KURZPROTOKOLL
AVETUX

Öffentlicher Titel	Avelumab und Cetuximab beim unbehandelten metastasierten Kolorektalkarzinom
Wissenschaftl. Titel	Avelumab and cetuximab in combination with FOLFOX in patients with previously untreated metastatic colorectal cancer – The phase II AVETUX-CRC trial
Kurztitel	AVETUX
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig
Studienphase	Phase II
Erkrankung	Verdauung: Darmkrebs (Kolorektales Karzinom): Erstlinie

Einschlusskriterien

- Patients with histologically confirmed, previously untreated RAS and BRAF wildtype, MSI or MSS metastastic colorectal cancer (primary tumor may be present)
- Patients with at least one measurable lesion acc. to RECIST v1.1
- ECOG Performance status <= 1
- Life expectancy > 3 months
- Age >= 18 years
- Haematologic function as follows: ANC >= 1.5 x 10^9/L, platelets >= 100 x10^9/L, hemoglobin >= 9 g/dL or 5.59 mmol/L
- Adequate liver function as measured by serum transaminases (AST & ALT) <= 2.5 x ULN (in case of liver metastases < 5 x ULN) and total bilirubin <= 1.5 x ULN. Patients with known Gilbert disease who have serum bilirubin level <= 3 × ULN may be enrolled.
- Adequate renal function: serum creatinine <= 1.5 x ULN
- Negative serum pregnancy test at screening for women of childbearing potential.
- Highly effective contraception for both male and female subjects if the risk of conception exists. (Note: The effects of the trial drug on the developing human fetus are unknown; thus, women of childbearing potential and men able to father a child must agree to use 2 highly effective contraception, defined as methods with a failure rate of less than 1 % per year. Highly effective contraception is required at least 28 days prior, throughout and for at least 30 days after avelumab treatment and 6 month after standard chemotherapy.
- At least 6 months after completion of adjuvant chemotherapy
- Written informed consent
- Ability to comply with the protocol for the duration of the study, including hospital/office visits for treatment and scheduled follow-up visits and examinations

Ausschlusskriterien

- Carcinoma in situ of the cervix, basal or squamous cell skin cancer, localized prostate cancer treated surgically with curative intent, ductal carcinoma in situ treated surgically with curative intent)
- All subjects with known brain metastases, except those meeting AIO-KRK-0216 / AVETUX-CRC page 12 of 72 Version Final 3.0, 30 Jun 2017 EudraCT: 2016-004434-26 the following criteria: (a) Brain metastases that have been treated locally and are clinically stable for at least 2 weeks prior to enrolment; (b) No ongoing neurological symptoms that are related to the brain localization of the disease (sequelae that are a consequence of the treatment of the brain metastases are acceptable); (c) Subjects must be either off steroids or on a stable or decreasing dose of <10mg daily prednisone (or equivalent)
- Prior organ transplantation, including allogeneic stem-cell transplantation
- Significant acute or chronic infections including, among others: (a) Known history of testing positive test for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS); (b) Positive test for HBV surface antigen and / or confirmatory HCV RNA (if anti-HCV antibody tested positive)

	- Active autoimmune disease that might deteriorate when receiving an immunostimulatory agent (Subjects with diabetes type I, vitiligo, psoriasis, hypo- or hyperthyroid disease not requiring immunosuppressive treatment are eligible) - Concomitant treatment with corticosteroids or other immunosuppressants, besides treatment of brain metastases as mentioned in criteria 2 or: (a) Subjects requiring hormone replacement with corticosteroids are eligible if the steroids are administered only for the purpose of hormonal replacement and at doses <= 10 mg or 10 mg equivalent prednisone per day; (b) Administration of steroids through a route known to result in a minimal systemic exposure (topical, intranasal, intro-ocular, or inhalation) are acceptable - Known severe hypersensitivity reactions to monoclonal antibodies (Grade >= 3 NCI-CTCAE v 4.03), any history of anaphylaxis, or uncontrolled asthma (that is, 3 or more features of partially controlled asthma) - Pregnancy or lactation - Known alcohol or drug abuse - Clinically significant (i.e., active) cardiovascular disease: AIO-KRK-0216 / AVETUX-CRC page 13 of 72 Version Final 3.0, 30 Jun 2017 EudraCT: 2016-004434-26 cerebral vascular accident/stroke (< 6 months prior to enrolment), myocardial infarction (< 6 months prior to enrolment), unstable angina, congestive heart failure (>= New York Heart Association Classification Class II), or serious cardiac arrhythmia requiring medication. - Persisting toxicity related to prior therapy (NCI CTCAE v. 4.03 Grade > 1); however, alopecia, sensory neuropathy Grade <= 2, or other Grade <= 2 not constituting a safety risk based on investigator’s judgment are acceptable. - All other significant diseases (for example, inflammatory bowel disease, uncontrolled asthma, colitis and pneumonitis), which, in the opinion of the Investigator, might impair the subject’s tolerance of trial treatment - Any psychiatric condition that would prohibit the understanding or rendering of informed consent - Vaccination within 4 weeks of the first dose of avelumab and while on trial is prohibited except for administration of inactivated vaccines - Any approved anticancer therapy, including chemotherapy, hormonal therapy or radiotherapy, within 4 weeks prior to initiation of study treatment - Major surgical procedure within 28 days prior to treatment or anticipation of need for a major surgical procedure during the course of the study
Alter	18 Jahre und älter
Molekularer Marker	NRAS BRAF MSI-H MSS KRAS
Sponsor	AIO-Studien GmbH
Förderer	Merck KGaA
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03174405 EudraCT 2016-004434-26