KURZPROTOKOLL
CheckRad-CD8

Öffentlicher Titel	Phase II Studie zu Durvalumab/Tremelimumab/Radiotherapie bei neu diagnostiziertem Kopf-Hals-Krebs
Wissenschaftl. Titel	First-Line Treatment of locally advanced HNSCC double checkpoint Blockade and radiotherapy dependent on intratumoral CD+T cellinfiltration
Kurztitel	CheckRad-CD8
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Kopf-Hals: Kopf-Hals-Tumoren: Erstlinie
Einschlusskriterien	- Written informed consent and any locally-required authorization (e.g., HIPAA in the USA, EU Data Privacy Directive in the EU) obtained from the subject prior to performing any protocol-related procedures, including screening evaluations - Age > 18 years at time of study entry - Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 - Locally advanced HNSCC, UICC stage III-IVB (oral cavity, oropharynx, hypopharynx, supraglottic larynx) - Histological confirmation of HNSCC (regardless if p16 positive or negative) - Measureable CD8 density in provided archival tumor tissue - Body weight >30kg - Adequate normal organ and marrow function as defined: Haemoglobin >= 9.0 g/dL; Absolute neutrophil count (ANC) >= 3,000 per mm3; Platelet count >100,000 per mm3 - Serum bilirubin <= 1.5 x institutional upper limit of normal (ULN) - AST (SGOT)/ALT (SGPT) <= 2.5 x institutional upper limit of normal (ULN) - Creatinine Clearance >40ml/min (calculated from serum creatinine using the Cockcroft-Gault formula) - Female subject of childbearing potential should have a negative serum pregnancy within 72 hours prior to receiving the first dose of durvalumab and tremelimumab. A highly sensitive pregnancy test must be used. - Female subjects of childbearing potential must be willing to use a highly effective contraceptive measure as defined in the Clinical Trial Facilitation Group (CTFG) guideline (“Recommendations related to contraception and pregnancy testing in clinical trials.”) For details see Section 7.1.1 of the study protocol. Highly effective contraception is required from screening to 90 days after the last dose of durvalumab monotherapy or 180 days after the last dose of durvalumab + tremelimumab combination therapy. (Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.) - Male subjects of childbearing potential must agree to use a highly effective method of contraception as outlined in Section 7.1.1. Contraception, starting from screening to 90 days after the last dose of durvalumab monotherapy or 180 days after the last dose of durvalumab + tremelimumab combination therapy. (Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.) - 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	- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site) - Participation in another clinical study with an investigational product during the last 4 weeks

- 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
- Distant metastases
- Prior systemic anti-cancer therapy (chemotherapy, immunotherapy, endocrine therapy, targeted therapy, biologic therapy, tumour embolization, monoclonal antibodies) of the locally advanced HNSCC
- Any other concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment, except the induction chemotherapy in the protocol. Concurrent use of hormonal therapy for non-cancer-related conditions (e.g., hormone replacement therapy) is acceptable
- Prior radiotherapy of HNSCC
- Radiotherapy to more than 30% of the bone marrow or with a wide field of radiation within 4 weeks of the first dose of study drug
- Major surgical procedure of the current locally advanced HNSCC (as defined by the Investigator). Note: Local surgery of isolated lesions for palliative intent is acceptable
- History of allogenic organ transplantation.
- Active or prior documented autoimmune or inflammatory disorders (including inflammatory bowel disease [e.g., colitis or Crohn's disease], diverticulitis [with the exception of diverticulosis], 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 areata
- -> Patients with hypothyroidism (e.g., 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
- -> Patients with celiac disease controlled by diet alone
- 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 IP and of low potential risk for recurrence
- -> Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease
- -> Adequately treated carcinoma in situ without evidence of disease
- 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 (e.g., CT scan premedication) - Receipt of live attenuated vaccine within 30 days prior to the first dose of IP. Note: Patients, if enrolled, should not receive live vaccine whilst receiving IP and up to 30 days after the last dose of IP - Female patients who are pregnant or breastfeeding or male or female patients of reproductive potential who are not willing to employ effective birth control from screening to 90 days after the last dose of durvalumab monotherapy or180 days after the last dose of durvalumab + tremelimumab combination therapy. This also applies to patients who receive only induction chemotherapy before the restaging endoscopy with biopsy - Known allergy or hypersensitivity to any of the study drugs or any of the study drug excipients - Prior randomisation or treatment in a previous durvalumab and/or tremelimumab clinical study regardless of treatment arm assignment - Known active bleeding diathesis - Past medical history of ILD, drug-induced ILD, radiation pneumonitis which required steroid treatment, or any evidence of clinically active interstitial lung disease - Judgment by the investigator that the patient is unsuitable to participate in the study and the patient is unlikely to comply with study procedures, restrictions and requirements - Known allergy or hypersensitivity to durvalumab, tremelimumab, cisplatin/carboplatin, docetaxel or any excipient - Cisplatin/carboplatin induced polyneuropathy or hearing disorder
Alter	18 Jahre und älter
Prüfzentren	**Strahlentherapie** (Nachbeobachtung) Theodor-Stern-Kai 7 60590 Frankfurt am Main Prof. Dr. med. Claus Rödel studien-strahlen@unimedizin-ffm.de
Sponsor	Universität Erlangen-Nürnberg
Förderer	Astra Zeneca
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03426657 (primäres Register) EudraCT 2017-003226-33