

the three groups. At presentation, disease severity was similar in all groups; However, patients in GI were more likely to have detectable toxin A/B by EIA compared with GII and GIII (53% vs. 23%, $P = 0.015$) and higher treatment failure rates (56%) when compared with GI (15% $P = 0.007$) and GIII (16%, $P = 0.004$). Bacteremia was more common in GIII (28%) compared with GII (0%) $P = 0.041$ and GI 7% $P = 0.007$. Patients in GI experienced fewer complications when compared with those in GIII $P = 0.025$. No differences in sustained clinical response, recurrence, ICU stay or all cause 90-day mortality were found between the groups.

Conclusion. Cancer patients with CDI due to GII ribotypes are more likely to excrete fecal toxin A/B and fail conventional therapy. In contrast, patients in GI and GIII were more likely to respond to therapy. GI was associated with fewer complications. Of interest, GIII was associated with bacteremia. Evaluation of *C. difficile* ribotypes is clinically relevant in cancer patients with CDI.

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1266. Bezlotoxumab (BEZ) for Prevention of Clostridium Difficile Infection (CDI) Recurrence (rCDI): Outcomes in Patients with Substantial Renal Impairment (SRI)

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Background. CDI in patients with SRI is harder to treat and is associated with higher recurrence. MODIFY I/II found that BEZ, a monoclonal antibody against *C. difficile* toxin B, is superior to placebo (PBO) at preventing rCDI in patients receiving standard of care antibiotics (SoC). This post hoc analysis assessed efficacy of BEZ in patients with SRI in the MODIFY studies.

Methods. MODIFY I/II mITT populations were pooled to estimate initial clinical cure (ICC), rCDI, and mortality through 12 weeks. Estimated glomerular filtration rate (eGFR) was calculated with the Modified Diet in Renal Disease (MDRD) method. SRI was defined as eGFR <60 mL/minute/1.73 m². ICC was defined as SOC ≤16 days and no diarrhea on the 2 days after SoC end. rCDI was defined as diarrhea and toxigenic *C. difficile* in stool. Mortality within 90 days after randomization was summarized.

Results. Of the included 1554 patients, 1101 had no SRI (≥90: n = 612; 60 to < 90: n = 489); 430 had SRI (30 to <60: n = 290; 15 to <30: n = 71; <15: n = 69); 23 had unknown eGFR. 87% of SRI patients had ≥1 risk factor for rCDI. Relative to patients without SRI, more patients with SRI were ≥65 years (69% vs. 44%), immunocompromised (25 vs. 20%), had ribotype 027 (25% vs. 17%), and used concomitant antibiotics during SoC (41% vs. 31%) or after SoC (36% vs. 28%). SRI patients had more severe CDI (21% vs. 14%), lower CDI cure (78.4% vs. 80.1%), higher rCDI (31.6% vs. 27.8%), and death (11.6% vs. 5.3%). In the SRI cohort, more BEZ vs. PBO patients were inpatients (81% vs. 72%), ≥65 years (72% vs. 65%), immunocompromised (28 vs. 22%), and used systemic antibiotics after SoC ended (40% vs. 32%). The rate of ICC was similar between treatment groups and the rCDI rate was significantly less the BEZ vs. PBO group (Table).

Conclusion. SRI was associated with worse CDI outcomes. BEZ given with SoC significantly reduced rCDI in patients with SRI and could benefit this hard to treat population.

	Endpoints of interest in patients with renal impairment		
	BEZ (n/N)	PBO (n/N)	Unadjusted Difference [95%CI]†
ICC	80.6 (174/216)	76.2 (163/214)	4.4 (-3.4, 12.2)
rCDI	17.8 (31/174)	31.9 (52/163)	-14.1 (-23.2, -4.9)

†Based on the Miettinen and Nurminen method without stratification.
 ‡BEZ=bezlotoxumab; ICC=initial clinical cure; n=number of patients in the analysis population meeting the criteria for endpoint; N=number of patients included in the analysis population; PBO=placebo; rCDI=C. difficile infection recurrence

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1267. Successful Response to Microbiota-Based Drug RBX2660 in Patients with Recurrent Clostridium Difficile Infection is Associated with More Pronounced Alterations in Microbiome Profile

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Background. Recurrent *Clostridium difficile* infections (rCDI) are associated with decreased diversity and altered intestinal microbiome compared with healthy patients. RBX2660, a standardized microbiota-based drug, is designed to restore microbiome diversity and composition in patients. The effect of RBX2660 on rCDI patient microbiomes was evaluated by comparing pre- and post-treatment samples from PUNCH CD 2—a randomized, double-blind, placebo-controlled study.

Methods. rCDI subjects were randomized to receive blinded treatments of 2 doses of RBX2660 (Group A), 2 doses of placebo (Group B), or 1 dose each of RBX2660 and placebo (Group C), by enema 7 days apart. Subjects submitted stool samples at baseline, day 7, 30, and 60 after treatment. Stool samples from responders to RBX2660 treatment per protocol defined as the absence of CDI for 8 weeks after treatment were compared with non-responders.

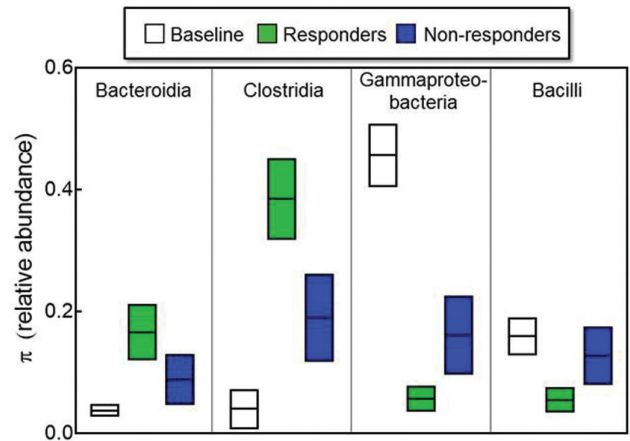
Relative taxonomic abundances at the class level were determined using 16s rRNA sequencing analysis for 94 stool samples from 45 patients in Groups A and C. Relative abundance data were grouped longitudinally using Bray-Curtis dissimilarity index. Analyses were performed based on the Dirichlet-Multinomial distribution to compare group mean relative taxonomic abundances; Simpson and Shannon diversity indices were compared among groups longitudinally.

Results. Baseline patient microbiomes were similar across response groups. RBX2660 treatment shifted the relative microbiome densities with taxa-specific increase in Bacteroidia, Clostridia, and decrease in Gamma-proteobacteria abundance. A larger shift from baseline microbiome was seen in responders to RBX2660 compared with non-responders (Figure 1). Microbiome changes in responders were durable to 60 days. RBX2660 treatment increased Shannon and Simpson diversity at 7 days post-treatment in responders but not in non-responders ($P < 0.05$).

Conclusion. RBX2660 treatment shifts patient intestinal microbiomes with greater alterations seen in those with a successful clinical outcome.

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Figure 1. Responders to RBX2660 have a greater change in taxa abundance from baseline relative to non-responders at 30 days. Dirichlet-Multinomial parameter pi presented as mean (95% CI).



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1268. Changes to the Composition of the Gastrointestinal Microbiome after Probiotics for Clostridium difficile Infection in Adults

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