# Effectiveness of Bezlotoxumab for Prevention of Recurrent *Clostridioides difficile* Infection in Patients at High Risk for Recurrence

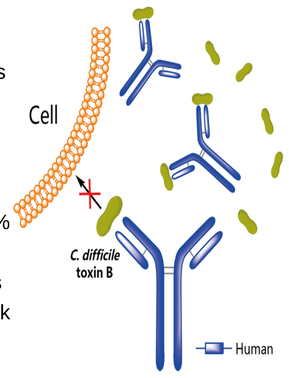
Tanner Johnson, PharmD[1,2], Amanda Howard, PharmD[1], Gerard Barber, RPh, MPH[2], Kerry Schwarz, PharmD, MPH[1,2], Lorna Allen, FNP-C[1,3], Misha Huang, MD, MS[1,3], Valida Bajrovic, MD[1,3], Matthew Miller, PharmD[1,2]

[1]UCHealth University of Colorado Hospital, Aurora, CO, USA. [2]University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO, USA.
[3]University of Colorado School of Medicine, Aurora, CO, USA.

Email: tanner.johnson@uchealth.org
Twitter: @johnsontannerm

## Introduction

- Risk of recurrent *Clostridioides difficile* infection (rCDI) increases with each successive episode and recurrences within 180 days are associated with a 33% increase in mortality
- Bezlotoxumab is a monoclonal antibody against toxin B produced by *C. difficile* and is indicated for the prevention of rCDI when used in combination with standard of care (SoC) treatment
- Subgroup of Phase 3 clinical trials for bezlotoxumab, MODIFY I & II, showed a 13% absolute reduction in rCDI
- Post-hoc analyses of the MODIFY I & II trials suggest increased benefit in patients with risk factors for rCDI




## Objectives

- Evaluate effectiveness of bezlotoxumab in rCDI prevention
- Assess the impact of number of risk factors on bezlotoxumab effectiveness
- Evaluate patient-specific characteristics and their impact on bezlotoxumab response

## Study Design and Methods

- Multi-center, retrospective cohort comparing patients who received bezlotoxumab to historical matched controls
- Controls were matched to treatment arm in a 2:1 fashion
- Bezlotoxumab dosing was 10mg/kg IV once, doses were capped at 1,000mg for those weighing >100kg
- Medical records reviewed from 139 patients within the UCHealth system
- Information collected: demographics, comorbidities, number of past CDI episodes, severity of index CDI, CDI treatment and duration, and patient-specific risk factors for rCDI

Inclusion Criteria:

- *C. difficile* diagnosis
- SoC treatment: PO vancomycin or fidaxomicin
- Entire bezlotoxumab infusion received at a UCHealth facility

| Control Matching Criteria |
|---|
| Transplant Status (SOT/BMT) |
| Number of past CDI episodes |
| Receipt of concomitant antibiotics |

## Results

**Table 1.** Patient Baseline Characteristics

| Variable | Total Population n=120 | Bezlotoxumab n=47 | Control n=73 | P-value |
|---|---|---|---|---|
| Age, mean | 55 (16, 20-87) | 56 (16, 21-81) | 55 (16, 20-87) | NS |
| Charlson Comorbidity Index, mean | 4.2 (2.8, 0-12) | 4.3 (2.8, 0-11) | 4.2 (2.8, 0-12) | NS |
| Number of lifetime CDI, mean | 3.1 (2.0, 1-11) | 3.3 (2.2, 1-10) | 3.1 (2.0, 1-11) | NS |
| *C. difficile* Complication | 24 (20%) | 5 (11%) | 19 (26%) | NS |
| Risk Factors for Recurrence | | | | |
| Immunocompromised (>1 allowed) | 90 (75%) | 35 (75%) | 54 (74%) | NS |
| SOT/BMT | 76 (63%) | 27 (57%) | 49 (67%) | NS |
| Concomitant Antibiotic Use | 87 (73%) | 27 (57%) | 51 (70%) | NS |
| Past *C. difficile* episode* | 68 (57%) | 34 (72%) | 34 (47%) | **0.010** |
| Age ≥65 years old | 32 (27%) | 18 (38%) | 14 (19%) | **0.036** |
| PPI Use | 57 (48%) | 19 (40%) | 38 (52%) | NS |
| Proteinuria | 71 (59%) | 24 (51%) | 47 (64%) | NS |
| Severe CDI (Zar Score ≥2) | 37 (31%) | 11 (23%) | 26 (36%) | NS |
| FMT (any history) | 12 (10%) | 6 (13%) | 6 (8.2%) | NS |
| PO Vancomycin Receipt | 114 (95%) | 43 (92%) | 71 (97%) | NS |
| Extended-Duration anti-CDI Treatment† | 84 (70%) | 36 (77%) | 48 (66%) | NS |

**Table 1**. Baseline characteristics of the 120 patients included in the study. Continuous variables are reported as mean values, with standard deviations and ranges in parentheses. Categorical variables are reported as the absolute number of participants, followed by the percentage of the patient population in parentheses. Other immunocompromising conditions included active malignancy, HIV, medication-induced, splenectomy, and hypogammaglobulinemia.
Abbreviations: CDI=*C difficile* Infection; SOT=Solid Organ Transplant; BMT=Bone Marrow Transplant; PPI=Proton Pump Inhibitor; FMT=Fecal Microbiota Transplant; NS=Not Significant
* Indicates p=value <0.05 comparing bezlotoxumab to control cohort
† Extended-duration defined as treatment for >14days

**Outcomes within 90 days of Completing *C. difficile* Treatment**

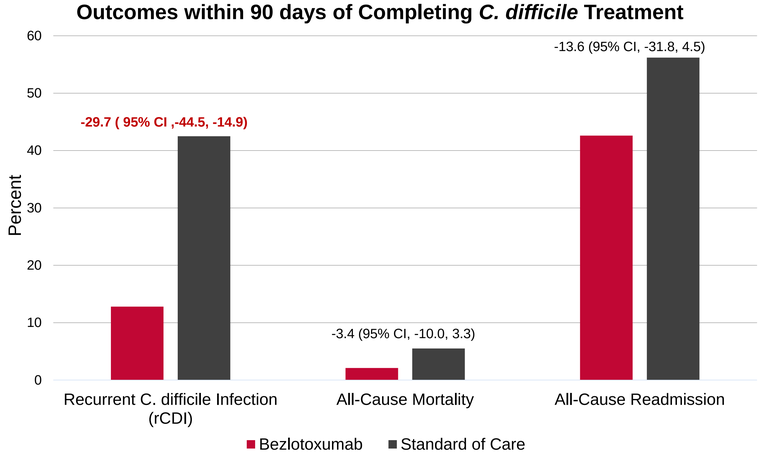



**Figure 1**. Study outcomes within 90 days of completion of standard of care treatment (metronidazole, oral vancomycin, or fidaxomicin) for *C. difficile*. Numbers listed are the absolute risk reduction with 95% confidence intervals in parentheses. Bold-faced and maroon-colored values indicate statistical significance.

The number needed to treat to prevent one rCDI at 90 days was 4

**Table 2.** Safety Outcomes

| Outcome | Bezlotoxumab n=47 | Control n=73 |
|---|---|---|
| Heart Failure Exacerbation (90-day) | 1 (2.1%) | 2 (2.7%) |
| Infusion-Related Reactions | 1 (2.1%) | N/a |

## Results (continued)

**Incidence of rCDI at 90 days Stratified by Number of Risk Factors for Recurrence**

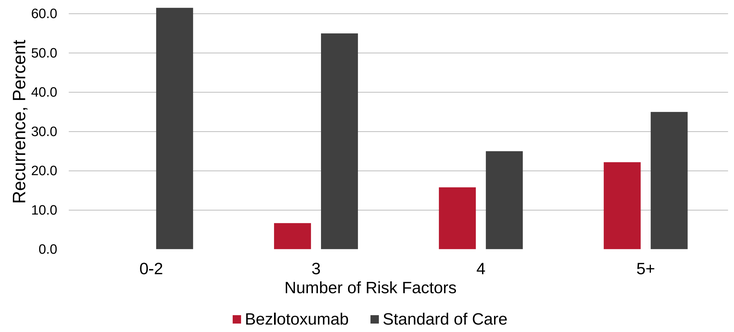



**Figure 2**. Incidence of rCDI at 90 days stratified by number of risk factors for recurrence. Risk factors evaluated included immunocompromised status, concomitant antibiotic use, past CDI episode, age ≥65 years, PPI use, proteinuria, & severe CDI.

**Table 3.** Bezlotoxumab Subgroup Analysis (n=47)

| Variable | Values | Recurrence at 90 days | P-value |
|---|---|---|---|
| Timing of bezlotoxumab administration in relation to SoC treatment initiation | ≥14 days<br><14 days | 4/29 (14%)<br>2/18 (11%) | NS |
| *C. difficile* Severity (Zar Score) | Severe<br>Non-Severe | 2/11(18%)<br>4/36 (11%) | NS |
| Received FMT before bezlotoxumab administration | Yes<br>No | 0/6 (0.0%)<br>6/41 (15%) | NS |
| Body weight | >100 kg<br>≤100 kg | 0/5 (0.0%)<br>6/42 (14%) | NS |
| Index *C. difficile* Event | Primary Infection<br>Recurrent Infection | 3/13 (23%)<br>3/34 (8.8%) | NS |

## Conclusions and Limitations

- Bezlotoxumab, in combination with SoC treatment, reduced the 90-day incidence of rCDI when compared to SoC treatment alone
- Timing of bezlotoxumab administration, patient weight, nature of index CDI event, CDI severity, and prior receipt of FMT did not significantly impact bezlotoxumab's effectiveness
- Conclusions are limited by small sample size, retrospective nature of data collection, and presence of undetected confounding variables

## References

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- Conflict of Interest Disclosure: None