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Efficacy of fecal microbiota-based therapies for prevention of recurrent *Clostridioides difficile* infection in patients with cancer

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Abstract

Background Patients with cancer are vulnerable to recurrent *Clostridioides difficile* infection due to immunosuppression, antibiotic exposure and microbiota disruption. While colonoscopy-delivered fecal microbiota transplantation (FMT) is an established treatment, microbiota-based products, such as fecal microbiota live-jslm and fecal microbiota spores live-brpk, offer less invasive alternatives; however, real-world oncology data are limited. This study evaluated their safety and efficacy in cancer patients with rCDI.

Methods This single-center retrospective cohort study included adults with cancer who received colonoscopy-delivered FMT, fecal microbiota live-jslm or fecal microbiota spores live-brpk between October 2017 and March 2025. The primary outcome was rCDI within 8 weeks. Secondary outcomes included adverse events and cancer status at follow up. Subgroup analysis compared outcomes between FMT and fecal microbiota live-jslm.

Results In 69 patients, colonoscopy-delivered FMT was most common (68.1%), followed by fecal microbiota live-jslm (17.4%) and fecal microbiota spores live-brpk (7.2%). The overall 8-week recurrence rate was 5.8%. Adverse events were rare and mild. Subgroup analysis showed similar recurrence rates for colonoscopy-delivered FMT (n=3, overall recurrence 4.3%, subgroup 6.4%) and fecal microbiota live-jslm (n=1, overall recurrence 1.5%, subgroup 8.3%), with no recurrences among fecal microbiota spores live-brpk recipients. No new immune-related adverse events occurred in patients receiving immune checkpoint inhibitors after microbiota-based therapy during the study period.

Conclusions All 3 approaches were associated with low 8-week recurrence and few, mild adverse events in patients with cancer, supporting their feasibility in an underrepresented population but warranting confirmation in larger prospective studies. Selection should consider clinical context, product availability, and resources.

Keywords *Clostridioides difficile,* fecal microbiota transplantation, microbiome, cancer

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Introduction

Clostridioides difficile infection (CDI) remains one of the most common healthcare-associated infections worldwide, contributing significantly to patient morbidity, mortality, and healthcare costs [1]. Despite appropriate antibiotic therapy, 20-30% of patients experience a first recurrence, and up to 60% may suffer multiple episodes [1-4]. Recurrent CDI (rCDI), defined as the return of diarrhea with a positive test for CDI within 8 weeks after completing treatment for the initial episode, remains particularly challenging [1,5]. This is especially true in patients with cancer, who are particularly vulnerable because of frequent exposure to broad-spectrum antibiotics, chemotherapy-induced mucosal injury, repeated hospitalizations and immunosuppressive treatments. These

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factors collectively disrupt the gut microbiome and increase susceptibility to both initial CDI and recurrence [2,6-14]. The high risk of rCDI in this population underscores the urgent need for effective preventive strategies to reduce disease burden and improve outcomes [6,15,16].

In recent years, restoring the gut microbiota has emerged as an effective approach to interrupt the cycle of CDI recurrence [5,13,17]. Fecal microbiota transplantation (FMT) has demonstrated the ability to reestablish microbial diversity and restore colonization resistance, with reported success rates ranging from 60-90% in the general population [3,13,18-21]. Current clinical guidelines recommend FMT or standardized microbiota-based therapies, such as fecal microbiota live-jslm or fecal microbiota spores live-brpk, for patients with multiple CDI recurrences or those at high risk of severe disease [22]. Among the available delivery methods, oral capsules or colonoscopy are preferred, with enemas reserved for situations in which other routes are not feasible [5].

While these strategies are becoming increasingly well established in the general population, evidence supporting their use in patients with cancer remains limited. Most published reports focus on conventional FMT delivered via colonoscopy, which is highly effective; however, this approach may not always be feasible in oncology care, given the procedural and anesthesia-related risks, patient-specific factors and resource availability. These limitations underscore the need to explore the full spectrum of available microbiota-based options [4,23,24]. Recently approved live biotherapeutic products, such as fecal microbiota live-jslm (rectally administered) and fecal microbiota spores live-brpk (oral spores), offer standardized alternatives that may be suitable for patients who are at high risk for invasive procedures. However, real-world data on their safety and effectiveness for rCDI prevention in oncology populations are scarce [16,25-29].

Given the heightened risk of CDI recurrence in this population and the practical considerations associated with existing treatments, there is a clear need to understand how these microbiota-based approaches perform in routine oncology practice. This study aims to describe real-world outcomes, effectiveness and safety of colonoscopy-delivered FMT, fecal microbiota live-jslm, and fecal microbiota spores live-brpk, specifically in patients with cancer, with the goal of expanding the evidence base for preventive strategies in this vulnerable group.

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Patients and methods

Study design and population

This retrospective cohort study was conducted at The University of Texas MD Anderson Cancer Center and was approved by the institutional review board (PA18-0472). Eligible patients were adults (≥18 years) with a documented history of CDI or rCDI who received microbiota-based therapy between October 2017 and March 2025 (Fig. 1). The CDI diagnosis was based on clinical criteria (≥3 loose stools within 24 h), along with positive toxin gene nucleic acid amplification testing (NAAT) and/or enzyme immunoassay (EIA) positivity, or endoscopic evidence of pseudomembranous colitis. Recurrence was defined as a recurrence of diarrhea and a confirmatory positive test (NAAT or EIA) within 8 weeks after completion of treatment for an initial episode of CDI.

Interventions

Patients received colonoscopy-delivered FMT, a fecal microbiota live-jslm rectal enema, or fecal microbiota spores live-brpk in oral capsules (Fig. 2). Intervention selection was guided by physician discretion, patient preference and product availability. In accordance with institutional practice patterns, a subset of patients also received bezlotoxumab at the treating physician's discretion.

The 3 protocols differed in source material, route and schedule. Colonoscopy-delivered FMT used processed stool from screened, qualified donors, instilled into the colon during colonoscopy after standard bowel preparation [22]. Fecal microbiota, live-jslm (REBYOTA; Ferring Pharmaceuticals; formerly RBX2660) is a single-dose 150-mL microbiota suspension administered as a rectal enema; it was the first microbiota-based product approved by the US Food and Drug Administration (FDA) for prevention of rCDI (November 2022), and is given 24 to 72 h after completion of antibiotic therapy [30]. Fecal microbiota spores, live-brpk (VOWST; Seres Therapeutics; formerly SER-109) is an orally administered

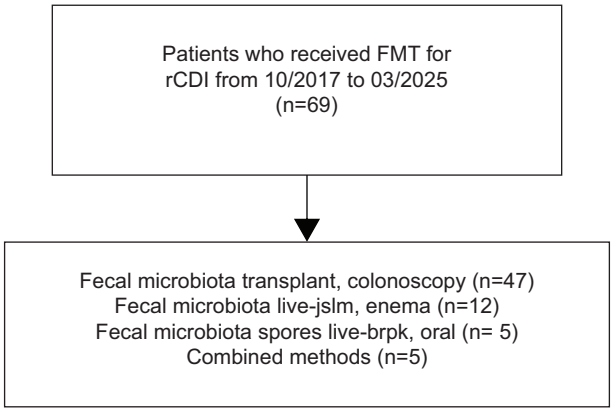

Figure 1 Patient selection diagram

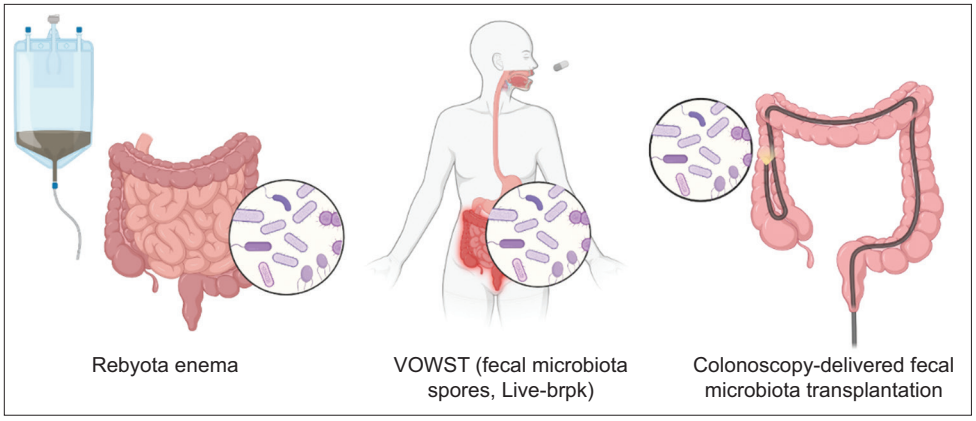

Figure 2 Fecal microbiota transplantation delivery methods

preparation of purified Firmicutes spores supplied as capsules; it was the first oral microbiota-based product approved by the FDA (April 2023), and is given as 4 capsules once daily for 3 consecutive days, starting 2 to 4 days after completion of antibiotic therapy and preceded by a magnesium citrate preparation [31]. The 4-letter suffixes "jslm" and "brpk" are FDA-designated distinguishing suffixes for licensed biological products and carry no inherent meaning.

Safety procedures were consistent across approaches. Donor-derived material was obtained from qualified donors, screened and tested for a panel of transmissible pathogens, in accordance with the FDA requirements for the licensed products and established donor-screening practice for colonoscopy-delivered FMT [22]. Therapy was administered only after completion of anti-CDI antibiotics, observing the product-specific interval, and avoiding antibacterial therapy concurrent with the oral spore product [30,31].

Data collection and outcomes

Data were extracted from electronic medical records and included demographic characteristics, cancer type and stage, active treatment status, CDI history, diagnostic testing, concurrent conditions (e.g., immune checkpoint inhibitor [ICI]-colitis, graft-versus-host disease [GVHD], inflammatory bowel disease [IBD]), and antibiotic regimens. The primary outcome was CDI recurrence within 8 weeks following microbiota-based intervention. Secondary outcomes included any recurrence during follow up, adverse events within 8 weeks, and cancer status at last follow up. Subgroup analysis compared outcomes between colonoscopy-delivered FMT and fecal microbiota live-jslm.

Statistical analysis

Descriptive statistics were used to summarize patient characteristics and outcomes. Continuous variables were reported as medians with interquartile ranges (IQR), and categorical variables as frequencies and percentages. Univariate logistic regression was performed to assess associations between selected clinical factors and CDI recurrence, including cancer type, cancer stage, ICI use, bezlotoxumab administration and post-procedure antibiotic exposure. Analyses were performed using SPSS version 24 (IBM Corp.).

Results

Patient characteristics

A total of 69 patients with a history of CDI or rCDI were included (Table 1). The median age was 67 years (IQR: 57-76), and 63.4% were female. The majority were white (74.6%), and the most common cancer types were hematological malignancies (31.9%), followed by genitourinary cancers (14.5) and breast cancer (11.3%). Advanced cancer (stage III-IV) was present in 47.8% of patients. At the time of their most recent CDI/rCDI episode prior to microbiota-based intervention, 20.3% were receiving chemotherapy, 26.1% were receiving ICIs, and 8.7% were on combined chemotherapy and immunotherapy. The remaining patients were not undergoing active cancer treatment. Absolute neutrophil count data were available within 30 days of intervention, and only a minority of patients had values below 500/μL (4.3%).

Interventions included colonoscopy-delivered FMT in 47 patients (68.1%), fecal microbiota live-jslm in 12 (17.4%), fecal microbiota spores live-brpk in 5 (7.2%), and combination strategies in 5 (7.2%). Combination approaches included fecal microbiota live-jslm with colonoscopy-delivered FMT (n=4, 5.8%) and fecal microbiota live-jslm with fecal microbiota spores live-brpk (n=1, 1.4%). The overall all-cause mortality rate was 40.6%, with a median follow up of 11 months (IQR 3-35.5).

CDI/rCDI clinical features, treatment, and outcomes

Before the microbiota-based intervention, the median number of CDI episodes within 180 days and 1 year was 1 (IQR 1-2) and 2 (IQR 1-3), respectively. The majority of patients (59.4%) experienced fewer than 3 episodes. Diarrhea was the most prevalent symptom (98.6%), followed by abdominal pain (26.1%), and blood or mucus in the stool (15.9%). ICI-related colitis was present in 17.4% of patients, GVHD in 8.7% and IBD in 4.3%. Positive results for both *C. difficile* NAAT and EIA tests were documented in 63.8% of patients, whereas 23.2% were NAAT-positive but EIA-negative in the most recent laboratory result before intervention. The median time from symptom onset to intervention was 28 days (IQR 12.5-61.2). Anti-CDI treatments included vancomycin (20.3%), fidaxomicin (18.8%) and combination regimens. Bezlotoxumab was administered in 18.8% of cases (n=13). Hospitalization for the index CDI occurred in 44.9% of patients, with a median length of stay of 8 days (IQR 5-16.5).

Recurrence within 8 weeks after FMT occurred in 4 patients (5.8%): 3 after colonoscopy-delivered FMT and 1 after fecal microbiota live-jslm (Table 2). No recurrence was observed in patients who received fecal microbiota spores live-brpk. The median interval from intervention to recurrence was 49 days and the median length of hospitalization for rCDI was 7 days (IQR 4.2-12.5). Adverse events within 8 weeks of FMT occurred in 2 patients (2.9%) and were limited to mild symptoms (constipation and vomiting), both following colonoscopy-delivered FMT. No adverse events were reported after administration of fecal microbiota live-jslm or fecal microbiota spores live-brpk. At last follow up, no patients had experienced any immune-related adverse events. Cancer outcomes included stable disease in 36.2% of patients, remission in 26.1%, and progression in 26.1%.

Table 1 Patient demographic characteristics, n=69

Characteristic	No. (%)
Age, median (IQR), *years*	67 (57-76)
Female sex	45 (63.4)
White race	53 (74.6)
Cancer type	
Hematological	22 (31.9)
Lung	7 (10.1)
Genitourinary	10 (14.5)
Breast	7 (10.1)
Head and neck	5 (7.2)
Gastrointestinal	5 (7.2)
Endocrine	3 (4.3)
Melanoma	2 (2.9)
Other	8 (11.6)
Cancer stage	
I-II	2 (2.9)
III-IV	33 (47.8)
Baseline hematologic status within 30 days prior to intervention	
ANC ≥500 /μL	66 (95.7)
ANC <500 /μL	3 (4.3)
Cancer response status at the time of FMT intervention	
Stable	21 (30.4)
Remission	16 (23.2)
Progression	25 (36.2)
Type of cancer therapy received during the CDI/rCDI[1]	
Chemotherapy only	14 (20.3)
Immune-checkpoint inhibitors only	18 (26.1)
Combined therapy[2]	6 (8.7)
No concurrent treatment	31 (44.9)
FMT delivery method	
Colonoscopy	47 (68.1)
Fecal microbiota live-jslm enema	12 (17.4)
Fecal microbiota spores live-brpk	5 (7.2)
Fecal microbiota live-jslm and colonoscopy	4 (5.8)
Fecal microbiota live-jslm and fecal microbiota spores live-brpk	1 (1.4)
All-cause mortality	28 (40.6)
Length of follow up, median (IQR), *months*	11 (3-35.5)

[1]Last CDI/rCDI related to intervention
[2]Chemotherapy and Immunotherapy
IQR, interquartile range; ANC, absolute neutrophil count; FMT, fecal microbiota transplantation; CDI, Clostridioides difficile infection; rCDI, recurrent Clostridioides difficile infection

Table 2 Clinical outcomes after FMT for rCDI prevention in patients with cancer (n=69)

Parameter	No. (%)
8-week recurrence after FMT	
Colonoscopy	4 (5.8)
Fecal microbiota live-jslm	3 (4.3)
Fecal microbiota spores live-brpk	1 (1.5)
Time from intervention to recurrence, median (IQR), *days*	0
Length of hospitalization for recurrence, median (IQR), *days*	49 (24-61.25) 7 (4.2-12.5)
Adverse events after FMT[1]	2 (2.9)
Colonoscopy[2]	2 (4.2)
Fecal microbiota live-jslm[2]	0
Fecal microbiota spores live-brpk [2]	0
Immune-related adverse events after FMT[3]	0
Cancer outcomes after FMT[3]	
Stable	22 (36.2)
Remission	18 (26.1)
Progression	18 (26.1)

[1]Within 8 weeks after intervention; Adverse events included constipation (1 patient) and vomiting (1 patient)
[2]The denominator for these rows is based on the total number of patients who received each single delivery method (FMT:47 patients, fecal microbiota live-jslm: 12, fecal microbiota spores live-brpk: 5 patients)
[3]Until last follow-up date
FMT, fecal microbiota transplantation; rCDI, recurrent Clostridioides difficile infection; IQR, interquartile range

Comparative outcomes: colonoscopy-delivered FMT vs. fecal microbiota live-jslm

A subset analysis was performed in 59 patients who received either colonoscopy-delivered FMT (n=47) or fecal microbiota live-jslm enema (n=12) Table 3. Baseline CDI characteristics, including the number of prior episodes and the time from symptom onset to intervention, were comparable between groups. The prevalence of ICI-colitis, GVHD and IBD did not differ significantly between cohorts. The use of fidaxomicin or vancomycin monotherapy was more frequent in the colonoscopy-delivered FMT group, although the difference was not statistically significant. Hospitalization rates and lengths of stay prior to intervention were also similar. Time to recurrence and re-hospitalization rates following recurrence were not significantly different. Median follow-up duration was longer in the colonoscopy-delivered FMT group (26 vs. 13 months, P=0.004).

Risk factors for recurrent CDI

Univariate analysis did not identify any statistically significant predictors of rCDI following colonoscopy-delivered FMT or fecal microbiota live-jslm (Table 4). Variables assessed included cancer type (hematological vs. solid), cancer stage, treatment modality, presence of ICI-colitis, hospitalization and use of bezlotoxumab. Trends toward lower odds of recurrence were observed in patients receiving bezlotoxumab (odds ratio [OR] 0.2, 95% confidence interval [CI] 0.026-1.605; P=0.131) and in those receiving post-procedure anti-CDI antibiotics (OR 0.2, 95%CI 0.021-1.772; P=0.157), although these did not reach statistical significance. In contrast, post-procedure use of high- and moderate-risk antibiotics for CDI was associated with slightly higher odds of recurrence, but the association was not statistically significant (OR 1.1, 95%CI 0.103-10.918; P=0.959).

Table 3 Comparison of clinical features and outcomes among CDI/rCDI patients treated with colonoscopy-delivered FMT versus fecal microbiota live-jslm enema, n= 59

Feature	No. (%)		P-value
	Colonoscopy-delivered FMT, n= 47	Fecal microbiota live-jslm, n=12	
Number of CDI episodes within 180 days before intervention, median (IQR)	1 (1-2)	2 (1-2)	0.813
<3 episodes	28 (59.6)	10 (83.3)	0.102
≥3 episodes	7 (14.9)	1 (8.3)	0.102
Laboratory results[1]			
NAAT (+)/ EIA (+)	30 (63.8)	9 (75)	0.555
NAAT (+)/ EIA (-)	9 (19.1)	2 (16.7)	0.313
Time from start of symptoms to intervention, median (IQR), *days*	18 (9.5-50.7)	30 (18-72)	0.377
Other comorbidities			
ICI-colitis	9 (19.1)	3 (25)	0.261
GVHD	2 (4.3)	3 (25)	0.074
IBD	1 (2.1)	1 (8.3)	0.410
Associated anti-CDI treatment[1]			
Fidaxomicin	10 (21.3)	0	0.151
Vancomycin	11 (23.4)	0	0.141
Vancomycin and fidaxomicin	13 (27.7)	5 (41.7)	0.642
Fidaxomicin and metronidazole	3 (6.4)	0	0.480
Vancomycin and metronidazole	4 (8.5)	2 (16.7)	0.665
Vancomycin, fidaxomicin, and metronidazole	2 (4.3)	2 (16.7)	0.313
Bezlotoxumab	8 (17)	3 (25)	0.815
Hospitalization before intervention[1]	19 (40.4)	7 (58.3)	0.793
Length of hospitalization, median (IQR), *days*	8 (5-14)	3 (3-3)	0.435
Outcomes			
Recurrence within 8 weeks*	3 (6.4)	1 (8.3)	0.675
Time from intervention to CDI recurrence, *days*	146 (52.5-499)	89 (89-89)	0.346
Length of follow up, median (IQR), *months*	26 (9-42)	3 (2-10.5)	0.004

[1]Index CDI/rCDI previous to intervention;
*This section uses the total number of patients who received only the referred interventions as denominator
CDI, Clostridioides difficile infection; rCDI, recurrent Clostridioides difficile infection; FMT, fecal microbiota transplantation; NAAT, nucleic acid amplification testing for C. difficile toxin gene testing; EIA, C. difficile toxin enzyme immunoassay; IQR, interquartile range; ICI-colitis, immune-checkpoint inhibitor colitis; GVHD, graft-versus-host disease; IBD, inflammatory bowel disease

Table 4 Univariate analysis of factors associated with rCDI after colonoscopy-delivered FMT or fecal microbiota live-jslm enema, n=59

Factor	Odds ratio (confidence interval)	P-value
Cancer type: hematological vs solid cancer	1.3 (0.137-14.263)	0.779
Stage: 3-4 vs. 1-2	0.9 (0.128-7.312)	0.975
Chemotherapy vs. immunotherapy	0.7 (0.062-8.901)	0.815
Active anti-cancer therapy vs. no active therapy	1.2 (0.165-9.358)	0.834
Multiple antibiotic therapy for index event vs. single therapy	0.4 (0.043-4.463)	0.488
Time from start of symptoms to intervention	0.9 (0.831-1.029)	0.150
Intervention associated with bezlotoxumab[2]	0.2 (0.026-1.605)	0.131
CDI with concurrent other GI condition[3]	1.2 (0.131-13.6)	0.808
Length of hospitalization[2]	1 (0.984-1.018)	0.922

[1]Recurrences until last follow up
[2]Within 8 weeks before intervention
[3]Immune-mediated diarrhea and colitis, graft versus host disease, or inflammatory bowel disease
rCDI, recurrent Clostridioides difficile infection; CDI, Clostridioides difficile infection; FMT, fecal microbiota transplantation

Discussion

This single-center study adds real-world data on the use of colonoscopy-delivered FMT, fecal microbiota live-jslm and fecal microbiota spores live-brpk for preventing rCDI in patients with cancer, an especially vulnerable population given several predominantly non-modifiable risk factors [6,12,14,16,32-34]. To our knowledge, this is the first real-world report to describe outcomes for all 3 microbiota-based prevention strategies in oncology patients, a group frequently underrepresented in the existing literature.

In this cohort, the 8-week recurrence rate was low at 5.8%, supporting the benefit of restoring the gut microbiota to break the cycle of recurrence, even in this high-risk population with complex medical conditions. These findings are consistent with previous studies showing high success rates for colonoscopy-delivered FMT, with recurrence rates as low as 13-16% in 8 weeks [15,25]. While colonoscopy-delivered FMT remains the most extensively studied approach, and has shown durable responses even in severe or fulminant cases [4,5], our results suggest that newer standardized products like fecal microbiota live-jslm and fecal microbiota spores live-brpk may also be effective for real-world rCDI prevention in patients with cancer. In our study, fecal microbiota live-jslm was associated with an overall recurrence of 1.5% and a subgroup recurrence rate of 8.3% (n=1) within 8 weeks, while no recurrences were observed in the fecal microbiota spores live-brpk subgroup; however, the latter comprised a very small sample. Larger studies are needed to confirm the effectiveness of these approaches in this population [35].

Guidelines support the use of microbiota-based therapies for preventing rCDI after multiple recurrences, recommending colonoscopy-delivered FMT or capsules when feasible, and enema delivery if other routes are unavailable [5,22]. Meta-analyses and randomized controlled trials in the general population have shown that capsules are non-inferior to colonoscopy-delivered FMT and can reduce procedural risks in individuals at high risk for invasive procedures [5,36]. In patients with cancer, who may be frail, or at increased risk for endoscopy-related complications, ready-to-use options like fecal microbiota live-jslm and fecal microbiota spores live-brpk may help overcome these barriers by avoiding sedation and intensive bowel preparation, simplifying delivery while ensuring consistent dosing. Medical decision-making should consider patient-specific needs, product availability, and institutional resources [5,27,37]. However, current guidelines note insufficient evidence to recommend fecal microbiota spores live-brpk or fecal microbiota live-jslm in immunocompromised patients, including those receiving active cytotoxic therapy for solid tumors or hematologic malignancies, reflecting the limited representation of these populations in existing studies [22].

In this cohort, no serious adverse events or new infections were observed, a finding consistent with prior reports in immunocompromised patients [5,25]. Adverse events were limited to mild constipation in 1 patient and vomiting in another, both of which resolved spontaneously within 24 h without intervention. Appropriate patient selection remains critical, and factors such as neutropenia should be carefully considered, as the latter is a well-documented risk factor for post-FMT infections, including bacteremia and mortality in vulnerable populations [38]. In our cohort, absolute neutrophil count data were available within 30 days of intervention, and only a minority of patients had values below 500/μL (4.3%), suggesting that most were not profoundly neutropenic at the time of FMT or fecal microbiota live-jslm administration. This probably contributed to the favorable safety outcome observed.

Evidence from early-phase clinical trials suggests that fecal microbiota transplantation (FMT) can modulate the gut microbiome to potentially enhance responsiveness to ICIs without increasing the incidence of immune-related adverse events (irAEs) [39,40]. In our cohort, patients who received FMT for rCDI prevention during immunotherapy did not develop new irAEs. Notably, 12 had concomitant immune-mediated diarrhea and colitis (IMDC), with 11 receiving FMT after their first CDI episode, and none

experienced recurrence within 90 days. These findings support early FMT as a potential strategy for patients with both CDI and IMDC, though confirmation in prospective studies is required [41].

Several meta-analyses have confirmed that FMT can reduce severe CDI-related complications, including colectomy and sepsis, and may lower mortality compared with standard antibiotic therapy alone [42-44]. Mechanistically, microbiota-based therapies restore colonization resistance by reestablishing protective bacterial taxa that compete with *C. difficile*, produce short-chain fatty acids and modulate host immunity, with benefits that may persist for more than a year after intervention [24,45-50].

This study had several limitations. The retrospective, single-center design and relatively small sample size, particularly for the fecal microbiota spores live-brpk subgroup, may have limited both generalizability and statistical power. There was no control group treated with antibiotics alone, and treatment selection was influenced by physician preference, patient characteristics and product availability, potentially introducing selection bias. Microbiome sequencing was not performed to confirm engraftment, and follow-up duration varied, precluding assessment of long-term durability. In addition, practical considerations, such as cost, insurance coverage and local infrastructure, may affect the broader implementation of these therapies. Larger prospective studies are warranted to confirm these findings, clarify the role of standardized products, and explore cost-effectiveness and patient-reported outcomes to guide practical prevention strategies in oncology care. Accordingly, these results should be regarded as hypothesis-generating, and should not be extrapolated to other centers, products or patient populations without confirmation in larger, comparative studies.

In this single-center experience, colonoscopy-delivered FMT, fecal microbiota live-jslm, and fecal microbiota spores live-brpk were each associated with low 8-week recurrence rates and few, mild adverse events when used to prevent rCDI in patients with cancer, a population at particularly high risk. As a retrospective, single-center, non-comparative analysis with a small sample, this study cannot establish comparative efficacy or safety, and its findings should not be generalized beyond comparable settings. To our knowledge, this is the first real-world report to describe outcomes for all 3 approaches together in this population, a cohort often underrepresented in clinical trials.

Selection of the most appropriate strategy should consider each patient's condition, preferences, and the practical factors unique to each setting. Our findings highlight the value of having multiple effective microbiota-based options that can be tailored to different clinical scenarios. Larger studies are needed to confirm these results, assess long-term outcomes and cost-effectiveness, and define best practices for integrating these therapies into routine oncology care.

Summary Box

What is already known:

- Cancer patients experience a high rate of recurrent *Clostridioides difficile* infection (rCDI), and while fecal microbiota transplantation (FMT) is effective in the general population, evidence in oncology patients remains limited
- Standardized microbiota-based products are now available as alternatives to colonoscopy-delivered FMT
- Concerns about safety in immunocompromised patients may limit the use of these therapies in oncology settings

What the new findings are:

- Three microbiota-based treatment approaches were used in this cohort of 69 cancer patients: colonoscopy-delivered FMT, fecal microbiota live jslm, and fecal microbiota spores live brpk
- Recurrence within 8 weeks was low (5.8 percent) across all delivery methods
- No infectious complications or new immune-related adverse events were observed, including among patients receiving immune checkpoint inhibitors
- These findings suggest that microbiota-based therapy is a feasible option for preventing rCDI n in oncology patients and warrant confirmation in larger prospective studies

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