



Treatment Patterns and Economic Burden of Ulcerative Colitis in Japan: A Retrospective Claims Analysis

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Received: October 2, 2024 / Accepted: December 13, 2024 / Published online: January 24, 2025
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ABSTRACT

Introduction: This retrospective claims analysis characterized contemporary ulcerative colitis (UC) treatment patterns and investigated the economic burden of UC in Japan.

Methods: This study used anonymized claims data in the Medical Data Vision database. Patients were included if they had a confirmed UC diagnosis and ≥ 1 claim of systemic treatment for UC (index date) between June 2018 and December 2022, in addition to continuous enrollment for ≥ 6 months before and ≥ 12 months after the index date. Patients were excluded if they were aged < 18 years at index or if they had claimed systemic UC

treatment during the pre-index period, had a confirmed diagnosis of Crohn's or Behçet's disease, or had a record of colectomy during the pre-index period. Outcomes of interest were treatment patterns, healthcare resource utilization (HCRU), and UC-related costs per person per month (PPPM). Further exploratory analyses were conducted to understand whether real-world treatment patterns with conventional therapy were optimally aligned with guideline recommendations. Two definitions of suboptimal treatment with conventional therapies were identified: prolonged treatment with corticosteroids (i.e., consecutive use for > 90 days) and corticosteroid cycling (i.e., three or more ≥ 30 -day corticosteroid courses over 1 year, with a ≥ 60 -day gap between courses).

Results: Overall, 15,429 patients were included. The most frequently observed class of first-line treatment was 5-aminosalicylic acid monotherapy (75.0%); treatment modification was observed in 39.7% of patients. Within 1 year of follow-up, patients had a mean (SD) of 9.8 (6.8) outpatient visits, and a hospital stay was reported in 23.9% of patients. Mean total cost PPPM was ¥76,374. Of patients with ≥ 1 course of corticosteroids, 39.8% received suboptimal treatment with conventional therapies. HCRU and total costs were higher for patients with versus without suboptimal treatment with conventional therapies.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s12325-024-03096-1>.

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Conclusions: Japanese patients with UC would benefit from treatment options that can reduce costs, HCRU, and suboptimal treatment with conventional therapies.

Keywords: Claims analysis; Corticosteroid; Health care costs; Inflammatory bowel disease; Japan; Observational study; Ulcerative colitis

Key Summary Points

Why carry out this study?

This retrospective claims analysis characterized ulcerative colitis (UC) treatment patterns and investigated the economic burden of UC in Japan using data through 2022, allowing observation of treatment patterns with recently launched UC medications.

Further analyses were conducted to understand whether real-world treatment patterns with conventional therapy were optimally aligned with guideline recommendations and to investigate the implications of suboptimal treatment for healthcare resource utilization (HCRU) and costs.

What was learned from the study?

The most frequently observed class of first-line treatment was 5-aminosalicylic acid monotherapy (75.0%); patients had a mean (SD) of 9.8 (6.8) outpatient visits, and the mean (SD) total cost per person per month was ¥76,374 (215,983).

Suboptimal treatment with conventional therapies was observed in 39.8% of patients who received ≥ 1 course of corticosteroids; HCRU and total costs were higher for patients with versus without suboptimal treatment.

Japanese patients with UC would benefit from treatment options that can reduce costs, HCRU, and suboptimal treatment with conventional therapy.

INTRODUCTION

Ulcerative colitis (UC) represents one of the two major forms of inflammatory bowel disease [1, 2]. Characterized by ulceration of the colonic mucosa that may extend from the rectum to involve the entire colon, the disease follows a relapsing–remitting course; its symptom flares include bloody diarrhea, abdominal pain, and fatigue [2]. Patients may also present with extraintestinal manifestations (EIMs) of disease that affect the musculoskeletal system, skin, hepatobiliary tract, and eyes [3]. The prevalence of UC in Japan has risen in recent decades; estimates of crude period prevalence rates suggest an increase from 158 cases per 100,000 people in 2010 to 266 per 100,000 people in 2019 [4]. What was once a rare disease managed in specialized hospitals is now common in community hospitals, under the care of nonspecialist physicians [5].

While UC prevalence has increased markedly in recent decades, treatment options for managing the disease have expanded, and the treatment guidelines have evolved [1, 6, 7]. Japanese guidelines endorse a treat-to-target approach in UC; the goal of treatment is the induction and maintenance of remission, defined as endoscopic healing [7]. Treatment algorithms for the induction and maintenance of remission are complex and consider disease extent (i.e., how much of the colon is affected), severity, current activity, and steroid-dependence status [1, 7]. In addition to 5-aminosalicylic acid (5-ASA), which remains the first-line mainstay of pharmacologic treatment, Japanese guidelines recommend immunomodulators, immunosuppressants, several Janus kinase (JAK) inhibitors, and a range of biologic therapies to treat moderately to severely active UC [1, 6, 7]. The guidelines recommend corticosteroids for the induction but not the maintenance of remission, due to the side effects resulting from long-term corticosteroid administration [7]. The 2020 guidelines issued by the Japanese Society of Gastroenterology recommend reducing the dose of corticosteroids to less than the equivalent of prednisolone 10 mg or budesonide 3 mg per day within 3 months [1], whereas the 2024 guidelines issued under

the auspices of the Ministry of Health, Labour, and Welfare of Japan endorse the 2022 European Crohn's and Colitis Organisation recommendation that steroids be discontinued entirely by 3 months after initial administration [7, 8]. Together, this guidance reflects an international consensus that steroid use be considered a key performance indicator in the management of inflammatory bowel disease [9, 10]. In addition to pharmacologic treatment, Japanese guidelines recommend cytapheresis (i.e., blood cell depletion therapy) for patients with steroid-refractory or steroid-dependent UC; surgery for patients with severe, fulminant, or treatment-refractory disease; and surgery for those who have experienced serious side effects from medication [7].

The complex and evolving UC treatment landscape in Japan warrants attention to the unmet needs of patients receiving the current standard of care. While the available evidence indicates that biologic treatments are associated with poor persistence [11], that rates of suboptimal treatment with corticosteroids are high [12], and that patients with UC incur a substantial economic burden [13], the data supporting this evidence were procured ≥ 5 years ago. In the interim, new treatments have been approved and new treatment guidelines issued [1, 6, 7]. A recent study conducted in the United States found approximately half of the patients with UC had suboptimal treatment with conventional therapies and that these patients incurred significantly higher UC-related costs and rates of healthcare resource utilization (HCRU) during follow-up than those who had not received suboptimal treatment [14]. However, there are no studies in Japan exploring such outcomes.

Using data from an administrative claims database, this study investigates contemporary UC treatment patterns in Japan and characterizes the economic burden presented by UC. The study's primary objectives were to describe the demographic and clinical characteristics of patients with UC treated with systemic drug therapy and the treatment patterns associated with systemic drug therapy. As a secondary objective, this study estimated HCRU and costs for patients receiving systemic UC treatment. To understand whether real-world treatment patterns were optimally aligned with guideline

recommendations, we further examined treatment patterns with conventional therapies—and their associated cost and HCRU burden—in patients who moved to advanced therapy (i.e., a biologic agent or JAK inhibitor) within a year of their first claim of systemic treatment. Suboptimal treatment with conventional therapies was defined with reference to Japanese UC guidelines and clinical expert advice. Since the guidelines specify conditional parameters for corticosteroid use, two definitions of suboptimal treatment with conventional therapies, each related to corticosteroids, were identified: prolonged treatment with corticosteroids (i.e., consecutive use for >90 days) and corticosteroid cycling (i.e., three or more ≥ 30 -day courses of corticosteroids over 1 year, with a ≥ 60 -day gap between courses). As exploratory objectives, this study sought to identify factors associated with suboptimal treatment with corticosteroids and to characterize EIMs before and after treatment with systemic therapy.

METHODS

Data Source and Ethics Approval

This real-world, retrospective, observational study used anonymized patient data from June 2018 to December 2022, obtained from Medical Data Vision, a hospital-based claims database (Medical Data Vision, Tokyo, Japan) that covers approximately 42 million patients across 474 acute care hospitals in Japan. As all data were anonymized, requirements for ethics approval and informed consent under the Ethical Guidelines for Epidemiological Research in Japan do not apply to this study. Permission was obtained to access and use data by Medical Data Vision.

Data Collection

Patients were included if they had a confirmed UC diagnosis (International Classification of Diseases, Tenth Revision [ICD-10]: code K51) during the study period and, within the same month or 1 month before, were treated with an eligible systemic drug therapy: 5-ASA,

corticosteroid, cyclosporine, tacrolimus, carotegrast methyl, azathioprine, 6-mercaptopurine hydrate, infliximab, adalimumab, golimumab, ustekinumab, vedolizumab, tofacitinib, filgotinib, or upadacitinib. The first claim of systemic treatment within the study period was defined as the index date. Patients were also required to have had continuous enrollment in the database for ≥ 6 months prior to and ≥ 12 months after the index date. Patients were excluded if they had a claim of systemic treatment during the pre-index period, were aged < 18 years at the index date, or had a confirmed diagnosis of Crohn's disease or Behçet's disease or a record of colectomy during the pre-index period.

Outcomes

Demographic variables collected included age, sex, and disease extent at the index date, and Charlson comorbidity index (CCI) score during the pre-index period, which was calculated using a validated method [15]. Outcomes of interest for the primary objectives included treatment classes at each line of therapy, with each line defined by the initiation of a treatment regimen for ≥ 30 days until that regimen's modification (i.e., discontinuation, switch, add-on, reduction, or restart); number of lines of therapy; number of patients discontinuing, switching, adding-on, reducing, or restarting treatments; number of patients prescribed a course of corticosteroids (defined with a ≥ 60 -day gap between courses); and number of patients suboptimally treated with corticosteroids. Treatment discontinuation was defined as no prescription of the index treatment during the 60 days after the period covered by the previous prescription, with no further treatment line initiated. Treatment switch was defined as the prescription of a new treatment during the period covered by the last prescription or during the following 60 days, but with the same total number of drugs in the index regimen. Treatment add-on was defined as the prescription of a new treatment during the period covered by the last prescription or during the following 60 days, with a greater number of drugs in the subsequent regimen than in the previous regimen. Treatment reduction was

assessed for patients receiving ≥ 2 treatments and was defined as discontinuation of ≥ 1 treatment. Treatment restart was defined as initiating a subsequent line of therapy using the same regimen as in the previous line. For the line of therapy analysis but not for the other objectives, patients with inpatient records only were excluded from analysis.

Outcomes for the secondary and exploratory objectives included HCRU, costs, and presence of EIMs pre- and post-index. HCRU was described by the number of UC-related outpatient visits, UC-related hospitalizations, UC-related surgeries, and cytapheresis use within 1 year from the index date. Mean direct costs in Japanese yen were adjusted for inflation with 2022 as the reference year (based on the calendar year average of the Consumer Price Index) and are reported per person per month (PPPM) for UC-related inpatient visits, UC-related outpatient visits, and UC medication, measured separately and in total. HCRU and costs are reported for the overall population as well as for patients who moved to advanced therapy within 1 year of their index date and who did and did not experience suboptimal treatment with corticosteroids.

Patients who experienced EIMs at baseline and those who developed EIMs during the study period are reported, and treatment patterns before and after observation of an EIM code are described.

Statistical Analyses

This study was primarily descriptive in nature. Categorical variables are described with counts and frequencies, while mean values and standard deviation (SD) are given for continuous variables. *P* values for differences in HCRU and costs between patients who did and did not receive suboptimal treatment with corticosteroids were derived using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables.

Univariate logistic regression analyses were used to identify factors associated with suboptimal treatment with corticosteroids in patients who moved to advanced therapy within 1 year of their index date, such as age, sex, CCI score,

disease extent, treatment changes (including adding a thiopurine in a subsequent line of therapy), cytopheresis use, or UC-related hospitalization.

Statistical analyses were conducted using R Statistical Software (version 4.2; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient Population

Overall, 15,429 patients were included in this analysis; an attrition flowchart is shown in Fig. 1. Patients were followed for a median 884 (interquartile range: 620–1168) days. Table 1 displays patient demographic and baseline clinical characteristics. The mean (SD) age was 47.7 (18.6) years, and 58.4% of patients were male. Pancolitis was the most common disease

extent code in patients who had disease extent recorded. A CCI score ≥ 1 was observed in 11.5% of patients.

Primary Objective: Treatment Patterns

At least one line of therapy was observed in 12,402 patients; of these patients, 39.7% had ≥ 2 lines of therapy. Most patients initiated a new line within 6 months of the index date, with a median of 126 days to second line. The most frequently observed first-line treatment class was 5-ASA monotherapy, received by 75.0% of patients, followed by 5-ASA and corticosteroid combination therapy (6.0%) (Fig. 2). In the second line, most patients were treated with 5-ASAs, immunomodulators, and/or corticosteroids. Advanced therapies (biologics and JAK inhibitors) were prescribed to 1238 (25.1%) patients in the second line, either as monotherapy or in combination with other therapies.

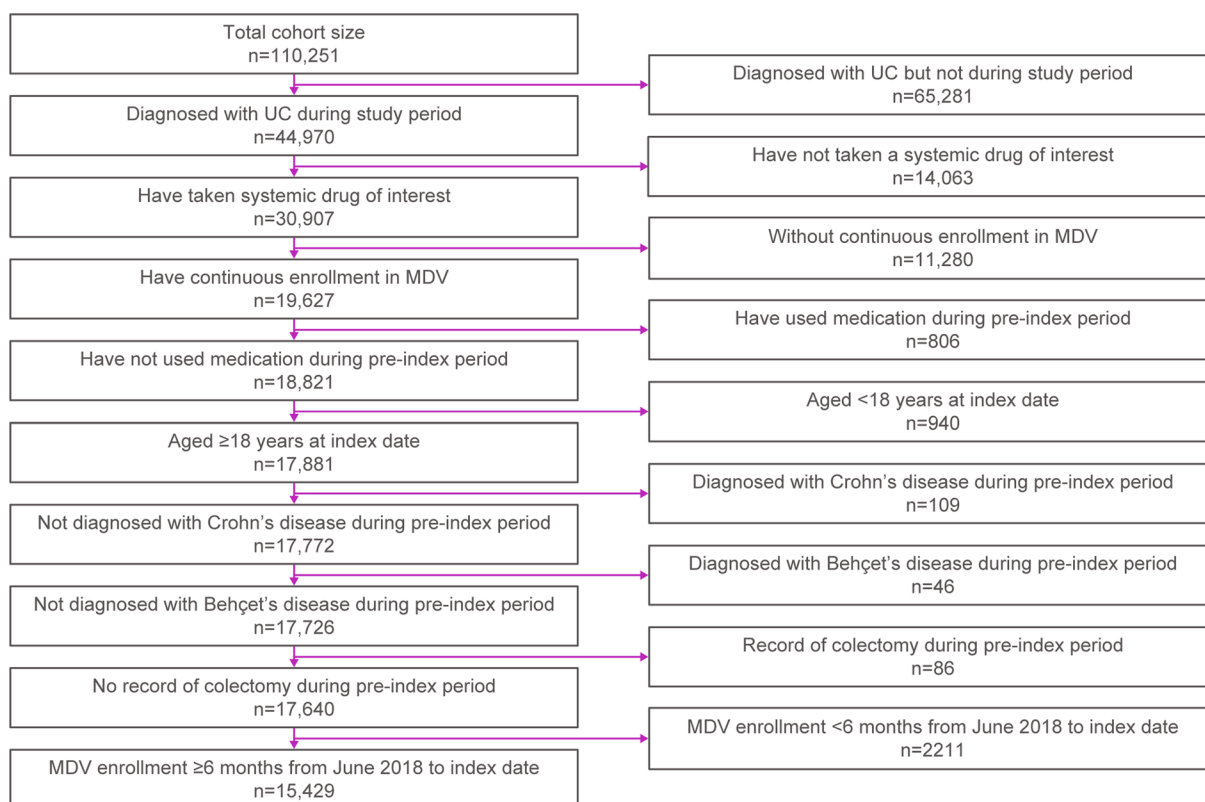


Fig. 1 Patient attrition. *MDV* Medical Data Vision; *UC* ulcerative colitis

Table 1 Demographic and baseline clinical characteristics

Characteristic	Patients (<i>n</i> = 15,429)
Sex, <i>n</i> (%)	
Male	9003 (58.4)
Female	6426 (40.5)
Age, years	
Mean (SD)	47.7 (18.6)
Median (IQR)	46.0 (32.0–62.0)
Age category, years, <i>n</i> (%)	
18–29	3126 (20.3)
30–39	2659 (17.2)
40–49	2939 (19.0)
50–59	2402 (15.6)
60–69	1888 (12.2)
≥ 70	2415 (15.7)
Disease extent, ^a <i>n</i> (%)	
Pancolitis	2957 (19.2)
Left-sided colitis	979 (6.3)
Proctitis	819 (5.3)
Rectosigmoiditis	233 (1.5)
Unspecified	11,056 (71.7)
CCI score, <i>n</i> (%)	
0	13,653 (88.0)
1	321 (2.1)
2	812 (5.3)
3	247 (1.6)
≥ 4	396 (2.6)

CCI Charlson Comorbidity Index; IQR interquartile range; SD standard deviation

^aPatients could have > 1 disease extent code recorded.

These patients most commonly received tumor necrosis factor inhibitors (45.8%). Most patients who initiated second-line treatment received combination therapy.

Within each line of therapy, 39.7–52.6% of patients initiated subsequent treatment (Fig. 3).

Patients moving from line 1 to line 2 most frequently had a treatment added (16.5%); most of these add-on treatments were immunomodulators or corticosteroids (Fig. 2). Patients moving from lines 2 or 3 to lines 3 or 4 most commonly had a reduction in the number of treatments they were prescribed. Corticosteroid treatment was frequently reduced in these later lines of therapy.

A total of 2460 patients had ≥ 1 course of treatment with corticosteroids (Fig. S1 in the Supplementary Material). Of these patients, 978 (39.8%) received suboptimal treatment with corticosteroids. Steroid cycling was observed in 62 patients, while prolonged corticosteroid use was observed in 939 patients.

Secondary Objectives: HCRU and Costs, Overall and by Suboptimal Treatment with Corticosteroids

Overall, the mean (SD) number of outpatient visits during 1 year of follow-up was 9.8 (6.8) (Table 2). A hospital stay was reported in 23.9% of patients, with a mean (SD) stay of 29.3 (25.2) days. Of the patients who progressed to advanced therapy within 1 year of their index date, 425 (11.6%) received suboptimal treatment with corticosteroids and 3250 (88.4%) did not; the group that did not receive suboptimal treatment included 391 patients who did not meet the line of therapy definition (≥ 30 consecutive days of treatment). Compared with patients who did not receive suboptimal treatment with corticosteroids, those with suboptimal treatment with corticosteroids had significantly more UC-related outpatient visits (18.2 vs 12.6; $P < 0.001$) and a higher rate of UC-related hospitalizations (55.3% vs 49.2%; $P = 0.020$). The mean time to advanced therapy was 3 times longer in patients who received suboptimal treatment with corticosteroids than in those who did not (191.3 days vs 62.5 days; $P < 0.001$).

Table 3 shows that overall, patients incurred a mean (SD) total UC-related cost PPPM of ¥76,374 (215,983). Patients who received suboptimal treatment with corticosteroids incurred significantly higher total costs than patients who did not (¥199,506 vs ¥183,394; $P < 0.001$).

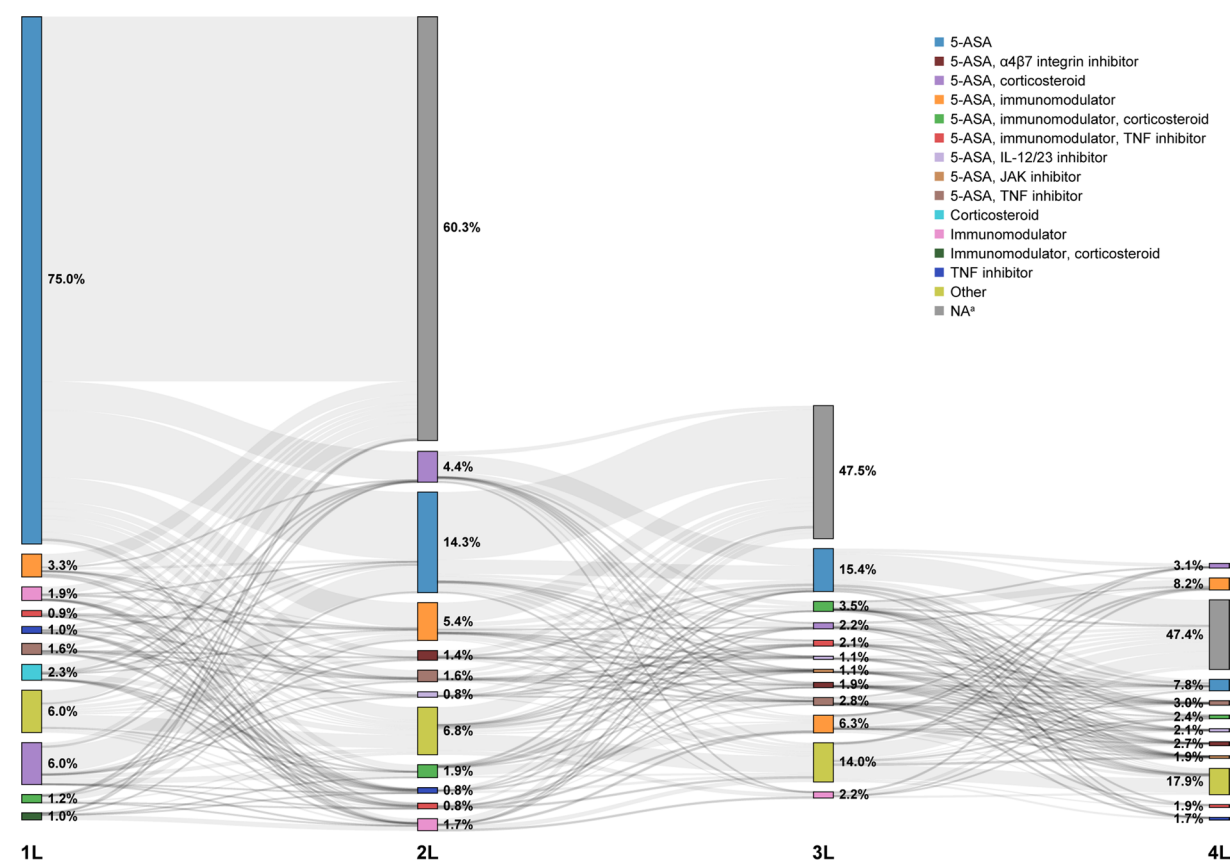


Fig. 2 Treatment patterns across four lines of therapy. ^aPatients discontinued treatment or continued treatment with no additional modifications until the end of the study period. *1L* first line; *2L* second line; *3L* third line; *4L*

fourth line; *5-ASA* 5-aminosalicylic acid; *IL* interleukin; *JAK* Janus kinase; *NA* not applicable; *TNF* tumor necrosis factor

Exploratory Objective: Factors Associated with Suboptimal Treatment with Corticosteroids

Suboptimal treatment with corticosteroids was associated with higher odds of UC-related hospitalization ($P=0.018$); greater disease extent (i.e., pancolitis; $P<0.001$); and treatment modifications ($P<0.001$) (Table S1 in the Supplementary Material). Patients who received thiopurines in the first line had a lower probability of experiencing suboptimal treatment with corticosteroids. Demographic variables, such as age, gender, or CCI score, were not associated with suboptimal treatment with corticosteroids.

Exploratory Objective: EIMs Pre- and Post-Index

In the pre-index period, EIMs were reported in 4.9% of patients; in the post-index period, EIMs were reported in 7.9% of patients (Table S2 in the Supplementary Material). Rheumatoid arthritis and spondylopathy were the most common EIMs in both the pre- and post-index periods. An increase in cases of herpes zoster and acute pancreatitis was observed after the index prescription of systemic treatment for UC. Most post-index EIMs occurred within the first and second line of therapy (84.6%); patients had been most commonly receiving 5-ASA monotherapy (54.2%)

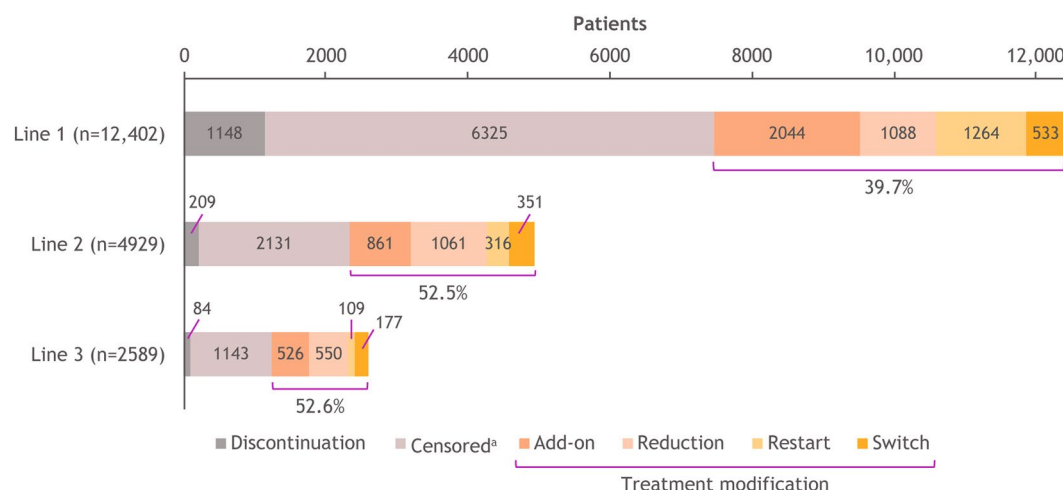


Fig. 3 Treatment patterns over three lines of therapy. Line 1 implies patients moving from first- to second-line treatment; line 2 implies patients moving from second- to third-line treatment; and line 3 implies patients moving from

third- to fourth-line treatment. ^aPatients were censored if they continued their treatment with no modifications for the remainder of the study period

Table 2 Healthcare resource utilization, overall and for patients who moved to AT^a within 1 year of index with and without suboptimal treatment with corticosteroids

Variable	Overall (N = 15,429)	Treatment		
		Suboptimal treatment with corticosteroids (n = 425)	No suboptimal treatment with corticosteroids (n = 3250)	P value
≥ 1 UC-related outpatient visit, n (%)	14,318 (92.8)	425 (100.0)	3098 (95.3)	< 0.001
Visits, mean (SD)	9.8 (6.8)	18.2 (7.0)	12.6 (7.0)	< 0.001
≥ 1 UC-related hospitalization, n (%)	3680 (23.9)	235 (55.3)	1599 (49.2)	0.020
Length of stay, days, mean (SD)	29.3 (25.2)	31.9 (21.6)	34.5 (28.9)	0.5
≥ 1 UC-related surgery, n (%)	257 (1.7)	2 (0.5)	100 (3.1)	< 0.001
Time to AT, ^a days, mean (SD)	77.4 (97.1)	191.3 (75.2)	62.5 (89.5)	< 0.001

AT advanced therapy; SD standard deviation; UC ulcerative colitis

^aATs were defined as biologics or Janus kinase inhibitors.

or combination therapy with 5-ASA and corticosteroids (8.3%). Of 542 patients who experienced a first EIM within a line of therapy

after their index date, 85 (15.7%) modified their treatment within 30 days (Table S3 in the Supplementary Material).

Table 3 UC-related costs, overall and for patients who moved to AT^a within 1 year of index with and without suboptimal treatment with corticosteroids

UC-related costs ^b	Overall (N = 15,429)	Treatment		P value
		Suboptimal treatment with corticosteroids (n = 425)	No suboptimal treatment with corticosteroids (n = 3250)	
Inpatient cost, PPPM, mean (SD)	26,149 (71,755)	66,891 (92,593)	69,727 (115,117)	0.12
Outpatient cost, PPPM, mean (SD)	16,989 (38,805)	37,408 (51,159)	23,122 (32,498)	< 0.001
Pharmacy cost, PPPM, mean (SD)	33,236 (193,342)	95,208 (99,543)	90,545 (129,314)	< 0.001
Total cost PPPM, mean (SD)	76,374 (215,983)	199,506 (151,880)	183,394 (178,961)	< 0.001

AT advanced therapy; PPPM per person per month; SD standard deviation; UC ulcerative colitis

^aATs were defined as biologics or Janus kinase inhibitors.

^bUC-related costs are reported in 2022 Japanese yen.

DISCUSSION

This real-world study using data from a large, hospital-based administrative database confirms that 5-ASAs remain the mainstay of first-line treatment for patients with UC in Japan. The second line also frequently featured 5-ASAs, either as monotherapy or in combination with corticosteroids or immunomodulators. These findings corroborate Miyazaki et al., who reported a first-line 5-ASA monotherapy rate of 77.5%, and are in line with Japanese guidelines for UC treatment [1, 7, 13]. The mean age of patients in this study was slightly greater than that reported by Miyazaki et al., who used data from salaried workers and their family members included in the Japan Medical Data Center health claims database [13]; this database may underrepresent older patients [16].

Approximately 40% of patients experienced treatment modification from their first-line prescription after a median of 126 days; studies conducted in the United States report that up to 77% of patients with UC initiate second-line therapy [17, 18], while Miyazaki et al. reported a treatment modification rate of just 26% in Japan [13]. Notably, the database used by Miyazaki et al. generally includes patients with

less severe disease than the database we used in this study [16]. Most patients receiving second-line treatment were prescribed conventional therapies (5-ASAs, immunomodulators, and corticosteroids), but a quarter were prescribed an advanced therapy (biologics or JAK inhibitors). Of these patients, nearly half were prescribed a tumor necrosis factor inhibitor; this finding is consistent with Taida et al., who report that tumor necrosis factor inhibitors are the most commonly used advanced therapy in a diversifying field of therapeutic strategies [5]. The most frequent treatment modification from first- to second-line therapy was adding a treatment, such as corticosteroids or immunomodulators. The prevalence of combination therapy in the second line may hold implications for treatment adherence and disease management: in UC, as in other disease areas, pill burden is associated with diminished treatment adherence [19–21].

Matsuoka et al. have observed that although 59.0% of patients prescribed corticosteroids in 2016 used them for ≥ 90 days, the proportion of patients with prolonged use of corticosteroids for UC declined from 2011 through 2016 [12]. A more recent study confirms the encouraging trend that the median duration of corticosteroid use has declined from 103 days over the period

from 2006 through 2011 to 86 days over the period from 2016 through 2020 [22]. However, of the 2460 patients in our study who received ≥ 1 course of treatment with corticosteroids, approximately 40% experienced suboptimal treatment (prolonged use or steroid cycling), suggesting that a discrepancy between clinical practice and treatment guidelines nevertheless persists in Japan. The mean time to initiation of advanced therapy was 3 times higher in patients who received suboptimal treatment with corticosteroids; this finding may be indicative of clinical inertia in UC management [23–25]. However, it should be noted that as one of the defining parameters of suboptimal treatment with corticosteroids in this study was consecutive corticosteroid use for ≥ 90 days, immortal time bias may have been introduced [26]. Thus, time to advanced therapy initiation in the population who received suboptimal treatment with corticosteroids may be overestimated compared with patients without suboptimal treatment with corticosteroids. Suboptimal treatment with corticosteroids was also associated with higher odds of pancolitis, UC-related hospitalization, and treatment modifications. These findings should be considered in conjunction with the established risks of prolonged corticosteroid use, which include complications, such as osteoporosis, venous thromboembolism, and infections [27]. As corticosteroids are not suitable for the maintenance of remission, universal efforts are warranted to introduce therapies with improved clinical efficacy in maintenance of remission at an earlier treatment stage.

Overall, UC was associated with a high economic burden, including mean total costs of ¥76,374 PPPM; these costs are notably higher than the mean ¥50,960 PPPM over 12 months reported by Miyazaki et al. [13]. Suboptimal treatment with corticosteroids in patients who progressed to advanced therapy was associated with an even greater HCRU and cost burden than in similar patients who were not suboptimally treated with corticosteroids.

EIMs occurred in 7.9% of patients who received UC treatment; however, as only diagnoses with active treatment were observable in the database, this rate may be an underestimation. Most EIM

occurred within the first or second lines of therapy, and 15.7% of patients with a first EIM within a line of therapy after their index date changed treatment. The number of patients experiencing herpes zoster infection or acute pancreatitis increased during the post-index period; while this study cannot confirm whether the increases were treatment-induced adverse events or complications of the underlying disease, the increase highlights the importance of safer treatment options for patients with UC and efforts to prevent EIM in daily practice.

This study provides updated data on real-world treatment patterns in Japan since the introduction of new biologics for UC. Furthermore, this is the first study in Japan to investigate HCRU and cost outcomes for patients with suboptimal treatment with corticosteroids. Nevertheless, certain limitations must be acknowledged. While the Medical Data Vision database is large and considered broadly generalizable to the wider Japanese population, the sample only includes patients treated at acute care hospitals, who may have more severe disease than those treated at a clinic. The study could not follow patients who were discharged or moved to clinics or other hospitals not included in the Japanese healthcare system's Diagnosis Procedure Combination reimbursement database; however, patients had a mean follow-up period of approximately 2.5 years, which mitigated this limitation. Causal relationships between treatment exposure and economic or health outcomes cannot be assumed, since several risk factors, including disease severity, were not observed in the database. Moreover, the research identified patients using ICD-10 diagnosis codes, which poses a risk of inappropriate inclusion or exclusion of patients whose disease was miscoded. Finally, the comparison of outcomes between patients who did and did not experience suboptimal treatment with corticosteroids did not adjust for disparities in time on treatment.

CONCLUSIONS

We conclude that treatment modification is common in patients with UC in Japan, that patients incur a high economic burden, and

that many receive suboptimal treatment with standard of care, a circumstance associated with poorer economic and health outcomes. Japanese patients with UC would benefit from treatment options that can reduce treatment modification, costs, HCRU, and suboptimal treatment with conventional therapies. As the treatment landscape evolves, additional real-world research on how other treatment options may address these burdens is needed.

Medical Writing/Editorial Assistance. Writing and editorial assistance was provided by Eleanor Bush, MA, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Bristol Myers Squibb. The authors thank Sumit Verma and Pulkit Parashar of Mu Sigma, Inc., for their contribution to the statistical analysis of the data. The analysis was a professional assistance funded by Bristol Myers Squibb.

Author Contributions. Shingo Kato, Yoshiyuki Yamada, Kiran Dave, Shweta Shah, and Hyunchung Kim contributed to the conceptualization of the study, and Bruno Casaes Teixeira and Thomas Laurent to the study's methodology. Yoshiyuki Yamada and Hyunchung Kim were responsible for the study investigation, and Bruno Casaes Teixeira and Thomas Laurent for data analysis. Shingo Kato, Thomas Laurent, and Hyunchung Kim were responsible for data validation. Shingo Kato and Hyunchung Kim provided study supervision. Shingo Kato, Bruno Casaes Teixeira, Thomas Laurent, Yoshiyuki Yamada, Kiran Dave, Shweta Shah, and Hyunchung Kim contributed to the writing, review, and editing of the draft, and approved its publication.

Funding. This study was funded by Bristol Myers Squibb, Princeton, NJ, USA. Bristol Myers Squibb provided the funding for the journal's Rapid Service and Open Access fees.

Data Availability. Bristol Myers Squibb's policy on data sharing may be found at: <https://www.bms.com/researchers-and-partners/independent-research/data-sharing-request-process.html>. The datasets generated or analyzed during

the current study are available from Bristol Myers Squibb on reasonable request.

Declarations

Conflict of Interest. Shingo Kato received honoraria from AbbVie, Janssen Pharmaceutical K.K., Kissei, Mitsubishi Tanabe, and Takeda. Bruno Casaes Teixeira, Thomas Laurent, Yoshiyuki Yamada, Kiran Dave, Shweta Shah, and Hyunchung Kim are employees and/or shareholders of Bristol Myers Squibb.

Ethical Approval. This real-world, retrospective, observational study used anonymized patient data from June 2018 to December 2022, obtained from Medical Data Vision, a hospital-based claims database (Medical Data Vision, Tokyo, Japan) that covers approximately 42 million patients across 474 acute care hospitals in Japan. As all data were anonymized, requirements for ethics approval and informed consent under the Ethical Guidelines for Epidemiological Research in Japan do not apply to this study. Permission was obtained to access and use data by Medical Data Vision.

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