Biomarker/BioSensor development using Modulife to achieve intestinal healing in Crohn*s disease

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In this study, we are looking at the effectiveness of following phase 3, the maintenance phase, of the Crohn's Disease Exclusion Diet (CDED) compared to normal diet (with or without standard maintenance treatment) in children and adults with...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON57360

Source
ToetsingOnline

Brief title
BIO-MODEM

Condition

- Gastrointestinal inflammatory conditions

Synonym
chronic bowel inflammation, Inflammatory Bowel Disease (IBD)

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: beurs van het ministerie van Volksgezondheid;Welzijn en Sport (VWS) (TKI-PPP Health Holland) in samenwerking met

Nestlé Health Science,Nestlé Health Science

Intervention

Keyword: Crohn's Disease, Crohn's Disease Exclusion Diet (CDED), Heartrate Variability (HRV), Intestinal Ultrasound (IUS)

Outcome measures

Primary outcome

We will assess a composite outcome of steroid-free clinical remission as Harvey Bradshaw Index (HBI) < 5 + calprotectin remission (calprotectin <200 ug/g) at week 24.

Secondary outcome

1. Composite outcome + normal CRP at week 24

2. IUS response at week 6, 12, 24

3. IUS remission at week 6, 12, 24

4. Composite steroid-free clinical remission + calprotectin response + intestinal ultrasound (IUS) response at week 24

5. Composite steroid-free clinical remission + calprotectin response + intestinal ultrasound (IUS) response + normal CRP at week 24

6. (Primary) non-response to dietary therapy at week 6 and loss of response at weeks 12, 16, 24 (with good compliance)

7. Survival analysis of loss of remission during CDED phase 3 versus normal diet, based on HBI and biweekly calprotectin measurements (week 12, 14, 16, 18, 20, 22, 24)

8. Clinical remission (HBI <5) at week 6, 12, 16, 24 with and without calprotectin response

9. Clinical remission (HBI < 5) + normal CRP at week 6, 12, 16, 24

10. Biochemical changes (CRP, calprotectin) at weeks 6, 12, 14, 16, 18, 20, 22, 24

11. Need for further therapeutic intervention at weeks 6, 12, 16, 24

12. Phase 1-2-3 of CDED and/or PEN compliance at weeks 6, 12, 16. 20, 24

13. Changes in patient reported outcomes (PRO) (Quality of Life (QoL), fatigue) at weeks 0, 6, 12, 24

14. Compliance with instructions to record HRV (x days measurements/24 (=2 days per week for first 12 weeks))

15. Changes in anthropometrics at weeks 6, 12, 16, 24, as well as body composition and hand grip strength at week 24

16. Multi-omics of dietary response, non-response and loss-of-response

17. HRV-patterns of active disease, remission/response and early signs of loss-of-response during phase 1 and 2 of the CDED

18. Association analysis of HRV, biomarkers, immune phenotyping and multi-omics of Crohn*s disease

The overarching goal of these secondary objectives is to compare CDED + PEN phase 3 and normal diet. For the observational study of HRV, analysis of HRV-data of patients from disease to response/remission will in time enable integration of biomarkers (CRP/calprotectin) and immune-phenotyping together with multi-omics analyses (epigenetics, microbiome, metabolome, transcriptomics).

Study description

Background summary

The increasing incidence of Crohn*s disease causes considerable morbidity and poses challenges for our health care due to costs of therapy/hospitalisation/surgery. We and others have shown in randomized trials that dietary self-management using the Crohn*s Disease Exclusion Diet (CDED) phase 1 and 2 + Partial Enteral Nutrition (PEN) can induce remission in children and adults, increase quality of life and reduce the need for immune-suppressing medication.
While CDED phase 1 and 2 are now included in European guidelines (presented at ESPEN 2022 and published ECCO/ESPGHAN 2020) as an alternative to Exclusive Enteral Nutrition (EEN), the CDED maintenance phase (phase 3) still lacks a strong evidence-base regarding the introduction of new foods once remission is achieved. The recently completed paediatric DIETOMICS trial and the first adult CDED study by Yanai et al. have shown clinical benefit of this approach, both in terms of maintenance of remission and mucosal healing (only Yanai et al.).
We aim to assess the efficacy of CDED + PEN phase 3 compared to a normal diet with standard-of-care (SOC) maintenance treatment in patients with mild-to-moderate CD.

To date, disease management is guided by markers of inflammation in blood and feces together with relapse of symptoms. Therefore, a secondary aim is to observationally study heart-rate-variability (HRV) as a potential non-invasive biomarker for active disease.

Study objective

In this study, we are looking at the effectiveness of following phase 3, the maintenance phase, of the Crohn's Disease Exclusion Diet (CDED) compared to normal diet (with or without standard maintenance treatment) in children and adults with mild to moderate Crohn's Disease. Secondarily, we want to investigate whether we can use Heart Rate Variability (HRV) measurement, as a non-invasive measurable indicator of active disease and remission during the first 12 weeks of the CDED.

Study design

This is an interventional open-label Randomized Controlled Trial where patients with clinical remission with CDED + PEN at week 12 (with or without stable concomitant treatment) will be randomized to continue CDED phase 3 as maintenance therapy (group A), or resume their normal diet (group B).

Intervention

1. RCT: CDED phase 3 (maintenance phase) for patients after remission with CDED phase 1 and 2 as induction of remission or as adjuvant concomitant treatment (to ongoing standard of care stable treatment)
2. Observational: Firstbeat biosensor
- Weeks 0-12: continued optional biosensor use for all participants

Study burden and risks

For some patients, following CDED + PEN will help avoid medication altogether. For patients already requiring immune suppressive medication, our approach may yield better control with their current treatment and avoid escalation or changing of expensive immune-suppression therapy. The potential benefit of the trial is that of better control of CD symptoms with a therapy that has no medical complications. Study burden consists of maintaining dietary records, optional use of a heart-rate-monitor + the accompanying app to assess HRV and stress-score, assessment of intestinal healing at baseline, week 6, 12, and 24 by means of ultrasounds and more frequent stool collection for calprotectin.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

Inclusion criteria for entering study at week 0:
1. Male or female, children >=10 years old or adults <=70 years old
2. Proven diagnosis of CD according to standard clinical guidelines
3. Mild to moderate disease activity, defined as: Harvey-Bradshaw Index (HBI) 5-14
OR evidence of active inflammation based on faecal calprotectin level >= 250 microgram/g within 30 days
prior to week 0 visit
4. Provision of signed and dated informed consent form with stated willingness to comply with all study procedures and availability for the duration of the study

Inclusion criteria for entering the RCT (maintenance phase) of the study (weeks 12-24):
1. Corticosteroid-free clinical remission
a. HBI <= 4
b. Without need for surgery / therapy escalation / therapy switch / dietary intensification (such as returning to Phase 1 CDED or starting Exclusive Enteral Nutrition)

Exclusion criteria

1. Stricturing, penetrating (intestinal or perianal) and/or fistulising disease, specifically symptoms of stenosis/sub-obstruction or radiological evidence of significant stenosis (pre-stenotic dilatation) which renders the use of CDED contraindicated
2. Inflammation limited to the rectum (proctitis)
3. Inflammation limited to intestinal segments proximal to the terminal ileum
4. Having undergone intestinal resection
5. Laboratory diagnosis of Clostridium Difficile Infection (CDI) or any other infections (SSYC), if performed for clinical indication
6. Pregnancy/lactation
7. Dual biologic therapy
8. Biologic dose escalation within previous 6 weeks

9. Present or past history of eating disorder including anorexia nervosa
10. Adhering to a vegan diet

Patients with known pre-existing conditions that may affect HRV (e.g. (congenital) heart disease or use of anti-arrhythmic drugs, other inflammatory conditions (such as SLE, JIA) and anxiety disorders), will not be offered the observational HRV measurements but can join the study without HRV measurement.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2024
Enrollment:	80
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	27-02-2025
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85226.018.24