Lengthening Adalimumab Dosing Interval in IBD patients in long term remission, the LADI study.

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To assess the safety of lengthening the adalimumab dosing interval from 2 to 3 weeks, in patients with Crohn*s disease or ulcerative colitis in long term (6 months) remission.

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

Summary

ID

NL-OMON40962

Source
ToetsingOnline

Brief title
LADI study

Condition

- Gastrointestinal inflammatory conditions

Synonym
Inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,fonds NutsOhra aangevraagd;indien nodig financiering uit 1e geldstroom

Intervention

Keyword: Adalimumab, Crohn's disease, Remission, Ulcerative colitis

Outcome measures

Primary outcome

Non-inferiority, defined as no significant difference in HBI and SCCAI scores

between control and intervention groups

Secondary outcome

adherence to therapy

quality of life

cost-effectiveness

Study description

Background summary

The inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the gastrointestinal tract. Two entities exist within IBD, namely Crohn*s disease (CD) and ulcerative colitis (UC). These two entities differ in type, site and extent of inflammation, disease history and extraintestinal manifestations. Though the pathogenesis of these diseases is not fully understood, it is known that a chronic up-regulation of the enteric mucosal immune system, reacting to intestinal bacterial flora, plays an important role. IBD is a common disease that affects many people, it*s incidence is similar to diabetes mellitus type I and epilepsy. Furthermore, the incidence of IBD has been rising over the last few decades, most likely due to a non-genetic, life-styleassociated influence on the disease course. A particular increase in incidence has been observed for young CD patients. For the Netherlands it is expected that the prevalence of IBD will increase by 7% in the coming decade, on top of approximately 80.000 Dutch patients already diagnosed with IBD. The goal of IBD therapy is to induce rapid and sustained disease remission. Currently, guidelines advise a step-up approach, where initial therapy consists of the least effective and simultaneously least toxic medication. Currently, the first tier of therapy is mesalazine is for mild-to-moderate UC and CD. If this therapy fails, corticosteroids and immunosuppressives form the second tier of the step-up approach. Finally, if these therapies also fail to induce or

maintain remission, anti-TNFα therapy is initiated. The use of such therapies is currently widely established for both CD and UC patients. In the previously reported DELTA1 cohort, 50% of the newly diagnosed IBD patients received anti-TNFα treatment within 18 months of their diagnosis. However, this anti-TNFα treatment is associated with high monetary costs.Specifically, in a representative Dutch population of CD patients, anti-TNFα therapies are the cause of 64.1% of all CD related healthcare costs, with adalimumab (ADA) accounting for 33.9% of all CD related costs.
ADA is a fully human monoclonal IgG antibody against TNFα. It*s effectiveness for inducing and maintaining remission in IBD patients has been studied in several trials. The ADA dose in the maintenance phase of these studies was 40mg, administered subcutaneously every other week.
Original phase-I pharmacokinetic studies of ADA have shown that the mean half-life after the first administration lies between 15 to 19 days. However, after 5 months of treatment, the mean half-life increases to 21 days.
Given these pharmacokinetic data, it seems feasible to lengthen the dosing interval of ADA from 2 to 3 weeks in IBD patients in longterm remission. If this increased interval does not result in more disease relapse, the cost-effectiveness of ADA would clearly improve. To our knowledge, no such studies have been performed in IBD patients, nor in other patient populations. As such, the aim of this study is to investigate the effects on the efficacy of ADA maintenance therapy in IBD patients in long term remission, after lengthening the ADA dose interval from 2 to 3 weeks.

Study objective

To assess the safety of lengthening the adalimumab dosing interval from 2 to 3 weeks, in patients with Crohn*s disease or ulcerative colitis in long term (6 months) remission.

Study design

Single center, randomized controlled,open label non inferiority study with two treatment arms

Intervention

Adalimumab every 3 weeks

Study burden and risks

In this study patients will have to visit the site more frequently and additional blood samples will be drawn each visit.
The work-up in case of suspected relapse is not different from daily practice, and does not result in additional burden.

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
Written informed consent.
Previous diagnosis of ileocolonic Crohn*s disease or ulcerative colitis
In sustained clinical remission for at least 6 months whilst being treated with adalimumab
Adalimumab dosed at 40mg, once every 2 weeks
Full clinical response and disease control, defined as
-Absence of intestinal or extra-intestinal symptoms, as judged by both patient and physician
-Fecal calprotectin < 200 µg/g and CRP within normal range
-Full endoscopic remission (no ulcera) assessed at least within 12 months before inclusion
Permitted concomitant therapy: aminosalicylates, azathioprine, 6-mercatopurine and methotrexate at stable dose for 12 weeks

Exclusion criteria

Concomitant corticosteroid usage
Imminent need for IBD-related surgery
Actively draining perianal fistula
Pregnancy or lactation
Other significant medical illness that might interfere with this study (such as current malignancy, immunodeficiency syndromes and psychiatric illness)

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2014
Enrollment:	80
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	28-05-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-08-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-10-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-03-2015
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	EUCTR2014-001919-39-NL
CCMO	NL48890.078.14