**ABSTRACT**

**Background:** The balance of the gut microbiome is linked to human health, and disruption of this balance is associated with many diseases from obesity to inflammatory bowel disease. The gut microbiome is also a major conduit for the spread of antibiotic-resistant bacteria, and loss of diversity in the gut microbiome is associated with the development of antibiotic resistance. In a recent study of patients on intensive care units, ribaxamase (Syn-004) was identified as a promising organism to protect and maintain the diversity of the gut microbiome.

**Methods:** In this study, patients were randomized to receive ribaxamase or placebo in addition to antibiotics. Fecal samples were collected before and after the treatment period. DNA was extracted, and 16S rRNA sequencing was performed to determine the composition of the gut microbiome. Comparisons were made to determine the effects of ribaxamase.

**Results:** The primary endpoint was the change in the gut microbiome from the start to the end of the treatment period. Ribaxamase significantly reduced the incidence of C. difficile infection by 78% compared to placebo. The gut microbiome of patients who received concurrent ribaxamase recovered faster and had a higher diversity.

**Conclusions:** Ribaxamase is a promising organism to protect the gut microbiome from antibiotic-mediated dysbiosis.

**Efficacy Study Design**

**Rifaximin Efficacy Study**

Patients admitted to the hospital for treatment of T1 or T2 gastrointestinal or systemic infections were randomized to receive rifaximin or placebo, with follow-up samples collected after 7 days. A total of 412 patients were enrolled, with 214 patients in each group.

**Exploratory Endpoints**

**Protection of the Gut Microbiome**

16S r RNA Sequencing (DNA Genotek)

**Number of Samples**

- Total Samples Collected: 677
- Sample Sequences (screening sample required): 672
- Sample Sequences with benefit: 25

**Number of Patients**

- Ribaxamase: 112
- Placebo: 117

**Alpha Diversity**

- Difference in alpha diversity in the placebo group was significant compared to the ribaxamase group.

**Beta Diversity**

- Difference in beta diversity in the placebo group was significant compared to the ribaxamase group.

**Relative Abundance of Certain AMR Genes T0 vs. T1**

- Identification of many genes of interest including, β-lactamases, vancomycin and macrolide resistance genes.

**Ribaxamase Prevented Emergence of Antimicrobial Resistance**

- Statistical analysis was performed to determine which genes significantly changed from the screening sample (T0) to the post antibiotic sample (T1) in the placebo vs. the ribaxamase patients.

**Conclusions**

- Ribaxamase reduced the incidence of new onset CDI by 78% as compared with placebo (confirmed at the central lab), p<0.043.

- Ribaxamase protected the diversity of the gut microbiome.

- Ribaxamase reduced new colonization with VRE.

- Some VRE colonized patients appeared to display monoclonal growth.

- Ribaxamase prevented ceftriaxone-mediated changes in the gut resistome.

**SYN-004 (ribaxamase) Protects the Diversity of the Gut Microbiome in Patients Receiving Intravenous Ceftriaxone Treatment**

John F. Kokai-Kun*, Sheila Connelly, Charles Le, Ken Trout and Joseph Sliman

Synthetic Biologics, Inc., Rockville, MD