# Clinical Trials Data BRAF - Document 51

# Onalespib, Dabrafenib, and Trametinib in Treating Patients With BRAF-Mutant Melanoma or Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery

## Clinical Trial: https://clinicaltrials.gov/study/NCT02097225

"eligibilityCriteria": "Inclusion Criteria:\n\n\* Patients must have histologically confirmed, BRAF-mutant (V600E/K) solid tumor (molecularly confirmed using Cobas assay or a comparable Food and Drug Administration \\[FDA\\]-approved assay) that is metastatic or unresectable, have received and tolerated prior BRAF or BRAF and MEK inhibitor (BRAF targeted) therapy at full dose or not previously received BRAF targeted therapy, and for which standard curative measures do not exist or are no longer effective\n\n \* If test at Clinical Laboratory Improvement Act (CLIA)-certified laboratory (lab) used a non-FDA approved method, information about the assay must be provided; (FDA approved tests for BRAF V600 mutations in melanoma include: THxID BRAF Detection Kit and Cobas 4800 BRAF V600 Mutation Test)\n\* Patients must have measurable disease, defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded for non-nodal lesions and short axis for nodal lesions) as \\>= 20 mm with conventional techniques or as \\>= 10 mm with spiral computed tomography (CT) scan, magnetic resonance imaging (MRI), or calipers by clinical exam\n\* Prior therapy is allowed; patients may have received any number of prior lines of therapy, including treatment with a BRAF and/or MEK inhibitor\n\* All prior anti-cancer treatment-related toxicities must be less than or equal to grade 1 according to the Common Terminology Criteria for Adverse Events version 5 (CTCAE version 5.0; National Cancer Institute \\[NCI\\], 2017) at the time of enrollment; a notable exception are endocrinopathies caused by immune checkpoint inhibitors that are appropriately treated with medical management (e.g. hormone replacement therapy, anti-diabetic agents)\n\* Eastern Cooperative Oncology Group (ECOG) performance status =\\< 1 (Karnofsky \\>= 70%)\n\* Life expectancy of greater than 3 months\n\* Leukocytes \\>= 3,000/mcL\n\* Absolute neutrophil count \\>= 1,200/mcL\n\* Hemoglobin \\>= 9 g/dl (patients may be transfused to this level)\n\* Platelets \\>= 100,000/mcL\n\* Total bilirubin \\< 1.5 x institutional upper limit of normal OR \\> 1.5 x institutional upper limit of normal allowed if direct bilirubin is within normal range\n\* Aspartate aminotransferase (AST) (serum glutamic oxaloacetic transaminase \\[SGOT\\])/alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase \\[SGPT\\]) =\\< 2.5 x institutional upper limit of normal\n\* Prothrombin time (PT) \\< 1.3 x upper limit of normal (ULN)\n\* International normalized ratio (INR) \\< 1.3 x ULN\n\* Partial thromboplastin time (PTT) \\< 1.3 x ULN\n\* Serum creatinine =\\< 1.5 mg/dL OR creatinine clearance \\>= 50 mL/min/1.73 m\\^2\n\* Potassium \\> 3 and \\< 5.5 mEq/L\n\* Magnesium \\> 1.2 and \\< 2.5 mEq\n\* Left ventricular \\>= institutional lower limit of normal (LLN) by echocardiogram (ECHO) ejection fraction\n\* Women of child-bearing potential must have a negative serum pregnancy test within 14 days prior to randomization and agree to use effective contraception (barrier method of birth control, or abstinence; hormonal contraception is not allowed) from 14 days prior to randomization, throughout the treatment period, and for 4 months after the last dose of study treatment; should a woman become pregnant or suspect she is pregnant while she is participating in this study, she should inform her treating physician immediately\n\* Therapeutic level dosing of warfarin can be used with close monitoring of PT/INR by the site; exposure may be decreased due to enzyme induction when on treatment, thus warfarin dosing may need to be adjusted based upon PT/INR; consequently, when discontinuing dabrafenib, warfarin exposure may be increased and thus close monitoring via PT/INR and warfarin dose adjustments must be made as clinically appropriate; prophylactic low dose warfarin may be given to maintain central catheter patency\n\* Ability to understand and the willingness to sign a written informed consent document\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\nExclusion Criteria:\n\n\* Patients who received prior systemic anti-cancer therapy (chemotherapy with delayed toxicity, extensive radiation therapy, immunotherapy, biologic therapy, or vaccine therapy) within the last 3 weeks prior to day 1 of cycle 1; patients are permitted to be on dabrafenib and trametinib standard of care at start of therapy without wash-out period prior to day 1 of cycle 1; dosing will change to protocol determined dose levels on day 1 of cycle 1\n\* Patients must not have received prior HSP90 inhibitor therapy\n\* Patients who are receiving any other investigational agents; patients who have taken an investigational drug within 28 days or 5 half-lives (minimum 14 days), whichever is shorter, prior to randomization\n\* Patients with history of activating RAS mutation positive tumors regardless of interval from current study; however, patients may have concurrent BRAFV600 and RAS mutations in the tumor to be treated with protocol therapy\n\* Patients must have no clinical evidence of leptomeningeal or brain metastasis causing spinal cord compression that are symptomatic or untreated or not stable for \\>= 4 weeks (must be documented by imaging) or requiring corticosteroids; subjects on a stable dose of corticosteroids \\> 1 month or who have been off of 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 of enzyme-inducing anticonvulsants for \\> 4 weeks\n\* History of known immediate or delayed hypersensitivity reactions attributed to compounds of similar chemical or biologic composition to AT13387, dabrafenib, or trametinib, or excipients or to dimethyl sulfoxide (DMSO)\n\* Uncontrolled intercurrent illness including, but not limited to, ongoing or active serious infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, uncontrolled diabetes, or psychiatric illness/social situations that would limit compliance with study requirements\n\* Pregnant women are excluded from this study; breastfeeding should be discontinued prior to the mother being treated with the study drugs\n\* Patients known to be human immunodeficiency virus (HIV)-positive patients and on combination antiretroviral therapy are ineligible\n\* History of another malignancy other than the study indication under this trial within 5 years of study enrollment; does not apply to subjects who underwent successful definitive resection of basal or squamous cell carcinoma of the skin, superficial bladder cancer, in situ cervical cancer, in situ breast cancer, or other in situ cancers\n\n \* Exception: patients with history of RAS mutation-positive tumors are not eligible regardless of interval from the current study; prospective RAS testing is not required; however, if the results of previous RAS testing are known, they must be used in assessing eligibility\n\* History of interstitial lung disease or pneumonitis\n\* History or current evidence/risk of retinal vein occlusion (RVO) or retinal pigment epithelial detachment (RPED):\n\n \* History of RVO or RPED, or predisposing factors to RVO or RPED (e.g., uncontrolled glaucoma or ocular hypertension, uncontrolled systemic disease such as hypertension, diabetes mellitus, or history of hyperviscosity or hypercoagulability syndromes)\n \* Visible retinal pathology as assessed by ophthalmic exam that is considered a risk factor for RVO or RPED such as evidence of new optic disc cupping, evidence of new visual field defects, and intraocular pressure \\> 21 mm mercury (Hg)\n\* History or evidence of cardiovascular risk including any of the following:\n\n \* An average of the three most recent QT intervals corrected for heart rate using the Bazett's formula QTcB \\>= 460 msec\n \* History or evidence of current clinically significant uncontrolled arrhythmias (exception: patients with controlled atrial fibrillation for \\> 30 days prior to randomization are eligible)\n \* History of acute coronary syndromes (including myocardial infarction and unstable angina), coronary angioplasty, or stenting within 6 months prior to randomization\n \* History or evidence of current \\>= class II congestive heart failure as defined by the New York Heart Association (NYHA) functional classification system\n \* Treatment-refractory hypertension defined as a blood pressure of systolic \\> 140 mmHg and/or diastolic \\> 90 mmHg which cannot be controlled by anti-hypertensive therapy\n \* 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 be entered on study\n \* Prior placement of an implantable defibrillator\n \* History of or identification on screening imaging of intracardiac metastases\n\* No known active infection with hepatitis B virus (HBV), or hepatitis C virus (HCV); patients with chronic or cleared HBV infection and HCV infection are eligible\n\* Current use of a prohibited medication; the following medications or non-drug therapies are prohibited:\n\n \* Other anti-cancer therapy while on study treatment; (note: megestrol \\[Megace\\] if used as an appetite stimulant is allowed)\n \* Concurrent treatment with bisphosphonates is permitted; however, treatment must be initiated prior to the first dose of study therapy; prophylactic use of bisphosphonates in patients without bone disease is not permitted, except for the treatment of osteoporosis\n \* The concurrent use of all herbal supplements is prohibited during the study (including, but not limited to, St. John's wort, kava, ephedra \\[ma huang\\], ginkgo biloba, dehydroepiandrosterone \\[DHEA\\], yohimbe, saw palmetto, or ginseng)\n \* Current use of a prohibited medication; patients receiving any medications or substances that are strong inhibitors or inducers of CYP3A or CYP2C8 are ineligible; current use of, or intended ongoing treatment with: herbal remedies (e.g., St. John's wort), or strong inhibitors or inducers of P-glycoprotein (Pgp) or breast cancer resistance protein 1 (Bcrp1) should also be excluded",  
 "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:  
Based on the provided clinical trial information, a patient with a BRAF gene mutation would be eligible for the trial if they meet the following inclusion criteria and none of the exclusion criteria:  
  
1. \*\*Presence of BRAF Mutation\*\*: The patient must have a histologically confirmed, BRAF-mutant (V600E/K) solid tumor. This must be molecularly confirmed using the Cobas assay or a comparable FDA-approved assay.  
  
2. \*\*Tumor Status\*\*: The tumor must be metastatic or unresectable, and the standard curative measures should not exist or be effective anymore.  
  
3. \*\*Measurable Disease\*\*: The patient must have measurable disease, with at least one lesion that can be accurately measured.  
  
4. \*\*Prior Therapy\*\*: Patients are allowed to have received BRAF targeted therapy or no prior BRAF targeted therapy at all. They may have had any number of prior therapies, including BRAF and/or MEK inhibitors.  
  
5. \*\*Performance Status and Other Health Criteria\*\*: The patient must meet specific health criteria, including an ECOG performance status of ≤ 1, and have certain laboratory values within specified limits.  
  
6. \*\*Ability to Consent and Comply\*\*: The patient must understand and be willing to sign a consent document, and be able to comply with study requirements.  
  
They must not have any of the exclusion criteria, such as:  
  
- Prior HSP90 inhibitor therapy.  
- Known immediate or delayed hypersensitivity reactions to the study drugs.  
- Active RAS mutation-positive tumors, unless it is concurrent with the BRAF V600 mutation.  
- Uncontrolled illnesses or active systemic infections.  
- Recent use of prohibited medications or investigational agents.  
  
If a patient with a BRAF gene mutation meets these conditions and does not fall under the outlined exclusions, they would be eligible for participation in the clinical trial.