Immunotherapy With Nivolumab or Nivolumab Plus Ipilimumab vs. Double Placebo for Stage IV Melanoma w. NED

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

Verified December 2015 by University Hospital, Essen

Sponsor:
Prof. Dr. med. Dirk Schadendorf

Information provided by (Responsible Party):
Prof. Dr. med. Dirk Schadendorf, University Hospital, Essen

ClinicalTrials.gov Identifier:
NCT02523313

First received: August 5, 2015
Last updated: December 1, 2015
Last verified: December 2015
History of Changes

Purpose

This is a prospective, double-blind placebo-controlled, multicenter, randomized phase II trial testing the adjuvant immunotherapy with Nivolumab plus Ipilimumab Placebo or Nivolumab plus Ipilimumab versus Double Placebo Control as a post-surgical/post-radiation treatment for stage IV melanoma with no evidence of disease (NED).

Condition	Intervention	Phase
Malignant Melanoma	Drug: Nivolumab + Placebo Drug: Nivolumab + Ipilimumab Drug: Double Placebo Control	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Intervention Model: Crossover Assignment
Masking: Double Blind (Subject, Caregiver, Investigator)
Primary Purpose: Treatment

Official Title: A Phase II Randomized, Double-Blind Trial of Immunotherapy With Nivolumab or Nivolumab Plus Ipilimumab Versus Double-Placebo Control as a Post-Surgical/Post-Radiation Treatment for Stage IV Melanoma With No Evidence of Disease

Resource links provided by NLM:

MedlinePlus related topics: Melanoma

Drug Information available for: Ipilimumab Nivolumab

Genetic and Rare Diseases Information Center resources: Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by University Hospital, Essen:

Primary Outcome Measures:

- Efficacy of adjuvant immunotherapy with Nivolumab alone or in combination with Ipilimumab (Progression-free survival) [Time Frame: 24 months after LPI] [Designated as safety issue: No]

  Progression-free survival (PFS) defined as the time from the first study treatment date until documented tumor progression date or date of death, whichever occurs first.

Secondary Outcome Measures:

- Overall survival [Time Frame: 24 months after LPI] [Designated as safety issue: No]

  Overall survival of a patient defined as the time from the first study treatment date until documented date of death

Other Outcome Measures:

- Safety / Toxicity All adverse events ≥ Grade 3 according to CTCAE Version 4.0 criteria [Time Frame: until 90 days after discontinuation of dosing] [Designated as safety issue: Yes]

  All adverse events ≥ Grade 3 according to CTCAE Version 4.0 criteria, that are related to the administration of the investigational agents will be assessed

Estimated Enrollment:	312
Study Start Date:	July 2015
Estimated Study Completion Date:	June 2021
Estimated Primary Completion Date:	June 2021 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: Nivolumab + Placebo Nivolumab (3 mg/kg) i.v. every 2 weeks + Placebo instead of Ipilimumab on weeks 1, 4, 7 and 10 + Placebo instead of Nivolumab on weeks 4 and 10	Drug: Nivolumab + Placebo Nivolumab will be applied at a dose of 3 mg/kg given as IV infusion every 2 weeks for up to 1 year after initial dosing or until PD + Placebo instead of Ipilimumab on weeks 1, 4, 7 and 10 + Placebo instead of Nivolumab on weeks 4 and 10. Other Name: Treatment Arm A
Experimental: Nivolumab + Ipilimumab Nivolumab (1 mg/kg) and Ipilimumab (3 mg/kg) i.v. every 3 weeks for 4 doses. Both study drugs are administered on the same day over the first 12 weeks + Placebo instead of Nivolumab on weeks 3, 5, 9 and 11. After week 12: Nivolumab as maintenance and at a dose of 3 mg/kg IV every 2 weeks for up to 1 year after initial dosing (of the combination) or until PD.	Drug: Nivolumab + Ipilimumab Nivolumab (1 mg/kg) and Ipilimumab (3 mg/kg) will be applied as IV infusion every 3 weeks for 4 doses. Both study drugs are to be administered on the same day over the first 12 weeks + Nivolumab-Placebo on weeks 3, 5, 9 and 11. After week 12 Nivolumab is given as maintenance and will be applied at a dose of 3 mg/kg IV every 2 weeks for up to 1 year after initial dosing (of the combination) or until PD. Other Name: Treatment Arm B
Placebo Comparator: Double Placebo Control Placebo instead of Nivolumab and Placebo instead of Ipilimumab i.v. every 3 weeks for 4 doses. Both placebos are administered on the same day over the first 12 weeks + Placebo instead of Nivolumab on weeks 3, 5, 9 and 11. After week 12 Placebo instead of Nivolumab as maintenance and applied as IV every 2 weeks for up to 1 year after initial dosing (of the combination) or until PD.	Drug: Double Placebo Control Placebo instead of Nivolumab and Placebo instead of Ipilimumab will be applied as IV infusion every 3 weeks for 4 doses. Both placebos are to be administered on the same day over the first 12 weeks + Placebo instead of Nivolumab on weeks 3, 5, 9 and 11. After week 12 Placebo instead of Nivolumab is given as maintenance and will be applied intravenously every 2 weeks for up to 1 year after initial dosing (of the combination) or until PD. Other Name: Treatment Arm C

Detailed Description:
This study will allow for direct comparison of the clinical benefit provided by Nivolumab monotherapy or Nivolumab combined with Ipilimumab versus double placebo control. Furthermore, it will also allow for direct comparison of the respective safety profiles of Nivolumab monotherapy or Nivolumab combined with Ipilimumab. Nivolumab monotherapy was chosen as one of the experimental arms because of a favourable risk-benefit ratio assessed in the large Phase 1 study (MDX1106-03/CA209-003). The combination of Nivolumab and Ipilimumab was chosen as an experimental arm because of the preliminary evidence from the Phase 1 study CA209-004 suggesting synergy between Nivolumab and Ipilimumab resulting in a higher frequency of patients with increased tumour burden reduction. Evaluating both Nivolumab monotherapy and the combination of Nivolumab and Ipilimumab will provide clinical data allowing clinicians to select the appropriate treatment for each patient based on their individual risk-benefit ratio.

Eligibility

Ages Eligible for Study:	18 Years and older (Adult, Senior)
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Stage IV melanoma arising from a primary cutaneous site or metastatic from an unknown primary site with no evidence of disease (NED) after surgery or radiation therapy (conducted within 8 weeks before enrolment)
- Signed written informed consent
- Known BRAF status
- Subjects must be willing and able to comply with scheduled visits, treatment schedule, laboratory testing, and other requirements of the study
- Minimum life expectancy of five years excluding their melanoma diagnosis
- ECOG performance status of 0 or 1
- Tumor tissue from the resected site of disease must be provided for biomarker analyses. In order to be randomized a subject must have a PD-L 1 expression classification (positive (≥ 5% tumor cells expressing PD-L1) or negative (< 5% tumor cells expressing PD-L1)). If an insufficient amount of tumor tissue from the resected site is provided for analysis, acquisition of additional archived tumor tissue (block and/or slides) for the biomarker analyses is required.
- Prior radiotherapy must have been completed at least 2 weeks prior to study drug administration
- Required laboratory values

- Negative pregnancy test for female subjects and effective contraception (Pearl-Index <1) for both male and female subjects if the risk of conception exists

Exclusion Criteria:

- History of primary uveal or mucosal melanoma
- Prior therapy with CTLA4 or PD1 antibodies
- The patient has psychiatric or addictive disorders that may compromise his/her ability to give informed consent or to comply with the trial procedures.
- Lack of availability for clinical follow-up assessments.
- Any immunosuppressive therapy given within the past 30 days prior to study drug administration (excluding physiologic steroid hormone replacement)
- Other malignancies within the past five years requiring treatment except basal or squamous skin carcinomas or carcinoma in situ of the cervix
- Serious cardiac, gastrointestinal, hepatic or pulmonary disease reducing life expectancy to less than five years
- Patients with serious intercurrent illness, requiring hospitalization.
- Other serious illnesses, e.g., serious infections requiring antibiotics or bleeding disorders.
- The patient is known to be positive for Human Immunodeficiency Virus (HIV) or other chronic infections (HBV, HCV) or has another confirmed or suspected immunosuppressive or immunodeficient condition.
- Known hypersensitivity reaction to any of the components of study treatment
- Pregnancy (absence to be confirmed by ß-HCG urinary test, minimum sensitivity 25IU/L or equivalent units of HCG)) or lactation period
- Women of childbearing potential (WOCBP): Refusal or inability to use effective means of contraception (Pearl-Index <1). WOCBP will be instructed to adhere to contraception until 31 weeks after the last dose of investigational product
- Men who are sexually active with WOCBP must use any contraceptive method with a failure rate of less than 1% per year (Pearl-Index <1). Men receiving Nivolumab and who are sexually active with WOCBP will be instructed to adhere to contraception until 31 weeks after the last dose of investigational product
- Known alcohol or drug abuse
- Participation in another clinical study and use of any investigational or non-registered product (drug or vaccine) within the 30 days before registration
- Significant disease or condition which, in the investigator's opinion, would exclude the patient from the study
- Legal incapacity or limited legal capacity

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: NCT02523313

Contacts

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Locations

Germany

Charité Berlin — **Recruiting**
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Contact: Felix Kiecker, Dr. felix.kiecker@charite.de

Elbe Klinikum Buxtehude — **Recruiting**
Buxtehude, Germany, 21614
Contact: Peter Mohr, Dr. peter.mohr@elbekliniken.de

Universitätsklinikum Dresden — **Recruiting**
Dresden, Germany, 01307
Contact: Friedegund Meier, Prof. Dr. friedegund.meier@uniklinikum-dresden.de

Studienzentrum Hautklinik Universitätsklinikum Essen (AöR) Klinik für Dermatologie — **Not yet recruiting**
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SRH Wald-Klinikum Gera GmbH — **Recruiting**
Gera, Germany, 07548
Contact: Martin Kaatz, PD Dr. kaatz.studienzentrum@wkg.srh.de

Medizinische Hochschule Hannover — **Recruiting**
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Contact: Ralf Gutzmer, Prof. Dr. gutzmer.ralf@mh-hannover.de

SLK Kliniken Heilbronn GmbH — **Recruiting**
Heilbronn, Germany, 74078

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Sponsors and Collaborators

Prof. Dr. med. Dirk Schadendorf

Investigators

Principal Investigator: Dirk Schadendorf, Prof. Dr. Studienzentrum Hautklinik Universitätsklinikum Essen (AöR) Klinik für Dermatologie

More Information

Responsible Party:	Prof. Dr. med. Dirk Schadendorf, Prof. Dr. med., University Hospital, Essen
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Health Authority:	Germany: Paul-Ehrlich-Institut

Additional relevant MeSH terms:

Melanoma	Nevi and Melanomas
Neuroendocrine Tumors	Antibodies, Monoclonal
Neuroectodermal Tumors	Nivolumab
Neoplasms, Germ Cell and Embryonal	Immunologic Factors
Neoplasms by Histologic Type	Physiological Effects of Drugs
Neoplasms	Antineoplastic Agents
Neoplasms, Nerve Tissue	

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