PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

Multicenter, Open-label Phase II Trial on Post-surgery Chemoradiation in Combination With Cetuximab in Squamous Cell Carcinoma of the Head and Neck With High Risk of Locoregional Recurrence.

Trial Acronym

ACCRA-HN

URL of the trial

[---]*

Brief Summary in Lay Language

This multicenter, open-label, uncontrolled phase II trial evaluates safety and efficacy of post-operative chemoradiation in combination with cetuximab in squamous cell carcinoma of the head and neck.

Brief Summary in Scientific Language

Advanced squamous cell carcinoma of the head and neck still has a poor prognosis and loco-regional recurrence frequently occurs. Efforts have been made to improve response rates and survival and different therapeutic regimens including concurrent chemo-radiotherapy or sequential chemo-radiotherapy have been developed.

To further increase the outcome of patients with locally advanced SCCHN effective new treatments with minimal toxicities are needed. Molecular targeted agents, which do not demonstrate overlapping toxicities with commonly used chemotherapy agents, have therefore been investigated. The EGFR is widely expressed at high levels in SSCHN and is associated with poor prognosis.

Cetuximab has already been investigated in combination with radiotherapy or chemotherapy in patients with head and neck cancer. The immunoradiotherapy was well

tolerated with most of the side effects related to the high dose irradiation. The most common side effects are mucositis and dysphagia. Additionally, skin reactions appear sometimes more frequently in cetuximab administration. Grade 3 to 4 infusion reactions were observed in 3% of the patients treated with cetuximab. Based on the current promising results with RCT in patients with locally advanced head and neck cancer and clinical results with EGFR-antibodies plus RT, the present study was primarily designed to define the acute grade 3/4 toxicity.

We expect to show effective results in reducing the risk of distant metastasis, with administration of an additional six month adjuvant cetuximab treatment, in patient with recurrent SCCHN.

Organizational Data

- DRKS-ID: **DRKS00003939**
- Date of Registration in DRKS: **2012/05/09**
- Date of Registration in Partner Registry or other Primary Registry: **2008/11/13**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **MC-LKP_233 , Ethik-Kommission an der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf**

Secondary IDs

- Primary Registry-ID: **NCT00791141 (ClinicalTrials.gov)**
- Sponsor-ID: **ACCRA-HN (Heinrich-Heine University, Duesseldorf)**

Health condition or Problem studied

- Free text: **Head and Neck Cancer**
- ICD10: **C13 - Malignant neoplasm of hypopharynx**
- ICD10: **C10 - Malignant neoplasm of oropharynx**
- ICD10: **C32 - Malignant neoplasm of larynx**

Interventions/Observational Groups

- Arm 1: **Drug: Cetuximab**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Rate of patients experiencing grade 3/4 acute toxicities not considering grade 3/4 skin tox. outside the radiation portals combined with 2-years disease-free survival rate.; time frame: any toxicities occurring within 90 days post radiation start

Secondary Outcome

- Incidence of Loco-regional relapse; time frame: assessment after patient has completed follow-up
- Disease-free survival; time frame: time from start of surgery to the first evidence of loco-regional or distant tumor relapse or death
- Progression-free survival; time frame: from start of surgery to the first observation of disease progression or death
- Overall survival; time frame: censored at the time of last documented efficacy
- The rate of patients with secondary primary neoplasm; time frame: assessment after patient has completed follow-up
- The incidence of late toxicity; time frame: beyond 90 days after start of radiation therapy

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- **Department of Radiotherapy and Radiological Oncology, University Hospital Munich, Munich**
- **Department of Radiotherapeutics of the University Hospital Freiburg, Freiburg**
- **Department of Radiological Oncology University Hospital Heidelberg, Heidelberg**
- **Department of Radiotherapy and Radiological Oncology University Hospital Tuebingen, Tuebingen**
- **Department of Radiotherapy and Radiological Oncology University Hospital Ulm, Ulm**
- **Department of Radiotherapy an Radiological Oncology University Hospital Essen, Essen**
- **Department of Radiotherapy and Radiological Oncology University Hospital Mainz, Mainz**
- **Department of Radiotherapy, University Hospital Schleswig Holstein, Campus Lübeck, Lübeck**
- **Department of Radiotherapy and Radiological Oncology Universität Hospital Jena, Jena**
- **Charité University Medicine, Department of Radiotherapy and Radiological Oncology, Berlin**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2008/08/31**
- Target Sample Size: **80**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **70 Years**

Additional Inclusion Criteria

- Signed written informed consent;

- Males or females between 18 and 70 years of age;

- Surgically resected squamous cell carcinomas of the hypopharynx, oropharynx, larynx and oral cavity with high risk of locoregional recurrence not more than 6-9 weeks (maximum) ago;

- To be categorized as high risk patients have to fulfil at least one of the

following criteria:

- **R0 - resection <5 mm margin**
- **R1 - resection**
- **Extracapsular nodal extension;**

- **no previous chemotherapy, radiotherapy;**
- **Performance status ECOG: 0 - 1;**
- **Contraception in male and female patients if of childbearing potential, willingness to use effective contraceptive method for the study duration and 2 months post-dosing;**
- **Adequate renal, liver and hematological functions (within maximum 9 weeks until surgery):**
  - **Adequate bone marrow function: neutrophils > 1.5 x 10^9/L, platelets > 100 x 10^9/L, hemoglobin > 10.0 g/dL**
  - **Adequate liver function: Bilirubin < 2.0 mg/dL, AST, ALT, AP, γ-GT < 3 x ULN**
  - **Adequate renal function: creatinine clearance > =60 ml/min**
- **No distant metastases;**

Exclusion criteria

- **Nasopharyngeal carcinoma;**
- **R2 resection;**
- **Invalid informed consent;**
- **Performance Status > 1;**
- **Previous chemotherapy or radiotherapy for carcinoma of the head and neck;**
- **Prior exposure to EGFR pathway targeting therapy;**
- **Other serious illness or medical conditions:**
  - **Unstable cardiac disease despite treatment, congestive heart failure NYHA grade 3 and 4;**
  - **Clinically significantly abnormal electrocardiogram (ECG) or left ventricular**

ejection fraction (LVEF) below the institutional range of the normal

- Significant neurologic or psychiatric disorders including dementia or seizures;

- Active uncontrolled infection;

- Active disseminated intravascular coagulation;

- Other serious underlying medical conditions which could impair the ability of the patient to participate in the study;

- Symptomatic peripheral neuropathy National Cancer Institute-Common Toxicity Criteria (NCI-CTC v3.0) grade 2 or ototoxicity grade 2, except if due to trauma or mechanical impairment due to tumor mass;

- Having participated in another therapeutic clinical trial or any investigational agent in the preceding 30 days;

- Known allergic/hypersensitivity reaction to any of the components of the treatment;

- Pregnancy (absence confirmed by serum/urine β-HCG) or breast-feeding;

- Known drug abuse;

- Other previous malignancy within 5 years, with exception of a history of a previous basal cell carcinoma of the skin or pre-invasive carcinoma of the cervix;

- Legal incapacity or limited legal capacity;

- Sensitivity and incompatibility against 5-Fluorouracil

- Sensitivity and incompatibility against platinum-compounds

- Known incompatibilities >grade 3 towards cetuximab

- expected incompliance of patient (e.g. in case of severe alcohol addiction)

- Dental evaluation: Pre treatment dental care before start of radiochemotherapy (approximately 8 to 10 days lapse-time is needed for complete recovery before initiation of radiation therapy).

Addresses

■ **Primary Sponsor**

Heinrich-Heine University, Duesseldorf

Primary Sponsor

Heinrich-Heine University, Duesseldorf

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Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
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E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting complete, follow-up continuing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Further trial documents **Budach W, Bölke E, Homey B. Severe cutaneous reaction during radiation therapy with concurrent cetuximab. N Engl J Med. 2007 Aug 2;357(5):514-5. No abstract available.; 17671265**