Adalimumab dose reduction aiming low serum concentration with control of disease activity

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24020

Source
Nationaal Trial Register

Brief title
ADDORA-low

Health condition

Rheumatoid arthritis

Sponsors and support

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

Intervention

Outcome measures

Primary outcome

The primary objective is to evaluate the disease activity after dose reduction, aiming adalimumab concentration of 2 mg/L or 5 mg/L

Secondary outcome

The secondary objectives are 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 and to study the difference in cumulative incidence of flares between the two study groups

Study description

Background summary

Biological agents are frequently prescribed to optimize rheumatoid arthritis care. In order to prevent joint destruction it is necessary to maintain remission or low disease activity. Up to now clinicians used to continue the initial treatment regimen to maintain remission or low disease activity. Since biologic therapy is expensive, and is associated with patient burden as dose dependant risk for serious infections, multiple studies have been performed to show that a large proportion of patients with rheumatoid arthritis with stable low disease activity can reduce their dose without relapse of disease. Currently, most clinicians use Disease Activity Score in 28 joints (DAS28) and the Clinical Disease Activity Index (CDAI) to monitor dose reduction strategies. Although disease activity guided dose reduction is safe and cost-effective, a relatively novel strategy is dose reduction using serum drug concentrations (therapeutic drug monitoring).The rationale behind therapeutic drug monitoring is that medication dose correlates with serum drug levels and drug concentration correlates with therapeutic effect. The latter notion is demonstrated for adalimumb by Pouw et al. Adalimumab serum concentration in a range 5–8 mg/L is sufficient for adequate response. In the first phase of treatment, drug concentration must be high enough to control immunogenicity. To control disease activity in the 2nd phase (after 28 weeks), lower concentrations than 5 mg/L are probably sufficient. Our study group illustrated in 2018 that reducing adalimumab dose by prolonging the dosing interval with 50%, is non-inferior to continuation in patients with adalimumab levels > 8mg/L. In addition, recent published data suggest that concentrations of 0.1-0.5 mg/L are enough to control TNF in this phase. 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

We hypothesize that serum adalimumab concentration of 2 mg/L is sufficient to control disease activity in patients with stable rheumatoid arthritis disease.

Study design

-2,0,12,24 weeks

Intervention

Rheumatoid arthritis patients using adalimumab for at least 28 weeks and trough serum concentration of >5mg/L will be randomly assigned to dose reduction aiming a drug level of respectively 2 mg/L or 5 mg/L

Contacts

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Eligibility criteria

Inclusion criteria

Rheumatoid arthritis patient, according to ACR 1987 ACR/EULAR 2010 criteria
Treated for at least 28 weeks with adalimumab
Adalimumab trough concentration >5mg/L
Who has agreed to participate (written informed consent);
Age 18 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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-12-2019
Enrollment:	89
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
To avoid duplication of research, the gathered data will be shared once all desirable data analysis have been performed and the results are published

Ethics review

Positive opinion

Date:	03-12-2019
Application type:	First submission

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
NTR-new	NL8209
Other	METC VU : METC 2019.250 CCMO NL69883.029.19 EudraCT 2019-001793-28

Study results

Summary results
N/A