Efficacy and Safety of RBX2660 in PUNCH CD3, a Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial with a Bayesian Primary Analysis for the Prevention of Recurrent *Clostridioides difficile* Infection

Khanna S, Assi M, Lee C, Yoho D, Louie T, Knapple W, Aguilar H, Garcia-Diaz J, Wang GP, Berry SM, Marion J, Su X, Braun T, Bancke L, Feuerstadt P. *Drugs* 82, 1527–1538 (2022). https://doi.org/10.1007/s40265-022-01797-x

Recurrent ***Clostridioides difficile*** infection (CDI) is a major health problem worldwide –especially among older adults

RBX2660 is a microbiota-based live biotherapeutic that is rectally administered for the prevention of recurrence of CDI

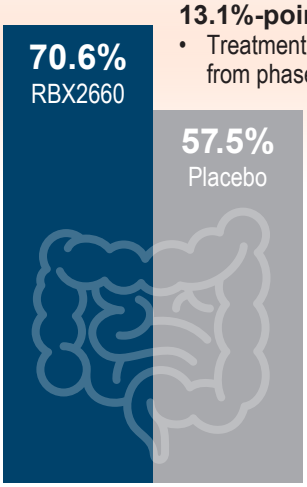
The microbiota suspension contains a broad consortium of **live microbes** sourced from **healthy donors**

The PUNCH CD3 trial found RBX2660 superior to placebo in patients with recurrent CDI

PUNCH CD3

- A randomized, double-blind, placebo-controlled, phase 3 study
- Patients enrolled had either ≥1 recurrence of CDI after a primary episode and completed ≥1 round of antibiotic therapy or ≥2 episodes of severe CDI that resulted in hospitalization in the past year
- Treatment arms: single-dose RBX2660 (n = 180) or placebo (n = 87)
- Primary endpoint: Treatment success, absence of CDI-related diarrhea at 8 weeks
- Patients were followed up for 6 months

EFFICACY

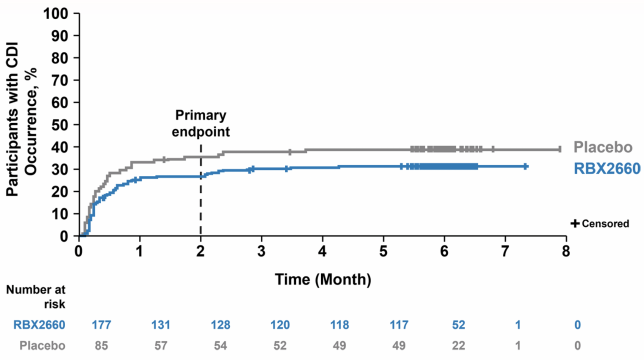


Posterior probability of superiority of 0.991

13.1%-point Treatment Difference

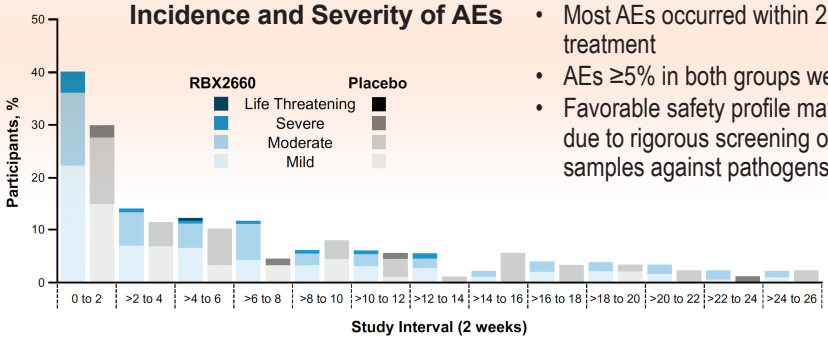
- Treatment success based on a Bayesian analysis integrating data from phase 2b study

- **92.1%** of patients with success at 8 weeks remained free of CDI recurrence for 6 months



SAFETY & TOLERABILITY

Incidence and Severity of AEs



- Most AEs occurred within 2 weeks of treatment
- AEs ≥5% in both groups were GI-related
- Favorable safety profile may be partially due to rigorous screening of donors and samples against pathogens

Limitations, potentially leading to high placebo response rate:

- PCR assay used in >70% of patients
- 1/3 of patients enrolled after one rCDI occurrence

RBX2660 was well tolerated and prevented rCDI in patients following antibiotic therapy

Abbreviations: CDI: *Clostridioides difficile* infection; AEs: adverse events; GI: gastrointestinal