Lack of Association with Patient Demographics and Outcomes in PUNCH CD 2, a Randomized Controlled Trial of RBX2660, a Microbiota-based Drug for Recurrent *Clostridium difficile* Infection

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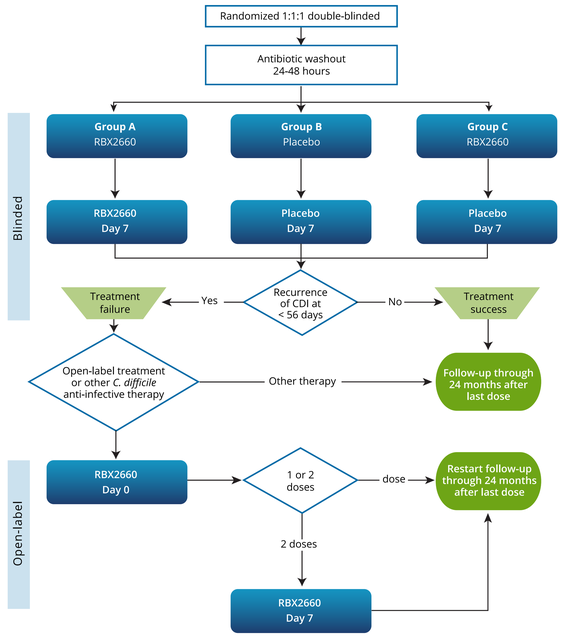
Background

- Microbiota therapy is gaining acceptance for preventing recurrent Clostridium difficile infection (CDI).
- RBX2660 is a microbiota-based drug derived from healthy human donors using a standardized, quality-controlled manufacturing process.
- One dose of RBX2660 was demonstrated to be safe and effective for preventing rCDI in a randomized, double-blind, placebo controlled study (PUNCH CD 2; reported by Dubberke et al., ID Week, Oct 2016).
- Recent microbiota-based trials suggested suggested that outcomes may correlate with patient demographics.
- Key demographics of subjects treated in the PUNCH CD 2 trial were evaluated for impact on treatment.

Methods

- A total of 133 patients with recurrent CDI were enrolled in the PUNCH CD 2 clinical trial at 21 sites in the USA and Canada (Trial #: NCT02299570).
- Patients were randomized to receive: 2 doses of RBX2660 (Group A); 2 doses of placebo (Group B); or 1 dose of RBX2660 followed by 1 dose of placebo (Group C).
- Therapies were administered via enema 7 days apart.
- The first blinded treatment dose was administered 24-48 hours after completion of antibiotic treatment.
- Success was defined as the absence of *C. difficile*-associated diarrhea at 8 weeks following completion of the last blinded treatment.
- Demographic information was collected at the time of enrollment, with success and failure designations applied after the study blind was lifted.
- Logistic regression was used to determine whether outcomes correlated with specific demographic characteristics.

The PUNCH CD 2 Trial (A Phase 2B Study)



RBX2660

- One dose of RBX2660 contains 50 g of human stool per 150 mL of suspension in a single-dose ready-to-use enema bag.
- Stored frozen at ≤−80°C at the manufacturer and shipped frozen to the site as needed in a temperature-controlled container.
- Manufactured using standardized, quality-controlled processes with guaranteed minimum quantity of microbes.

Results

Logistic regression analysis was conducted with data from 127 patients treated in the blinded phase of the PUNCH CD 2 trial.

Table 1: Patient Outcomes Classified by Each Covariate		OUTCOMES	
		Fail	Success
TREATMENT	Placebo	24	20
	RBX2660 (Groups A & C)	30	53
REGION OF TRIAL SITE	Canada	14	13
	East (USA)	10	11
	Midwest (USA)	22	34
	South (USA)	0	4
	West (USA)	8	11
PRE-TREATMENT ANTIOBIOTIC	Vancomycin	49	64
	Fidaxomicin*	2	3
	Other*	3	6
SEX	Female	34	45
	Male	20	28
AGE (yrs)	Under 65	29	38
	65+	24	35

Treatment is the only significant covariate that impacted treatment outcome. (Table 2) A logistic regression model was used to determine the probability of success according to treatment received, age, gender.

	ESTIMATE	STD ERROR	2 VALUE	Pr(>|z|)
(Intercept)	0.1452	0.7881	0.23	0.8202
TREATMENT (RBX2660)	0.7123	0.3844	1.85	0.0639
PRETREATMENT ANTIBIOTIC (Vancomycin)	-0.3414	0.6033	-0.57	0.5715
SEX (Male)	-0.0591	0.3828	-0.15	0.5715
AGE (65+)	0.0885	0.3724	0.14	0.8850

Region of trial site does not significantly impact treatment outcome. (Table 3) A separate logistic model was fit to determine the significance of Region. Note: Canada is the reference level.

	ESTIMATE	STD ERROR	Z VALUE	Pr(>|z|)
(Intercept)	-0.5856	0.4824	-1.21	0.2247
TREATMENT (RBX2660)	0.7203	0.3938	1.83	0.0673
EAST	0.2362	0.5922	0.40	0.6900
MIDWEST	0.5288	0.4791	1.10	0.2698
SOUTH	11.4314	1199.7724	0.01	0.9891
WEST	0.6120	0.6260	0.98	0.3283

Conclusions

- The efficacy outcome of RBX2660 did not depend on sex, age, region of the clinical trial center, or the antibiotic regimen completed prior to RBX2660 treatment.
- The broad benefit of RBX2660 among patient demographics underscores its merit for further clinical evaluation for preventing rCDI.