# Clinical Trials Data EGFR - Document 112

# Study of Tivantinib (ARQ 197) Plus Cetuximab in EGFR Inhibitor-Resistant MET High Subjects

## Clinical Trial: https://clinicaltrials.gov/study/NCT01892527

"eligibilityCriteria": "Inclusion Criteria:Subjects must satisfy all of the following criteria to be included in the study:\n\n1. Subjects with surgically unresectable locally advanced or metastatic disease who have received \u2265 1 prior line of systemic therapies for advanced or metastatic disease. The last treatment regimen must include EGFR inhibitor (cetuximab or panitumumab) on which the patient had a best response as CR or PR or SD, and must have either progressed on or after EGFR inhibitor based therapy within 3 months before enrollment. Subjects must have radiologically documented disease progression prior to enrollment.\n2. All subjects must express the wild-type form of the gene KRAS. Previously existing KRAS mutation status from an accredited local laboratory will be accepted.\n3. Fresh tumor biopsy tissue must be available for molecular sequencing and biomarker expression in \\>70% of patients. If prior radiotherapy, tissue biopsy must be outside radiotherapy field. In a minor percentage of patients (\\<30%) archival tumor tissue could be considered acceptable for molecular sequencing and biomarker expression.\n4. Patients must be MET High testing by IHC (IHC 2+ or 3+ in \u226550% of tumor cells) analyzed by Ventana Test Kit.\n5. Measurable disease according to RECIST criteria, Version 1.1.\n6. Male or female \u2265 18 years of age.\n7. Eastern Cooperative Oncology Group (ECOG) performance status of \u2264 2.\n8. Resolution of any toxic effects of prior therapy to NCI CTCAE, Version 4.0, grade \u2264 1 (with the exception of alopecia and grade \u2264 2 neuropathy).\n9. Adequate bone marrow, liver, and renal functions, defined as: Hemoglobin \u2265 9.0 g/dL (transfusion and/or growth factor support allowed).\n\n Absolute neutrophil count (ANC) \u2265 1.5 \u00d7 109/L. Platelet count \u2265 75 \u00d7 109/L. Serum creatinine \u2264 1.5 \u00d7 upper limit of normal (ULN) or creatinine clearance \u2265 60 mL/min. Alanine transaminase (ALT), and aspartate transaminase (AST) \u2264 2.5 x ULN in subjects with no liver metastasis and \u2264 5.0 x ULN in subjects with liver metastasis. Total bilirubin \u2264 1.5 x ULN (\u2264 4 x ULN and direct bilirubin \u2264 1.5 x ULN is acceptable for subjects with Gilbert's syndrome).\n10. Male and female subjects of child-bearing potential must agree to use double-barrier contraceptive measures, oral contraception, or avoidance of intercourse during the study and for 90 days after last investigational drug dose received. 11. All female subjects of childbearing potential must each have a negative pregnancy test (serum or urine) result before initiating study treatment.\n\n12. Subjects must be fully informed about their illness and the investigational nature of the study protocol (including foreseeable risks and possible side effects) and must sign and date an IEC- or IRB-approved ICF (including HIPAA authorization, if applicable) before performance of any study-specific procedures or tests.\n\nExclusion Criteria:\n\nSubjects who meet any of the following criteria will be disqualified from entering the study:\n\n1. History of malignancy other than CRC, unless there is an exception that the malignancy has been cured and no tumor- specific treatment for the malignancy has been administered within the 3 years prior to initiation of study treatment (subjects with a history of basal cell carcinoma or benign tumor of cervix can be enrolled if diagnosis and treatment occurred \\< 3 years prior to enrollment).\n2. Anticipation of need for a major surgical procedure or radiation therapy (RT) during the study.\n3. Treatment with chemotherapy, radiotherapy, surgery, immunotherapy, biological therapy, or any other investigational anticancer agent within 3 weeks prior to start of study treatment.\n4. History of cardiac disease: Congestive heart failure defined as Class II to IV per New York Heart Association (NYHA) classification; active coronary artery disease (CAD); Previously diagnosed bradycardia (subjects with asymptomatic bradycardia and hear rate above 50 bpm are allowed) or other cardiac arrhythmia defined as \u2265Grade 2 or higher according to NCI CTCAE, version 4.0, or uncontrolled hypertension; myocardial infarction that occurred within 6 months prior to start of study treatment (myocardial infarction that occurred \\> 6 months prior the start of study treatment is permitted).\n5. Malabsorption syndrome, chronic diarrhea (lasting \\> 4 weeks), inflammatory bowel disease, or partial bowel obstruction.\n6. Known metastatic brain or meningeal tumors, unless the subject is \\> 6 months from definitive therapy, has a negative imaging study within 4 weeks of first dose of study treatment, and is clinically stable (no concomitant therapy, including supportive therapy with steroids or anticonvulsant medications) with respect to the tumor at the time of first dose of study treatment.\n7. Uncontrolled seizure disorder, spinal cord compression, or carcinomatous meningitis.\n8. Pericardial or pleural effusion (requiring drainage) or pericardial involvement with the tumor. Subjects with minimal pleural effusion may be eligible upon request by Investigator and approval by Sponsor.\n9. Clinically significant active infection that requires antibiotic therapy.\n10. Previous administration of any MET inhibitor (including tivantinib) or EGFR inhibitor (except cetuximab or panitumumab).\n11. Substance abuse or medical, psychological or social conditions that may, in the opinion of the Investigator, interfere with the subject's participation in the clinical trial or evaluation of the clinical trial results.\n12. Any condition that is unstable or that could jeopardize the safety of the subject and the subject's protocol compliance.\n13. Inability to swallow oral medications.\n14. Pregnant or nursing females.",  
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Question:  
Based on the following clinical trial information, would a patient with a EGFR gene mutation be eligible for the clinical trial?

Answer:  
To determine if a patient with an EGFR gene mutation would be eligible for this clinical trial, we need to review the inclusion and exclusion criteria provided in the trial details.  
  
\*\*Inclusion Criteria Highlights:\*\*  
1. The subject must have received at least one prior line of systemic therapy for advanced or metastatic disease.  
2. The last treatment regimen must include an EGFR inhibitor (cetuximab or panitumumab), and the patient must have shown either CR, PR, or SD and then progressed within 3 months before enrollment.  
3. Subjects must express the wild-type form of the KRAS gene.  
4. Other biological and performance status criteria, as well as age and laboratory test requirements.  
  
\*\*Exclusion Criteria Highlights:\*\*  
- Previous administration of any EGFR inhibitor is not allowed except for cetuximab or panitumumab.   
- Subjects with other stable existing conditions or recent therapies that contradict trial policies.  
  
The presence of an EGFR gene mutation itself is not listed as an exclusion criterion; however, key eligibility revolves around KRAS status and prior treatment responses to specific EGFR inhibitors. The criteria explicitly state that the last treatment regimen must include an EGFR inhibitor (cetuximab or panitumumab) and that patients must have progressed following such treatment.  
  
So, an EGFR gene mutation alone would not disqualify a patient from participating, but their treatment history, including responses to EGFR inhibitors like cetuximab or panitumumab, along with KRAS wild-type status, are crucial eligibility determinants. If a patient with an EGFR mutation meets these specific conditions, they could be eligible for this trial.