APPLICANT/ COORDINATING INVESTIGATOR	Prof. Dr. M. Ebert, Department of Medicine II, University Hospital Mannheim, Heidelberg University, 68167 Mannheim, Phone: 0621-383 3284, matthias.ebert@umm.de
CONDITION	Patients receiving palliative chemotherapy for metastasized or locally recurrent gastrointestinal cancer before their last established palliative treatment line
OBJECTIVE(S)	With this study, we aim to establish precision oncology for patients with advanced gastrointestinal cancer by ex-vivo drug screening of individual patient derived organoids (PDOs). In particular, we aim 1) to establish individual PDOs and to perform a drug screen for identification of drugs with highest efficacy. 2) To assess the efficacy of a systemic treatment chosen by ex-vivo screening of individual PDOs in regards to response rate (≤5% vs. ≥20%, primary end-point) 3) To characterize molecular alterations of the PDOs and tumor and analyze gene-drug associations as potential predictive biomarkers
INTERVENTION(S)	Experimental intervention: 1. Biopsy to establish PDOs, 2. Treatment of the patient with best performing drug in PDO-based drug-screen Control intervention: No control intervention is performed Duration of intervention per patient: 1. Biopsy: 30-60minutes, 2. Treatment after last line therapy (until disease progression) Follow-up per patient: 24 months
KEY INCLUSION AND EXCLUSION CRITERIA	Key inclusion criteria: 1. Patients ≥ 18 years of age. 2. Performance status ECOG 0-2. 3. Histologically confirmed metastatic or locally recurrent colorectal cancer prior last line therapy. 4. Tumor accessible to biopsy and patient willing to undergo biopsy. 5. At least one measurable lesion of disease according to RECIST criteria. 5. Signed informed consent prior to any screening procedures Key exclusion criteria: 1. HIV, HBV or HCV infection. 2. Inadequate end organ function
OUTCOME(S)	Primary efficacy endpoint: Best objective response rate (ORR) per central review in last-line treated subjects (≤5% vs. ≥20%) determined by RECIST criteria Key secondary endpoint(s): Progression-free survival, overall survival, toxicity, quality of life (QoL), predictive value of PDO screens for treatment efficiency, treatment duration and dose intensity Assessment of safety: Patients will be closely monitored for the occurrence of adverse events (AE) and serious adverse events (SAE).
STUDY TYPE	Multicentered, single armed, phase II interventional clinical trial
STATISTICAL ANALYSIS	Efficacy: Objective response rate (≤5% vs. ≥20%, primary end-point) Description of the primary efficacy analysis and population: Descriptive analysis. The primary objective is to estimate best objective response rate (ORR) per investigator assessment in last-line treated subjects. A Fleming single-stage Phase II design will be used to test the null-hypothesis that the true ORR is 5% (P0) against a one-sided alternative that the ORR = 20% (PA). H0 : P ≤ P0 HA : P ≥ PA Safety: Rates of complications, adverse events and serious adverse events will be calculated with 95% confidence intervals for group comparisons. Secondary endpoint(s): Progression-free survival, Toxicity, QoL

SAMPLE SIZE	To be assessed for eligibility: (n = 70) To be allocated to trial: (n = 40) To be analyzed: (n = 30)
TRIAL DURATION	Time for preparation of the trial (months): 6 Recruitment period (months): 24 First patient in to last patient out (months): 48 Time for data clearance and analysis (months): 3 Duration of the entire trial (months): 57 (6 preparation, 48 study, 3 analysis)
PARTICIPATING CENTERS	To be involved (n): 3 High volume centers with expertise in treatment of advanced gastrointestinal cancer