Low Dose Naltrexone for the induction of remission in patients with mild to moderate Crohn*s Disease that failed conventional treatment

Published: 08-10-2019
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Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON52463

Source
ToetsingOnline

Brief title
The LDN Crohn study

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Crohn's Disease, Naltrexone, Remission

Outcome measures

Primary outcome

Endoscopic remission at week 12 defined as SES-CD <=2 and ulcerated surface subscore <=1 in all five segments.

Secondary outcome

• Proportion of patients in steroid free clinical remission defined as a by an HBI score of <=4 and complete tapering of systemic corticosteroids and endoscopic remission at week 12

• Response defined by a decrease in HBI of >=3 points compared to baseline and endoscopic response defined as a reduction of SES-CD score by >=50% vs baseline at week 12

• Changes in laboratory measures of inflammation (CRP, fecal calprotectin) from baseline at week 12,24 and 52

• Adverse events at every visit

• Quality of life, via the disease specific and validated sIBDQ at screening, week 4, 12, 24 and 52

• Fatigue, via the FACIT-F and MFI at screening, week 4, 12, 24 and 52

• Anxiety, Depression, Sleepdisturbance, via the PROMIS NIH at screening, week 4, 12, 24 and 52

• Healthcare costs and utilization, via WPAI and EQ5D at screening, week 4, 12, 24 and 52

• PROM, via the IBD validated PRO2-tool (at screening, week 2, 4, 8, 12, 24 and

52)

• Proportion of patients in corticosteroid free clinical remission at week 24

and 52

• Response (HBI) at week 24 and 52

• Endoscopic remission and response at week 52

• Anxiety, Depression, Sleepdisturbance, via the PROMIS NIH at screening,

week 4, 12, 24 and 52

Study description

Background summary

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder, which includes Crohn*s disease (CD) and ulcerative colitis (UC). Several drugs exist to induce and maintain remission, and these drugs are usually prescribed in a step up fashion. In contrast to UC, for patients with CD after induction of remission with corticosteroids, maintenance of remission is only achieved with immunosuppressive drugs, mainly thiopurines. Although these drugs are effective in 60% for remaining clinical remission after 12 months, the drawback of these drugs are the side effects that include bone marrow suppression, liver test abnormalities and malignancies. Pilot studies in patients with CD showed a positive effect of low dose naltrexone (LDN) therapy, with 15 of 17 patients showing a clinical response. A subsequent randomized, placebo-controlled, double blind study in 34 patients found a response rate of 88% in the LDN group versus 40% in the placebo group after 12 weeks of therapy. In addition LDN was also shown to be safe in pediatric IBD patients, and resulted in significantly reduced PCDAI scores, with 25% of patients achieving remission and 67% showing improvement of disease.(1-4)

Study objective

The aim of this preliminary study is to prospectively assess the efficacy of LDN as induction therapy in CD.

Study design

This is a multicentre, prospective, randomized, placebo-controlled study. Patients with mild to moderate active CD will be randomized 1:1 to receive

treatment with either LDN 4.5 mg or placebo for 12 weeks. After week 12 patients will be invited to participate in an open label exploratory extension study with visits at week 24, 26 and 52.

Intervention

LDN induction therapy 4.5 mg once daily or placebo orally for 12 weeks followed by open label maintenance therapy of 4.5 mg LDN once daily during one year.

Study burden and risks

Patients participating in this study will come to their habitual check-ups at the department of Gastroenterology and Hepatology. As additional burden, they will undergo a colonoscopy during screening and at week 12 and will be asked to fill out questionnaires during visits and telephone calls. During the visits blood samples and fecal samples will be collected as normal follow-up of patients with an active disease. Telephone interviews are planned at randomization, week 2 and week 6. During these calls the patients reported outcomes and clinical disease activity (HBI) will be recorded. Benefits of the proposed therapy are the anti-inflammatory effects on CD disease activity. This study will have direct impact on the management of IBD patients by determining if LDN is involved in the treatment of mild to moderate Crohn*s disease. If LDN is possible to induce remission, this drug might be regarded as a first line therapy after failure of conventional treatment in the treatment of active CD because of the oral administration and anticipated low frequency of side effects.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Doctor Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Doctor Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Age 18 or older; must have the ability to understand and sign a written ICF
• Diagnosis of Crohn*s disease >=3 months before screening.
• Objective evidence of inflammation at baseline as defined by endoscopy with mucosal ulcers in the ileum or colon or both, and a SES-CD score of 3-15.
• Concurrent therapies with stable doses of azathioprine, mercaptopurine, MTX or steroids

Exclusion criteria

• Current use of i.v. corticosteroids.
• Imminent need for in-hospital treatment.
• Pregnancy or lactation.
• Current treatment with investigational drug; current or past treatment within 3 months prior to randomization with a biological agent.
• Stool sample positive for Clostridium difficile (C. diff) toxin, pathogenic Escherichia coli (E. coli), Salmonella species (spp), Shigella spp, Campylobacter spp, or Yersinia spp.
• Other significant illnesses that may interfere with the study, stricture causing obstructive symptoms, or fistulising disease complicated by infection.
• Opiates use or drugs and/or alcohol abuse.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	14-01-2021
Enrollment:	122
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Naltrexone
Generic name:	Naltrexone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	08-10-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	31-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	23-11-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2019-000852-32-NL
CCMO	NL69149.078.19

Study results

Date completed: 01-05-2024

Summary results
Trial ended prematurely