

Donors are Universal in the Fight Against *Clostridium difficile*: Results from Two Trials Investigating the Safety and Efficacy of RBX2660, a Microbiota-based Drug

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Background: Questions have been raised about donor impact on the treatment outcomes of microbiota-based therapies for recurrent *Clostridium difficile* Infection (CDI); specifically is there such thing as a super donor? We report patient outcomes in two separate human clinical studies of RBX2660, a donor derived microbiota based drug for recurrent CDI: PUNCH CD, an open label clinical trial, and PUNCH CD 2, a randomized, double-blind, placebo-controlled trial.

Methods: RBX2660 is manufactured from donor stool using standardized and quality-controlled procedures, including a pre-enrollment pathogen screen and blood testing at the end of each donation cycle (min. 14 days after last stool screen). In the case of a positive result on any of the tests, all drug product associated with that donor during a cycle was destroyed. Donor material is not pooled, allowing for direct donor to patient traceability.

Patients in the PUNCH CD study received a single dose of RBX2660 and were eligible to get another treatment if the first one failed. Patients in the blinded phase of the PUNCH CD 2 trial were randomized to receive either: 2 doses of RBX2660; 2 doses of placebo; or 1 dose of RBX2660 and 1 dose of placebo via enema with doses 7 days apart. In both studies, donor batches were randomized to the patient, and randomized again for the second dose. Patients could receive product from the same or different donors. For analysis, a generalized linear mixed effects model with binomial distribution was used to evaluate outcomes, treating the donor and patient as a random effect.

Results: A total of 34 patients enrolled in the PUNCH CD Phase 2 trial (mean age 68.8 years, 67.6% female) were treated with at least one dose of RBX2660. Fifteen received a second dose. Four donors were used throughout the entire study. In the Phase 2B PUNCH CD2 clinical trial, a total of 83 patients (mean age 62 years; 59% female) received at least 1 dose of RBX2660. Seventeen donors were used throughout the entire study. The donor effect was not significant ($P > .05$, variance = 0) for predicting patient success or failure responses in either study.

Conclusion: For patients with recurrent CDI treated with RBX2660, success or failure is not determined by donor. The data from two separate clinical studies demonstrate that RBX2660 prepared from a universal group of donors who pass screening criteria, does not impact patient outcomes and that a super donor was not identified. Indications other than CDI will require further study.

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