Pembrolizumab With or Without Talimogene Laherparepvec or Talimogene Laherparepvec Placebo in Unresected Melanoma

This study is currently recruiting participants. (see Contacts and Locations)

Verified June 2016 by Amgen

Sponsor:
Amgen

Collaborator:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Amgen

ClinicalTrials.gov Identifier:
NCT02263508

First received: September 26, 2014
Last updated: June 27, 2016
Last verified: June 2016
History of Changes

Purpose

Phase 1b Subjects will be treated with talimogene laherparepvec until all injectable tumors have disappeared, disease progression per modified Immune-Related Response Criteria (irRC), or intolerance of study treatment, up to a maximum of 24 months of study treatment. Subjects will be treated with MK-3475 (pembrolizumab) until complete response (CR) disease progression per irRC, or intolerance of study treatment, up to a maximum of 24 months of study treatment. In Phase 3, Subjects will be treated with talimogene laherparepvec plus pembrolizumab(arm 1) or placebo plus pembrolizumab (arm 2) until 24 months from the date of the first dose of pembrolizumab or end of treatment due to disappearance of injectable lesions, complete response, disease progression per irRC-RECIST or intolerance of study treatment.

Condition	Intervention	Phase
Melanoma	Drug: talimogene laherparepvec Drug: pembrolizumab (MK-3475) Drug: 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 1b/3, Multicenter, Trial of Talimogene Laherparepvec in Combination With Pembrolizumab (MK-3475) for Treatment of Unresectable Stage IIIB to IVM1c Melanoma (MASTERKEY-265)

Resource links provided by NLM:

MedlinePlus related topics: Melanoma

Drug Information available for: Talimogene laherparepvec Pembrolizumab

Genetic and Rare Diseases Information Center resources: Carcinoid Tumor Neuroepithelioma

U.S. FDA Resources

Further study details as provided by Amgen:

Primary Outcome Measures:

- Incidence of dose limiting toxicities (DLT) [Time Frame: Start of treatment until 6 weeks from the initial administration of pembrolizumab (MK-3475)] [Designated as safety issue: Yes]

  Phase 1b: To evaluate the safety, as assessed by incidence of dose limiting toxicity (DLT), of talimogene laherparepvec in combination with pembrolizumab (MK-3475)

- Progression Free Survival (PFS) (response evaluation by blinded central review assessed modified RECIST 1.1) [Time Frame: up to 24 months of treatment] [Designated as safety issue: No]

  Phase 3: To evaluate the efficacy of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by progression-free survival (PFS) (response evaluation by blinded central review using modified Response Evaluation Criteria in Solid Tumors 1.1 [RECIST]).

- Overall Survival [Time Frame: up to 24 months of treatment] [Designated as safety issue: No]

  Phase 3: To evaluate the efficacy of talimogene laherparepvec with pembrolizumab versus placebo with pembrolizumab, as assessed by overall survival (OS).

Secondary Outcome Measures:

- Incidence of adverse events (AEs) [Time Frame: Start of treatment to 30 (+7) days after end of treatment] [Designated as safety issue: Yes]

  Incidence of treatment-emergent and treatment-related adverse events (all AEs, grade ≥ 3 AEs, serious adverse events, fatal AEs, and AEs defined as events of interest)

- Overall Response Rate (ORR) [Time Frame: Start of treatment and every 12 weeks until confirmed disease progression]
  [Designated as safety issue: No]

  To evaluate the efficacy, as assessed by ORR of treatment with talimogene laherparepvec in combination with pembrolizumab in Phase 1b and talimogene laherparepvec in combination with pembrolizumab verses placebo in Phase 3.

- Best overall response (BOR) [Time Frame: Start of treatment and every 12 weeks until confirmed disease progression]
  [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- Durable response rate (DRR) defined as rate of objective responses for a duration of 6 months or longer [Time Frame: Start of treatment and every 12 weeks until confirmed disease progression] [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- Duration of response (DOR) [Time Frame: Start of treatment and every 12 weeks until confirmed disease progression]
  [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- Disease Control Rate (DCR) [Time Frame: Start of treatment and every 12 weeks until confirmed disease progression]
  [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- Progression-free survival (PFS) [Time Frame: Start of treatment and every 12 weeks until 60 months after the last subject enrolled in Phase 3. Calculated from date of Randomization to date of disease progression or death whichever comes first.] [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- Overall survival (OS) [Time Frame: Start of treatment and every 12 weeks during long term follow up until 60 months after last subject enrolled. Calculated from date of Randomization to date of death.] [Designated as safety issue: No]

  To be assessed for Phase 1b, Phase 3

- As assessed by the EQ-5D and QLQ-C30 subject questionnaires [Time Frame: weeks 0, then every 3, 6, 9, 12 weeks then every 6 weeks until the end of the study and at safety follow up.] [Designated as safety issue: No]

  Phase 3: To evaluate patient reported outcomes (PRO)

Estimated Enrollment:	660
Study Start Date:	December 2014
Estimated Study Completion Date:	May 2022
Estimated Primary Completion Date:	May 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Phase 1b; Phase 1b: talimogene laherparepvec and pembrolizumab (MK-3475)	Drug: talimogene laherparepvec Phase 1b: talimogene laherparepvec will be administered by intralesional injection at Day 1, Week -5; then every 2 weeks starting at Day 1, Week -2; Phase 3, Arm 1 talimogene laherparepvec will be administered by intralesional injection at Day 1 Week 0, 3, 5, 7 then every 3 weeks starting at Day 1 Week 9. Drug: pembrolizumab (MK-3475) Phase 1b: pembrolizumab will be administered intravenously every 2 weeks starting at Day 1 Week 0; Phase 3, Arm 1 and Arm 2 pembrolizumab will be administered intravenously on Day 1 Week 0, then every 3 weeks starting at Day 1 Week 3.
Experimental: Phase 3 Arm 1; Phase 3 Arm 1: talimogene laherparepvec and pembrolizumab (MK-3475)	Drug: talimogene laherparepvec Phase 1b: talimogene laherparepvec will be administered by intralesional injection at Day 1, Week -5; then every 2 weeks starting at Day 1, Week -2; Phase 3, Arm 1 talimogene laherparepvec will be administered by intralesional injection at Day 1 Week 0, 3, 5, 7 then every 3 weeks starting at Day 1 Week 9. Drug: pembrolizumab (MK-3475)

	Phase 1b: pembrolizumab will be administered intravenously every 2 weeks starting at Day 1 Week 0; Phase 3, Arm 1 and Arm 2 pembrolizumab will be administered intravenously on Day 1 Week 0, then every 3 weeks starting at Day 1 Week 3.
Experimental: Phase 3 Arm 2; Phase 3 Arm 2: placebo and pembrolizumab (MK-3475)	Drug: pembrolizumab (MK-3475) Phase 1b: pembrolizumab will be administered intravenously every 2 weeks starting at Day 1 Week 0; Phase 3, Arm 1 and Arm 2 pembrolizumab will be administered intravenously on Day 1 Week 0, then every 3 weeks starting at Day 1 Week 3. Drug: placebo Phase 3, Arm 2 placebo will be administered by intralesional injection at Day 1 Week 0, 3, 5, 7 then every 3 weeks starting at Day 1 Week 9.

Eligibility

Ages Eligible for Study: 18 Years to 95 Years (Adult, Senior)
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Key Inclusion Criteria:

- Age ≥ 18 years with histologically confirmed diagnosis of melanoma and stage IIIB to IVM1c for whom surgery is not recommended.
- Subjects must have measurable disease and be a candidate for intralesional therapy administration into cutaneous, subcutaneous, or nodal lesions.
- ECOG performance status of 0 or 1.
- Adequate hematologic, hepatic, renal, and coagulation function.
- Subjects with BRAFV600 wild-type tumors must not have received any prior systemic anticancer treatment consisting of chemotherapy, immunotherapy, or targeted therapy given in a non-adjuvant setting for unresectable stage IIIB to IVM1c melanoma.
- Subjects with B-Raf V600 (BRAFV600) mutated tumors who have received prior BRAF inhibitor therapy either alone or in combination with MEK inhibitor as their only prior systemic therapy are eligible.
- Subjects who received prior adjuvant therapy for melanoma will not be excluded (including, but not limited to, interferon, ipilimumab, limb infusion/perfusion, or use of investigational agents in the adjuvant setting) with the exception that prior adjuvant therapy with inhibitors of PD-1 or PD-L1 is not allowed. However, if the subject received adjuvant therapy, the subject must have completed therapy at least 28 days prior to enrollment.
- Subjects must have a tumor sample that is adequate for PD-L1 assessment prior to randomization.

Key Exclusion Criteria:

- Subjects must not have clinically active cerebral metastases.
- Subjects must not have primary uveal or mucosal melanoma, history or evidence of melanoma associated with immunodeficiency states or history of other malignancy within the past 3 years.
- Subjects may not have been previously treated with talimogene laherparepvec, any other oncolytic virus, pembrolizumab, or any other inhibitor of PD-1, PD-L1, or PD-L2.
- Subjects must not have history or evidence of symptomatic autoimmune pneumonitis, glomerulonephritis, vasculitis, other symptomatic autoimmune disease, documented history of autoimmune disease or syndrome requiring systemic treatment in the past 2 years (ie, with use of disease modifying agents, steroids or immunosuppressive agents) except vitiligo or resolved childhood asthma/atopy, or evidence of clinically significant immunosuppression.
- Subjects must not have active herpetic skin lesions or prior complications of herpetic infection and must not require intermittent or chronic treatment with an antiherpetic drug (eg, acyclovir), other than intermittent topical use.

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: NCT02263508

Contacts

Contact: Amgen Call Center 866-572-6436

Show 39 Study Locations

Sponsors and Collaborators

Amgen

Merck Sharp & Dohme Corp.

Investigators

Study Director: MD Amgen

More Information

Additional Information:

AmgenTrials clinical trials website

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ClinicalTrials.gov Identifier:	NCT02263508 History of Changes
Other Study ID Numbers:	20110265 2014-000185-22
Study First Received:	September 26, 2014
Last Updated:	June 27, 2016
Health Authority:	United States: Institutional Review Board United States: Food and Drug Administration Australia: Therapeutic Goods Administration UK: Medicines HealthCare Products and Regulatory Agency (MHRA) Switzerland: Swissmedic Sweden: Medical Products Agency Spain: Spanish Agency for Medicines and Health Products Austria: Bundesamt für Sicherheit im Gesundheitswesen / AGES Medizinmarktaufsicht Belgium: FAMHP (Federal Agency for Medicines and Health Products) France: Agence nationale de sécurité du médicament et des produits de santé (ANSM) Germany: Paul-Ehrlich-Institut (PEI) Greece: National Organization for Medicines Italy: Agenzia Italiano del Farmaco (AIFA) Netherlands: Centrale Commissie Mensgebonden Onderzoek (CCMO) Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products S. Africa: Medicines Control Council (MCC) Canada: Health Canada Biologics and Genetic Therapies Directorate South Korea: MFDS The Ministry of Food and Drug Safety Hong Kong: Department of Health Singapore: Health Sciences Authority (HSA) Malaysia: National Pharmaceutical Control Bureau (NPCB) Brazil: National Agency of Sanitary Surveillance (ANVISA) Czech Republic: Ministry of Health Finland: Finnish National Agency for Medicines Norway: Norwegian Institute of Public Health Portugal: National Pharmacy and Medicines Institute Russia: Ministry of Health of the Russian Federation

Keywords provided by Amgen:
pembrolizumab
Keytruda

Additional relevant MeSH terms:

Melanoma	Neoplasms
Neuroendocrine Tumors	Neoplasms, Nerve Tissue
Neuroectodermal Tumors	Nevi and Melanomas
Neoplasms, Germ Cell and Embryonal	Pembrolizumab
Neoplasms by Histologic Type	Antineoplastic Agents

ClinicalTrials.gov processed this record on July 05, 2016