CRS3123 with High Cure Rate and Low Recurrence In Toxin Positive *Clostridioides difficile* Infection

Poster: E0883

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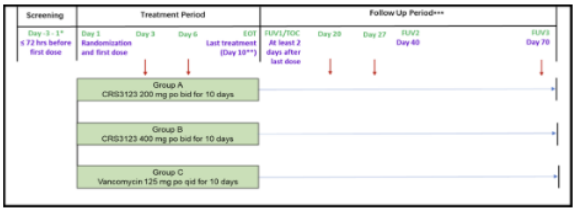
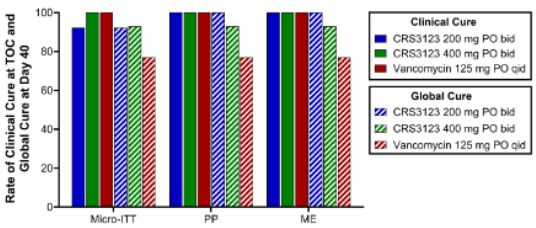
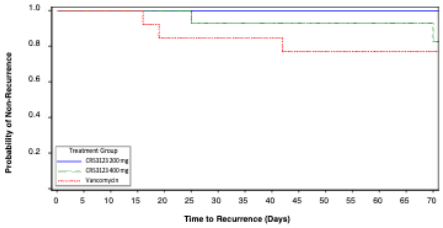
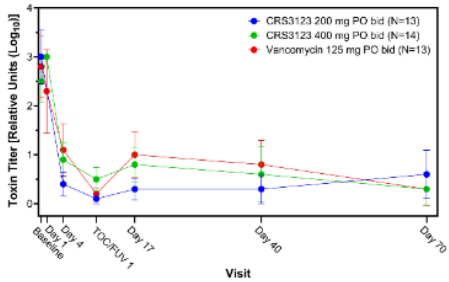
Methods: This randomized, double-blind, Phase 2 study was conducted at 31 sites in North America to evaluate the safety and efficacy of 2 oral twice daily dosages of CRS3123 (200 mg and 400 mg) and oral 4 times daily vancomycin (125 mg) for 10 days in adults with a primary episode or first recurrence of CDI. Subject enrollment required the presence of *C. difficile* toxin A or B, clinical symptoms of CDI, >3 unformed bowel movements with a Bristol Stool Score of 5, 6, or 7. A test-of-cure (TOC) assessment by the investigator was conducted at least 2 full days after end of therapy. The rate of CDI recurrence was assessed through Day 70. The primary efficacy endpoint was clinical cure at the TOC visit in the intent-to-treat (ITT) population. Key secondary endpoints included rate of recurrence of CDI through Day 40, Global Clinical cure through Day 40, and quantification of *C. difficile* toxins and spores. Plasma and fecal concentrations of CRS3123, and fecal samples for analysis of microbiome, biomarkers of inflammation, and metabolomics were obtained.

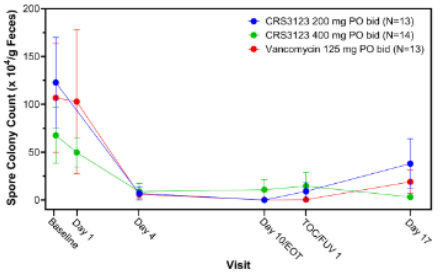


Results: 43 subjects were randomized; 14 to CRS3123 200 mg, 15 to CRS3123 400 mg, and 14 to vancomycin 125 mg. The mean age was 58.4 years. gender, race, BMI, and mean C-reactive protein were comparable across treatment groups. 31 (72.1%) subjects had a primary episode of CDI and 12 (27.9%) had a first recurrence of CDI. Clinical cure in the ITT population was achieved in 13/14 (92.86%) subjects in each of the CRS3123 200 mg and vancomycin groups, and in 15/15 (100%) subjects in the CRS3123 400 mg group. The rate of Global Cure through Day 40 in the Micro-ITT population was 12/13 (92.3%) in CRS3123 200 mg recipients, 13/14 (92.9%) in CRS3123 400 mg recipients, and 10/13 (76.9%) in vancomycin recipients. *C. difficile* toxin titers were 2.5-3.0 (log10) relative units (RU) at baseline and were rapidly reduced by Day 4 and remained lowest in CRS3123 groups post-treatment. Similarly, C. difficile spore counts were rapidly reduced by Day 4. Recurrence through Day 40 in the micro-ITT population were 3.8% (1/26) in the combined CRS3123 groups and 23.1% (3/13) in the vancomycin group. The most frequently reported treatment emergent adverse events were primarily gastrointestinal in nature and headache, mild to moderate and comparable across treatment groups.









Conclusions: Compared to oral vancomycin, CRS3123 200 and 400 mg BID for 10 days demonstrated high cure rates, lower rates of recurrence and were well tolerated. Future trials of this promising agent in CDI are warranted.

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