COMPLETED

Study of MK-3475 in Patients With Microsatellite Unstable (MSI) Tumors (Cohorts A, B and C)

ClinicalTrials.gov ID NCT01876511

Sponsor Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Information provided by Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins (Responsible Party)

Last Update Posted 2020-02-06

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.

☐	1	2013-06-10	• None (earliest version on record)
☐	2	2013-06-12	• Study Status • Outcome Measures
☐	3	2013-09-20	• Recruitment Status • Study Status • Contacts/Locations
☐	4	2014-05-21	• Study Status • Conditions
☐	5	2014-06-25	• Study Status • Contacts/Locations • Outcome Measures
☐	6	2014-09-15	• Study Status • Contacts/Locations
☐	7	2014-12-26	• Study Status • Contacts/Locations

Compare

☐	8	2015-01-29	• Study Status • Contacts/Locations
☐	9	2015-02-26	• Study Status • Contacts/Locations
☐	10	2015-04-15	• Study Status • Eligibility • Contacts/Locations
☐	11	2015-06-09	• Study Status • Study Design • Eligibility
☐	12	2016-01-04	• Study Status • Eligibility
☐	13	2016-06-28	• Study Status
☐	14	2016-11-10	• Study Status
☐	15	2017-05-03	• Study Status • Contacts/Locations
☐	16	2017-08-28	• Study Status
☐	17	2017-10-05	• Study Status • Contacts/Locations • Study Description • Conditions • Arms and Interventions • Outcome Measures • Eligibility
☐	18	2017-12-13	• Study Status • Conditions
☐	19	2018-02-27	• Study Status • Contacts/Locations
☐	20	2018-03-27	• Study Status • Eligibility • References • Conditions
☐	21	2019-01-08	• Study Status • Eligibility • Contacts/Locations
☐	22	2019-02-18	• Study Status

			• Contacts/Locations • Eligibility • Conditions
☐	23	2019-02-18	• Study Status • Contacts/Locations
☐	24	2019-03-04	• Study Status • Conditions **Results Submission Events (1)** • 2019-11-06: Returned after QC review: 2019-11-27
☐	25	2019-12-20	• Recruitment Status • Study Status • Adverse Events • Study Identification • Oversight • Study Description

	Version	Date submitted (YYYY-MM-DD)	Changes
			• Arms and Interventions • Outcome Measures • Eligibility • IPDSharing • Participant Flow • Baseline Characteristics • More Information • Document Section
☐	26	2020-01-17	• Study Status • Adverse Events
☐	27	2020-02-03	• Study Status
☐	28	2020-02-04	• Study Status

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Version 12: 2016-01-04

	Version	Date submitted (YYYY-MM-DD)	Changes

Study Details

Study Identification

Unique Protocol ID
J1365

Brief Title
Phase 2 Study of MK-3475 in Patients With Microsatellite Unstable (MSI) Tumors

Official Title
Phase 2 Study of MK-3475 in Patients With Microsatellite Unstable (MSI) Tumors

Secondary IDs
MK-3475-016, NA_00085756

Study Status

Record Verification
2016-01

Overall Status
Recruiting

Study Start
2013-09

Primary Completion
2017-06 [Estimated]

Study Completion
2020-10 [Estimated]

First Submitted
2013-06-10

First Submitted that Met QC Criteria
2013-06-10

First Posted
2013-06-12 [Estimated]

Last Update Submitted that Met QC Criteria
2016-01-04

Version	Date submitted (YYYY-MM-DD)	Changes

Sponsor/Collaborators

Sponsor
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Responsible Party
Sponsor

Collaborators
Merck Sharp & Dohme LLC

Oversight

U.S. FDA-regulated Drug

U.S. FDA-regulated Device

Data Monitoring
Yes

Study Description

Brief Summary
This study will be looking at whether MK-3475 (an antibody that blocks negative signals to T cells) is effective (anti-tumor activity) and safe in three different patient populations. These include: 1. patients with MSI positive colon cancer, 2. patients with MSI negative colon cancer, and 3. patients with other MSI positive cancers.

Detailed Description

Conditions

Condition
MSI Positive Colorectal Cancer MSI Negative Colorectal Cancer MSI Positive Non-Colorectal Cancers

Keywords
MSI MSS MLH 1 MSH 2 MSH 6 PMS2 BRAF pV600E

TGFBR2

Study Design

Study Type
Interventional

Primary Purpose
Treatment

Study Phase
Phase 2

Interventional Study Model
Parallel Assignment

Number of Arms
3

Masking
None (Open Label)

Allocation
Non-Randomized

Enrollment
171 [Estimated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: MSI Positive Colorectal Cancer	Drug: MK-3475 • MK-3475 10 mg/kg every 14 days
Experimental: MSI Negative Colorectal Cancer	Drug: MK-3475 • MK-3475 10 mg/kg every 14 days
Experimental: MSI Positive Non-Colorectal Cancer	Drug: MK-3475 • MK-3475 10 mg/kg every 14 days

Outcome Measures

Primary Outcome Measures
1. Immune-related progression free survival (irPFS) rate at 20 weeks in patients with MSI positive and negative colorectal adenocarcinoma using immune related response criteria (irRC) [Time Frame: 4 years]

2. Objective response rate (irORR) at 20 weeks in patients with MSI positive and negative colorectal adenocarcinoma using immune related response criteria (irRC)
   [Time Frame: 4 years]
3. Immune-related progression free survival (irPFS) rate in patients with MSI positive non-colorectal adenocarcinoma using immune related response criteria (irRC) at 20 weeks
   [Time Frame: 4 years]

Secondary Outcome Measures

1. Overall survival
   [Time Frame: 4 years]
2. irPFS and PFS in patients with MSI positive and negative tumors at 28 weeks using irRC and RECIST 1.1
   [Time Frame: 4 years]
3. Best overall response rate and disease control rate in patients with MSI positive and negative tumors
   [Time Frame: 4 years]
4. Number of participants experiencing immune-related toxicities (IRAEs)
   [Time Frame: 4 years]
5. Does MSI as a marker predict treatment response
   [Time Frame: 4 years]
6. Identify alternative markers of MSI status. This includes but is not limited to MLH 1, MSH 2, MSH 6, PMS2, BRAF pV600E, and TGFBR2.
   [Time Frame: 4 years]

Eligibility

Minimum Age

18 Years

Maximum Age

Sex

All

Gender-based Eligibility

Gender Eligibility Description

Accepts Healthy Volunteers

No

Criteria

Inclusion Criteria:

1. Arm 1 only: Patients with MSI positive colorectal cancer
2. Arm 2 only: Patients with MSI negative colorectal cancer
3. Arm 3 only: Patients with MSI positive non-colorectal cancer
4. Have measurable disease
5. ECOG Performance Status of 0 to 1
6. Adequate organ function as defined by study-specified laboratory tests

7. Must use acceptable form of birth control through the study and for 28 days after final dose of study drug
8. Signed informed consent form
9. Willing and able to comply with study procedures
10. Agree to have a biopsy of their cancer
11. Patients with colon cancer must have received at least two prior cancer therapy regimens.
12. Patients with other cancer types must have received at least one prior cancer therapy

Exclusion Criteria:

1. Patients with uncontrolled intercurrent illness, including but not limited to ongoing or active infection, systematic congestive heart failure, unstable angina pectoris, cardiac arrhythmia or psychiatric condition that would limit compliance with study requirements
2. Patients who have had chemotherapy or biological cancer therapy within 2 weeks prior to the first dose of study drug
3. Patients who have had radiation within 2 weeks prior to the first dose of study drug
4. Patients who have undergone major surgery within 4 weeks of dosing of investigational agent
5. Patients who have received another investigational product or investigational device within 4 weeks prior to receiving study drug
6. Patients who have received any of the following concomitant therapy: IL-2, interferon, or other non-study immunotherapy regimens, immunosuppressive agents, other investigational therapies or chronic use of systemic corticosteroids within one week prior to first dose of study drug
7. Patients who have received a live vaccine within 4 weeks prior to or after any dose of MK-3475
8. Patients who have received growth factors, including but not limited to granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), erythropoietin, etc. within 2 weeks of study drug administration
9. Patient who have had prior treatment with anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, anti-OX-40, anti-CD40, or anti-CTLA-4 antibodies
10. Patients with history of any autoimmune disease:inflammatory bowel disease, (including ulcerative colitis and Crohn's Disease), rheumatoid arthritis, systemic progressive sclerosis (scleroderma), systemic lupus erythmatosus (SLE) autoimmune vasculitis, CNS or motor neuropathy considered to be of autoimmune origin.
11. Patients who have known history of infection with HIV, hepatitis B, or hepatitis C
12. Patients with evidence of interstitial lung disease
13. Systemically active steroid use
14. Patients on home oxygen
15. Patients with oxygen saturation of <92% on room air by pulse oximetry
16. Pregnant or lactating
17. Conditions, including alcohol or drug dependence, or intercurrent illness that would affect the patient's ability to comply with study visits and procedures

Contacts/Locations

Central Contact Person

Study Officials

- Name
  Dung Le, MD

  Role
  Principal Investigator

Affiliation
Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Location

- **Stanford, California, United States, 94305**
  Status:
  Recruiting

  Facility:
  Stanford University

  Contact:
  - Contact
    - George Fisher, MD
    - georgeaf@stanford.edu
  - Principal Investigator
    - George Fisher, MD

- **Baltimore, Maryland, United States, 21231**
  Status:
  Recruiting

  Facility:
  Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

  Contact:
  - Contact
    - Holly Kemberling, RN
    - 443-287-5013
    - hkember1@jhmi.edu
  - Principal Investigator
    - Dung Le, MD

- **Bethesda, Maryland, United States, 20892**
  Status:
  Recruiting

  Facility:
  Investigator Thoracic and Gastrointestinal Oncology Branch, Center for Cancer Research, NIH

  Contact:
  - Contact
    - Tim F. Greten, MD
    - gretentf@mail.nih.gov
  - Principal Investigator
    - Tim F Greten, MD

- **Columbus, Ohio, United States, 43210**
  Status:
  Recruiting

  Facility:
  Ohio State University

  Contact:
  - Contact
    - Richard Goldberg, MD
    - Richard.goldberg@osumc.edu
  - Principal Investigator
    - Richard Goldberg, MD

- **Portland, Oregon, United States, 97213**
  Status:
  Recruiting

Facility:
Providence Portland Medical Center

Contact:
- Contact
  - Todd Crocenzi, MD
  - Todd.Crocenzi@providence.org
- Principal Investigator
  - Todd Crocenzi, MD

- **Pittsburgh, Pennsylvania, United States, 15232**
  Status:
  Recruiting

  Facility:
  University of Pittsburgh Cancer Institute

  Contact:
  - Contact
    - James Lee, MD, PhD
    - leejj@upmc.edu
  - Principal Investigator
    - James Lee, MD; PhD

IPD Sharing

IPD information

References

Citations

Links

Available IPD/Information

Document Section