Synopsis

TITLE OF TRIAL	(EN) A Randomised Controlled Trial on Pulmonary Metastasectomy vs. Standard of Care in Colorectal Cancer Patients with ≥ 3 Lung Metastases (DE) Eine randomisiert-kontrollierte Studie zum Vergleich der pulmonalen Metastasektomie mit der Standardtherapie bei Patienten mit ≥ 3 pulmonalen Metastasen eines kolorektalen Karzinoms
SHORT TITLE	PUCC trial
PROTOCOL NUMBER	P001781
HEALTH CONDITION STUDIED	stage IV colorectal cancer
PHASE	n/a
OBJECTIVE(S)	The primary objective is to assess the effect of pulmonary metastasectomy compared to standard of care in patients with stage IV colorectal cancer on overall survival. Secondary objectives include Progression-free survival (PFS), Quality of life (QoL questionnaire), Complete remission, time without systemic therapy, impact of mutational status on treatment response and survival.
TREATMENT(S)	**Experimental treatment (Arm A):** pulmonary metastasectomy **Control treatment (Arm B):** standard of care **Duration of treatment per patient:** up to 6 weeks (pulmonary metastasectomy in Arm A) Treatment duration for Arm B not predefined **Follow-up per patient:** 36-60 months
KEY INCLUSION CRITERIA	1. Histologically confirmed colorectal adenocarcinoma 2. ≥ 3 technically resectable (R0) pulmonary metastases 3. Male or female patients aged ≥ 18 years without upper age limit 4. Resected primary tumour with intent to cure (sole prior (chemo) radiation of a rectal cancer with documented complete remission is permitted) 5. In case of previous treatment of hepatic metastases: no radiologic sign of residual hepatic disease at the time of trial randomisation 6. A minimum of 12 weeks of systemic therapy with the last treatment applied within 6 months prior to randomisation 7. Good performance status (ECOG 0-1)
KEY EXCLUSION CRITERIA	1. Active extra-thoracic tumour disease (including primary tumour *in situ*) 2. Prior resection of lung metastases (diagnostic resection is allowed) 3. Requirement of a pneumonectomy to achieve complete resection 4. Other malignancy in the past 5 years (except non-melanoma skin cancer or *in situ* cancer) 5. Histologically proven intrathoracic lymph node metastasis (except resectable single level mediastinal, hilar and pulmonary)
ENDPOINTS	**Primary endpoint:** Overall Survival (OS) **Secondary endpoint(s):** Progression-free survival (PFS), quality of life (QoL), complete remission, total duration of systemic therapy and further exploratory endpoints **Assessment of safety**: Adverse events and adverse events of Special Interest in Arm A

TRIAL DESIGN	Randomised controlled trial with two treatment arms	
STATISTICAL ANALYSIS	**Statistical methods used to compare groups for primary and secondary outcomes:** The primary analysis will be based on the intention-to-treat (ITT) principle. The effects of pulmonary metastasectomy and standard of care with respect to the primary endpoint overall survival will be estimated and tested by Cox regression. The regression model will include treatment and study site as independent variables, as well as age, disease-free interval at baseline, metachronicity vs. synchronicity, presence of lymph node metastasis, previous treatment of hepatic metastasis, mutational status and colon- vs rectal cancer. Analyses of the secondary endpoints will be performed in similar regression models as for the primary endpoints as appropriate for the respective type of data. **Methods for additional analyses, such as subgroup analyses and adjusted analyses:** As a sensitivity analysis, the analysis will be repeated in the per-protocol (PP) set, excluding patients with major protocol violations.	
SAMPLE SIZE	To be assessed for eligibility:	n = 260
	To be randomised to trial:	n = 152 (76:76)
	To be analysed:	n = 152
TRIAL DURATION	Recruitment period (months):	24
	First patient in to last patient out (months):	60
	Treatment duration per patient (weeks):	6
	Follow up duration per patient (months):	36-60
PLANNED DATES	Enrolment of first patient, first patient in (FPI)	1st quarter 2022
	Enrolment of last patient, last patient in (LPI)	1st quarter 2024
	End of trial defined as last patient last visit (LPLV)	1st quarter 2027
	Final statistical analysis	2nd quarter 2028
PARTICIPATING SITES	ca.15 sites in Germany	
FUNDER(S)	Deutsche Forschungsgemeinschaft (DFG) DFG project number: 418151269	