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

## Trial Description

### Title

**Multimodal Therapy With and Without Cetuximab in Patients With Locally Advanced Esophageal Carcinoma - An Open-Label Phase III Trial**

### Trial Acronym

**[---]***

### URL of the trial

**[---]***

### Brief Summary in Lay Language

**RATIONALE: Radiation therapy uses high-energy x-rays and to kill tumor cells. Drugs used in chemotherapy, such as docetaxel and cisplatin, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. Monoclonal antibodies, such as cetuximab, can block tumor growth in different ways. Some block the ability of tumor cells to grow and spread. Others find tumor cells and help kill them or carry tumor-killing substances to them. It is not yet known whether giving radiation therapy together with chemotherapy is more effective with or without cetuximab in treating patients with esophageal cancer.**

**PURPOSE: This randomized phase III trial is studying giving radiation therapy together with chemotherapy, with or without cetuximab, followed by surgery in treating patients with locally advanced esophageal cancer that can be removed by surgery.**

### Brief Summary in Scientific Language

**OBJECTIVES:**

**Primary**

**- To determine the efficacy of neoadjuvant radiochemotherapy comprising docetaxel,**

**cisplatin, and radiotherapy in combination with cetuximab followed by surgery and adjuvant cetuximab versus neoadjuvant radiochemotherapy comprising docetaxel, cisplatin, and radiotherapy followed by surgery in patients with locally advanced esophageal carcinoma.**

**Secondary**

**- To compare the toxicity of the two therapy arms.**

**- To determine patterns of failure overall and with regard to histology.**

**- To evaluate economic aspects in a subproject and to perform a radiotherapy quality assurance program.**

**OUTLINE: This is a multicenter study. Patients are stratified according to center, histology (adenocarcinoma vs squamous cell carcinoma), primary tumor (T2 vs T3-4), and gender (male vs female). Patients are randomized to 1 of 2 treatment arms.**

**- Arm A:**

**- Induction chemotherapy (docetaxel and cisplatin) and concurrent cetuximab Patients receive docetaxel IV over 1 hour and cisplatin IV over 1 hour on day 1 and cetuximab IV over 1-2 hours on day 1, 8, and 15. Treatment repeats every 21 days for 2 courses.**

**- Chemotherapy (docetaxel and cisplatin), cetuximab, and concurrent radiotherapy Beginning in week 7, patients receive cetuximab IV over 1 hour, docetaxel IV over 30 minutes, cisplatin IV over 1 hour on days 43, 50, 57, 64, and 71 and undergo radiotherapy 5 days a week for 5 weeks. Patients then undergo surgery 4-7 weeks after completion of radiotherapy.**

**- Adjuvant cetuximab Beginning 3-6 weeks after completion of surgery, patients receive cetuximab IV over 1-2 hours once every 2 weeks for a total of 6 doses.**

**- Arm B: Patients receive induction chemotherapy comprising docetaxel IV and cisplatin IV for 2 courses as in arm A. Beginning in week 7, patients receive docetaxel IV, cisplatin IV, and concurrent radiotherapy for 5 weeks as in arm A. Patients then**

**undergo surgery 4-7 weeks after completion of radiotherapy.**

**After completion of study therapy, patients are followed up at 1 (arm B) or 6 (arm A) months, every 3 months for 3 years, and then every 6 months for 2 years.**

**Do you plan to share individual participant data with other researchers?**

**[---]***

**Description IPD sharing plan**

**[---]***

## Organizational Data

- DRKS-ID: **DRKS00003758**
- Date of Registration in DRKS: **2012/05/03**
- Date of Registration in Partner Registry or other Primary Registry: **2010/04/20**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

## Secondary IDs

- EudraCT-No. (for studies acc. to Drug Law): **2009-016584-10**
- Primary Registry-ID: **NCT01107639 (ClinicalTrials.gov)**
- Sponsor-ID: **SAKK 75/08 (Swiss Group for Clinical Cancer Research)**
- Other Secondary-ID: **SWS-SAKK-75/08**
- Other Secondary-ID: **EU-21024**
- Other Secondary-ID: **EUDRACT-2009-016584-10**
- Other Secondary-ID: **CDR0000669249**

## Health condition or Problem studied

- Free text: **Adenocarcinoma of the Gastroesophageal Junction**
- Free text: **Esophageal Cancer**
- ICD10: **C15 - Malignant neoplasm of oesophagus**

## Interventions/Observational Groups

- Arm 1: **Biological: cetuximab**
- Arm 2: **Drug: cisplatin**
- Arm 3: **Drug: docetaxel**
- Arm 4: **Procedure: adjuvant therapy**
- Arm 5: **Procedure: neoadjuvant therapy**

## Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Active control (effective treament of control group)**
- Purpose: **Treatment**
- Assignment: **Factorial**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

### Primary Outcome

**- Progression-free survival (PFS); time frame: time from randomization to a defined event.; time from randomization to one of the following events, whichever comes first:**
**Tumor progression at any time (progression of primary tumor or local lymph nodes, appearance of new lesions)**
**Recurrence at local, regional or distant site after surgery**
**Death from any cause**

### Secondary Outcome

**- Progression-free survival after surgery; time frame: from date of surgery to an event as defined in PFS.**
**- Adverse events according to CTCAE version 4.0 and major postoperative complications; time frame: during treatment and follow-up period.**
**- Pathological remission; time frame: Assessed according to the tumor regression model of Mandard**
**- Overall survival; time frame: time from trial randomization to the date of death from any cause**
**- Time to locoregional failure after R0 resection; time frame: from date of surgery to date of first documented loco-regional failure**

**- Time to systemic failure after R0 resection; time frame: from date of surgery to date of first documented systemic failure**
**- In-hospital mortality; time frame: occurring after surgery but while the patient remains in hospital**
**- Time to progression (TTP); time frame: Time to progression is defined as time from randomization to one of the following events, whichever comes first: - Tumor progression at any time. - Recurrence at local, regional or distant site after surgery. - Death due to tumor**

## Countries of recruitment

- AT **Austria**
- FR **France**
- DE **Germany**
- HU **Hungary**
- CH **Switzerland**

## Locations of Recruitment

- **Charite University Hospital - Campus Virchow Klinikum, Berlin**
- **Universitaetsklinikum Duesseldorf, Duesseldorf**
- **Kliniken Essen - Mitte, Essen**
- **Universitaetsklinikum Freiburg, Freiburg**
- **SLK-Kliniken Heilbronn GmbH, Heilbronn**
- **Klinikum Herford, Herford**
- **Klinikum Ludwigsburg, Ludwigsburg**
- **Universitaetsklinikum Giessen und Marburg GmbH, Marburg**
- **Klinikum der Universitaet Muenchen - Grosshadern Campus, Munich**
- **Staedtisches Klinikum Solingen, Solingen**
- **Klinikum Stuttgart - Katharinenhospital, Stuttgart**
- **Universitaetsklinikum Tuebingen, Tuebingen**

## Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2010/04/30**
- Target Sample Size: **300**
- Monocenter/Multicenter trial: **Multicenter trial**

Planned/Actual: **[---]***

(Anticipated or Actual) Date of First Enrollment: **2010/04/30**

Target Sample Size: **300**

Monocenter/Multicenter trial: **Multicenter trial**

- National/International: **International**

## Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **75 Years**

## Additional Inclusion Criteria

**DISEASE CHARACTERISTICS:**

**- Histologically confirmed esophageal carcinoma**

**- Meets the following criteria:**

**- Resectable, locally advanced disease as determined by the combination of CT scan, endoluminal ultrasound (EUS), PET scan, and a multidisciplinary team discussion**

**- T2, N1-3; T3, any N; or T4a, any N (if technically resectable with curative intent [R0] as decided by a multidisciplinary team discussion)**

**- EUS-guided fine-needle aspiration (FNA) allowed, but determines nodal status only if positive FNA**

**- No T1, any N, M0; or T2, N0, M0; T4a (due to infiltration of the trachea-bronchial tree or organ involvement that cannot be operated on with curative intent [R0] as decided by a multidisciplinary team discussion); T4b; or distant metastasis (M1)**

**- Type I or II disease according to the Siewert classification**

**- Squamous cell carcinoma (including basaloid-squamous cell and adenosquamous carcinoma) or adenocarcinoma of the thoracic esophagus or the esophagogastric junction (from 5 cm below the entrance of the esophagus into the thorax to the gastric cardia)**

**- Patients with obstructive tumors are eligible (obstructive tumors will be considered as locally advanced tumors)**

**- No cervical esophageal carcinoma and tumors involving the first 5 cm of the thoracic esophagus**

**- No airway infiltration in case of tumors at or above the tracheal bifurcation**

**- No peritoneal carcinomatosis in case of adenocarcinomas infiltrating the gastric cardia (i.e., esophagogastric junction carcinoma Siewert type I or II)**

**PATIENT CHARACTERISTICS:**

**- WHO performance status 0-1**

**- Neutrophil count ≥ 1.5 x 10^9/L**

**- Platelet count ≥ 100 x 10^9/L**

**- Creatinine clearance > 60 mL/min**

**- Bilirubin ≤ 1.0 times upper limit of normal (ULN)**

**- Alkaline phosphatase ≤ 2.5 times ULN**

**- AST ≤ 1.5 times ULN**

**- INR normal**

**- PTT ≤ 1.0 times ULN**

**- Not pregnant or nursing**

**- Negative pregnancy test**

**- Fertile patients must use effective contraception during and for 12 months after completion of study therapy**

**- FEV_1 ≥ 1.5 L OR ≥ 75% of the reference value**

**- Must be compliant and geographically proximal for staging and follow-up**

**- Considered operable (i.e., appropriate organ functions and ability to undergo general anesthesia)**

**- No other malignancies within the past 5 years except nonmelanomatous skin cancer or adequately treated carcinoma in situ of the cervix**

**- No severe or uncontrolled cardiovascular disease, including any of the following:**

**- NYHA class III-IV congestive heart failure**

**- Unstable angina pectoris**

**- Myocardial infarction within the past 12 months**

**- Significant arrhythmias**

**- No psychiatric disorder precluding understanding of information on trial related topics, giving informed consent, and answering questionnaires**

**- No active uncontrolled infection**

**- No serious underlying medical condition that, in the opinion of the investigator, could impair the ability of the patient to participate in the trial (e.g., uncontrolled diabetes mellitus or active autoimmune disease)**

**- No preexisting peripheral neuropathy > grade 1**

**- No definite contraindications for the use of corticosteroids and antihistamines as premedication**

**- No known hypersensitivity to trial drugs or hypersensitivity to any other component of the trial drugs**

**PRIOR CONCURRENT THERAPY:**

**- No prior chemotherapy or radiotherapy to the chest**

**- At least 30 days since prior treatment in another clinical trial**

**- No concurrent drugs contraindicated for use with the trial drugs**

**- No other concurrent anticancer treatments**

**- No other concurrent experimental drugs or investigational treatments**

### Exclusion criteria

**[---]***

## Addresses

■ **Primary Sponsor**

**Swiss Group for Clinical Cancer Research**

**Primary Sponsor**

**Swiss Group for Clinical Cancer Research**

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

- **Contact for Scientific Queries**

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URL: **[---]***

## Sources of Monetary or Material Support

- **[---]***

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

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

## Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

## Trial Publications, Results and other documents

- Further trial documents **Clinical trial summary from the National Cancer Institute's PDQ® database**

*The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.*

*- Translation on version: 124*

*- Last processed date by ClinicalTrials.gov: 2013/12/01*

* *This entry means the parameter is not applicable or has not been set.*

*** *This entry means that data is not displayed due to insufficient data privacy clearing.*