# Clinical Trials Data BRAF - Document 34

# Influence of BRAF and PIK3K Status on the Efficacy of 5-Fluorouracil/Leucovorin/Oxaliplatin (FOLFIRI) Plus Bevacizumab or Cetuximab in Patients With RAS Wild-type Metastatic Colorectal Carcinoma and < 3 Circulating Tumor Cells (CTC)

## Clinical Trial: https://clinicaltrials.gov/study/NCT01640444

"eligibilityCriteria": "Inclusion Criteria:\n\n1. Patient's Informed consent in written.\n2. Age between 18-70 years old.\n3. ECOG 0-1.\n4. Life expectancy of at least 3 months.\n5. Histological confirmation of adenocarcinoma of the colon or rectum.\n6. Sample of tumour tissue available for evaluation of genes RAS, BRAF and PI3K. To be included in the study patients should present \\< 3 CTC in peripheral blood and RAS wild-type present in the sample of tumor tissue.\n7. Measurable metastatic stage IV disease with at least 1 measurable metastatic lesion following RECIST criteria v 1.1 (non suitable for radical surgery at the inclusion time).\n8. Prior radiotherapy is allowed but must be completed at least 4 weeks before randomization (if applicable).\n9. Adequate bone marrow, liver and renal function.\n10. Women of childbearing potential must have a negative serum or urine pregnancy test. Postmenopausal women must have been amenorrheic for at least 12 months.Both men and women participating in this study must use adequate contraception.\n11. Subject must have the ability, in the opinion of the investigator, to comply with all the study procedures and follow-up examinations.\n\nExclusion Criteria:\n\n1. Previous chemotherapy for metastatic disease.\n2. Prior treatment with Bevacizumab, or EGFR inhibitors\n3. Any anticancer treatment (chemotherapy, hormonal treatment, radiation treatment, surgery , immunotherapy, biologic therapy or tumour embolization) within 4 weeks before randomization.\n4. Use of any investigational drug within 4 weeks before start the treatment.\n5. Clinical or radiographic evidence of brain metastasis.\n6. Uncontrolled hypertension (systolic blood pressure \\>150 mmHg and/or diastolic blood pressure \\>100 mmHg on repeated measurement) despite optimal medical management.\n7. Previous history of hypertensive encephalopathy or hypertensive crises.\n8. Current or history of peripheral neuropathy \\> or equal to 1 NCICTCAE.\n9. Patients classified as fragile according to criteria listed in the protocol.\n10. Significant cardiovascular disease (e.g. AVC, myocardial infarction, within 6 months before randomization). Unstable angina, congestive heart failure New York Heart Association (NYHA) \u2265 class II, arrhythmia that requires treatment within 3 months before randomization.\n11. Significant vascular disease (e.g. aortic aneurism requiring surgical intervention, pulmonary embolic, peripheral arterial thrombosis) within 6 months before randomization.\n12. Previous history of significant haemorrhage /severe, within 1 month before randomization.\n13. Major surgery, open surgical biopsy or significant traumatic injury within 4 weeks before randomization.\n14. Large bore needle biopsy of a major organ within 14 days before randomization. Placement of central venous access port \\> or equal to 7 days before randomization is permitted.\n15. Evidence or history of bleeding diathesis or coagulopathy.\n16. INR \\>1.5 within 14 days prior to starting study treatment. EXEMPTION: patients on full anticoagulation must have an in-range INR\\[usually between 2-3\\]. Any anticoagulation therapy must be at stable dosing prior to enrolment.\n17. History of previous abdominal fistula or gastrointestinal perforation within 6 months before randomization.\n18. Serious non-healing wound, ulcer or bone fracture.\n19. Acute or sub-acute of intestinal occlusion or history of intestinal inflammatory disease.\n20. History of uncontrolled convulsive crises.\n21. History of pulmonary fibrosis, acute lung disease or interstitial pneumonia.\n22. Chronic, actual o recent use (10 days prior first drug administration) of acetylsalicylic acic (aspirin) \\> 325 mg/day or clopidogrel (75mg/day) or other treatments that can cause gastrointestinal ulcer (low-dose aspirin is permitted \\< or equal to 325 mg/day).\n23. Urinary protein excretion \\> or equal to 2+ (dipstick). If \\> or equal 2 g proteinuria is detected with dipstick, a 24-hour period urine test will be performed and the result should be \\< or equal to 1 g/24 hours to permit the inclusion of the patient in the clinical trial\n24. Known human immunodeficiency virus infection or chronic hepatitis B or C infection or other uncontrolled, severe concurrent infection .\n25. Current infection \\> or equal to Grade 2 (NCI-CTCAE).\n26. Any previous or concurrent cancer different to colorectal carcinoma within 5 years before to start the treatment. Subjects with successfully treated, non-invasive cancers, including cervical cancer in situ, basal cell carcinoma will be allowed to participate in the clinical trial. Or those cancer treated with curative intention without disease evidence in the last 5 years at least\n27. Known or suspected allergy or hypersensitivity to any component of bevacizumab, cetuximab, irinotecan, or 5-FU/LV.\n28. Any medical, psychological, or social condition that may interfere with the subject's participation in the study or evaluation of the study results.\n29. Any psychological, familial or geographic situation that interferes in the adequate follow-up and adherence to the study protocol.\n30. Women who are pregnant or breast-feeding.",  
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"ADULT",  
"OLDER\_ADULT"  
]

Question:  
Based on the following clinical trial information, would a patient with a BRAF gene mutation be eligible for the clinical trial?

Answer:  
No. Inclusion criteria #6 states that patients must have RAS wild-type to be included, meaning they \*cannot\* have a RAS mutation. While the criteria require testing for BRAF, it does \*not\* specify that a BRAF mutation is required or permitted. Therefore, having a BRAF mutation does not automatically disqualify someone, but the presence of a RAS mutation \*does\*.