Adalimumab dose reduction aiming low serum concentration with control of disease activity (ADDORA-LOW) : a single blind, non-inferiority, randomised clinical trial

Published: 18-10-2019
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Primary objective: to evaluate the disease activity after dose reduction, aiming adalimumab concentration of 2 mg/L or 5 mg/L, in rheumatoid arthritis patients responding to adalimumab.Secondary objectives: to evaluate whether reducing adalimumab...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON55177

Source
ToetsingOnline

Brief title
ADDORA-low

Condition

- Autoimmune disorders

Synonym
Rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Reade
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Adalimumab, Dose reduction, Rheumatoid arthritis

Outcome measures

Primary outcome

The primary study endpoint is the difference in mean time weighted DAS28-CRP

between week 0 and 24.

Secondary outcome

Difference in mean time weighted DAS28-CRP between study groups after 12 weeks

Direct medical costs (medication, non-scheduled visits due flares, cost TDM

testing) over 24 weeks

Agreement between algorithm predicted and measured adalimumab concentrations at

week 24.

Number of flares and dose-interval shortenings after 24 weeks.

Study description

Background summary

Several prior studies have shown that dose reduction or discontinuation of tumor necrosis factor (TNF)-inhibitors, like adalimumab, is possible in substantial number of patients with a rheumatic disease without an increase in disease activity. Prior studies showed that patients with concentrations higher than 5 mg/L are overexposed to adalimumab and can safely reduce the dose. In the first phase of treatment, an adalimumab concentration of 5mg/L is needed to achieve adequate clinical response. However to control disease activity after 28 weeks, lower concentration than 5 mg/L are probably sufficient. Recent published data suggest that concentrations of 0.1-0.5 mg/L are enough to

control TNF blockade in this state. Yet, a study which investigates the lowest effective drug serum concentration is missing so far. We hypothesize that serum adalimumab concentration of 2 mg/L is sufficient to control disease activity.

Study objective

Primary objective: to evaluate the disease activity after dose reduction, aiming adalimumab concentration of 2 mg/L or 5 mg/L, in rheumatoid arthritis patients responding to adalimumab.
Secondary objectives: to evaluate whether reducing adalimumab dose aiming a concentration of 2 mg/L is superior in costs savings compared to dose tapering aiming adalimumab concentration of 5 mg/L; to evaluate the algorithm used to achieve target concentration of 2 mg/L or 5 mg/L; to study the difference in cumulative incidence of flares between the two study groups

Study design

single blinded randomized, non-inferiority, trial

Intervention

Patients are randomly assigned to dose reduction aiming a drug level of respectively 2 mg/L or 5 mg/L

Study burden and risks

We hypothesize that dose reduction aiming a drug level of 2 mg/L is possible with disease activity remaining stable, however, an increased disease activity risk cannot be excluded.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

Rheumatoid arthritis patient, according to ACR 1987/2010 criteria;
Treated for at least 28 weeks with adalimumab
Adalimumab trough concentration >5mg/L
Who has agreed to participate (written informed consent);
Age 16 years or older.

Exclusion criteria

Scheduled surgery during the follow-up of the study or other pre-planned reasons for treatment discontinuation
Life expectancy shorter than follow-up period of the study;
No other disease that might flare if adalimumab is tapered like psoriasis, inflammatory bowel disease

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-05-2019
Enrollment:	89
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Humira, Amgevita, Hulio, Hyrimoz, Imraldi, Amgevita
Generic name:	Adalimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-10-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	05-11-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	12-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	25-01-2022
Application type:	Amendment
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
EudraCT	EUCTR2019-001793-28-NL
CCMO	NL69883.029.19