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

Published: 25-10-2016 Last updated: 16-04-2024

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 titleCAMARO

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

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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

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 auidelines
- 3. Age \geq 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
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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

Application type:

Date: 05-04-2017

Review commission: METC Leiden-Den Haag-Delft (Leiden)

Amendment

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)

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Approved WMO

Date: 09-07-2019

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO

Date: 10-10-2019

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO

Date: 27-08-2020

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO

Date: 21-05-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO

Date: 12-05-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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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