorts. *IBD* inflammatory bowel disease

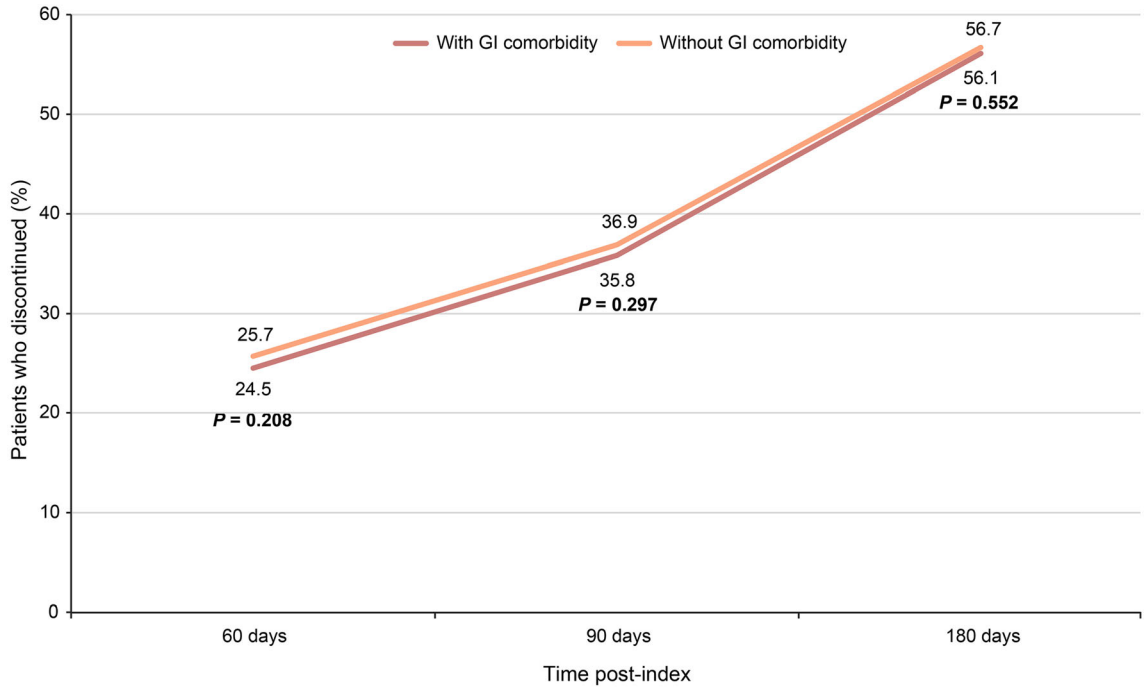


Fig. 4 Discontinuation rates for GI comorbidities. [a]GI comorbidities included gastroenteritis, colitis, vascular disorder of the intestine, intestinal obstruction, diverticulitis, fissure/fistula, abscess, and hemorrhoids. *GI* gastrointestinal

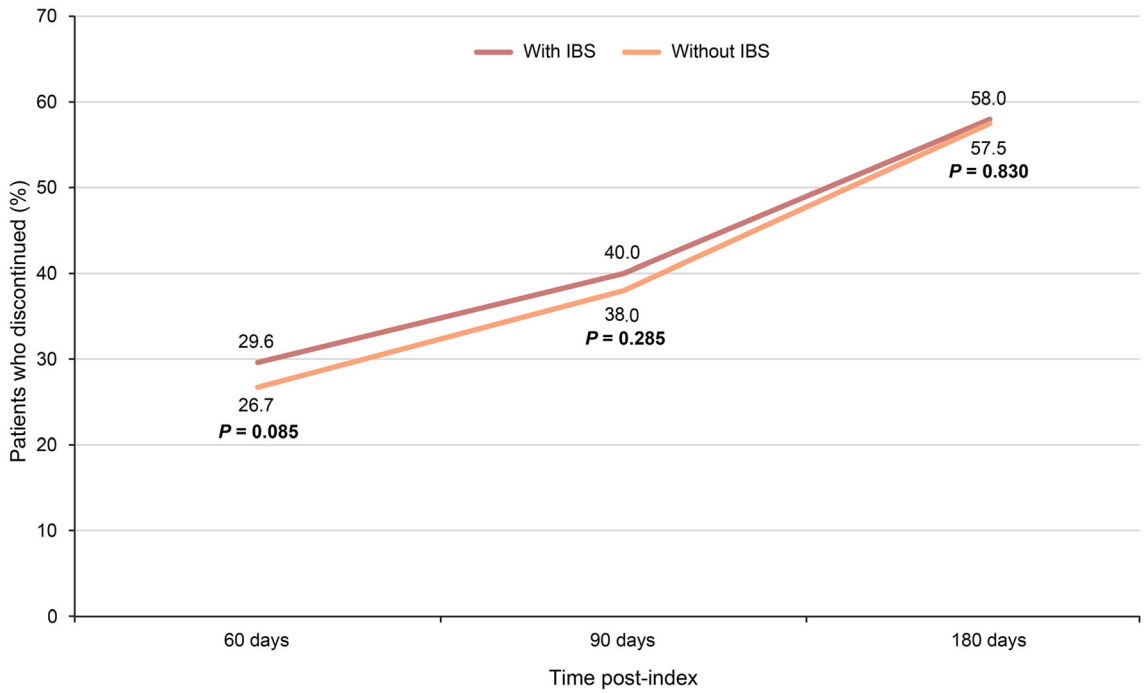


Fig. 5 Discontinuation rates for IBS. *IBS* irritable bowel syndrome

comorbidities and the elderly, while also capturing a wide geographic dispersion of patients.

Several limitations should be considered when interpreting these results. Discontinuations within the first 30 days could not be examined since prescription claims data only record dispensed medications and most initial prescriptions were for a 30-day supply. Claims data capture only prescriptions submitted for insurance payment; thus, patients who initiated apremilast using samples provided by healthcare providers were not recorded. In addition, although prescriptions for apremilast were filled, it is uncertain if patients took the medication as prescribed, and reinitiation of apremilast after a prescription refill gap of longer than 30 days was not captured in this analysis. The claims contained only data regarding prescription fills and did not record the reasons for treatment discontinuation. Treatment discontinuation rates may be higher in biologic-experienced versus biologic-naive patients because the former patients are aware of the numerous types of psoriasis treatments available, and they may be less willing to wait for a treatment to become effective or to manage side effects. These patients may also be frustrated with previously used systemic treatments and may be more likely to abandon one in favor of a potentially more effective option. Further research, including primary data collection studies, is needed to better understand the reasons for discontinuation. As in all claims-based studies, medical claims were submitted by healthcare providers for reimbursement, not for research purposes, and may have contained coding errors or used coding for the purposes of ruling out a diagnosis rather than submitting an actual diagnosis. All patients in the claims database had commercial insurance; thus, these findings may not be generalizable to patients who are uninsured or who have other types of insurance, or to patients outside the USA.

CONCLUSIONS

High rates of early discontinuation are a cause of concern for patients receiving apremilast, regardless of GI comorbidity status, although the rates are slightly higher at 60 and 180 days in patients with IBD than in those without IBD. High rates of early discontinuation, whether attributable to poor tolerability or effectiveness, suggest the need for additional oral treatment options. A chart review or survey study of the rates and reasons for early discontinuation of apremilast would build on these findings and could help address the limitations of the current study.

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Author Contributions. L Schmidt, CA Wang, V Patel, D Davidson, S Kalirai, and L Seigel contributed to the study design. CA Wang and A Panda participated in the collection and assembly of data and in data analysis. All authors had full access to the data and contributed to the drafting, critical review, and revision of the manuscript. All authors granted approval of the final manuscript for submission.

Prior Presentation. This study was presented in part at the 31st Congress of the European Academy of Dermatology and Venereology, September 7–10, 2022, in Milan, Italy.

Disclosures. L Schmidt has served as a speaker for AbbVie, Amgen, Eli Lilly, Incyte, and Janssen. CA Wang, V Patel, S Kalirai, and L Seigel are employees of Bristol Myers Squibb and may be shareholders in the company. At the time of the study, D Davidson was an employee of Bristol Myers Squibb, and A Panda was an employee of Mu Sigma, which received support from Bristol Myers Squibb for data analysis.

Compliance with Ethics Guidelines. This retrospective cohort study using administrative medical claims data complies with the Helsinki Declaration of 1964. No patients were directly involved in the study, and only de-identified patient information was used; thus, institutional review board approval was waived. Permission to access the claims data was obtained through a licensing agreement.

Data Availability. Data for these analyses were made available to the authors through a third-party license from IBM® (now Merative™) MarketScan®, a commercial data provider of commercial and Medicare claims data in the United States. As such, the authors cannot make these data publicly available due to a data use agreement. Other researchers can access these data by purchasing a license through Merative™. Inclusion criteria specified in the Methods section would allow other researchers to identify the same cohort of patients used in these analyses. Interested parties may see https://www.merative.com/real-world-evidence for more information on these data.

REFERENCES

1. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. Int J Mol Sci. 2019;20(6):1475.

2. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. J Am Acad Dermatol. 2023;88(1):29–39.

3. Strober B, Thaçi D, Sofen H, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, Program fOr Evaluation of TYK2 inhibitor psoriasis second phase 3 trial. J Am Acad Dermatol. 2023;88(1):40–51.

4. Armstrong AW, Robertson AD, Wu J, Schupp C, Lebwohl MG. Undertreatment, treatment trends, and treatment dissatisfaction among patients with psoriasis and psoriatic arthritis in the United States: findings from the National Psoriasis Foundation surveys, 2003–2011. JAMA Dermatol. 2013;149(10):1180–5.

5. Feldman SR, Goffe B, Rice G, et al. The challenge of managing psoriasis: unmet medical needs and stakeholder perspectives. Am Health Drug Benefits. 2016;9(9):504–13.

6. Schafer P. Apremilast mechanism of action and application to psoriasis and psoriatic arthritis. Biochem Pharmacol. 2012;83(12):1583–90.

7. FDA approves first oral treatment for all psoriasis severities [press release]. National Psoriasis Foundation, 2021. https://www.psoriasis.org/advance/fda-approves-first-oral-treatment-for-all-psoriasis-severities/. Accessed 12 Dec 2022.

8. Otezla [package insert]. Thousand Oaks, CA: Amgen Inc., 2021.

9. Lebwohl MG, Bachelez H, Barker J, et al. Patient perspectives in the management of psoriasis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis Survey. J Am Acad Dermatol. 2014;70(5):871–81.

10. Papp K, Reich K, Leonardi CL, et al. Apremilast, an oral phosphodiesterase 4 (PDE4) inhibitor, in patients with moderate to severe plaque psoriasis: results of a phase III, randomized, controlled trial (Efficacy and Safety Trial Evaluating the Effects of Apremilast in Psoriasis [ESTEEM] 1). J Am Acad Dermatol. 2015;73(1):37–49.

11. Paul C, Cather J, Gooderham M, et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). Br J Dermatol. 2015;173(6):1387–99.

12. Menter MA, Armstrong AW, Gordon KB, Wu JJ. Common and not-so-common comorbidities of psoriasis. Semin Cutan Med Surg. 2018;37(2s):S48–S51.

13. Kapniari E, Dalamaga M, Papadavid E. Comorbidities burden and previous exposure to biological agents may predict drug survival of apremilast for psoriasis in a real-world setting. Dermatol Ther. 2020;33(6):e14168.

14. Papadavid E, Rompoti N, Theodoropoulos K, Kokkalis G, Rigopoulos D. Real-world data on the efficacy and safety of apremilast in patients with moderate-to-severe plaque psoriasis. J Eur Acad Dermatol Venereol. 2018;23(7):1173–9.

15. Feldman SR, Tian H, Wang X, Germino R. Health care utilization and cost associated with biologic treatment patterns among patients with moderate to severe psoriasis: analyses from a large US claims database. J Manag Care Spec Pharm. 2018;25(4):479–88.

16. Kishimoto M, Komine M, Kamiya K, Sugai J, Ohtsuki M. Drug survival of apremilast in a real-world setting. J Dermatol. 2019;46(7):615–7.

17. Graier T, Weger W, Sator PG, et al. Effectiveness and clinical predictors of drug survival in psoriasis patients receiving apremilast: a registry analysis. JAAD Int. 2021;2:62–75.