Does the Donor Matter? Results from PUNCH CD 2, a Randomized Controlled Trial of a Microbiota-based Drug for Recurrent *Clostridium difficile* Infection

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Background: Questions about applicability of a universal donor vs. donor-to-patient matching have been raised in regards to microbiota-based therapies for recurrent *Clostridium difficile* Infection (CDI). We report on donor-to-patient outcomes in the PUNCH CD 2 trial, a randomized, placebo-controlled study of RBX2660.

Methods: 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. RBX2660 is a microbiota-based drug manufactured from human-derived microbes using standardized processes in donor-specific batches that can be tracked to individual patients and outcomes; donors were randomized to patients for each dose. A generalized linear mixed effects model with binomial distribution was used to evaluate outcomes. Both the donors and patients were treated as random effects.

Results: A total of 83 patients in the intention-to-treat population (mean age 62 years; 59% female) who received at least 1 dose of RBX2660 were included in the analysis. The donor was not significant ($P > 0.99$) for predicting responses (Table 1). The variance = 0 indicating that no difference in outcome by donor was expected and that the treatment rates for success and failure were the same for each donor.

Discussion: This analysis of the PUNCH CD 2 study demonstrates that the donor does not matter with regard to the efficacy of RBX2660 administration for recurrent CDI. The results are consistent with a previously reported analysis of the PUNCH CD study, a prospective open-label study of RBX2660.[1] Thus, the data from two clinical studies demonstrate that RBX2660 prepared from a universal donor pool is appropriate without donor-to- patient matching. However, this may not be the case for indications other than CDI.

References:

1. Ray A and Jones C. Does the donor matter? Donor vs patient effects in the outcome of a next-generation microbiota-based drug trial for recurrent *Clostridium difficile* infection. *Future Microbiol.* 2016. Mar 17. Epub ahead of print.

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Table 1. Outcomes for Donors and Patients

	Estimate	P Value
Fixed Effect	Coefficient	
Intercept	11.042	4.07e-12
Random Effect	Variance	
Donor	0	> 0.99