Adalimumab drug optimisation in rheumatoid arthritis using therapeutic drug monitoring (ADDORA): multi-centre open label randomised controlled trail

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Adalimumab dose reduction based on serum drug concentration will not affect clinical efficacy of adalimumab, while it will minimize medical costs.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26185

Bron
Nationaal Trial Register

Verkorte titel
ADDORA

Aandoening

Rheumatoid arthritis

Ondersteuning

Primaire sponsor: Reade Rheumatology Research Institute
Overige ondersteuning: ZonMw: The Netherlands Organisation for Health Research and Development

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The main objective is to evaluate whether adalimumab dose reduction using adalimumab serum concentration will minimize medical costs, compared to disease activity guided dose reduction in rheumatoid arthritis patients

Toelichting onderzoek

Achtergrond van het onderzoek

Since the introduction of biologics in rheumatology, as well as treat-to-target (measuring disease activity and adapting treatment accordingly) the prognosis of patients has improved substantially. Obviously, patient burden due to self-injection or infusion, the risk of adverse events and costs demand responsible use of these agents. Multiple studies have shown that a large proportion of patients with rheumatoid arthritis with stable low disease activity can taper their dose or stop without relapse of disease activity. This can be done by using disease activity guided tapering. Drawbacks, however, include increased risk for short lived flares, the effort of slowly and carefully tapering, and somewhat more risk of radiographic damage due to higher mean disease activity.As most biologics are characterized by wide variation in pharmacokinetics between patients, therapeutic drug monitoring (TDM), i.e. dose based on serum trough concentration, might be an attractive approach to lower the dose quickly while remaining clinical efficacy. Although some data suggest that the minimal effective concentration varies between patients, we demonstrated in an earlier study that serum adalimumab concentration of 5 mg/L is enough for initial response to adalimumab. In the first phase of treatment, drug concentration must be high enough to control immunogenicity. To control disease activity after 28 weeks, lower concentrations than 5 mg/L are probably sufficient. Since around 70% of the patients have an adalimumab concentration above 5 mg/l, we assume that dose reduction to achieve these lower targets (for example direct doubling of interval in patients with levels > 10 mg/L) will result in the lowest effective drug dose. Our study group illustrated in 2018 that dose reduction by extending the dosing interval with 50% is non inferior to continuation of standard dose in patients with adalimumab levels > 8mg/L. In other words, measuring drug concentrations can help clinicians to select overexposed patients to reduce the dose of adalimumab without adversely affecting clinical efficiency. We posit that therapeutic drug monitoring can attribute to a more efficient dose reduction strategy. Since steady state drug concentrations are achieved within 16 weeks of treatment, we expect that the dose can be reduced from this point. This is earlier in treatment compared to the strategy using disease activity alone, namely after 6 months of treatment. Conceptually, such a test can improve disease activity guided dose reduction in two ways: 1) flaring caused by empirical tapering (i.e. through trial and error) below the minimal effective concentration would be avoided, and 2) patients can be directly given their minimum effective dose instead of empirical tapering, thereby saving time and drugs. Our aim is to investigate whether the use of drug levels can attribute to a

more efficient dose reduction strategy of adalimumab in patients with RA. In this study we will compare costs and clinical efficiency of two dose reduction strategies: a strategy using drug concentration versus a strategy using disease activity scores. We expect that direct medical costs will be lower in the ‘drug concentration guided’ strategy because: 1) overexposed patient can reduce the dose more timely and, 2) adalimumab dose can be further reduced after 6 months of treatment since we posit that adalimumab concentration of 2 mg/L is sufficient to control disease.

Doel van het onderzoek

Adalimumab dose reduction based on serum drug concentration will not affect clinical efficacy of adalimumab, while it will minimize medical costs.

Onderzoeksopzet

0,4,16,28,40,52,80 weeks

Onderzoeksproduct en/of interventie

Rheumatoid arthritis patients treated with adalimumab will be randomly assigned to a dose reduction strategy using disease activity scores or to a dose reduction strategy using serum drug concentrations

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Rheumatoid arthritis patient, according to ACR 1987 or ACR/EULAR 2010 criteria;
Starting adalimumab as the first biological therapy
Who has agreed to participate (written informed consent);
Age 18 years or older.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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;
Other disease that might flare if adalimumab is tapered like psoriasis, inflammatory bowel disease.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	03-12-2019
Aantal proefpersonen:	267
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

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

Ethische beoordeling

Positief advies

Datum:	03-12-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8208
Ander register	METC VUmc : METC 2019.190 CCMO NL68946.029.19 EudraCT 2019-001554-25

Resultaten

Samenvatting resultaten
N/A