Ipilimumab With or Without Talimogene Laherparepvec in Unresected Melanoma

This study is ongoing, but not recruiting participants.

Sponsor:
Amgen

Information provided by (Responsible Party):
Amgen

ClinicalTrials.gov Identifier:
NCT01740297

First received: November 14, 2012
Last updated: March 28, 2016
Last verified: March 2016
History of Changes

Purpose

Phase 1b of the study will evaluate the safety of talimogene laherparepvec in combination with ipilimumab. Phase 2 is a randomized study that will evaluate the safety and efficacy of talimogene laherparepvec in combination with ipilimumab versus ipilumumab alone. Talimogene laherparepvec will be administered by intratumor injection, and ipilimumab will be administered by intravenous infusion for a total of 4 infusions. Subjects will be treated with talimogene laherparepvec until complete response, all injectable tumors have disappeared, disease progression per a modified Immune-Related Response Criteria (irRC), or intolerance of study treatment.

Condition	Intervention	Phase
Melanoma	Drug: Talimogene laherparepvec plus ipilimumab Drug: Ipilimumab	Phase 1 Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Phase 1b/2, Multicenter, Open-label Trial to Evaluate the Safety and Efficacy of Talimogene Laherparepvec and Ipilimumab Compared to Ipilimumab Alone in Subjects With Unresected, Stage IIIB-IV Melanoma

Resource links provided by NLM:

MedlinePlus related topics: Melanoma

Drug Information available for: Ipilimumab Talimogene laherparepvec

Genetic and Rare Diseases Information Center resources: Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by Amgen:

Primary Outcome Measures:

- Safety and Tolerability [Time Frame: 12 weeks following last subject enrolled] [Designated as safety issue: Yes]

  Phase 1b: Determine the safety and tolerability of talimogene laherparepvec in combination with ipilimumab as assessed by incidence of dose-limiting toxicities (DLT) in subjects with previously untreated, unresected, stages IIIB to IV melanoma

- Efficacy [Time Frame: 24 months following last subject randomized] [Designated as safety issue: No]

  Phase 2: Evaluate the efficacy as assessed by confirmed objective response rate (ORR) of treatment with talimogene laherparepvec in combination with ipilimumab versus ipilimumab alone in subjects with unresected, stages IIIB to IV melanoma.

Secondary Outcome Measures:

- Efficacy [Time Frame: 24 months following last subject enrolled] [Designated as safety issue: No]

  Phase 1b: Objective Response Rate (ORR)

- Safety [Time Frame: 24 months following last subject enrolled] [Designated as safety issue: Yes]

Phase 1b and Phase 2: Incidence of all AEs, grade 3 or greater AEs, Serious adverse events, events requiring discontinuation of study drug, local effects on tumor, clinically significant laboratory changes, and clinically significant changes in vital signs

- Efficacy [Time Frame: 24 months following last subject randomized] [Designated as safety issue: No]

  Phase 2: Best Overall Response (BOR), Disease Control Rate (DCR), Deep Response Rate, Durable Response Rate (DRR), Duration of Response (DOR), Time to response (TTR), Progression free survival (PFS), resection rate, Overall Survival (OS), landmark OS by year

Enrollment:	217
Study Start Date:	February 2013
Estimated Study Completion Date:	February 2019
Estimated Primary Completion Date:	August 2016 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Phase 1b and Phase 2 Arm 1 Talimogene laherparepvec plus ipilimumab	Drug: Talimogene laherparepvec plus ipilimumab Talimogene laherparepvec administered by intratumoral injection on Day 1 of Week 1, Day 1 of Week 4, then every two weeks thereafter. Ipilimumab administered intravenously on Day 1 of Week 6, Week 9, Week 12, and Week 15 for a total of 4 infusions. Subjects will be treated wtih talimogene laherparepvec until complete response, all injectable tumors have disappeared, confirmed disease progression per the modified irRC, or intolerance of study treatment, whichever occurs first. Other Name: Talimogene laherparepvec plus Yervoy
Active Comparator: Phase 2 Arm 2 Ipilimumab	Drug: Ipilimumab Ipilimumab administered intravenously on Day 1 of Week 1, 4, 7, and 10 for a total of 4 infusions. Other Name: Yervoy

Eligibility

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

Criteria

Inclusion Criteria:

- Histologically confirmed diagnosis of malignant melanoma.
- Stage IIIB, IIIC, IVM1a, IVM1b, or IVM1c disease that is not suitable for surgical resection
- Phase1: Treatment naïve: Must not have received any prior systemic anticancer treatment consisting of chemotherapy, immunotherapy, or targeted therapy for unresected stage IIIB to IV melanoma.
- Phase 2: Either treatment naïve or received only one line of systemic anticancer therapy if BRAF wild-type or up to two lines of systemic anticancer therapy including one BRAF inhibitor-containing regimen if BRAF mutant. Treatments given in an adjuvant setting (eg, interferon, radiotherapy, isolated limb perfusion, or investigational agents) are not considered as prior lines of therapy. No prior talimogene laherparepvec, other oncolytic virus therapies, or tumor vaccines are allowed, even if given in the adjuvant setting.
- Phase 2: Subjects treated with prior ipilimumab must have had PR, CR, or at least 6 months of stable disease followed by disease progression.
- Phase 2: Subjects previously treated with anti-PD1 or anti-CTLA-4 antibodies must not have discontinued therapy due to any treatment-related adverse events including immune-related adverse events. Prior treatment-related adverse events should also be fully resolved and not requiring treatment for at least 28 days prior to randomization.
- Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
- Adequate hematologic, hepatic, renal, and coagulation functions

Exclusion Criteria:

- Primary uveal or mucosal melanoma
- History or evidence of melanoma associated with immunodeficiency states (eg, hereditary immune deficiency, organ transplant, or leukemia)
- Phase 1b: History or evidence of central nervous system (CNS) metastases
- Phase 2: Clinically active cerebral melanoma metastases. Subjects with up to 3 cerebral metastases, and neurological performance status of 0 may be enrolled,provided that all lesions have been adequately treated with stereotactic radiation therapy, craniotomy, or Gamma knife therapy, with no evidence of progression, and have not required steroids, for at least 2 months prior to enrollment.
- History or evidence of symptomatic autoimmune disease (such as pneumonitis, glomerulonephritis, vasculitis, rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, scleroderma, or other), or history of autoimmune disease that required systemic treatment (ie, use of corticosteroids, immunosuppressive drugs or biological agents used for treatment of autoimmune diseases) in past 2 months prior to enrollment. Replacement therapy (eg, thyroxine for hypothyroidism, insulin for diabetes mellitus) is not considered a form of systemic treatment for autoimmune disease.
- History of or plan for splenectomy or splenic irradiation
- Active herpetic skin lesions or prior complications of HSV-1 infection (eg, herpetic keratitis or encephalitis).
- Requires intermittent or chronic systemic (intravenous or oral) treatment with an antiherpetic drug (eg, acyclovir), other than intermittent topical use
- Known human immunodeficiency virus (HIV) disease

- Known acute or chronic hepatitis B or hepatitis C infection
- Phase 1b: Prior talimogene laherparepvec, ipilimumab, other Cytotoxic T-lymphocyte associated antigen 4 (CTLA-4) inhibitors, programmed death-1 (PD-1) inhibitors, or tumor vaccine
- Phase 2: Prior talimogene laherparepvec, other oncolytic virus therapies, or tumor vaccines
- Currently receiving or less than 28 days since ending systemic anticancer treatment for unresected stage IIIB to IV melanoma

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: NCT01740297

Show 40 Study Locations

Sponsors and Collaborators

Amgen

Investigators

Study Director: MD Amgen

More Information

Additional Information:

AmgenTrials clinical trials website

Responsible Party:	Amgen
ClinicalTrials.gov Identifier:	NCT01740297 History of Changes
Other Study ID Numbers:	20110264
Study First Received:	November 14, 2012
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Health Authority:	United States: Food and Drug Administration Germany: Paul-Ehrlich-Institut

Keywords provided by Amgen:
melanoma, talimogene laherparepvec, ipilimumab, metastatic melanoma, melanoma, immunotherapy, unresectable melanoma, oncolytic immunotherapy,

Additional relevant MeSH terms:

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

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