Purpose

The NOA-16 trial is the first-in-man trial of the IDH1 (isocitrate dehydrogenase type 1) peptide vaccine targeting the IDH1R132H mutation (amino acid exchange from arginine to glutamine at position 132 of IDH1). The aim of this trial is to evaluate the safety and tolerability of and immune response to the IDH1 peptide vaccine in patients with IDH1R132H-mutated, WHO grade III-IV gliomas.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
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<tbody>
<tr>
<td>Glioma</td>
<td>Drug: IDH1 peptide vaccine</td>
<td>Phase 1</td>
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</tbody>
</table>

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

Official Title: Targeting IDH1R132H in WHO Grade III-IV IDH1R132H-mutated Gliomas by a Peptide Vaccine - a Phase I Safety, Tolerability and Immunogenicity Multicenter Trial (NOA-16)

Primary Outcome Measures:
- safety and tolerability of repeated fixed dose vaccinations of the IDH1 peptide vaccine administered with topical imiquimod (Aldara®) assessed by Regime Limiting Toxicity (RLT). [Time Frame: 15 months] [Designated as safety issue: Yes]
- immunogenicity of the IDH1 peptide vaccine [Time Frame: 15 months] [Designated as safety issue: No]

The primary immunogenicity endpoint is the presence of an IDH1R132H-specific T-cell and/or antibody response at any time point during the trial measured by IFN-gamma ELISpot and ELISA, respectively (response Yes/No).
Secondary Outcome Measures:

- Immunogenicity by assessing the IDH1R132H-specific T-cell and antibody response [Time Frame: 15 months] [Designated as safety issue: No]
- Progression-free survival (PFS) [Time Frame: 15 months] [Designated as safety issue: No]
- Overall response rate (ORR) [Time Frame: 15 months] [Designated as safety issue: No]
- Association between immunogenicity (IDH1R132H-specific T-cell and antibody response) and the clinical outcome parameters (ORR, PFS) [Time Frame: 15 months] [Designated as safety issue: No]

assessed by Logistic regression and Proportional Hazard models

Estimated Enrollment: 39
Study Start Date: June 2015
Estimated Study Completion Date: August 2018
Estimated Primary Completion Date: August 2018 (Final data collection date for primary outcome measure)

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<th>Arms</th>
<th>Assigned Interventions</th>
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<tr>
<td>Experimental: IDH1 peptide vaccine</td>
<td>Drug: IDH1 peptide vaccine</td>
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The IDH1 peptide vaccine is a 20mer peptide encompassing the IDH1R132H-mutated region emulsified in Montanide®. It is injected subcutaneously and administered in combination with topical imiquimod. The vaccine is administered 8 times every 2 or 4 weeks.

Detailed Description:

The patient population will be molecularly defined and include IDH1R132H mutant grade III and IV gliomas without co-deletion of 1p/19q and with loss of alpha-thalassemia/mental retardation syndrome X-linked (ATRX) expression.

Within this trial, the IDH1 peptide vaccine will be administered to 39 patients.

In treatment group 1 vaccination treatment will be done alone starting 4-6 weeks post radiotherapy. In treatment groups 2 and 3 vaccination treatment will be done in parallel with temozolomide (TMZ) chemotherapy starting at day 10 of the 4th TMZ cycle (treatment group 2) or at day 10 of the 1st TMZ cycle post concomitant radiochemotherapy (treatment group 3).

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Patients present with histologically confirmed diagnosis of an IDH1R132H-mutated glioma (with or without measurable residual tumor after primary tumor resection or biopsy)
- Histology may be astrocytoma, oligodendroglioma, or oligoastrocytoma WHO grade III or IV
- Absence of chromosomal 1p/19q co-deletion in the tumor tissue
- Loss of ATRX expression in the tumor tissue
- Availability of primary tumor tissue for molecular screening (FFPE bulk tissue or biopsy)
- Patients have received radiotherapy (54 - 60 Gy) alone, 3 cycles of chemotherapy with TMZ (150-200 mg/m2, 5/28 days) or standard combined radiochemotherapy with TMZ prior to enrollment.
- Patients should be immunocompetent (i.e. no concomitant treatment with dexamethasone (or equivalent), or receive stable/decreasing steroid levels not exceeding 2 mg/day dexamethasone (or equivalent) during the last 3 days prior to clinical screening; no severe lymphopenia)
- ≥18 years old, smoking or non-smoking, of any ethnic origin and gender
- Karnofsky Performance Status ≥ 70
- Ability of patient to understand character and individual consequences of the clinical trial
- Evidence of two informed consent documents personally signed and dated by the patient (or a witness in case the patient is unable to write) covering the molecular screening procedure (short IC) and the remaining trial-related procedures (extended IC) and indicating that the patient has been informed of all pertinent aspects of the study and that the patient consents to participate in the trial.
Women of child-bearing potential (WOCBP; i.e., those who have not undergone a hysterectomy, bilateral salpingectomy and bilateral oophorectomy or who have not been post-menopausal for at least 24 consecutive months) must have a negative serum pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 72 hours prior to the start of the investigational medicinal product (IMP).

WOCBP must be using an effective method of birth control to avoid pregnancy throughout the study and for 24 weeks after the last dose of the IMP. This includes two different forms of effective contraception (e.g., hormonal contraceptive and condom, IUD/IUS and condom) or sterilization, resulting in a failure rate less than 1% per year.

Men must be willing and able to use an effective method of birth control throughout the study for up to 24 weeks after the last dose of the IMP if their sexual partners are WOCBP (acceptable methods see above).

Patients who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures

Exclusion Criteria:

- Progressive (incl. pseudoprogression) or recurrent disease after radiation therapy, chemotherapy or radiochemotherapy based on local MRI assessment
- Previous or concurrent experimental treatment for the tumor. This includes local therapies such as interstitial radiotherapy or local chemotherapy (i.e., BCNU wafers), loco-regional hyperthermia, and antiangiogenic therapy (such as bevacizumab)
- Antitumor treatment other than standard radiotherapy and/or standard TMZ chemotherapy. Daily metronomic TMZ or intensified dosing scheduled as a substitute for maintenance TMZ cycles are not allowed. (Dose reductions of standard TMZ chemotherapy are allowed.)
- Abnormal (≥ Grade 2 CTCAE v4.0) laboratory values for hematology, liver and renal function (serum creatinine). In detail the following values apply as exclusion criteria:
  a. Hemoglobin < 10 g/dL (6.2 mmol/L)
  b. White blood cell count (WBC) decrease (<3.0 x 10^9/L) or increase (>10.0 x 10^9/L)
  c. Absolute neutrophil count (ANC) decrease (< 1.5 x 10^9/L)
  d. Platelet count decrease (<75 x 10^9/L)
  e. Bilirubin > 1.5 x ULN (upper limit of normal according to the performing lab’s reference range)
  f. ALT > 3 x ULN
  g. AST > 3 x ULN
  h. GGT > 2.5 x ULN
  i. Serum creatinine increase (> 1.5 x ULN)
- Pregnancy and lactation
- Patients with history or presence of HIV and/or HBV/HCV
- Patients with history or known presence of tuberculosis
- Patients with severe infection(s) or signs/symptoms of infection within 2 weeks prior to the first administration of the study drug
- Patients who have received a live, attenuated vaccine within 4 weeks prior to the first administration of the study drug
- Patients with a prior solid organ transplantation or haematopoietic stem cell transplantation
- History of hypersensitivity to the IMP or to any drug with similar chemical structure or to any excipient present in the pharmaceutical form of the IMP
- Participation in other clinical trials or their observation period during the last 30 days before the first administration of the IMP

**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](https://clinicaltrials.gov/). Please refer to this study by its ClinicalTrials.gov identifier: NCT02454634

**Contacts**

Contact: Michael Platten, MD  +49 (0)6221 / 56-6804  michael.platten@med.uni-heidelberg.de
Contact: Wolfgang Wick, MD  +49 (0)6221 / 56-7075  wolfgang.wick@med.uni-heidelberg.de

**Locations**

**Germany**

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Recruiting</th>
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<tbody>
<tr>
<td>Charité Berlin, Neurosurgery</td>
<td>Recruiting</td>
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<td>Berlin, Germany</td>
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<tr>
<td>University Hospital Dresden, Neurosurgery</td>
<td>Recruiting</td>
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<tr>
<td>Dresden, Germany</td>
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</tbody>
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University Hospital Essen, Internal Medicine
Essen, Germany
Recruiting

University Hospital Frankfurt, Neurooncology
Frankfurt/Main, Germany
Recruiting

University Hospital Freiburg, Neurosurgery
Freiburg, Germany
Recruiting

University Hospital Heidelberg, Neurology Clinic
Heidelberg, Germany
Recruiting

LMU, University Hospital Munich
Munich, Germany
Recruiting

University Hospital Tuebingen, Neurooncology
Tuebingen, Germany
Recruiting

Sponsors and Collaborators
National Center for Tumor Diseases, Heidelberg
University Hospital Heidelberg
German Cancer Research Center
Neuro-Oncology Working Group of the German Cancer Society

Investigators
Principal Investigator: Michael Platten, MD University Hospital Heidelberg, Neurology Clinic; Neurooncology Program at the NCT

More Information
No publications provided

Responsible Party: National Center for Tumor Diseases, Heidelberg
ClinicalTrials.gov Identifier: NCT02454634 History of Changes
Other Study ID Numbers: NCT-2013-0216 2014-000503-27
Study First Received: May 12, 2015
Last Updated: October 22, 2015
Health Authority: Germany: Paul-Ehrlich-Institut

Keywords provided by National Center for Tumor Diseases, Heidelberg:
IDH1R132H peptide vaccine immunotherapy IDH1R132H-mutated glioma

Additional relevant MeSH terms:
Glioma Neoplasms, Glandular and Epithelial
Neoplasms Neoplasms, Nerve Tissue
Neoplasms by Histologic Type Neoplasms, Neuroepithelial
Neoplasms, Germ Cell and Embryonal Neuroectodermal Tumors

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