Trial Description

Title

**GvHD prophylaxis with ATG-Fresenius S in allogeneic Stem Cell Transplantation from matched unrelated donors:
A randomised phase III multicenter trial comparing a standard GvHD prophylaxis with cyclosporine A and methotrexate with additional pretransplant ATG-FRESENIUS S**

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

The principle of allogeneic hematopoietic stem cell transplantation is based on the destruction of the malignant cells by high dose chemotherapy or combination of chemotherapy and irradiation. The high dose chemotherapy (conditioning) also leads to the destruction of normal blood cells and their precursors (bone marrow cells or stem cells). Therefore following conditioning chemotherapy the patient must receive a bone marrow from a healthy donor (bone marrow or stem cell transplantation). The transplant also contains specialized cells of the immune system (lymphocytes) . The transferred lymphocytes can help to eliminate any malignant cells remaining after chemotherapy. This phenomenon is called graft versus leukemia/lymphoma effect and is a substantial therapy principle of allogeneneic transplantation. Unfortunately the tissue difference between donor and recipient (especially if the donor is not related to the recipient) frequently leads to the unwanted effect that the transferred Lymphozyten attacks the body of the patient, which is called graft versus host disease, (GvHD). The graft versus host disease primarily affects the skin, the intestine and the liver and can lead to death. . The GvHD can be prevented and treated with so called immune suppressive medications. Standard therapy consists of cyclosporine A, which has to taken for several months after transplantation and methotrexate, which is given on the days +1, +3, +6 and +11 after transplantatio. A more novel therapy is the addition of anti-T-cell globulin (ATG) to the standard therapy. This treatment strategy is compared with the the standard therapy in the current trial.

Brief Summary in Scientific Language

**The goal of this study is to compare standard GvHD prophylaxis consisting of cyclosporine A and methotrexate with standard GvHD prophylaxis plus pre-transplant ATG-FRESENIUS S with respect to efficacy and safety.
All patients receive myeloablative therapy. Recommended regimens: For patients with ALL: fractionated TBI (8-12 Gy) plus cyclophosphamide (1-2 x 60 mg/kg). For all other indications: either TBI (8-12 Gy) or busulfan (14-16 mg/kg) plus cyclophosphamide (1-2 x 60 mg/kg) or thiotepa = 15 mg/kg or BCNU = 300 mg/m2. Conditioning regimens may differ from center to center; each center decides for**

constant (disease specific) regimen(s) throughout the whole study period. Standard GvHD prophylaxis consists of cyclosporine A (target trough level = 200 ng/ml starting from day -1 until day +100) and short course methotrexate (15 mg/m2 at day +1, 10 mg/m2 at days +3, +6 and +11).

Organizational Data

- DRKS-ID: **DRKS00000002**
- Date of Registration in DRKS: **2008/08/08**
- Date of Registration in Partner Registry or other Primary Registry: **2005/09/13**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **238/02 , Ethik-Kommission der Albert-Ludwigs-Universität Freiburg**

Secondary IDs

- EudraCT-No.
  (for studies acc. to Drug Law): **2004-000232-91**
- Primary Registry-ID: **NCT00655343 (ClinicalTrials.gov)**
- Partner Registry-ID: **UKF000501 (Register Klinischer Studien des Universitätsklinikums Freiburg)**

Health condition or Problem studied

- ICD10: **C95 - Leukaemia of unspecified cell type**
- Free text: **GvHD prophylaxis**

Interventions/Observational Groups

- Arm 1: **Standard GvHD Prophylaxis with Cyclosporin A and Methotrexat which additionally includes the application of Anti-T Lymphocyte Globulins ATG FRESENIUS S**
- Arm 2: **Standard GvHD Prophylaxis with Cyclosporin A and Methotrexat**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***

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Blinding: **[---]***

- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

The primary endpoint is the appearance of acute GvHD (Level III-IV) and premature mortality in the first 100 days following transplantation.

Secondary Outcome

**Time to onset of acute GvHD (grade I-IV, II-IV, III-IV), incidence and severity of infections until
day +100, time to engraftment, incidence of chronic GvHD (limited and extensive, extensive) over time,
disease free survival, incidence of relapse over time, incidence of death without relapse over time, overall
survival, safety and tolerability.**

Countries of recruitment

- DE **Germany**
- IL **Israel**
- FI **Finland**
- CZ **Czech Republic**
- AT **Austria**
- BE **Belgium**
- FR **France**
- IT **Italy**
- CH **Switzerland**
- ES **Spain**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2003/05/26**
- Target Sample Size: **200**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **60 Years**

Additional Inclusion Criteria

- Patients, 18-60 years of age;
- Patients suffering from one of the following diseases:
- AML: 1st complete remission, beyond 1st remission, in relapse not in remission (induction failure, primary refractory);
- ALL: 1st complete remission, beyond 1st remission, in relapse not in remission (induction failure, primary refractory);
- MDS: RA (with poor risk factors as classified by the International Prognostic Scoring System of MDS), RARS, RAEB, RAEB-t, CMML;
- CML: beyond 1st chronic phase: accelerated phase, blast crisis, chronic phase (CP) 2, CP 3;
- Patients designated to undergo allogeneic bone marrow transplantation or allogeneic peripheral blood stem cell transplantation;
- Patients with an HLA-A, -B (serologic and DNA-based), HLA-DRB1, -DQB1 (high DNA-based resolution) matched (8 out of 8 alleles) unrelated donor;
- Patients with a Karnofsky Performance Score (KPS): ? 60%;
- Patients who underwent all obligatory screening examinations (special examinations within the last 4 weeks);
- Patients who have given their written informed consent to participate in the study.

Exclusion criteria

- Patients with significant cardiac, renal, metabolic and/or CNS disease, currently uncontrolled by treatment, which may interfere with the completion of the study;
- Patients with any bacterial, viral, or fungal infections not under adequate antimicrobial control;

- Patients who are known to have serum hepatitis or who are carriers of the Hepatitis B surface antigen (HBs-Ag), or Hepatitis C antibody, or who are known to have a positive result to the test of HIV antibodies;
- Patients with any additional concurrent or previous malignant disease;
- Patients with known hypersensitivity to rabbit immunoglobulin antibodies in past patient history or with known allergy to any substance chemically related to the study medication;
- Pregnant or lactating women;
- Patients who formerly underwent transplantation;
- Patients who cannot communicate reliably with the investigator or who are not likely to cope with the requirements of the study.

Addresses

■ **Primary Sponsor**

Neovii Biotech GmbH
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82166 Gräfelfing
Germany

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URL: **[---]***

■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

- **Commercial (pharmaceutical industry, medical engineering industry, etc.)**

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  Am Haag 6-7
  82166 Gräfelfing
  Germany

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **2015/02/26**

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.*