Onderzoek naar non inferioriteit van afbouw en stop behandelstrategieën van adalimumab of etanercept bij patiënten met reumatoïde artritis: Kosten besparen tegen welke prijs?

Gepubliceerd: 21-12-2011 Laatst bijgewerkt: 15-05-2024

Dose reduction and withdrawal is non inferior to continuation of adalimumab or etanercept in RA patients with respect to disease activity.

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

Samenvatting

ID

NL-OMON20595

Bron
NTR

Verkorte titel
DRESS (Dose REduction Strategies of Subcutaneous TNF inhibitors)

Aandoening

Rheumatoid Arthritis, adalimumab, etanercept, dose reduction

Ondersteuning

Primaire sponsor: Sint Maartenskliniek Nijmegen, department of rheumatology
Overige ondersteuning: Sint Maartenskliniek Nijmegen, department of rheumatology

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

17-03-2013: Newly formulated primary outcome:

Asses whether the difference in cumulative incidence in persistent RA flares (DAS28 increase of more than 1.2 or a DAS28 increase of more than 0.6 with a current DAS28≥3.2) with a duration of >3 months between the intervention group and the usual care group does not exceed the non-inferiority margin of 20% after 18 months follow up.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:
TNF Blocking agents are effective in the treatent of Rheumatoid Arthritis (RA), with adalimumab and etanercept being the two most frequently used agents in the Netherlands. These drugs are associated with side effects, including a dose dependent increased risk for infection. Also, these agents are much more expensive than traditional anti-rheumatic drugs (DMARDs), thus increasing the costs of treatment. Therefore, it seems rational to give these drugs in the lowest effective dose and stop the treatment when it is no longer necessary.

There are data that suggest that dose reduction and withdrawal of TNF blocking agents is feasible in a subgroup of patients without relevant increase in disease activity. However, a number patients will not be able to reduce doce and will develop a temporary increase in disease activity. Therefore it is usefull to find predictive factors for succesfull dose reduction.
Objectives:
The main objectives are to evaluate effectiveness, cost effectiveness and safety of a dose reduction and withdrawal strategy compared to usual care and to find predictive factors for succesfull down titration/withdrawal.
Study design:
Pragmatic open randomised controlled cost effectiveness strategy trial, stratified for anti-TNF agent. This study has an induction phase from 0-9 months and a maintenance phase from 6 to 18 months.
Study population:
Patients with rheumatoid arthritis using adalimumab or etanercept for at least 6 months and stable low disease activity during this time.
Intervention:
Control group: usual care with tight control. A visit is planned every three months, DAS28 measurement is provided on the day of the outpatient clinic visit. There is a standardised protocol wich offers treatment suggestions in case of loss of response and patients are encouraged to contact the outpatient clinic when they experience more complaints.
Intervention group:

Background treatment, monitoring of disease, tight control and flare criteria is the same as in the usual care group.

With addition of a dose reduction and withdrawal strategy advice to the treating rheumatologist. If a patient uses adalimumab, the interval will be stepwise increase every three months: 14,21,28 days and stop. For etanercept: 7,10,14 days and stop. In case of a persistant flare, the interval is shortened back to the last effective interval.
Outcomes:
The primary outcome of this study will be the cumulative incidence of flare in intervention and usual care group after 8 and 18 months of follow up.

Secondary outcomes of this study include cost effectiviness ratio between intervention and usual care group. Predictive factors for succesfull dose reduction and progression of radiological damage.

Doel van het onderzoek

Dose reduction and withdrawal is non inferior to continuation of adalimumab or etanercept in RA patients with respect to disease activity.

Onderzoeksopzet

Visit at 0,3,6,9,12,15,18 months in both groups
In case of flare of disease activity an extra visit is planned.

Onderzoeksproduct en/of interventie

Randomisation into control or intervention group.
In the control group usual care and tight control (visit every 3 months, extra visit in case of flare, DAS28 measurement on day of outpatient clinic visit, standardised treatment protocol)is provided.

In the intervention group tight control is provided and the treating rheumatologist is advised to try to increase the interval of adalimumab or etanercept.
If a patient uses adalimumab the dosage will be kept the same and the interval will be stepwise increased every three months from 14 to 21 to 28 days, after that the adalimumab will be stopped. If a patient uses etanercept, the dosage will be kept the same and the interval will be stepwise increased very three months from 7 to 10 to 14 days, after that the etanercept will be stopped. When a persistent flare occurs in disease activity, the treatment is intensified and interval is shortened back to the last effective interval.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Rheumatoid arthritis (either 2010 ACR RA20 and/or 1987 RA21 criteria and/or clinical diagnosis of the treating rheumatologist, fulfilled at any time point between start of the disease and inclusion);
2. Using either adalimumab or etanercept (all dose/interval regimens, all background medication including DMARDs and corticosteroids up to 5 mg, higher doses of steroids should be reduced first);
3. 6 months of stable low disease activity while using adalimumab or etanercept (operationalised by either a DAS28 < 3.2 or judgment of low disease activity by rheumatologist at at least two subsequent visits);
4. 6 months stable treatment with adalimumab or etanercept (previous dose reduction/interval increase is allowed when more than three months ago) and stable DMARDs and corticosteroids for more than 4 weeks;
5. Previous (unsuccessful) dose de-escalation of current or previous biological is no exclusion criterion;
6. Informed consent
7. Ability to measure the outcome of the study in this patient (e.g. life expectancy > 1 year, no planned relocation);
8. Ability to read and communicate well in Dutch.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

Co morbidity that also requires treatment with anti-TNF and thus prevents dose reduction.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	12-12-2011
Aantal proefpersonen:	180
Type:	Werkelijke startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Ethische beoordeling

Positief advies

Datum:	21-12-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 38325
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3068
NTR-old	NTR3216
CCMO	NL37704.091.11
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON38325

Resultaten

Samenvatting resultaten
https://pubmed.ncbi.nlm.nih.gov/25858265/