KURZPROTOKOLL
INSIGHT

Öffentlicher Titel	Phase I Studie zu IMP321 bei verschiedenen fortgeschrittenen soliden Tumoren
Wissenschaftl. Titel	An explorative, single center, open-labeled, phase I study to evaluate the feasibility and safety of intra-tumoral, intra-peritoneal, and subcutaneous injections with IMP321 (LAG-3Ig fusion protein) for advanced stage solid tumor entities
Kurztitel	INSIGHT
Studienart	prospektiv, Therapiestudie, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase I
Erkrankung	Bewegungsapparat: Knochenkrebs (Sarkome): sonstige Therapiestudien Drüsen/Hormone/Stoffwechsel: Neuroendokrine Tumoren: sonstige Therapiestudien Geschlechtsorgane: Brustkrebs: sonstige Therapiestudien Geschlechtsorgane: Krebserkrankungen der männlichen Geschlechtsorgane: sonstige Therapiestudien Geschlechtsorgane: Krebserkrankungen der weiblichen Geschlechtsorgane: sonstige Therapiestudien Haut: Hautkrebs: sonstige Therapiestudien Kopf-Hals: Kopf-Hals-Tumoren: sonstige Therapiestudien Lunge: Lungenkrebs: sonstige Therapiestudien Nervensystem: Gliome: sonstige Therapiestudien Niere/Harnwege: Harnblasenkrebs: sonstige Therapiestudien Niere/Harnwege: Nierenzellkrebs: sonstige Therapiestudien Verdauung: Analkrebs: sonstige Therapiestudien Verdauung: Gastrointestinale Stromatumoren (GIST): sonstige Therapiestudien Verdauung: Gallengangs-/Gallenblasenkrebs (maligne biliäre Tumoren): sonstige Therapiestudien Verdauung: Darmkrebs (Kolorektales Karzinom): sonstige Therapiestudien Verdauung: Leberkrebs (Hepatozelluläres Karzinom): sonstige Therapiestudien Verdauung: Magen-/Speiseröhrenkrebs (Magen-/Ösophaguskarzinom): sonstige Therapiestudien Verdauung: Bauchspeicheldrüsenkrebs (Pankreaskarzinom): sonstige Therapiestudien Weichteile: Sarkome: sonstige Therapiestudien
Einschlusskriterien	- Histologically confirmed locally advanced or metastatic solid tumor - Tumor is accessible for repeated injections and biopsies (only for Stratum A) - Peritoneal carcinomatosis (only for Stratum B) - Patient failed standard therapy or refused standard therapy or is intolerable towards standard therapy (Strata A, B) or who receives standard-of-care chemotherapy indicated for his/her tumor entity (only for Stratum C) - Patient does not receive a concurrent chemotherapy (only for Strata A and B) - Female and male patients >= 18 years. Patients in reproductive age must be willing to use highly effective contraception during the study and 3 months after the end of the study (appropriate contraception is defined as combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation, progestogen-only hormonal contraception associated with inhibition of ovulation, intrauterine device (IUD), intrauterine hormone-releasing system (IUS), vasectomized partner, bilateral tubal occlusion, sexual abstinence. If an oral contraception is used, a barrier method of contraception (e.g. male condom, female condom, cervical cap, diaphragm, contraceptive sponge) has to be applied additionally.).. Female patients with childbearing potential need to have a negative pregnancy test within 7 days before study start. - ECOG 0 or 1

- Adequate hematological, hepatic and renal function parameters: (a) ANC (absolute neutrophil count) >= 1.500/µl; (b) Leukocytes >= 3.000/µl; (c) Platelets >= 75.000/µl; (d) Serum creatinine <= 1.5 x upper limit of normal, or GFR >= 50 ml/min; (e) Bilirubin <= 1.5 - 3 x upper limit of normal; (f) AST and ALT <= 3 x upper limit of normal (<= 5 x if liver metastases are present); (g) Alkaline phosphatase <= 6 x upper limit of normal; (h) Hemoglobin >= 9g/dL
- Adequate coagulation functions as defined by International Normalized Ratio (INR) <= 1.5, and a partial thromboplastin time (PTT) <= 5 seconds above the ULN (unless receiving anticoagulation therapy). Patients receiving warfarin/ phenprocoumon must be switched to low molecular weight heparin and have achieved stable coagulation profile.
- Patient able and willing to provide written informed consent and to comply with the study protocol and with the planned surgical procedures

Ausschlusskriterien

- Inability to understand the aims of the study and/or protocol procedures
- Bleeding ulcerative tumors (only for Stratum A)
- Patients with contraindication versus a laparoscopy or refusing a laparoscopy (only for Stratum B)
- Hypersensitivity to IMP321 or any ingredient of the injection solution
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Any other concurrent antineoplastic treatment including irradiation (only Strata A and B)
- Prior treatment with CD137 agonists, anti-CTLA4, anti-PD-1, or anti-PD-L1 therapeutic antibody or pathway-targeting agents
- Cirrhosis of the liver (Child > Grade A), pronounced alcohol abuse with anticipated detoxification, severe pulmonary infection with considerable reduction of pulmonary function
- Clinically significant active coronary heart disease, cardiomyopathy or congestive heart failure, NYHA III-IV
- Clinically active brain metastases, defined as untreated symptomatic, or requiring therapy with steroids or anticonvulsants to control associated symptoms. Subjects with treated brain metastases that are no longer symptomatic and require no treatment with steroids may be included in the study if they have recovered from the acute toxic effect of radiotherapy and have no evidence of disease progression on imaging studies (MRI/CT scan).
- Chronic inflammatory bowel disease
- Active infection requiring intravenous antibiotics at the start of study treatment or chronic infection
- QTcF >480 ms, family or personal history of long or short QT syndrome, Brugada syndrome or known history of QTc prolongation, or Torsade de Pointes (TdP)
- Uncontrolled electrolyte disorders that can worsen the effects of a QTc-prolonging drug (e.g., hypocalcaemia, hypokalaemia, hypomagnesemia)
- Positive test for human immunodeficiency virus (HIV)
- Active hepatitis B (defined as having a positive hepatitis B surface antigen [HBsAg] test) or hepatitis C Note: Patients with past hepatitis B virus (HBV) infection or resolved HBV infection (defined as having a negative HBsAg test and a positive antibody to hepatitis B core antigen antibody test) are eligible. Note: Patients positive for hepatitis C virus (HCV) antibody are eligible only if polymerase chain reaction testing is negative for HCV ribonucleic acid (RNA).
- Active tuberculosis
- Active autoimmune disease requiring immunosuppressive therapy

	- Administration of a live, attenuated vaccine within four weeks prior to start of maintenance treatment or anticipation that such a live attenuated vaccine will be required during the remainder of the study. - Any condition requiring continuous systemic treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immunosuppressive medications within 2 weeks prior to first dose of study treatment. Inhaled or topical steroids and physiological replacement doses of up to 10 mg daily prednisone equivalent are permitted in the absence of active autoimmune disease. - Treatment with systemic immunostimulatory agents (including but not limited to interferons or interleukin-2) within four weeks or five half-lives of the drug, whichever is shorter, prior to start of study treatment - Any previous venous thromboembolism > National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Grade 3 within the last 12 months - Past history of severe allergic episodes and/ or Quincke's oedema - Prior organ transplantation or stem cell transplantation - On-treatment participation in another clinical study in the period 30 days prior to start of study treatment and during the study - Patients in a closed institution according to an authority or court decision (AMG § 40, Abs. 1 No. 4) - Pregnancy or lactation
Alter	18 Jahre und älter
Status	Rekrutierung beendet
Sponsor	Institut für Klinisch-Onkologische Forschung
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03252938 EudraCT 2016-002309-20