INTRODUCTION

- Ulcerative colitis (UC) is a relapsing-remitting chronic inflammatory disorder affecting the mucosal surface of the colon (Denson and Fasold 2011). The role of the microbiome in the development, progression, and treatment of UC has been a subject of considerable interest.
- SER-301 is an oral, rationally-designed investigational microbiome therapeutic composed of cultivated spores and vegetative bacterial strains intended to treat UC by modifying the gastrointestinal microbiome to reduce intestinal inflammation and repair epithelial barrier damage that are central to UC pathogenesis.
- We used mouse models of colitis to evaluate the ability of SER-301 to promote immune homeostasis in the colon and counterbalance inflammatory conditions to prevent the development of colitis.

In multiple preclinical models, SER-301 demonstrated the ability to modulate gut immune cell populations towards a noninflammatory phenotype, promoting the development of regulatory T cells and decreasing the frequency of inflammatory Th1 and Th17 effectors cells.

SER-301 MODULATES COLONIC CD4+ T CELLS IN THE DSS-INDUCED COLITIS MODEL TOWARDS A NONINFLAMMATORY PHENOTYPE

In the dextran sodium sulfate (DSS)-induced model of colitis, germ-free (GF) and wild-type (WT) C57BL/6 mice were colonized with either SER-301 or a composition containing strains isolated from UC patients with proinflammatory properties ("INFL+"), SER-301 colonization modulated colonic CD4+ T cell populations towards a noninflammatory phenotype resulting in a significantly lower frequency of proinflammatory Th1 and Th17 effectors cells, and increased peripheral regulatory T cells, compared to mice colonized with INFL+.

Experimental Design

SER-301 was evaluated in a spontaneous colitis model using GF 101° C57BL/6 mice. Mice were colonized with either SER-301 or a human fecal microbial transplant prepared from IBD patients (IBD FMT) and monitored for 5-8 weeks (Experiment 2a). The severity of intestinal inflammation was assessed by fecal lipocalin, histopathology (crom, colon, rectum) and flow cytometric characterization of colonic immune cell populations. The same evaluation was repeated in a second experiment (Experiment 2b), colonizing mice with SER-301 or the inflammatory composition INFL+. In both experiments, SER-301 colonization induced a noninflammatory phenotype in the colon and did not induce colitis, while colonization with IBD FMT or INFL+ significantly increased levels of lipocalin and frequency of proinflammatory T cell populations, indicative of intestinal inflammation and colitis.

Histology and Lipocalin Results

- Flow Cytometry Results

- Conclusion

CONCLUSIONS

- Preclinical assessments of SER-301 in two prophylactic mouse models of colitis show that SER-301 treatment promotes a noninflammatory immune profile in the colon and does not induce the development of colitis in germ-free (GF) C57BL/6 mice.
- Additionally, intestinal dosing of SER-301 in the 101° mouse model showed that SER-301 is capable of reversing established intestinal inflammation and the development of colitis.
- SER-301 design and in vitro properties will be presented in the Microbiome and Host Response in IBD session at 1637.
- A Phase 1b study evaluating SER-301 for the treatment of active mild-to-moderate UC is currently enrolling (ACTRN12620020853251).