ForPatients
by Roche

Wild Type MelanomaMetastatic MelanomaSkin Cancer

A Study Evaluating the Safety and Efficacy of Cobimetinib Plus Atezolizumab in BRAFV600 Wild-type Melanoma With Central Nervous System Metastases and Cobimetinib Plus Atezolizumab and Vemurafenib in BRAFV600 Mutation-positive Melanoma With Central Nervous System Metastases

Trial Status	Trial Runs In	Trial Identifier
Completed	8 Countries	NCT03625141 2018-000759-41 MO39136

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 II Two Cohort Study Evaluating the Safety and Efficacy of Cobimetinib Plus Atezolizumab in BRAFV600 Wild-type Melanoma With Central Nervous System Metastases and Cobimetinib Plus Atezolizumab and Vemurafenib in BRAFV600 Mutation-positive Melanoma With Central Nervous System Metastases

Trial Summary:

This study will evaluate the efficacy and safety of cobimetinib plus atezolizumab in participants with BRAFV600 wild-type melanoma with central nervous system (CNS) metastases and of cobimetinib plus atezolizumab and vemurafenib in BRAFV600 mutation-positive melanoma patients with CNS metastases.

Hoffmann-La Roche
Sponsor

Phase 2
Phase

NCT03625141 2018-000759-41 MO39136
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	# 18 Years	No

Inclusion Criteria:

Disease-specific inclusion criteria:

- Histologically confirmed melanoma with radiologically confirmed brain metastases
- Documented BRAFV600 mutation status of melanoma tumour tissue using a validated genetic test.
- Measurable brain metastases
- Prior systemic therapy for metastatic melanoma is allowed with exceptions as detailed in the exclusion criteria
- Prior SRT or surgical therapy of # 10 brain metastases is allowed but prior WBRT is not allowed
- Adverse effects of all prior systemic or local treatment must have either returned to baseline or become stable and manageable prior to initiation of study treatment.

General inclusion criteria:

- Age #18 years
- Able to comply with the study protocol, in the investigator's judgment
- ECOG Performance Status # 2
- Life expectancy of > 3 months
- Willing and able to complete health and quality of life questionnaires required by the protocol
- Adequate hematologic and end-organ function
- Female patients of childbearing potential and male patients with partners of childbearing potential must agree to always use two effective forms of contraception during the course of this study and for at least six months after completion of study therapy.
- Male patients must agree to refrain from donating sperm for at least six months after the last dose of cobimetinib

Exclusion Criteria:

Disease-specific exclusion criteria:

- Ocular melanoma
- Leptomeningeal involvement
- Uncontrolled tumour-related pain
- Uncontrolled pleural effusion, pericardial effusion, or ascites requiring repeated drainage more than once every 28 days.
- Prior WBRT treatment for CNS disease
- Increasing corticosteroid dose during the seven days prior to initiation of study treatment or current dexamethasone or equivalent dose of > 8 mg/day
- Prior treatment with a BRAF or MEK inhibitor
- For patients assigned to Cohort 1 only: prior immunotherapy in the metastatic setting is not allowed. Prior immunotherapy is allowed in the adjuvant setting, provided it is completed # 90 days prior to study treatment initiation.

For patients assigned to Cohort 2 only: prior immunotherapy in either the adjuvant or metastatic setting is not allowed.

- Major surgical procedure other than for diagnosis within four weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the course of the study
- Known hypersensitivity to biopharmaceutical agents produced in Chinese hamster ovary cells or to any formulation component of cobimetinib or atezolizumab or, for patients assigned to Cohort 2 only, vemurafenib

- Any anti-cancer therapy, including chemotherapy, hormonal therapy and radiotherapy, within two weeks prior to initiation of study treatment
- Patients assigned to Cohort 2 only: Concomitant treatment with anticonvulsants other than gabapentin, vigabatrin and levetiracetam
- Patients assigned to Cohort 2 only: acetaminophen is prohibited within seven days prior to initiation of study treatment unless the patient has an absolute contraindication to the to the use of non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin
- Active malignancy (other than melanoma) or a prior malignancy within the past three years

General exclusion criteria:

- Known risk factors for ocular toxicity
- History of clinically significant cardiac dysfunction
- Inability to swallow medications
- Malabsorption condition that would alter the absorption of orally administered medications
- Traumatic injury within two weeks prior to initiation of study treatment
- Prior allogeneic stem cell or solid organ transplantation
- Active or history of autoimmune disease or immune deficiency
- 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
- Uncontrolled diabetes or symptomatic hyperglycaemia
- Any Grade # 3 haemorrhage or bleeding event within 28 days of study treatment initiation
- History of stroke, reversible ischemic neurological defect, or transient ischemic attack within six months prior to study treatment initiation
- Positive human immunodeficiency virus (HIV) test at screening
- Hepatitis B virus (HBV) infection (chronic or acute)
- Active hepatitis C virus (HCV) infection
- Active tuberculosis
- History of severe allergic, anaphylactic or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins
- Severe infection within four weeks prior to initiation of study treatment
- Signs or symptoms of infection within two weeks prior to initiation of study treatment
- Any serious medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the patient's safe participation in, and completion of, the study
- Any psychological, familial, sociological, or geographical condition that may hamper compliance with the protocol and follow-up after treatment discontinuation
- Pregnancy, breastfeeding, or intention of becoming pregnant during the study. Women of childbearing potential must have a negative serum pregnancy test result within seven days prior to initiation of study treatment.
- Treatment with therapeutic oral or IV antibiotics within two weeks prior to initiation of study treatment
- Administration of a live, attenuated vaccine within four weeks prior to initiationof study treatment or anticipation of need for such a vaccine during the study
- Treatment with systemic immunostimulatory agents within 28 days or 5 half-lives of the drug, whichever is shorter, prior to study treatment initiation
- Treatment with systemic immunosuppressive medications within two weeks prior to study treatment initiation
- Treatment with investigational drug within 28 days or 5 half-lives of the drug, whichever is longer, prior to initiation of study treatment
- For patients to be assigned to Cohort 2 only: anticipated use of any concomitant medication during or within seven days prior to initiation of study treatment that is known to cause QT prolongation
- Consumption of foods, supplements, or drugs that are strong or moderate CYP3A4 enzyme inducers or inhibitors at least seven days prior to initiation of study treatment.

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