

KURZPROTOKOLL **TransValid-B-Studie**

Öffentlicher Titel	Präoperativen Radiochemotherapie 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	<ul style="list-style-type: none">- 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	<ul style="list-style-type: none">- 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

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Ausschlusskriterien	<ul style="list-style-type: none">- Life expectancy \leq weeks- Adequate bone marrow function: WBC $>3.0 \times 10^9/L$, neutrophils $>1.5 \times 10^9/L$, thrombocytes $>100 \times 10^9/L$, 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 > 50 ml/min, serum creatinine ≤ 1.5 mg/dl- Written and signed informed consent of competent patient- 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 analogues- Known Dihydropyrimidine dehydrogenase deficiency- Cardiac infarction/failure within 3 months before start of multimodal therapy- Disseminated infection or sepsis- Activated disseminated intravascular coagulopathy- 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
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Sponsor	Universität Göttingen
Förderer	Deutsche Forschungsgemeinschaft
Registrierung in anderen Studienregistern	Deutsches Register Klinischer Studien DRKS00004186 EudraCT 2011-004228-37
Anmerkung	TransValid-KFO179/GRCSSG-Trial-B