

## **KURZPROTOKOLL** **AVETUX**

<b>Öffentlicher Titel</b>	Avelumab und Cetuximab beim unbehandelten metastasierten Kolorektalkarzinom
<b>Wissenschaftl. Titel</b>	Avelumab and cetuximab in combination with FOLFOX in patients with previously untreated metastatic colorectal cancer – The phase II AVETUX-CRC trial
<b>Kurztitel</b>	AVETUX
<b>Studienart</b>	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig
<b>Studienphase</b>	Phase II
<b>Erkrankung</b>	Verdauung: Darmkrebs (Kolorektales Karzinom): Erstlinie
<b>Einschlusskriterien</b>	<ul style="list-style-type: none"> <li>- Patients with histologically confirmed, previously untreated RAS and BRAF wildtype, MSI or MSS metastatic colorectal cancer (primary tumor may be present)</li> <li>- Patients with at least one measurable lesion acc. to RECIST v1.1</li> <li>- ECOG Performance status <math>\leq 1</math></li> <li>- Life expectancy <math>&gt; 3</math> months</li> <li>- Age <math>\geq 18</math> years</li> <li>- Haematologic function as follows: ANC <math>\geq 1.5 \times 10^9/L</math>, platelets <math>\geq 100 \times 10^9/L</math>, hemoglobin <math>\geq 9</math> g/dL or 5.59 mmol/L</li> <li>- Adequate liver function as measured by serum transaminases (AST &amp; ALT) <math>\leq 2.5 \times</math> ULN (in case of liver metastases <math>&lt; 5 \times</math> ULN) and total bilirubin <math>\leq 1.5 \times</math> ULN. Patients with known Gilbert disease who have serum bilirubin level <math>\leq 3 \times</math> ULN may be enrolled.</li> <li>- Adequate renal function: serum creatinine <math>\leq 1.5 \times</math> ULN</li> <li>- Negative serum pregnancy test at screening for women of childbearing potential.</li> <li>- 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.</li> <li>- At least 6 months after completion of adjuvant chemotherapy</li> <li>- Written informed consent</li> <li>- 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</li> </ul>
<b>Ausschlusskriterien</b>	<ul style="list-style-type: none"> <li>- 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)</li> <li>- 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 <math>&lt;10</math>mg daily prednisone (or equivalent)</li> <li>- Prior organ transplantation, including allogeneic stem-cell transplantation</li> <li>- 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)</li> </ul>

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- 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  $\leq 10$  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  $\geq 3$  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 ( $\geq$  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  $\leq 2$ , or other Grade  $\leq 2$  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

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