In vitro activity of tebipenem against a recent collection of fastidious organisms recovered from respiratory tract infections

**Background.** Tebipenem is a cephalosporin derivative with potent in vitro activity against fastidious organisms that cause respiratory tract infections (RTIs) such as *S. pneumoniae* and *H. influenzae*. It is designed for use in the treatment of community-acquired respiratory tract infections (CARTIs) and pneumonia.

**Methods.** This study evaluated the activity of tebipenem against a recent collection of fastidious organisms recovered from community-acquired respiratory tract infections (CARTIs). The isolate collection included fastidious organisms that are commonly associated with respiratory tract infections, such as *S. pneumoniae* and *H. influenzae*, and other fastidious pathogens such as *Haemophilus parainfluenzae* and *Streptococcus pneumoniae*.

**Results.** Tebipenem had MIC₅₀ values of 0.5 mg/L against *H. influenzae* and 1 mg/L against *H. parainfluenzae* isolates. All 18 BNLAR isolates from these two species were inhibited at ≤ 0.12 mg/L of tebipenem. The MIC₅₀ values observed for tebipenem were 0.25 mg/L for these organisms. Tebipenem displayed good activity against *S. pneumoniae* isolates at ≤0.12 mg/L. Tebipenem activity (MIC₅₀) was 8-fold greater than ertapenem (MIC₉₀) against *S. pneumoniae* isolates. Greater than 99.7% of all *H. influenzae* isolates, including all BNLAR, were inhibited at ≤0.12 mg/L. All *M. catarrhalis* isolates were inhibited at ≤0.03 mg/L. Although tebipenem activity correlated with penicillin resistance, all *S. pneumoniae* isolates were inhibited at ≤0.12 mg/L. Tebipenem activity in vitro was greater than ertapenem when tested against *S. pneumoniae* isolates. This data supports the possible development of tebipenem as an oral option for combating CARTIs caused by these organisms.

**Conclusion.** Tebipenem displayed potent activity against fastidious organisms causating respiratory tract infections. Greater than 99.7% of all *H. influenzae* isolates, including all BNLAR, were inhibited at ≤0.12 mg/L. All *M. catarrhalis* isolates were inhibited at ≤0.03 mg/L. Although tebipenem activity correlated with penicillin resistance, all *S. pneumoniae* isolates were inhibited at ≤0.12 mg/L. Tebipenem activity in vitro was greater than ertapenem when tested against *S. pneumoniae* isolates. This data supports the possible development of tebipenem as an oral option for combating CARTIs caused by these organisms.

**Table:** Summary of culture and CFU log reduction among infected prosthetics

| Species of culture | PLG 0266 Dose | CFU Unreated | CFU Treated | Log Reduction |
|--------------------|---------------|-------------|-------------|---------------|
| S. epidermidis     | 1.00E+07      | 0           | 7.0         |
| S. epidermidis     | 1.00E+07      | 0           | 7.0         |
| S. aureus (MSSA)  | No isolate*   | N/A         |             |
| S. aureus (MRSA)  | 0.1          | 0           | 7.0         |
| S. hemolytica      | 3.7E+02       | 0           | 2.9         |
| E.coli            | 3.5E+03       | 60          | 1.8         |
| E.coli            | 3.5E+03       | 30          | 2.1         |
| Enterococcus      | 1.4E+04       | 80          | 4.1         |
| S. epidermidis     | 1.00E+04      | 90          | 2.3         |
| H. parainfluenzae | 1.00E+07      | 0           | 7.0         |
| H. parainfluenzae | 1.00E+07      | 0           | 7.0         |
| S. aureus (MRSA)  | 1.1E+04       | 0           | 4.0         |

* CFU 1E07-07 is an estimate of uncounted isolate: CFU directly from micro lab measurements.

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1042. Safety of Investigational Microbiota-Based Live Biotherapeutic RXB2660 in Individuals with Recurrent Clostridioides difficile Infection: Data from Five Prospective Clinical Studies

**Background.** Microbiota-based treatments have shown promise to reduce recurrence, morbidity, and mortality for recurrent Clostridioides difficile infections (rCDI), but consistent and reliable safety data are needed to support regulatory approvals and broaden patient access. Here we provide cumulative safety data from 5 prospective clinical studies evaluating RXB2660—a standardized, microbiota-based investigational live biotherapeutic—for reducing rCDI.

**Methods.** This analysis included three Phase 2 (PUNCH CD, PUNCH CD2, PUNCH CD Open Label) and two Phase 3 trials (PUNCH CD3, PUNCH CD3-OLS add-on placebo). Participants were ≥18 years old with documented rCDI who completed standard-of-care oral antibiotic therapy prior to treatment with RXB2660. PUNCH CD3-OLS allowed participants with comorbidities of irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD). Depending on the trial, assigned study treatment was 1 or 2 doses of RXB2660 (or placebo), administered rectally. Participants whose CDI recurred within 8 weeks were eligible for additional RXB2660 treatment. Treatment-emergent adverse events (TEAEs) were recorded for at least 6 months following last study treatment; CD2 and CD Open Label recorded TEAEs for 24 months.

**Results.** Among 620 participants who received at least one RXB2660 dose (assigned treatment or after recurrence), 324 (52.3%) received 1, 270 (43.5%) received 2, 14 (2.3%) received 3, and 12 (1.9%) received 4. 83 participants received blinded placebo only; A total of 1980 TEAEs were reported from 432 (69.7%) RXB2660-treated participants, compared to 174 total TEAEs in 50 (60.2%) placebo-only treated participants. Most TEAEs were mild or moderate in severity, with diarrhea common in all treatment groups. No potentially life-threatening TEAEs were considered related to RXB2660. Study discontinuation due to TEAEs was minimal (<1%) with none related to RXB2660 treatment. There were no reported infections for which the causative pathogen was traced to RXB2660.

**Conclusion.** Across five clinical studies with consistent investigational product, RXB2660 was well-tolerated in ICDI participants. In aggregate, this data provides cumulative and consistent safety data for RXB2660.

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