Liver toxicity of azathioprine and 6-mercaptopurine in IBD patients.

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The primary goal of the study is the prevalence of NRH in patients with IBD, who have been treated for at least five years with azathioprin or 6-mercaptopurin. A MRI of the liver, using the Seiderer protocol, and a percutaneous liver biopsy will be...

Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON31453

Source
ToetsingOnline

Brief title
Liver toxicity of azathioprine and 6-mercaptopurine

Condition

- Gastrointestinal inflammatory conditions

Synonym
Nodular regenerative hyperplasia; non cirrhotic portal hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 6-mercaptopurine, azathioprine, IBD, Livertoxicity

Outcome measures

Primary outcome

prevalence of NRH (histologically) with percutaneous liver biopsy

prevalence of NRH with MRI, uing the Seiderer protocol, sensitivity and

specificity compared to histology.

Secondary outcome

Secundary goals are the correlation between NRH and the cumulative dose of

azathioprin and 6-mercaptopurin and the correlation between NRH and the 6-TGN

levels.

Other secundary goals are the correlation between radiological and histological

findings and correlation between radiological or histological findings and

blood constituents (livertests and thrombocytes).

Study description

Background summary

Azathioprine and 6-mercaptopurine are widely used in the treatment of inflammatoru bowel disease. 6-Thioguanin (Lanvis) was introduced in 2001, because this thiopurine is closely related to the active 6TGN metabolites. With 6-thioguanin a high frequency of Nodular regenerative hyperplasia has been reported.

Liver biopsy is most sensitive for detecting NRH and MRI has been suggested as an alternative diagnostic test.

Study objective

The primary goal of the study is the prevalence of NRH in patients with IBD,

who have been treated for at least five years with azathioprin or 6-mercaptopurin. A MRI of the liver, using the Seiderer protocol, and a percutaneous liver biopsy will be performed.

Secundary goals are the correlation between NRH and the cumulative dose of azathioprin and 6-mercaptopurin and the correlation between NRH and the 6-TGN levels.
Other secundary goals are the correlation between radiological and histological findings and correlation between radiological or histological findings and blood constituents (livertests and thrombocytes).

Study design

Observational

Study burden and risks

Burden:
1. MRI-liver:
- one hour
- no radiation is used, specfic contra-indications.

2. ultrasonography monitored percutaneous liver biopsy
- 3,5 hour
- before the biopsy venapunction
- afterwards observation

Risks:
2. Liver biopsy:
- 25% mild pain inupper quadrant or right shoulder; mild hypotension
- Risks; bleeding: 0.3%, infection and hemobilia 0.1%. Motality: 1 in 10.000 to 1 in 12.000

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

IBD patients
18 years or older
who have been treated at least 5 years with azathioprine and/or 6-mercaptopurine
who give permission for ultrasound guided liverbiopsy and MRI

Exclusion criteria

anaemia (Hb < 6.5 mmol/L), thrombocytopenia (Thr < 50 * 10 9/L), prolonged INR (INR > 1.5), ascites.
exclusioncriteria for MRI: pacemaker, ICD, metal intracerebral clips, known allergy for contrast agents that are used, claustrophobia.

Study design

Design

Study phase:	4
Study type:	Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	10-06-2008
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	29-05-2008
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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
CCMO	NL20965.096.08