

# Supplementary Appendix

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## **Inclusion and exclusion criteria for the participants**

### Inclusion criteria:

1. Patients of both genders, over 18 years.
2. Patients that undergo an episode of CD infection (either the first episode or subsequent recurrences).
3. Presence of an episode of diarrhea, defined as  $\geq 3$  stools/24 hours, at the beginning of the episode.
4. Confirmation of the presence of CD toxin A and/or B in feces, by a direct toxin detection test or by PCR for the detection of toxin's producing genes, at the start of the episode that is going to be treated in the clinical trial (the toxin test must be positive within 7 days prior to the enrollment of the patient).

### Exclusion criteria:

1. Previous FMT.
2. Transplanted patients, except those with a solid organ transplant of more than 2 years, with good organ function.
3. Absolute neutrophil count  $< 500$  cells / $\mu$ L at the time of the enrolment in the study.
4. Pregnancy, breastfeeding, or pregnancy intentions over the course of the study.

5. Active treatment with bile acid sequestrants.
6. Positive patients for HIV except those patients with lymphocytes T CD4 count >200 cells/ $\mu$ L and viral load less than 20 copies.
7. Swallowing dysfunction or no oral motor coordination.
8. Patient admitted in an intensive care unit or expected to be admitted in an intensive care unit due to serious illness.
9. History of significant medical conditions that would not allow an adequate evaluation or follow-up of the patient.

**Table S1. Stool donor inclusion Criteria.**

<b>Inclusion Criteria</b>
Age 18-50 years (50-60 if screening for negative colorectal cancer)
Body mass index (BMI) 18-30 kg/m <sup>2</sup>
Ability to donate 2 to 5 times a week
Good overall health

**Table S2. Stool donor exclusion criteria.**

<b>Exclusion Criteria</b>
<b><i>Infectious</i></b>
History of infection or exposure to HIV, hepatitis B, or hepatitis C, syphilis, primate T-lymphotropic viruses (PTLVs), malaria, or tuberculosis
At-risk sexual contacts or behaviors or partner change in the past three months
Sexual contact, in the past 12 months, with someone who has used needles for drug or steroid use or for anything else that has not been prescribed by a doctor
Sexual contact, within the past 12 months, with someone with HIV, Hepatitis B, or Hepatitis C, with hemophilia, or receiving clotting factor concentrates. Contacting someone with hepatitis

<b>Exclusion Criteria</b>
Infection and/or treatment of any sexually transmitted disease within the past 12 months
Illicit drug use within the past three months
Previous organ or tissue transplantation
Have been in contact, within the past six months, with blood from another person, or have been punctured/cut with material that could be contaminated with blood or fluids from another person
Tattoos, piercings, acupuncture, or accidental needle stick within the past 12 months
Risk factors for Creutzfeldt-Jakob disease
Recent gastrointestinal infection (Rotavirus, <i>Giardia lamblia</i> , etc.)
Travel in the past 12 months to tropical countries with endemic diarrheal illnesses or high-risk of traveler's diarrhea
Vaccination within the last 12 months with live attenuated vaccines or any injection
Healthcare personnel or workers from hospitals and healthcare institutions (risk of transmission of multi-resistant microorganisms) or if working with animals (risk of transmission of zoonoses)
Those who have been in a prison or reformatory facility within the past 12 months or have been under arrest for more than 72 hours
Those who have experienced malaria, Chagas disease, or babesiosis or trypanosomiasis
Those who have suffered, or have anyone in their environment who has suffered, COVID-19
If you have been exposed to or are infected with monkeypox virus
Fever, frequent cough, or feeling short of breath in the past two weeks
Working with animals (to avoid the risk of transmission of zoonoses)
<b>Gastrointestinal comorbidities</b>
Inflammatory bowel disease
Irritable bowel syndrome, chronic functional constipation, or chronic functional diarrhea (per ROME IV)
Celiac disease and other chronic digestive disorders
History or high risk for gastrointestinal cancer or polyposis

<b>Exclusion Criteria</b>
A family member diagnosed with Crohn's disease or ulcerative colitis (parents, siblings or children)
Family history of colon cancer (parents, siblings or children)
Diarrhea, blood in stool, abdominal pain, or other significant digestive symptomatology within the past three months, or routinely
<b><i>Consumption of drugs that may alter gut microbiota</i></b>
Use of antibiotics, antifungals, or antivirals within the past three months
Use of Proton-pump inhibitors (PPIs) in the past three months
Use of systemic anti-cancer agents within the past three months
Taking medications related to gastric reflux, heartburn, within the past three months
Use of immunosuppressive medication or chemotherapy within the past three months
<b><i>Other reasons</i></b>
Legal inability to give consent
Active cancer process or cancer history in the past 10 years
Consumer of >28 Alcohol Standard Drink Unit (SDU) per week
Have had surgery for something in the past three months
Gastroscopy or colonoscopy within the past three months
Prior major digestive system surgery (excluding appendectomy) (parents, siblings or children)
Have had a transplant within the last 12 months
Evolved liver disease
Chronic kidney disease
Autoimmune and systemic diseases
Chronic or autoimmune systemic diseases with GI involvement
Diabetes mellitus
Metabolic syndrome
Neurological, neurodegenerative or psychiatric diseases

<b>Exclusion Criteria</b>
Symptoms of eczema or psoriasis in the past eight weeks
Food, seasonal, animal, medication, latex, dust, other allergies
Asthma in the past 12 months
Experienced symptoms or taken treatment in the past 12 months for attention deficit, hyperactivity, anxiety, and/or depression
Pregnancy or delivery or termination of pregnancy in the last six months
Vaccinations not correctly received per the vaccine schedule
Significant vascular disease