STUDY TYPE	Non-interventional, exploratory
PRINCIPAL INVESTIGATOR	Dr. Benedikt Westphalen Medizinische Klinik und Poliklinik III, Klinikum der Universität München Marchioninistr. 15, 81377 München
TRIAL OFFICE	ClinAssess
SPONSOR	Klinikum der Universität München
CONDITION	Resectable pancreatic adenocarcinoma
DESIGN	Non interventional, exploratory.
INDICATION	Resectable pancreatic adenocarcinoma
Primary Objective	Comparison of disease-free survival (DFS) of patients with preoperative presence of ctDNA (Group A) and absence of ctDNA (Group B)
INTERVENTION(S)	None
OBJECTIVES of OPTIONAL TRANSLATIONAL RESEARCH	Comparison between preoperative and postoperative ctDNA levels (only in patients in Group A) Comparison between mutational status in tissue and blood (only in patients in Group A) Comparison of DFS based on tumor tissue mutational status (patients in Group A and Group B) Stratified by ctDNA status, molecular subtypes of FoundationOne CDx (F1CDx) and clinical parameters
BACKROUND/RATIONALE	Pancreatic ductal adenocarcinoma (PDAC) remains an almost uniformly lethal disease. Although significant progress has been made in the understanding of the molecular biology of pancreatic cancer, this knowledge has not translated into an improved prognosis for patients suffering from this devastating disease. Especially, mechanisms underlying early relapse after potentially curative surgery, resistance to therapeutic interventions as well as response to chemotherapy are incompletely understood. Alarmingly, pancreatic cancer is on the rise and will become the second leading cause of cancer-related death in Germany and the US by 2020 In order to treat a patient with potentially harmful systemic chemotherapy, a diagnosis has to be made. Many countries such as Germany demand a histological confirmation of malignancy in order to allow for treatment with chemotherapy. Due to its delicate location, biopsies of the pancreas are technically challenging and pose the risk of complications. Furthermore, cytological and histological diagnosis of pancreatic malignancy is highly depended on the expertise of the gastroenterologist, the underlying pancreatic disease and the on-site pathologists. Accordingly, novel means to diagnose and monitor patients with pancreatic cancer are of major clinical significance. Liquid biopsies have the potential to close this diagnostic gap as they rely on tumor-specific signatures in the circulation and are thus more specific than traditional tumor markers. Generally, analysis of circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) holds the biggest promise to adequately diagnose and monitor malignant disease based on liquid biopsies. While capturing and analyzing CTCs is complex, isolation and processing of ctDNA is relatively simple. Genetically, pancreatic cancer is defined by near ubiquitous activating mutations in the KRAS oncogene. Furthermore, mutations in p53, SMAD4/DPC4 and CDKN2A are observed with a high frequency. This overrepresentation of a relatively small group of highly conserved mutations renders pancreatic cancer especially suitable for ctDNA-based approach. While limited data based on small single center studies on liquid biopsies in pancreatic cancer exist a comprehensive and methodically standardized analysis of the value of ctDNA in the diagnosis, management and prognosis of pancreatic cancer is missing. Preliminary data from small clinical trials suggest, that the presence of preoperative ctDNA has a major prognostic impact on the disease-free and overall survival in patients undergoing curative surgery for resectable pancreatic cancer

KEY EXCLUSION CRITERIA	1. Non-resectable disease as determined by a local tumor board 2. Metastatic pancreatic disease 3. Previous neoadjuvant chemotherapy 4. Previous neoadjuvant radiotherapy 5. Histology other than PDAC such as acinar, neuroendocrine, mixed histology etc. in the resection specimen 6. Malignant disease other than PDAC within previous year (***exception***: patients with adequately treated and completely resected basal cell or squamous cell skin cancer; in situ cervical, breast or prostate cancer within previous year may be included)
KEY INCLUSION CRITERIA	1. Adult patients ≥ 18 years of age 2. Pancreatic mass, suspicious of pancreatic cancer, deemed resectable and resection planned. 3. Patient deemed medically fit for adjuvant chemotherapy by the investigator 4. Patient's legal capacity to consent to study participation 5. Signed and dated informed consent to participate in the study
STATISTICAL ANALYSIS	The analysis of the study will be exploratory and primarily use descriptive statistical methods. The primary analysis of the study will compare the disease-free survival time of patients with preoperative ctDNA positivity (Group A) to patients with preoperative ctDNA negativity (Group B) based on a Cox Proportional Hazards model with adjustments for relevant covariates.
SAMPLE SIZE	Under the assumptions of proportional hazards and exponential distribution, the study is planned to detect a difference (ratio of 1.8) in disease-free survival between ctDNA positive (Group A) and ctDNA negative patients (Group B) with a power of 80%, which requires a total number of 119 events (tumor disease recurrence or death) to be observed. To take deviations from assumptions into account, inclusion of 132 patients overall (about 44 patients with preoperative ctDNA positivity) in total is planned. An interim analysis will be conducted after 60 events have occurred to detect deviations from the statistical assumptions.
TRIAL DURATION	***Accrual period:*** The accrual period is estimated to last 24 months. ***Duration of individual observation*** Until occurrence of relapse (or death if death occurs earlier than relapse) for a maximum of 36 months after the date of surgery ***Estimated study duration:*** 5 years from the first patient enrolled until the end of study ***Start of the study:*** First patient First visit (FPFV): Date of the informed consent by the first patient enrolled *Planned* QII/2019 ***End of the study:*** Last patient's last Follow up visit *Planned* QII/2024