Substudy 02A: Safety and Efficacy of Pembrolizumab in Combination With Investigational Agents in Participants With Programmed Cell-death 1 (PD-1) Refractory Melanoma (MK-3475-02A/KEYMAKER-U02)

STUDY DESCRIPTION

Brief Summary

Substudy 02A is part of a larger research study that is testing experimental treatments for melanoma, a type of skin cancer. The larger study is the umbrella study. The goal of substudy 02A is to evaluate the safety and efficacy of investigational treatment arms in participants with PD-1 refractory melanoma to identify the investigational agent(s) that, when used in combination, are superior to the current treatment options/historical control available.

Condition or Disease: Melanoma

Intervention/treatment:
- Biological: Pembrolizumab
- Biological: Quavonlimab
- Biological: Vibostolimab
- Drug: Lenvatinib

Phase: Phase 1/Phase 2

DETAILED DESCRIPTION

N/A

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment: 200 participants

Intervention Model: Parallel Assignment

Masking: None (Open Label)

Primary Purpose: Treatment

Official Title: A Phase 1/2 Open-Label Rolling-Arm Umbrella Platform Design of Investigational Agents With or Without Pembrolizumab or Pembrolizumab Alone in Participants With Melanoma (KEYMAKER-U02): Substudy 02A

Actual Study Start Date: June 2020

Estimated Primary Completion Date: April 2030

Estimated Study Completion Date: April 2030

ARMS AND INTERVENTIONS

<table>
<thead>
<tr>
<th>Arm</th>
<th>Intervention/treatment</th>
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<tbody>
<tr>
<td>Experimental: Pembrolizumab + Quavonlimab + Lenvatinib</td>
<td>Biological: Pembrolizumab&lt;br&gt;Administered via IV infusion at a specified dose on specified days&lt;br&gt;Biological: Quavonlimab&lt;br&gt;Administered via IV infusion at a specified dose on specified days&lt;br&gt;Drug: Lenvatinib&lt;br&gt;Administered via oral capsules at a specified dose on specified days</td>
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<tr>
<td>Participants will receive pembrolizumab IV plus quavonlimab IV plus lenvatinib orally at specified doses on specified days for a total treatment duration of up to approximately 2 years.</td>
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OUTCOME MEASURES

Primary Outcome Measures:
1. Percentage of participants who experience an adverse event (AE) [Time Frame: Up to ~28 months]
   An AE is any untoward medical occurrence in a clinical study participant, temporarily associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who experience an AE will be reported.
2. Percentage of participants who discontinue study treatment due to an AE [Time Frame: Up to ~24 months]
   An AE is any untoward medical occurrence in a clinical study participant, temporarily associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who discontinue study treatment due to an AE will be reported.
3. Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors 1.1 (RECIST 1.1) [ Time Frame: Up to ~30 months ]

ORR is defined as the percentage of participants in the analysis population who have a complete response (CR: disappearance of all target lesions) or partial response (PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters). Responses are according to RECIST 1.1 as assessed by blinded independent central review (BICR). RECIST 1.1 has been modified for this study to include a maximum of 10 target lesions and a maximum of 5 target lesions per organ.

1. Duration of Response (DOR) per RECIST 1.1 [ Time Frame: Up to ~30 months ]

For participants in the analysis population who demonstrate a confirmed CR (disappearance of all target lesions) or confirmed PR (at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters), DOR is defined as the time from first documented evidence of CR or PR until progressive disease (PD) or death due to any cause, whichever occurs first. Responses are according to RECIST 1.1 as assessed by BICR. RECIST 1.1 has been modified for this study to include a maximum of 10 target lesions and a maximum of 5 target lesions per organ.

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 to 120 Years (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
- Has histologically or cytologically confirmed melanoma
- Has unresectable Stage III or Stage IV melanoma, not amenable to local therapy
- Has progressed on treatment with an anti-PD-1/L1 monoclonal antibody (mAb) administered either as monotherapy, or in combination with other therapies
- Has submitted prestudy imaging
- Has not received more than 3 lines of therapy for their advanced melanoma
- Has provided a tumor biopsy
- Male participants who receive lenvatinib are abstinent from heterosexual intercourse or agree to use contraception during the intervention period and for at least 7 days after the last dose of lenvatinib; for male participants who only receive pembrolizumab, quavonlimab, vibostolimab, or a combination, no contraception measures are needed
- Female participants are not pregnant or breastfeeding and are either not a woman of child-bearing potential (WOCBP) OR use a contraceptive method that is highly effective or are abstinent from heterosexual intercourse during the intervention period and for at least 120 days after the last dose of pembrolizumab, quavonlimab, vibostolimab or 30 days after the last dose of lenvatinib, whichever occurs last
- Has adequate organ function
- Has resolution of toxic effect(s) of the most recent prior therapy to Grade 1 or less (except alopecia)

Exclusion Criteria:
- Has a diagnosis of immunodeficiency or is receiving immunosuppressive therapy within 7 days before the first dose of study intervention
- Has a known additional malignancy that is progressing or requires active treatment within the past 2 years
- Has known central nervous system (CNS) metastases and/or carcinomatous meningitis
- Has ocular or mucosal melanoma
- Has known hypersensitivity including previous clinically significant hypersensitivity reaction to treatment with another mAb
- Has an active autoimmune disease that has required systemic treatment in the past 2 years
- Has an active infection requiring systemic therapy
- Has known history of human immunodeficiency virus (HIV)
- Has known history of hepatitis B
- Has a history of (noninfectious) pneumonitis
- Has a history of active tuberculosis (TB)
- Has received prior systemic anticancer therapy within 4 weeks prior to randomization
- Has received prior radiotherapy within 2 weeks of first dose of study intervention
- Has had major surgery <3 weeks prior to first dose of study intervention
- Has received a live vaccine within 30 days before the first dose of study intervention
- Has participated in a study of an investigational agent within 4 weeks prior to the first dose of study intervention
- Has had an allogeneic tissue/solid organ transplant - Has a pre-existing Grade ≥3 gastrointestinal fistula or nongastrointestinal fistula - Has radiographic evidence of encasement of invasion of major blood vessel or of intratumoral cavitation - Has clinically significant hemoptysis or tumor bleeding within 2 weeks prior to the first dose of study intervention
- Has clinically significant cardiovascular disease within 12 months from first dose of study intervention

CONTACTS AND LOCATIONS

Contacts
Contact: Toll Free Number 1-888-577-8839 Trialsites@merck.com

Locations

France, Gironde
- Hopital Saint Andre ( Site 1108) Bordeaux
- Hopital La Timone ( Site 1103) Marseille

France, Haute-Garonne
- Institut Claudius Regaud ( Site 1105) Toulouse cedex 9

France, Rhone
- Centre Hospitalier Lyon Sud ( Site 1102) Pierre Benite

France, Val-de-Marne
- Gustave Roussy ( Site 1101) Villejuif

France
- A.P.H. Paris, Hopital Saint Louis ( Site 1107) Paris

United States, California
- The Angeles Clinic and Research Institute ( Site 1009) Los Angeles

United States, California
- UCLA Hematology & Oncology ( Site 1004) Los Angeles
Sponsors and Collaborators
Merck Sharp & Dohme Corp.

Investigator
Study Director : Medical Director Merck Sharp & Dohme Corp.

MORE INFORMATION
Responsible Party : Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier : NCT04305041
Other Study ID Numbers :
First Posted : March 12, 2020
Last Update Posted : October 8, 2021
Last Verified : October 2021
Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: Yes
Plan Description:
url:
Studies a U.S. FDA-regulated Drug Product:
Yes
Studies a U.S. FDA-regulated Device Product:
No
Keywords provided by Merck Sharp & Dohme Corp.:
programmed cell death 1 (PD-1, PD1)
receptor tyrosine kinase inhibitor T cell immunoreceptor with immunoglobulin and immunoreceptor tyrosine receptor motif domains (TIGIT)
programmed cell death ligand 1 (PD-L1, PDL1)
Additional relevant MeSH terms: Melanoma