Trial Description

Title

Translational Validation Trial-B (add-on phase I/II study to the Clinical Research Unit (Klinische Forschergruppe) KFO179-2: Preoperative radiochemotherapy (RCT) combined with 5-fluorouracil (5-FU) and oxaliplatin followed by 3 cycles of FOLFOX chemotherapy (5-FU+folinic acid+oxaliplatin) and total mesorectal excision (TME-surgery) in advanced rectal cancer (clinically staged as UICC stages II, III or IV) accompanied by molecular and cell biological (translational) analysis.

Trial Acronym

TransValid-KFO179/GRCSG-B-Trial

URL of the trial

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Brief Summary in Lay Language

Within the TransValid-KFO179/GRCSG-Trial-B the treatment modalities are modified by placing the chemotherapy part before surgery. The trial tests, if modification of the treatment sequences radiochemotherapy followed by 3 cycles of FOLFOX (5-Fluorouracil, oxaliplatin, folinic acid) and surgery with total mesorectal excision can improve the response rate for rectal cancer and reduce side-effects of chemotherapy. This approach avoids the problem of major compliance problems associated with post-operative adjuvant chemotherapy and is combined with biomolecular analysis of biomaterials.

Brief Summary in Scientific Language

TransValid-KFO179/GRCSG-Trial-B study tests the modification of the sequence of the three treatment modalities by placing the chemotherapy part before TME surgery.
All patients will receive preoperative RCT (total dose: 50.4 Gy, 28 fractions with a single dose of 1.8 Gy) combined with 5-FU (250 mg/m2 civ infusion on d1-d14 and d22-d35) and oxaliplatin (50 mg/m2 2h iv on d1, d8, d22 and d35). Three weeks after completion of RCT, patients will receive 3 applications of a shortened FOLFOX regimen [(400 mg FA/m2, 2-h civ, d 1; 100 mg oxaliplatin/m2 2-h civ in 500 ml Glucose 5%, d 1; 2400 mg 5-FU/m2 as 46-h civ infusion) on d1+d15+d30] as recently used within the CAO/AIO/ARO-04 trial (in adjuvant postoperative intent). TME-surgery will be performed 3-4 weeks after completion of RCT+CTx.
This innovative preoperative sequence of RCT followed by chemotherapy and TME-surgery is postulated to be beneficial according to response kinetics considerations and by maintaining an enhanced locoregional treatment in first place. This approach avoids the problem of major compliance problems associated with post-operative adjuvant chemotherapy.

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

[---]*

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[---]*

Description IPD sharing plan

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Organizational Data

- DRKS-ID: **DRKS00004186**
- Date of Registration in DRKS: **2012/10/26**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **23/10/11 , Ethik-Kommission der Medizinischen Fakultät der Georg-August-Universität Göttingen**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1132-0235**
- EudraCT-No.
(for studies acc. to Drug Law): **2011-004228-37**
- BfArM-No.: **4038135**

Health condition or Problem studied

- ICD10: **C20 - Malignant neoplasm of rectum**

Interventions/Observational Groups

- Arm 1: **- All patients receive preoperative RCT (radiochemotherapy) (total dose: 50.4 Gy, 28 fractions with a single dose of 1.8 Gy, applied as three-dimensional conformal irradiation by a three-field box technique combined with 5-FU (5-Fluorouracil) (250 mg/m2/d civ infusion on d1-d14 and d22-d35) and oxaliplatin (50 mg/m2 2h iv on d1, d8, d22 and d35 in 500 ml glucose 5%).**
- Three weeks after completion of RCT, patients receive 3 applications of a shortened FOLFOX regimen [(400 mg FA (folinic acid) (/m2, 2-h civ, d 1; 100 mg oxaliplatin/m2 2-h civ in 500 ml Glucose 5%, d 1; 2400 mg 5-FU/m2 as 46-h civ infusion) on d1+d15+d30] as recently used within the CAO/AIO/ARO-04 trial.
- TME-surgery is performed 3-4 weeks after completion of RCT+CTx.
- The follow-up procedures take place according to national guidelines (S3-Guideline, Dt. Krebsgesellschaft.

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: **I-II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **N/A**

Primary Outcome

Toxicity and histopathologically confirmed complete remission (pCR) will be compared exploratively to the TransValid-KFO179/ GRCSG-A-Trial.

The aim of this study is to establish the feasibility and to receive first data on the efficacy of an innovative sequential combination of established pre-operative intensified RCT (5-FU+Oxaliplatin) with consecutively intensive but shortened preoperative FOLFOX-chemotherapy (5-FU+Oxaliplatin) followed by TME-surgery.

Secondary Outcome

The results will be used in planned studies of the GRCSG (e.g. the CAO/AIO/ ARO-12 Trial, a randomized multicentric phase IIb trial).

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- University Medical Center **Klinik für Allgemein- und Viszeralchirurgie, Göttingen**
- University Medical Center **Klinik für Strahlenklinik und Onkologie, Frankfurt a.M.**

Recruitment

- Planned/Actual: **Actual**
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Planned/Actual: **Actual**

(Anticipated or Actual) Date of First Enrollment: **2013/04/05**

- Target Sample Size: **50**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **80 Years**

Additional Inclusion Criteria

- Males and females with histologically confirmed resectable advanced primary rectal cancer of the lower thirds of the rectum (localized within 0 to 12 cm above the anocutaneous verge as measured by rigid rectoscopy), clinically (c) classified as cT3/cT4 or cN+ carcinomas or with evidence for synchronous, but resectable distant metastases (liver metastases, pulmonary metastases)
- Aged 18 to 80 years, inclusive
- WHO/ECOG status ≤2
- Life expectancy >12weeks
- Adequate bone marrow function: WBC >3.0x109/L, neutrophils >1.5x109/L, thrombocytes >100x109/L, hemoglobin ≥10 g/dl
- Adequate liver function: bilirubin ≤2.0 mg/dl, SGOT, SGPT, AP, gamma-GT < three point five fold of upper level of normal range
- Creatinine clearance > 50ml/min, serum creatinine <1.5 mg/dl
- Written and signed informed consent of competent patient

Exclusion criteria

1. Prior or concurrent malignancy except non-melanoma skin cancer or cervical carcinoma FIGO stage 0-1 if the patient is successfully treated. Patients with other tumors that have been successfully treated and have not reappeared during the last 3-5 years, may be included at the principal investigator's discretion
2. Simultaneous therapy with other anti-cancer drugs
3. Major surgery at the pelvic region 2-3 weeks prior to inclusion
4. Previous chemotherapy (last 2 years before diagnosis of rectal cancer)
5. Chronic colonic diseases
6. Chronic diarrhea (>grade 1 according NCI CTCAE)
7. Allergic reaction to platin derivates or study medication
8. Known Dehydropyrimidindehydrogenase (DPD) deficiency
9. Symptomatic neuropathia (NCI CTC >1)
10. Concomitant treatment with sorivudin and analogous
11. Disseminated infection or sepsis
12. Disseminated intravascular coagulopathy
13. Patients (man and woman) with uncontrolled, serious physical or mental diseases, e.g.: instable cardiac disease in spite of medical treatment, myocardial infarction during the last 3 months prior to start of trial participation

14. Men and women unwilling or unable to use highly effective methods of contraception (per institutional standard) during treatment and for 6 months (male or female) after the end of treatment.
15. Patients (man and woman) who are not able or willing to accept treatment and follow-up care according to trial protocol.
16. Participation in an AMG-clinical trial in the period 30 days prior to inclusion
17. Current drug abuse
18. neurological or psychiatric dysfunction including dementia or seizure disorder

Addresses

- **Primary Sponsor**

  Universitätsmedizin Göttingen
  Georg-August-Universität
  Robert-Koch-Straße 40
  37075 Göttingen
  Germany

  Telephone: **0551398323**
  Fax: **05513914155**
  E-mail: **Studiensek-chirurgie at med.uni-goettingen.de**
  URL: **www.chirurgie-goettingen.de**

- **Contact for Scientific Queries**

  Universitätsmedizin GöttingenGeorg-August-UniversitätKlinik für Allgemein-, Viszeral- und Kinderchirurgie
  Mr. Prof. Dr. Torsten Liersch
  Robert-Koch-Straße 40
  37075 Göttingen
  Germany

  Telephone: **0551398323**
  Fax: **055114155**
  E-mail: **tliersc at gwdg.de**
  URL: **www.med.uni-goettingen.de**

- **Contact for Public Queries**

  Universitätsmedizin Göttingen
  Georg-August-Universität
  Ms. MA Johanna Kreutzer
  Robert-Koch-Straße 40
  37075 Göttingen
  Germany

  Telephone: **0551398323**
  Fax: **05513914155**
  E-mail: **Studiensek-chirurgie at med.uni-goettingen.de**
  URL: **www.med.uni-goettingen.de**

Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

  Deutsche Forschungsgemeinschaft (DFG)
  Kennedyallee 40
  53175 Bonn
  Germany

  Telephone: **022-8851**
  Fax: **0228-8852777**
  E-mail: **postmaster at dfg.de**
  URL: **www.dfg.de**

Status

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

Trial Publications, Results and other documents

** 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.*