KURZPROTOKOLL
ISA101b-HN-01-17

Öffentlicher Titel	Phase II Studie zu Cemiplimab mit und ohne ISA101b bei HPV16-positivem Mundrachenkrebs
Wissenschaftl. Titel	A Randomized, Double-blind, Placebo-Controlled, Phase 2 Study of Cemiplimab Versus the Combination of Cemiplimab With ISA101b in the Treatment of Subjects With HPV16-Positive Platin-Resistant Oropharyngeal Cancer (OPC)
Kurztitel	ISA101b-HN-01-17
Studienart	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
Studienphase	Phase II
Erkrankung	Kopf-Hals: Kopf-Hals-Tumoren: Erstlinie Kopf-Hals: Kopf-Hals-Tumoren: Zweitlinie oder höher

Einschlusskriterien

- Subjects must have signed and dated an IRB/IEC approved written informed consent form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol related procedures that are not part of normal subject care
- Subjects must be willing and able to comply with scheduled visits, treatment schedule, laboratory tests and other requirements of the study
- Men and women >= 18 years of age
- Eastern Cooperative Oncology Group (ECOG) performance status of <= 1
- Subjects with histologically- or cytologically-documented incurable Human Papillomavirus (HPV)-positive OPSCC. HPV-16 serotype will be assessed by Cervista assay
- Subjects can be treatment naïve or may have had two prior regimens for recurrent cancer. They must be naive to treatment with PD-1/L1 or CTLA-4 inhibitors
- Subjects must have progression within 6 months of platin exposure during definitive or palliative therapy
- Subjects must have measurable disease by CT or MRI per RECIST 1.1 criteria; Radiographic Tumor Assessment performed within 28 days of study inclusion
- Target lesions may be located in a previously irradiated field if there is documented (radiographic) disease progression in that site
- Subject entering the study will need to consent for mandatory biopsy at study entrance and as an optional procedure prior to C3 for biomarker evaluation. Biopsy should be excisional, incisional or core needle. Fine needle aspiration is insufficient
- Prior chemotherapy, monoclonal antibody therapy, must have been completed at least 4 weeks prior to start. Radiotherapy or radiosurgery must have been completed at least 2 weeks prior to start
- All baseline laboratory requirements will be assessed and should be obtained within -14 days of study registration. Screening laboratory values must meet the following criteria i) White blood cells (WBCs) >= 2000/microL ii) Neutrophils >= 1500/microL iii) Platelets >= 100 x 10^3/microL iv) Hemoglobin >= 9.0 g/dL Patients must not be transfused for at least 14 days prior to study entry v) Serum creatinine of <=1.5 x upper limit of normal(ULN) or creatinine clearance(CrCl) > 50 mL/minute (using Cockcroft/Gault formula) Female CrCl= 0.85 x [(140 - age in years) x weight in kg]/(72 x serum creatinine in mg/dL) Male CrCl= 1.00 x [(140 - age in years) x weight in kg]/(72 x serum creatinine in mg/dL) vi) AST <= 2.5 x ULN vii) ALT <= 2.5 x ULN viii) Total bilirubin<= 1.5 x ULN (except subjects with Gilbert Syndrome who must have total bilirubin <3.0 mg/dl)

- Women of childbearing potential (WOCBP) must use method(s) of contraception for 30 days + 5 half-lives (60 days) of the study drugs. For a teratogenic study drug and/or when there is insufficient information to assess teratogenicity (preclinical studies have not been done), a highly effective method(s) of contraception (failure rate of less than 1% per year) is required. Highly effective birth control in this study is defined as a double barrier method. Examples include a condom (with spermicide) in combination with a diaphragm, cervical cap, or intrauterine device (IUD). The individual methods of contraception should be determined in consultation with the investigator.
- WOCBP must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of investigational product
- Women must not be breastfeeding
- Men who are sexually active with WOCBP must use any contraceptive method with a failure rate of less than 1% per year. The investigator shall review contraception methods and the time period that contraception must be followed. Men that are sexually active with WOCBP must follow instructions for birth control for a period of 90 days plus the time required for the investigational drug to undergo 5 half- lives (60 days)

Ausschlusskriterien

- Subjects with active CNS metastases are excluded. Subjects are eligible if CNS metastases are adequately treated and subjects are neurologically returned to baseline (except for residual signs or symptoms related to the CNS treatment) for at least 4 weeks prior to enrollment. In addition, subjects must be either off corticosteroids, or on a stable or decreasing dose of <= 10 mg daily prednisone (or equivalent) for 2 weeks.
- Subjects with carcinomatous meningitis
- Subjects with active, known or suspected systemic autoimmune disease. Subjects with vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune thyroiditis only requiring hormone replacement, or conditions not expected to recur in the absence of an external trigger are permitted to enroll
- Subjects with a condition requiring systemic treatment with either corticosteroids (>10 mg daily prednisone equivalent) or other immunosuppressive medications within 14 days of start. Inhaled or topical steroids, and adrenal replacement steroid doses > 10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease
- Prior therapy with anti-CD137 or ISA101
- Subjects with a history of interstitial lung disease
- Other active malignancy requiring concurrent intervention
- Subjects with previous malignancies (except non-melanoma skin cancers, and the following in situ cancers: bladder, gastric, colon, endometrial, cervical/dysplasia, melanoma, or breast) are excluded unless a complete remission was achieved at least 2 years prior to study entry AND no additional therapy is required during the study period
- Subjects with toxicities attributed to prior anti-cancer therapy other than alopecia and fatigue that have not resolved to grade 1 (NCI CTCAE version 4.03) or baseline before administration of study drug
- Subjects who have not recovered from the effects of major surgery or significant traumatic injury at least 14 days before the first dose of study treatment
- Treatment with any investigational agent within 28 days of first administration of study treatment
- Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS)

	- Positive test for hepatitis B virus surface antigen (HBV sAg) or hepatitis C virus ribonucleic acid (HCV RNA) indicating acute or chronic infection - History of allergy or intolerance (unacceptable adverse event) to study drugs components - WOCBP who are pregnant or breastfeeding - Women with a positive pregnancy test at enrollment or prior to administration of study medication - Any other serious or uncontrolled medical disorder, active infection, physical exam finding, laboratory finding, altered mental status, or psychiatric condition that, in the opinion of the investigator, would limit a subject's ability to comply with the study requirements, substantially increase risk to the subject, or impact the interpretability of study results - Prisoners or subjects who are involuntarily incarcerated - Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness
Alter	18 - 99 Jahre
Molekularer Marker	HPV
Sponsor	Isa Therapeutics
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03669718 (primäres Register) EudraCT 2018-000789-13