# Clinical Trials Data BRAF - Document 22

# Study of XL888 With Vemurafenib for Patients With Unresectable BRAF Mutated Stage III/IV Melanoma

## Clinical Trial: https://clinicaltrials.gov/study/NCT01657591

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Must have cytologically or histologically-confirmed unresectable melanoma that harbors a BRAF V600 E or K mutation determined by pyrosequencing assay or equivalent genotyping assay in a Clinical Laboratory Improvement Amendments (CLIA) certified laboratory, meeting one of the following American Joint Committee on Cancer (AJCC) staging criteria:\n\n \* AJCC Stage IV (Tany, Nany, M1a, b, or c)\n \* AJCC Stage III B or C with unresectable nodal/locoregional involvement\n\* Adequate hepatic, renal, and bone marrow function as defined by the following parameters obtained within 2 weeks prior to initiation of study treatment:\n\n \* Hematologic Criteria: leukocytes \u22653,000/mcL; absolute neutrophil count \u22651,500/mcL; platelets \u2265100,000/mcL\n \* Renal Criteria: serum creatinine within normal institutional limits or a creatinine clearance \u226560 mL/min for patients with creatinine levels above institutional normal\n \* Hepatic Criteria: aspartate aminotransferase (AST)/alanine transaminase (ALT) \u22642.5 X institutional upper limit of normal; if liver metastasis present, then AST/ALT may be less than or equal to 5 times the upper limit of normal\n\* Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1\n\* Willing to give written informed consent per institutional guidelines and must be able to adhere to dose and visit schedules\n\* Female and male participants must agree to use a medically acceptable method of birth control prior to screening and agree to continue its use throughout the study. Females of childbearing potential should be counseled in the appropriate use of birth control while on this study.\n\* Treatment-na\u00efve and previously treated patients will be included; however, patients may not have received a BRAF or HSP90 inhibitor in the past.\n\* Patients must be at least 4 weeks from any prior systemic therapy (6 weeks for nitrosoureas or mitomycin C), surgery or radiation.\n\* Must have measurable disease as defined by RECIST 1.1\n\nExclusion Criteria:\n\n\* Females who are pregnant, intend to become pregnant or are nursing. Females with child-bearing potential must have a negative pregnancy test within one week of enrollment.\n\* Previously treated with BRAF or HSP90 inhibitor therapy\n\* Patients who have had chemotherapy or radiotherapy within 4 weeks (6 weeks for nitrosoureas or mitomycin C) prior to entering the study or those who have not recovered from adverse events due to agents administered more than 4 weeks earlier.\n\* Patients who are receiving any other investigational agents.\n\* History of allergic reactions attributed to compounds of similar chemical or biologic composition (i.e. ethanol) to XL888 or vemurafenib (i.e., ethanol).\n\* Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, uncontrolled or symptomatic cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements\n\* HIV-positive patients on combination antiretroviral therapy are ineligible because of the potential for pharmacokinetic interactions with XL888 and vemurafenib.\n\* Untreated or uncontrolled brain metastases or evidence of leptomeningeal disease. Brain metastases that have been appropriately treated with radiation and/or surgery will be allowed as long as the central nervous system (CNS) disease has been stable for at least 4 weeks post-treatment.\n\* Must be at least 3 years from any prior malignancy and have no evidence of the malignancy at the time of enrollment. Patients with adequately treated squamous cell or basal cell carcinomas of the skin, multiple primary melanomas, or any carcinoma in situ will be allowed.\n\* Corrected QT interval (QTc) greater than 460 ms at baseline",  
 "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 V600E or V600K mutation \*could\* be eligible for this trial, but more information is needed. Simply having the mutation isn't enough. They must also meet \*all\* of the other inclusion criteria and \*none\* of the exclusion criteria.  
  
Here's a breakdown of why a BRAF V600 mutation alone isn't sufficient:  
  
\* \*\*Specific Mutation:\*\* The trial specifies BRAF V600E \*or\* V600K mutations. Other BRAF mutations wouldn't qualify.  
\* \*\*Confirmation and Testing:\*\* The mutation must be confirmed by a specific type of test (pyrosequencing or equivalent) in a CLIA-certified lab.  
\* \*\*Stage and Resectability:\*\* The patient's melanoma must be unresectable and meet specific AJCC staging criteria (Stage IV or specific Stage III).  
\* \*\*Organ Function:\*\* Adequate liver, kidney, and bone marrow function is required, with specific lab value thresholds.  
\* \*\*Performance Status:\*\* The patient must have an ECOG performance status of 0 or 1.  
\* \*\*Prior Treatments:\*\* The patient cannot have received prior BRAF or HSP90 inhibitors. Restrictions also exist on other prior systemic therapies, surgery, or radiation.  
\* \*\*Other Criteria:\*\* Numerous other criteria must be met, including measurable disease, no pregnancy or breastfeeding (for females), agreement to birth control, no conflicting medications or conditions, and no uncontrolled brain metastases.  
  
In short, the BRAF V600E/K mutation is a necessary but not sufficient condition for eligibility. A physician would need to evaluate the patient's full medical history and current status to determine if they meet all the criteria.