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

Submission date
28/02/2008

Recruitment status
No longer recruiting

Registration date
14/03/2008

Overall study status
Completed

Last Edited
30/12/2020

Condition category
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

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

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)

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?
Results article	results	01/07/2008	30/12/2020	Yes	No