STORM: Temsirolimus, Rituximab and DHAP for Relapsed and Refractory Diffuse Large B-cell Lymphoma

Purpose

The STORM-trial consists of two parts. In the part I (dose escalation of Temsirolimus) the primary objective is to establish a maximum tolerated dose of Temsirolimus in combination with Rituximab and DHAP. Secondary objective is to prove ability to mobilize stem cells in patients scheduled to high dose therapy.

In the part II (full target dose) the primary objective is to evaluate the ORR in patients with relapsed diffuse large B cell lymphoma (DLBCL). The secondary objective is to evaluate progression free survival (PFS), overall survival (OS) and Toxicity.

Condition | Intervention | Phase
----------|-------------|------
Diffuse Large B-Cell Lymphoma | Drug: Rituximab, Temsirolimus, DHAP, intravenous | Phase 2

Study Type: Intervventional
Study Design:
- Endpoint Classification: Safety/Efficacy Study
- Intervention Model: Single Group Assignment
- Masking: Open Label
- Primary Purpose: Treatment

Official Title: A Phase II Trial to Evaluate the Safety, Feasibility and Efficacy of a Salvage Therapy Consisting of Temsirolimus Added to the Standard Therapy R-DHAP for the Treatment of Patients With Relapsed or Refractory DLBCL - the STORM Trial

Resource links provided by NLM:
- MedlinePlus related topics: Lymphoma
- Drug Information available for: Dexamethasone, Cytarabine, Dexamethasone sodium phosphate, Stilbesterol, Dexamethasone acetate, Everolimus, Temsirolimus, Rituximab
- Genetic and Rare Diseases Information Center resources: B-cell Lymphomas, Lymphosarcoma
- U.S. FDA Resources

Further study details as provided by University Hospital Heidelberg:

Primary Outcome Measures:
- Safety, Tolerability and Efficacy of a combination therapy of Temsirolimus added to the standard therapy, Rituximab and DHAP (Cytarabine, Cisplatin, Dexamethasone) [Time Frame: 09-2012 to 06-2018 (up to six years)] [Designated as safety issue: Yes]
  - In the part I (dose escalation of Temsirolimus) the primary objective is to establish a maximum tolerated dose of Temsirolimus in combination with Rituximab and DHAP.

Secondary Outcome Measures:
- Safety, Tolerability and Efficacy of a combination therapy of Temsirolimus added to the standard therapy, Rituximab and DHAP (Cytarabine, Cisplatin, Dexamethasone) [Time Frame: 09-2012 to 06-2018 (up to six years)] [Designated as safety issue: Yes]
  - In the part I (dose escalation of Temsirolimus) secondary objective is to prove ability to mobilize stem cells in patients scheduled to high dose therapy.
- Safety, Tolerability and Efficacy of a combination therapy of Temsirolimus added to the standard therapy, Rituximab and DHAP (Cytarabine, Cisplatin, Dexamethasone) [Time Frame: 09-2012 to 06-2018 (up to six years)] [Designated as safety issue: Yes]
  - In the part II (full target dose) the secondary objective is to evaluate Progression Free Survival
In the part II of the trial 40 patients will be included to receive the full target dose, established within the part I of the study.

Estimated Enrollment: 88
Study Start Date: September 2012
Estimated Study Completion Date: July 2018
Estimated Primary Completion Date: June 2018 (Final data collection date for primary outcome measure)

### Arms

<table>
<thead>
<tr>
<th>Experiment: Rituximab, Temsirolimus, DHAP, intravenous</th>
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| This is a multicenter, open label, single arm, phase II study. There will be no placebo usage within this trial. In the part I, dose escalation part, of this trial 6 patients will be included in each dose level. There will be 4 cohorts, administering up to a maximum of 4 cycles 25 mg, 50 mg, 75 mg or 100 mg Temsirolimus in combination with Rituximab and DHAP. Treatment regimen part I: Part I - Cohort A, B, C, D, X Temsirolimus 25 (A), 50 (B), 75 (C), 100 (D) or 15 (X) mg, Day 1, 8, Rituximab (375 mg/m² day 2) Dexamethasone 40 mg day 3-6 Cisplatine 100 mg/m² day 3 Cytarabine 2x2 g/m² day 4 ...
| assigned interventions |

### Experimental: Rituximab, Temsirolimus, DHAP, intravenous

- Drug: Rituximab, Temsirolimus, DHAP, intravenous
- Maximum tolerated dose of Temsirolimus Rituximab (375 mg/m²) Dexamethasone (120 mg) Cisplatin (100 mg/m²) Cytarabine (2x2g/m²)
- Other Names: Temsirolimus-R-DHAP, Torisel, MabThera, Fortecortin, ARA-C, ARA-cell, Depocyte, R-DHAP, Rituximab-DHAP
- Temsirolimus, Rituximab, Dexamethasone, Cisplatin, Cytarabine
- Temsirolimus-Rituximab-DHAP

### Eligibility

- Ages: 18 Years and older
- Genders: Both
- Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

- Patients with histologically proven diagnosis of diffuse large cell B-cell lymphoma (DLBCL) according to the World Health Organization classification.
- Documented relapse or progression following at least one treatment but a maximum of 2 prior treatments. Prior treatment must have included at least 3 cycles of anthracycline containing chemotherapy (e.g. CHOP-like).
- Any of the following: at least 1 measurable tumor mass (>1.5 cm x >1.0 cm), involvement of any organ or bone marrow infiltration
- Subjects 18 years or older
- Subjects (or their legally acceptable representatives) must have signed an informed consent document indicating that they understand the purpose of and procedures required for the study and are willing to participate in the study.
- Adequate bone marrow reserve: Platelets of at least 75000/µl, absolute neutrophil count at least 1500/µl
- Alanine aminotransferase (ALT) < 2.5 x upper limit of normal (ULN); Aspartate aminotransferase (AST) < 2.5 x ULN; Total bilirubin < 1.5 x ULN
- Calculated creatinine clearance (MDRD) > 70 mL/min
- Eastern Cooperative Oncology Group [ECOG] performance Status < 3
- Female subject must be postmenopausal (for at least 6 months), surgically sterile, abstinent, or, if sexually active, be practicing an effective method of birth control (e.g., prescription oral contraceptives, contraceptive injections, intrauterine device, double-barrier method, contraceptive patch, male partner sterilization) before entry and throughout the study; and have a negative serum ß-hCG pregnancy test at screening

#### Exclusion Criteria:

- Active central nervous System lymphoma. Brain MRT is required only if clinically indicated
- Pregnant or breast feeding women
- Lymphoma other than DLBCL
- Severe concomitant disease (e.g. uncontrolled arterial hypertension, heart failure (NYHA II-IV), uncontrolled diabetes mellitus, pulmonary fibrosis, uncontrolled hyperlipoproteinemia)
- Active uncontrolled infections including HIV-positivity, active Hep B or C
- Mental status precluding patient's compliance
- Prior treatment with Temsirolimus
- Known CD30 negativity
- Patients refractory to DHAP in a prior treatment line
- Prior autologous or allogeneic stem cell or bone marrow transplantation
- Peripheral neuropathy or neuropathic pain of Grade 2 or worse
Diagnosed or treated for a malignancy other than NHL except: adequately treated non-melanoma skin cancer, curatively treated in-situ cancer of the cervix, DCIS of the breast, or other solid tumors curatively treated with no evidence of disease for >5 years

Concurrent treatment with another investigational agent during the conduct of the trial.

Concurrent participation in non-treatment studies is not excluded

Known intolerance to Sirolimus or derivates, Cytarabine, Cisplatine or Rituximab.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01653067

Contacts

Contact: Mathias Witzens-Harig, MD 0049 6221 56 8199 mathias.witzens-harig@med.uni-heidelberg.de

Locations

Germany

University Hospital Freiburg
Freiburg, Baden-Württemberg, Germany, 79106
Contact: Gerald Berhaus, MD 0049-761-27037850
Principal Investigator: Gerald Berhaus, MD

University of Heidelberg Hospital
Heidelberg, Baden-Württemberg, Germany, 69120
Contact: Mathias Witzens-Harig, MD +49 6221 568008 mathias.witzens-harig@med.uni-heidelberg.de
Principal Investigator: Mathias Witzens-Harig, MD

University Hospital Ulm
Ulm, Baden-Württemberg, Germany, 89081
Contact: Andreas Viardot, MD 0049-731-50045539
Principal Investigator: Andreas Viardot, MD

University Hospital Erlangen
Erlangen, Bayern, Germany, 91054
Contact: Stefan W. Krause, Prof. 0049-9131-8535957
Principal Investigator: Stefan W. Krause, Prof.

Ludwig-Maximilians-University of Munich
Munich, Bayern, Germany, 81377
Contact: Martin Dreyling, Prof. 0048-89-70952202
Principal Investigator: Martin Dreyling, Prof.

Technische Universität München
Munich, Bayern, Germany, 81675
Contact: Ulrich Keller, MD 0049-89-41407435
Principal Investigator: Ulrich Keller, MD

Johann Wolfgang Goethe University Hospitals, Frankfurt
Frankfurt, Hessen, Germany, 60590
Contact: Johannes Atta, MD
Principal Investigator: Johannes Atta, MD

Johannes Gutenberg University Mainz
Mainz, Rheinland-Pfalz, Germany, 55101
Contact: Georg Heß, MD 0049-6131-175040
Principal Investigator: Georg Heß, MD

Charité University Berlin
Berlin, Germany, 12200
Contact: Agnieszka Korfel, MD 0049-30-84452337
Principal Investigator: Agnieszka Korfel, MD

Sponsors and Collaborators

Mathias Witzens-Harig
Johannes Gutenberg University Mainz
Technische Universität München
Ludwig-Maximilians - University of Munich
University Hospital Ulm
University Hospital Erlangen
Charité University, Berlin, Germany
University Hospital Freiburg
Johann Wolfgang Goethe University Hospitals

Investigators

Principal Investigator: Mathias Witzens-Harig, MD University Hospital of Heidelberg, Department 5 Hematology, Oncology, Rheumatology, Im Neuenheimer Feld 410, 69120 Heidelberg, Germany

More Information

No publications provided by University Hospital Heidelberg

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Responsible Party: Mathias Witzens-Harig, PD Dr. med. Mathias Witzens-Harig, University Hospital Heidelberg

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Study First Received: July 17, 2012

Last Updated: December 11, 2014

Health Authority: Germany: Ethics Commission
Germany: Federal Institute for Drugs and Medical Devices

Keyw ords provided by University Hospital Heidelberg:
Non Hodgkin’s Lymphoma
Diffuse Large B-Cell Lymphoma
Aggressive Lymphoma
Aggressive Non Hodgkin’s Lymphoma
NHL
aNHL
Temsirolimus

Additional relevant MeSH terms:
Lymphoma
Lymphoma, B-Cell
Lymphoma, Large B-Cell, Diffuse
Immune System Diseases
Immunoproliferative Disorders
Lymphatic Diseases
Lymphoma, Non-Hodgkin
Lymphoproliferative Disorders
Neoplasms
Neoplasms by Histologic Type
BB 1101
Cytarabine
Dexamethasone
Dexamethasone 21-phosphate
Dexamethasone acetate

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