Adjuvant Therapy of Completely Resected Merkel Cell Carcinoma With 3 mg/kg BW Ipilimumab (Yervoy®) Versus Observation (ADMEC)

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

Verified December 2015 by University Hospital, Essen

Sponsor:
Prof. Dr. med. Dirk Schadendorf

Collaborator:
Bristol-Myers Squibb

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

ClinicalTrials.gov Identifier:
NCT02196961

First received: June 20, 2014
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History of Changes

Purpose

Primary Objective:

To estimate the efficacy of adjuvant ipilimumab therapy in completely resected Merkel cell carcinoma (MCC) patients; i.e. the primary endpoint is disease-free survival (DFS) rate at 12 months, defined as the number of patients alive and free of disease at 12 months after randomization divided by the total number of patients randomized.

Secondary Objectives:

To assess safety and additional efficacy parameters of the ipilimumab treatment in MCC, as well as to characterize potential biomarkers; secondary endpoints are: (i) adverse events according to CTCAE (Common Terminology Criteria for Adverse Events), Version 4.0 criteria, that are definitely, probably, or possibly related to the administration of ipilimumab, (ii) Overall survival rate at 12 months, defined as the number of patients surviving at 12 months after randomization divided by the total number of patients randomized.

Condition	Intervention	Phase
Merkel Cell Carcinoma	Drug: Ipilimumab	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Prospective Randomized Trial of an Adjuvant Therapy of Completely Resected Merkel Cell Carcinoma (MCC) With 3 mg/kg BW Ipilimumab (Yervoy®) Every 3 Weeks for 12 Weeks Versus Observation

Resource links provided by NLM:

Drug Information available for: Ipilimumab

Genetic and Rare Diseases Information Center resources: Merkel Cell Carcinoma Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by University Hospital, Essen:

Primary Outcome Measures:

- Disease-free survival (DFS) rate at 12 months [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: No]

  The number of patients alive and free of disease at 12 months after randomization divided by the total number of patients randomized.

Secondary Outcome Measures:

- Number of adverse events [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: Yes]

  Adverse events according to CTCAE, Version 4.0 criteria, that are related to the administration of Ipilimumab

- Overall survival rate at 12 months [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: No]

  Overall survival rate at 12 months, defined as the number of patients alive at 12 months after randomization divided by the total number of patients randomized.

Other Outcome Measures:

- Disease free survival [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: No]

  Number of patients free of disease at the end of study

- Overall survival [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: No]

  Number of patients still alive at the end of study

- Identification of prognostic/predictive biomarkers [Time Frame: 1 year post last patient first treatment/randomization] [Designated as safety issue: No]

  Identify and validate prognostic/predictive biomarkers such as immune status, kinetics of the absolute lymphocyte count (ALC), or tumor microenvironment characteristics

Estimated Enrollment:	222
Study Start Date:	June 2014
Estimated Study Completion Date:	June 2018
Estimated Primary Completion Date:	June 2017 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
No Intervention: Observation After complete resection of Merkel cell carcinoma, patients randomized to the observational arm will be observed only	
Experimental: Ipilimumab After complete resection of Merkel cell carcinoma, patients randomized to the treatment arm will receive ipilimumab as a single agent (3 mg/kg) administered intravenously over a 90 minute period every 3 weeks for a total of four doses, as tolerated, i.e. day 1 (week 1), day 22 (week 4), day 43 (week 7), day 64 (week 10).	Drug: Ipilimumab adjuvant treatment of completely resected Merkel cell carcinoma Other Name: Yervoy

Show Detailed Description

Eligibility

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

Criteria

Inclusion Criteria:

1. The patient is willing and able to give written informed consent.
2. Central histological confirmation of diagnosis of Merkel cell carcinoma (MCC).
3. All MCC manifestations have been completely resected by surgery within 12 weeks before enrolment.
4. No currently present metastases (as confirmed by standard imaging studies (e.g. suggested by S2k guidelines)).
5. No previous systemic therapy for MCC.
6. Required values for initial laboratory tests:
   - WBC ≥ 2000/uL
   - ANC ≥ 1000/uL
   - Platelets ≥ 75 x 103/uL
   - Hemoglobin ≥ 8 g/dL (≥ 80 g/L; may be transfused)
   - Creatinine ≤ 2.0 x ULN
   - AST/ALT ≤ 2.5 x ULN
   - Total Bilirubin ≤ 2.0 x ULN, (except patients with Gilbert's Syndrome, who must have a total bilirubin less than 3.0 mg/dL)
7. ECOG performance status 0 or 1.
8. No active or chronic infection with HIV, Hepatitis B (HBV) or C (HCV).
9. Men and women, ≥ 18 years of age.
10. Women of childbearing potential (WOCBP) must be using an adequate method of contraception (Pearl-Index < 1) to avoid pregnancy for up to 12 weeks after the last dose of ipilimumab, in such a manner that the risk of pregnancy is minimized. WOCBP include any female who has experienced menarche and who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation, or bilateral

oophorectomy) or is not post-menopausal. WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 72 hours before the start of ipilimumab.

11. Men of fathering potential must be using an adequate method of contraception to avoid conception for up to 12 weeks after the last dose of investigational product in such a manner that the risk of pregnancy is minimized.

Exclusion Criteria:

1. Autoimmune disease: Patients with a history of inflammatory bowel disease, including ulcerative colitis and Crohn's Disease, are excluded from this study, as are patients with a history of symptomatic disease requiring systemic steroids (e.g., rheumatoid arthritis, systemic progressive sclerosis, systemic lupus erythematosus, autoimmune vasculitis); autoimmune motor neuropathy.
2. Other serious illnesses, e.g., serious infections requiring i.v. antibiotics.
3. 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 immune deficient condition.
4. Any underlying medical or psychiatric condition, which in the opinion of the investigator will make the administration of ipilimumab hazardous or obscure the interpretation of AEs, such as a condition associated with frequent diarrhea.
5. Any non-oncology vaccine therapy for up to 1 month before or after any dose of ipilimumab.
6. A history of prior or current treatment with a T cell potentiating agent (e.g. IL-2, interferon, anti-CTLA-4, anti-CD137, anti-PD1, anti-PDL1, or anti-OX40 antibody).
7. Chronic use of immunosuppressive agents or systemic corticosteroids.
8. Women of childbearing potential (WOCBP), defined above in Section 5.1, who:
    - are unwilling or unable to use an acceptable method of contraception to avoid pregnancy for up to 12 weeks after the last dose of investigational product
    - have a positive pregnancy test at baseline
    - are pregnant or breastfeeding.
9. The patient has psychiatric or addictive disorders that may compromise his/her ability to give informed consent or to comply with the trial procedures.
10. Prisoners or subjects who are compulsorily detained (involuntarily incarcerated) for treatment of either a psychiatric or physical (e.g., infectious) illness.
11. Men of reproductive potential unwilling to use an adequate method to avoid pregnancy for up to 12 weeks after the last dose of investigational product.
12. Use of any investigational or non-registered product (drug or vaccine) other than the study treatment.

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: NCT02196961

Contacts

Contact: Dirk Schadendorf, Prof. Dr. +49 201-723 4342 ext 4342 Dirk.Schadendorf@uk-essen.de

Locations

Germany

University Hospital Essen, Dermatology — **Recruiting**
Essen, NRW, Germany, 45122
Contact: Dirk Schadendorf, Prof. Dr. +49-201- 723 ext 4342 dirk.schadendorf@uk-essen.de
Contact: Lisa Zimmer, Dr. med. lisa.zimmer@uk-essen.de
Principal Investigator: Dirk Schadendorf, Prof. Dr.

Elbeklinikum Buxtehude — **Recruiting**
Buxtehude, Germany, 21614
Contact: Peter Mohr, Dr. med. peter.mohr@elbekliniken.de
Contact: Leonie Bluhm, Dr. med. leonie.bluhm@elbekliniken.de
Principal Investigator: Peter Mohr, Dr. med.

University Hospital Dresden, Dermatology — **Recruiting**
Dresden, Germany, 01307
Contact: Friedegund Meier, Prof. Dr. friedegund.meier@uniklinikum-dresden.de
Contact: Marlene Garzarolli, Dr. med. marlene.garzarolli@uniklinikum-dresden.de
Principal Investigator: Friedegund Meier, Prof. Dr.

National Centre for Tumour Diseases (NCT) — **Recruiting**
Heidelberg, Germany, 69120
Contact: Jessica Hassel, Dr. med. jessica.hassel@med.uni-heidelberg.de
Contact: Martin Hartmann, Dr. med. martin.hartmann@med.uni-heidelberg.de
Principal Investigator: Jessica Hassel, Dr. med.

University Hospital Schleswig-Holstein, Kiel — **Recruiting**
Kiel, Germany, 24105

Contact: Katharina Kähler, Dr. med. kkaehler@dermatology.uni-kiel.de
Contact: Axel Hauschild, Prof. Dr. ahauschild@dermatology.uni-kiel.de
Principal Investigator: Axel Hauschild, Prof. Dr.

University Hospital München (LMU) **Recruiting**
Munich, Germany, 80337
Contact: Carola Berking, Prof. Dr. carola.berking@med.uni-muenchen.de
Contact: Tanja Maier, Dr. med. tanja.maier@med.uni-muenchen.de
Principal Investigator: Carola Berking, Prof. Dr.

University Hospital Tübingen **Recruiting**
Tübingen, Germany, 72076
Contact: Claus Garbe, Prof. Dr. claus.garbe@med.uni-tuebingen.de
Contact: Thomas Eigentler, Dr. med. thomas.eigentler@med.uni-tuebingen.de
Principal Investigator: Claus Garbe, Prof. Dr.

Sponsors and Collaborators

Prof. Dr. med. Dirk Schadendorf

Bristol-Myers Squibb

Investigators

Principal Investigator: Dirk Schadendorf, Prof. Dr. University Hospital, Essen

More Information

Responsible Party:	Prof. Dr. med. Dirk Schadendorf, University Hospital, Essen
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Keywords provided by University Hospital, Essen:
Merkel cell carcinoma
Ipilimumab
Adjuvant

Additional relevant MeSH terms:

Carcinoma	Carcinoma, Neuroendocrine
Carcinoma, Merkel Cell	Neuroendocrine Tumors
Neoplasms, Glandular and Epithelial	Neuroectodermal Tumors
Neoplasms by Histologic Type	Neoplasms, Germ Cell and Embryonal
Neoplasms	Adenocarcinoma
Polyomavirus Infections	Neoplasms, Nerve Tissue
DNA Virus Infections	Antibodies, Monoclonal
Virus Diseases	Immunologic Factors
Tumor Virus Infections	Physiological Effects of Drugs

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