Study Synopsis

Applicant(s) / coordinating investigator(s)	**Coordinating investigator**: Florian Lordick, Prof. Dr. University Cancer Center Leipzig (UCCL) Leipzig University Medical Center, Liebigstr. 22, D- 04103 Leipzig, Germany E-mail: florian.lordick@medizin.uni-leipzig.de
Statistician	Dr. Aziz Ali (Cytel Inc. Stockholm, Sweden)
Title of trial (English)	Randomised Phase III Trial of First Line Intraperitoneal Paclitaxel and Systemic Therapy versus Systemic Therapy Alone in Gastric Cancer Patients with Peritoneal Metastases, IPa-Gastric trial
Title of trial (German)	Randomisierte Phase-III-Studie zur Erstlinienbehandlung mit intraperitonealem Paclitaxel und systemischer Therapie im Vergleich zur alleinigen systemischen Therapie bei Magenkrebspatienten mit Peritonealmetastasen, IPa-Gastric Studie
Medical condition	Gastric Cancer
Hypothesis	Intraperitoneal paclitaxel and Systemic Therapy provides better overall survival compared to Systemic Therapy alone.
Participants / study population	**Key inclusion criteria:** • Gastric or gastro-oesophageal junction Siewert type II or III adenocarcinoma verified by biopsy or cytology from the primary tumour. • Peritoneal metastasis verified by biopsy, or cytology from ascites or peritoneal wash fluid. • Staging laparoscopy with assessment of peritoneal cancer index (PCI) performed less than four weeks before enrolment. • Patients with tumour positive cytology (CYT+) without clinically manifest peritoneal metastases at baseline (PCI 0) staging laparoscopy can be included if they persist to be CYT+ after at least four cycles of systemic chemotherapy. • Adequate haematology assessment and serum chemistry • Eastern Cooperative Oncology Group (ECOG) performance status 0-1. • Age of at least 18 years. • Life expectancy of at least three months. **Key exclusion criteria:** • Comorbidity that does not allow treatment with ST or IP paclitaxel. • Confirmed or suspected severe abdominal adhesions • Distant metastases (including M1 lymph node metastases) other than peritoneal, with the specific exception of ovarian metastases. • Symptomatic ascites already requiring drainage for palliation, or expected to require drainage in the short term. • Previously received palliative-intent systemic chemotherapy (with the specific exception of cytology positive patients without manifest peritoneal metastases) for the current gastric • cancer. Perioperative chemotherapy within previous curative context is allowed. • Another malignancy that can affect survival within the next three years. • Known or suspected allergies against any product included in the trial interventions. • DYPD deficiency. • Pregnancy or recent delivery within 28 days postpartum or ongoing breastfeeding. • Active sex-life without use of secure contraceptive method. • If the investigator considers the patient inappropriate for participation in the study for any other reason. • Ongoing or recent participation (within 30 days) in a clinical trial with an investigational medicinal product.

Trial type	IPa-Gastric trial is an open-label, randomized, controlled, phase III, multicentre trial.
Treatments / procedures	**Experimental intervention:** The experimental arm treatment will consist of the same standard systemic investigator's choice treatment described as control intervention combined with IP paclitaxel. IP paclitaxel will be administered through a subcutaneous intraperitoneal port catheter (SIPC), surgically placed in the ventral abdominal wall for simple administration of IP paclitaxel and easily accessible intraperitoneal fluid sampling. **Control intervention:** The control arm treatment in the study will consist of standard investigator's choice therapy with systemic chemotherapy and any targeted therapies indicated in the standard clinical practice setting, for example anti-HER2 and/or immunotherapy. **Follow-up per patient:** All patients will be followed for survival status every 12 weeks (± 2 weeks) from the time at which study treatment is ended until their death, or for a period of up to 24 months after the last patient has been randomised in the trial, whichever occurs first. **Duration of intervention per patient:** Patients will receive treatment until peritoneal disease progression, unacceptable side effects, other diseases that do not allow continued administration of the drug, the investigator's decision to end the patient's participation in the study, death or other reasons that require treatment to be discontinued or until End of Study.
Endpoint(s)	**Primary endpoint:** Overall survival (OS) **Secondary endpoint(s):** Toxicity/adverse Events, HRQoL (EORTC QLQ-C30 and EORTC OG-25), Progression-free survival, Radiological response, Amount of ascites **Assessment of safety:** At each trial visit, adverse events (AE) are registered, starting after first intervention in the trial, up to and including 4 weeks after the subject has ended their treatment with the investigational medicinal products.
Trial duration	**First patient in to last patient out (months): 60** **Duration of the entire trial (months): 60** **Recruitment period (months): 36**
Sample size	**To be assessed for eligibility: n = 262/340, whole trial** **To be assigned to the trial, i.e. recruited: n = 262/340, whole trial** **To be recruited (Germany): n = 50** **To be analysed: n = 262**
Participating sites	**No. of cities to be involved: 5** **No. of centres to be involved: 6** **Names of cities and centres:** (1) **Leipzig** University Medical Center**,** (2) **Berlin** Charité, (3) **Berlin** Vivantes Friedrichshain, (4) **Hannover** MHH**,** (5) **München** TUM, (6) **Frankfurt/M**. Krankenhaus Nordwest