ISRCTN86571875 https://doi.org/10.1186/ISRCTN86571875

Granulocyte colony-stimulating factor (G-CSF) and liver regeneration in patients with alcoholic steatohepatitis

Submission date	Recruitment status
28/02/2008	No longer recruiting
Registration date	**Overall study status**
14/03/2008	Completed
Last Edited	**Condition category**
30/12/2020	Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 2005DR2212

Study information

Scientific Title
Granulocyte colony-stimulating factor (G-CSF) induces proliferation of hepatic progenitors in alcoholic steatohepatitis: a randomized trial

Study objectives
Liver failure is a major cause of death in patients with alcoholic steatohepatitis. Many patients are not candidates for liver transplantation, and no therapy has proven useful to promote liver regeneration. Granulocyte colony stimulating factor (G-CSF) showed promising results in ischemic heart disease in the repopulation of the parenchyma by pluripotent cells issued from the bone marrow following a mobilization course by G-CSF.

Hypothesis:
The effects of a 5-day course of G-CSF in patients with alcoholic steatohepatitis associated with cirrhosis is well tolerated and is associated with signs of liver cell proliferation in the short-term.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Protocol N°05-089 approved by the local Ethics Committee of the University Hospital of Geneva (Hôpitaux Universitaires de Genève, Comite Departemental d'Ethique de Medecine Interne et Medecine Communautaire, 24, Rue Micheli-du-Crest, CH-1211 Genève, Switzerland). Date of approval: 14/06/2005

This study was also approved by the Swiss Agency for therapeutic products (Swissmedic)(ref: 2005DR2212)

Study design
Single-center randomized controlled pilot trial (not blinded).

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Alcoholic steatohepatitis

Interventions
Thirteen patients were randomized to standard care + G-CSF, and 11 patients to standard care only. The random allocation of participants to the two arms of the study were carried out using the sealed envelope technique by an independent nurse.

Baseline assessments (both intervention and control arms):
1. Patients had a transjugular liver biopsy as part of the diagnostic work-up of decompensated alcoholic liver disease.
2. Physical examination, blood sampling for routine values (coagulation, blood chemistry and liver function tests) and cytokines measurements: alfa-foetoprotein (AFP), hepatocyte growth factor (HGF)
3. Measurement of CD34+ hematopoietic stem cells (flow cytometry)
4. Aminopyrine breath test (microsomal liver function)
5. Immunohistochemistry for CK7 and Ki67 (identification of hepatic progenitor cells with proliferative activity)

Patients randomized to G-CSF: Mobilization course by G-CSF (10 mcg/kg/day) for 5 days.

Assessments for both arms at day 7:
1. Repeat liver biopsy with similar immunohistochemistry studies
2. Physical examination
3. Repeat routine blood tests and cytokines
4. Measurement of CD34+ hematopoietic stem cells (flow cytometry)
5. Aminopyrine breath test

Assessments for both arms at day 28 visit:
1. Physical examination
2. Routine blood tests and cytokines

Both arms at day 90:
Clinical outcome

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Ability of G-CSF to increase circulating CD34 + cells (see Interventions for timepoints of assessment)

Secondary outcome measures
1. Safety of filgrastim in patients with liver failure
2. Effects of filgrastim on liver regeneration assessed using biological markers and immunohistochemistry
3. Possible influence of filgrastim on liver function

See Interventions for details of assessments

Overall study start date

01/09/2005

Completion date
31/08/2006

Eligibility

Key inclusion criteria
1. Age 18-70 years
2. Recent heavy alcohol intake (>80 g/day)
3. Biopsy-proven alcoholic steatohepatitis
4. Maddrey's score >20 and <70
5. Leucocyte count <15 g/L
6. Ability to give an informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
70 Years

Sex
Both

Target number of participants
24

Total final enrolment
24

Key exclusion criteria
1. Platelet count <20 g/L
2. International Normalised Ratio (INR) >1.9
3. Known hypersensitivity to filgrastim (G-CSF)
4. Creatinine >150 µmol/L
5. Recent (10 days) infection or gastrointestinal hemorrhage
5. Documented hepatocellular carcinoma, hepatitis B, C, or HIV seropositivity
6. Ongoing pregnancy

Date of first enrolment
01/09/2005

Date of final enrolment
31/08/2006

Locations

Countries of recruitment
Switzerland

Study participating centre
Gastroenterology and Hepatology
Geneva
Switzerland
CH-1211

Sponsor information

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

Sponsor details
12, Rue Adrien Lachenal
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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	01/07/2008	30/12/2020	Yes	No