

**First name Last name**

**Therapeutic manipulation of the human microbiome: Fecal microbiota transplantation in patients with active ulcerative colitis through superdonor selection – The RESTORE TRIAL**

**INTRODUCTION:** The gut microbiota play a pivotal role in the pathogenesis of ulcerative colitis (UC). Manipulation of the gut microbiota to restore normobiosis has therapeutic potential in IBD and could be a good alternative for the current immunosuppressive therapies. Faecal microbiota transplantation (FMT) is a novel technique of microbiome manipulation and its efficacy has been evaluated in 3 RCT’s so far (Moayeddi et al., Rossen et al., and Paramsothy et al.) with improving efficacy. There are still a lot of unanswered questions regarding the optimum treatment preparation, treatment intensity, route of administration and the role of donor pre-screening.

**AIMS AND METHODS:** The AIM of this study is to investigate whether the FMT success rate in active UC patients can be increased by intensive donor pre-screening, anaerobic preparation of the FMT and by repeated FMT. METHODS: An international multi-centre double-blind randomized sham-controlled trial will start in March 2017 at 6 hospitals in Belgium and 2 in The Netherlands. We will randomly allocate 108 patients with active ulcerative colitis (Mayo score 4-10, endoscopic Mayo score 2 or 3) in a 1:1 ratio, using a pre-established randomization list, to either ‘superdonor’ faecal microbiota transplantation or autologous fecal microbiota transplantation (=sham). Each patient will receive 4 FMT’s. At baseline FMT will be performed during sigmoidoscopy. At week 1, 2 and 3, the FMT will be administered through rectal instillation. Each FMT will be derived from one donor. Donors will be preselected based on a species richness and abundance of taxa of interest. The primary outcome will be steroid-free clinical and endoscopic remission at week 8 (Mayo score ≤2, all subscores ≤ 1, and ≥1 point reduction in endoscopy subscore). Fecal, blood and mucosal samples and questionnaires will be collected at different time points. 16S rRNA stool analysis will be performed to assess the microbial changes after FMT.

**RESULTS:** Patients will be enrolled in our trial from March 2017 until March 2019. Assuming a success rate of 40% to achieve mucosal healing at week 8 in the donor FMT arm, a treatment difference of 25% in the autologous FMT arm, a sample size of 49 patients per group is required to obtain a power of 80% and a statistical significance at the 5% level. In addition, considering 10% dropouts, a total of 108 patients will be included.

**CONCLUSION:** Since the trial will start in March 2017, results aren’t available yet, but with this promising trial design, we hope through using superdonors and by strict anaerobic preparation of the FMT, to improve the FMT success rate.