Summary results

Feasibility studies to investigate the role of ursodeoxycholic acid in the prevention of recurrence of *C. difficile* infection.

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The aim of this study was to recruit thirty patients who had recently been treated for *C. difficile* infection and involved taking increasing doses of ursodeoxycholic acid for a period of 6 weeks, with follow up after a further 6 weeks.

The study was terminated early after recruitment of 6 participants, for the following reasons: (i) there was major disruption related to COVID pandemic, (ii) there has been variation in the number of eligible cases of *C. difficile* infection, (iii) potential participants are predominantly frail elderly patients, with significant co-existing illnesses and most developed *C. difficile* infection during admission to hospital for another illness. Many of those eligible considered hospital study visits to be too burdensome.

Six patients (5 female, 1 male) were recruited from 2019 to 2023. Five had been treated for first episode of *C. difficile* infection and for a second episode (1st recurrence of the infection) in the sixth subject. Three were able to tolerate gradually increasing doses (5 to 15 mg /kg) of ursodeoxycholic acid over 6 weeks and there was no recurrence of *C. difficile* infection over the 12 week study period. Three patients were able to tolerate 5 mg/kg of ursodeoxycholic acid but not a higher dose (10 mg/kg) because of symptoms (gastrointestinal symptoms and one also complained of an itchy rash). Milder episodes of most of the gastrointestinal symptoms had previously been experienced by two of these subjects and had been deemed to be due to irritable bowel syndrome. The third patient had symptoms consistent with functional dyspepsia prior to recruitment. One of the three patients that could not complete the study had a second recurrence of *C. difficile* infection 3 days after withdrawal from the study.

Preliminary conclusions of this trial that was terminated early: (i) the study protocol enabled the identification of patients with varying levels of tolerance to ursodeoxycholic acid that was started within 7 days of completion of antibiotic treatment for *C. difficile* infection (ii) for future clinical investigations of the role of ursodeoxycholic acid in the prevention of recurrence of *C. difficile* infection, recruitment may be improved by undertaking study visits in the patient's place of abode (iii) absence of preceding symptoms suggestive of functional gastrointestinal disorders may predict tolerance to higher doses of ursodeoxycholic acid.