Lengthening Adalimumab Dosing Interval in quiescent Crohn*s disease patients: the LADI study.

Published: 08-12-2016
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To assess non-inferiority of extending the adalimumab dosing interval, under strict disease monitoring in CD patients in sustained (>9months) clinical remission, compared to standard care.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational non invasive

Summary

ID

NL-OMON47881

Source
ToetsingOnline

Brief title
Lengthening Adalimumab Dosing Interval in Crohn*s disease.

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohn's disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Adalimumab, Crohn's disease, Lengthening dosing interval

Outcome measures

Primary outcome

Primary outcome: The difference in cumulative incidence of persistent flares

between the dose reduction and usual care groups at 48-week follow-up.

Secondary outcome

Secondary outcomes

• Cumulative incidence of patients with transient flare (duration <8 weeks)

• Disease activity measured by HBI

• PROM: PRO-2 (abdominal pain and stool frequency).

• Adalimumab trough levels

• Anti-adalimumab antibody levels

• Adverse event rates (including injection site reactions and infections)

• Quality of life (IBDQ and EQ-5D-5L)

• Costs from a health care and societal perspective

• Medication changes during 2 year observational follow-up

Study description

Background summary

Adalimumab is both an effective induction and maintenance therapy for Crohn*s disease (CD). Due to the risk of side effects (infection, infusion reaction) and high costs, this drug should be used as efficient as possible. Lengthening the dosing interval has never been investigated in a randomized controlled trial in CD patients.

Study objective

To assess non-inferiority of extending the adalimumab dosing interval, under strict disease monitoring in CD patients in sustained (>9months) clinical remission, compared to standard care.

Study design

Multicenter, randomized controlled, open label non-inferiority trial, with two treatment arms.

Study burden and risks

In this study patients will have to visit the site every 12 weeks which is slightly more than the usual 2-3 times per year. This will allow strict monitoring of disease control and timely intervention in case of flares. In terms of diagnostics, blood tests/ fecal tests and questionnaires will be performed 4 times per year. Additionally, patients in both arms will be interviewed via telephone every 6 weeks in between clinical visits to assess for symptoms and potential disease activity. The work-up in case of a suspected disease relapse includes switching back to the prior injection interval. Risk of intevral extension includes a higher risk of disease flare. It is anticipated that most patients will enter remission upon subsequent adjusting the injection interval. Study patients may benefit from reduced exposure to adalimumab, reduced risk of injection reactions, and potentially less side effects including risk of infectious complications.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age 18 or older
- Diagnosis of colonic and/or distal ileal CD
- Sustained steroid-free clinical remission for 9 months whilst being treated with adalimumab at a stable dose
- Adalimumab dosed at 40 mg every 2 weeks
- Full clinical response and disease control, all three criteria below need to be fulfilled prior to enrollment:
1. Absence of intestinal or extra-intestinal symptoms, as judged by both patient and physician
2. Fecal calprotectin (FC) lower than 150 µg/g and CRP <10 mg/L
- If endoscopic remission was recently confirmed, FC can be lower than 250 µg/g
3. Harvey Bradshaw Index (HBI) <5

Exclusion criteria

- Absence of written informed consent
- Concomitant corticosteroid usage
- Need for IBD-related surgery
- Actively draining peri-anal fistula
- Pregnancy or lactation
- Other significant medical conditions that might interfere with this study (such as current/recent malignancy, immunodeficiency syndromes and psychiatric illness)
- Impossibility to measure outcomes, e.g. planned relocation, language issues, short life expectancy

Study design

Design

Study phase:	4
Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-05-2017
Enrollment:	174
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-12-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-01-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	29-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-07-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-08-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	30-07-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-04-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 21837
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2016-003321-42-NL
ClinicalTrials.gov	NCT03172377
CCMO	NL58948.091.16
OMON	NL-OMON21837