ForPatients
by Roche

Skin Cancer

Cobimetinib (Targeted Therapy) Plus Atezolizumab (Immunotherapy) in Participants With Advanced Melanoma Whose Cancer Has Worsened During or After Treatment With Previous Immunotherapy and Atezolizumab Monotherapy in Participants With Previously Untreated Advanced Melanoma

Trial Status	Trial Runs In	Trial Identifier
Completed	7 Countries	NCT03178851 2016-004402-34 CO39721

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase Ib Study Evaluating Cobimetinib Plus Atezolizumab in Patients With Advanced BRAF V600 Wild-Type Melanoma Who Have Progressed During or After Treatment With Anti-PD-1 Therapy and Atezolizumab Monotherapy in Patients With Previously Untreated Advanced BRAF V600 Wild-Type Melanoma

Trial Summary:

This study will evaluate the preliminary efficacy, safety, and pharmacokinetics of cobimetinib and atezolizumab in participants with advanced BRAF V600-wild type (WT), metastatic, or unresectable locally advanced melanoma who have progressed on prior anti-PD-1 therapy. In addition, this study will evaluate the efficacy, safety, and pharmacokinetics of atezolizumab monotherapy in participants with BRAFV600-WT metastatic or unresectable locally advanced melanoma, who have not been previously treated.

Hoffmann-La Roche
Sponsor

Phase 1
Phase

NCT03178851 2016-004402-34 CO39721
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

Inclusion Criteria:

Disease-Specific Inclusion Criteria: Cohorts A and B:

- Histologically confirmed Stage IV (metastatic) or unresectable Stage IIIc BRAF V600 WT (locally advanced) melanoma
- Documentation of BRAF V600 mutation-negative status in melanoma tumor tissue (archival [< 5 years old] or newly obtained) through use of a clinical mutation test approved by the local health authority
- Measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1
- Disease progression on or after treatment with a programmed death (PD)-1 inhibitor either as monotherapy or in combination with other agent(s)

Additional Disease-Specific Inclusion Criteria in Cohort B (Biopsy Cohort):

- Progressed on or after anti-PD-1 therapy within 12 weeks before study start
- Received a minimum of two cycles of anti-PD-1 therapy
- Meet the following criteria for resistance to an anti-PD-1 agent: primary resistance defined as disease progression, according to RECIST v1.1, as best response; secondary resistance defined as disease progression after initial confirmed response according to RECIST v1.1
- Consent to undergo tumor biopsies of accessible lesions, before and during treatment and at radiographic progression, for biomarker analyses.
- Have at least two accessible lesions that are amenable to excisional or core-needle (minimum three cores and minimum diameter 18 gauge; however, 16 gauge is desirable) biopsy without unacceptable risk of a major procedural complication. Exceptions may be made if patient has only one lesion that allows multiple biopsies.

Disease-Specific Inclusion Criteria: Cohort C:

- Histologically confirmed Stage IV (metastatic) or unresectable Stage IIIc BRAFV600-WT (locally advanced) melanoma
- Naive to prior systemic anti-cancer therapy for melanoma
- Documentation of BRAFV600 mutation-negative status in melanoma tumor tissue (archival [< 5 years old] or newly obtained) through use of a clinical mutation test approved by the local health authority
- A representative, formalin-fixed, paraffin-embedded (FFPE) tumor specimen in a paraffin block (preferred) or 20 slides containing unstained, freshly cut, serial sections must be submitted along with an associated pathology report prior to study entry.
- Measurable disease according to RECIST v1.1.

General Inclusion Criteria:

- Ability to comply with the study protocol, in the investigator's judgment
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- Available and adequate baseline tumor tissue sample
- Life expectancy # 18 weeks
- Adequate hematologic and end-organ function, defined by laboratory test results, obtained within 14 days before initiation of study treatment
- For women of childbearing potential: abstinent or use an effective form of contraceptive method for at least 3 months for cobimetinib and at least 5 months for atezolizumab. Women must refrain from donating eggs during this same period.
- For men: abstinent or use contraceptive measures and agreement to refrain from donating sperm for at least 3 months after cobimetinib and atezolizumab

Exclusion Criteria:

- Prior treatment with a mitogen activated-protein kinase (MAPK) inhibitor
- Ocular melanoma
- Major surgical procedure other than for diagnosis within 4 weeks before initiation of study treatment, or anticipation of need for a major surgical procedure during the course of the study
- Traumatic injury within 2 weeks before initiation of study treatment
- Palliative radiotherapy within 14 days before initiation of study treatment
- Active malignancy (other than BRAF V600 mutation-negative melanoma) or malignancy within 3 years
- Treatment with any anti-cancer agent 14 days prior to Cycle, Day 1 other than aPD-1 based therapy
- Adverse events from prior anti-cancer therapy that have not resolved to Grade # 1. Clinically stable patients with manageable immune-related adverse events resulting from prior cancer immunotherapy may be eligible for the study.
- For Cohort C only: any prior anti-cancer therapy for advanced melanoma
- History or evidence of ongoing serous retinopathy or retinal vein occlusion (RVO) at baseline
- History of clinically significant cardiac dysfunction
- Active or untreated central nervous system (CNS) metastases
- History of metastases to brain stem, midbrain, pons, or medulla, or within 10 millimeter (mm) of the optic apparatus (optic nerves and chiasm)
- History of leptomeningeal metastatic disease
- Human immunodeficiency virus (HIV) infection
- Active tuberculosis
- Severe infection within 4 weeks before initiation of study treatment
- Signs or symptoms of infection within 2 weeks before initiation of study treatment
- Treatment with oral or intravenous (IV) antibiotics within 2 weeks prior to Day 1 of Cycle 1
- Active or chronic viral hepatitis B or C infection
- Active or history of autoimmune disease or immune deficiency
- Prior allogeneic stem cell or solid organ transplantation
- History of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- Treatment with systemic immunosuppressive medications with the following exceptions:
- Patients who have received acute, low-dose systemic immunosuppressant medication (# 10 mg/day oral prednisone or equivalent) or a one-time pulse dose of systemic immunosuppressant medication (e.g., 48 hours of corticosteroids for a contrast allergy) are eligible for the study after Medical Monitor approval has been obtained.
- Patients who received mineralocorticoids (e.g., fludrocortisone), corticosteroids for chronic obstructive pulmonary disease (COPD) or asthma, or low-dose corticosteroids for orthostatic hypotension or adrenal insufficiency are eligible for the study.
- Current severe, uncontrolled systemic disease other than cancer
- Any Grade >/=3 hemorrhage or bleeding event within 28 days of Day 1 of Cycle 1
- History of stroke, reversible ischemic neurological defect, or transient ischemic attack within 6 months prior to Day 1
- Anticipated use of any concomitant medication during or within 7 days before initiation of study treatment that is known to cause QT prolongation
- Any psychological, familial, sociological, or geographic condition that may hamper compliance with the protocol and follow-up after treatment discontinuation
- History of malabsorption or other clinically significant metabolic dysfunction that may interfere with absorption of oral study treatment
- Pregnant or breastfeeding, or intending to become pregnant during the study
- Known clinically significant liver disease

- Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the participant at high risk for treatment complications
- Treatment with a live, attenuated vaccine within 4 weeks before initiation of study treatment, or anticipation of need for such a vaccine during the course of the study
- Known hypersensitivity to any component of the atezolizumab or cobimetinib formulations
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Treatment with any other investigational agent or participation in another clinical study with therapeutic intent
- Inability or unwillingness to swallow pills
- Requirement for concomitant therapy or food that is prohibited during the study