OC-007

VSL#3 FOR THE PREVENTION OF ANTIBIOTIC ASSOCIATED DIARRHOEA (AAD) AND CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA (CDAD): AN INTERIM ANALYSIS

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Introduction CDAD is the most common health care-acquired infection in the United Kingdom and causes significant morbidity and mortality. Previous studies have reported incidences of CDAD as high as 17%. Prevention of CDAD by Probiotics co-administration during antibiotic exposure is an appealing concept, but the few previously published trials showed inconclusive data and were hindered by flaws in trial design. This trial aims to investigate whether VSL#3 will prevent AAD and CDAD in hospitalised patients exposed to systemic antibiotics.

Methods This multi-centre, randomised, double-blind, placebo-controlled trial will recruit 445 patients. One sachet of VSL#3 or placebo is given twice daily for the length of the antibiotics course and 7 days thereafter with follow-up for 28 days after the last antibiotic dose. Primary outcomes are occurrence of AAD and CDAD and secondary outcomes are length of stay (LOS) and 30-day mortality.

Results This interim analysis reports on 124 patients enrolled in the trial so far. 62 patients were randomised to the active and 62 to the placebo group. Both groups were well matched for baseline demographic patient data. The study drug was generally well tolerated, and there was no difference in the rate of serious adverse events (3 in each group). Exposure to high risk antibiotic regimens was 85.5% (active) and 74.4% (placebo), respectively. No statistically significant differences were found in primary and secondary outcomes between the active and the placebo group at interim analysis. There was, however, a trend towards less AAD in the active group on per protocol analysis (active 0%, placebo 11.4%, p = 0.11). Assuming CDAD incidences of 5% in the placebo group and 0.1% in the active group 175 participants per group (350 in total) would give 90% power to detect a difference at a significance level of 0.05.

Table 1 OC-007 Results of the interim per protocol (PP) analysis

	Active group (PP)	Placebo group (PP)	p-Value (PP)
AAD	0	4 (11.4%)	p = 0.11
CDAD	0	0	p = 1.0
LOS (days)	8	10.2	p = 0.31
30-day mortality	0	0	p = 1.0

Conclusion VSL#3 is well tolerated, and no drug-related SAE were reported. The incidences of both AAD and CDAD are much lower than previously reported. This may reflect improved infection control measures (hygiene, isolation rooms, and antibiotic policy) at the participating sites. Updated power calculations based on the lower incidences find that the original sample size is still suitable to confirm or refute the primary hypothesis.

Competing interests C. Selinger Grant / Research Support from: Ferring Pharmaceuticals, M. Lockett Grant / Research Support from: Ferring Pharmaceuticals, A. Bell Grant / Research Support from: Ferring Pharmaceuticals, S. Sebastian Grant / Research Support from: Ferring Pharmaceuticals, N. Haslam Grant / Research Support from: Ferring Pharmaceuticals.

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