Perspectives on the PUNCH CD Trial of a Microbiota-Based Drug Targeted at Recurrent *C. difficile* Infection

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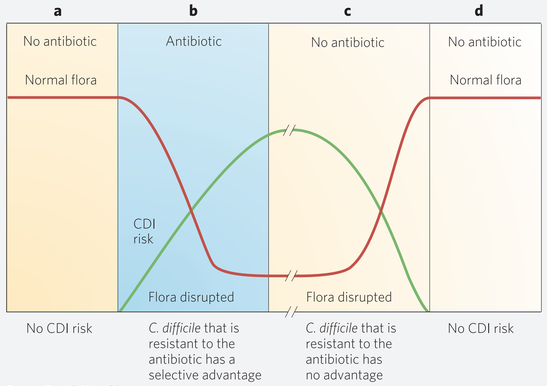
Antibiotics and the Recurrence of *Clostridium difficile* Infection

- Antibiotic-mediated disruption of the intestinal microbiota is a risk factor for *Clostridium difficile* (C. diff.) infection
- Approximately 25% of patients suffer from recurrence of disease following standard antibiotic therapy[1]
- After an initial recurrence, approximately 45% to 65% of patients will go on to experience repeated, sometimes chronic episodes.[2]
- There is increasing recognition that restoration of a healthy gut microbiota is necessary to limit C. diff. colonization[3]

Role of Antibiotics in Intestinal Microbiota Disruption

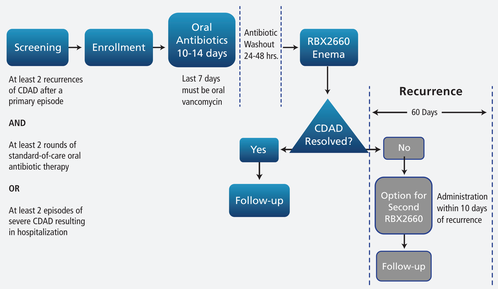


Source: Rupnik M et al.[4]
A. Prior to antibiotic exposure, patients are resistant to C. diff. infection. B. The risk of C. diff. infection increases after exposure due to disruptions to the gut microbiota. Antibiotic resistant strains of C. diff. have a selective advantage. C. The gut microbiota remains disrupted for a variable period even after antibiotics have been discontinued, and the patient can be re-infected. D. Only after the normal gut flora are restored, is resistance to C. diff. infection is restored.

PUNCH CD Study

- Phase 2 open label study of RBX2660 (microbiota suspension) for recurrent C. diff. infection
- Objective: Evaluate the safety and effectiveness of RBX2660, a next-generation fecal microbiota transplant (FMT)
- First multi-center study of FMT under a unified protocol conducted under an FDA IND

PUNCH CD Study Design



RBX2660 Compared with FMT

- Designed to mimic FMT
- Donors rigorously screened
- Patients do not have to find their own donor; have donor undergo testing; wait for the results of the testing
- Contains a minimum guaranteed quantity of microbes
- Formulated to have a long shelf-life
- Manufactured using standardized, quality controlled processes
- Supplied in a ready-to-use enema format

Epidemiology of Recurrent C. diff.

- Patients with recurrent C. diff. are typically older (median age 64.8, range 18.3 - 98.2 years); with a higher comorbidity burden evidenced by a higher Charlson score[5]
- Additionally, high-risk antimicrobials, particularly when administered after completion of the initial C. diff. treatment; gastric acid suppression; ≥ 2 hospitalizations within the prior 60 days are among the factors found to increase the risk of recurrence.[5]

PUNCH CD PATIENT POPULATION

Age (years)	
Mean (SD)	66.8 (15.1)
Range	26.7 - 89.6
Gender	
Female	23/34 (67.6%)
Race	
American Indian or Alaska Native	1/34 (2.9%)
Asian	0/34 (0.0%)
Black or African American	1/34 (2.9%)
Native Hawaiian or Other Pacific Islander	0/34 (0.0%)
White	32 (94.2%)
BMI (kg/m²)	
Mean (SD)	24.4 (5.2)
Range	15.0 - 37.0
Prior Medical History	
Head, eyes, ears, nose and throat	15/34 (44.1%)
Cardiovascular	19/34 (55.9%)
Gastrointestinal	21/34 (61.8%)
Musculoskeletal	13/33 (39.4%)
Neurological	5/34 (14.7%)
Genitourinary	18/26 (69.2%)
Psychiatric	9/32 (28.1%)

CAPITAL DIGESTIVE CARE PATIENT POPULATION

Age (years)	
Mean (SD)	71.5 (21.2)
Range	26 - 89
Gender	
Female	5/6 (83.3%)
Race	
White	6 (100%)
BMI (kg/m²)	
Mean (SD)	21 (5.0)
Range	16-31
Prior Medical History	
Head, eyes, ears, nose and throat	3 (50%)
Cardiovascular	6 (100%)
Gastrointestinal	3 (50%)
Musculoskeletal	3 (50%)
Neurological	1 (16.7%)
Genitourinary	3 (50%)
Psychiatric	1 (16.7%)

Clinical Takeaways:

- PUNCH CD population predominantly elderly with multiple co-morbidities
- Typical recurrent C. diff. population
- PUNCH CD was an "all-comer study" that reflects the real-world recurrent C. diff. population seen in clinical practice – not sub-selected.

RBX2660 Administration

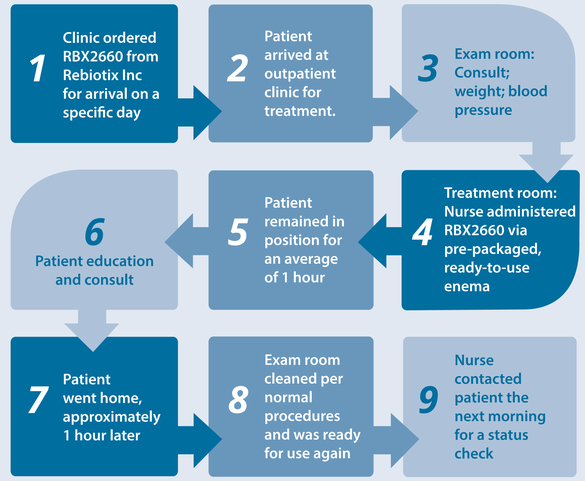
WHY ENEMA ADMINISTRATION?

- Has been shown to work in previous case series[6,7]
- Safe for patient; minimal risk as compared to colonoscopy or nasogastric tube method
- No bowel prep required
- No sedation required
- Can be administered by a nurse; no special procedure room or extra personnel needed.
- Family members can remain in the treatment room

Results

- Of the 8 patients enrolled at Chevy Chase Clinical Research, 6 were treated with RBX2660.
- Five patients had efficacy data at 8 weeks.
- Overall efficacy was 80.0% (4/5) at Chevy Chase Clinical Research.

Impact on Clinic Logistics



Conclusion

The PUNCH CD study to assess RBX2660 for recurrent C. diff. infection provided patient access to a new therapy with minimal disruption to clinic operation.

What's Next?

- Participating in PUNCH CD 2 Study
- Randomized double-blind, placebo controlled study of RBX2660

References

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