500. Efficacy of 30-Day Fidaxomicin for Treatment of Acute *Clostridium difficile* Infection With History of Multiple Recurrences

Christine Lee, MD, FRCPC[1]; Minahz Habib, BSc[2]; Christiana Kim, BSc[3]; Peyman Goldeh, B. Eng[3]; Salaheddin Abouanaser, MD, FRCPC[4] and Peter Kim, PhD[5]; [1]Microbiology, Vancouver Island Health Authority, Victoria, BC, Canada, [2]University of Guelph, Guelph, ON, Canada, [3]Vancouver Island Health Authority, Victoria, BC, Canada, [4]St. Joseph's Healthcare Hamilton, Hamilton, ON, Canada, [5]Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

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Background. Multiple recurrent *Clostridium difficile* (mrCDI) infections pose major challenges to patients and to the healthcare system. mrCDI is associated with multiple, prolonged hospitalizations and significantly higher costs. It can also lead to chronic, severe diarrhea, colectomy, or death. Fecal microbiota transplantation (FMT) is an effective treatment, but its long-term safety remains unknown, and approximately 10% of patients do not respond to multiple FMTs. A 30-day course of fidaxomicin was evaluated for treatment of acute episode of CDI superimposed on mrCDI, including those who did not respond to multiple FMTs. Fidaxomicin was chosen because it disrupts the fecal microbiome less than vancomycin.

Methods. Twenty-nine adult patients with at least two episodes of recurrent CDI were initiated on fidaxomicin 200 mg when they experienced new episode of CDI (symptoms plus positive for CD toxin gene by polymerase chain reaction). These patients continued with fidaxomicin 200 mg twice daily for 10 days, and 200 mg once daily for 20 additional days in an open-label clinical trial. The primary endpoints were a clinical response at the completion of 30-day course of fidaxomicin and a sustained clinical response at week 8 from the last dose of fidaxomicin. Patient health-related quality of life was evaluated throughout the treatment using the RAND-36 Item Health Survey (copyright© the RAND Corporation).

Results. Twenty-four of the 29 patients (83%) experienced clinical resolution of CDI-related symptoms at the completion of 30-day fidaxomicin treatment. Twenty-two of the 29 patients had a sustained clinical response with the overall cure rate of 76% (22/29). Eleven of the 29 patients had multiple FMTs and were enrolled into this study as they failed FMTs. Eight of the 11 patients (73%) of these patients had a sustained clinical response. Statistically significant improvements ($P < 0.05$) in multiple domains of quality of life according to the RAND-36 Item Health Survey were also observed.

Conclusion. An extended regimen of fidaxomicin is an effective treatment for adults with multiple rCDI and in restoring quality of life, including those who failed FMTs.

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501. Evaluation of Bezlotoxumab in Prevention of Recurrent *C. difficile* Infection: A Multicenter Single-Arm Study in Outpatient Infusion Centers

Richard L. Hengel, MD[1]; Timothy E. Ritter, MD[2]; Ramesh V. Nathan, MD, FIDSA[3]; Lucinda J. Van Anglen, PharmD[4]; Claudia P. Schroeder, PharmD, PhD[4]; Stephen Marcella, MD, MPH[5] and Kevin W. Garey, PharmD, MS[6]; [1]Atlanta ID Group, Atlanta, Georgia, [2]Luminal Research Division, Texas Digestive Disease Consultants, Southlake, Texas, [3]Mazur, Statner, Dutta, Nathan, PC, Thousand Oaks, California, [4]Healix Infusion Therapy, Sugar Land, Texas, [5]Center for Observational and Real World Evidence, Merck & Co., Inc., Kenilworth, New Jersey, [6]Pptr, University of Houston College of Pharmacy, Houston, Texas

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Background. Bezlotoxumab (BEZ) was approved in October 2016 for the prevention of recurrent *C. difficile* (rCDI) infection in patients receiving standard-of-care (SoC) antibiotic therapy for active CDI who are at high risk for CDI recurrence. Presently, there are little real-world data on recurrence rates and factors associated with recurrence in patients receiving BEZ. This study describes characteristics of patients receiving BEZ in US Outpatient Infusion Centers (OICs) and analyzes subsequent CDI recurrences.

Methods. Medical records from 24 OICs were retrospectively reviewed of all patients treated with BEZ through December 2017. Data collected included demographics, comorbidities, and all therapy parameters, including SoC antibiotic therapy. Risk factors for rCDI were assessed and included age, immunocompromised status, prior number of CDI episodes, use of gastric acid suppressants, inflammatory bowel disease (IBD), and history of fecal microbiota transplant (FMT). rCDI, defined as diarrhea lasting ≥2 days with treatment for CDI with or without a positive stool test for toxigenic *C. difficile*, was assessed through a follow-up visit or phone call 90 days post BEZ administration. Risk factors for rCDI were evaluated using Student's t-test and Pearson χ^2 test.

Results. Eighty patients received BEZ (10 mg/kg) with 78 available for follow-up evaluation for rCDI ≥90 days post treatment. Mean age was 65 ± 16 years with 51% female. Mean number of CDI episodes were 3 ± 1 with a mean Charlson score of 4 ± 3. SoC antibiotics included vancomycin (66% of patients) with 41% on long-term taper, fidaxomicin (33% of patients), and metronidazole (25% of patients). Nineteen (24%) patients received more than one SoC antibiotic during their treatment course, most commonly with metronidazole and another SoC antibiotic. Of the 78 patients with follow-up data, 17 (22%) developed rCDI with a mean time to recurrence of 33 ± 22 days. Risk factors for rCDI are shown in the table. The use of BEZ earlier in the disease course (first or second CDI episode) was associated with a decreased risk of rCDI (OR: 0.21 95% CI: 0.04–0.98; $P = 0.033$).

Assessment of risk factors for recurrent CDI in patients receiving bezlotoxumab

Parameter (n=78)	No CDI recurrence (n=61)	CDI recurrence (n=17)	P-value
Age, years*	65±16	66±13	0.39
Weight, kg*	77±20	68±22	0.10
Charlson score*	4.3±3.3	4.1±2.9	0.85
Inflammatory bowel disease (n=35)	11%	18%	0.50
Gastric acid suppressant (n=36)	44%	53%	0.26
Failed prior FMT (n=10)	13%	12%	0.88
>2 CDI episodes (n=52)	61%	88%	0.033
Time from referral to BEZ infusion, days*	12±16	8±5	0.21

*Mean ± standard deviation.

Conclusion. In highly comorbid patients with recurrent *C. difficile* infection, bezlotoxumab use was effective in prevention of recurrence at 90 days and consistent with that of the randomized trials.

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502. Enhanced Sporulation and Vancomycin Resistance Associated With *Clostridium difficile* From Recurrent Infections

Laura E. Tijerina-Rodriguez, MSc[1]; Adrián Martínez-Meléndez, MSc[1]; Licet Villarreal-Treviño, PhD[1]; Rayo Morfín-Otero, MD, PhD[2]; Adrian Camacho-Ortiz, MD, PhD[3]; Simon D. Baines, PhD[4]; Eduardo Rodríguez-Noriega, MD, PhD[5] and Elvira Garza-González, PhD[6]; [1]Facultad de Ciencias Biológicas, Universidad Autónoma de Nuevo León, Monterrey, Mexico, [2]Hospital Civil de Guadalajara, "Fray Antonio Alcalde," Guadalajara, Mexico, [3]Infectious Diseases, Hospital Universitario "Dr. José Eleuterio González." Universidad Autónoma de Nuevo León, Monterrey, Mexico, [4]University of Hertfordshire, Hertfordshire, UK, [5]Instituto de Patología Infecciosa "Dr. Francisco Ruiz Sánchez." CUCS. UDG, Guadalajara, Mexico, [6]Hospital Universitario "Dr. José Eleuterio González." Universidad Autónoma de Nuevo León, Monterrey, Mexico

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Background. Recurrent *Clostridium difficile* infection (R-CDI) remains a significant healthcare problem. Our aim was to analyze sporulation and antimicrobial resistance of *C. difficile* in biofilms as a potential reservoir for recurrence.

Methods. *C. difficile* isolates obtained from patients with initial CDI (I-CDI) (n = 93) and from patients with R-CDI (n = 39) were analyzed. Isolates were identified by PCR and MALDI-TOF MS and ribotyped using 16S RNA amplification and capillary electrophoresis. Biofilm production was assessed by the crystal violet microtiter-plate method. Susceptibilities to vancomycin and linezolid were determined both in planktonic and in biofilm cells and total viable cells and spore were quantified in biofilm cells.

Results. All I-CDI and R-CDI isolates were biofilm producers and >75% were ribotype 027. MICs for vancomycin and linezolid were higher in biofilm than in planktonic cells in both I-CDI and R-CDI isolates ($P < 0.05$) (Table 1). Isolates recovered from R-CDI showed a higher vancomycin resistance (MIC >2 mg/L) and sporulated 2 $\log_{10}$ higher than isolates from I-CDI ($P < 0.01$ and $P = 0.086$, respectively).

Table 1. Antimicriobial Susceptibilities of *C. difficile* From I-CDI and R-CDI Patients.

		Vancomycin			Linezolid		
Group	Phase	Range (mg/L)	GM (mg/L)	% R	Range (mg/L)	GM (mg/L)	% R
I-CDI	Planktonic	0.25-4	1.68*	9.2 (6/69)*	0.03-32	3.38*	34.8 (24/69)
	Biofilm	8 >128	73.9*	100 (73/73)	4 >128	60.85*	98.5 (66/67)
R-CDI	Planktonic	2-4	1.69*	27.3 (9/33)*	0.25-128	3.31*	35.1 (14/37)
	Biofilm	4 >128	72.6*	100 (34/34)	8 >128	59.5*	93.5 (29/31)

*Significant difference $P < 0.05$; GM: Geometric mean; %R: Resistant.

Conclusion. *C. difficile* isolates in biofilms were 100-fold more resistant to vancomycin than planktonic cells. Isolates recovered from patients with R-CDI showed higher sporulation capacities than *C. difficile* recovered from I-CDI patients. Our data suggest that biofilm formation ability may play a key role in R-CDI by contributing to vancomycin resistance/tolerance. Furthermore, *C. difficile* from recurrent episodes sporulated to a greater capacity which may facilitate prolonged *C. difficile* persistence in the gut following therapy for R-CDI.

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503. Risk and Timing of *Clostridium difficile* Infection Relapse After Antibiotic Exposure

Joel Szela, DO[1], Neethi Venkatappa, MD[2] and Matthew Sims, MD, PhD[3]; [1]Internal Medicine, Beaumont Hospital Royal Oak, Royal Oak, Michigan, [2]Infectious Diseases, Beaumont Hospital Royal Oak, Royal Oak, Michigan and [3]Beaumont Health System, Royal Oak, Michigan