Using adalimumab serum concentration to choose a subsequent biological DMARD in rheumatoid arthritis patients failing adalimumab treatment

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We hypothesis that a switching strategy based on adalimumab concentration is superior to usual care switching in rheumatoid arthritis patients failing adalimumab.

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

Samenvatting

ID

NL-OMON24414

Bron
NTR

Verkorte titel
ADDORA-switch

Aandoening

Rheumatoid arthritis

Ondersteuning

Primaire sponsor: Reade Rheumatology Research Institute
Overige ondersteuning: ZonMw, Sanquin diagnostics

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary objective is to evaluate whether a switching strategy based on adalimumab concentration is superior to usual care switching in rheumatoid arthritis patients failing adalimumab treatment with regard to mean time weighted DAS28CRP at 28 weeks.

Toelichting onderzoek

Achtergrond van het onderzoek

Over the last decades biopharmaceuticals such as agents against tumor necrosis factor (TNF), are frequently prescribed to optimize rheumatoid arthritis treatment. Although TNF-inhibitors such as adalimumab, etanercept and infliximab, have improved the treatment of rheumatoid arthritis, a proportion of patients discontinue the treatment because of inefficacy or intolerance. Where TNF-inhibitor have failed, mainly two treatment approaches are available: switch to another TNF-inhibitor or to a biological with a different mode of action (notably rituximab, abatacept or tocilizumab) or to a target synthetic DMARDs. The EULAR recommendation for the management of rheumatoid arthritis advocate that any biologic agent including a subsequent TNF-inhibitor can be used with equal chance for effect in case of non-response to a previous TNF-inhibitor. Although it seems that indeed on a group level response to a non-TNF-inhibitor is comparable to a second TNF-inhibitor after the first TNF-inhibitor has failed, using therapeutic drug monitoring could identify subgroups of patient who would benefit more from either a non TNF-inhibitor or a TNF-inhibitor as next treatment. Here we explore the underlying pathophysiological mechanisms for this hypothesis. Nonresponse on adalimumab in RA can have different causes. Firstly, the patient might not be sensitive to TNF blockade at all, or the patient develops this trait later on (primary nonresponse or secondary nonresponse). In these patients, switching to a non-TNF-inhibitor might conceptually be superior to starting a second TNF-inhibitor. However, in other patients nonresponse (either primary or secondary) might be caused by inefficient drug concentration because of development of antidrug antibodies against adalimumab. In these patients a TNF-inhibitor might be just as effective as a non-TNF-inhibitor, as these patients have drug- but not class failure. Thus, testing of adalimumab levels might be helpful in channelling patients to their most optimal treatment.However, a diagnostic study comparing a serum concentration guided versus usual care switching strategy has not yet been performed.

Doel van het onderzoek

We hypothesis that a switching strategy based on adalimumab concentration is superior to usual care switching in rheumatoid arthritis patients failing adalimumab.

Onderzoeksopzet

-2,4,12,24 weeks

Onderzoeksproduct en/of interventie

Rheumatoid arthritis patients failing adalimumab treatment will be randomly assigned to switching strategy using drug concentration or usual care switching

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;
Recently failed treatment with adalimumab (defined as DAS28-CRP >2.9) and not treated with a subsequent biological DMARD (bDMARD) or target synthetic DMARD (tsDMARD)
Who has agreed to participate (written informed consent);
Received adalimumab for at least 10 weeks in standard dosing (40mg subcutaneously every other week, either in monotherapy or combined with methotrexate or leflunomide);
Stop adalimumab due to inefficacy, either alone or combined with side effects;
Age 16 years or older.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Treatment with another TNF inhibitor prior to adalimumab
Treatment with all non-TNFi options (abatacept, rituximab, sarilumab and tocilizumab) prior to adalimumab

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 possibility to safely receive an TNF-inhibitor or a non TNF-inhibitor

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	31-07-2020
Aantal proefpersonen:	84
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	NL8210
Ander register	Commissie Mensgebonden Onderzoek Regio Arnhem-Nijmegen : METC 2019-5397 CCMO NL69841.091.19 EudraCT 2019-001754-25

Resultaten

Samenvatting resultaten
N/A