The THRIVE Study: Repurposing Fecal Microbiota Transplantation For the Treatment of Severe Acute Malnutrition in South Africa

The THRIVE study will investigate the safety and clinical response to fecal microbiota transplantation in children with severe acute malnutrition unresponsive to standard therapy.

**DISEASE/CONDITION**
- ~19 million children under the age of five are affected by severe acute malnutrition (SAM) annually.
- SAM is a life threatening condition characterized by very low weight for height and severe muscle wasting.
- There is emerging evidence that perturbations in the gut microbiota, the trillions of bacteria residing in the gastrointestinal tract, are causally related to poor recovery in malnutrition.

**CURRENT TREATMENT**
- Current approaches to treatment in correcting SAM have only modest effects with ~30% of children failing to respond to standard nutritional therapy.
- For these children who fail to respond there is a paucity of treatment options.

**SUMMARY STATEMENT**
In the THRIVE study (Transfer of Healthy Gut Flora for Restoration of Intestinal Microbiota via Enema), fecal microbiota transplantation (FMT) of healthy stool will be transferred into individuals suffering from SAM.

**PROPOSED TREATMENT**
In the THRIVE study, fecal microbiota transplantation (FMT) of healthy stool will be transferred into individuals suffering from SAM.

FMT is derived from minimally processed stool from screened, healthy donors, and is upending our understanding of seemingly intractable diseases with ongoing trials in diseases such as pediatric inflammatory bowel disease, autism and graft-versus-host disease.

FMT is widely used for the treatment of C. difficile infection and is recommended in clinical guidelines for adults and children. In this study, FMT will be delivered via enema, a standard approach for delivering FMT in pediatric patients.

This study will assess if microbiome restoration through FMT can enhance recovery in SAM and potentially unlock a new therapeutic class.

**PROJECT**
We will investigate the safety and clinical response to FMT in children with severe acute malnutrition, and assess whether microbiome restoration through FMT can enhance SAM recovery.

The THRIVE study is a single-center, two-armed, randomized controlled trial that will compare the safety of FMT administered via enema (followed by standard of care) to the standard of care only in participants 18-60 months of age with uncomplicated, non-edematous SAM not responsive to standard therapy.

Primary Objective: To evaluate the safety and tolerability of FMT compared to standard of care in pediatric patients in the rehabilitation phase of SAM who are unresponsive to standard therapy.

Secondary Objectives:
- To gather preliminary data on nutritional recovery.
- To gather preliminary data on the clinical response.
- Assess engraftment of donor microbial communities into recipients.
- Assess the capacity for FMT to normalize biomarkers associated with recovery and survival in SAM.
- Assess the regulatory and operational feasibility of scaling FMT in an LMIC context.