**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 Sequencing. Differences between probiotic and placebo groups were compared using analysis of variance and permutation 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* pathogenicity. 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

Ciaran P. Kelly, MD,1; Ian R. Poxton, PhD,2; Judong Shen, PhD,3; Radha Raikar, PhD,3; Dalya Guris, MD4; and Mary Beth Dorr, PhD2; Gastroenterology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, 1University of Edinburgh, Edinburgh, United Kingdom, 2Merck & Co., Inc., Kenilworth, New Jersey

**Session:** 148. C. difficile: From the Bench to Bedside

**Background.** MODIFY I/II were global trials of the efficacy and safety of bezlotoxumab (BEZ) and actoxumab (ACT) in patients with *C. difficile* infection (CDI) at baseline with low or absent endogenous IgG antibodies against *C. difficile* toxin A (eAb-A) and/or toxin B (eAb-B). The rise in eAb-A and eAb-B titers over time is consistent with a specific immune response to toxins A and B following CDI. The lack of correlation between eAb-A or eAb-B levels and the rate of recurrence (rCDI) at any time point suggests that higher eAb levels are associated with a better clinical outcome. The proportion of patients with higher eAb-A and eAb-B titers increased from 9% at baseline to 83% at 12 weeks post-CDI (P < 0.0001). Patients with low eAb-B titers had a 50% increased risk of rCDI compared with patients with high eAb-B titers at baseline. Therefore, higher eAb-B titers at baseline are associated with lower risk for rCDI, consistent with the efficacy of BEZ. 22.1% of patients with high eAb-B titers at baseline had 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 diagnostic characteristics such as advanced age, compromised immunity, and CDI history.

**Disclosures.** C. P. Kelly, TBD: Investigator, Speaker honorarium, J. Shen, Merck & Co., Inc.: Employee, may hold stock/hold stock options in the Company; R. Raikar, 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; Mary Beth 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

Ilan Youngster, MD, MMS3; Zepora Lazarovitch, PhD; Marina Bondencorno, MD4; Betlehem Mengesha, MD3; Limor Toledano, MD4; Yaed Kachlon, MD4; Dror Marchaim, MD4; Assaf Harofeh Medical Center, Zerifin, Israel, 1Infected Diseases, Assaf Harofeh Medical Center, Zerifin, Israel

**Session:** 148. C. difficile: From the Bench to Bedside

**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, but some instances of 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 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 in 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)

Mary Beth Dorr, PhD1; Zhen Zeng, PhD; Mark Wilcox, MD2; Junhua Li, PhD3; Ian Poxton, PhD, DSc; Hailong Zhao, MS4; Xiaoyun Li, MS5; Dalya Guris, MD6; and Peter Shaw, PhD7; Merck & Co., Inc., Kenilworth, New Jersey, 2Merck & Co., Inc., Kenilworth, New Jersey, 3Beijing Institute of Biomedical and Clinical Sciences, 4University of Leeds, Leeds, United Kingdom, 5BGI-Shenzhen, Shenzhen, China, 6Assaf Harofeh Medical Center, Zerifin, Israel, 7University of Edinburgh, Edinburgh, United Kingdom

**Session:** 148. C. difficile: From the Bench to Bedside

**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 −48% 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 sequencing (WGS).
sequencing (WGS). rCDI was defined as diarrhea with toxigenic *C. difficile* in stool. Relapse and reinfection were differentiated by comparing ribotype (RT) and pair-wise single-nucleotide WGS variations (PWSNV). Relapse was assigned if the baseline RT and the RT isolated during rCDI were the same and PWSNVs were ≤2. Reinfection was defined as rCDI cases with a different RT compared with baseline or the same RT with >10 PWSNVs. Patients treated with AC and AC+BEZ were pooled and patients receiving PBO or ACT were pooled. The effect of BEZ on the cumulative incidence of relapse and reinfection was estimated by Fine & Gray’s competing risks survival model.

Results. Among 514 patients with rCDI in MODIFY I/II, 259 (50.4%) had a baseline and a post-baseline *C. difficile* isolate. There were 198 (76.4%) relapse and 50 (19.3%) reinfection cases (Table). Among rCDI cases, proportions of reinfection and relapse were similar between treatments. Proportion of relapses was higher for RT 027. Significant differences in crude cumulative incidence for relapse (P < 0.001) were observed for BEZ and ACT+BEZ groups compared with PBO and ACT groups. Similar changes were observed for reinfection but results were not significant. Cumulative incidence curves showed that relapses occurred earlier and at a higher rate than reinfections, but the reduction in rCDI was similar (Figure).

Conclusion. The BEZ-induced reduction in rCDI observed in MODIFY I/II reflects the prevention of relapses due to the same strain. A reduction in reinfections was also observed, but likely due to a smaller number of reinfection cases, the difference was not significant.

| Table: Proportion of rCDI Cases Designated as Relapse vs Reinfection by Treatment Group in MODIFY I/II |
|-------------|--------|--------|--------|
| RT          | BEZ and ACT+BEZ | PBO and ACT | RT 027 |
| Recurrence (%) | 123 | 138 | 58 |
| Relapse | 91 (74.0) | 107 (78.7) | 49 (84.8) |
| Reinfection | 26 (21.3) | 24 (17.6) | 7 (12.1) |
| Unknown* | 6 (4.9) | 0 (0.0) | 2 (3.4) |
| *P value for relapse vs reinfection | 0.53 | 0.13 |

*Includes all treatment groups: ACT, ACT+BEZ, BEZ, and PBO

**Results.** Among 514 patients with rCDI in MODIFY I/II, 259 (50.4%) had a baseline and a post-baseline *C. difficile* isolate. There were 198 (76.4%) relapses and 50 (19.3%) reinfections. Among individual cases, proportions of reinfection and relapse were similar between treatments. Proportion of relapses was higher for RT 027. Significant differences in crude cumulative incidence for relapse (P < 0.001) were observed for BEZ and ACT+BEZ groups compared with PBO and ACT groups. Similar changes were observed for reinfection but results were not significant. Cumulative incidence curves showed that relapses occurred earlier and at a higher rate than reinfections, but the reduction in rCDI was similar (Figure).

**Conclusion.** The BEZ-induced reduction in rCDI observed in MODIFY I/II reflects the prevention of relapses due to the same strain. A reduction in reinfections was also observed, but likely due to a smaller number of reinfection cases, the difference was not significant.