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

No registrations found.

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

Summary

ID

NL-OMON22458

Source
NTR

Brief title
REDIX

Health condition

Crohn's disease
Ziekte van Crohn

Sponsors and support

Primary sponsor: Academic Medical Center
Source(s) of monetary or material Support: Academic Medical Center

Intervention

Outcome measures

Primary outcome

Proportion of patients with sustained clinical remission

Secondary outcome

1. Quality of life

2. Economic evaluation and pharmacoeconomic evaluation (yearly costs of IFX per QALY)

3. Incidence and severity of adverse events / side effects

4. Proportion of patients in clinical remission (additional analyses)

5. Proportion of patients in biochemical remission

6. Proportion of patients in sustained clinical remission

7. Proportion of patients in sustained biochemical remission

8. Time to clinical relapse

9. Time to biochemical relapse

10. Presence of predictive factors for successful IFX dose reduction (with specific focus on smoking status, body mass index and extent of disease)

11. Yearly total IFX dose per person

Study description

Background summary

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.

Study objective

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.

Study design

Primary endpoint: after 24 months of treatment.

Intervention

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.

Contacts

Public
Academic Medical Center
Department of Gastroenterology and Hepatology
Meibergdreef 9
M. Löwenberg
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5667621
Scientific
Academic Medical Center
Department of Gastroenterology and Hepatology
Meibergdreef 9
M. Löwenberg
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5667621

Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	01-06-2014
Enrollment:	54
Type:	Anticipated

Ethics review

Positive opinion

Date:	08-04-2013

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40729
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

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

Study results

Summary results
N/A