KURZPROTOKOLL
Focus

Öffentlicher Titel	Phase III Studie zu Melphalan/HDS bei metastasiertem okulärem Melanom
Wissenschaftl. Titel	A Single-arm, Multi-Center, Open-Label Study to Evaluate the Efficacy, Safety and Pharmacokinetics of Melphalan/HDS Treatment in Patients with Hepatic-Dominant Ocular Melanoma (PHP-OCM-301A)
Kurztitel	Focus
Studienart	prospektiv, Therapiestudie, offen/unverblindet, einarmig
Studienphase	Phase III
Erkrankung	Haut: Hautkrebs: Schwarzer Hautkrebs (Malignes Melanom) - Alle Stadien
Einschlusskriterien	- Male or female patients >=18 years of age - Patients must weigh >= 35 kg (due to possible size limitations with respect to percutaneous catheterization of the femoral artery and vein using the Delcath Hepatic Delivery System) - 50% or less histologically or cytologically-proven ocular melanoma metastases in the parenchyma of the liver - Disease in the liver must be measurable by computed tomography (CT) and/or magnetic resonance imaging (MRI) - Evidence of limited extrahepatic disease on preoperative radiological studies is acceptable if the life threatening component of disease is in the liver. Limited extrahepatic disease is defined in this protocol as follows: metastasis in bone, subcutaneous, lung or lymph nodes that is amenable to resection or radiation and has a defined treatment plan. Patients with extra-hepatic tumor burden which does not have a defined treatment plan (i.e. monitor or is unable to be resected or radiated) must not be included in the trial - Scans used to determine eligibility (CT scan of the chest/abdomen/pelvis and MRI of the liver) must be performed within 28 days prior to eligibility. An MRI of the liver is required at screening to validate that CT accurately reflects the extent of disease in the liver. For patients with MRI intolerance, a 3-phase liver CT is to be done in place of liver MRI - Patients must not have had chemotherapy, radiotherapy, chemoembolization, radioembolization, or immunoembolization for their malignancy within 30 days prior to treatment and must have recovered from all side effects of therapeutic and diagnostic interventions except those listed in Appendix B of the study protocol - Patients receiving anti programmed cell death protein 1 (PD-1) immunotherapy such as pembrolizumab or nivolumab, or human cytotoxic T-lymphocyte antigen 4 blocking antibody such as ipilimumab must have completed treatment 8 weeks prior to study eligibility - Patients must have an ECOG PS of 0-1 at screening - Patients must have adequate hepatic function as evidenced by total serum bilirubin <=1.5 x the upper limit of normal (ULN) and a prothrombin time (PT) within 2 seconds of the upper normal limit. Aspartate aminotransferase/alanine aminotransferase (AST/ALT) must be <= 2.5 x ULN - Patients must have a platelet count > 100,000/µL, hemoglobin >= 10.0 gm/dL, white blood cell count (WBC) > 2,000/uL, absolute neutrophil count >= 1.5 x 109/L, and a serum creatinine <= 1.5 mg/dL unless the measured creatinine clearance is > 40 mL/min/1.73 m2 - Women of childbearing potential (WOCBP) must have a negative serum pregnancy test (-human chorionic gonadotropin) within 7 days prior to eligibility - Provided signed informed consent
Ausschlusskriterien	- Patients with Child-Pugh Class B or C cirrhosis or with evidence of portal hypertension by history, endoscopy, or radiologic studies

- Those with New York Heart Association functional classification II, III or IV active cardiac conditions, including unstable coronary syndromes (unstable or severe angina, recent myocardial infarction), worsening or new-onset congestive heart failure, significant arrhythmias and severe valvular disease must be evaluated for risks of undergoing general anesthesia
- History or evidence of clinically significant pulmonary disease that precludes the use of general anesthesia
- Women of childbearing potential (WOCBP) i.e. fertile meaning not permanently sterilized and having had a menstrual period within the past 12 months) unable to undergo hormonal suppression to avoid menstruation during treatment
- WOCBP and fertile males (not permanently sterile by bilateral orchiectomy) unwilling or unable to use highly effective contraception method from consent to at least 6 months after the last administration of study treatment (e.g. combined hormonal contraception; progestogen-only hormonal contraception; Intrauterine device, intrauterine hormone-releasing system; bilateral tubal occlusion, vasectomized partner or sexual abstinence)
- Females that are pregnant or are breastfeeding
- Patients taking immunosuppressive drugs, however, oral corticosteroids <= 10 mg/ day are allowed
- Patients who are unable to be temporarily removed from chronic anti-coagulation therapy
- Patients with active bacterial infections with systemic manifestations (malaise, fever, leucocytosis) are not eligible until completion of appropriate therapy
- Patients with severe allergic reaction to iodine contrast, which cannot be controlled by premedication with antihistamines and steroids
- Patients with a history of or known hypersensitivity to melphalan or the components of the Melphalan/HDS system
- Patients with latex allergy
- Patients with a history of hypersensitivity to heparin or the presence of heparin-induced thrombocytopenia
- Patients with a history of bleeding disorders or evidence of intracranial abnormalities which would put them at risk for bleeding with anti-coagulation (e.g., strokes, active metastases)
- Patients with a history of gastrinoma, hepatic vasculature incompatible with perfusion, hepatofugal flow in the portal vein or known unresolved venous shunting
- Known varices at risk of bleeding, including medium or large esophageal or gastric varices, or active peptic ulcer
- Patients with prior Whipple’s procedure
- Patients with brain metastases or presence of other intracranial lesions at risk for bleeding by history or baseline radiologic imaging
- Patients with an active infection, including Hepatitis B and Hepatitis C infection. Patients with anti-hepatitis B core antibody (HBc) positive, or hepatitis B surface antigen (HBsAg) but DNA negative are exception(s)
- Uncontrolled endocrine disorders including diabetes mellitus, hypothyroidism, or hyperthyroidism
- Received any investigational agent for any indication within 30 days prior to first treatment
- Not recovered from side effects of prior therapy to <= Grade 1 (according to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE v. 4.03). Certain side effects that are unlikely to develop into serious or life–threatening events (e.g. alopecia) are allowed at > Grade 1

	- Patients who have been institutionalized by governmental or legal decree or who are employees of the sponsor, Investigator, or study site - Cancers other than ocular melanoma for which the patient is currently under treatment or still deemed to be not cancer free
Alter	18 Jahre und älter
Prüfzentren	**Universitätsklinikum Gießen und Marburg, Standort Marburg** (Geschlossen) Baldingerstraße 35043 Marburg Anna Estor Tel: 06421 58 62919 anna.estor@med.uni-marburg.de
Sponsor	Delcath Systems Inc.
Registrierung in anderen Studienregistern	EudraCT 2015-000417-44 ClinicalTrials.gov NCT02678572 (primäres Register)