

A Lyophilized, Non-Frozen, Oral Microbiota-Based Drug Rbx7455 Is Safe, Reduces *Clostridium Difficile* Infection Recurrence, and Restores the Microbiome

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Background

To broaden access to microbiota-based therapeutics therapies, RBX7455—a lyophilized, non-frozen, orally-administered microbiota-restoring drug candidate was developed. We report interim results from an open-label Phase 1 trial of RBX7455 for preventing recurrent *Clostridium difficile* infections (rCDI).

Methods

Nineteen patients with ≥ 2 CDI episodes following ≥ 2 courses of antibiotic therapy were enrolled. Patients received 8 RBX7455 capsules for 4 days (cohort 1) or 2 days (cohort 2). Success was defined as absence of CDI recurrence through 8 weeks after treatment completion, and adverse events were monitored during and after treatment.

Patients submitted stool samples prior to and at 1, 7, 30, and 60 days after treatment. Stool and representative RBX7455 product samples were sequenced using an ultra-shallow shotgun sequencing method. Operational taxonomic unit (OTU) data were grouped by cohort and compared using a Bray-Curtis dissimilarity calculation. Relative OTU abundances at the class level were compared among time points.

Results

Nine of ten patients in cohort 1 (median age=67, 90% female) and seven of nine patients in cohort 2 (median age=54, 55% female) were recurrence-free at the 8-week endpoint. A total of 37 non-serious adverse events(AE) were observed, with gastrointestinal AEs being most common. There were no serious AEs observed.

Prior to treatment, the taxonomic compositions of responder microbiomes were dissimilar from the RBX7455 composition and were dominated by Gammaproteobacteria and Bacilli. After treatment, patient microbiomes converged toward the RBX7455 composition, with Bacteroidia and Clostridia becoming more predominant. Microbiome changes were comparable among responders in both cohorts.

Conclusion

RBX7455 had 90% and 78% success preventing rCDI with no serious AEs in two cohorts of rCDI patients. For this small observational study, both cohorts showed acceptable outcomes. In addition, RBX7455 appears to restore patient microbiomes toward the RBX7455 composition. Microbiome and safety data collection will continue for 6 months after treatment.

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