DC Vaccination in CML

This study is currently recruiting participants. (see Contacts and Locations)

Verified September 2015 by Charite University, Berlin, Germany

Sponsor:
Charite University, Berlin, Germany

Information provided by (Responsible Party):
Jörg Westermann, MD, Charite University, Berlin, Germany

ClinicalTrials.gov Identifier:
NCT02543749

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History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

The aim of this phase I/II trial is induction of anti leukemic T cell immunity in a clinical situation of "minimal residual disease". This might be a strategy to immunologically eradicate the residual leukemia cells. Patients to be included are chronic phase bcr/abl+ CML (chronic myeloid leukemia) patients in stable cytogenetic and/or molecular remission.

These patients can be included if they have:

1. not achieved a CMR (complete molecular response) or
2. achieved bcr/abl < 10% on qPCR (quantitative polymerase chain reaction) (=MCyR) (Major cytogenic Response), but less than a CCyR (complete cytogenic Response).

Autologous DC (Dendritic cells), generated under GMP (Good manufacturing conditions) conditions, are used as a vaccine. These DC constitutively express all putative tumor antigens. In order to ensure sufficient presentation of distinct CML-related antigens, particularly in good responders to TKIs, DC are additionally pulsed with peptides from bcr/abl, WT-1 (Wilms Tumor Protein) and proteinase-3. Monitoring of T cell reactivity against these peptides can then serve as surrogate marker for anti leukemic immunity induced by the vaccine. Vaccination is performed with 10^7 DC i.d. (intra dermal) in weeks 1, 3, 5, 8, 11, 14, 17, 20, 23 and 26. KLH (keyhole limpet hemocyanin) is used as an adjuvant for vaccine preparations in weeks 3, 5 and 8 (and 11).

Condition	Intervention	Phase
Myeloid Leukemia, Chronic	Biological: DC vaccine	Phase 1 Phase 2

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

Official Title: Dendritic Cells as Autologous Vaccine in Patients With Chronic Myeloid Leukemia

Resource links provided by NLM:

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Genetic and Rare Diseases Information Center resources: Chronic Myeloid Leukemia Chronic Myeloproliferative Disorders Myeloid Leukemia

U.S. FDA Resources

Further study details as provided by Charite University, Berlin, Germany:

Primary Outcome Measures:

- DC toxicity Parameters using CTC (Common toxicity criteria) [Time Frame: 30 w eeks] [Designated as safety issue: No]

  Number of Participants With Treatment-Related Adverse Events as Assessed by CTCAE v4.0 (Treatment: long-term vaccination w ith peptide-pulsed autologous DC in patients w ith chronic phase CML w ho have persistent residual cytogenetic and/or molecular disease after at least 18 months therapy w ith a tyrosine kinase Inhibitor)

Secondary Outcome Measures:

- Molecular/cytogenetic Response under vaccination as measured by qPCR for bcr/abl in % IS (International scale) [Time Frame: 30 w eeks] [Designated as safety issue: No]
- T-cell Response: Antigen specific T-cell Response in % CD8+ T-cells for bcr/abl [Time Frame: 30 w eeks] [Designated as safety issue: No]
- T-cell Response: Antigen specific T-cell Response in % CD4+ T-cells for bcr/abl [Time Frame: 30 w eeks] [Designated as safety issue: No]
- T-cell Response: Antigen specific T-cell Response in % CD8+ T-cells for WT-1 (only in HLA-A2+ patients) [Time Frame: 30 w eeks] [Designated as safety issue: No]
- T-cell Response: Antigen specific T-cell Response in % CD8+ T-cells for Proteinase 3 (only in HLA-A2+ patients) [Time Frame: 30 w eeks] [Designated as safety issue: No]

Estimated Enrollment:	30
Study Start Date:	July 2014
Estimated Study Completion Date:	January 2019
Estimated Primary Completion Date:	July 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interv entions
Experimental: DC vaccine Autologous DC pulsed w ith leukemia-associated peptides+adjuvant. Ten vaccinations over 26 w eeks w ith 10 x 106 freshly thaw ed DC Intradermal injections (1-2 ml volume)	Biological: DC vaccine Autologous DC pulsed w ith leukemia-associated peptides+adjuvant

Eligibility

Ages Eligible for Study:	18 Years to 80 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Patients w ith bcr/abl-positive CML in stable cytogenetic / molecular remission after at least 18 months therapy w ith tyrosine kinase Inhibitors (TKI). The follow ing groups of patients w ill be included:
   - complete cytogenetic remission (CCyR), but stable detection of bcr/abl-transcript on qPCR (at least on tw o different time points over a period of at least 6 months). A stable molecular remission is assumed, if the difference betw een the qPCR values does not exceed a factor 5 (< 0,5log).
   - No CCyR, but qPCR for bcr/abl transcript < 10% (= MCyR (Major cytogenetic Response)) after at least 24 months on 2nd generation TKI therapy.
2. Treatment w ith a TKI inhibitor and an additional anti leukemic drug is no exclusion criterion.
3. Age 18-80 years
4. Performance status of 0 or 1 according to WHO index or Karnofsky index >70 %
5. Life expectancy > 18 months
6. Hematological function should be at least partially conserved (platelets count >50.000/ µl, Hb > 8g/dl)
7. w ritten informed consent
8. No breast feeding
9. if of childbearing potential, negative pregnancy test (serum/urine ß- HCG (human chorionic gonadotropin)) and w illingness to use highly effective contraceptive methods (Pearl Index <1, e.g.: birth control pill, loop, hormone implant, transdermal hormone patch, a combination of tw o barrier methods [condom and vaginal diaphragm] sterilisation or sexual abstinence) for the study duration and

thereafter as long as under treatment w ith antileukemic drugs

Exclusion Criteria:

1. Clinically relevant autoimmune disorders
2. Immunodeficiency syndromes
3. Know n allergy to GM-CSF (granulocyte macrophage colony-stimulating factor), TNF-α (Tumor necrosis factor Alpha) , IL-4 (interleukine 4) or KLH (keyhole limpet hemocyanin)
4. Pregnancy (absence confirmed by serum/urine ß-HCG) or breastfeeding
5. Women of childbearing age w ithout highly effective contraception
6. Active infectious disease requiring treatment
7. Continuous therapy w ith corticosteroids or other immunosuppressive drugs
8. Severe psychiatric disorders
9. Organ dysfunction:
   - Thrombin Time / Partial Thromboplastin Time > 1,5 x upper normal limit
   - creatinine > 2,0 mg/ml
   - Bilirubin > 3,0 mg/ml, ALAT/ASAT (Alanine aminotransferase/ aspartate aminotransferase) > 3x upper normal limit
   - pulmonary disfunction (dyspnea at rest or w ith minimal exertion)
   - clinically relevant coronary heart disease or ventricular arrhythmia, congestive heart failure > grade II NYHA (New York Heart Association)
10. Persons w ho are detained officially or legally to an official institute
11. Subjects for w hom there is concern about compliance w ith the protocol procedures
12. Present History of substance abuse (drug or alcohol) or any other factor (e.g., serious psychiatric condition) that could limit the subject's ability to comply w ith study procedures

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith 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: NCT02543749

Contacts

Contact: J. Westermann, Prof. Dr. +49-30-450-553141 joerg.w estermann@charite.de

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Locations

Germany

Charité - University Medicine Berlin — **Recruiting**
Berlin, Germany, 13353
Contact: Jörg Westermann, Prof. Dr. +49-30-450-553141 joerg.w estermann@charite.de

Klinikum Bremen Mitte — **Not yet recruiting**
Bremen, Germany, 28177
Contact: Bernd Hertenstein, Prof. Dr.

Sponsors and Collaborators

Charite University, Berlin, Germany

Investigators

Principal Investigator: J. Westermann, Prof. Dr. Charite University, Berlin, Germany

More Information

No publications provided

Responsible Party: Jörg Westermann, MD, Representative of the sponsor, Charite University, Berlin, Germany
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Other Study ID Numbers:	**CSTI571ADE60**, 2006-006962-41
Study First Received:	August 25, 2015
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Keyw ords provided by Charite University, Berlin, Germany:
CML
DC vaccine

Additional relevant MeSH terms:

Leukemia, Myelogenous, Chronic, BCR-ABL Positive	Leukemia
Leukemia, Myeloid	Myeloproliferative Disorders
Bone Marrow Diseases	Neoplasms
Hematologic Diseases	Neoplasms by Histologic Type

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