KURZPROTOKOLL
TransValid-B-Studie

Öffentlicher Titel	Präoperativen Radichemotherapie gefolgt von FOLFOX und OP bei fortgeschrittenem Rektumkarzinom
Wissenschaftl. Titel	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.
Kurztitel	TransValid-B-Studie
Studienart	multizentrisch, prospektiv, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase I/II
Erkrankung	Verdauung: Darmkrebs (Kolorektales Karzinom): neoadjuvant
Ziele	- The primary objectives for this evaluation will be toxicity and histopathologically confirmed complete tumor remission (pCR). - The data will be compared exploratively to the separate TransValid-KFO179/GRCSG -Trial-A (validation study, n=200 patients) and to expectations derived from historical data (e.g. the large CAO/AIO/ARO-94 as well as -04 trial of the German Rectal Cancer Study Group [GRCSG] and others). - R0-rate of resection, circumferential resection margin, resection status -Rate of sphincter-sparing surgery - Clinical response after each treatment step - TRG - residual tumor infiltration depth - residual lymph node status incl. residual metastases in mesorectal lymph nodes - post-operative 30-day mortality, morbidity and late complications - quality of TME-surgery - acute and late toxicity of the RCT and CTx according to the CTC/ NCI - DFS after 2 and 3 ys - cumulative incidence of local relapses and/or distant metastases - overall cancer-specific survival (CSS) after 3 and 5 ys - Quality of life - Translational/biomarker trial: Re-evaluate the prognostic relevance of the KFO179 scores [A predictive microarray-based gene expression signatures and single gene biomarkers in patients treated with 5-FU based RCT] + primary clinicopathological parameters/biomarkers in a follow-up. Developing an improved 5-FU dose adjustment by measuring 5-FU blood levels during preoperative RCT and CTx.
Einschlusskriterien	- 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 syn- chronous, but resectable distant metastases (liver metastases, cM+): a) Transrectal endoscopic ultrasound is the mandatory local staging procedure; b) Additional high-resolution, thin-sliced (i.e. 3 mm) magnetic resonance imaging (MRI) of the pelvis to classify infiltration depth and/or cN+ status or extramural venous cancer invasion (based on MRI-criteria) ; c) abdominal sonography and chest x-ray /or contrast-enhanced computed tomography scan of the thorax and abdomen (and pelvis, if EUS and/or MRI are not available) to complete UICC staging classification - Aged 18 to 80 years, inclusive - WHO/ECOG status <=2

	- Life expectancy <=weeks - Adequate bone marrow function: WBC >3.0x10^9/L, neutrophils >1.5x10^9/L, thrombocytes >100x10^9/L, hemoglobin >=10 g/dl - Adequate liver function: bilirubin <=2.0 mg/dl, SGOT, SGPT, AP, gamma-GT < threefold of upper level of normal range - Creatinine clearance > 50ml/min, serum creatinine <=1.5 mg/dl - Written and signed informed consent of competent patient
Ausschlusskriterien	- Prior or concurrent malignancy (<=3 years prior to enrolment in study) except non-melanoma skin cancer or cervical carcinoma FIGO stage 0-1 if the patient is continuously disease-free patients with other tumors that have been successfully treated and have not reappeared during the last 3 years, may be included at the principal investigator's discretion - Simultaneous therapy with other anti-cancer drugs - Major surgery at the pelvic region 2-3 weeks prior to inclusion - Previous multimodal treatment of rectal cancer - Chronic colonic diseases - Chronic diarrhea (>grade 1 according NCI CTCAE) - Allergic reaction to platin-derivates or study medication - Symptomatic neuropathia (NCI CTC >=2) - Simultaneous treatment with sorivudin and analogous - Known Dihydropyrimidine dehydrogenase deficiency - Cardiac infarction/failure within 3 months before start of multimodal therapy - Disseminated infection or sepsis - Activated disseminated intravasal coagulopathia - Subject pregnant or breast feeding, or planning to become pregnant within 6 months after the end of treatment - 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 (adequate: oral contraceptives, intrauterine device or barrier method in conjunction with spermicidal jelly) - Participation in an AMG-clinical trial in the period 30 days prior to inclusion - Current drug abuse - Psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule (these conditions should be discussed with the patient before registration in the trial) - Insufficient compliance of the patient
Alter	18 - 80 Jahre
Prüfzentren	**Universitätsmedizin Frankfurt** (Rekrutierung beendet) Klinik für Strahlentherapie und Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Prof. Dr. med. Claus Rödel studien-strahlen@unimedizin-ffm.de
Sponsor	Universität Göttingen
Förderer	Deutsche Forschungsgemeinschaft
Registrierung in anderen Studienregistern	Deutsches Register Klinischer Studien DRKS00004186 EudraCT 2011-004228-37
Anmerkung	TransValid-KFO179/GRCSG-Trial-B