KURZPROTOKOLL
Ramona

Öffentlicher Titel	Phase II Studie zu second-line Nivolumab und Ipilimumab bei fortgeschrittenem ösophagealem Plattenepithelkarzinom
Wissenschaftl. Titel	A Multicenter Open-label Phase II Trial to Evaluate Nivolumab and Ipilimumab for 2nd Line Therapy in Elderly Patients With Advanced Esophageal Squamous Cell Cancer
Kurztitel	Ramona
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Verdauung: Magen-/Speiseröhrenkrebs (Magen-/Ösophaguskarzinom): Zweitlinie oder höher
Einschlusskriterien	- Written informed consent including participation in translational research and any locally-required authorization (EU Data Privacy Directive in the EU) obtained from the subject prior to performing any protocol-related procedures, including screening Evaluations - Age >= 65 years at time of study entry - Histologically confirmed advanced stage esophageal squamous cell carcinoma in 2nd line: - - stage 4 OR - - stage 3 non-responder to radio-chemotherapy OR - - stage 3 with early relapse < 6 month after chemo-radiation - Patients treated with Carboplatin/Paclitaxel (+/- radiotherapy) or other chemotherapy in 1st line - Geriatric status: SlowGo or GoGo according to G8 and DAFI assessment (G8 > 14 points or CGA/DAFI 0.2 < 0.35) - At least 1 measurable lesion according to RECIST 1.1 - Karnofsky performance status >= 50 - Sufficient cardiac functional reserve defined as ejection fraction > 50% - Adequate blood count, liver-enzymes, and renal function: - - neutrophil count > 1.5 x 10^6/mL - - WBC >= 3000/L - - Platelet count >= 100 x 10^9/L (>100,000 per mm^3) - - hemoglobin >= 9 g/dL - - INR <= 1.5 and PPT <= 1.5 x lower limit during the last 7 days before therapy - - AST (SGOT)/ALT (SGPT) < 3 x institutional upper limit of normal (5 x lower limit in case of liver metastases) - - bilirubin < 1.5 x ULN - - Serum creatinine <= 1.5 x institutional ULN or creatinine clearance (CrCl) >= 30 mL/min (if using the Cockcroft-Gault formula below): - -> Female CrCl = (140 - age in years) x weight in kg x 0.85 / 72 x serum creatinine in mg/dL Male CrCl = (140 - age in years) x weight in kg x 1.00 / 72 x serum creatinine in mg/dL - Men who are sexually active with WOCBP must use any contraceptive method with a failure rate of less than 1% per year. Men receiving Nivolumab and who are sexually active with WOCBP will be instructed to adhere to contraception for a period of 7 months after the last dose of investigational products (Nivolumab, Ipilimumab). Women who are not of childbearing potential (i.e., who are postmenopausal or surgically sterile) as well as azoospermic men do not require contraception)

- Subject is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up

Ausschlusskriterien

- Patients < 65 years of age
- Frail patients (DAFI score >= 0.35)
- Esophageal adenocarcinomas, neuroendocrine tumors
- Prior therapy with an anti-programmed cell death protein 1 (anti-PD-1), anti-PDL1, anti-programmed cell death-ligand 2 (anti-PD-L2), anti-CD137 (4-1BB ligand, a member of the Tumor Necrosis Factor Receptor [TNFR] family), or anti-cytotoxic T-lymphocyte-associated antigen-4 (anti-CTLA-4) antibody (including Ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways)
- Participation in another clinical study with an investigational product during the last 30 days before inclusion or 7 half-lifes of previously used trial medication, whichever is longer
- Previous treatment in the present study (does not include screening failure).
- Any condition or comorbidity that, in the opinion of the investigator, would interfere with evaluation of study treatment or interpretation of patient safety or study results, including but not limited to:
- - Major surgery <= 28 days prior first dose of study treatment
- - Anticancer treatment during the last 30 days prior to start of Nivolumab monotherapy treatment, including systemic therapy or major surgery [palliative radiotherapy has to be completed at least 2 weeks prior to start of study treatment]
- - History of interstitial lung disease
- - Known acute or chronic pancreatitis
- - Known active HBV, HCV or HIV infection
- - Active tuberculosis
- - Any other active infection (viral, fungal or bacterial) requiring systemic therapy
- - History of allogeneic tissue/solid organ transplant
- - Diagnosis of immunodeficiency or patient is receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of Nivolumab monotherapy treatment.
- - Has an active autoimmune disease requiring systemic treatment within the past 3 months or a documented history of clinically severe autoimmune disease, or a syndrome that requires systemic steroids or immunosuppressive agents. Exceptions: Subjects with vitiligo, hypothyroidism, diabetes mellitus type I or resolved childhood asthma/atopy are an exception to this rule. Subjects that require intermittent use of bronchodilators or local steroid injections would not be excluded from the study. Subjects with Hashimoto thyroiditis, hypothyroidism stable on hormone replacement or psoriasis not requiring treatment are not excluded from the study.
- - Live vaccine within 30 days prior to the first dose of Nivolumab monotherapy treatment or during study treatment.
- - Other clinically significant active malignancy requiring treatment OR less then 5 years disease free interval of another primary malignancy
- - Clinically significant or symptomatic cardiovascular/cerebrovascular disease (incl. myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) within 6 months before enrollment

- - History or clinical evidence of CNS metastases Exceptions are: Subjects who have completed local therapy and who meet both of the following criteria: i. are asymptomatic AND ii. have no requirement for steroids 6 weeks prior to start of Nivolumab monotherapy treatment. Screening with CNS imaging (CT or MRI) is required only if clinically indicated or if the subject has a history of CNS metastases
- Medication that is known to interfere with any of the agents applied in the trial
- Has known hypersensitivity to Nivolumab or Ipilimumab or any of the constituents of the products
- Any other efficacious cancer treatment except protocol specified treatment at study start
- Patient has received any other investigational product within 28 days of study entry
- Patient has had a prior monoclonal antibody within 4 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier. [Subjects with <= Grade 2 neuropathy or alopecia are an exception to this criterion and may qualify for the study.]
- Female subjects who are pregnant, breast-feeding or male/female patients of reproductive potential who are not employing an effective method of birth control (failure rate of less than 1% per year). [Acceptable methods of contraception are: implants, injectable contraceptives, combined oral contraceptives, intrauterine pessaries (only hormonal devices), sexual abstinence or vasectomy of the partner]. Women of childbearing potential must have a negative pregnancy test (serum beta-HCG) at screening.
- Patient with any significant history of non-compliance to medical regimens or with inability to grant reliable informed consent.
- Patient who has been incarcerated or involuntarily institutionalized by court order or by the authorities § 40 Abs. 1 S. 3 Nr. 4 AMG.
- Patients who are unable to consent because they do not understand the nature, significance and implications of the clinical trial and therefore cannot form a rational intention in the light of the facts [§ 40 Abs. 1 S. 3 Nr. 3a AMG].

Alter	65 Jahre und älter
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