



Record 1 of 1



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Study of Pembrolizumab (MK-3475) in Participants With Progressive Locally Advanced or Metastatic Carcinoma, Melanoma, or Non-small Cell Lung Carcinoma (P07990/MK-3475-001/KEYNOTE-001) (KEYNOTE-001)

ClinicalTrials.gov ID NCT01295827

Sponsor Merck Sharp & Dohme LLC

Information provided by Merck Sharp & Dohme LLC (Responsible Party)

Last Update Posted 2019-12-13

Completed

No longer looking for participants

Record History Tab

Study Record Versions

- This table shows all the versions of this study record arranged in order by submitted date.
 - To view one version of the study record, click the submitted date.
 - To compare two versions, select them using the check boxes and click "Compare" at the bottom of the list.
 - Data that is changed in the study record is color coded:
 - Deletions from the study record are shown crossed out in **red highlights**.
 - Additions to the study record are shown in green highlights.

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	1	2011-02-14	<ul style="list-style-type: none">None (earliest version on record)
☐	2	2011-03-10	<ul style="list-style-type: none">Study IdentificationStudy StatusSponsor/CollaboratorsConditionsArms and InterventionsOutcome Measures

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
			<ul style="list-style-type: none"> Eligibility
☐	3	2011-04-01	<ul style="list-style-type: none"> Recruitment Status Study Status Contacts/Locations
☐	4	2011-06-02	<ul style="list-style-type: none"> Study Status
☐	5	2011-07-28	<ul style="list-style-type: none"> Study Status
☐	6	2011-08-09	<ul style="list-style-type: none"> Study Status
☐	7	2011-09-29	<ul style="list-style-type: none"> Study Status
☐	8	2011-10-21	<ul style="list-style-type: none"> Study Identification Study Status Sponsor/Collaborators Study Description Conditions Study Design Arms and Interventions Outcome Measures Eligibility
☐	9	2011-11-30	<ul style="list-style-type: none"> Study Status Contacts/Locations
☐	10	2011-12-29	<ul style="list-style-type: none"> Study Status Contacts/Locations
☐	11	2012-01-04	<ul style="list-style-type: none"> Study Status Contacts/Locations
☐	12	2012-02-29	<ul style="list-style-type: none"> Study Status Contacts/Locations
☐	13	2012-04-17	<ul style="list-style-type: none"> Study Identification Study Status Study Description Study Design Arms and Interventions Outcome Measures Eligibility Contacts/Locations
☐	14	2012-04-24	<ul style="list-style-type: none"> Study Status
☐	15	2012-05-25	<ul style="list-style-type: none"> Study Status

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	16	2012-06-08	<ul style="list-style-type: none"> • Study Identification • Study Status • Sponsor/Collaborators
☐	17	2012-06-27	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	18	2012-09-06	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Study Design • Arms and Interventions • Outcome Measures • Eligibility • Contacts/Locations
☐	19	2012-12-04	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Study Design • Arms and Interventions • Outcome Measures • Eligibility
☐	20	2012-12-13	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	21	2012-12-14	<ul style="list-style-type: none"> • Study Status • Conditions
☐	22	2013-01-23	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	23	2013-02-08	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	24	2013-02-25	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	25	2013-03-22	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	26	2013-05-09	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Study Design • Arms and Interventions

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
			<ul style="list-style-type: none"> • Outcome Measures • Eligibility • Contacts/Locations
☐	27	2013-05-16	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	28	2013-06-28	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	29	2013-07-16	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	30	2013-08-02	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	31	2013-09-03	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Study Design • Arms and Interventions • Outcome Measures • Eligibility • Contacts/Locations
☐	32	2013-09-11	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	33	2013-09-18	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	34	2013-10-09	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	35	2013-11-12	<ul style="list-style-type: none"> • Study Status
☐	36	2013-11-15	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	37	2013-12-03	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	38	2013-12-17	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	39	2013-12-30	<ul style="list-style-type: none"> • Study Status • Contacts/Locations

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	40	2014-01-09	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	41	2014-01-27	<ul style="list-style-type: none"> • Study Status • Study Description • Arms and Interventions • Outcome Measures • Eligibility
☐	42	2014-01-30	<ul style="list-style-type: none"> • Study Status
☐	43	2014-02-20	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Study Design • Arms and Interventions • Eligibility • Contacts/Locations
☐	44	2014-02-28	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	45	2014-03-05	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	46	2014-03-18	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	47	2014-03-20	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	48	2014-04-23	<ul style="list-style-type: none"> • Study Status
☐	49	2014-04-30	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	50	2014-06-02	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Arms and Interventions • Outcome Measures • Eligibility • Contacts/Locations
☐	51	2014-06-18	<ul style="list-style-type: none"> • Study Status • Contacts/Locations

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	52	2014-06-26	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	53	2014-07-02	<ul style="list-style-type: none"> • Study Status • Contacts/Locations
☐	54	2014-07-10	<ul style="list-style-type: none"> • Recruitment Status • Study Status • Contacts/Locations
☐	55	2014-09-17	<ul style="list-style-type: none"> • Study Status • References
☐	56	2015-01-30	<ul style="list-style-type: none"> • Study Status
☐	57	2015-03-30	<ul style="list-style-type: none"> • Study Status • Study Design
☐	58	2015-04-09	<ul style="list-style-type: none"> • Study Status
☐	59	2015-08-26	<ul style="list-style-type: none"> • Study Status
☐	60	2016-02-03	<ul style="list-style-type: none"> • Study Status
☐	61	2016-04-05	<ul style="list-style-type: none"> • Study Status
☐	62	2016-05-09	<ul style="list-style-type: none"> • Study Identification • Study Status • Study Description • Arms and Interventions • Outcome Measures • Eligibility
☐	63	2016-06-16	<ul style="list-style-type: none"> • Study Status • References
☐	64	2016-09-13	<ul style="list-style-type: none"> • Study Status
☐	65	2016-12-02	<ul style="list-style-type: none"> • Study Status
☐	66	2017-04-17	<ul style="list-style-type: none"> • Study Status
☐	67	2017-08-18	<ul style="list-style-type: none"> • Study Status
☐	68	2017-11-08	<ul style="list-style-type: none"> • Study Status

Compare

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	69	2018-01-28	<ul style="list-style-type: none">• Study Identification• Study Status• Oversight• Study Design
☐	70	2018-03-15	<ul style="list-style-type: none">• Study Status
☐	71	2018-06-19	<ul style="list-style-type: none">• Study Status
☐	72	2018-09-12	<ul style="list-style-type: none">• Study Status
☐	73	2018-11-19	<ul style="list-style-type: none">• Study Status• IPDSharing
☐	74	2018-12-19	<ul style="list-style-type: none">• Recruitment Status• Study Status
☐	75	2019-03-29	<ul style="list-style-type: none">• Study Status• Study Description• Arms and Interventions• Outcome Measures• Eligibility <div>Results Submission Events (1)<ul style="list-style-type: none">• 2019-10-21: Returned after QC review: 2019-11-08</div>
☐	76	2019-11-22	<ul style="list-style-type: none">• Study Identification• Study Status• Study Description• Conditions• Arms and Interventions• Outcome Measures• Eligibility• Document Section• Participant Flow• Baseline Characteristics• Outcome Measures (Results)• Adverse Events• More Information

[Compare](#)[<>](#)

Viewing **V56** (2015-01-30)**Study Details****Study Identification**

Unique Protocol ID
P07990
Brief Title
Study of Pembrolizumab (MK-3475) in Participants With Progressive Locally Advanced or Metastatic Carcinoma, Melanoma, or Non-small Cell Lung Carcinoma (P07990/MK-3475-001/KEYNOTE-001)
Official Title
Phase I Study of Single Agent MK-3475 in Patients With Progressive Locally Advanced or Metastatic Carcinoma, Melanoma, and Non-Small Cell Lung Carcinoma
Secondary IDs
MK-3475-001, 2011-002371-42

Study Status

Record Verification
2015-01
Overall Status
Active, not recruiting
Study Start
2011-03
Primary Completion
2016-07 [Estimated]
Study Completion
2016-07 [Estimated]
First Submitted
2011-02-10
First Submitted that Met QC Criteria
2011-02-14
First Posted
2011-02-15 [Estimated]
Last Update Submitted that Met QC Criteria

2015-01-30
Last Update Posted
2015-02-02 [Estimated]

Sponsor/Collaborators

Sponsor
Merck Sharp & Dohme LLC
Responsible Party
Sponsor
Collaborators

Oversight

U.S. FDA-regulated Drug
U.S. FDA-regulated Device
Data Monitoring
No

Study Description

Brief Summary
<p>This study will be done in 6 parts. In Part A the dose of intravenous (IV) pembrolizumab (MK-3475) will be escalated to find the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D) for participants with a histologically or cytologically confirmed diagnosis of any type of carcinoma or melanoma (MEL). Part B of the study will explore the safety, tolerability, and efficacy of the drug in participants with advanced or metastatic MEL and compare every 2 week to every 3 week dosing. Part C of the study will explore the safety, tolerability, and efficacy of the drug in participants with non-small cell lung carcinoma (NSCLC) that is locally advanced or metastatic. Part D of the study will explore the low and high doses of study drug identified in Parts A and B in participants with advanced or metastatic MEL. Part E (closed with Amendment 7) will explore low, medium, and high doses of study drug in combination with standard chemotherapy in participants with locally advanced or metastatic NSCLC. Part F will explore low and high doses of study drug in treatment-naive and previously-treated participants with NSCLC with programmed cell death 1 ligand (PD-L1) gene expression. In Parts D and F and some of Part B participants will be randomized to one dose level. The primary hypotheses are the following: that pembrolizumab has acceptable safety and tolerability; and that pembrolizumab shows a clinically meaningful response rate (RR) or disease-control rate (DCR) in participants with melanoma (ipilimumab-refractory or not), and a clinically meaningful RR in participants with NSCLC, especially a clinically meaningful RR in those participants with either cancer, whose tumors express PD-L1.</p>

Detailed Description

Part F (NSCLC) is the only part currently enrolling participants.

Conditions**Condition**

Cancer, Solid Tumor

Keywords

Melanoma
Carcinoma
Cancer
Advanced cancer
Metastatic cancer
Metastatic melanoma
PD-1
PD1

Study Design**Study Type**

Interventional

Primary Purpose

Treatment

Study Phase

Phase 1

Interventional Study Model

Parallel Assignment

Number of Arms

12

Masking

None (Open Label)

Allocation

Randomized

Enrollment

1137 [Estimated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Part A: Pembrolizumab 1 mg/kg (Closed) Participants receive pembrolizumab intravenous (IV) infusion over 30 minutes on Day 1 of each cycle, at dose of 1 mg/kg	Drug: Pembrolizumab 1 mg/kg <ul style="list-style-type: none"> IV infusion over 30 minutes on Day 1 of each cycle, at dose of 1 mg/kg
Experimental: Part A: Pembrolizumab 3 mg/kg (Closed) Participants receive pembrolizumab intravenous (IV) infusion over 30 minutes on Day 1 of each cycle, at dose of 3 mg/kg	Drug: Pembrolizumab 3 mg/kg <ul style="list-style-type: none"> IV infusion over 30 minutes on Day 1 of each cycle, at dose of 3 mg/kg
Experimental: Part A: Pembrolizumab 10 mg/kg (Closed) Participants receive pembrolizumab intravenous (IV) infusion over 30 minutes on Day 1 of each cycle, at dose of 1 mg/kg	Drug: Pembrolizumab 10 mg/kg <ul style="list-style-type: none"> IV infusion over 30 minutes on Day 1 of each cycle (every 2 or 3 weeks depending on study arm) at a dose of 10 mg/kg.
Experimental: Part B: Pembrolizumab MEL (Closed) Participants receive pembrolizumab IV infusion over 30 minutes on Day 1 of each cycle.	Drug: Pembrolizumab MEL <ul style="list-style-type: none"> IV infusion over 30 minutes on Day 1 of each cycle
Experimental: Part C: Pembrolizumab NSCLC (Closed) Participants receive pembrolizumab IV infusion over 30 minutes on Day 1 of each cycle	Drug: Pembrolizumab NSCLC <ul style="list-style-type: none"> IV infusion over 30 minutes on Day 1 of each cycle
Experimental: Part D: Pembrolizumab MEL Low Dose (Closed) participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab MEL Low Dose <ul style="list-style-type: none"> IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation
Experimental: Part D: Pembrolizumab MEL High Dose (Closed) Participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab MEL High Dose <ul style="list-style-type: none"> IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation
Experimental: Part E: Pembrolizumab NSCLC Low Dose (Closed) Participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab NSCLC Low Dose <ul style="list-style-type: none"> IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation
Experimental: Part E: Pembrolizumab NSCLC Med. Dose (Closed) Participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab NSCLC Medium Dose <ul style="list-style-type: none"> IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation
Experimental: Part E: Pembrolizumab NSCLC High Dose (Closed)	Drug: Pembrolizumab NSCLC High Dose <ul style="list-style-type: none"> IV infusion over 30 minutes every 2 or 3

Participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	weeks at dose determined during dose escalation
Experimental: Part F: Pembrolizumab NSCLC PD-L1 Low Dose Participants receive pembrolizumab IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab NSCLC Low Dose • IV infusion over 30 minutes every 3 weeks at dose determined during dose escalation
Experimental: Part F: Pembrolizumab NSCLC PD-L1 High Dose Participants receive pembrolizumab IV infusion over 30 minutes every 2 or 3 weeks at dose determined during dose escalation	Drug: Pembrolizumab NSCLC High Dose • IV infusion over 30 minutes every 2 or 3 weeks at dose determined during dose escalation

Outcome Measures

Primary Outcome Measures	
1.	Number of participants experiencing dose-limiting toxicities (DLTs) [Time Frame: Cycle 1 (28 days)]
2.	Number of participants experiencing clinical and laboratory adverse events (AEs) [Time Frame: First dose to 30 days post last dose]
3.	Number of all study participants who demonstrate a response rate (RR) [Time Frame: Weeks 12 and 24]
4.	Number of MEL participants who demonstrated a response rate (RR) and/or disease control rate (DCR) [Time Frame: Weeks 12 and 24]
5.	Number of NSCLC participants who demonstrated a response rate (RR) [Time Frame: Week 9 and Week 18]
6.	Change from Baseline in candidate biomarker expression levels in MELS and NSCLC participants [Time Frame: Week 12 and Week 24 (MEL), Week 9 and Week 18 (NSCLC)]
Secondary Outcome Measures	

1. The area under the curve (AUC) of plasma concentration of drug against time after administration of pembrolizumab (Part A)
[Time Frame: Pre-dose, 30 minutes, 6, 24, and 48 hours post-dose, and on Days 8, 15, 22, and 29 of Cycle 1; pre- and post-dose on Day 1 of every other subsequent 14-day cycle up to 12 months]
2. Maximum concentration (C_{max}) after first dose interval of pembrolizumab
[Time Frame: Part A, Cycle 1 + Day 1 of Cycle 2 and then every 14-day cycle for up to 12 months; Part B Q2W, Cycles 1 and 3; Part B Q3W, Cycles 1 and 2; Part C, Cycles 1 and 2; Part D, Cycles 1 and 6; Part E, Cycles 1 and 6; Part F, Cycles 1 and 6.]
3. Time at which maximum concentration (T_{max}) occurs for pembrolizumab (Part A)
[Time Frame: Pre-dose, 30 minutes, 6, 24, and 48 hours post-dose, and on Days 8, 15, 22, and 29 of Cycle 1; pre- and post-dose on Day 1 of every other subsequent 14-day cycle up to 12 months]
4. Lowest plasma concentration (C_{trough}) of pembrolizumab
[Time Frame: Part A, Cycle 1 + Day 1 Cycle 2, and each 14-day cycle for up to 12 mo.; Part B Q2W, Cycles 1,3,7 + every 4 cycles for 12 mo.; Parts B/C Q3W, Cycles 1, 2, 5 + every 4 cycles for 12 mo.; Parts D/E/F, Cycles 1, 2, 3, 6, 8 + every 4 cycles for up to 2 yrs.]
5. Terminal half-life (t_{1/2}) of pembrolizumab (Parts B, C, D, E and F)
[Time Frame: Pre-dose, 30 minutes, 6, 24, and 48 hours post-dose, and on Days 8, 15, 22, and 29 of Cycle 1; pre- and post-dose on Day 1 of every other subsequent 14-day cycle starting with Cycle 2 for up to 12 months.]
6. Progression free survival (PFS) in MEL and NSCLC participants
[Time Frame: From first documented response up to 2 years]
7. Overall survival (OS) in MEL and NSCLC participants
[Time Frame: From first dose of study drug until death or lost to follow-up (up to 2 years)]
8. Duration of response (DR) in MEL and NSCLC participants
[Time Frame: From first documented response up to 2 years]

Eligibility

Minimum Age
18 Years
Maximum Age
Sex
All
Gender-based Eligibility
Gender Eligibility Description
Accepts Healthy Volunteers
No
Criteria

Inclusion criteria (Part F is the only part currently enrolling participants).

- In Part A: Histological or cytological diagnosis of MEL or any type of carcinoma, progressive metastatic disease, or progressive locally advanced disease not amenable to local therapy. In Parts B and D of the study, histological or cytological diagnoses of metastatic MEL with progressive locally advanced or metastatic disease. In Parts C and F, histological or cytological diagnosis of NSCLC. In Part F, participants with Stage IV NSCLC without prior systemic therapy may be eligible.
- Failure of established standard medical anti-cancer therapies for a given tumor type or intolerance to such therapy.
- In Parts B, C, D, or F of the study, MEL or NSCLC must be measurable by imaging.
- In Part F of the study, NSCLC with PD-L1 gene expression.
- Performance status of 0 or 1 on the Eastern Cooperative Oncology Group (ECOG) Performance Scale.
- Adequate organ function.

Exclusion criteria (Part F is the only part currently enrolling participants)

- Chemotherapy, radioactive, or biological cancer therapy within 4 weeks prior to the first dose of study therapy, or not recovered to Common Terminology Criteria for Adverse Events (CTCAE) Grade 1 or better from the adverse events caused by therapy administered more than 4 weeks prior to first dose.
- Participation in a study of an investigational agent or using an investigational device within 30 days of administration of pembrolizumab, with the exception of participants in the follow-up phase.
- Other form(s) of antineoplastic therapy anticipated during the period of the study.
- History of pneumonitis requiring treatment with steroids, or has a history of interstitial lung disease.
- Medical condition that requires chronic systemic steroid therapy, or on any other form of immunosuppressive medication, excepting use of inhaled steroids.
- History of acute diverticulitis, intra-abdominal abscess, GI obstruction, abdominal carcinomatosis.
- History of a hematologic malignancy, malignant primary brain tumor, malignant sarcoma, or another malignant primary solid tumor, unless no evidence of that disease for 5 years.
- Active central nervous system (CNS) metastases and/or carcinomatous meningitis.
- Previous severe hypersensitivity reaction to another monoclonal antibody (mAb).
- Active autoimmune disease or a documented history of autoimmune disease or syndrome that requires systemic steroids or immunosuppressive agents, except vitiligo or resolved childhood asthma/atopy.
- Prior therapy with another anti-programmed cell death (PD)-1 agent or previously enrolled in any pembrolizumab trial.
- Active infection requiring therapy.
- Positive for Human Immunodeficiency Virus (HIV), Hepatitis B (Hepatitis B Surface Antigen [HBsAg] reactive), or Hepatitis C virus (Hepatitis C Virus Ribonucleic Acid [HCV RNA] (qualitative) is detected).
- Regular use of illicit drugs or a recent history (within the last year) of substance abuse (including alcohol).
- Symptomatic ascites or pleural effusion.
- Participant is pregnant or breastfeeding, or expecting to conceive or father children within the projected duration of the study.

Contacts/Locations

Central Contact Person

Study Officials
<ul style="list-style-type: none">Name Medical DirectorRole Study DirectorAffiliation Merck Sharp & Dohme LLC
Location

IPD Sharing

IPD information

References

Citations
<ul style="list-style-type: none">[Results] Robert C, Ribas A, Wolchok JD, Hodi FS, Hamid O, Kefford R, Weber JS, Joshua AM, Hwu WJ, Gangadhar TC, Patnaik A, Dronca R, Zarour H, Joseph RW, Boasberg P, Chmielowski B, Mateus C, Postow MA, Gergich K, Elassaiss-Schaap J, Li XN, Iannone R, Ebbinghaus SW, Kang SP, Daud A. Anti-programmed-death-receptor-1 treatment with pembrolizumab in ipilimumab-refractory advanced melanoma: a randomised dose-comparison cohort of a phase 1 trial. <i>Lancet</i>. 2014 Sep 20;384(9948):1109-17. doi: 10.1016/S0140-6736(14)60958-2. Epub 2014 Jul 15. (https://pubmed.ncbi.nlm.nih.gov/25034862)
Links
Available IPD/Information

Document Section