**Trial Description**

<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Phase I/II Pilotstudy: Feasability, safety and efficacy of transplantation of retrovirus-transduced hematopoetic stem cells for the treatment of Wiskott-Aldrich-Syndrome</th>
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<tbody>
<tr>
<td><strong>Trial Acronym</strong></td>
<td>WAS-GT</td>
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**URL of the trial**

[---]*

**Brief Summary in Lay Language**

The Wiskott-Aldrich-Syndrome (WAS) is an inherited disorder of the immune system characterized by recurrent infections, bleeding tendency, eczema and patients are likely to develop malignant lymphomas (cancer of the lymph nodes). WAS is a uniformly lethal disease, the only curative treatment option consists in the transplantation of allogeneic hematopoietic stem cells. However, this approach is associated with severe side effects. WAS is caused by mutations in the gene encoding the Wiskott-Aldrich-Syndrome-Protein, which is present in all hematopoietic cells. A defective version of this gene leads to loss/impairment of function of the white blood cells and blood platelets. Although therapy of WAS has improved substantially in the last years, most of the patients with WAS die of complications of the immune deficiency as young adults. The only long lasting therapy is the blood stem cell transplantation, which has however some severe side effects. The aims of this protocol are to assess feasibility, safety and efficacy of a hematopoietic stem cell gene therapy approach. Blood stem cells from WAS patients will be isolated and genetically modified using a retroviral vector which contains a correct version of the WAS gene. A mild preparatory chemotherapy consisting of Busulfan will be given to patients to enhance engraftment of genetically modified cells. The patient will receive a transfusion of the genetically modified blood stem cells. After 10 to 14 days the genetically correct cells are expected to have engrafted.

**Brief Summary in Scientific Language**

The Wiskott-Aldrich-Syndrome (WAS) is a primary immunodeficiency disorder characterized by recurrent infections, thrombocytopenia, eczema and propensity to malignant lymphomas. WAS is a uniformly lethal disease, the only curative treatment option consists in the transplantation of allogeneic hematopoietic stem cells. However, this approach is associated with severe side effects. The aims of this protocol are to assess feasibility, safety and efficacy of a hematopoietic stem cell gene therapy approach. CD 34+ cells from WAS patients will be isolated or cleaned after G-CSF mediated mobilisation and after cytokin-stimulation transduced with GALV-pseudotyped retroviral vectors. The retroviral vector encodes for a modified version of the WASP-gene. A mild preparatory...
regimen of Busulfan will be given to patients to enhance engraftment of the genetically modified cells. Thereafter the modified autologous hematopoietic stem cells will be transfused.

Organizational Data

- DRKS-ID: DRKS00000330
- Date of Registration in DRKS: 2010/09/30
- Date of Registration in Partner Registry or other Primary Registry: 2005/04/05
- Investigator Sponsored/Initiated Trial (IST/IIT): yes
- Ethics Approval/Approval of the Ethics Committee: Approved
- (leading) Ethics Committee Nr.: 2783, Ethikkommission der Medizinischen Hochschule Hannover

Secondary IDs

- Partner Registry-ID: DeReG-Nr: 77 (Deutsches Register für somatische Gentransferstudien)
- BfArM-No.: 4022911
- PEI-No.: 1271/01

Health condition or Problem studied

- ICD10: D82.0 - Wiskott-Aldrich syndrome
- ICD10: [---]* - [---]*

Interventions/Observational Groups

- Arm 1: transfusion of gene-corrected hematopoietic stem/progenitor cells

Characteristics

- Study Type: Interventional
- Study Type Non-Interventional: [---]*
- Allocation: Single arm study
- Blinding: Open (masking not used)
- Who is blinded: [---]*
- Control: Uncontrolled/Single arm
- Purpose: Other
Study Type: **Interventional**
Study Type Non-Interventional: [---]*
Allocation: **Single arm study**
Blinding: **Open (masking not used)**
Who is blinded: [---]*
Control: **Uncontrolled/Single arm**
Purpose: **Other**
- Assignment: **Single (group)**
- Phase: I-II
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): [---]*

### Primary Outcome

1. Feasibility of ex vivo gene marking of autologous hematopoietic cells which contribute to short- and long-term hematopoiesis after partially myeloablative conditioning
2. Safety of retroviral gene transfer into hematopoietic stem cells, in particular with regards to the absence of replication-competent retroviral particles and analysis of insertional mutagenesis after transfusion of genetically modified stem cells
3. Efficacy of WASP reconstitution in the hematopoietic system, as demonstrated by reconstitution of immunologic effector cell function, normalization of blood parameters and decrease of infectious complications

### Secondary Outcome

Determination of frequency and functionality of the gene therapy vector encoding WASP by molecular insertion site analysis and demonstration of genetic correction using cell biological assays in peripheral blood and bone marrow leukocytes
2. Determination of the engraftment potential and efficacy of differentiation into multiple hematopoietic cell lineages
3. Determination of persistence of molecular cell clones in diverse cell lineages of the hematopoietic system
4. Monitoring of hematopoiesis with an emphasis on the potential contribution of genetically marked and reconstituted cells to the development of myelodysplastic syndrome or malignant transformation
5. Determination of the expression level of WASP in hematopoietic cells and correction of cellular phenotype

### Countries of recruitment

- DE Germany
Locations of Recruitment

Recruitment

- Planned/Actual: Actual
- (Anticipated or Actual) Date of First Enrollment: 2006/10/13
- Target Sample Size: 15
- Monocenter/Multicenter trial: Monocenter trial
- National/International: National

Inclusion Criteria

- Gender: Male
- Minimum Age: 12 Months
- Maximum Age: no maximum age

Additional Inclusion Criteria

1. Classic Wiskott-Aldrich-Syndrome verified by molecular analysis of the WASP-gene. Patients with residual protein expression can be enrolled, if they experienced at least one episode of life-threatening complications (severe infection or bleeding)
2. Age > 12 months
3. No signs of a malignant disease (exclusion of lymphoma by ultrasonic abdomen examination, chest x-ray, bone marrow cytological analysis)
4. informed consent or informed assent by patients or legal representative
5. Sufficient number of vital CD34+ cells (>1 x 10^5 CD34+ cells/kg bodyweight) isolated from bone marrow or mobilised apherese preparation

Exclusion Criteria

1. WASP mutations in the context of congenital neutropenia (GBD-mutations) or congenital thrombocytopenia (XLT)
2. Positive screening result for WASP proviral sequences by PCR analysis, or
3. Patients who are participating in other clinical trials with investigational drugs
4. Patients or legal representatives respectively with a medical or psychiatric condition that compromises the ability to participate in the study or to give informed consent

Addresses

- **Primary Sponsor**
  
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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.)

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  URL: http://www.bmbf.de

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

Status

- Recruitment Status: Recruiting complete, follow-up continuing
- Study Closing (LPLV): [---]*
**Trial Publications, Results and other documents**

- Trial results **Boztug et al NEJM 2010**

* 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.