



ORIGINAL ARTICLE - GASTROENTEROLOGY (CLINICAL)

Fidaxomicin treatment for *Clostridioides difficile* infection in patients with inflammatory bowel diseaseAndree H Koop,*  Paul M Travers,[†]  Sahil Khanna,[‡] Darrell S Pardi,[‡] Francis A Farraye* and Jana G Hashash*[§]Divisions of *Gastroenterology and Hepatology, [†]Community Internal Medicine, Mayo Clinic, Jacksonville, Florida, [‡]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, USA; [§]Division of Gastroenterology and Hepatology, American University of Beirut, Beirut, Lebanon**Key words***Clostridioides difficile* infection, Crohn's disease, fidaxomicin, inflammatory bowel disease, ulcerative colitis.

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Email: koop.andree@mayo.edu**Declaration of conflict of interest:** SK receives research support from Rebiotix/Ferring, Vedanta, Finch, Seres, and Pfizer. SK serves as a consultant for Probio Tech, LLC, Shire/Takeda, Niche, and Immuron. DSP receives grants from Atlantic, Finch, Salix, Janssen, Pfizer, Seres, Applied Molecular Transport, and Takeda and consulting fees from AbbVie, Vedanta, Seres, Immunic, Merck, Otsuka, Ferring, Rise Therapeutics, Boehringer Ingelheim, and Summit Therapeutics. The remaining authors have nothing to disclose pertinent to this manuscript. Content from this manuscript was presented at the American College of Gastroenterology National meeting in Charlotte, NC, October 2022.**Introduction**

Clostridioides difficile infection (CDI) is a diarrheal illness from a spore-forming, anaerobic, gram-positive bacterium that can range from self-limited diarrhea to fulminant colitis with significant morbidity and mortality.¹ In patients with inflammatory bowel disease (IBD) including ulcerative colitis (UC) and Crohn's disease (CD), CDI is the most common infectious complication and is associated with worse clinical outcomes.^{2–5} Patients with IBD are more likely to develop CDI and have recurrent CDI.⁶ Additionally, hospitalized patients with IBD and CDI have a fourfold higher risk of mortality and CDI has been associated with increased risk for colectomy.^{7,8} Patients with CDI and IBD are more likely to have a flare of underlying IBD and require treatment escalation, although balancing immunosuppression in the setting of infection can be challenging.³

Abstract**Background and Aim:** Although fidaxomicin is an effective first-line treatment for *Clostridioides difficile* infection, it has not been well studied in patients with inflammatory bowel disease. We aimed to assess the effectiveness of fidaxomicin for the treatment of *C. difficile* infection in patients with inflammatory bowel disease.**Methods:** This was a multicenter retrospective study of adults with inflammatory bowel disease and *C. difficile* infection treated with fidaxomicin with at least 3 months of follow up. The primary outcomes were treatment response, defined as resolution of *C. difficile* infection-attributed diarrhea and/or negative *C. difficile* infection stool test, and time to *C. difficile* infection recurrence after fidaxomicin.**Results:** Thirty-three patients (median age 42 years; 60.6% female) were included. Most patients had ulcerative colitis (26, 78.8%), were receiving treatment with a biologic or small molecule medication (19, 57.6%), and had a prior episode of *C. difficile* infection (26, 78.8%, median 2 episodes, range 0–15). Fidaxomicin led to resolution of *C. difficile* infection in 20 (60.6%) patients, with 6/20 (30.0%) developing a recurrence at a median of 55 days. Most patients who failed to respond to fidaxomicin underwent fecal microbiota transplantation (10/13, 76.9%) with resolution.**Conclusions:** In this cohort of patients with inflammatory bowel disease and *C. difficile* infection, 60.6% responded to treatment with fidaxomicin. Of those who did not respond, fecal microbiota transplantation was an effective therapy.**Financial support:** No funding was received for this study.**Guarantor of the article:** Dr Andree Koop.

The initial treatment of CDI is antibiotic therapy with fidaxomicin or vancomycin as recommended in multiple guidelines including the Infectious Diseases Society of America and the American College of Gastroenterology.^{2,9} Most recent guidelines by the Infectious Diseases Society of America now suggest using fidaxomicin rather than standard course vancomycin for an initial episode.⁹ The effectiveness of both vancomycin and fidaxomicin in patients with IBD remains less clear, as clinical trials testing medications for CDI excluded patients with IBD due to the difficulty in following clinical endpoints.^{3,10} As such, these medications have not been rigorously studied in patients with IBD. The data for fidaxomicin in CDI and IBD are limited to one retrospective study of 21 patients in which all responded to treatment with either symptom improvement or a negative CDI test. Recurrence of CDI occurred in 19% of patients at a median

of 29 days.¹¹ Although the study evaluated patients on biologic therapy, they did not assess IBD activity or other clinical parameters of disease severity.

In this study, we aimed to assess the effectiveness of fidaxomicin for the treatment of CDI in IBD and assess risk factors for treatment failure and recurrence.

Methods

This was a retrospective multicenter study of all cases of CDI treated with fidaxomicin in patients with IBD from January 1, 2017, to December 31, 2021, at the Mayo Clinic sites in Jacksonville, FL, Rochester, MN, and Phoenix, AZ. All patients were age 18 years and older and had at least 3 months of follow up after treatment with fidaxomicin. The study was approved by the Mayo Clinic Institutional Review Board and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and later amendments. Data supporting the findings of this study are available from the corresponding author (A. H. K.) on request.

Patients with IBD, CDI, and treatment with fidaxomicin were identified by a search of the electronic medical record. All medical records from the three Mayo Clinic sites are linked and accessible through the same electronic system. The records were reviewed manually to identify patients who met the inclusion criteria. CDI was defined as a positive toxin enzyme immunoassay or polymerase chain reaction for toxigenic *C. difficile* and either ≥ 4 loose bowel movements per day or change from baseline in this patient cohort with IBD. All patients had IBD, either UC/indeterminate colitis or CD, confirmed by clinical, endoscopic, and/or histologic evidence from review of the patient record. All patients were treated with fidaxomicin of 200 mg twice daily for 10 days, or twice daily for 5 days followed by an extended regimen of every other day for days 7 through 25.

Collected information included patient demographics, clinical characteristics, prior CDI episodes and treatments, history of IBD including subtype, baseline endoscopic findings before CDI, and IBD treatment. Laboratory values, endoscopic findings, and cross-sectional imaging findings performed within 7 days of CDI diagnosis and fidaxomicin treatment were recorded. Episodes of CDI were defined as recurrent or subsequent if they occurred ≤ 56 or > 56 days, respectively, from the successful treatment of a prior CDI episode. The primary outcome was treatment response, defined as resolution of diarrhea or return to baseline symptoms in patients with active IBD and/or negative stool testing for CDI. Additionally, we evaluated the time to CDI recurrence after treatment response. We assessed the association of patient characteristics including demographics, clinical information, CDI history, and IBD history with treatment failure and CDI recurrence. Patients were defined as receiving salvage therapy with fidaxomicin if they had a non-response to prior treatment, such as vancomycin or metronidazole, immediately prior to treatment with fidaxomicin. Patients with a history of total abdominal colectomy and ileal pouch anal anastomosis (IPAA) were excluded from the primary analysis but described separately.

Continuous variables were summarized with the sample median, mean, and range. Categorical variables were summarized with the number and percentage of patients. Comparisons between two groups were compared using the Wilcoxon rank sum test

(continuous variables) or Fisher's exact test (categorical variables). All tests were two-sided with an alpha level set at 0.05 for statistical significance. Statistical analysis was performed with BlueSky statistics (version 7.40, Chicago, IL, USA).

Results

Of 127 patients identified through the electronic medical record, 33 met strict inclusion criteria. Sixty-five patients were excluded for not having a confirmed history of IBD, 24 patients were excluded for not receiving fidaxomicin, 1 patient was excluded for not having 3-month follow up, and 4 patients were analyzed separately due to a history of IPAA. The median age was 42 years old, 20 (60.6%) patients were female, and all patients were Caucasian. Thirty patients were treated with fidaxomicin of 200 mg twice daily for 10 days, and 3 patients received 200 mg twice daily for 5 days followed by an extended regimen. Other than diarrhea attributed to CDI and/or IBD, fidaxomicin was well tolerated and treatment course completed by all patients. Eleven (33.3%) patients were on treatment with a proton pump inhibitor, and a minority (5, 15.2%) had received antibiotics in the 3 months prior to CDI. Five patients were taking probiotics at the time of fidaxomicin treatment; no patients received probiotics to prevent CDI recurrence.

Patient characteristics and treatments of IBD are listed in Table 1. Most patients had UC (26, 78.8%) and 19 (57.6%) were receiving treatment with a biologic or small molecule therapy (Table S1). The most common distribution of UC was extensive occurring in 17/24 (70.8%) patients. Only 3/18 (16.7%) patients had findings of endoscopic remission on their prior baseline colonoscopy. Table 2 summarizes characteristics of CDI treated with fidaxomicin. Most patients (26, 78.8%) had a history of one or more episodes of CDI (median 2, 0–15), and 10 (30.3%) had undergone prior fecal microbiota transplantation (FMT) at a median of 28.0 months before CDI treatment with fidaxomicin. This was the first occurrence of CDI in 7 (21.2%) patients, a recurrent episode in 4 (12.1%) patients, and a subsequent episode in 22 (66.7%) patients. Regarding prior treatments for CDI, 29 (87.9%) patients had received vancomycin and 16 (48.5%) metronidazole. Of the seven patients with a first episode of CDI, three were treated with fidaxomicin after not responding to vancomycin and four were treated with fidaxomicin as first-line therapy. In addition to diarrhea, approximately one half of patients had symptoms of hematochezia (16, 48.5%) and only a minority (6, 18.2%) underwent colonoscopy within 7 days of CDI diagnosis. All patients had moderate or severe findings on endoscopy, and no patients had findings of pseudomembranes. Nearly all (5, 83.3%) patients with cross-sectional imaging within 1 week of CDI diagnosis had radiographic findings of colonic inflammation.

Patient outcomes are listed in Table 3 and a flow diagram of treatment response is illustrated in Figure 1. Resolution of CDI occurred in 20 (60.6%) patients, and 13 (39.4%) failed to respond. Of the 13 patients who failed to respond, 7 achieved response after FMT, 3 after vancomycin bridge to FMT, 1 after vancomycin treatment, 1 after vancomycin, metronidazole, and bezlotoxumab treatment, and 1 after colectomy. Four (12.1%) patients were hospitalized during their treatment with fidaxomicin for severe diarrhea. Of the 20 patients who initially responded to fidaxomicin treatment, 6 (30.0%) developed CDI at a median of 55.0 days

Table 1 Characteristics of inflammatory bowel disease

Type of inflammatory bowel disease (#, %)	33, 100
Ulcerative colitis	26, 78.8
Crohn's disease	7, 21.2
Baseline colonoscopy/flexible sigmoidoscopy before CDI	
Time before CDI, days (mean, median, range)	324, 107, 21–2920
Mayo endoscopic subscore (#, %)	17, 100
0	2, 11.8
1	6, 35.3
2	6, 35.3
3	3, 17.6
Simple endoscopic score for Crohn's disease (1)	0
Treatment for IBD (#, %)	25, 75.8
Biologic or small molecule	19, 57.6
Azathioprine	4, 12.2
Combination therapy (azathioprine and biologic)	3, 9.1
Oral steroid (prednisone or budesonide)	6, 18.2
Oral 5-ASA	8, 24.2
Treatment duration at time of CDI, months (mean, median, range)	18.9, 7.0, 0.5–180
Ulcerative colitis phenotype (#, %)	
Proctitis	1, 4.2
Left sided	6, 25.0
Extensive	17, 70.8
Crohn's disease phenotype (#, %)	7, 100
Ileal	1, 14.3
Colonic	2, 28.6
Ileocolonic	4, 57.1
Isolated upper digestive	0, 0.0
B1 non-stricturing, non-penetrating	3, 42.9
B2 stricturing	1, 14.3
B3 penetrating	3, 42.9
Perianal disease	2, 28.6
Surgery for Crohn's disease (#, %)	7, 100
Small bowel resection	1, 14.3
Large bowel resection	1, 14.3
Stricturoplasty	1, 14.3

CDI, *Clostridioides difficile* infection; IBD, inflammatory bowel disease.

following treatment, of which 3 patients underwent FMT. One patient again developed CDI 104 days after FMT and was treated with fidaxomicin and bezlotoxumab. Due to non-response and severe UC, he underwent colectomy. Of the other three patients with recurrence after treatment with fidaxomicin, two responded to treatment with vancomycin and one responded to treatment with fidaxomicin.

Table 4 lists the association of clinical factors with fidaxomicin treatment response and CDI recurrence in patients who responded. The only variable significantly associated with treatment response was use of azathioprine, which was more common in patients without treatment response (30.8% vs 0.0% patients, $P = 0.017$). Three of the four patients on azathioprine were on combination therapy (one infliximab and two adalimumab, $P = 0.052$). A lower hemoglobin ($P = 0.073$) and a higher C-reactive protein ($P = 0.128$) occurred in more patients with treatment response but did not reach statistical significance. There was no difference in treatment response between patients with a prior history of

Table 2 Characteristics of *Clostridioides difficile* infection

History of CDI (#, %)	26, 78.8
# of prior episodes (mean, median, range) (#, %)	2.61, 2, 0–15
0	7, 21.2
1	6, 18.2
2	5, 15.2
3 or more	15, 45.5
Prior treatments for CDI (#, %)	
0 treatments	4, 12.1
1 treatment	12, 36.4
2 treatments	8, 24.2
3 or more	9, 27.3
Prior treatments for CDI (#, %)	
Vancomycin	29, 87.9
Metronidazole	16, 48.5
Rifaximin	2, 6.1
Bezlotoxumab	1, 3.0
FMT	10, 30.3
Time from FMT to fidaxomicin treatment, months (mean, median, range)	29.8, 28.0, 0.5–83.0
Symptoms (#, %)	
Hematochezia	16, 48.5
Colonoscopy within 7 days of CDI (#, %)	6, 100
Mayo endoscopic score	
0	0, 0
1	0, 0
2	4, 80.0
3	1, 20.0
Simple endoscopic score for Crohn's disease (1)	9
Cross-sectional imaging within 7 days of CDI (6)	6, 100
Findings of colitis (wall thickening, inflammatory stranding)	5, 83.3

CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation.

CDI ($P = 1$), prior history of FMT ($P = 0.461$), by type of IBD ($P = 0.393$), treatment with a biologic or small molecule medication ($P = 0.310$), or use of fidaxomicin as initial *versus* salvage therapy ($P = 1.00$). No factors were associated with CDI recurrence.

One patient with UC underwent colectomy for CDI after treatment with fidaxomicin. She was a 45-year-old woman with severe UC who had been initiated on prednisone and infliximab 3 months earlier. Testing for CDI was performed for ongoing diarrhea and returned positive. She was treated with 10 days of oral vancomycin without clinical improvement and transitioned to fidaxomicin. Due to severe symptoms including diarrhea, abdominal pain, and 15-pound weight loss, she required hospitalization 4 days later. Testing for CDI was not repeated on hospital admission. She was treated with intravenous corticosteroids and continued fidaxomicin. Computed tomography imaging of the abdomen revealed pancolitis without concern for toxic megacolon. After multi-disciplinary discussion, due to ongoing symptoms despite treatment, she underwent subtotal colectomy with end ileostomy.

In addition to the referenced patient who underwent colectomy, three other patients were hospitalized during CDI and fidaxomicin treatment, one patient with UC and two patients with CD of the colon. All three patients had severe activity of their IBD and a prior

Table 3 Outcomes of treatment with fidaxomicin

Resolution of CDI attributed diarrhea and/or negative stool test for CDI after fidaxomicin (#, %)	20/33, 60.6
Persistent diarrhea and/or positive stool test for CDI after fidaxomicin (#, %)	13, 39.4
Hospitalization for CDI (#, %)	4, 12.1
Length of stay, days (mean, median, range)	5.5, 5.0, 2–10
Intensive care unit stay (#, %)	0, 0.0
Readmission (#, %)	0, 0.0
Colectomy (#, %)	1, 3.0
Treatments after failed fidaxomicin (#, %)	13, 100
Vancomycin	5, 38.5
Rifaximin	0, 0.0
Bezlotoxumab	1, 7.7
FMT	7, 76.9
Time to FMT, days (mean, median, range)	62.3, 57.5, 5–175
Recurrent CDI after treatment response to fidaxomicin (#, %)	6, 30
Time to recurrence, days (mean, median, range)	63.8, 55.0, 20–150
Treatments (#, %)	
Vancomycin	1, 16.7
Fidaxomicin	2, 33.3
Rifaximin	0, 0.0
Bezlotoxumab	0, 0.0
FMT	3, 50.0

CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation.

history of CDI treated with oral vancomycin. Two patients had significant clinical improvement with prednisone and a prolonged course of fidaxomicin. Both patients had negative follow-up CDI testing. The third patient did not respond to a 10-day course of fidaxomicin and was treated with two prolonged courses of oral vancomycin.

Four patients who were not included in the overall patient cohort had a history of IBD, CDI, and an IPAA. All patients responded to treatment with fidaxomicin, although one developed a subsequent episode 3 months later. These patients are summarized in Table S2. All four patients with IPAA initially underwent total abdominal colectomy and IPAA for UC, and three patients were subsequently diagnosed with CD due to inflammation in the pre-pouch ileum. Two of the patients with CD had persistent diarrhea after treatment with fidaxomicin, although repeat CDI testing was negative. Of these two patients, one was diagnosed with *Plesiomonas shigelloides* infection through stool studies, and the other had treatment escalation for CD with vedolizumab. The third patient with CD initially responded to fidaxomicin, however had a recurrence of CDI 3 months later treated with FMT. The patient with IPAA and a history of UC responded to fidaxomicin after not responding to two courses of vancomycin.

Discussion

In this multicenter retrospective study of patients with CDI and IBD treated with fidaxomicin, the overall response rate was 60.6%, and 30.0% of patients who responded developed another CDI episode at a median of 55 days. This is the largest study to date reporting outcomes in patients with CDI and IBD treated with fidaxomicin. Of the patients who did not respond to fidaxomicin, most were treated successfully with FMT. The only factor associated with a lack of treatment response was azathioprine use, with three of four of these patients on combination therapy with a biologic medication. Factors not associated included type of IBD, phenotype of UC, and treatment with biologic or small molecule medications. Characteristics of CDI including prior CDI, prior FMT, and fidaxomicin as salvage therapy were similarly not associated with treatment response.

The only prior study evaluating outcomes of CDI in patients with IBD treated with fidaxomicin was performed by Spiceland *et al.*, evaluating 21 patients reviewed over a 4-year time period.¹¹ There was no overlap of patients between these two studies. Our studies

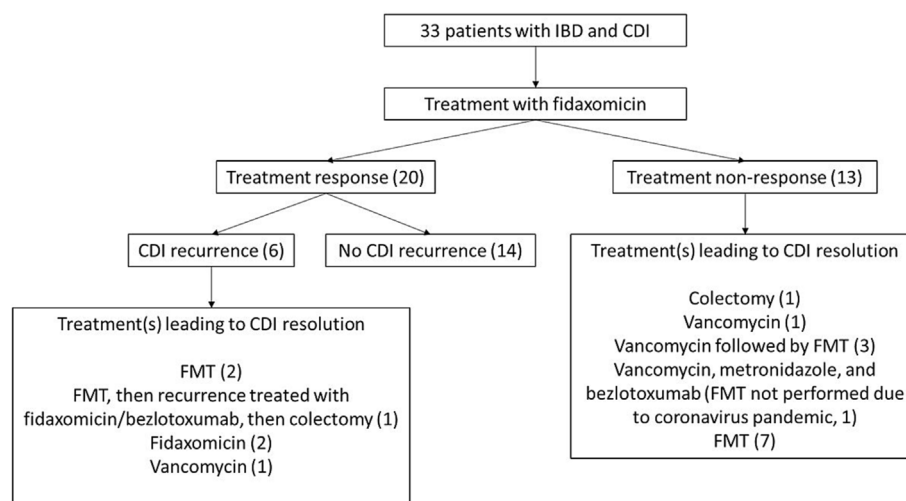


Figure 1 Flow chart depicting treatment response to fidaxomicin and treatments for non-response and recurrence. CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation; IBD, inflammatory bowel disease.

Table 4 Association of clinical factors with CDI treatment response and recurrence following fidaxomicin

Variable (# of patients)	Treatment response (20)	No treatment response (13)	CDI recurrence (6)	No CDI recurrence (14)
Age, years (mean)	51.4	41.2	43.3	54.8
Sex, female (#, %)	11, 55.0	9, 69.2	4, 66.7	7, 50.0
# prior episodes of CDI, mean	2.70	2.46	1.33	3.29
History of 1 or more episodes of CDI (#, %)	16, 80.0	10, 76.9	4, 66.7	12, 85.7
Prior FMT (#, %)	5, 25.0	5, 38.5	1, 16.7	4, 28.6
PPI use (#, %)	7, 35.0	4, 30.8	2, 33.3	5, 35.7
Labs (median)				
White blood cells, mean ($\times 1000/\text{mm}^3$)	8.83	7.88	11.5	7.6
Hemoglobin, mean (g/dL)	11.52	13.27	11.2	11.7
Creatinine, mean (mg/dL)	1.07	0.818	1.37	0.94
Albumin, mean (g/L)	3.85	3.96	3.45	4.0
C-reactive protein, mean (mg/dL)	53.54	25.52	20.5	66.76
IBD history				
Ulcerative colitis (#, %)	17, 85.0	9, 62.9	6, 100.0	11, 78.6
Crohn's disease (#, %)	3, 15.0	4, 30.8	0, 0.0	3, 21.4
Baseline colonoscopy (#, %)				
Baseline Mayo score 2 or higher (#, %)	7, 63.6	2, 33.3	2, 50.0	5, 71.4
Extensive ulcerative colitis phenotype	11, 55.0	6, 46.2	2, 33.3	9, 64.3
Treatment for IBD (#, %)				
Any	14, 70.0	11, 84.6	4, 66.7	10, 71.4
Biologic or small molecule	10, 50.0	9, 69.2	2, 33.3	6, 42.9
Azathioprine	0, 0.0	4, 30.8*	0, 0.0	0, 0.0
Combination therapy (azathioprine and biologic)	0, 0.0	3, 23.1	0, 0.0	0, 0.0
Oral steroid	5, 25.0	1, 7.7	1, 16.7	4, 28.6
Oral 5-ASA	5, 25.0	3, 23.1	3, 50.0	2, 14.3
Fidaxomicin as CDI salvage therapy (#, %)	12, 60.0	7, 53.8	3, 50.0	9, 64.3
Rectal bleeding (#, %)	11, 55.0	5, 38.5	5, 83.3	6, 42.9

*P-value < 0.05 on comparison between treatment response and no treatment response.

Laboratory values were recorded if obtained within 1 week of CDI diagnosis. Comparisons between two groups were compared using the Wilcoxon rank sum test (continuous variables) or Fisher's exact test (categorical variables). CDI, *Clostridioides difficile* infection; FMT, fecal microbiota transplantation; IBD, inflammatory bowel disease; PPI, proton pump inhibitor.

used similar outcomes and defined treatment response as resolution of symptoms attributed to CDI or a negative stool test after treatment. Our study demonstrated a worse treatment response to fidaxomicin (60.6% vs 100%) and a higher recurrence rate (30.0% vs 19%). Notably, most patients in both studies had a prior history of CDI (78.8% and 76%), and more patients in our study underwent prior FMT (30.3% vs 5%). Additionally, we included more patients with UC (78.8% vs 48%). The lower treatment response in our study may reflect greater disease severity as illustrated by more patients with prior FMT and UC, which is associated with greater morbidity and mortality from CDI than CD.¹²

Clinical trials evaluating vancomycin and fidaxomicin in CDI have excluded patients with IBD, and their effectiveness in these patient populations remains unclear.^{10,13,14} The medical literature for vancomycin in CDI and IBD is more robust than that for fidaxomicin. Treatment with vancomycin compared with metronidazole was associated with shorter hospital length of stay, fewer readmissions, and decreased rate of colectomy in patients with IBD.^{15,16} A prolonged duration of treatment (21–42 days) of vancomycin compared with a short duration (10–14 days) was associated with decreased CDI recurrence.¹⁷ Compared with vancomycin, the primary disadvantage of fidaxomicin is its high cost,

although studies have demonstrated cost-effectiveness by preventing readmissions.^{18,19} CDI recurs in as high as 32% of patients with IBD compared with 24% of non-IBD patients.²⁰

In the clinical trials of non-IBD patients treated with fidaxomicin, the response rate was non-inferior to vancomycin and ranged from 87% to 92%, although fidaxomicin demonstrated a lower recurrence rate of 13–16%.^{10,13} In this study, patients with CDI and IBD treated with fidaxomicin had both lower treatment response and higher recurrence than reported in non-IBD patients. This likely reflects the impacts of IBD on CDI, as it is well established that CDI may lead to a flare of IBD and require escalation of immunosuppression. In patients with flares of IBD, guidelines recommend testing for CDI.^{21,22} Theoretically, increased immunosuppression may lead to worsening of CDI, versus treatment with antibiotic therapy alone, although studies have demonstrated conflicting results.^{3,23–25} At this time, withholding immunosuppression during treatment of CDI in IBD is generally not recommended, and escalation of immunosuppressive therapy can be performed after several days of antibiotic therapy and symptom assessment. The association of azathioprine and lack of treatment response in this study may reflect the severity of underlying IBD, as three of these patients were on combination therapy with biologic medications.

Fecal microbiota transplantation is generally safe and effective for patients with IBD and recurrent CDI, with a pooled response rate of 80% and increasing to 90% with two or more treatments.^{26,27} In both CDI and IBD, the gut microbiota is disrupted and FMT acts to reconstitute the diversity of the gut flora. In this study, 10 patients who had a non-response to fidaxomicin ultimately responded to FMT. Three of these 10 patients were treated with vancomycin as a bridge to FMT, and 7 patients went directly to FMT. Of the six patients who developed CDI recurrence after response to fidaxomicin, three were treated with FMT, of which two responded. The patient who did not respond had UC, was dependent on prednisone, and had not responded to treatment with infliximab, vedolizumab, or ustekinumab. He underwent colectomy in the setting of severe UC and recurrent CDI. This study illustrates that FMT can be an effective treatment for patients with IBD and CDI who do not respond to fidaxomicin.

The strengths of this study include the largest cohort of patients reported to date with IBD, CDI, and treatment with fidaxomicin from three tertiary medical centers. The primary study limitation is its retrospective nature and lack of a control group such as patients treated with vancomycin or patients without IBD. Although most patients were treated with fidaxomicin of 200 mg twice daily for 10 days, 3 patients received 200 mg twice daily for 5 days followed by an extended regimen. Due to small sample size, differences in outcomes between these two regimens could not be assessed and further studies are needed to assess the effectiveness of fidaxomicin in this population. Finally, assessing treatment response for CDI in patients with IBD is difficult given overlapping symptoms and the close interplay between these conditions. In the absence of a negative CDI test, assessing treatment response is somewhat subjective and based on clinical judgement. Nevertheless, this is a situation frequently encountered in clinical practice and represented by this study.

In conclusion, this retrospective study found that patients with underlying IBD treated for CDI with fidaxomicin had approximately a 60% response rate and a 30% recurrence rate. Most patients who did not respond to fidaxomicin did respond to FMT. Further studies are needed to evaluate the effectiveness of fidaxomicin in patients with IBD and identify the optimal treatment in this patient population.

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Data availability statement. The data that support the findings of this study are available from the corresponding author upon reasonable request and completion of necessary privacy and ethical approvals.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1: Treatments for IBD.

Table S2: Patients with a history of IBD and ileal pouch anal anastomosis treated with fidaxomicin for CDI.