# Clinical Trials Data BRAF - Document 25

# BKM120 Combined With Vemurafenib (PLX4032) in BRAFV600E/K Mutant Advanced Melanoma

## Clinical Trial: https://clinicaltrials.gov/study/NCT01512251

"eligibilityCriteria": "Inclusion Criteria\n\n1. Histologically or cytologically confirmed diagnosis of unresectable stage III and stage IV melanoma\n2. BRAFV600E or BRAFV600K mutation-positive\n3. Age \\>= 18 years\n4. Eastern Cooperative Oncology Group (ECOG) performance status \\<= 2\n5. Patients must have at least one site of measurable disease (per RECIST for solid tumors)\n6. Life expectancy of \u2265 12 weeks\n7. Adequate bone marrow function as shown by: Absolute Neutrophil Count (ANC) \\>= 1.5 x 109/L, Platelets \\>= 100 x 109/L, Hb \\>9 g/dL\n8. Total calcium (corrected for serum albumin) within normal limits (biphosphonate use for malignant hypercalcemia control is not allowed)\n9. Magnesium \u2265 the lower limit of normal\n10. Potassium within normal limits for the institution\n11. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) within normal range (or \\<= 3.0 x upper limit of normal (ULN) if liver metastases are present)\n12. Serum bilirubin within normal range (or \\<= 1.5 x ULN if liver metastases are present; or total bilirubin \\<= 3.0 x ULN with direct bilirubin within normal range in patients with well documented Gilbert Syndrome)\n13. Serum creatinine \\<= 1.5 x ULN or 24-hour clearance \\>= 50 mL/min\n14. Serum amylase \\<= ULN\n15. Serum lipase \\<= ULN\n16. International Normalized Ratio (INR) \\<= 2\n17. Fasting plasma glucose \\<= 120 mg/dL (6.7 mmol/L)\n18. Negative serum pregnancy test within 48 hours before starting study treatment\n\nExclusion Criteria\n\n1. Patients who have received prior treatment with a PI3K inhibitor or a BRAF inhibitor, prior treatment with sorafenib is permitted.\n2. Patients with a known hypersensitivity to BKM120 or to its excipients\n3. Patients with untreated brain metastases are excluded; however, patients with metastatic central nervous system (CNS) tumors may participate in this trial, if the patient is \\> 4 weeks from therapy completion (incl. radiation and/or surgery) and clinically stable at the time of study entry\n4. Patients with acute or chronic liver, renal disease or pancreatitis\n5. Patients with the following mood disorders as judged by the Investigator or a psychiatrist, or as a result of patient's mood assessment questionnaire:\n\n \* Medically documented history of or active major depressive episode, bipolar disorder (I or II), obsessive-compulsive disorder, schizophrenia, history of suicidal attempt or ideation, or homicidal ideation\n \* \\>= CTCAE grade 3 anxiety\n \* Meets the cut-off score of \\>= 10 in the Patient Health Questionnaire-9 (PHQ-9) or a cut-off of \\>= 15 in the General Anxiety Disorder-7 (GAD-7) mood scale, respectively, or selects a positive response of \"1, 2, or 3\" to question number 9 regarding potential for suicidal thoughts in the PHQ-9 (independent of the total score of the PHQ-9) will be excluded from the study unless overruled by the psychiatric assessment\n6. Patients with diarrhea \\>= CTCAE grade 2\n7. Patient has active cardiac disease including any of the following:\n\n \* Left ventricular ejection fraction (LVEF) \\< 50% as determined by multigated acquisition (MUGA) or echocardiogram (ECHO)\n \* QTc \\> 480 msec on screening ECG (using the QTcF formula)\n \* Personal or family history of prolonged QT syndrome\n \* Angina pectoris that requires the use of anti-anginal medication\n \* Ventricular arrhythmias except for benign premature ventricular contractions\n \* Supraventricular and nodal arrythmias requiring a pacemaker or not controlled with medication\n \* Conduction abnormality requiring a pacemaker\n \* Symptomatic pericarditis\n8. Patient has a history of cardiac dysfunction including any of the following:\n\n \* Myocardial infarction within the last 6 months, documented by persistent elevated cardiac enzymes or persistent regional wall abnormalities on assessment of left ventricular ejection fraction (LVEF) function\n \* History of documented congestive heart failure (New York Heart Association functional classification III-IV)\n \* Documented cardiomyopathy\n9. Poorly controlled diabetes mellitus (HbA1c \\> 8 %)\n10. Other concurrent severe and/or uncontrolled concomitant medical conditions that could cause unacceptable safety risks or compromise compliance with the protocol\n\n - Significant symptomatic deterioration of lung function; if clinically indicated, pulmonary function tests including measures of predicted lung volumes, Diffusing capacity of the lungs for carbon monoxide (DLCO), oxygen (O2) saturation at rest on room air should be considered to exclude pneumonitis or pulmonary infiltrates\n11. Impairment of gastrointestinal (GI) function or GI disease that may significantly alter the absorption of BKM120 (e.g., ulcerative diseases, uncontrolled nausea, vomiting, diarrhea, malabsorption syndrome, or small bowel resection)\n12. Patients who have been treated with any hematopoietic colony-stimulating growth factors (e.g., Granulocyte colony-stimulating factor (G-CSF), Granulocyte-macrophage colony-stimulating factor (GM-CSF)) \\<= 2 weeks prior to starting study drug; erythropoietin or darbepoetin therapy, if initiated at least 2 weeks prior to enrollment, may be continued\n13. Patients who are currently receiving treatment with medication with a known risk to prolong the QT interval or inducing Torsades de Pointes and the treatment cannot either be discontinued or switched to a different medication prior to starting study drug\n14. Patients receiving chronic treatment with steroids or another immunosuppressive agent; topical applications, inhaled sprays, eye drops or local injections are allowed; patients with previously treated brain metastases, who are on stable low dose corticosteroids treatment for at least 14 days before start of study treatment are eligible\n15. Patients who have taken herbal medications and certain fruits within 7 days prior to starting study drug - herbal medications include, but are not limited to St. John's Wort, Kava, ephedra (ma huang), gingko biloba, dehydroepiandrosterone (DHEA), yohimbe, saw palmetto, and ginseng; fruits include CYP3A inhibitors: Seville oranges, grapefruit, pomelos, or exotic citrus fruits\n16. Patients who are currently treated with drugs known to be moderate and strong inhibitors or inducers of isoenzyme CYP3A, and the treatment cannot be discontinued or switched to a different medication prior to starting study drug; note that co-treatment with weak inhibitors of CYP3A is allowed).\n17. Patients who have received chemotherapy or targeted anticancer therapy \\<= 4 weeks (6 weeks for nitrosourea, antibodies or mitomycin-C) prior to starting study drug must have resolution of treatment related adverse events to baseline or grade 1 before starting the trial\n18. Patients who have received wide field radiotherapy \\<= 4 weeks or limited field radiation for palliation \u2264 2 weeks prior to starting study drug or who have not recovered from side effects of such therapy\n19. Patients who have undergone major surgery \\<= 2 weeks prior to starting study drug or who have not recovered from side effects of such therapy\n20. Patients who are currently taking therapeutic doses of warfarin sodium or any other coumadin-derivative anticoagulant\n21. Women who are pregnant or breast feeding or adults of reproductive potential not employing an effective method of birth control; women of child-bearing potential must have a negative serum pregnancy test \\<= 72 hours prior to initiating treatment; double barrier contraceptives must be used through the trial by both sexes; oral, implantable, or injectable contraceptives are therefore not considered effective for this study\n\n \* Women are considered post-menopausal and not of child bearing potential if they have had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g. age appropriate, history of vasomotor symptoms) or six months of spontaneous amenorrhea with serum follicle stimulating hormone (FSH) levels \\> 40 milli-international units per millilitre (mIU/mL) \\[for US only: and estradiol \\< 20 pg/mL\\] or have had surgical bilateral oophorectomy (with or without hysterectomy) at least six weeks ago. In the case of oophorectomy alone, only when the reproductive status of the woman has been confirmed by follow up hormone level assessment is she considered not of child bearing potential.\n \* Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, must use highly effective contraception during treatment for 3 months in total after study drug discontinuation. Highly effective contraception is defined as either: True abstinence-when this is in line with the preferred and usual lifestyle of the subject, periodic abstinence and withdrawal are not acceptable methods of contraception; Sterilization-have had surgical bilateral oophorectomy (with or without hysterectomy) or tubal ligation at least six weeks ago; Male partner sterilization-for female subjects, the vasectomised male partner should be the sole partner for that patient; Use of a combination of any two of the following barrier methods of contraception-condom or Occlusive cap with spermicidal foam/gel/film/cream/vaginal suppository\n \* Fertile males, defined as all males physiologically capable of conceiving offspring must use condom during treatment, for 3 months in total after study drug discontinuation and should not father a child in this period\n22. Known diagnosis of human immunodeficiency virus (HIV) infection\n23. History of another malignancy within 3 years, except cured or curable basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ of the cervix; patients with lesions curable by excision must have these lesions excised prior to the initiation of treatment on study\n24. Patient is unable or unwilling to abide by the study protocol or cooperate fully with the investigator",  
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Question:  
Based on the following clinical trial information, would a patient with a BRAF gene mutation be eligible for the clinical trial?

Answer:  
Based on the inclusion criteria provided for the clinical trial, a patient with a BRAF gene mutation would be eligible if they meet the following specific criteria:  
  
1. The patient must have an unresectable stage III or stage IV melanoma.  
2. The patient must be BRAFV600E or BRAFV600K mutation-positive.   
  
If the patient has a BRAF mutation but it is not specifically noted as BRAFV600E or BRAFV600K, they would not be eligible based on this criterion.  
  
Make sure to double-check all other inclusion and exclusion criteria to ensure the patient is otherwise eligible for the trial.