***Study Title**:*
*Personalized Microbiome Modulation in Pediatric Patients with Inflammatory Bowel Disease (IBD): An Interventional Study at Louis Țurcanu Children's Emergency Hospital*

NB302 identifier

---

**Background and Rationale**

Inflammatory Bowel Disease (IBD), encompassing Crohn's disease and ulcerative colitis, is a chronic, immune-mediated condition that significantly impacts pediatric patients' quality of life and long-term health. Current standard therapies, though effective for some patients, often fail to achieve sustained remission or lead to adverse effects, underscoring the need for adjunctive strategies that improve clinical outcomes. Emerging evidence highlights the intestinal microbiome's role in modulating immune responses and influencing IBD pathogenesis, positioning it as a promising target for therapeutic intervention.

This study, initiated by NostraBiome in collaboration with the Louis Țurcanu Children's Emergency Hospital, aims to evaluate the impact of AI-guided, personalized microbiome modulation on the clinical outcomes of pediatric IBD patients receiving standard therapy. Through advanced shotgun metagenomic sequencing (Next-Generation Sequencing, NGS) and comprehensive data integration, this study seeks to optimize therapeutic strategies, potentially setting a new paradigm in IBD management.

---

**Study Objectives**

**Primary Objective**

- To evaluate the effectiveness of personalized microbiome modulation, guided by AI-driven analysis, in improving clinical and paraclinical outcomes for pediatric patients undergoing standard IBD therapy.

**Secondary Objectives**

- Assess the correlation between microbiome signatures and changes in clinical symptoms, laboratory markers, and endoscopic findings.
- Identify unique microbiome signatures that may predict response to microbiome modulation.
- Build a repository of biological samples for future research on the microbiome's role in pediatric IBD.

---

**Study Design**

**Type**
Single-arm, interventional, open-label study conducted at the Louis Țurcanu Children's Emergency Hospital, Timișoara, Romania.

**Intervention**
All enrolled patients will receive the standard IBD treatment per national guidelines, along with a personalized microbiome modulation therapy. The personalized intervention is informed by AI analysis of

microbiome data and incorporates patient-specific clinical profiles, including blood tests and symptom questionnaires. Personalized microbiome therapy may include probiotics, synbiotics, postbiotics, dietary adjustments, lifestyle modifications, or selective use of antivirals or antibiotics.

**Sample Size**
Approximately 30 to 60 pediatric patients diagnosed with Crohn's disease or ulcerative colitis.

---

**Eligibility Criteria**

**Inclusion Criteria**

- Written informed consent from patients' guardians.
- Pediatric patients aged 6-18 years.
- Clinically confirmed diagnosis of Crohn's disease or ulcerative colitis.
- Receiving or eligible for standard IBD therapy as per national guidelines.
- Willingness to comply with study procedures, including microbiome sample collection and clinical assessments.

**Exclusion Criteria**

- Severe infections or concurrent diseases that may interfere with study participation.
- Recent use of systemic corticosteroids or immunosuppressants exceeding protocol limits.
- Current participation in other interventional trials involving microbiome or immune-modulating agents.

---

**Study Interventions and Schedule**

| Step | Description |
|---|---|
| **Patient Identification** | Pediatric patients with IBD referred to the Louis Țurcanu Children's Emergency Hospital. |
| **Baseline Assessment** | Collection of informed consent, baseline stool sample for microbiome analysis, blood tests, and patient questionnaires. |
| **AI-Driven Microbiome Analysis** | AI analyzes the microbiome profile, integrating shotgun metagenomic NGS data with clinical data to guide personalized therapy. |
| **Personalized Microbiome Therapy** | Following baseline analysis, a tailored microbiome modulation plan is developed, possibly including dietary modifications, probiotics, and other supportive therapies. |
| **Monitoring and Adjustments** | At Months 3 and 6, stool samples and blood tests are repeated, and patient questionnaires are administered to track clinical progress and adjust therapy if needed. |
| **Final Evaluation at Month 6** | Comprehensive assessment including stool and blood sampling, symptom evaluation, and analysis of treatment outcomes. |

Patients continue receiving standard IBD therapy throughout the study, with microbiome modulation serving as an adjunct intervention.

---

**Study Measures**

**Primary Outcome**

- Improvement in clinical symptoms and laboratory markers assessed by physician evaluations, patient-reported outcomes, and paraclinical findings (e.g., blood tests, colonoscopy results).

**Secondary Outcomes**

- Changes in microbiome composition and diversity, as measured by metagenomic sequencing, correlated with clinical outcomes.
- Identification of microbiome signatures predictive of therapeutic response.
- Repository of biospecimens (stool, blood) for future research in pediatric IBD.

---

**Sample and Biospecimen Retention**

**Biospecimens**

- Stool samples collected at baseline, Month 3, and Month 6 for microbiome analysis.
- Blood samples collected at baseline, Month 3, and Month 6 for additional biomarker analysis as needed.

---

**Timeline and Study Flowchart**

| Study Timeline | Events |
|---|---|
| **Month 0 (Baseline)** | Patient registration, informed consent, baseline microbiome and blood sampling, questionnaire completion, and initiation of personalized therapy. |
| **Month 3** | Follow-up assessments, including stool and blood sampling, clinical evaluation, and therapy adjustments based on microbiome response. |
| **Month 6 (Final Evaluation)** | Final assessments, including comprehensive stool and blood analysis, clinical evaluation, and therapy completion. |

---

**Study Schema**

| Step | Description |
|---|---|
| **Patient Identification** | Pediatric patients with Crohn’s disease or ulcerative colitis receiving standard IBD therapy. |

| | |
|---|---|
| **Baseline Sampling** | Initial stool and blood sample collection for metagenomic NGS and clinical baseline data. |
| **AI-Guided Microbiome Modulation** | Personalized microbiome modulation therapy based on patient-specific microbiome analysis and clinical profile. |
| **Monitoring at Months 3 and 6** | Stool and blood sampling, clinical evaluations, and modulation adjustments if needed. |
| **Final Evaluation** | Comprehensive clinical and paraclinical assessment to evaluate the impact of microbiome modulation therapy. |

---

**Ethical Considerations**

All participants will continue to receive the standard IBD therapy per national guidelines throughout the study. Informed consent will be obtained from patients' guardians, and the study will adhere to ethical standards to ensure patient safety, confidentiality, and integrity.

This interventional study is designed to evaluate whether AI-guided, personalized microbiome modulation can optimize clinical outcomes for pediatric IBD patients. By integrating microbiome data with comprehensive clinical profiles, this study aims to identify therapeutic microbiome signatures that could potentially transform the standard approach to pediatric IBD management.