

Recurrent *Clostridioides Difficile* Infection (CDI) Worsens Anxiety-Related Patient-Reported Quality of Life

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BACKGROUND

- Clostridioides difficile* infection (CDI) is associated with long-term symptoms and substantial impact on quality of life (QOL).^{1,2}
- The Cdiff32 Health-related QOL (HR-QOL) instrument contains 32 elements related to physical, mental and social health of CDI patients, which allows assessment of disease-specific QOL changes associated with recurrent CDI.³
- There are currently no data on HR-QOL of CDI patients after receiving a single infusion of bezlotoxumab in the outpatient setting.

OBJECTIVES

- To determine HR-QOL differences using the highly relevant anxiety sub-domain of the Cdiff32 tool in patients with and without CDI recurrence ≥90 days post bezlotoxumab infusion.
- To evaluate changes of the anxiety-related HR-QOL score associated with a patient's history of CDI, specifically the number of prior CDI episodes.

METHODS

- Study design:** A qualitative QOL assessment as part of a multicenter real-world outcome study conducted in patients who received bezlotoxumab for prevention of recurrent CDI in 25 U.S. outpatient infusion centers.
- Patient population:** CDI patients (≥18 years of age) with confirmed positive *C. difficile* test, completing a HR-QOL questionnaire at the time of receiving bezlotoxumab and again at the ≥90 days follow-up assessment post infusion. Study period was September 2017 through March 2019.
- Data collection:** demographics, comorbidities, number of prior CDI episodes, patient-reported QOL at baseline (day of infusion) and ≥90 days post bezlotoxumab.
- Outcome measures:** A patient-reported HR-QOL questionnaire related to the anxiety sub-domain of Cdiff32³ was used to document changes in the QOL at two different time points. Response scores from the survey (1 to 5) were recorded and transformed to a score between 0 (worst QOL) and 100 (best QOL). Averages were calculated at baseline (day of infusion) and at ≥90 days follow-up post bezlotoxumab. Recurrence was defined as new onset of diarrhea for at least 2 days requiring CDI-active antibiotics.

- Statistical analysis:** Continuous data are reported as mean and standard deviation (SD), or median and interquartile range (IQR); categorical data as counts and percentages or frequencies as percentages. A stepwise linear regression with backward elimination approach was used and only clinical variables that met criteria P<0.05 (statistical significance) were retained.

RESULTS

Table 1. Demographics and Disease Characteristics of Recurrent vs. Non-Recurrent Patients post Bezlotoxumab

Variable	All Patients (n=107)	Recurrence of CDI ≥90 Post Bezlotoxumab Infusion	
		Yes (n=14, 13%)	No (n=93, 87%)
Age, years (mean ± SD)	68±14	64±14	69±14
Female, n (%)	71 (66.4)	12 (85.7)	59 (63.4)
Charlson index (mean ± SD)	4.5±3.4	3.4±2.7	5.8±3.8
CDI history, n (%)			
primary CDI	19 (17.8)	1 (7.1)	18 (19.4)
2 or 3 prior episodes	55 (51.4)	9 (64.3)	46 (49.5)
≥4 prior episodes	33 (30.8)	4 (28.6)	29 (31.2)
CDI risk factors n (%)			
≥65 years	75 (70.1)	7 (50.0)	68 (73.1)
CDI episode in previous 6 months	81 (75.7)	13 (92.8)	68 (73.1)
use of proton pump inhibitors	41 (38.3)	7 (50.0)	34 (36.6)
immunocompromised condition	41 (38.3)	4 (28.6)	37 (39.8)
inflammatory bowel disease	10 (9.3)	2 (14.3)	8 (8.6)
chronic renal disease	11 (10.3)	1 (7.1)	10 (10.8)

Table 2. Overall Patient-Reported Baseline Scores for Anxiety-Related Questionnaire Prior to Bezlotoxumab (N=107)

Domain	Sub-Domain	Question No.	Question	Scale	QOL Scores (All patients)			
					Pre Bezlotoxumab Infusion		90 Day Post Bezlotoxumab Infusion	
					Mean ± SD	Median IQR [Q1, Q3]	Mean ± SD	Median IQR [Q1, Q3]
Mental	Anxiety - present	1	Due to your <i>C. difficile</i> infection, do you have difficulties or disruptions carrying out your daily activities?	1 = least or No 5 = most or Yes	3.6 ± 1.6	4.0 [2.0-5.0]	1.9 ± 1.4	1.0 [1.0-3.0]
Mental	Anxiety - future	2	Are you afraid your <i>C. difficile</i> infection could come back?	1 = least or No 5 = most or Yes	4.3 ± 1.3	5.0 [4.0-5.0]	3.2 ± 1.7	3.0 [1.0-5.0]
Mental	Anxiety - present	3	I feel my life is less enjoyable because of my <i>C. difficile</i> infection	1 = least or No 5 = most or Yes	4.0 ± 1.4	5.0 [3.0-5.0]	2.4 ± 1.7	1.0 [1.0-4.0]
Mental	Anxiety - present	4	I feel irritable because of my <i>C. difficile</i> infection	1 = least or No 5 = most or Yes	3.2 ± 1.6	3.0 [1.0-5.0]	2.1 ± 1.6	1.0 [1.0-4.0]
Mental	Anxiety - present	5	I feel isolated from others because of my <i>C. difficile</i> infection	1 = least or No 5 = most or Yes	3.1 ± 1.7	3.0 [1.0-5.0]	2.0 ± 1.6	1.0 [1.0-3.0]
Mental	Anxiety - present	6	I feel depressed because of my <i>C. difficile</i> infection	1 = least or No 5 = most or Yes	2.8 ± 1.7	3.0 [1.0-3.0]	1.8 ± 1.4	1.0 [1.0-2.0]
Mental	Anxiety - present	7	I worry about transmitting my <i>C. difficile</i> infection to my family and/or friends	1 = least or No 5 = most or Yes	3.7 ± 1.6	5.0 [2.0-5.0]	2.2 ± 1.6	1.0 [1.0-3.0]

Changes of QOL Anxiety Scores from Baseline (Initial) to ≥90 Days Post Bezlotoxumab (Follow-up) Between Recurrent vs. Non-Recurrent Patients by Number of Previous Episodes

Figure 1. Changes in QOL in CDI patients with primary episode

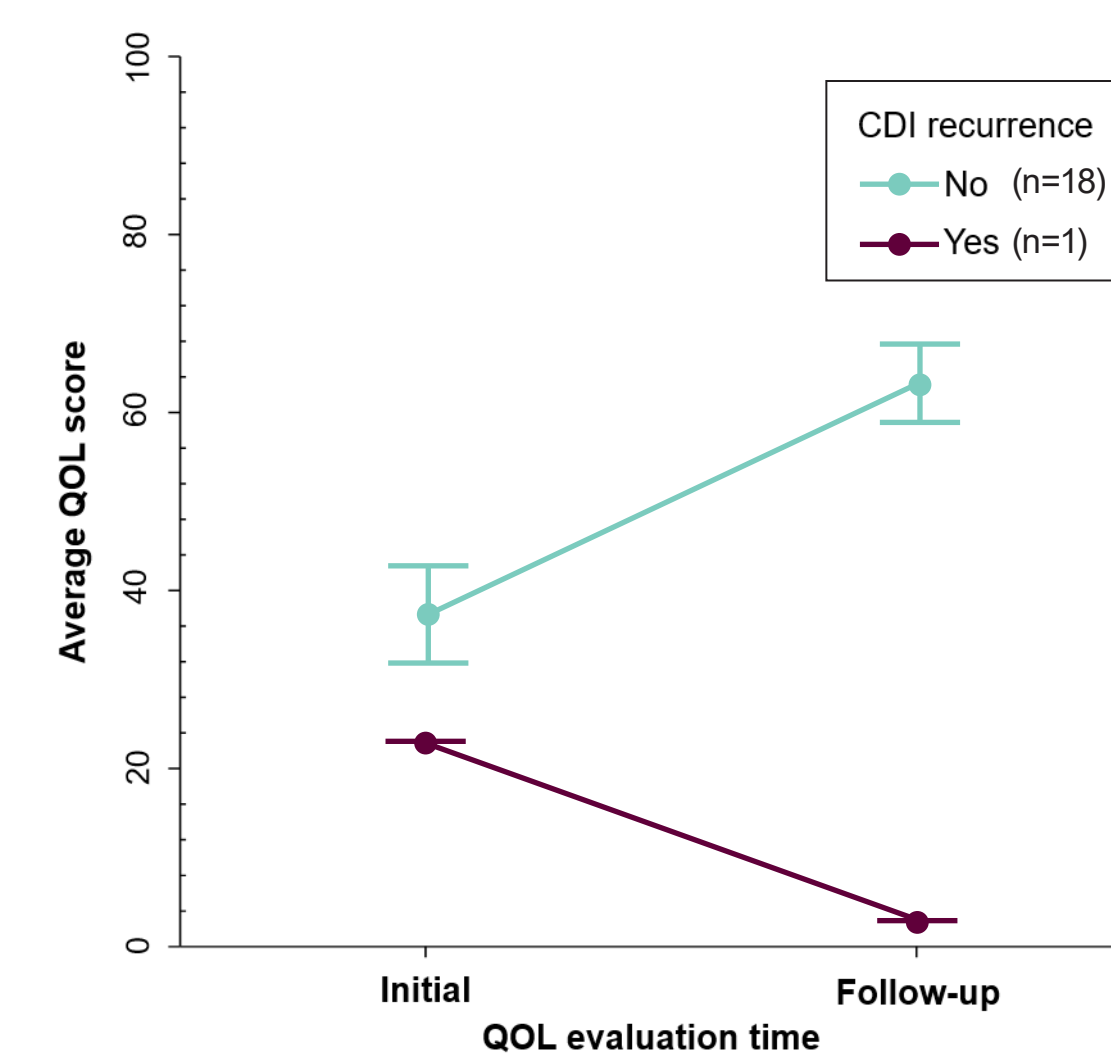


Figure 2. Changes in QOL in CDI patients with 2 or 3 prior episodes

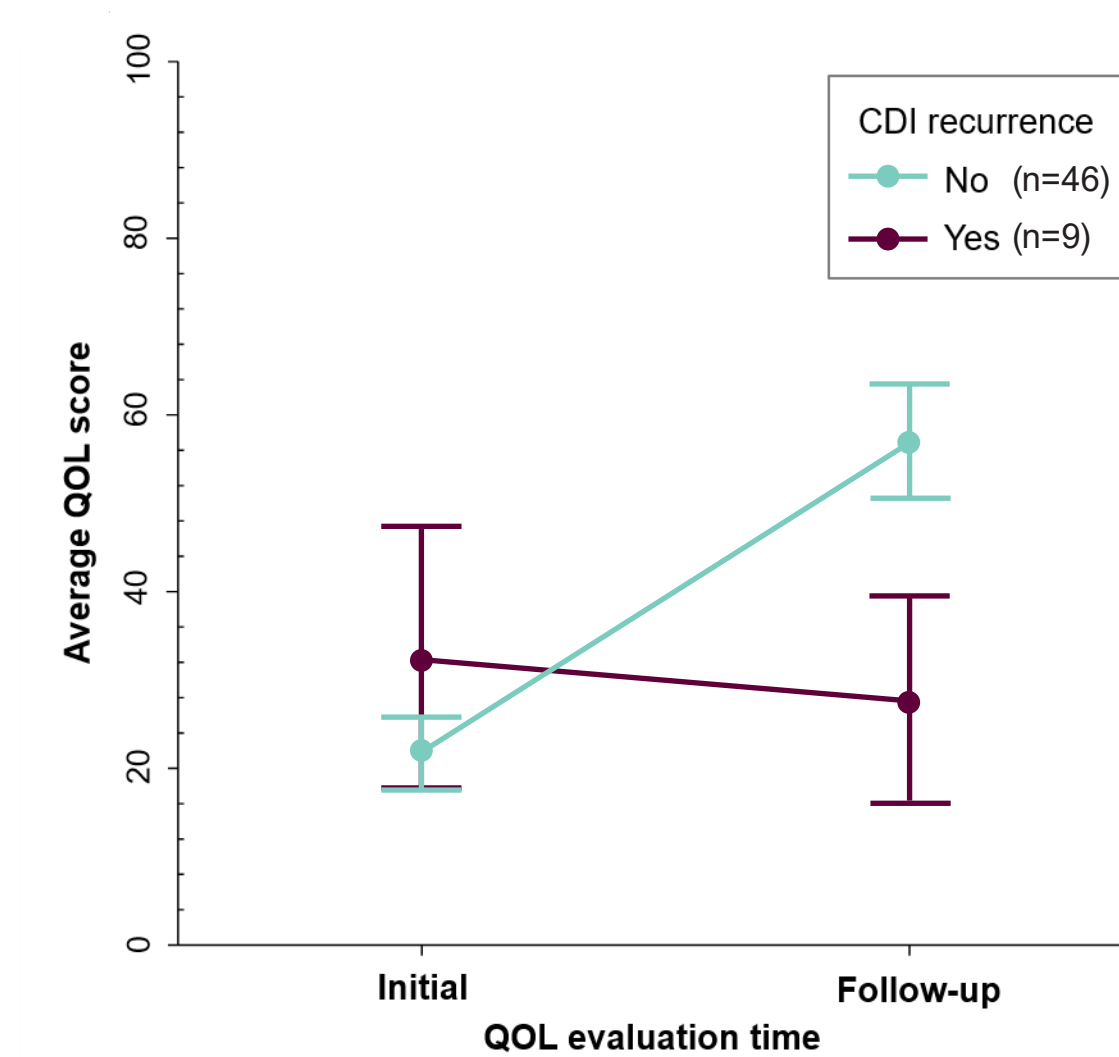


Figure 3. Changes in QOL in CDI patients with ≥4 prior episodes

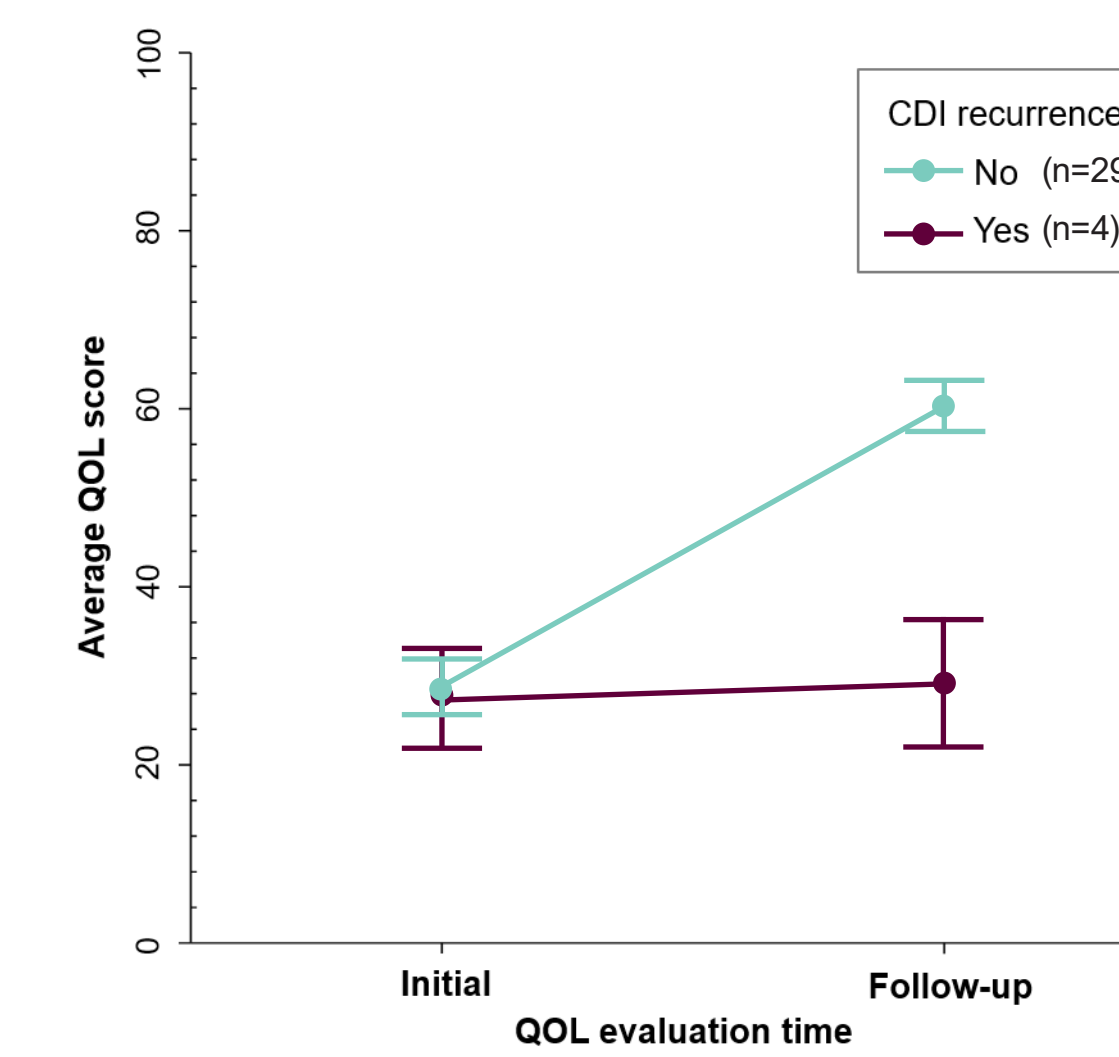


Table 3. Results from stepwise regression analysis assessing predictors of change in anxiety-related QOL post bezlotoxumab

Clinical Variable ¹	Change in Average QOL Score ± SD	P-value
CDI recurrence	-33.0 ± 8.0	<0.0001

¹: defined as statistically significant change (P<0.05).

- Strict elimination criteria resulted in a parsimonious model including only CDI recurrence assessed ≥90 days post bezlotoxumab infusion and was observed to be univariately associated with a decrease in average QOL score by 33.0 indicating worsening anxiety (P<0.0001)
- Other covariates analyzed, but did not meet the P<0.05 criteria for remaining in the model, included age ≥65, weight, Charlson comorbidity index, severe CDI, immunocompromised state, chronic renal disease, inflammatory bowel disease, primary use of fidaxomicin, previous fecal microbiota transplant, receipt of proton pump inhibitor, and concomitant use of systemic antibiotics.

- Overall baseline anxiety QOL score was 29±22, which was comparable for all 107 patients regardless of number of prior CDI episodes (Figs. 1, 2, and 3)
- Risk factors for overall lower baseline anxiety-related HR/QOL were immunocompromised conditions (p<0.046) and receipt of proton pump inhibitors (p<0.018)
- Average QOL scores increased for patients with no further CDI recurrence following bezlotoxumab, indicating an improvement in anxiety
- Changes in QOL scores between recurrent (n=1) vs. non-recurrent patients (n=18) appears highest in the group with primary CDI episode

DISCUSSION

This study assessed changes from baseline for anxiety-related QOL associated with recurrent CDI in patients receiving a single dose of bezlotoxumab in U.S. outpatient infusion centers.

- 107 patients from 25 sites responded to the anxiety sub-domain questionnaire of the Cdiff32 HR-QOL instrument.³
- Changes in QOL baseline scores are presented for 14 (13%) patients with CDI recurrence in comparison to 93 (87%) patients without CDI recurrence. Follow-up was assessed ≥90 days post bezlotoxumab and stratified by number of prior episodes. The findings included:
 - Levels of anxiety were similar for all patients at baseline. Initial QOL anxiety scores did not differ significantly regardless of CDI history.
 - QOL anxiety scores improved in patients without CDI recurrence indicating less anxiety at the 90-day follow-up.
 - QOL anxiety scores decreased in patients with CDI recurrence regardless of CDI history indicating worsening anxiety.
- Limitations of this study include a small sample size, especially for patients with a primary CDI and selection of only the anxiety-related sub-domain of the Cdiff32 HR-QOL instrument, which has not been separately validated.

CONCLUSIONS

- Poor anxiety-related HR-QOL was observed at baseline for all patients regardless of number of prior CDI episodes. However, QOL was improved 90 days after bezlotoxumab infusion in patients without further CDI recurrences and worsened in patients with a subsequent recurrence.
- These results suggest that the anxiety-related sub-domain of the Cdiff32 HR-QOL instrument may be useful to assess the impact of new therapies on disease-specific changes in the QOL for patients with recurrent CDI.

Disclosures

- This study was sponsored by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Ryan Dillon is an employee of Merck Sharp & Dohme Corp.

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