

Marrow stem cell therapy to improve liver function in alcoholic liver disease

Submission date 29/02/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 10/03/2008	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
Last Edited 05/07/2013	Condition category Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Swissmedic 2008DR2031

Study information

Scientific Title

Autologous human bone marrow stem cells mobilized by granulocyte colony-stimulating factor (G-CSF) to improve liver function in patients with decompensated alcoholic liver disease: a randomized study

Study objectives

Patients with advanced alcoholic liver disease often come to medical attention due to hepatic decompensation (fatigue, jaundice, ascites, bleeding and hepatic encephalopathy). The prognosis depends on the severity of the liver insufficiency. The characteristic features of patients who do not survive is profound liver failure and inability to achieve efficient parenchymal regeneration.

Study hypothesis:

The combination of stimulating autologous hematopoietic stem cells from the bone marrow after a 5-day mobilization course with G-CSF followed by a direct administration into the liver parenchyma via the hepatic artery translates into a better outcome during follow-up as compared to the standard care (which included only supportive measures).

Please note that as of 04/01/10 the anticipated end date for this trial has been extended from 31 /03/10 to 31/12/10.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Protocol N°07-145 approved by the local Ethics Committee (Comite Departemental D'Ethique de Médecine Interne et Médecine Communautaire, 24, Rue Micheli-du-Crest CH-1211 Geneve Switzerland) on November 6, 2007. Also approved by the national Swiss Agency for Therapeutic Products (2008DR2031) on February 7, 2008.

Study design

Single-center randomized controlled study, not blinded.

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Alcoholic liver disease

Interventions

The participants will be randomly allocated to the two study arms in equal numbers by an independent person using the sealed envelope technique.

Intervention arm: Stem cell embolisation in the hepatic artery

Control arm: supportive measures only

The following tests will be carried out in both arms at baseline:

1. Liver biopsy
2. Computed tomography (CT) with volumetry
3. Physical examination
4. Blood sampling for cytokines (tumor necrosis factor [TNF], Interleukin-6 [IL6], alpha-fetoprotein [AFP], Hepatocyte Growth Factor [HGF], transforming growth factor [TGF]-beta)
5. Routine hematology and coagulation studies
6. Blood chemistry with liver function test (to measure the MELD score)

Control arm: Supportive measures according to the standard care.

The following will be carried out at Day 28 visit:

1. Repeat liver biopsy
2. Physical examination
3. CT with volumetry
4. Blood sampling (idem)

Day 60 and day 90 visits will include only physical examination and blood tests.

In the treatment arm: Five-day mobilization course with lenograstim (G-CSF) 10 mcg/kg subcutaneously per day, followed by a 40 to 60 ml bone marrow aspiration from the iliac crest. Then, CD34+ and mesenchymal cells will be isolated from the aspirate using a classical Ficoll density separation. Within 36 h of aspiration, the suspension of cells (an average of 0.5×10^8 cells) will be selectively embolized via arteriography into the right and left hepatic artery branches, so as to distribute CD34+ and mesenchymal cells in both lobes of the liver. Day 28, 60 and 90 visits will be similar to the control arm.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

granulocyte colony-stimulating factor (G-CSF)

Primary outcome measure

Improvement of liver function, as assessed by a decrease in the MELD score of >3 between baseline, Day 28, 60, and 90 follow-up visits.

Secondary outcome measures

1. Improvement in liver function as assessed by the following parameters at Day 28, 60, and 90:

- 1.1. Bilirubin
- 1.2. Albumin
- 1.3. Coagulation times
- 1.4. Presence or absence of ascites
- 1.5. Presence or absence of hepatic encephalopathy)

This will allow the calculation of the Child-Pugh's score

2. Mortality at 3 and 6 months
3. Evolution of serum markers of liver regeneration (AFP, HGF), inflammation (TNF, IL6) and fibrosis (TGF-beta)
4. Changes in liver histology at Day 28

Overall study start date

01/03/2008

Completion date

31/12/2010

Eligibility

Key inclusion criteria

1. Age 18-75 years
2. Biopsy-proven alcoholic liver disease
3. Abnormal liver function with a Model for End-Stage Liver Disease (MELD) (assessment that include bilirubin, coagulation time and creatinine) score 10-26
4. Written informed consent

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Upper age limit

75 Years

Sex

Both

Target number of participants

60

Key exclusion criteria

1. Recent (10 days) infection or hemorrhage
2. Estimated survival <6 months
3. Coexistent HIV, hepatitis C virus (HCV), hepatitis B virus (HBV)

4. Portal vein obstruction
5. Documented hepatocellular carcinoma
6. Severe liver atrophy as defined by volumetry <0.6% body weight
7. Leucocytes >25g/L
8. Known hypersensitivity to G-CSF
9. Creatinine >150 µmol/L
10. Contraindication to arteriography
11. Clinically overt hepatic encephalopathy
12. Absence of written consent

Date of first enrolment

01/03/2008

Date of final enrolment

31/12/2010

Locations

Countries of recruitment

Switzerland

Study participating centre

University Hospital of Geneva

Geneva

Switzerland

CH-1211

Sponsor information

Organisation

Foundation for Liver and Gut Studies (FLAGS) (Switzerland)

Sponsor details

12, Rue Adrien Lachenal

Geneva

Switzerland

CH-1207

Sponsor type

Other

Funder(s)

Funder type

Other

Funder Name

Foundation for Liver and Gut Studies (FLAGS), a non profit organisation based in Geneva (Switzerland)

Funder Name

University Hospital of Geneva (Hôpitaux Universaires de Genève; HUG) (Switzerland)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2013		Yes	No