KURZPROTOKOLL
Immuchec

Öffentlicher Titel	Phase II Studie zu Durvalumab und Tremelimumab bei unbehandeltem Cholangio- oder Gallenkarzinom
Wissenschaftl. Titel	A randomized phase II trial of durvalumab and tremelimumab with gemcitabine or gemcitabine and cisplatin compared to gemcitabine and cisplatin in treatment-naïve patients with cholangio- and gallbladder carcinoma (IMMUCHEC)
Kurztitel	Immuchec
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, dreiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Verdauung: Gallengangs-/Gallenblasenkrebs (maligne biliäre Tumoren): Erstlinie
Einschlusskriterien	- Fully-informed written consent and locally required authorization (European Union [EU] Data Privacy Directive in the EU) obtained from the patient/legal representative prior to performing any protocol-related procedures, including screening evaluations - Age >= 18 years - Histologically documented diagnosis of cholangiocarcinoma or gall bladder carcinoma and available tumor tissue (block or at least 4 slides) for translational research - Performance status (PS) <= 1(ECOG scale) - At least one measurable site of disease as defined by RECISTv1.1 criteria - Adequate bone marrow and renal function including the following: Hemoglobin >= 9.0 g/dL; absolute neutrophil count >= 1.5 x 103/L; platelets >= 100 x 109 /L; Creatinine <= 1.5 x upper normal limit - Calculated creatinine clearance >=40 mL/min as determined by the Cockcroft- Gault equation (using actual body weight) - Adequate hepatic function (with stenting for any obstruction, if required) including the following: Total bilirubin <= 2x upper normal limit; AST (SGOT), ALT (SGPT) <= 5 x upper normal limit; prothrombin time >= 60%; albumin >= 30 g/L - Female patients with reproductive potential must have a negative urine or serum pregnancy test within 7 days prior to start of trial - Evidence of post-menopausal status or negative urinary or serum pregnancy test for female pre-menopausal patients. Women will be considered postmenopausal if they have been amenorrheic for 12 months without an alternative medical cause. The following age-specific requirements apply: - -> Women <50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of exogenous hormonal treatments and if they have luteinizing hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution or underwent surgical sterilization (bilateral oophorectomy or hysterectomy) - -> Women >=50 years of age would be considered post-menopausal if they have been amenorrheic for 12 months or more following cessation of all exogenous hormonal treatments, had radiation-induced menopause with last menses >1 year ago, had chemotherapy-induced menopause with last menses >1 year ago, or underwent surgical sterilization (bilateral oophorectomy, bilateral salpingectomy or hysterectomy) - The patient is willing and able to comply with the protocol for the duration of the study, including hospital visits for treatment and scheduled follow-up visits and examinations
Ausschlusskriterien	- Concurrent enrolment in another clinical study, unless it is an observational (non-interventional) clinical study, or during the follow-up period of an interventional study - Participation in another clinical study with an investigational product within 21 days prior to the first dose of the study treatment

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- Prior immunotherapy or use of other investigational agents, including prior treatment with an anti-Programmed Death receptor-1 (PD-1), anti-Programmed Death-1 ligand-1 (PD-L1), anti-PD-L2, or anti-cytotoxic T-lymphocyte associated antigen-4 (anti-CTLA-4) antibody, therapeutic cancer vaccines
- Prior chemotherapy with gemcitabine and cisplatin (exception: gemcitabine in the adjuvant setting, last infusion has to be >= 6 months prior randomization)
- Any unresolved toxicity NCI CTCAE Grade >= 2 from previous anticancer therapy with the exception of alopecia, vitiligo, and the laboratory values defined in the inclusion criteria:
- -> Patients with Grade >=2 neuropathy will be evaluated on a case-by-case basis after consultation with the Study Physician
- -> Patients with irreversible toxicity not reasonably expected to be exacerbated by treatment with durvalumab or tremelimumab may be included only after consultation with the Study Physician
- Any concurrent chemotherapy, IMP, biologic, or hormonal therapy for cancer treatment. Concurrent use of hormonal therapy for non-cancer-related conditions (eg, hormone replacement therapy) is acceptable. Note: Local treatment of isolated lesions for palliative intent is acceptable (eg, local radiotherapy)
- Radiotherapy treatment to more than 30% of the bone marrow or with a wide field of radiation within 4 weeks of the first dose of study drugs
- Major surgery (as defined by the Investigator) within 4 weeks prior to the first dose of the investigational product (IMP) of starting the study and patients must have recovered from effects of major surgery. Note: Local non-major surgery for palliative intent (eg, surgery of isolated lesions, per-cutaneous biliary drainage or biliary stenting) is acceptable
- History of allogenic organ transplantation
- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [eg, colitis or Crohn's disease], diverticulitis [with the exception of diverticulosis], celiac disease, systemic lupus erythematosus, Sarcoidosis syndrome, or Wegener syndrome [granulomatosis with polyangiitis, Graves' disease, rheumatoid arthritis, hypophysitis, uveitis, etc])
- The following are exceptions to this criterion:
- -> Patients with vitiligo or alopecia
- -> Patients with hypothyroidism (eg, following Hashimoto syndrome) stable on hormone replacement
- -> Any chronic skin condition that does not require systemic therapy
- -> Patients without active disease in the last 5 years may be included but only after consultation with the study physician
- Uncontrolled intercurrent illness, including but not limited to, ongoing or active infection, symptomatic congestive heart failure, uncontrolled hypertension, unstable angina pectoris, cardiac arrhythmia, interstitial lung disease, serious chronic gastrointestinal conditions associated with diarrhea, or psychiatric illness/social situations that would limit compliance with study requirement, substantially increase risk of incurring AEs or compromise the ability of the patient to give written informed consent
- History of another primary malignancy except for:
- -> Malignancy treated with curative intent and with no known active disease >=5 years before the first dose of IMP and of low potential risk for recurrence
- -> Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease

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	- -> Adequately treated carcinoma in situ without evidence of disease History of leptomeningeal carcinomatosis - Brain metastases or spinal cord compression. Patients with suspected brain metastases at screening should have a CT/ MRI of the brain prior to study entry. - History of active primary immunodeficiency - Active infection including tuberculosis (clinical evaluation that includes clinical history, physical examination and radiographic findings, and TB testing in line with local practice), hepatitis B (known positive HBV surface antigen [HBsAg) result], hepatitis C, or human immunodeficiency virus (positive HIV 1/2 antibodies). Patients with a past or resolved HBV infection (defined as the presence of hepatitis B core antibody [anti-HBc] and absence of HBsAg) are eligible. Patients positive for hepatitis C (HCV) antibody are eligible only if polymerase chain reaction is negative for HCV RNA - Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab or tremelimumab. The following are exceptions to this criterion: - -> Intranasal, inhaled, topical steroids, or local steroid injections (eg, intra articular injection) - -> Systemic corticosteroids at physiologic doses not to exceed 10 mg/day of prednisone or its equivalent - Steroids as premedication for hypersensitivity reactions (eg, CT scan premedication) Receipt of live attenuated vaccine within 30 days prior to the first dose of IMP
Alter	18 Jahre und älter
Prüfzentren	**Universitätsklinikum Frankfurt** (Geschlossen) Medizinische Klinik I, Gastroenterologie/Hepatologie Theodor-Stern-Kai 7 60590 Frankfurt am Main Wina Hensel Tel: 069 6301-87769 Fax: 069 6301-6580 wina.hensel@kgu.de
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