

## Avelumab and Cetuximab in Combination With FOLFOX in Patients With Previously Untreated Metastatic Colorectal Cancer - The Phase II AVETUX-CRC Trial. (AVETUX)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. **A** [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:

NCT03174405

[Recruitment Status](#) ⓘ: Recruiting

[First Posted](#) ⓘ: June 2, 2017

[Last Update Posted](#) ⓘ: October 10, 2017

See [Contacts and Locations](#)

### Sponsor:

AIO-Studien-gGmbH

### Information provided by (Responsible Party):

AIO-Studien-gGmbH

[Study Details](#)
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## Study Description

Go to

### Brief Summary:

AVETUX is a single arm multicentric phase II investigator initiated trial conducted by the Arbeitsgemeinschaft Internistische Onkologie (AIO) in 11 German sites in patients with previously untreated RAS/BRAF wildtype mCRC independent of MSI status.

<a href="#">Condition or disease</a> ⓘ	<a href="#">Intervention/treatment</a> ⓘ	<a href="#">Phase</a> ⓘ
Metastatic Colorectal Cancer	Drug: Avelumab	Phase 2

### Detailed Description:

The primary clinical objective is to determine the efficacy of a standard 1st line regimen (FOLFOX and cetuximab) in patients with RAS/v-Raf murine sarcoma viral oncogene homolog B (BRAF) wildtype, Microsatellite Instability (MSI) or icrosatellite Stability (MSS) MCRC with avelumab in terms of progression free survival rate after 12 months (acc. to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1).

The main secondary objective is to determine safety and tolerability, according to NCI Common Terminology Criteria for Adverse Events (CTCAE v4.03) and to the obtained data on vital signs, clinical parameters (oxygen saturation) and feasibility of the regimen. Further secondary objectives are to determine the efficacy of the experimental regimen in terms of objective response rate (acc. to RECIST v1.1 and irRECIST), and overall survival,

to correlate clonal dynamics (RAS/EGFR subclones) with immune response signature to determine control of mutant subclones by the combination of anti-Epidermal growth factor receptor (EGFR) with anti-PD-L1 and PD-L1 staining (and MSI status) with efficacy.

## Study Design

Go to

**Study Type** ⓘ: Interventional (Clinical Trial)

**Estimated Enrollment** ⓘ: 43 participants

**Intervention Model:** Single Group Assignment

**Masking:** None (Open Label)

**Primary Purpose:** Treatment

**Official Title:** Avelumab and Cetuximab in Combination With FOLFOX in Patients With Previously Untreated Metastatic Colorectal Cancer - The Phase II AVETUX-Colorectal Cancer (CRC) Trial.

**Actual Study Start Date** ⓘ: July 17, 2017

**Estimated Primary Completion Date** ⓘ: May 2020

**Estimated Study Completion Date** ⓘ: August 2021

### Resource links provided by the National Library of Medicine

[MedlinePlus](#) related topics: [Colorectal Cancer](#)



[Drug Information](#) available for: [Cetuximab](#) [Avelumab](#)

[U.S. FDA Resources](#)

## Arms and Interventions

Go to

<b>Arm</b> ⓘ	<b>Intervention/treatment</b> ⓘ
Experimental: AVELUMAB	<p>Drug: Avelumab</p> <p>All eligible patients will receive cetuximab and mFOLFOX6 combined avelumab from the second cycle onwards.</p> <p>Cetuximab at a dose of 250 mg/m<sup>2</sup> IV over 60 to 90 min (day 1 and 8) (first dose 400mg/m<sup>2</sup>) mFOLFOX6 (administration according to local standard) Oxaliplatin at a dose of 85 mg/m<sup>2</sup> IV (day 1) 5-FU 400 mg/m<sup>2</sup> IV bolus (day 1) LV at a dose of 400 mg/m<sup>2</sup> iv (day 1) 5-FU at a dose of 2400 mg/m<sup>2</sup> IV (day 1-3) Avelumab at a dose of 10mg/kg IV over 60 to 90 min (day 1 from cycle 2 onwards)</p>

## Outcome Measures

Go to

### Primary Outcome Measures

 ⓘ:

1. Progression Free Survival Rate (PFS) @ 12 months [ Time Frame: during 12 months of treatment ]  
PFS according to RECIST 1.1 at 12months of treatment

### Secondary Outcome Measures

 ⓘ:

1. Safety [ Time Frame: 21 months ]

Safety and tolerability (acc. to NCI CTC AE v4.03 and to the obtained data on vital signs, clinical parameters (oxygen saturation) and feasibility of the regimen)

2. Response Rate (RR) [ Time Frame: 4 years ]

Response Rate (RR) according to RECIST v1.1 and modified RECIST (mRECIST)

3. Progression Free Survival (PFS) [ Time Frame: 4 years ]

Progression Free Survival (PFS) according to RECIST v1.1 and mRECIST

4. Overall survival (OS) [ Time Frame: 4 years ]

Overall survival (OS)

5. Translational research [ Time Frame: 48 months ]

Translational research (correlation of clonal dynamics (RAS/EGFR subclones) with immune response signature to determine control of mutant subclones by the combination of anti-EGFR with anti-PD-L1, and PD-L1 (and MSI) status with efficacy

## Eligibility Criteria

Go to 

### Information from the National Library of Medicine



*Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).*

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

### Criteria

#### Inclusion Criteria:

1. Patients with histologically confirmed, previously untreated RAS and BRAF wildtype, MSI or MSS metastatic colorectal cancer (primary tumor may be present)
2. Patients with at least one measurable lesion acc. to RECIST v1.1
3. ECOG Performance status  $\leq 1$
4. Life expectancy  $> 3$  months
5. Age  $\geq 18$  years.
6. Haematologic function as follows: ANC  $\geq 1.5 \times 10^9/L$ , platelets  $\geq 100 \times 10^9/L$ , hemoglobin  $\geq 9$  g/dL or 5.59 mmol/L
7. Adequate liver function as measured by serum transaminases (AST & ALT)  $\leq 2.5 \times$  ULN (in case of liver

metastases < 5 x ULN) and total bilirubin  $\leq$  1.5 x ULN. Patients with known Gilbert disease who have serum bilirubin level  $\leq$  3 x ULN may be enrolled.

8. Adequate renal function: serum creatinine  $\leq$  1.5 x ULN
9. Negative serum pregnancy test at screening for women of childbearing potential. 10. 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 90 days after avelumab treatment and 6 month after standard chemotherapy.
11. At least 6 months after completion of adjuvant chemotherapy. 12. Written informed consent 13. 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

Exclusion Criteria:

1. Malignancies other than disease under study within 5 years prior to inclusion, with the exception of those with a negligible risk of metastasis or death (e.g., expected 5-year OS > 90%) treated with expected curative outcome (such as adequately treated 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)
2. All subjects with known brain metastases, except those meeting the following criteria:
  1. Brain metastases that have been treated locally and are clinically stable for at least 2 weeks prior to enrolment
  2. 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)
  3. Subjects must be either off steroids or on a stable or decreasing dose of <10mg daily prednisone (or equivalent)
3. Prior organ transplantation, including allogeneic stem-cell transplantation
4. Significant acute or chronic infections including, among others:
  1. Known history of testing positive test for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome (AIDS)
  2. Positive test for HBV surface antigen and / or confirmatory HCV RNA (if anti-HCV antibody tested positive)
5. 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)
6. Concomitant treatment with corticosteroids or other immunosuppressants, besides treatment of brain metastases as mentioned in criteria 2 or:
  1. 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
  2. Administration of steroids through a route known to result in a minimal systemic exposure (topical, intranasal, intro-ocular, or inhalation) are acceptable
7. 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)
8. Pregnancy or lactation
9. Known alcohol or drug abuse 10. Clinically significant (i.e., active) cardiovascular disease: 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.

11. 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.

12. 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 13. Any psychiatric condition that would prohibit the understanding or rendering of informed consent 14. Vaccination within 4 weeks of the first dose of avelumab and while on trial is prohibited except for administration of inactivated vaccines 15. Any approved anticancer therapy, including chemotherapy, hormonal therapy or radiotherapy, within 4 weeks prior to initiation of study treatment 16. Major surgical procedure within 28 days prior to treatment or anticipation of need for a major surgical procedure during the course of the study

## Contacts and Locations

Go to

### Information from the National Library of Medicine



*To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.*

*Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT03174405***

### Contacts

Contact: Aysun Karatas, Dr. 0308145344 ext 31 [info@aio-studien-ggmbh.de](mailto:info@aio-studien-ggmbh.de)

### Locations

#### Germany

Universitätsklinikum Hamburg-Eppendorf **Recruiting**  
Hamburg, Germany  
Contact: Alexander Stein, PD Dr.

### Sponsors and Collaborators

AIO-Studien-gGmbH

### Investigators

Principal Investigator: Alexander Stein, PD Dr. Universitätsklinikum Hamburg-Eppendorf

## More Information

Go to

### Additional Information:

[Homepage of the AIO \(Arbeitsgemeinschaft Internistische Onkologie in der Deutschen Krebsgesellschaft e.V.\)](#)

Responsible Party: AIO-Studien-gGmbH

ClinicalTrials.gov Identifier: [NCT03174405](#) [History of Changes](#)

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2016-004434-26 ( EudraCT Number )  
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First Posted: June 2, 2017 [Key Record Dates](#)  
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Individual Participant Data (IPD) Sharing Statement:  
Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No  
Studies a U.S. FDA-regulated Device Product: No

Additional relevant MeSH terms:

Colorectal Neoplasms	Colonic Diseases
Intestinal Neoplasms	Intestinal Diseases
Gastrointestinal Neoplasms	Rectal Diseases
Digestive System Neoplasms	Cetuximab
Neoplasms by Site	Antibodies, Monoclonal
Neoplasms	Antineoplastic Agents
Digestive System Diseases	Immunologic Factors
Gastrointestinal Diseases	Physiological Effects of Drugs