

Trial record 1 of 1 for: 2016-002482-54

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A Study of Atezolizumab Plus Cobimetinib and Vemurafenib Versus Placebo Plus Cobimetinib and Vemurafenib in Previously Untreated BRAFv600 Mutation-Positive Participants With Metastatic or Unresectable Locally Advanced Melanoma

This study is not yet open for participant recruitment. (see [Contacts and Locations](#))

Verified October 2016 by Hoffmann-La Roche

Sponsor:
Hoffmann-La Roche

Information provided by (Responsible Party):
Hoffmann-La Roche

ClinicalTrials.gov Identifier:

NCT02908672

First received: September 19, 2016

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[History of Changes](#)

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[No Study Results Posted](#)

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Purpose

This is a Phase III, double-blinded, placebo-controlled, randomized, multicenter study designed to evaluate the efficacy, safety, and pharmacokinetics of combination of atezolizumab (ATZ), cobimetinib and vemurafenib compared with combination of ATZ placebo, cobimetinib and vemurafenib in participants with previously untreated BRAFv600 mutation-positive metastatic or unresectable locally advanced melanoma.

| Condition | Intervention | Phase |
|---------------------------|---|-----------------------|
| Melanoma | Drug: Atezolizumab Drug: Atezolizumab Placebo Drug: Cobimetinib Drug: Vemurafenib Drug: Vemurafenib Placebo | Phase 3 |

Study Type: **Interventional**
Study Design: **Allocation: Randomized**
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: **A Phase III, Double-Blinded, Randomized, Placebo-Controlled Study of Atezolizumab Plus Cobimetinib and Vemurafenib Versus Placebo Plus Cobimetinib and Vemurafenib in Previously Untreated BRAFV600 Mutation-Positive Patients With Unresectable Locally Advanced or Metastatic Melanoma**

Resource links provided by NLM:

[MedlinePlus](#) related topics: [Melanoma](#)

[Drug Information](#) available for: [Vemurafenib](#) [Cobimetinib](#) [Atezolizumab](#)

[Genetic and Rare Diseases Information Center](#) resources: [Carcinoid Tumor](#) [Neuroepithelioma](#)

[U.S. FDA Resources](#)

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measures:

- Progression-Free Survival (PFS), as Determined by Investigator Using Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 [Time Frame: Baseline up to disease progression or death due to any cause, whichever occurs first (up to approximately 90 months)] [Designated as safety issue: No]

Secondary Outcome Measures:

- Progression-Free Survival (PFS), as Determined by Independent Review Committee Using RECIST v1.1 [Time Frame: Baseline up to disease progression or death due to any cause, whichever occurs first (up to approximately 90 months)] [Designated as safety issue: No]
- Percentage of Participants With Objective Response, as Determined by Investigator Using RECIST v1.1 [Time Frame: Baseline up to disease progression or death due to any cause, whichever occurs first (up to approximately 90 months)] [Designated as safety issue: No]
- Duration of Response, as Determined by Investigator Using RECIST v1.1 [Time Frame: Baseline up to disease progression or death due to any cause, whichever occurs first (up to approximately 90 months)] [Designated as safety issue: No]
- Overall Survival [Time Frame: Baseline up to death due to any cause (up to approximately 90 months)] [Designated as safety issue: No]
- Percentage of Participants Who are Alive at Year 2 [Time Frame: 2 years] [Designated as safety issue: No]
- Time to Deterioration in Global Health Status Using The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30) Global Health Status Scale Score [Time Frame: Baseline up to end of treatment (approximately 90 months)] [Designated as safety issue: No]

- Time to Deterioration in Physical Functioning Using EORTC QLQ-30 Physical Functioning Scale Score [Time Frame: Baseline up to end of treatment (approximately 90 months)] [Designated as safety issue: No]
- Percentage of Participants with Adverse Events and Serious Adverse Events [Time Frame: Baseline up to 6 months after the last dose of study treatment (approximately 90 months)] [Designated as safety issue: No]
- Serum Concentration of ATZ [Time Frame: Pre-infusion (0 hour) and 30 minutes (min) post-infusion (infusion duration=30-60 min) on Day 1 (D1) of Cycles (Cy) 1-4; Pre-infusion on D1 of Cy 8 & every 8 Cy thereafter up to ATZ discontinuation (approximately 90 months overall) (1 Cy=28 days)] [Designated as safety issue: No]
- Plasma Concentration of Cobimetinib [Time Frame: Pre-dose (0 hour) and 3 to 6 hours post dose on Day 15 of Cy 1 and 4 (1 Cy = 28 days)] [Designated as safety issue: No]
- Plasma Concentration of Vemurafenib [Time Frame: Pre-dose (0 hour) and 3 to 6 hours post dose on Day 15 of Cy 1 and 4 (1 Cy = 28 days)] [Designated as safety issue: No]
- Percentage of Participants With Anti-Therapeutic Antibodies (ATA) to Atezolizumab [Time Frame: Pre-infusion (0 hour) on D1 of Cy 1-4; Pre-infusion on D1 of Cy 8 & every 8 Cy thereafter up to atezolizumab discontinuation (approximately 90 months overall) (1 Cy=28 days) (approximately up to 90 months)] [Designated as safety issue: Yes]

Estimated Enrollment: 500
 Study Start Date: February 2017
 Estimated Study Completion Date: February 2020
 Estimated Primary Completion Date: February 2020 (Final data collection date for primary outcome measure)

| <u>Arms</u> | <u>Assigned Interventions</u> |
|--|---|
| <p>Experimental: ATZ + Cobimetinib + Vemurafenib + Vemurafenib Placebo</p> <p>Run-In Period (Cycle 1=28 days): Participants will receive vemurafenib 960 mg (four, 240 mg tablets) PO BID along with cobimetinib 60 mg (three, 20 mg tablets) PO QD on Days 1 to 21 followed by vemurafenib 720 mg (three, 240 mg tablets) PO BID on Days 22 to 28 and vemurafenib placebo (1 tablet) PO BID on Days 22 to 28. Triple Combination Period (Cycle 2 onwards): Participants will receive ATZ 840 mg IV infusion on Day 1 and 15, cobimetinib 60 mg (three, 20 mg tablets) PO QD on Days 1 to 21, vemurafenib 720 mg (three, 240 mg tablets) PO BID on Days 1 to 28, and vemurafenib placebo (1 tablet) PO BID on Days 1 to 28 of each 28-day cycle. Study treatment will continue until investigator-determined disease progression, death, unacceptable toxicity, withdrawal of consent, or pregnancy, whichever occurs first.</p> | <p>Drug: Atezolizumab Will be administered as per the schedule described in individual arm.</p> <p>Drug: Cobimetinib Will be administered as per the schedule described in individual arm.</p> <p>Drug: Vemurafenib Will be administered as per the schedule described in individual arm.</p> <p>Drug: Vemurafenib Placebo Will be administered as per the schedule described in individual arm.</p> |
| <p>Experimental: ATZ Placebo + Cobimetinib + Vemurafenib</p> <p>Run-In Period (Cycle 1=28 days): Participants will receive vemurafenib 960 milligrams (mg) (four, 240 mg tablets) orally (PO) twice a day (BID) along with cobimetinib 60 mg (three, 20 mg tablets) PO once a day (QD) on Days 1 to 21 followed by vemurafenib 960 mg (four, 240 mg tablets) PO BID on Days 22 to 28. Triple Combination Period (Cycle 2 onwards): Participants will receive ATZ placebo by intravenous (IV) infusion on Day 1 and 15, cobimetinib 60 mg (three, 20 mg tablets) PO QD on Days 1 to 21, and vemurafenib 960 mg (four, 240 mg tablets) PO BID on Days 1 to 28 of each 28-day cycle. Study treatment will continue until investigator-determined disease progression, death, unacceptable toxicity, withdrawal of consent, or pregnancy, whichever occurs first.</p> | <p>Drug: Atezolizumab Will be administered as per the schedule described in individual arm.</p> <p>Drug: Atezolizumab Placebo Will be administered as per the schedule described in individual arm.</p> <p>Drug: Cobimetinib Will be administered as per the schedule described in individual arm.</p> <p>Drug: Vemurafenib Will be administered as per the schedule described in individual arm.</p> |

► Eligibility

Ages Eligible for Study: 18 Years and older (Adult, Senior)
 Genders Eligible for Study: Both
 Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Age greater than or equal to (>=) 18 years

- Females of child bearing potential and males with female partners must use of contraceptive methods with a failure rate of less than or equal to (<=)1% per year is required during treatment and for 6 months post treatment. Males should not expose pregnant partners to sperm and refrain from donating sperm for 6 months post treatment
- Histologically confirmed Stage IV (metastatic) or unresectable Stage IIIc (locally advanced) melanoma
- Naive to prior systemic anti-cancer therapy for melanoma (example: chemotherapy, hormonal therapy, targeted therapy, immunotherapy, or other biologic therapies) except adjuvant treatment with interferon (IFN), interleukin (IL)-2, or vaccine therapies or herbal therapies
- Documentation of BRAFv600 mutation-positive status in melanoma tumor tissue (archival or newly obtained) through use of a clinical mutation test approved by the local health authority
- Eastern Cooperative Oncology Group Performance (ECOG) Status of 0 or 1
- Measurable disease according to RECIST v1.1
- Life expectancy >=18 weeks
- For participants not receiving therapeutic anticoagulation: International normalized ratio (INR) or activated partial thromboplastin time (aPTT) less than or equal to (<=) 1.5*upper limit of normal (ULN) within 28 days prior to initiation of study treatment
- For participants receiving therapeutic anticoagulation: stable anticoagulant regimen and stable INR during the 28 days immediately preceding initiation of study treatment

Exclusion Criteria:

Cancer-Related Exclusion Criteria:

- Major surgical procedure within 4 weeks prior study treatment initiation
- Traumatic injury or palliative radiotherapy within 2 weeks prior study treatment initiation
- Active malignancy (other than BRAFv600 mutation-positive melanoma) or malignancy within 3 years prior to screening, with the exception of resected melanoma, resected basal cell carcinoma (BCC), resected cutaneous squamous cell carcinoma (SCC), resected carcinoma in situ of the cervix, resected carcinoma in situ of the breast, in situ prostate cancer, limited-stage bladder cancer, or other curatively treated malignancies from which the participant has been disease-free for at least 3 years

Ocular Exclusion Criteria:

- History of or evidence of retinal pathology on ophthalmologic examination that is considered a risk factor for neurosensory retinal detachment, central serous chorioretinopathy, retinal vein occlusion (RVO), or neovascular macular degeneration

Cardiac Exclusion Criteria:

- History of clinically significant cardiac dysfunction
- Left ventricular ejection fraction (LVEF) below the institutional lower limit of normal or below 50%

Central Nervous System (CNS) Exclusion Criteria:

- Untreated or actively progressing CNS lesions (carcinomatous meningitis)
- History of metastases to brain stem, midbrain, pons, or medulla, or within 10 millimeter (mm) of the optic apparatus (optic nerves and chiasm); or leptomeningeal metastatic disease; or intracranial hemorrhage

Additional Exclusion Criteria:

- Current severe, uncontrolled systemic disease (including, but not limited to, clinically significant cardiovascular, pulmonary, or renal disease) other than cancer
- History of malabsorption or other clinically significant metabolic dysfunction
- Pregnant or breastfeeding, or intending to become pregnant during the study
- Prior allogeneic stem cell or solid organ transplantation
- History of idiopathic pulmonary fibrosis, organizing pneumonia (example: bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest computed tomography (CT) scan
- History of autoimmune disease
- Known clinically significant liver disease, inherited liver disease and active viral disease
- Active tuberculosis
- Treatment with therapeutic oral or intravenous (IV) antibiotics; or with a live, attenuated vaccine; or systemic immunosuppressive medication
- Known hypersensitivity to biopharmaceutical agents produced in Chinese hamster ovary cells or any component of the atezolizumab, cobimetinib, or vemurafenib formulations

▶ **Contacts and Locations**

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see [Learn About Clinical Studies](#).

Please refer to this study by its ClinicalTrials.gov identifier: NCT02908672

Contacts

Contact: Reference Study ID Number: CO39262 www.roche.com/about_roche/roche_worldwide.htm 888-662-6728 (U.S. and Canada) global.rocheagentechtrials@roche.com

Sponsors and Collaborators

Hoffmann-La Roche

Investigators

Study Director: Clinical Trials Hoffmann-La Roche

▶ **More Information**

Responsible Party: Hoffmann-La Roche
 ClinicalTrials.gov Identifier: [NCT02908672](https://clinicaltrials.gov/ct2/show/study/NCT02908672) [History of Changes](#)
 Other Study ID Numbers: CO39262 **2016-002482-54**

Study First Received: September 19, 2016
Last Updated: October 12, 2016
Health Authority: United States: Food and Drug Administration

Additional relevant MeSH terms:

| | |
|------------------------------------|--------------------------------|
| Melanoma | Neoplasms, Nerve Tissue |
| Neuroendocrine Tumors | Nevi and Melanomas |
| Neuroectodermal Tumors | Antibodies, Monoclonal |
| Neoplasms, Germ Cell and Embryonal | Immunologic Factors |
| Neoplasms by Histologic Type | Physiological Effects of Drugs |
| Neoplasms | |

ClinicalTrials.gov processed this record on January 04, 2017