# Clinical Trials Data BRAF - Document 21

# A Study to Evaluate the Effect of Repeat Oral Dosing of GSK2118436 on Cardiac Repolarization in Subjects With V600 BRAF Mutation-Positive Tumors

## Clinical Trial: https://clinicaltrials.gov/study/NCT01738451

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Has provided signed, written informed consent for this study.\n\* Male or female, age \\>=18 years of age at the time of signing the informed consent form\n\* Has confirmed diagnosis of a V600 BRAF-mutation positive tumor as determined by appropriate genetic testing.\n\* Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.\n\* Has adequate baseline organ function as defined by: Absolute neutrophil count\\>=1.2 \u00d7 10\\^9/liter (L), hemoglobin\\>=9 gram (g)/deciliter (dL), platelets\\>= 75 \u00d7 10\\^9/L, prothrombin time (PT), international normalization ratio (INR) and partial thromboplastin time (PTT)\\<=1.3 times upper limit of normal (ULN), total bilirubin\\<=1.5 times ULN, alanine aminotransferase (ALT)\\<=2.5 times ULN; \\<5 times ULN if liver metastases are present, creatinine or\\<=1.5 times ULN, calculated creatinine clearance or 24-hour urine creatinine clearance\\>=60 mL/min and left ventricular ejection fraction (LVEF)\\>= institutional lower limit of normal (LLN) by echocardiogram (ECHO).\n\* For Part 2 subjects only: Have serum potassium, serum magnesium, and total serum calcium levels within normal limits.\n\* Able to swallow and retain orally administered medication and does not have any clinically significant GI abnormalities that may alter the absorption such as malabsorption syndrome or major resection of the stomach or bowels.\n\* If a female subject of childbearing potential, must have a negative serum pregnancy test within 14 days of first dose of study treatment and agree to use effective contraception, during the study and for 4 weeks following the last dose of study treatment.\n\nExclusion Criteria:\n\n\* Known immediate or delayed hypersensitivity reaction to dabrafenib or excipients;\n\* Any of the following ECG findings: QT duration corrected using Fridericia's formula (QTcF) interval \\>450 milliseconds (msec), PR interval \\>220 msec or \\<=110 msec, bradycardia defined as sinus rate \\<50 beats per minute (bpm)\n\* Cardiac conduction abnormalities denoted by any of the following: evidence of second-degree (type II) or third-degree atrioventricular block, evidence of ventricular pre-excitation, electrocardiographic evidence of complete left bundle branch block (LBBB), intraventricular conduction delay with QRS duration \\>120 msec, evidence of atrial fibrillation or history of atrial fibrillation within the past 6 months or presence of cardiac pacemaker\n\* History of any one of the following cardiovascular conditions within the past 6 months: Class II, III, IV heart failure as defined by the New York Heart Association (NYHA), cardiac angioplasty or stenting, myocardial infarction, unstable angina or symptomatic peripheral vascular disease or other clinically significant cardiac disease\n\* LVEF, as measured by ECHO, below the institutional LLN, or if a LLN does not exist at an institution, \\<50%.\n\* Abnormal cardiac valve morphology (\\>=grade 2) documented by echocardiogram (subjects with minimal abnormalities \\[ie, mild regurgitation/stenosis\\] can be entered)\n\* Moderate valvular thickening\n\* Personal or immediate family history of long-QT syndrome.\n\* Anti-cancer therapy (e.g., chemotherapy with delayed toxicity, extensive radiation therapy, immunotherapy, biologic therapy, or major surgery) within 21 days prior to enrolment; chemotherapy regimens without delayed toxicity within 14 days prior to enrollment; or use of an investigational anti-cancer drug within 28 days preceding the first dose of study treatment.\n\* Current use of a prohibited medication(s) or requires any of these medications during treatment with study treatment\n\* Current use of therapeutic warfarin.\n\* Unresolved toxicity of Grade 2 or higher from previous anticancer therapy, except alopecia or hemoglobin.\n\* A history of known Human Immunodeficiency Virus, Hepatitis B Virus (HBV), or Hepatitis C Virus infection. Subjects with documented laboratory evidence of HBV clearance may be enrolled.\n\* A history of known glucose-6-phosphate dehydrogenase (G6PD) deficiency.\n\* Brain metastases that are: symptomatic, or treated (surgery, radiation therapy) but not clinically and radiographically stable 1 month after local therapy, or asymptomatic and untreated but \\>1 centimeter (cm) in the longest dimension\n\* Uncontrolled medical conditions (i.e., diabetes mellitus, hypertension), psychological, familial, sociological, or geographical conditions that do not permit compliance with the protocol; or unwillingness or inability to follow the procedures required in the protocol.\n\* History of another malignancy; Only (a) Subjects who have been successfully treated and are disease-free for 3 years, (b) a history of completely resected non-melanoma skin cancer, (c) successfully treated in situ carcinoma, (d) CLL in stable remission, or (e) indolent prostate cancer (definition: clinical stage T1 or T2a, Gleason score \\<=6, and PSA \\< 10 nanogram (ng)/mL) requiring no or only anti-hormonal therapy with histologically confirmed tumour lesions that can be clearly differentiated from lung cancer target and non-target lesions are eligible\n\* Pregnant or lactating/actively breastfeeding female.",  
 "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. The inclusion criteria specifically state "confirmed diagnosis of a V600 BRAF-mutation positive tumor." However, having the mutation is only \*one\* of the requirements. The patient must \*also\* meet all other inclusion criteria and \*not\* meet any of the exclusion criteria. For instance, the patient must have adequate organ function, an acceptable ECOG performance status, and no conflicting medications or medical conditions. Therefore, simply having the BRAF mutation does not guarantee eligibility.