KURZPROTOKOLL
RADIANCE

Öffentlicher Titel	Radiochemotherapie und Durvalumab bei Analkarzinom
Wissenschaftl. Titel	Radiochemotherapy +/- Durvalumab for locally advanced Anal Carcinoma
Kurztitel	RADIANCE
Studienart	multizentrisch, prospektiv, randomisiert, offen/unverblindet, zweiarmig, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Verdauung: Analkrebs: Erstlinie

Einschlusskriterien

- Histologically-confirmed ASCC (both genders) of the anal canal or the anal margin
- UICC-Stage IIB-IIIC including T2>4cm Nany (IIB: T3N0M0; IIIA: T1-2N1M0; IIIB: T4N0M0; IIIC: T3-4N1M0; T2>4cm Nany) according to proctoscopy, pelvic MRI, CT scan of thorax and abdomen, all within 30 days prior to recruitment
- Age >=18 years, no upper age limit
- ECOG-Performance score 0-1
- History/physical examination within 30 days prior to recruitment
- Written informed consent and any locally-required authorization (e.g. EU Data Privacy Directive in the EU) obtained from the patient prior to performing any protocol -related procedures, including screening evaluations
- Life expectancy of > 12 months
- Body weight >30kg
- Hemoglobin >=9.0 g/dl
- Leukocytes >3.5 x 10 ^9/l
- Absolute neutrophil count (ANC) 1.5 x 10 9/l (> 1500 per mm3)
- Platelet count >=100 x 109/l (>100,000 per mm3)
- Serum bilirubin <=1.5 x institutional upper limit of normal (ULN). (This will not apply to patients with confirmed Gilbert's syndrome (persistent or recurrent hyperbilirubinemia that is predominantly unconjugated in the absence of hemolysis or hepatic pathology), who will be allowed only in consultation with their physician
- AST (SGOT), ALT (SGPT), AP <=3x institutional ULN
- Calculated creatinine CL>40 mL/min by the Cockcroft-Gault formula creatinine clearance
- Female subject of childbearing potential should have a negative serum pregnancy within 72 hours prior to receiving the first dose of durvalumab. 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"). Highly effective contraception is required from screening to 90 days after the last dose of durvalumab. (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, starting from screening to 90 days after the last dose of durvalumab. (Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.) Male patients should refrain from fathering a child or donating sperm during the study and for 180 days after the last dose of durvalumab + any drug combination therapy or 90 days after the last dose of durvalumab monotherapy, whichever is the longer time period
- Patient 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

- For HIV-positive patients: running combined antiretroviral therapy (CART) on a stable dose at study entry and undetectable HIV-viral load (HIV Viral load <50 copies/mL and CD4>200/Mircoliter). Patients will be closely monitored and CART management will be performed according to appropriate labelling guidance of the antiviral therapy. CART should be on a stable dose at study entry

Ausschlusskriterien

- UICC-Stage I-IIA ASCC defined as cT1N0M0 or cT2 <4cm N0M0 disease
- Second malignancy other than basalioma or cervical/genital/ neoplasia in situ
- 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 durvalumab 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
- Known DPD-deficiency
- Participation in another clinical study with an investigational product during the last 12 months
- 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
- Any previous treatment with other immunotherapy, a PD1 or PD-L1 inhibitor
- QT interval corrected for heart rate (QTc) >=470 ms
- Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab, with the exceptions of intranasal and inhaled corticosteroids or systemic corticosteroids at physiological doses, which are not to exceed 10 mg/d of prednisone, or an equivalent corticosteroid. In case of recent introduction of CART, inclusion will be possible provided subjects had at least 4 weeks of treatment prior to inclusion
- 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 Chairman Patients with irreversible toxicity not reasonably expected to be exacerbated by treatment with durvalumab may be included only after consultation with the Study Chairman
- Any concurrent chemotherapy, biologic, or hormonal therapy for cancer treatment, other than the study medication. Concurrent use of hormonal therapy for non-cancer-related conditions (e.g., hormone replacement therapy) is acceptable
- Previous radiotherapy treatment to the pelvis or 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 drug
- Major surgical procedure (as defined by the Investigator) within 28 days prior to the first dose of durvalumab
- 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 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 chairman 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 diarrhoea, 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 leptomeningeal carcinomatosis or any other metastatic 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. 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
- Receipt of live attenuated vaccine within 30 days prior to the first dose of durvalumab. Note Patients, if enrolled, should not receive live vaccine whilst receiving durvalumab and up to 30 days after the last dose of durvalumab
- Known allergy or hypersensitivity to any of the study/investigational drugs or any of the study/investigational drug excipients and/or radiochemotherapy with 5-FU and Mitomycin C
- 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

Alter

18 Jahre und älter

Prüfzentren

Universitätsklinikum Gießen und Marburg, Standort Marburg (Aktiv)
Baldingerstraße
35043 Marburg
Inga Stanger
Tel: 06421 58 68050
inga.stanger@uk-gm.de

Strahlentherapie (Rekrutierung beendet)
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Prof. Dr. med. Claus Rödel
studien-strahlen@kgu.de

Klinikum Darmstadt GmbH (Rekrutierung beendet)
Institut fur Radioonkologie und Strahlentherapie
Grafenstraße 9
64283 Darmstadt
Prof. Dr. med. Christian Weiß
Tel: 06151 1076670
Fax: 06151 1076676
Onko-Studienzentrum@mail.klinikum-darmstadt.de

Universitätsklinikum Frankfurt (Rekrutierung beendet)
Klinik für Strahlentherapie und Onkologie
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Dr. med. Daniel Martin
studien-strahlen@kgu.de

Sponsor

Universitätsklinikum Frankfurt

Förderer

Deutsche Krebshilfe e.V.

Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT04230759 EudraCT 2018-003005-25 (primäres Register)
Links	Weiterführende Informationen