

# The effect of acetylcysteine on thiopurine use related liver injury.

No registrations found.

<b>Ethical review</b>	Positive opinion
<b>Status</b>	Recruiting
<b>Health condition type</b>	-
<b>Study type</b>	Interventional

## Summary

### ID

NL-OMON21974

### Source

NTR

### 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

Thiopurines 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 metabolism of thiopurines on one hand and due to low availability of reduced glutathione 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 be ameliorated after N-acetylcysteine supplementation.

### Study design

Eligible patients will be screened prior to definite 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 Weeks 9 to 12 both thiopurine therapy and N-acetylcysteine will be withdrawn.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

### Public

D.P. Asseldonk, van  
VU University Medical Center,  
De boelelaan 1118  
Amsterdam 1081 HV  
The Netherlands  
+31 (0)20 4440613

#### **Scientific**

D.P. Asseldonk, van  
VU University Medical Center,  
De boelelaan 1118  
Amsterdam 1081 HV  
The Netherlands  
+31 (0)20 4440613

## **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 following 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<sup>8</sup>;

## 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