The effect of acetylcysteine on thiopurine use related liver injury.

No registrations found.

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

Summary

ID

NL-OMON21974

Source
Nationaal Trial Register

Brief title
NACTOX

Health condition

Inflammatory bowel disease; IBD; Crohn's disease; de ziekte van Crohn; ulcerative colitis; colitis ulcerosa; thiopurines; oxidative stress; hepatotoxicity; levertestafwijkingen

Sponsors and support

Primary sponsor: VU University Medical Center
Source(s) of monetary or material Support: Fund=initiator=sponsor

Intervention

Outcome measures

Primary outcome

Change in liver tests.

Secondary outcome

1. Change in state of oxidative stress (plasma malondialdehyde, plasma myeloperoxidase, urinary 8-hydroxy- deoxyguanosine and urinary F2-isoprostane);

2. Change in plasma xanthine oxidase activity;

3. Change in amino acid profile.

Study description

Background summary

Thioprunes are pivotal in the treatment of inflammatory bowel disease such as Crohn's disease and ulcerative colitis. However, toxicity is a frequent cause of therapy cessation. Hepatotoxicity due to thiopurine therapy may be initiated by an increased state of oxidative stress due to the metabolization of thiopurines on one hand and due to low availability reduced glutathion and its amino acid precursors. By supplementation of N-acetylcysteine we try to reduce oxidative stress and thereby ameliorate hepatotoxicity.

Study objective

Thiopurine induced hepatotoxicity is related with an enhanced state of oxidative stress and may ameliorate after N-acetylcysteine supplementation.

Study design

Elligible patients will be screened prior to defenite inclusion. After inclusion they will be randomly assigned to one of the two groups and will visit the outpatient clinics five times with an interval of four weeks. During the first eight weeks thiopurine therapy will be continued and depending on the group patients will concomitantly receive N-acetylcysteine 2400mg daily during weeks 1 to 4 or weeks 5 to 8. Weeks 9 to 12 both thiopurine therapy and N-acetylcysteine will be withdrawn. Rechallenge of solely thiopurine therapy takes place during weeks 13 to 16.

Intervention

Continuation of thiopurine treatment during eight weeks. During four weeks 600mg N-acetylcysteine effervescent tablets four times daily.

Contacts

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Eligibility criteria

Inclusion criteria

1. Crohn's disease and ulcerative colitis;

2. Patients between 18 and 70 years old;

3. Thiopurine use (azathioprine, 6-mercaptopurine or 6-thioguanine) for at least eight consecutive weeks;

4. Grade 1 or 2 toxicity on the CTCAEv3.0 of at least one of the folowing liver tests: ALAT, ASAT, gamma-GT, alkaline phosphatase and bilirubine.

Exclusion criteria

1. Serological findings consistent with auto-immune or viral hepatitis (Hep A,B,C; EBV; CMV);

2. Currently known liver disease;

3. History of chemotherapy;

4. Ultrasonographic findings consistent with cholestasis;

5. Lactation or pregnancy;

6. 6-TGN concentrations above 1200 pmol/8x10*8;

7. Use of antioxidants during thiopurine therapy.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2009
Enrollment:	30
Type:	Anticipated

Ethics review

Positive opinion

Date:	25-05-2009
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	NL1723
NTR-old	NTR1833
Other	MEC VUMC : 2009/56
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A