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

Submission date	Recruitment status	[ ] Prospectively registered
29/02/2008	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
10/03/2008	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
05/07/2013	Nutritional, Metabolic, Endocrine	

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 x 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