Preservation of Gut Microbiome Following Ridinilazole versus Fidaxomicin Treatment of Clostridium difficile Infection

C. difficile infection (CDI) is one of the most common nosocomial infections in the USA. Therapeutic options are limited with recurrent disease a particular concern.1

CDI is associated with antibiotic-induced dysbiosis, compounded by antimicrobial CDI treatments further eroding colonisation resistance, leading to recurrent disease. There is therefore a pressing need for the development of novel antimicrobials that target 5'-ribosyltransferase (C. difficile) and are safe for use in microbiome maintenance.

Ridinilazole is a novel antimicrobial for CDI that is targeted at the CDI-causing spore to ensure that there is no concern over the development of resistance.

Key exclusion criteria:

- Male or female subjects >18-90 years of age
- > 1 prior episodes of CDI in the previous 12 months
- Concurrent use of medications intended to treat CDI
- Subjects with history of inflammatory bowel disease
- Concurrent use of medications intended to treat CDI
- Pregnant or breastfeeding
- Unstable cardiovascular or renal disease
- Acute kidney disease during study
- Severe (Modified ESCMID) 2 (14.3) 0
- Had a binary toxin (CDT)
- Had severe disease at baseline
- Use of probiotics, prebiotics, or antibiotics within 30 days prior to TOC
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Methods: Study Design

- Clinical trial (2-arm, open-label, randomized, double-blind)
- Subjects randomized 1:1 to ridinilazole (330 mg bid) or fidaxomicin (200 mg bid) treatment for 10 days.
- Clinical response assessed 2 days after end of therapy (ETO) at a test of cure (TOC) visit and subjects were monitored for 30 days post ETO to ensure response.

The primary objective for the study was to compare the safety and tolerability of ridinilazole compared with FDX.

A key secondary objective was to compare the relative quantitative and qualitative impact of ridinilazole and fidaxomicin on the microbiome.

The activity of CDI and FDX was assessed through Sustained Clinical Response (SCR) defined as cure at TOC and no recurrence to 30 days post TOC EOT.

- Overall SCR rates were similar between the ridinilazole and fidaxomicin despite a higher number of subjects randomised to the ridinilazole arm (Table 2).

- There were no safety concerns identified with a similar number of subjects on each treatment arm.

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