Dose reduction of infliximab in Crohn's disease, based on serum infliximab concentration.

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The per patient annual infliximab dose can be lowered in Crohn’s disease patients in stable remission using dose reduction guided by serial trough level measurements.

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

Samenvatting

ID

NL-OMON22458

Bron
NTR

Verkorte titel
REDIX

Aandoening

Crohn's disease
Ziekte van Crohn

Ondersteuning

Primaire sponsor: Academic Medical Center
Overige ondersteuning: Academic Medical Center

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Proportion of patients with sustained clinical remission

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: Recent observations suggest that not all Crohn’s disease (CD) patients who are in stable remission with infliximab (IFX) maintenance therapy may need the recommended dose of 5 mg/kg, as long as IFX trough levels (TLs) (e.g. serum drug level measured just before the next administration) remain therapeutic.

Objectives: To evaluate the efficacy and safety of infliximab dose reduction guided by serial trough level measurements, compared to treatment as usual (no dose reduction), in Crohn’s disease patients who are in stable remission with infliximab maintenance therapy.

Study design: Single-blind prospective controlled randomized trial.

Study population: Patients with CD older than 18 years, at least 6 months in remission defined as a Harvey Bradshaw index (HBI) ≤4, normal serum C-reactive protein (CRP) level (< 5 mg/l) and low fecal calprotectin level (< 250 ug/g) who have received IFX therapy >6 months at 5 mg/kg every 8 weeks without dose adjustments. These patients are eligible if they have an IFX TL >7 µg/ml.

Intervention (if applicable): Patients in the intervention arm will undergo stepwise dose reduction of IFX. IFX dose will be decreased by 1 mg/kg, every 16 weeks. Dose reduction ends in case of one or more of the following:

-Relapse, defined as:

- Rise of ≥3 points (compared to baseline) of total HBI score to a value of >4 (clinical relapse) in combination with CRP >5 mg/l

- AND/OR calpro >250 measured at previous infusion visit

-AND/OR IFX TL <7 prior to the latest infusion.

Patients in the control arm will receive continued IFX at 5 mg/kg at an 8 week interval.

Main study parameters/endpoints:
PRIMARY ENDPOINT: Proportion of patients with sustained clinical remission.
SECONDARY ENDPOINTS: Proportion of patients with clinical and biochemical relapse; Time to relapse; Presence of predictive factors for successful IFX dose reduction with specific focus on smoking status, body mass index and extent of disease; Laboratory tests (CRP and fecal calprotectin) at all study visits; Adverse events; Economic evaluation; Pharmaco-economic

evaluation; Quality of life; Yearly total IFX dose per patient.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participation will result in additional blood sampling, since TLs will be measured every 8 weeks. However, no additional venous punctures will be performed, since blood sampling is performed directly before IFX infusion. All other laboratory tests can be considered as routine care. No additional hospital visits are required.

Current evidence indicates that TLs >3 suffice, and dose reduction will be only performed when TLs remain >7. We expect that IFX dose reduction while maintaining adequate TLs is not associated with an increased risk of relapse. Moreover, we hypothesize that reducing IFX dose in patients with supratherapeutic TLs, will lead to less side effects.

Doel van het onderzoek

The per patient annual infliximab dose can be lowered in Crohn’s disease patients in stable remission using dose reduction guided by serial trough level measurements.

Onderzoeksopzet

Primary endpoint: after 24 months of treatment.

Onderzoeksproduct en/of interventie

Patients in the intervention arm will undergo stepwise dose reduction of IFX. IFX dose will be decreased by 1 mg/kg per step. The dose reduction phase ends in case of relapse and/or if trough levels drop below < 3 µg/ml.

Patients in the control arm will receive continued IFX at 5 mg/kg at an 8 week interval.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Diagnosis of CD based on endoscopy and pathology;

2. 18 years or older;

3. At least 6 months in remission, defined as:

A. Harvey Bradshaw Index score ≤4;

B. Normal serum C-reactive protein (CRP) level (< 5 mg/l), and;

C. Low fecal calprotectin level (< 250 ug/g).

4. IFX therapy > 6 months at 5 mg/kg every 8 weeks with or without concomitant immunosuppression;

5. IFX TL > 7 ug/ml.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Non-adherence to the 8 weekly infusions schedule in the past;

2. Participation in another therapeutic trial;

3. Prior dose adjustments or interval shortening of IFX;

4. In case of immunosuppression: start < 3 months prior to screening

Onderzoeksopzet

Opzet

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

Deelname

Nederland

Status:	Werving tijdelijk gestopt
(Verwachte) startdatum:	01-06-2014
Aantal proefpersonen:	54
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	08-04-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 40729
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3778
NTR-old	NTR3943
CCMO	NL48325.018.14
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON40729

Resultaten

Samenvatting resultaten
N/A