Treatment Patterns and Sequencing in Patients With Inflammatory Bowel Disease

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ABSTRACT

Purpose: Treatment options for patients with ulcerative colitis (UC) or Crohn disease (CD) have increased considerably in recent years with the advent of new biologics, but little is known about treatment pathways in clinical practice. We aimed to characterize treatment patterns and sequences in patients with UC or CD newly initiated on a biologic or an immunosuppressant (IMS).

Methods: This retrospective cohort study used US health insurance claims data dated from January 1, 2009, to December 31, 2013, from patients with UC or CD newly initiated on a biologic or an IMS. Treatment patterns and sequences were described during a 24-month follow-up period.

Findings: Among 5543 patients with UC and 7561 patients with CD, 2403 and 4677 patients, respectively, were initiated on a biologic; 3140 and 2884 patients were initiated on an IMS. In patients initiated on a biologic, monotherapy was chosen in 71% for UC (primarily infliximab [68%]) and in 79% for CD (primarily adalimumab [52%]). Approximately one third of patients remained on the first-line biologic during the follow-up period; 69% (UC) and 70% (CD) of patients were initiated on a second-line therapy, among whom 25% (UC) and 39% (CD) received a different biologic monotherapy, suggesting intolerance, inadequate response, or loss of response to first-line therapy. In patients initiated on an IMS, 58% (UC) and 66% (CD) were initiated on monotherapy; combination therapy with a corticosteroid was prescribed in 41% (UC) and 30% (CD) of patients; and second-line therapy was initiated in 72% (UC) and 75% (CD) of patients.

Implications: While current treatment options seem effective in a proportion of patients with UC and CD, others require multiple lines of therapy, suggesting an unmet need for alternative treatments in UC and CD to achieve disease control. (*Clin Ther.* 2018;■:1–13)

Key words: biologic, Crohn disease, treatment patterns, ulcerative colitis.

INTRODUCTION

Ulcerative colitis (UC) and Crohn disease (CD), the two main forms of inflammatory bowel disease (IBD), are characterized by phases of remission and acute exacerbations, during which patients may experience rectal bleeding, discomfort, abdominal pain, and diarrhea.[1] Treatment of IBD aims to induce and maintain clinical remission and to promote mucosal healing via a range of pharmaceutical therapies tailored to the needs and the clinical response of individual patients.[1,2] Surgery is required in patients with refractory chronic or severe active disease in which pharmaceutical therapies have not been successful; however, surgery is typically seen as a last resort and is not always curative, particularly in CD.[1,3]

In patients with mild to moderate UC, current US guidelines recommend first-line treatment with aminosalicylate (5-ASA) or sequential induction with corticosteroids (CS) followed by 5-ASA maintenance therapy.[4,5] In patients with moderate to severe UC, an immunosuppressant (IMS) such as azathioprine or 6-mercaptopurine may be prescribed as maintenance therapy following CS induction.[5] Alternatively, a biologic, typically an anti–tumor necrosis factor (TNF)-α antibody such as infliximab or adalimumab, can be prescribed with or without a concurrent IMS to promote and maintain mucosal healing and clinical remission.[4–9] In moderate to severe CD, anti-TNFs are recommended to

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induce remission.[10,11] While anti-TNFα monotherapy is recommended over IMS monotherapy in these patients, an anti-TNFα agent in combination with an IMS is the preferred strategy in patients who do not have risk factors precluding the use of IMSs.[10,11] Treatment guidelines may vary between countries.

In clinical practice, clinicians often attempt a variety of monotherapies or combination therapies in sequence until an adequate clinical response is achieved. In an attempt to delay the need for surgery, slow the progression of disease, and attain clinical remission and mucosal healing, an increasing uptake of IMSs and biologics for IBD has been observed in recent years.[7] However, studies have shown that, overall, between one third and one half of patients do not respond to anti-TNFs,[7,12] with a second biologic commonly prescribed when the first has failed.[12] In addition, some patients experience a loss of response over time, or develop intolerance to a specific biologic.[13,14] Alternatives include using a biologic with a different mechanism of action.[15–18] Furthermore, as loss of response or tolerance to anti-TNFα agents may occur in some patients due to immunogenicity, an IMS may be coprescribed with a biologic to reduce the risk for developing anti-drug antibodies.[13,19]

Approximately half of patients who discontinue their first biologic treatment are not restarted on, or switched to, another therapy.[6] While some patients may have successfully achieved remission, others may be discontinued from biologic treatment due to other reasons, such as side effects or a lack of efficacy.[20–22] The reasons for discontinuation are currently poorly understood, and the data from clinical practice that describe treatment pathways in patients with IBD are limited.

The aims of this study were to characterize the treatment patterns and sequencing in patients with UC or CD newly initiated on a biologic or an IMS, and to examine patterns of switching, adding, and discontinuing therapies in a cohort of patients with UC and CD from clinical practice. These data may allow for a better understanding of the unmet needs in these patients, inform future clinical trial design, and help to optimize medicine-development strategies.

PATIENTS AND METHODS

Ethical Considerations

This retrospective study evaluated deidentified database records. As this analysis did not meet the definition of research in human subjects, its protocol was exempt from institutional review board review.

Study Design and Objectives

A retrospective cohort study was conducted using the MarketScan Commercial (Truven Health Analytics, IBM Watson Health, New York, New York) and Medicare Supplemental databases. The MarketScan databases are compiled by the collection of data from employers, health insurance plans, and United States (US) state Medicaid agencies.[23] The data covers 240 million unique patients from across the US from 1995, providing a nationally representative data sample of Americans with employer-provided health insurance. The Medicare Supplemental Database provides data on retirees in the US with Medicare supplemental insurance paid by employers. Detailed cost, use, drug, and outcomes data are available from both inpatient and outpatient settings, providing valuable insight into the health care experiences of older Americans.[23] *New users* within the databases were identified from their first initiation on either a biologic or an IMS (*index date*) for the management of UC or CD in the study period (Figure 1). Retrospective medical and pharmaceutical claims were collated in the 12 months prior to index date (baseline period) and at least 24 months following the index date (follow-up period). Study objectives were to characterize the treatment patterns and treatment sequencing in patients with UC or CD who were newly were initiated on a biologic

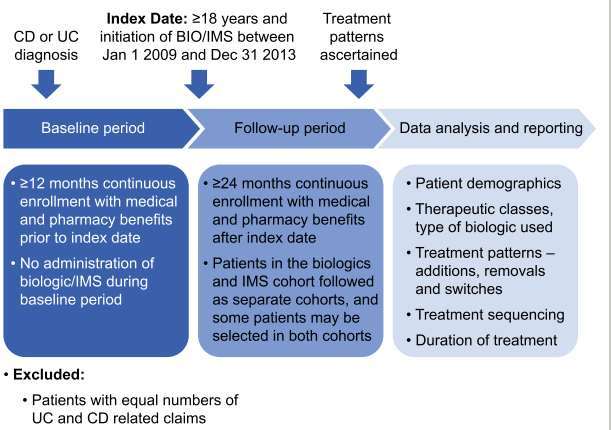

Figure 1. Study schema. BIO = biologic; CD = Crohn disease; IMS = immunosuppressants; UC = ulcerative colitis.