Trial Description

Title

Granulocyte colony stimulating factor (G-CSF) to treat acute-on-chronic liver failure: A multicentre randomized trial

Trial Acronym

GRAFT

URL of the trial

[---]*

Brief Summary in Lay Language

[---]*

Brief Summary in Scientific Language

ACLF is a condition with dismal prognosis, for which apart from OLT (liver transplantation) no therapeutic options exist. A treatment approach that helps to recover from this acute intercurrent event and hereby improves the very poor short-term survival would be of major clinical importance. Stem cells play a major role in the process of hepatic regeneration. Their mobilization from the bone marrow due to G-CSF in patients with liver failure could be demonstrated in several phase I/II trials. Although an impact on the hepatic regenerative capacity was obvious, the results for clinical endpoints like patients´ survival and liver function were controversial [Di Campli 2007, Lorenzini 2008, Gaia 2006, Spahr 2008]. This was most likely due to the fact, that the observation period was limited and the power was inadequate for these endpoints. Recently two small randomized trials have shown the potential of G-CSF in this patient population markedly improving patients´ outcome [Garg 2012, Duan 2013]. However, these results need to be confirmed in a large multicenter Trial.

Organizational Data

- DRKS-ID: DRKS00011572
- Date of Registration in DRKS: 2017/03/14
- Date of Registration in Partner Registry or other Primary Registry: 2016/01/29
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: 415/15-ff, Ethikkommission an der Medizinischen Fakultät der Universität Leipzig
Secondary IDs

- EudraCT-No. (for studies acc. to Drug Law): 2015-002212-32
- Primary Registry-ID: NCT02669680 (ClinicalTrials.gov)

Health condition or Problem studied

- ICD10: K72.0 - Acute and subacute hepatic failure
- Free text: acute-on-chronic liver failure

Interventions/Observational Groups

- Arm 1: Application of G-CSF (Filgrastim) in combination with standard care of acute-on-chronic liver failure (G-CSF subcutaneously, 5 μg/kg daily on day 0-4, then every 3rd day over 26 days (days 7, 10, 13, 16, 19, 22, 25) = 12 doses)
- Arm 2: Standard care of acute-on-chronic liver failure

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Randomized controlled trial
- Blinding: [---]*
- Who is blinded: [---]*
- Control: Active control (effective treatment of control group)
- Purpose: Treatment
- Assignment: Parallel
- Phase: N/A
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): N/A

Primary Outcome

Transplant-free survival up to 90 days (death or transplant count as events)

Secondary Outcome

- Overall survival at 360 days
- Transplant-free survival at 360 days
• Complications of ACLF within 90 days/within 360 days (hepatorenal syndrome, variceal bleeding, ascites, hepatic encephalopathy)
• Infections within 90 days/within 360 days (proven infection necessitating systemic use of antibiotics)
• Liver function during the course of treatment and follow-up (MELD-Score, Child-Pugh-Score)
• Duration of initial hospital stay

Assessment of safety:
In addition to the complications of ACLF listed above, further AEs and SAEs will be assessed. Laboratory values reflecting liver function as well as infection related parameters will be monitored during the course of treatment and follow-up.

Countries of recruitment

- DE Germany

Locations of Recruitment

- University Medical Center Allgemeine Innere Medizin 1, Kiel
- University Medical Center Medizinische Klinik Abteilung I, Tübingen
- University Medical Center Klinik u. Poliklinik für Gastroenterologie u. Rheumatologie, Leipzig
- University Medical Center Medizinische Klinik und Poliklinik I, Bonn
- University Medical Center Klinik für Gastroenterologie und Hepatologie - Zentrum für Innere Medizin, Essen
- University Medical Center Klinik f. Gastroenterologie u. Hepatologie am Abdominalzentrurn, Köln
- University Medical Center Klinik für Gastroenterologie, Hepatologie, Infektiologie, Düsseldorf
- Medical Center St. Georg, Leipzig
- University Medical Center Innere Medizin II, Gastroenterologie, Hepatologie, Endokrinologie, Saarland
- University Medical Center Medizinische Klinik III, Aachen
- Medical Center St. Josefs-Hospital, Wiesbaden
- University Medical Center Medizinische Klinik 1, Frankfurt a.M.
- University Medical Center Medizinische Klinik - Abt. IV Gastroenterologie/ Hepatologie, Heidelberg
- University Medical Center Innere Medizin II, Freiburg im Breisgau
- University Medical Center Klinik für Gastroenterologie, Hepatologie, Endokrinologie, Hannover
- University Medical Center Innere Medizin IV, Gastroenterologie, Hepatologie, Infektiologie, Jena
Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2016/02/29**
- Target Sample Size: **292**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

Acute-on-chronic liver failure according to the criteria defined by the CANONIC study [Moreau 2013] / age >= 18 years / Informed consent

Exclusion criteria

Prior not curatively treated or active malignancies / sickle cell disease / septic shock, defined by the following symptom complex: bacteraemia AND SIRS AND shock / WBC-count of > 50 x 10^9/L / known HIV infection / known intolerance to filgrastim / pregnancy, lactation or insufficient contraception / participation in other interventional clinical trials

Addresses

- **Primary Sponsor**
  Universität Leipzig
  Ritterstr. 26
  04109 Leipzig
  Germany
  Telephone: [--]*
  Fax: [--]*
  E-mail: [--]*
  URL: [--]*

- **Contact for Scientific Queries**
Contact for Scientific Queries

Universitätsklinikum Leipzig Sektion Hepatologie; Abteilung für Innere Medizin, Neurologie, Dermatologie
Mr. Prof. Thomas Berg
Liebigstraße 20
04103 Leipzig
Germany

Telephone: +49 341 97 12331
Fax: +49 341 97 12339
E-mail: thomas.berg at medizin.uni-leipzig.de
URL: [---]*

Contact for Public Queries

Universitätsklinikum Leipzig AöR Sektion Hepatologie, Klinik und Poliklinik für Gastroenterologie und Rheumatologie, Universitätsklinikum
Mr. Prof. Thomas Berg
Liebigstr. 20
04103 Leipzig
Germany

Telephone: +49 341 97 12331
Fax: [---]*
E-mail: thomas.berg at medizin.uni-leipzig.de
URL: [---]*

Sources of Monetary or Material Support

Public funding institutions financed by tax money/Government funding body
(German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)

Deutsche Forschungsgemeinschaft
Kennedyallee 40
53175 Bonn
Germany

Telephone: [---]*
Fax: [---]*
E-mail: [---]*
URL: www.dfg.de

Status

Recruiting Status: Recruiting stopped after recruiting started
Study Closing (LPLV): [---]*
Study Closing (LPLV): [---]*

**Trial Publications, Results and other documents**

* This entry means the parameter is not applicable or has not been set.

*** This entry means that data is not displayed due to insufficient data privacy clearing.