Effectiveness of fidaxomicin versus oral vancomycin in the treatment of recurrent *Clostridioides difficile*

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BACKGROUND

- *Clostridioides difficile* is a spore-forming Gram-positive bacteria responsible for approximately 500,000 cases of infectious diarrhea annually in the United States
- It is estimated that 20-30% of patients with *C. difficile* infection (CDI) will experience a recurrence, and that risk increases to approximately 40-60% following a second recurrence
- Recurrent CDI is associated with a 33% increased risk of mortality at 180 days as compared to patients who do not experience recurrence
- The 2017 IDSA/SHEA Clinical Practice Guidelines for *Clostridioides difficile* Infection in Adults and Children recommend treating recurrent episodes of CDI with either oral vancomycin (as a pulsed/tapered regimen or followed by rifaximin) or fidaxomicin
- Limited literature is available examining the impact of the treatment regimen on clinical outcomes beyond the first recurrence

METHODS

- Single-center, retrospective cohort study
- Study Timeframe: January 1, 2013 – May 1, 2019

Primary Outcome

- CDI recurrence in patients treated with fidaxomicin vs. oral vancomycin

Secondary Outcomes

- Treatment failure
- Presence and time to re-infection
- Infection-related length of stay (LOS)
- In-hospital all-cause mortality

Inclusion Criteria	Exclusion Criteria
• Age 18-19 years • Inpatient (+) *C. difficile* PCR for recurrent episode of CDI • Received oral vancomycin or fidaxomicin during the study period	• First episode of CDI • Received combination therapy of oral vancomycin and fidaxomicin >96 hours

METHODS (continued)

Definitions:

Recurrence	Symptoms consistent with CDI and (+) *C. difficile* PCR 2-8 weeks from (+) test for index episode
Re-infection	Symptoms consistent with CDI and (+) *C. difficile* PCR 8 weeks to 6 months from (+) test for index episode
Infection-related LOS	Time from (+) *C. difficile* PCR to hospital discharge, completion of CDI therapy, or in-hospital death, whichever occurred first

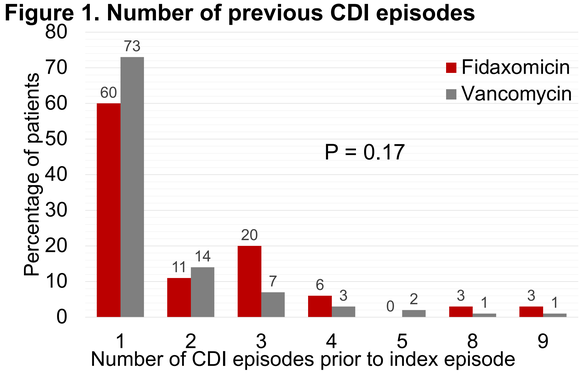
RESULTS

Table 1. Baseline characteristics

Variable	Fidaxomicin (n=35)	Vancomycin (n=100)
Age (years)	58 [43-66]	62 [48-70]
White race	29 (80)	72 (72)
Male gender	12 (34)	43 (43)
≥ 2 prior CDI episodes	14 (40)	28 (28)
Severity of Illness		
Non-severe	22 (63)	58 (58)
Severe	10 (29)	31 (31)
Fulminant	3 (9)	11 (11)
Secondary prophylaxis		
None	30 (86)	74 (74)
Vancomycin taper	4 (11)	25 (25)
Concomitant BSA*	15 (43)	60 (60)
Concomitant PPI*	19 (54)	37 (37)

*BSA: Broad spectrum antibiotic; PPI: proton pump inhibitor
Median [Interquartile Range, IQR]; Number (%)

Figure 1. Number of previous CDI episodes



RESULTS (continued)

Figure 2. CDI recurrence after index case

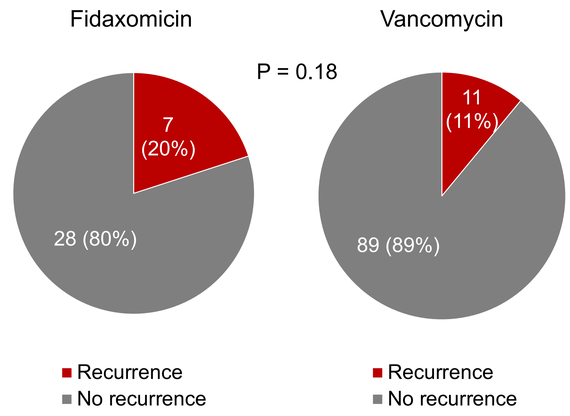


Table 2. Clinical outcomes

	Fidaxomicin (n=35)	Vancomycin (n=100)	P-value
Time to recurrence (days)*	37 [32-51]	29 [20-39]	0.27
Re-infection after index case	5 (14)	12 (12)	0.73
Time to re-infection** (days)	61 [60-80]	76.5 [67-95]	NC***
Infection-related LOS (days)	6 [4-10]	7.5 [4-14]	0.19
In-hospital all-cause mortality	2 (6)	4 (4)	0.65
Treatment failure	6 (17)	8 (8)	0.13
Anti-infective change	0 (0)	5 (5)	0.33
Colectomy	1 (3)	0 (0)	0.26
FMT***	5 (14)	3 (3)	0.03

*Reflective of fidaxomicin n=5 and vancomycin n=14 for patients with CDI re-infection
**Reflective of fidaxomicin n=7 and vancomcin n=11 for patients with CDI recurrence
***NC: Not calculated; FMT: fecal microbiota transplant
Median [Interquartile Range, IQR]; Number (%)

RESULTS (continued)

Table 3. Multivariable logistic regression model analyzing recurrence between groups

	Adjusted Odds ratio (aOR)	95% Confidence Interval
Vancomycin or fidaxomicin treatment	0.85	(0.27-2.7)
Treatment duration	0.91	(0.81-1.02)
Concomitant use of BSA*	0.54	(0.19-1.53)

*BSA: Broad spectrum antibiotic

DISCUSSION

- This represents the first analysis of CDI recurrence that has included patients with >2 prior episodes of CDI
- Similar rates of recurrence were observed between patients treated with fidaxomicin or oral vancomycin, even after controlling for differences in duration of therapy and concomitant BSA
- No difference in outcomes were noted with fidaxomicin or vancomycin therapy in regards to re-infection, treatment failure, infection-related length of stay, and in-hospital all-cause mortality

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