Trial Overview

Primary Endpoint: Progression Free Survival PFS

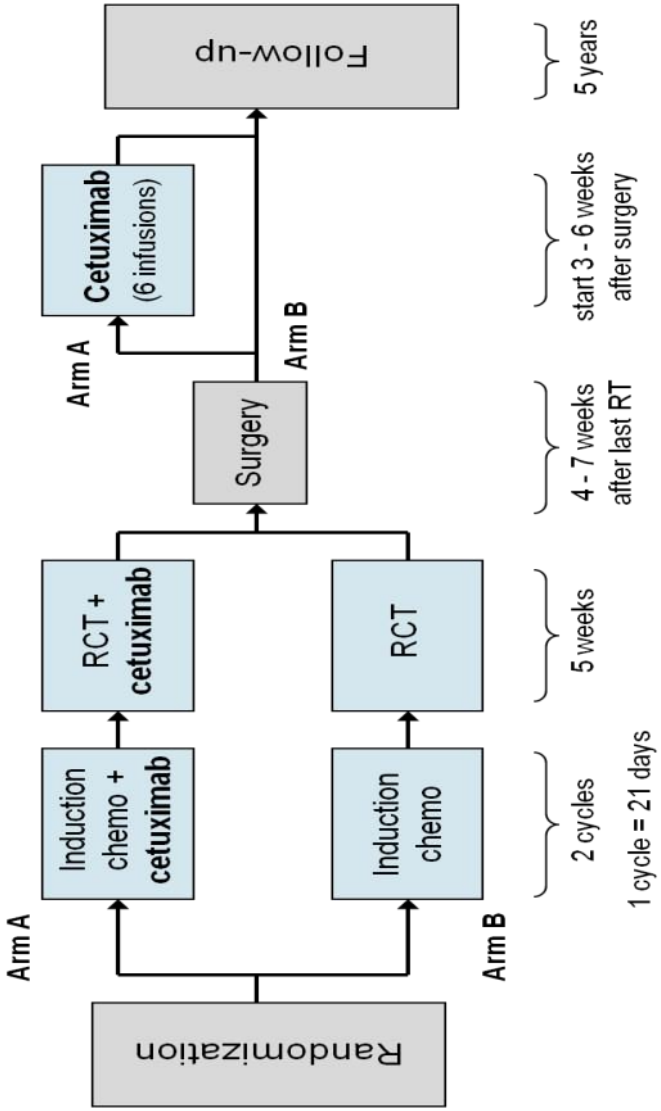
Secondary Endpoint:

- Progression-free survival after surgery
- Time to progression (TTP)
- Adverse events according to CTCAE version 4.0 and major postoperative complications
- Pathological remission (=TRG 1+2)
- R0-resection
- Overall survival
- Time to loco-regional failure after R0-resection
- Time to systemic failure after R0-resection
- Feasibility of the therapy: Completion of therapy, In-hospital mortality, Compliance with radio-therapy standards

Primary objective of the trial is to determine the efficacy of neoadjuvant radiochemotherapy (RCT) combined with immunotherapy followed by adjuvant immunotherapy compared with the same schedule without immunotherapy.

Secondary objectives of the trial are to compare the toxicity of the two therapy arms and to determine patterns of failure overall and with regard to histology; further to evaluate economic aspects in a subproject and to perform a radiotherapy quality assurance program.

Study design



AGMT Arbeitsgemeinschaft Medikamentöse Tumortherapie

SAKK 75/08

Multimodal therapy with and without cetuximab in patients with locally advanced esophageal carcinoma. An open-label phase III trial

EudraCT-Nr.: 2009-016584-10

COORDINATING INVESTIGATOR
Univ. Prof. Dr. Wolfgang Eisterer
Landeskrankenhaus-Universitätskliniken Innsbruck
Univ.-Klinik für Innere Medizin I
Contact: wolgang.eisterer@i-med.ac.at

PROJECT MANAGEMENT
Mag. Matthias Florian
m.florian@agmt.at - 0664/1296863

MONITORING
Barbara Meininger
b.meininger@agmt.at - 0664/88514814

An academic clinical trial by
Schweizerischen Arbeitsgemeinschaft für Klinische Krebsforschung (SAKK)
in cooperation with
Arbeitsgemeinschaft medikamentöse Tumortherapie (AGMT)

Inclusion Criteria

MOST IMPORTANT CRITERIA

Histologically confirmed 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 (=esophagogastric junction), types l and II according to the Siewert classification).

Resectable, locally advanced disease (the stage is determined by the combination of CT scan, EUS and PET and by a multidisciplinary team discussion): T2 N1-3 or T3 Nany or T4a Nany if technically resectable with curative intent (R0) as decided by a multidisciplinary team discussion

Health status: WHO performance status ≤ 1

Patient is considered operable (appropriate organ functions)

Age: 18-75 years

Adequate renal function, pulmonary function, hepatic function, hematologic values and normal coagulation according to local standard

Exclusion Criteria

MOST IMPORTANT CRITERIA

Distant metastasis (M1)

Cervical esophageal carcinoma and tumors involving the first 5 cm of the thoracic esophagus

Airway infiltration in case of tumors at or above the tracheal bifurcation

Previous malignancies within five years or concomitant malignancies, except: nonmelanomatous skin cancer or adequately treated in situ cervical cancer

Prior chemotherapy in oncological indication within the last 5 years or prior RT to the chest

Severe or uncontrolled cardiovascular disease

Active uncontrolled infection

Serious underlying medical condition

Pre-existing peripheral neuropathy (> grade 1) or pre-existing hardness of hearing

Concurrent treatment with other experimental drugs or other anti-cancer therapy-treatment in a clinical trial within 30 days prior to trial entry

Definite contraindications for the use of corticosteroids and antihistamines as premedication

Known hypersensitivity to trial drugs or hypersensitivity to any other component of the trial drugs

Any concomitant drugs contraindicated for use with the trial drugs according to the product information of the pharmaceutical companies

Additional research questions:

Translational research: Biobanking of tissue samples from initial biopsy and from surgical specimen (applicable for patients who gave consent for biobanking only)

Randomization and Stratification

Randomization is stratified for the factors:

- Center
- AC versus SCC (including basaloid-squamous cell and adenosquamous carcinoma)
- T2 versus T3/4
- male versus female

Amendment 2 + 3 (Abstract)

- Dexamethasone prior to all adjuvant cetuximab infusions to be administered at least two hours before
- Baseline thorax and abdomen CT may be omitted in case a diagnostic PET-CT, i.e. with intravenous contrast agent, is done
- Inclusion criteria for INR adapted (normal INR instead of ≤ 1.0 x ULN, since some centers do not have an ULN for INR)
- Secondary endpoints: Time to progression (TTP) added
- Trial termination is expected to be in Q2 2019