Phase IB Study of MK-3475 in Subjects with Select Advanced Solid Tumors

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON47029

Source
ToetsingOnline

Brief title
MK-3475 Solid All Comers

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer; solid tumor

Research involving
Human

Sponsors and support

Primary sponsor: Merck Sharp & Dohme (MSD)
Source(s) of monetary or material Support: Merck Sharp & Dohme (MSD)

Intervention

Keyword: Advanced Solid Tumors, all comers

Outcome measures

Primary outcome

To evaluate preliminary signals of potential anti-tumor activity of MK-3475 in subjects with a given a histopathologic type of PD-L1 positive advanced solid tumor based on RECIST 1.1 as determined by the investigator in the tumor indications below.

Secondary outcome

Across-Indication Secondary Objective

(1) Objective: To determine the safety and tolerability of MK-3475 across selected PD-L1 positive advanced solid tumors.

Within-Indication Secondary Objectives

The following secondary objectives will be evaluated separately in each of the 20 disease indications listed in Section 3.1.

(1) Objective: To evaluate the progression-free survival (PFS) in subjects with a given PD-L1 positive advanced solid tumor type receiving MK-3475.

(2) Objective: To evaluate the overall survival (OS) in subjects with a given PD-L1 positive advanced solid tumor type receiving MK-3475.

(3) Objective: To evaluate the response duration in subjects with a given PD-L1 positive advanced solid tumor type receiving MK-3475.

Study description

Background summary

Details regarding specific benefits and risks for subjects participating in this clinical trial may be found in the accompanying Investigators Brochure (IB) and Informed Consent documents.
This is a multicenter, nonrandomized, multi-cohort trial of MK-3475 in PD-L1 positive subjects with advanced solid tumors with no curative therapeutic options. Subjects will be enrolled into 1 of 20 solid tumor indications as outlined in Section 2.1. Given that immune checkpoints such as the PD-1/PD-L1 axis may be relevant in a variety of solid tumors in addition to the ones previously studied, exploration as to which of these tumors might be more responsive to PD-1 inhibition is being pursued in this protocol. Twenty indications with a significant unmet medical need in the metastatic/refractory setting for which there is internal PD-1/PD-L1 data were chosen for study. This indication discovery effort may lead to a better understanding of which tumor types may be more responsive to MK-3475.
Participation in this trial will be dependent upon supplying tissue from an archival tissue sample or newly obtained core or excisional biopsy of a tumor lesion to evaluate for PD-L1 expression by IHC. If an archival specimen is PD-L1 negative but a newly obtained biopsy is positive, the subject would be eligible. The specimen will be evaluated at a central laboratory for expression status of PD-L1. Only subjects with PD-L1 positive tumors will be enrolled in the trial. PD-L1 predicting potential response to anti-PD-1 therapy is based on the results from Topalian et al who examined PD-L1 expression in the archival specimens of 42 of the 296 subjects treated with the PD-1 inhibitor nivolumab. Of those 17 subjects whose tumor cells did not stain positive for PD-L1 using a 5% threshold of tumor cell surface expression, no objective response by RECIST 1.1 was observed. But among the 25 subjects whose tumor cells were considered positive for PD-L1, 9 responded (36%). Therefore, it is hypothesized that PD-L1 expression may be a predictive biomarker of anti-PD-1 activity, and this selection criterion will be utilized in this study as a necessary element for study enrollment.

Study objective

The primary objective of the trial is to evaluate a preliminary signal of potential anti-tumor activity of MK-3475 in subjects with PD-L1 positive advanced solid tumors. Secondary objectives include safety and tolerability, progression-free survival (PFS), overall survival (OS) and response duration.

Study design

This is a multicenter, nonrandomized, multi-cohort trial of MK-3475 in subjects with PD-L1 positive advanced solid tumors with no curative therapeutic options. Subjects will be enrolled into one of the following 20 solid tumor cohorts:

A1 Colon or Rectal Adenocarcinoma
A2 Anal Canal Squamous Cell Carcinoma
A3 Pancreas Adenocarcinoma
A4 Esophageal Squamous Cell Carcinoma or Adenocarcinoma (Including GE Junction)
A5 Biliary Tract Adenocarcinoma (Gallbladder and Biliary Tree but excluding Ampulla of Vater Cancers)
A6 Carcinoid Tumors
A7 Neuroendocrine Carcinomas (Well or moderately differentiated Pancreatic Neuroendocrine Tumor)
B1 ER Positive HER2 Negative Breast Cancer
B2 Ovarian Epithelial, Fallopian Tube or Primary Peritoneal Carcinoma
B3 Endometrial Carcinoma
B4 Cervical Squamous Cell Cancer
B5 Vulvar Squamous Cell Carcinoma
C1 Small Cell Lung Cancer
C2 Mesothelioma (Malignant Pleural Mesothelioma)
D1 Thyroid Cancer (Papillary or Follicular Subtype)
D2 Salivary Gland Carcinoma
D3 Nasopharyngeal Carcinoma
E1 Glioblastoma Multiforme
E2 Leiomyosarcoma
E3 Prostate Adenocarcinoma

Approximately 320 subjects will be enrolled in this trial to examine the safety and efficacy in these cohorts to the 10mg/kg dose of MK-3475 administered every 2 weeks. Subjects will be evaluated every 8 weeks (56 days ±7 days) with radiographic imaging to assess response to treatment. After 6 months, radiography imaging will be evaluated every 12 weeks (84 days ±7 days). RECIST 1.1 will be used as the primary efficacy endpoint of response rate.

Study burden and risks

• IV line for infusion of the study drug may cause: discomfort, irritation, mild bruising, bleeding, leakage of drug solution, and rarely infection, nausea, and lightheadedness.

• Blood samples: drawing blood from your arm may cause pain, bruising, lightheadedness, and rarely, infection.

• CT Scan: CT scans are used to create images of internal bones and organs using radiation. High dose radiation is known to produce cancer cells. The effect of exposure to radiation adds up over a lifetime. The amount of radiation exposure involved in this trial will not be significantly greater than for subjects with your disease who do not take part in the trial. The contrast solution that may be given for a CT scan may cause an allergic reaction (rare). Severe allergic reactions can be life threatening. CT contrast solution can cause kidney damage, especially if you are diabetic,

dehydrated (lost body water) or elderly.

• Magnetic Resonance Imaging (MRI): Risks of MRI include claustrophobia, discomfort due to lying still for a prolonged period of time, and other factors which will be described to you and discussed with you at the MRI center.

• Tumor Biopsy: Having biopsies performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling and/or infection at the site of the biopsy. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site. Other potential risks will be described to you and discussed with you by physicians who conduct these biopsies.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Have histologically or cytologically-documented, locally-advanced, or metastatic solid malignancy that has either (a) failed prior standard therapy, (b) for which no standard therapy exists, or (c) standard therapy is not considered appropriate by the patient and treating physician. There is no limit to the number of prior treatment regimens.;2. Have one of the following advanced (unresectable and/or metastatic) solid tumor indications for which no curative therapy exist:;A1 Colon or Rectal Adenocarcinoma
A2 Anal Canal Squamous Cell Carcinoma
A3 Pancreas Adenocarcinoma
A4 Esophageal Squamous Cell Carcinoma or Adenocarcinoma (Including GE Junction)
A5 Biliary Tract Adenocarcinoma (Gallbladder and Biliary Tree but excluding Ampulla of Vater Cancers)
A6 Carcinoid Tumors
A7 Neuroendocrine Carcinomas (Well or moderately differentiated Pancreatic Neuroendocrine Tumor)
B1 ER Positive HER2 Negative Breast Cancer a
B2 Ovarian Epithelial, Fallopian Tube or Primary Peritoneal Carcinoma
B3 Endometrial Carcinoma b
B4 Cervical Squamous Cell Cancer
B5 Vulvar Squamous Cell Carcinoma
C1 Small Cell Lung Cancer
C2 Mesothelioma (Malignant Pleural Mesothelioma)
D1 Thyroid Cancer (Papillary or Follicular Subtype)
D2 Salivary Gland Carcinoma b
D3 Nasopharyngeal Carcinoma
E1 Glioblastoma Multiforme c
E2 Leiomyosarcoma
E3 Prostate Adenocarcinoma d
a Note: ER positive HER2 negative status for breast cancer cohort defined by local standards.
b Note: All carcinoma subtypes are allowed however sarcomas or mesenchymal tumors are excluded.
c Note: Glioblastoma multiforme subjects with any prior bevacizumab treatment are NOT eligible.
d Note: Subjects with prostate cancer who are currently on LHRH analogs are eligible for this study and may continue to take the LHRH analogs while participating in this study.;3. Have provided tissue for biomarker analysis from an archival tissue sample or newly obtained core or excisional biopsy of a tumor lesion not previously irradiated (tumors progressing in a prior site of radiation are allowed for PD-L1 characterization, other exceptions may be considered after Sponsor consultation). ;4. Have a PD-L1 positive tumor as determined by IHC at a central laboratory from either an archived formalin fixed paraffin embedded (FFPE) tumor sample or a newly obtained biopsy.;5. Have measurable disease based on RECIST 1.1. Tumor lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions. ;6. Have a performance status of 0 or 1 on the ECOG Performance Scale.;7. Demonstrate adequate organ function as defined in the protocol.

Exclusion criteria

1. Is currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks of the first dose of treatment.;2. Has a diagnosis of immunodeficiency or is receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment. The use of physiologic doses of corticosteroids may be approved after consultation with the Sponsor.;Note: Systemic steroid therapy allowed for subjects in the GBM cohort as long as <= dexamethasone 4 mg, or its steroid equivalent (other exceptions may be considered after sponsor consultation).;3. Has had a prior anti-cancer monoclonal antibody (mAb) within 4 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to mAbs administered more than 4 weeks earlier. ;4. Has had prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to a previously administered agent.;Note: Subjects with <= Grade 2 neuropathy or <= Grade 2 alopecia are an exception to this criterion and may qualify for the study.;Note: If subject received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting therapy. ;5. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy or in situ cervical cancer.;6. Has known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Subjects with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least 7 days prior to trial treatment. This exception does not include carcinomatous meningitis which is excluded regardless of clinical stability.;7. Has an active autoimmune disease requiring systemic treatment within the past 3 months or a documented history of clinically severe autoimmune disease, or a syndrome that requires systemic steroids or immunosuppressive agents. Subjects with vitiligo or resolved childhood asthma/atopy would be an exception to this rule. Subjects that require intermittent use of bronchodilators, inhaled steroids, or local steroid injections would not be excluded from the study. Subjects with hypothyroidism stable on hormone replacement or Sjøgren*s syndrome will not be excluded from the study.;8. Has evidence of interstitial lung disease.;9. Has an active infection requiring systemic therapy.;10. Has received prior therapy with an anti-PD-1, anti-PD-L1, and anti-PD-L2 (including ipilimumab or any other antibody or drug specifically targeting T-cell co-stimulation or checkpoint pathways).;11. Has a known history of Human Immunodeficiency Virus (HIV) (HIV 1/2 antibodies).;12. Is or has an immediate family member (spouse or children) who is investigational site or sponsor staff directly involved with this trial, unless prospective IRB approval (by chair or designee) is given allowing exception to this criterion for a specific patient.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-04-2014
Enrollment:	13
Type:	Actual

Ethics review

Approved WMO Date:	22-01-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	28-03-2014
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-04-2014
Application type:	Amendment

Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-01-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	22-01-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-02-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-03-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	26-06-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO	

Date:	19-11-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-12-2015
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	21-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-11-2016
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-02-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	19-05-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-05-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	18-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-10-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	15-12-2017
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	31-01-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-02-2018

Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	13-08-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	24-08-2018
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-09-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	27-11-2019
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
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Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	14-05-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-004507-39-NL
CCMO	NL47685.031.14