KURZPROTOKOLL
ACO/ARO/AIO-21

Öffentlicher Titel	Phase I Studie zu Capecitabin-basierter Radiochemotherapie in Kombination mit Anakinra als neoadjuvante Behandlung bei Darmkrebs
Wissenschaftl. Titel	Capecitabin-basierte Radiochemotherapie in Kombination mit dem Interleukin-1-Rezeptorantagonisten Anakinra zur Behandlung von Patienten mit Rektumkarzinom
Kurztitel	ACO/ARO/AIO-21
Studienart	prospektiv, Therapiestudie, offen/unverblindet, einarmig, Pharma-Studie, Investigator Initiated Trial (IIT)
Studienphase	Phase I
Erkrankung	Verdauung: Darmkrebs (Kolorektales Karzinom): neoadjuvant
Einschlusskriterien	- Male and female patients with histologically confirmed diagnosis of rectal adenocarcinoma localized 0-12 cm from the anocutaneous line as measured by rigid rectoscopy (i.e. lower and middle third of the rectum) - Staging requirements: High-resolution, thin-sliced (i.e. 3 mm) magnetic resonance imaging (MRI) of the pelvis is the mandatory local staging procedure - Patients with MRI-defined low risk rectal cancer with the presence of at least one of the following conditions: - cT2N0 or cT3a/bN0 tumors <=6 cm from the anocutaneous line that would require abdominoperineal resection or permanent colostomy, - Any rectal cancer of the upper third (12-16 cm) requiring FU-CRT according to German S3 guideline recommendations (i.e. cT4, mrCRM+, extensive N+) - Patients with MRI-defined intermediate/high risk rectal cancer, but not eligible for TNT (oxaliplatin-containing) protocols: - any cT3 if the distal extent of the tumor is < 6 cm from the anocutaneous line, or - cT3c/d in the middle third of the rectum (>= 6-12 cm) with MRI evidence of extramural tumor spread into the mesorectal fat of more than 5 mm (>cT3b), or - cT3 with clear cN1 based on strict MRI-criteria (see appendix), - cT4 tumors, or - Tany middle/low third of rectum with clear MRI criteria for N2, - mrCRM+ (<= 1mm), or - Extramural venous invasion (EMVI+) - Trans-rectal endoscopic ultrasound (EUS) is additionally used when MRI is not definitive to exclude early cT1 disease in the lower third or middle third of the rectum - Spiral-CT of the abdomen and chest to exclude distant metastases - Aged at least 18 years. No upper age limit - WHO/ECOG Performance Status <=1 - Adequate hematological, hepatic, renal and metabolic function parameters: - Leukocytes >= 3.000/mm^3, ANC >= 1.500/mm^3, platelets >= 100.000/mm^3, Hb > 9 g/dl, - Serum creatinine <= 1.5 x upper limit of normal, - Bilirubin <= 2.0 mg/dl, SGOT-SGPT, and AP <= 3 x upper limit of normal - Informed consent of the patient
Ausschlusskriterien	- Distant metastases (to be excluded by CT scan of the thorax and abdomen) - Prior antineoplastic therapy for rectal cancer - Prior radiotherapy of the pelvic region - Major surgery within the last 4 weeks prior to inclusion - Subject pregnant or breast feeding, or planning to become pregnant within 6 months after the end of treatment - Subject (male or female) is not willing to use highly effective methods of contraception during treatment and for 6 months after the end of treatment - On-treatment participation in a clinical study in the period 30 days prior to inclusion - Previous or current drug abuse - Other concomitant antineoplastic therapy

- Serious concurrent diseases, including neurologic or psychiatric disorders (incl. dementia and uncontrolled seizures), active, uncontrolled infections, active, disseminated coagulation disorder
- Clinically significant cardiovascular disease in (incl. myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) <= 6 months before enrolment
- Prior or concurrent malignancy <= 3 years prior to enrolment in study (Exception: non -melanoma skin cancer or cervical carcinoma FIGO stage 0-1), if the patient is continuously disease-free
- Known allergic reactions on study medication
- Known dihydropyrimidine dehydrogenase deficiency
- 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)
- History of severe hepatic impairment (e.g. Child-Pugh = Grade C)
- Moderate (Creatinine Clearance 30 to 49 mL/minute), severe (Creatinine Clearance <30 mL/minute) renal impairment
- Neutropenia (neutrophil count <1.5x109/l)
- Known hypersensitivity to Anakinra or E. coli derived proteins, Anakinra or any of the components of the product
- Asthma
- Patients with clinically significant bacterial, fungal, parasitic or viral infection, which require acute therapy. Patients with acute bacterial infections requiring antibiotic use should delay screening/enrollment until the course of antibiotic therapy has been completed
- Patients with known active hepatitis B, C or who are HIV-positive or who are at risk for HBV reactivation. At risk for HBV reactivation is defined as hepatitis B surface antigen positive or anti-hepatitis B core antibody positive. Prior test results obtained as part of standard of care that confirm a subject is immune and not at risk for reactivation (ie, hepatitis B surface antigen negative, surface antibody positive) may be used for purposes of eligibility and tests do not need to be repeated. Subjects with prior positive serology results must have negative polymerase chain reaction results. Subjects whose immune status is unknown or uncertain must have results confirming immune status before enrollment
- Subjects who are already using the following medications will not be allowed: - Tumor necrosis alpha inhibitors: Use on any of these biologics within 8 weeks of screening or baseline visit. - IL-6 inhibitors: Use of any IL-6 inhibitors within 8 weeks of screening or baseline visit. - Janus Kinase inhibitors: Use of baricitinib, tofacinitib, upadacitinib, and ruxolitinib, oclacitinib, fedratinib, within 2 weeks from screening or baseline visit. - Bruton's tyrosine kinase inhibitors: Ibrutinib, acalabrutinib, zanubrutinib. - CCR5 antagonist (CCR5 = C-C Chemokine Receptor Type 5; DMARD = Disease Modifying Anti-Rheumatic Drug): Leronlimab is also an immunomodulator. - DMARDs: cyclosporine, cyclophosphamide, mycophenolic acid, chlorambucil, penicillamine, azathioprine: Use within 6 months prior to screening or baseline visit. - Rituximab: Use of rituximab within 1 year of screening or baseline visit. - Abatacept: Use of abatacept within 8 weeks of screening or baseline visit.
- Patients who have any severe and/or uncontrolled medical conditions or other conditions that could affect their participation such as severe impaired lung functions as defined as spirometry and DLCO that is 50% of the normal predicted value and/or O2 saturation that is 88% or less at rest on room air

	- Patients under ongoing treatment with another investigational medication or having been treated with an investigational medication within 30 days (incl. live attenuated vaccine) of screening or 5 half-lives (whichever is longer) prior to the first dose of investigational product - Patients receiving chronic, systemic treatment with corticosteroids or another immunosuppressive agent. Topical or inhaled corticosteroids are allowed - History of any other disease, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates use of an investigational drug, or that might affect interpretation of the results of this study, or render the subject at high risk for treatment complications
Alter	18 Jahre und älter
Prüfzentren	**Strahlentherapie** (Nachbeobachtung) Theodor-Stern-Kai 7 60590 Frankfurt am Main Prof. Dr. med. Claus Rödel studien-strahlen@kgu.de **Universitätsklinikum Frankfurt** (Nachbeobachtung) Klinik für Strahlentherapie und Onkologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Prof. Dr. med. Claus Rödel studien-strahlen@kgu.de
Sponsor	Goethe-Universität Frankfurt
Förderer	Frankfurt Cancer Institute
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT04942626 EudraCT 2021-000562-15 (primäres Register)
Links	Weiterführende Informationen