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

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.

Do you plan to share individual participant data with other researchers?

Description IPD sharing plan

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
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 Abdominalzentrum, 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
University Medical Center Charité, Berlin
University Medical Center 1. Medizinische Klinik, Mainz

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

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 AöRSektion 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

- Recruitment Status: Recruiting complete, follow-up complete
- Study Closing (LPLV): 2020/03/17

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.