Perioperative Chemotherapy Compared To Neoadjuvant Chemoradiation in Patients With Adenocarcinoma of the Esophagus (ESOPEC)

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

Verified May 2016 by University Hospital Freiburg

Sponsor:
University Hospital Freiburg

Collaborator:
Clinical Trials Unit Freiburg

Information provided by (Responsible Party):
Prof. Dr. Jens Hoeppner, University Hospital Freiburg

ClinicalTrials.gov Identifier:
NCT02509286

First received: July 22, 2015
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History of Changes

Purpose

The trial is designed to investigate differences in outcome of patients with esophageal adenocarcinoma and junctional adenocarcinoma treated with perioperative (neoadjuvant + adjuvant) chemotherapy (FLOT) plus surgical resection versus neoadjuvant chemoradiation (CROSS) plus surgical resection.

Condition	Intervention	Phase
Esophageal Adenocarcinoma (UICC TNM7) Adenocarcinoma of the Esophagogastric Junction	Drug: 5-Fluorouracil Drug: Leucovorin Drug: Oxaliplatin Drug: Docetaxel Drug: Carboplatin Drug: Paclitaxel Radiation: Neoadjuvant radiation	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Perioperative Chemotherapy (FLOT Protocol) Compared To Neoadjuvant Chemoradiation (CROSS Protocol) in Patients With Adenocarcinoma of the Esophagus

Resource links provided by NLM:

Drug Information available for: Fluorouracil Paclitaxel Carboplatin Oxaliplatin Docetaxel

Genetic and Rare Diseases Information Center resources: Esophageal Cancer

U.S. FDA Resources

Further study details as provided by University Hospital Freiburg:

Primary Outcome Measures:

- Overall survival [Time Frame: At end of trial- up to 3 years in follow up] [Designated as safety issue: No]

  Overall survival will be calculated as time from start of study treatment to death due to any cause.

Secondary Outcome Measures:

- Progression free survival time (PFS) [Time Frame: From randomisation up to 3 years in follow up] [Designated as safety issue: No]

  PFS will be calculated as the time interval from randomisation to the first event of locoregional failure, metastatic progression or death.

- Site of failure: local, regional or distant Failure [Time Frame: From time of surgery up to 3 years in follow up] [Designated as safety issue: No]
- Recurrence free survival time [Time Frame: From time of surgery up to 3 years in follow up] [Designated as safety issue: No]

  RFS will be calculated in resected patients who achieved an R0 or R1 resection as the time interval from surgery to the date of first recurrence (local, regional or distant) or death, whatever comes first.

- Postsurgical Quality of Life [Time Frame: From randomization up to 3 years in follow up] [Designated as safety issue: No]
- Postoperative complications [Time Frame: From time of surgery up to 90 days postoperatively] [Designated as safety issue: Yes]
- Non-surgical site complications [Time Frame: From time of surgery up to 90 days postoperatively] [Designated as safety issue: Yes]

Estimated Enrollment:	438
Study Start Date:	January 2016
Estimated Study Completion Date:	June 2023
Estimated Primary Completion Date:	January 2022 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Perioperative Chemotherapy (FLOT): The FLOT Arm consists of the FLOT protocol, which consists of 5-Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel. Repetition every 2 weeks (d15, q2w). Four neoadjuvant cycles (8 weeks) prior to surgery and four adjuvant cycles (8 weeks) postoperatively are given. Surgery is carried out by transthoracic subtotal esophagectomy or by transabdominal distal esophageal resection plus gastrectomy depending on tumor localization.	Drug: 5-Fluorouracil 2600 mg/m² (24 hours), d1 every two weeks; Drug: Leucovorin 200 mg/m² in 250 ml NaCl 0.9%, d1 every two weeks; Drug: Oxaliplatin 85 mg/m² in 500 ml G5% over 2h, d1 every two weeks; Drug: Docetaxel 50mg/m2 in 250 ml NaCl 0.9% over 1h, d1 every two weeks;
Active Comparator: Neoadjuvant Chemoradiation (CROSS): The CROSS Arm consists of the CROSS protocol, which consists of neoadjuvant radiation therapy (41.4Gy / 23fractions) and concurrent chemotherapy with Carboplatin and Paclitaxel (5 weeks) prior to surgery. Surgery is carried out by transthoracic subtotal esophagectomy or by transabdominal distal esophageal resection plus gastrectomy depending on tumor localization.	Drug: Carboplatin Dose-dependant: 2mg/ml/min AUC in 500ml Glucose 5%, day 1, 8, 15, 22 and day 29. Drug: Paclitaxel 50mg/m2 in 500ml NaCl 0.9% over 1 h, day 1, 8, 15, 22 and day 29; Radiation: Neoadjuvant radiation 41.4Gy given in 23 fractions of 1.8Gy on days 1-5, days 8-12, days 15-19, days 22-26 and days 29-31.

Detailed Description:
According to the given evidence a survival benefit of perioperative chemotherapy (periCTX) over Neoadjuvant chemoradiation (neoCRT) for patients with Esophageal adenocarcinomas (EAC) has not been proven in any randomized controlled trials (RCT). Data supporting the value of periCTX have all been obtained in studies including mixed patient cohorts with EAC and gastric adenocarcinoma (GAC). Due to relevant differences of histologic subtype distribution, response to periCTX and survival rates between EAC and GAC there is a clear need to obtain evidence concerning the value of periCTX for EAC. As nowadays periCTX is extensively and successfully applied in clinical practice in patients with EAC there is an obvious need to obtain evidence from a multicentre RCT. Moreover a confirmation of the superior survival rates of the recent RCT on neoCRT should be obtained in a RCT conducted exclusively on EAC. Therefore, this prospective RCT with the primary objective of longterm patient survival comparing periCTX and neoCRT was designed.

Eligibility

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

Criteria

Inclusion criteria:

- Histologically verified adenocarcinoma of the esophagus according to the UICC definition (TNM7)
- Pre-treatment stage cT1N+, M0 or cT2-4a, N0/+, M0
- Age ≥18 years
- No prior abdominal or thoracic radiotherapy
- ECOG Performance status 0-2
- Adequate cardiac function (Patients with a cardiac history (e.g. myocardial infarction, heart failure, coronary artery disease) should have a cardiology review)
- Adequate bone marrow function (WBC>3x10^9/l; Hb>9g/dl; platelets >100x10^9/l)
- Adequate respiratory function. Symptomatic Patients should have pulmonary function tests with FEV1>1,5l)

- Adequate renal function (GFR >60ml/min)
- Adequate liver function (serum bilirubin <1.5x Upper level of Normal (ULN); AST <2.5x ULN and ALT <3x ULN (ULN as per institutional standard)
- written informed consent

Exclusion Criteria:

- Tumors of squamous or other non-adenocarcinoma histology
- Patients with advanced inoperable or metastatic esophageal adenocarcinoma
- Stage cT1N0 and cT4b
- Gastric carcinoma
- Prior chemotherapy for cancer,
- Clinically significant (i.e. active) cardiac disease (e.g. symptomatic coronary artery disease or myocardial infarction within last 12 months)
- Clinical significant lung disease (FEV 1<1,5l)
- Peripheral neuropathy Grade >1

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: NCT02509286

Contacts

Contact: Jens Hoeppner, Professor +49 761 270-26970 jens.hoeppner@uniklinik-freiburg.de

Contact: Ulrich T Hopt, Professor +49 761 270-28060 ulrich.hopt@uniklinik-freiburg.de

Locations

Germany

Uniklinik RWTH Aachen — **Not yet recruiting**
Aachen, Germany
Principal Investigator: Maximilian Schmeding, PD Dr.
Sub-Investigator: Ulf Peter Neumann, Professor

Charité Berlin Campus Virchow-Klinikum (CVK) — **Not yet recruiting**
Berlin, Germany, 13353
Principal Investigator: Peter Thuß-Patience, PD Dr.
Sub-Investigator: Matthias Biebl, PD Dr.

Universitätsklinikum Carl Gustav Carus an der Technischen Universität Dresden — **Not yet recruiting**
Dresden, Germany, 03107
Principal Investigator: Gunnar Folprecht, PD Dr.
Sub-Investigator: Nuh N. Rahbari, PD Dr.

Universitätsklinikum Düsseldorf — **Not yet recruiting**
Düsseldorf, Germany
Principal Investigator: Matthias Schauer, PD Dr.
Sub-Investigator: Wolfram Knoefel, Prof.

Universitätsklinikum Freiburg — **Recruiting**
Freiburg, Germany
Principal Investigator: Jens Hoeppner, Professor
Sub-Investigator: Thomas Brunner, Professor

Universitätsmedizin Göttingen — **Not yet recruiting**
Göttingen, Germany, 37099
Principal Investigator: Jochen Gaedcke, PD Dr.
Sub-Investigator: Alexander König, Dr.

Universitätsklinikum Hamburg-Eppendorf — **Recruiting**
Hamburg, Germany
Principal Investigator: Jakob R. Izbicki, Professor
Sub-Investigator: Cordula Petersen, Professor

Universitätsklinikum Schleswig-Holstein, Campus Kiel — **Not yet recruiting**
Kiel, Germany
Principal Investigator: Thomas Becker, Professor
Sub-Investigator: Benedikt Reichert, Dr.

Universitätsklinikum Leipzig — **Recruiting**
Leipzig, Germany
Principal Investigator: Ines Gockel, Professor
Sub-Investigator: Orestis Lyros, Dr.

Universitätsklinikum Schleswig-Holstein, Campus Lübeck Lübeck, Germany Principal Investigator: Tobias Keck, Professor Sub-Investigator: Martin Hoffmann, PD Dr.	**Not yet recruiting**
Universitätsklinikum Magdeburg Magdeburg, Germany Principal Investigator: Benjamin Garlipp, Dr. Sub-Investigator: Marino Venerito, Dr.	**Recruiting**
Universitätsmedizin Mainz Mainz, Germany Principal Investigator: Peter Grimminger, PD Dr. Sub-Investigator: Stefan Heinrich, PD Dr.	**Recruiting**
Klinikum der Universität München (LMU) München, Germany Principal Investigator: Jens Werner, Professor Sub-Investigator: Martin Angele, Professor	**Recruiting**
Universitätsklinikum Münster Münster, Germany Principal Investigator: Daniel Palmes, Professor Sub-Investigator: Norbert Senninger, Professor	**Not yet recruiting**
Sana Klinikum Offenbach GmbH Offenbach, Germany, 63069 Principal Investigator: Thomas Haist, Dr. Sub-Investigator: Ernst Reitsamer, Dr.	**Recruiting**
Universitätsklinikum Würzburg Würzburg, Germany Principal Investigator: Burkhard von Rahden, PD Dr. Principal Investigator: Volker Kunzmann, Professor	**Recruiting**

Sponsors and Collaborators

University Hospital Freiburg

Clinical Trials Unit Freiburg

Investigators

Principal Investigator: Jens Hoeppner, Professor University Hospital Freiburg

More Information

Responsible Party:	Prof. Dr. Jens Hoeppner, Head of Upper GI Surgery Programm, University Hospital Freiburg
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Keywords provided by University Hospital Freiburg:

Esophageal neoplasms	surgery
gastro-esophageal junction neoplasms	radiotherapy
adenocarcinoma	chemotherapy
esophagectomy	

Additional relevant MeSH terms:

Adenocarcinoma	Oxaliplatin
Esophageal Neoplasms	Carboplatin
Carcinoma	Fluorouracil
Neoplasms, Glandular and Epithelial	Antineoplastic Agents, Phytogenic
Neoplasms by Histologic Type	Antineoplastic Agents
Neoplasms	Tubulin Modulators
Gastrointestinal Neoplasms	Antimitotic Agents
Digestive System Neoplasms	Mitosis Modulators
Neoplasms by Site	Molecular Mechanisms of Pharmacological Action
Head and Neck Neoplasms	Antimetabolites
Digestive System Diseases	Antimetabolites, Antineoplastic
Esophageal Diseases	Immunosuppressive Agents
Gastrointestinal Diseases	Immunologic Factors
Paclitaxel	Physiological Effects of Drugs
Docetaxel	

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