# Clinical Trials Data BRAF - Document 49

# Study to Investigate the Objective Response Rate of Dabrafenib in Combination With Trametinib in Subjects With BRAF V600 Mutation-Positive Melanoma

## Clinical Trial: https://clinicaltrials.gov/study/NCT02083354

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Signed written informed consent, which includes compliance with the requirements and restrictions listed in the consent form.\n\* \\>=18 years of age.\n\* Histologically confirmed acral lentiginous or cutaneous melanoma that is either Stage IIIC (unresectable) or Stage IV (metastatic), and BRAF V600 mutation-positive. The test was to have been conducted at a designated central laboratory.\n\* Measurable disease (i.e., present with at least one measurable lesion) by RECIST version1.1.\n\* Performance status score of 0 or 1 according to the Eastern Cooperative Oncology Group (ECOG) scale.\n\* All prior anti-cancer treatment-related toxicities (except alopecia and laboratory values) must be \\<=Grade 1 according to the Common Terminology Criteria for Adverse Events version 4 (CTCAE version 4.0) at the time of enrolment.\n\* Able to swallow and retain oral medication and must not have had any clinically significant gastrointestinal abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels.\n\* Women of child-bearing potential must have had a negative serum pregnancy test within 14 days of first dose of study treatment and agree to use effective contraception, from 14 days prior to enrolment, throughout the treatment period and for 4 months after the last dose of study treatment.\n\* Adequate baseline organ function as defined below: Absolute Neutrophil Count:\\>= 1.2 \u00d7 10\\^9/liter (L); Hemoglobin: \\>=9 grams (g)/deciliter (dL); Platelet count: \\>=100 x 10\\^9/L; Prothrombin Time/International Normalized Ratio (INR) (Subjects receiving anticoagulation treatment may be allowed to participate with INR established within the therapeutic range prior to enrolment) and Partial Thromboplastin Time: \\<=1.5 x Upper Limit of Normal (ULN); Albumin: \\>=2.5 g/dL; Total bilirubin: \\<=1.5 x ULN; Aspartate aminotransferase and Alanine aminotransferase: \\<=2.5 x ULN; Calculated creatinine clearance (Calculate creatinine clearance using standard Cockcroft-Gault formula): \\>=50 milliliter (mL)/ minute (min); Left Ventricular Ejection Fraction (LVEF) (ECHO scans must be used throughout the study) : \\>= Lower limit of normal (LLN) by ECHO.\n\* Subjects with East Asian origin.\n\nExclusion Criteria:\n\n\* Primary mucosal or ocular melanoma.\n\* Prior treatment with a BRAF inhibitor (including but not limited to dabrafenib, vemurafenib, LGX818, and XL281/BMS-908662) or a MEK inhibitor (including but not limited to trametinib, AZD6244, and RDEA119).\n\* Any major surgery, extensive radiotherapy, chemotherapy with delayed toxicity, biologic anti-cancer therapy, or immuno anti-cancer therapy within 21 days prior to enrolment /or daily or weekly chemotherapy without the potential for delayed toxicity within 14 days prior to enrolment. (Note: Ipilimumab, pembrolizumab and nivolumab treatment must ended at least 8 weeks prior to enrollment).\n\* Taken an investigational drug within 28 days or 5 half-lives (minimum 14 days), whichever is shorter, prior to enrolment. (Note: in case ipilimuamb, pembrolizmab and nivolumab are investigational drug in the regions and countries, and in case of PD-L1 antibody, these investigational treatment must have ended at least 8 weeks prior to enrollment ).\n\* Current use of a prohibited medication.\n\* Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the study treatments, their excipients, and/or dimethyl sulfoxide (DMSO).\n\* A history of Hepatitis B Virus (HBV), or Hepatitis C Virus (HCV) infection (subjects with laboratory evidence of cleared HBV and/or HCV will be permitted).\n\* Leptomeningeal or brain metastases or metastases causing spinal cord compression that were: symptomatic or untreated or not stable for 3 months (must be documented by imaging) or requiring corticosteroids. Subjects that were on a stable dose of corticosteroids \\>1 month or on replacement dose only, or have been off of corticosteroids for at least 2 weeks can be enrolled with approval of the medical monitor. Subjects must also have been off of enzyme-inducing anticonvulsants for \\>4 weeks.\n\* History of malignancy other than disease under study within 3 years of study enrolment with exceptions of subjects with a history of completely resected non-melanoma skin cancer, or subjects with indolent second malignancies were eligible only after the approval of the sponsor's medical monitor.\n\* History of malignancy with confirmed activating RAS mutation at any time. Note: Prospective RAS testing was not required. However, if the results of previous RAS testing were known, they must have been used in assessing eligibility\n\* Any serious or unstable pre-existing medical conditions (aside from malignancy exceptions specified above), psychiatric disorders, or other conditions that could have interfered with the subject's safety, obtaining informed consent, or compliance with study procedures.\n\* A history or evidence of cardiovascular risk including any of the following: Current LVEF \\< Institutional LLN; A QTc interval corrected for heart rate \\>=480 millisecond (msec) (using Bazett's formula); A history or evidence of current clinically significant uncontrolled arrhythmias. Clarification: Subjects with atrial fibrillation controlled for \\>30 days prior to dosing are eligible; A history of acute coronary syndromes (including myocardial infarction or unstable angina), coronary angioplasty, or stenting within 6 months prior to randomization; A history or evidence of current \\>=Class II congestive heart failure as defined by the New York Heart Association (NYHA) guidelines; Patients with intra-cardiac defibrillators; Treatment refractory hypertension defined as a blood pressure of systolic \\>140 millimeters of mercury (mmHg) and/or diastolic \\>90 mmHg which cannot be controlled by anti-hypertensive therapy; Known cardiac metastases; Abnormal cardiac valve morphology (\\>=grade 2) documented by echocardiogram (subjects with grade 1 abnormalities \\[i.e., mild regurgitation/stenosis\\] can be entered on study). Subjects with moderate valvular thickening should not have been entered in study.\n\* Uncorrectable electrolyte abnormalities (e.g. hypokalaemia, hypomagnesaemia, hypocalcaemia determined by blood chemistry), long QT syndrome or taking medicinal products known to prolong the QT interval.\n\* A history or current evidence of retinal vein occlusion (RVO) .\n\* Pregnant or nursing females.\n\* History of or current diagnosis of interstitial lung disease or pneumonitis.",  
 "healthyVolunteers": false,  
 "sex": "ALL",  
 "minimumAge": "18 Years",  
"stdAges": [  
"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:  
A patient with a BRAF V600 mutation \*could\* be eligible for this trial, but more information is needed. Here's why:  
  
\* \*\*Inclusion Criteria Met:\*\* The patient having a BRAF V600 mutation-positive acral lentiginous or cutaneous melanoma (Stage IIIC or IV) is a primary inclusion criterion.  
\* \*\*Other Criteria:\*\* The patient must ALSO meet \*all\* other inclusion criteria (age, measurable disease, performance status, prior treatments and toxicity, ability to take oral meds, organ function, East Asian origin, etc.) and \*none\* of the exclusion criteria. Many factors could disqualify the patient, including:  
 \* Prior treatment with a BRAF or MEK inhibitor.  
 \* Other health conditions (cardiovascular issues, other malignancies, etc.)  
 \* Specific lab values outside the acceptable range.  
 \* Use of certain medications.  
  
In short, having the BRAF V600 mutation is necessary but \*not sufficient\* for eligibility. A full review of the patient's medical history and current status is needed to determine final eligibility.