Clearance of vancomycin-resistant Enterococcus concomitant with administration of a microbiota-based drug targeted at recurrent Clostridium difficile infection

Erik Dubberke[1], Courtney Jones[2]

[1]Washington University School of Medicine, St. Louis, MO, USA.;[2]Rebiotix Inc., Roseville, MN, USA.

Objectives: Vancomycin-resistant Enterococcus (VRE) colonisation and Clostridium difficile infection (CDI) share similar risk factors. VRE is a major nosocomial pathogen and is a well-known complication among transplant and immune compromised patients. VRE carriers are at increased risk for infection due to VRE and a source of transmission to others. VRE shedding in stool increases with antimicrobial exposures and decreases with normalisation of the intestinal microbiota after antimicrobials are discontinued. We report on stool VRE clearance in a secondary analysis of data from the Phase 2 PUNCH CD assessing the safety and efficacy of RBX2660 (microbiota suspension) for recurrent CDI.

Methods: A total of 34 patients with recurrent CDI enrolled at 11 sites in the U.S. received 1 or 2 doses of RBX2660, a next-generation version of faecal transplant prepared from live human-derived microbes, between August 2013 and January 2014 as part of the PUNCH CD study. Patients were requested to voluntarily submit stool samples at baseline and at 7, 30 and 60 days and 6-months after the last administration of RBX2660. All VRE testing was conducted at Fairview Diagnostic Laboratories, Minneapolis, MN, U.S. Stool samples were shipped fresh overnight and were tested for VRE using bile esculin azide agar with 6 µg/ml vancomycin and gram staining. Vancomycin resistance was confirmed via blood agar and etest. Descriptive statistics were used for data analysis.

Results: VRE status (at least 1 test result) was available for 30 patients. All stool samples for 19 patients (63.3%, mean age 61.7 years, 68% female) tested VRE negative. Eleven patients (36.7%, mean age 75.5 years, 64% female) were VRE positive at the first test (baseline or 7-day follow-up). Of these patients, 72.7%, n=8 converted to negative as of the last available follow-up (30 or 60 days or 6-months). The status of the other 3 was as follows: 1 patient died (respiratory failure unrelated to RBX2660 administration) and follow-up data was not available; 1 patient remained positive at all follow-ups and 1 patient retested positive at 6-months after having tested negative during the interim. This patient had extenuating factors: multiple rounds of antibiotics including vancomycin for CDI recurrence.

Conclusions: Although based on a small sample size, this secondary analysis demonstrated the intriguing possibility of successfully converting a high percentage of VRE positive patients to negative in a recurrent CDI population. More study is needed to confirm the hypothesis that a microbiota-based drug may provide a method of VRE clearance.