# Clinical Trials Data BRAF - Document 43

# A Study of the Safety and Efficacy of Pembrolizumab (MK-3475) in Combination With Trametinib and Dabrafenib in Participants With Advanced Melanoma (MK-3475-022/KEYNOTE-022)

## Clinical Trial: https://clinicaltrials.gov/study/NCT02130466

"eligibilityCriteria": "Inclusion criteria:\n\n\* Histologically-confirmed diagnosis of advanced (unresectable Stage III) or metastatic (Stage IV) melanoma excluding mucosal, or ocular melanoma (or a histologically or cytologically-documented locally-advanced or metastatic solid malignancy in Parts 4 and 5)\n\* At least 1 measurable lesion as defined by RECIST 1.1 on imaging studies (computed tomography \\[CT\\] or magnetic resonance imaging \\[MRI\\])\n\* For solid tumors other than melanoma, (in Part 4 or 5 \\[dose confirmation only\\]), participants must have a malignancy that is incurable and has either: (a) failed prior standard therapy, (b) for which no standard therapy exists, or (c) standard therapy is not considered appropriate by the participants and treating physician. There is no limit to the number of prior treatment regimens, but prior treatment(s) should not include compounds targeting programmed cell death 1 (PD-1), programmed cell death ligand 1 (PD-L1), BRAF, or mitogen-activated protein kinase (MEK). Treatment must end at least 4 weeks prior to randomization\n\* BRAF mutation-positive (V600 E or K) melanoma for Parts 1, 2 and 3, or for Parts 1, 2, 4 and 5 only BRAF mutation-negative (wild type) melanoma with documented progression of \u22651 measurable lesion after prior therapy (if prior therapy was received). The inclusion criterion does not apply to participants with solid tumors in Parts 4 and 5 (dose confirmation only)\n\* Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1\n\* Anticipated life expectancy of at least 3 months\n\* Able to swallow and retain oral medication and no clinically significant gastrointestinal abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels\n\* Adequate organ function\n\* Provide tissue for biomarker analysis from a newly or recently-obtained biopsy (within 90 days of Study Day 1) of a tumor lesion not previously irradiated\n\* Female participants of non-childbearing potential must be willing to use highly effective contraceptive measures from the Screening Visit (Visit 1) through 120 days after the last dose of study drug; male participants must agree to use an adequate method of contraception starting with the first dose of study drug through 120 days after the last dose of study drug\n\* Female participants of childbearing potential should have a negative urine or serum pregnancy test within 72 hours prior to receiving the first dose of study drug\n\nExclusion criteria:\n\n\* Currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks of the first dose of study drug\n\* Prior systemic therapy (for participants who are BRAF mutation-positive), or BRAF mutation-negative and has received \\>1 prior systemic therapy for metastatic melanoma\n\* Prior therapy with compounds targeting PD-1, PD-L1, BRAF, MEK or other molecules in the mitogen-activated protein kinase (MAPK) pathway\n\* BRAF mutation-positive and has received prior systemic therapy with ipilimumab or other anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibodies. The BRAF exclusion criterion does not apply to participants with solid tumor in Parts 4 and 5 (dose confirmation only)\n\* Chemotherapy, radioactive, or biological cancer therapy within 4 weeks prior to the first dose of study drug, or not recovered from clinically significant adverse events due to cancer therapeutics administered more than 4 weeks prior to the first dose of study drug\n\* Expected to require any other form of systemic or localized antineoplastic therapy while in this study\n\* Has a known additional malignancy that is progressing or requires active treatment. Exceptions include early stage cancers (carcinoma in situ or stage 1) treated with curative intent, basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in situ cervical cancer, or in situ breast cancer that has undergone potentially curative therapy\n\* Active central nervous system (CNS) metastases and/or carcinomatous meningitis\n\* Active infection requiring systemic therapy\n\* Active autoimmune disease, or documented history of autoimmune disease, or a syndrome that requires systemic steroids or immunosuppressive agents\n\* Previous severe hypersensitivity reaction to treatment with another monoclonal antibody (mAb)\n\* On chronic systemic steroid therapy (\\>10 mg/day prednisone or equivalent) within 2 weeks prior to first dose of study drug or on any other form of immunosuppressive medication\n\* History or evidence of cardiovascular risk\n\* Uncorrectable electrolyte abnormalities, long QT syndrome or taking medications known to prolong the QT interval\n\* History of prior or current retinal vein occlusion (RVO)\n\* Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs chemically related to the study drugs, their excipients, and/or dimethyl sulfoxide (DMSO)\n\* Has had an allogeneic tissue/solid organ transplant, prior stem cell or bone marrow transplant\n\* History of (non-infectious) pneumonitis that required steroids or current pneumonitis\n\* Human immunodeficiency virus (HIV)\n\* Hepatitis B or C\n\* Received a live vaccine within 30 days prior to first dose of study drug\n\* Pregnant or breastfeeding or expecting to conceive or father children from the Screening Visit (Visit 1) through 120 days after last dose of study drug",  
 "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 \*parts\* of this trial, but not all of it. Here's the breakdown:  
  
\* \*\*Eligible for Parts 1, 2, and 3:\*\* The inclusion criteria specifically state "BRAF mutation-positive (V600 E or K) melanoma for Parts 1, 2 and 3".  
  
\* \*\*Eligible for Parts 1, 2, 4 and 5:\*\* If the patient is BRAF \*negative\*, they are eligible for these parts provided they meet the other inclusion/exclusion criteria, specifically the requirement for documented progression after prior therapy. For patients with solid tumors (not melanoma) in parts 4 and 5, BRAF status is not considered.  
  
\* \*\*Not eligible for parts 4 and 5 alone (dose confirmation only):\*\* These parts are specifically for BRAF \*negative\* melanoma patients who have progressed after prior therapy OR for patients with other solid tumors where BRAF status is not relevant. A BRAF positive melanoma patient would be excluded.  
  
\*\*Important Considerations:\*\* Even if a patient has the correct BRAF mutation for the applicable parts of the trial, they must \*also\* meet all other inclusion criteria and \*not\* meet any exclusion criteria. There are many other factors that could determine eligibility, such as prior treatments, overall health, and organ function.