

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

**Submission date**  
29/02/2008

**Recruitment status**  
No longer recruiting

Prospectively registered

Protocol

**Registration date**  
10/03/2008

**Overall study status**  
Completed

Statistical analysis plan

Results

**Last Edited**  
05/07/2013

**Condition category**  
Nutritional, Metabolic, Endocrine

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

**Protocol serial number**  
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

## **Study type(s)**

Treatment

## **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  $0.5 \times 10^8$  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(s)**

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.

### **Key secondary outcome(s)**

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

### **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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

75 years

**Sex**

All

**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)

## 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

### 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?
<a href="#">Results article</a>	results	01/12/2013		Yes	No