# 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:  
To determine whether a patient with a BRAF gene mutation is eligible for the clinical trial, we need to consider both the inclusion and exclusion criteria mentioned in the trial information.  
  
### Inclusion Criteria:  
1. The trial is investigating advanced or metastatic melanoma (Stage III or IV), among other solid malignancies.   
2. Specifically, for BRAF mutation-positive melanoma, the patient must have a V600 E or K mutation and meet the other trial criteria as outlined.  
3. The trial also specifies parts for BRAF mutation-positive candidates (Parts 1, 2, and 3), indicating that patients with these mutations are indeed considered for the study under certain trial parts.  
  
### Exclusion Criteria:  
1. Patients who have received prior systemic therapy targeting BRAF or MEK are not eligible.  
2. Additionally, BRAF mutation-positive patients who have previously received ipilimumab or other CTLA-4 inhibitors are excluded (except for solid tumors in Parts 4 and 5).  
  
Given this information, a patient with a BRAF gene mutation (specifically V600 E or K) could potentially be eligible for this clinical trial under Parts 1, 2, and 3, provided they have not received prior systemic therapy targeting BRAF/MEK or ipilimumab/CTLA-4 inhibitors, among other exclusionary criteria.  
  
In summary, eligibility for the trial would depend on the mutation type, the specific part of the trial, and the patient's treatment history. If the patient has not received these specific prior treatments, they may be eligible to participate.