# Clinical Trials Data BRAF - Document 24

# Dabrafenib in Treating Patients With Solid Tumors and Kidney or Liver Dysfunction

## Clinical Trial: https://clinicaltrials.gov/study/NCT01907802

"eligibilityCriteria": "Inclusion Criteria:\n\n\* PRE-REGISTRATION ELIGIBILITY CRITERIA\n\* Willing to provide tissue as required per protocol for central BRAF\\^V600X mutation testing\n\n \* NOTE: patients with prior BRAF\\^600X testing that demonstrate a mutation at V600X will be allowed to enroll prior to central testing if the assay was performed at a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory assay; this includes THxID, BRAF Detection Kit, Cobas 4800 BRAF600 mutation test and other CLIA-certified assays available at participating institutions\n\* Patients with unknown BRAF\\^600X status: histologically confirmed melanoma, papillary thyroid, cholangiocarcinoma or testicular cancer that is metastatic or unresectable and for which the investigator feels a BRAF\\^600X targeted agent is a reasonable treatment\n\n \* NOTE: patient must be screened by central BRAF testing and must demonstrate a V600 mutation prior to start of study agent\n \* Note: other tumor types without known BRAF\\^600X mutations will not be eligible for central testing\n\* Ability to understand and willingness to sign written informed consent\n\* Life expectancy of \\> 3 months\n\* REGISTRATION ELIGIBILITY CRITERIA\n\* Patients with known BRAF\\^V600X mutation: patients must have BRAF\\^V600X mutated, histologically confirmed cancer that is metastatic or unresectable and for which curative or standard therapies do not exist or are no longer effective\n\n \* NOTE: colorectal cancers with BRAF mutations ARE NOT allowed\n \* NOTE: any mutation at the V600 position that results in a change from V (valine) is allowed; this includes E, D, K, R or other mutations not noted here at the V600 position\n\* Any number of the following prior therapies is allowed:\n\n \* Chemotherapy \\>= 28 days prior to registration\n \* Mitomycin C/nitrosoureas \\>= 42 days prior to registration\n \* Immunotherapy \\>= 28 days prior to registration\n \* Biologic therapy \\>= 28 days prior to registration\n \* Radiation therapy \\>= 28 days prior to registration\n \* Radiation to \\< 25% of bone marrow\n\* Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (Karnofsky \\>= 70%)\n\* Able to swallow and retain oral medication and must not have any clinically significant gastrointestinal abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels\n\* Absolute neutrophil count (ANC) \\>= 1.2 x 10\\^9/L\n\* Hemoglobin \\>= 9 g/dL\n\* Platelets \\>= 100 x 10\\^9/L\n\* Albumin \\>= 2.5 g/dL\n\n \* NOTE: this applies to patient in the normal and renal dysfunction cohorts (N, R3 and R4); abnormal albumin is allowed for patients in the liver dysfunction cohorts\n\* Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) =\\< 2.5 x institutional upper limit of normal (ULN)\n\n \* NOTE: this applies to patient in the normal and renal dysfunction cohorts (N, R3 and R4); patients with elevated AST and/or ALT may be assigned to liver dysfunction cohorts\n\* Prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) =\\< 1.3 x institutional ULN; subjects receiving anticoagulation treatment may be allowed to participate with INR established within the therapeutic range prior to randomization\n\n \* NOTE: this applies to patient in the normal and renal dysfunction cohorts (N, R3 and R4); elevated PT/INR is allowed for patients in the liver dysfunction cohorts\n\* Left ventricular ejection fraction \\>= institutional lower limit of normal (LLN) by echocardiogram (ECHO)\n\* Hepatic and renal function meeting the strata below:\n\n \* Group N: Hepatic: normal function (bilirubin =\\< ULN; AST =\\< ULN); renal: normal function (creatinine clearance \\[CrCl\\] \\>= 60 mL/min as estimated by the Cockcroft and Gault equation)\n \* Group R3: Hepatic: normal function (bilirubin =\\< ULN; AST =\\< ULN); renal: severe dysfunction (CrCl \\>= 15 and \\< 30 mL/min as estimated by the Cockcroft and Gault equation)\n \* Group R4: Hepatic: normal function (bilirubin =\\< ULN; AST =\\< ULN; renal: renal failure (hemodialysis)\n \* Group H1: Hepatic: mild dysfunction (bilirubin =\\< ULN; AST \\> ULN); renal: acceptable function (CrCl \\>= 60 mL/min as estimated by the Cockcroft and Gault equation)\n \* Group H2: Hepatic: moderate dysfunction (bilirubin \\> ULN and =\\< 3 x ULN; AST \\> ULN); renal: acceptable function (CrCl\\>=\u2265 60 mL/min as estimated by the Cockcroft and Gault equation)\n \* Group H3: Hepatic: severe dysfunction (bilirubin \\> 3 x ULN and up to investigators discretion; AST \\> ULN); renal: acceptable function (CrCl \\>= 60 mL/min as estimated by the Cockcroft and Gault equation)\n\* Women of childbearing potential must have a negative serum pregnancy test =\\< 7 days prior to registration\n\* Women of child-bearing potential and men must agree to use adequate contraception (barrier method of birth control; abstinence) prior to study entry and for the duration of study participation; should a woman become pregnant or suspect she is pregnant while she or her partner is participating in this study, she should inform her treating physician immediately; men treated or enrolled on this protocol must also agree to use adequate contraception prior to the study, for the duration of study participation, and 1 month after completion of dabrafenib administration\n\* Ability to understand and the willingness to sign a written informed consent document\n\* Willingness to provide blood and tissue samples as required per protocol\n\* Patients with a history of clinical benefit from prior RAF inhibitor therapy, as judged by the investigator, will be allowed\n\nExclusion Criteria:\n\n\* Patients with active biliary obstruction; NOTE: patients for which a shunt has been in place for at least 10 days prior to the first dose of dabrafenib are allowed\n\* Reduced left ventricular ejection fraction (\\< 50%) or other evidence of cardiac dysfunction as determined by the investigator\n\* Use of an investigational anti-cancer drug within 28 days preceding the first dose of dabrafenib\n\* Patients receiving any medications or substances that are strong inhibitors or inducers of cytochrome P450, family 3, subfamily A (CYP3A) or cytochrome P450 family 2, subfamily C, polypeptide 8 (CYP2C8) are ineligible\n\n \* For patients on intermediate inducers or inhibitors, attempts should be made to switch to an alternative agent or delay enrollment until treatment course with concomitant agent completed; if not possible, patient may be enrolled if it is felt to be in the patients best interest as decided by the investigator\n \* Weak inhibitors of CYP3A or CYP2C8 should be used with caution and attempts made to limit their use or find alternative agents, if possible\n\* Warfarin use is provisionally allowed\n\* Unresolved toxicity of National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0 (NCI CTCAE v4.0) grade 2 or higher from previous anti-cancer therapy, except alopecia\n\* Human immunodeficiency virus (HIV)-positive patients on combination antiretroviral therapy are ineligible; Note: patients not on antiretroviral therapies are eligible for this study\n\* Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, diabetes mellitus, hypertension, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements\n\* Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection\n\* Presence of malignancy other than the study indication under this trial within 5 years of study enrollment\n\* History or evidence of cardiovascular risks including any of the following:\n\n \* QT interval corrected for heart rate using the Bazett's formula QTcB \\>= 480 msec\n \* History of acute coronary syndromes (including myocardial infarction or unstable angina), coronary angioplasty, or stenting within the past 24 weeks prior to randomization\n \* History or evidence of current class II, III, or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system\n \* Intra-cardiac defibrillators\n \* Abnormal cardiac valve morphology (\\>= grade 2) documented by ECHO; (subjects with grade 1 abnormalities \\[i.e., mild regurgitation/stenosis\\] can be entered on study); subjects with moderate valvular thickening should not be entered on study\n \* History or evidence of current clinically significant uncontrolled cardiac arrhythmias; clarification: subjects with atrial fibrillation controlled for \\> 30 days prior to dosing are eligible\n \* Treatment refractory hypertension defined as a blood pressure of systolic \\> 140 mmHg and/or diastolic \\> 90 mm Hg which cannot be controlled by anti- hypertensive therapy\n\* Brain metastases that are symptomatic or untreated or not stable for \\>= 3 months (must be documented by imaging) or requiring corticosteroids; subjects on a stable dose of corticosteroids \\> 1 month or who have been off corticosteroids for at least 2 weeks can be enrolled with approval of the Cancer Therapy Evaluation Program (CTEP) medical monitor; subjects must also be off enzyme-inducing anticonvulsants for \\> 4 weeks\n\* History of acute coronary syndromes (including unstable angina), coronary angioplasty, or stenting within the past 24 weeks; class II, III, or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system; or history of known cardiac arrhythmias unless it has been stably controlled\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition to dabrafenib or other agents used in this study\n\* Pregnant women are excluded from this study; breastfeeding should be discontinued if the mother is treated with dabrafenib\n\* Any condition or medical problem in addition to the underlying malignancy and organ dysfunction which the investigator feels would pose unacceptable risk",  
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"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:  
Yes, a patient with a BRAF gene mutation \*could\* be eligible for this trial. Here's why:  
  
\* \*\*BRAF V600X Mutation Required:\*\* The trial explicitly seeks patients with a BRAF V600X mutation. The information provided confirms the patient has a BRAF mutation, but it's crucial that it's specifically a V600X mutation (meaning any mutation at the V600 position). Other BRAF mutations would likely exclude the patient.  
  
\* \*\*Eligible Cancers:\*\* The patient's cancer type must be one of the following: melanoma, papillary thyroid cancer, cholangiocarcinoma, or testicular cancer. Colorectal cancer with a BRAF mutation is \*not\* allowed.  
  
\* \*\*Metastatic or Unresectable Disease:\*\* The cancer must be metastatic or unresectable, and standard therapies must be ineffective or non-existent.  
  
\* \*\*Other Criteria:\*\* The patient must also meet the other inclusion criteria (e.g., age, performance status, organ function, etc.) and not have any of the exclusion criteria (e.g., active biliary obstruction, severe heart dysfunction, certain medications, etc.).  
  
  
\*\*In summary:\*\* Having a BRAF mutation is a necessary but not sufficient condition for eligibility. The specific V600X mutation, cancer type, disease stage, and other inclusion/exclusion criteria must also be met. The patient should consult with their oncologist and the clinical trial team to determine definitive eligibility.