The influence of adalimumab on thiopurine metabolism in Crohn's disease patients.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON24966

Source
NTR

Brief title
N/A

Health condition

interaction, adalimumab, azathioprine, 6-mercaptopurine, 6-thioguanine, thiopurines, 6-TGN, 6-MMPR

Sponsors and support

Primary sponsor: none
Source(s) of monetary or material Support: none

Intervention

Outcome measures

Primary outcome

The influence of adalimumab therapy on the red blood cell levels of the active thiopurine metabolites (6-TGN and 6-MMPR) in Crohn's disease patients treated with stable azathioprine,

6-mercaptopurine or 6-thioguanine monotherapy.

Secondary outcome

1. The efficacy of concurrent treatment with the thiopurines azathioprine, 6-mercaptopurein or 6-thioguanine and adalimumab in Crohn's disease patients;

2. The safety during concurrent use of the thiopurines azathioprine, 6-mercaptopurine or 6-thioguanine and adalimumab in Crohn's disease patients.

Study description

Background summary

The influence of adalimumab on thiopurine metabolism in Crohn’s disease (CD) patients.

Background:
The novel anti–tumor necrosis factor monoclonal antibody adalimumab was significantly superior to placebo for long-term treatment of CD irrespective of concomitant immunosuppressive therapies, including the thiopurines azathioprine (AZA) and 6-mercaptopurine (6-MP). In 2003 Roblin et al. provided evidence for a drug interaction between infliximab and azathioprine in CD patients.
The mean erythrocyte level of the active thiopurine metabolites, the 6-thioguanine nucleotides (6-TGN), was comparable before and 3 months after the first infusion, but a significant increase was observed within 1–3 weeks after the first infusion. A mean increase of 50% of the basal level was seen.
An increase of the active thiopurine metabolites, 6-TGN, may on one hand result in a greater efficacy, but on the other hand may result in more (dangerous) adverse events, for instance myelotoxicity.

Objective:
To investigate the influence of adalimumab on the level of the active thiopurine metabolites, 6-TGN and 6-methylmercaptopurine ribonucleotides (6-MMPR), in CD patients treated with a stable maintenance therapy of azathioprine, 6-mercaptopurine or 6-thioguanine (6-TG).

Methods:
CD-patients treated with standard dose AZA (2-2,5mg/kg), 6-MP (1-1,5mg/kg) or 6-TG (10-40mg/day) who require adalimumab for active Crohn’s disease are included prospectively.
Patients receive adalimumab induction therapy with 160mg s.c. (week 0), 80mg s.c. (week 2), and subsequently 40mg s.c. every two weeks.
Efficacy, safety (adverse events), active thiopurine metabolite red blood cell levels and hematological and biochemical safety parameters will be evaluated at week 0 (inclusion), week 2, week 4, week 6 and week 12. The clinical outcome is evaluated by the Crohn’s

Disease Acitvity Index (CDAI) at week 0 (inclusion), week 4 and week 12. The duration of the study is twelve weeks. The dose of concomitant medication will be maintained, except for predniso(lo)ne, which can be dosed based on disease activity.

Outcome measures:
The alteration, which means a significant rise or decrease, of 6-TGN and/or 6-MMPR red blood cell levels resulting from concurrent adalimumab therapy.
Efficacy of therapy is evaluated at week 0, week 4 en week 12 by CDAI.
Safety is evaluated by measurement of hematological and biochemical parameters at week 0, 2, 4, 6 and 12 and clinical evaluation.

Study objective

The novel anti–tumor necrosis factor monoclonal antibody adalimumab was significantly superior to placebo for long-term treatment of CD irrespective of concomitant immunosuppressive therapies, including the thiopurines azathioprine (AZA) and 6-mercaptopurine (6-MP). In 2003 Roblin et al. provided evidence for a drug interaction between infliximab and azathioprine in CD patients. The mean erythrocyte level of the active thiopurine metabolites, the 6-thioguanine nucleotides (6-TGN), was comparable before and 3 months after the first infusion, but a significant increase was observed within 1–3 weeks after the first infusion. A mean increase of 50% of the basal level was seen. An increase of the active thiopurine metabolites, 6-TGN, may on one hand result in a greater efficacy, but on the other hand may result in more (dangerous) adverse events, for instance myelotoxicity. Objective. To investigate the influence of adalimumab on the level of the active thiopurine metabolites, 6-TGN and 6-methylmercaptopurine ribonucleotides (6-MMPR), in CD patients treated with a stable maintenance therapy of azathioprine, 6-mercaptopurine or 6-thioguanine (6-TG).

Study design

Week 0, 2, 4, 6 en 12.

Intervention

None.

Contacts

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Eligibility criteria

Inclusion criteria

1. Adult patients, aged between 18 – 70 years;

2. Diagnosis of CD for at least 6 months (histological and endoscopically confirmed);

3. AZA, 6-MP or 6-TG use for at least 3 months;

4. Steady state AZA, 6-MP or 6-TG use, with an unchanged thiopurine regime for at least 6 weeks (in combination with Infliximab);

5. Normal liver and kidney function (ALAT / AP / creatinin < 2 x upper normal limit, MDRD>60ml/min.);

6. 5-ASA use for at least 8 weeks, and an unchanged dose regime for at least 6 weeks.

Exclusion criteria

1. Bone marrow suppression (platelets / leucocytes < 1 x lower normal level);

2. Presence of tuberculosis or active infection (fever and CRP > 1 x upper normal limit);

3. Anemia (hemoglobine < 6 mmoll);

4. Symptomatic stenosis of the ileum;

5. Small bowel surgery interfering significantly with resorptive area;

6. Known intolerance to Humira compounds;

7. Moderate-severe congestive failure (NYHA III/IV);

8. Current use of Humira;

9. Current use of methotrexate;

10. Start or dose regime change of 5-ASA compounds within the last 45 days;

11. Concomitant use of allopurinol, 5-ASA, mycofenolate, furosemide within the past 6 weeks;

12. Pregnancy, expected pregnancy or lactation within 6 months.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2008
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	05-08-2009
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
NTR-new	NL1826
NTR-old	NTR1936
Other	n/a : n/a
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A