SYN-004 (ribaxamase) Protects the Gut Microbiome of Patients Treated with Ceftriaxone from Disruption and Reduces the Emergence of Antimicrobial Resistance

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ABSTRACT

Background: β-lactam antibiotics are administered intravenously, a significant portion of each dose can be excreted through the gastrointestinal tract if not metabolized. These antibiotics disrupt the gut microbiome, leading to an increased risk of Clostridium difficile infection (CDI) and the development of antimicrobial resistance (AMR) to β-lactam antibiotics (BPA) and other antimicrobial agents. Ribaxamase is a β-lactamase designed to be given with IV β-lactam antibiotics (including most cephalosporins) to degrade excess antibiotics excreted into the intestine. This excess antibiotic disrupts the balance of the gut microbiome making the recipient more susceptible to Clostridium difficile infection (CDI) and other infections. Meanwhile, the development of AMR to these antibiotics is a critical public health concern. The use of ribaxamase may also have the added benefit of reducing the development of antibiotic resistance in the gut microbiome and gut resistome and may help limit the emergence of AMR induced by these antibiotics. Results: Sequence analyses revealed that ribaxamase protected the integrity of the gut microbiome, including preventing CDI onset by 71% (7 vs. 2, confirmed at the central lab), p=0.045 and VRE and prevented enterococcal domination as compared with placebo (21% vs. 61%; odds ratio 95% CI of 2.73 to 10.59, p=0.002). Statistical analyses were performed to determine correlations between changes in the gut microbiome and clinical study parameters including β-lactamase, vancomycin and macrolide resistance genes.

CONCLUSION

Ribaxamase reduced ceftriaxone-mediated changes in the gut microbiome and gut resistome and has the potential to reduce the emergence of AMR.