A randomised, open-label clinical trial assessing the efficacy and safety of mycophenolate mofetil versus azathioprine for induction of remission in treatment naive autoimmune hepatitis

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To assess the efficacy and safety of mycophenolate mofetil as induction therapy in patients with treatment naive autoimmune hepatitis.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON52983

Source
ToetsingOnline

Brief title
CAMARO

Condition

- Hepatic and hepatobiliary disorders
- Autoimmune disorders

Synonym
Autoimmune hepatitis

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: autoimmune hepatitis, azathioprine, liver disease, mycophenolate mofetil

Outcome measures

Primary outcome

The primary outcome is the proportion of patients in remission, defined as normalization of serum ALT and IgG levels after 24 weeks of treatment, per treatment group. Secondary endpoints include safety and tolerability of mycophenolate mofetil, time to remission, changes in MELD-score (and its components bilirubine, INR, creatinine), albumin, pseudocholinesterase and N-terminal procollagen-III-peptide, ELF-score and aspects of quality of life.

In a sub-study, drug levels will be measured.

Secondary outcome

A. Biochemical remission at 24 weeks and at anytime

B. Time to biochemical remission

C. Partial remission, defined as ALT and AST serum levels >1x ULN and <2x ULN

D. Minimal response, defined as decrease of ALT and AST serum levels but still >2x ULN

E. Treatment failure, defined as no improvement or increase of ALT and AST serum levels

F. Changes in MELD score (and its components bilirubin, INR, creatinine) and in albumin and pseudocholinesterase

G. N-terminal procollagen-III-peptide, ELF score

H. Changes in quality of life measured with SF-36

I. Assessment of safety of MMF versus AZA in patients with AIH

J. The level of ALT, AST, GGT in both groups

K. Steroid and other side-effects scores consisting of VAS scores (0 - 10) by the physician for Cushing-face, buffalo hump, acne, striae, bruising and hirsutism.

L. Percentage of patients with biochemical remission

M. Ratio of ALAT to lowest ALAT ever

N. Mood alterations, headache, insomnia

O. Diabetes (requiring medication)

P. Hypertension (requiring medication)

Q. Bone fractures, osteoporosis and muscular weakness

R. Glaucoma and increased intraocular pressure

S. Number of infections

T. Extrahepatic AIH manifestations (e.g. arthralgia)

U. Patient survival

V. Fatigue index

W. Pruritis VAS score

Study description

Background summary

Current standard therapy of autoimmune hepatitis consists of a combination of prednisolone and azathioprine. However, a significant proportion of patients

does not respond to, or is intolerant for, azathioprine. Mycophenolate mofetil (MMF) has surpassed azathioprine as therapy to prevent organ transplant rejection and is sometimes used as an alternative option for autoimmune hepatitis. Several case series and one prospective study have documented the efficacy and safety of mycophenolate mofetil as induction therapy for autoimmune hepatitis. Robust evidence from a formal randomized clinical trial is lacking.

Study objective

To assess the efficacy and safety of mycophenolate mofetil as induction therapy in patients with treatment naive autoimmune hepatitis.

Study design

Multicenter, randomised, open-label intervention study

Intervention

The intervention group will receive oral mycophenolate mofetil for 24 weeks. The control group will be treated with azathioprine for 24 weeks. Both groups will be treated with steroid induction which will closely follow the schedule from the recent EASL Clinical Practice Guidelines.

Study burden and risks

The burden of the study consists of extra blood samples. Randomisation will be in a 1:1 ratio and patients will be treated with azathioprine, which is the current standard of care or mycophenolate mofetil. In both arms the standard prednisolone schedule is given. The potential benefit for participating patients is that mycophenolate mofetil may be more effective as induction therapy in autoimmune hepatitis and may possibly have less side-effects.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Probable or definite diagnosis of autoimmune hepatitis according to the International Autoimmune Hepatitis Study Group criteria (table 2) 9:
• Definite autoimmune hepatitis: >= 7
• Probable autoimmune hepatitis >= 6
2. First presentation of AIH requiring treatment according to the current EASL guidelines
3. Age >= 18 years
4. Must provide informed consent and agree to comply with the trial protocol

Exclusion criteria

1. Overlap syndrome with PSC or PBC (Paris criteria 29, strong positive AMA, past liver biopsy or cholangiographic findings compatible with PBC or PSC).2. Presence of clinical significant hepatic decompensation including:• History of liver transplantation, current active placement on a liver transplant waiting list.
• Portal hypertension with complications including: poorly controlled or diuretic resistant ascites, history of variceal bleeding or related therapeutic interventions (e.g. variceal banding, transjugular intrahepatic portosystemic shunts) or hepatic encephalopathy.
• Cirrhosis with complications, including history or presence of: spontaneous bacterial peritonitis, hepatocellular carcinoma, hepatorenal syndrome
a. N.B. cirrhosis without complications as mentioned above, is not an exclusion criterion

3. Current treatment with predniso(lo)ne and/or immunosuppressive medication for an indication other than autoimmune hepatitis4. Current systemic infection5. Other clinically significant medical conditions that could interfere with the trial6. If female of childbearing potential: known pregnancy, or unwilling to practice anticontraceptive measures. 7. History of noncompliance with medical regimens, or patients who are considered to be potentially unreliable or unable to participate8. Mental instability or incompetence, such that the validity of informed consent or compliance with the trial is uncertain

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2017
Enrollment:	70
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	azathioprine
Generic name:	azathioprine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	mycophenolate mofetil

Generic name:	mycophenolate mofetil
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	prednisolone
Generic name:	prednisolone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	25-10-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	18-11-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	23-01-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-04-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-08-2018

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	29-11-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	09-07-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	10-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	12-05-2022

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
EudraCT	EUCTR2016-001038-91-NL
ClinicalTrials.gov	NCT02900443
CCMO	NL57115.058.16

Study results

Date completed:	01-06-2023
Actual enrolment:	66

Summary results
Trial is onging in other countries