the three groups. At presentation, disease severity was similar in all groups; However, patients in GII were more likely to have detectable toxin A/B by EIA compared with GI 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.

Disclosures. **All authors:** No reported disclosures.

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 m^2. 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. rCDIsubjects 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 RBX2600 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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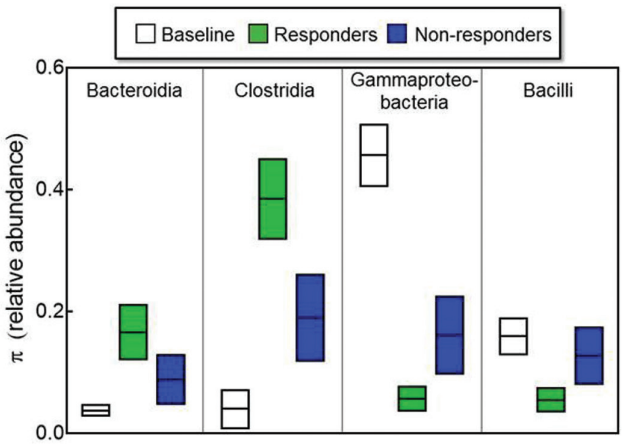
Figure 1. Responders to RBX2660 have a greater change in taxa abundance from baseline relative to non-responders at 30 days. Dirichlet-Multinomial parameter pi presented as mean (95% CI).



Disclosures. **S. Khanna**, Rebiotix, Inc.: Scientific Advisor, Consulting fee; **K. Blount**, Rebiotix, Inc.: Employee, Salary; **C. Jones**, Rebiotix, Inc.: Employee, Salary; **B. Shannon**, Rebiotix, Inc.: Research Contractor, Consulting fee; **S. Carter**, Rebiotix, Inc.: Research Contractor, Consulting fee

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

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Background. *Clostridium difficile* infections (CDI) in the US have markedly increased. Disturbances to the gastrointestinal (GI) microbiome due to antibiotic use predisposes patients to CDI. Probiotics are recommended to prevent GI microbiota changes during CDI antibiotic treatment, but efficacy is unknown. We conducted a randomized, double-blinded, placebo-controlled, examination of clinical and GI microbiota changes in subjects administered probiotics during a primary episode of CDI.

Methods. 33 subjects with a primary episode of CDI were randomized to once daily oral probiotic, consisting of four different bacterial strains, or placebo for 4-weeks (week 0–4) concurrent to antibiotic treatment. Subjects completed a daily stool diary, and stool samples were collected at enrollment (week 0), at the end of the probiotic or placebo adjunct regimen (week 4), and 4 weeks post-treatment (week 8). DNA was extracted for 16S rRNA sequencing with Illumina MiSeq. Microbial diversity, richness, and community structure were compared using analysis of variance and permutational analysis of variance. Similarity percentage analysis identified the operational taxonomic units driving the variation in β diversity.

Results. The duration of diarrhea ($P = 0.039$) and total days of diarrhea ($P = 0.005$) both decreased in the probiotic group compared with the placebo group. Analysis of community structure showed significant differences between treatment groups overall ($P = 0.017$) and in both groups over time ($P = 0.007$), but not between groups at each individual time point. Subjects in the probiotic group had a higher abundance of the family *Lachnospiraceae* at week 4 than subjects in the placebo group. By week 8 the abundance of *Lachnospiraceae* did not differ between subjects administered probiotic or placebo.

Conclusion. Lack of difference in overall community structure between groups at each time point is likely due to concurrent antibiotic therapy. The differential abundance of *Lachnospiraceae* likely contributes to the differences in the diarrheal outcomes observed between groups, as it has previously been associated with attenuated *C. difficile* pathology. Shortening the duration of diarrhea from an initial CDI may reduce the spread of *C. difficile* and improve clinical outcomes.

Disclosures. **All authors:** No reported disclosures.

1269. Endogenous Serum IgG Antibodies to *Clostridium difficile* Toxin B Are Associated with Protection against *C. difficile* Infection Recurrence

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Background. MODIFY I/II were global trials of the efficacy and safety of bezlotoxumab (BEZ), a monoclonal antibody (mAb) against *C. difficile* toxin B, alone and with actoxumab (ACT), a mAb against *C. difficile* toxin A. BEZ was superior to placebo (PBO) at preventing recurrent CDI (rCDI) in patients (patients) receiving antibacterials for CDI. The addition of ACT did not improve efficacy. The aims were to explore potential biomarkers for rCDI risk in the patients receiving PBO by measuring endogenous IgG Abs against Cd toxins A and B (eAb-A and eAb-B); it was expected that patients with low eAb levels might be at increased risk of rCDI.

Methods. Serum samples were collected pre-dose (PRE), at Week 4, and Week 12 postdose. eAb titers were measured using an electrochemiluminescence immunoassay. **Results** were reported as <1:1000, 1:1000, 1:5000, 1:25000, and ≥1:125000. As there is no clearly defined immunological surrogate of efficacy for rCDI tied to a specific eAb-A or eAb-B level, eAb levels were arbitrarily categorized as low (≤1:1,000), medium (1:5000), or high (≥1:25000). The rCDI rate was summarized by eAb category at each time point.

Results. The proportion of patients with higher eAb-A and eAb-B titers increased following the initial CDI episode (Tables 1 and 2). There was no evident correlation between eAb-A titers and the rCDI rate at any time point. The proportion of patients who experienced rCDI within 12 weeks after randomization was highest in patients with low eAb-B titers PRE and at Week 4. rCDI rate in those with low eAb-B titer at all timepoints and in patients who had low titer only at PRE was similar.

Conclusion. The rise in eAb-A and eAb-B titers over time is consistent with a convalescent humoral immune response to toxins A and B following CDI. The lack of correlation between eAb-A titers and rCDI is consistent with the lack of efficacy of ACT in prevention of rCDI. Conversely, higher eAb-B titers are associated with lower risk for rCDI, consistent with the efficacy of BEZ. 22.1% of patients with high eAb-B titers at PRE experienced rCDI. Therefore, eAb-B titers may have marginal utility as a biomarker for rCDI risk and are not likely to improve predictive value over clinical and demographic characteristics such as advanced age, compromised immunity, and CDI history.

Table 1. Distribution of PBO Patients by eAb-A titer Category and Proportion of PBO Subjects with rCDI by eAb-A titer Category at each Scheduled Timepoint (MODIFY I/II, mITT Population who Achieved Initial Clinical Cure and so were Eligible to develop rCDI)

	Percentage of placebo group (n)			% rCDI (m/n)		
Timepoint # in Pop	PRE N=606	Week 4 N=548	Week 12 N=497	PRE* N=606	Week 4* N=548	Week 12* N=497
Low	37.1 (225)	30.1 (165)	32.0 (159)	34.7 (78/225)	36.4 (60/165)	35.2 (56/159)
Medium	50.8 (308)	52.2 (286)	49.1 (244)	29.9 (92/308)	31.1 (89/286)	31.1 (76/244)
High	12.0 (73)	17.7 (97)	18.9 (94)	45.2 (33/73)	40.2 (39/97)	44.7 (42/94)

*One-sided Cochran-Armitage trend test p-value = 0.78, 0.62 and 0.88 at PRE, Week 4 and Week 12 respectively.

Table 2. Distribution of PBO Patients by eAb-B titer Category and Proportion of PBO Subjects with rCDI by eAb-B titer Category at each Scheduled Timepoint (MODIFY I/II, mITT Population who Achieved Initial Clinical Cure)

	Percentage of placebo group (n)			% rCDI (m/n)		
Timepoint # in Pop	PRE N=604	Week 4 N=545	Week 12 N=494	PRE* N=604	Week 4* N=545	Week 12* N=494
Low	38.1 (230)	30.8 (168)	23.9 (118)	38.7 (89/230)	38.1 (64/168)	34.7 (41/118)
Medium	44.7 (270)	40.9 (223)	40.9 (202)	32.6 (88/270)	35.0 (78/223)	35.1 (71/202)
High	17.2 (104)	28.3 (154)	35.2 (174)	22.1 (23/104)	27.2 (42/154)	33.9 (59/174)

*One-sided Cochran-Armitage Trend Test p-value = 1.60E-03, 0.02 and 0.43 at PRE, Week 4 and Week 12 respectively.

Disclosures. **C. P. Kelly**, TBD: Investigator, Speaker honorarium; **J. Shen**, Merck & Co., Inc.: Employee, may hold stock/hold stock options in the Company; **R. Railkar**, Merck & Co., Inc.: Employee, may own stock/hold stock options in the Company; **D. Guris**, Merck & Co., Inc.: Employee, may own stock/hold stock options in the Company; **M. B. Dorr**, Merck & Co., Inc.: Employee and Shareholder, may own stock/hold stock options in the Company

1270. Comparative Effectiveness of Vancomycin vs. Metronidazole in Mild *Clostridium difficile* Infections, and Potential Impact on Subsequent Vancomycin-Resistant *Enterococcus* (VRE) Isolation

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Background. The epidemiology and clinical characteristics of *Clostridium difficile* infections (CDI) have evolved dramatically in the past decade. Vancomycin is the treatment of choice for moderate to severe CDI, with superior cure rates observed in comparative trials. However, controlled comparative efficacy data pertaining to mild CDI is lacking. Furthermore, the potential impact of vancomycin treatment on subsequent Vancomycin-Resistant *Enterococcus* (VRE) isolation rates remains unknown at the individual patient level.

Methods. A Retrospective cohort analysis was executed at the Assaf Harofeh Medical Center, Israel, from 2010 to 2015. Adult patients (>18 years) with a first episode of acute CDI, determined per pre-established criteria, were enrolled. The efficacy of vancomycin vs..metronidazole was evaluated in the subset of patients with mild CDI. The outcomes of patients, who received vancomycin or metronidazole (but not both), were compared by Cox regression. A prediction score was used to control for possible confounders associated with being treated with vancomycin. The independent association of oral vancomycin treatment during the acute CDI and later (up to 18 months) VRE isolation was analyzed using Cox regression.

Results. A total of 413 patients with CDI were included in the study. The majority were elderly (median age 75 years, range 19–120), and had extensive comorbidities (mean Charlson's combined condition score 6.7 ± 3.4) and significant acute illness indices (35% with severe to fulminant Horn index). Among 126 patients with mild disease, no differences were observed in terms of clinical outcomes between vancomycin or metronidazole treatment. Metronidazole remained non-inferior even after incorporating a prediction score to control for confounders associated with being a "vancomycin case". Ten patients had new post-CDI VRE isolation. In multivariable analysis, oral vancomycin treatment during the acute CDI was the strongest independent predictor for later isolation of VRE (aOR=6.7, $P = 0.04$).

Conclusion. Our study suggests that metronidazole should remain the recommended treatment of choice for mild CDI, due to clinical non-inferiority and an apparent association between vancomycin therapy and subsequent VRE isolation on an individual patient level analysis.

Disclosures. **All authors:** No reported disclosures.

1271. Bezlotoxumab (BEZ) for Prevention of *Clostridium difficile* Infection (CDI) Recurrence (rCDI): Distinguishing Relapse from Reinfection with Whole Genome Sequencing (WGS)

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Background. Bezlotoxumab (BEZ) and actoxumab (ACT) are monoclonal antibodies against *C. difficile* toxins B and A, respectively. Patients receiving a single infusion of BEZ alone or with ACT in the MODIFY I/II trials showed an absolute 10% (relative ~40%) reduction in rCDI over 12-weeks compared with placebo (PBO). The addition of ACT did not improve efficacy. This *post hoc* analysis investigated whether BEZ prevented relapse with the same strain and/or reinfection with a new strain.

Methods. *C. difficile* strains isolated from patient stool samples were typed by PCR ribotyping, PCR free library construction and Illumina whole genome