A Clinical Trial of Pembrolizumab (MK-3475) Evaluating Predictive Biomarkers in Subjects with Advanced Solid Tumors (KEYNOTE 158)

Published: 04-01-2016
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This study has been transitioned to CTIS with ID 2022-501253-37-00 check the CTIS register for the current data. The primary efficacy objective of this trial is to evaluate the anti-tumor activity of pembrolizumab in subjects with any of a *basket*...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON53123

Source
ToetsingOnline

Brief title
KEYNOTE-158

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
solid tumors

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Biomarkers, Pembrolizumab, Solid Tumors

Outcome measures

Primary outcome

Objective Response Rate, ORR

Secondary outcome

Duration of Respons (DOR)

Progressionfree survival (PFS)

Overall survival (OS)

Study description

Background summary

The Phase II trial described in this protocol will evaluate the anti-tumor effect of pembrolizumab in a *basket* of rare malignancies and determine if any of three primary biomarkers predicts response to pembrolizumab treatment across multiple tumor types, regardless of specific tumor histology.

Subjects with any of ten specified solid tumor types (Groups A-J) will be enrolled, as outlined in Section 2.1 of the protocol. These tumor types were selected because (1) each is a rare malignancy, (2) each represents a significant unmet medical need in the metastatic/refractory setting, (3) there is preliminary evidence of clinical response to pembrolizumab in these malignancies, and (4) preliminary data in these rare tumor indications (and in other tumor types) has identified three primary biomarkers that may be predictive of response to pembrolizumab.

Study objective

This study has been transitioned to CTIS with ID 2022-501253-37-00 check the CTIS register

for the current data.

The primary efficacy objective of this trial is to evaluate the anti-tumor activity of pembrolizumab in subjects with any of a *basket* of rare malignancies (biomarker unselected and biomarker selected). ORR will be used as the primary endpoint per RECIST 1.1 criteria (see Section 12.7), as assessed by independent central radiologic review.

The ultimate goal of this trial is to gain regulatory approval for pembrolizumab treatment across multiple different rare tumor types.

Study design

This is a non-randomized, multi-site, open-label trial of pembrolizumab (MK-3475) in subjects with multiple types of advanced (unresectable and/or metastatic) rare cancers

Intervention

Subjects will receive 200 mg Pembrolizumab every three weeks intravenously or 400 mg Pembrolizumab every 6 weeks

Study burden and risks

The patient will receive the study drug every 3 weeks or every 6 weeks for up to 24 months. Additional treatment is possible (under certain conditions) for an extra year.

The patient will visit the doctor every 6 weeks or every 3 weeks. The first visit a tumor biopsy will take place (if necessary). Each visit, a physical examination will be performed, and blood samples will be taken. Volume will range from 8 - 26.5 ml per visit. At specified moments the patient will also fill in two questionnaires each visit, namely a 'quality-of-life questionnaire' (EORTC QLQ C30) and a questionnaire which asked about the health of the patient (eEuroQoL EQ-50).

The patient may experience physical and I or psychological discomfort with some of the procedures performed during a visit, such as blood sampling, the IV line, ECG, CT scan, MRI and tumor biopsy.

The main side effect reported with the use of MK3475 are fatigue, itching, rash, frequent or excessive bowel movements, joint pain and nausea.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

1.Have a histologically or cytologically-documented, advanced (metastatic and/or unresectable) solid tumor that is incurable and for which prior standard first-line treatment have failed. Patients must have progressed on or be intolerant to therapies that are known to provide clinical benefit. There is no limit to the number of prior treatment regimens.
2.Have one of the following advanced (unresectable and/or metastatic) tumor types:
(A)Anal Squamous Cell Carcinoma,
(B)Biliary Adenocarcinoma (gallbladder and biliary tree (intrahepatic or extrahepatic cholangiocarcinoma) except Ampulla of Vater Cancers,
(C)Neuroendocrine Tumors (well- and moderately-differentiated), of the lung, appendix, small intestine, colon, rectum, or pancreas,

(D)Endometrial Carcinoma (sarcomas and mesenchymal tumors are excluded)
(E)Cervical Squamous Cell Carcinoma,
(F)Vulvar Squamous Cell Carcinoma,
(G)Small Cell Lung Carcinoma,
(H)Mesothelioma (Malignant Pleural Mesothelioma),
(I)Thyroid Carcinoma (Papillary or Follicular Subtype),
(J)Salivary Gland Carcinoma (sarcomas and mesenchymal tumors are excluded)
OR
(K)Any advanced solid tumor (except CRC), which is MSI-H.
(L) Any advanced solid tumor (including CRC*) which is dMMR/MSI-H in patients from mainland China who are of Chinese descent.
(M) Any advanced solid tumor that has failed at least one line of therapy and is TMB-H (>=10 mut/Mb, F1CDx assay), excluding dMMR/MSI-H tumors.
3. Have submitted an evaluable tissue sample for biomarker analysis from a tumor lesion not previously irradiated (exceptions may be considered after Sponsor consultation). The tumor tissue submitted for analysis must be from a single tumor tissue specimen and of sufficient quantity and quality to allow assessment of ALL required primary biomarkers.
Note: SUBJECTS WILL NOT BE ELIGIBLE TO ENROLL INTO GROUPS A-J UNLESS ALL THREE PRIMARY BIOMARKERS (TUMOR PD-L1 EXPRESSION, GEP SCORE, AND MSI-H STATUS) CAN BE ASSESSED USING TISSUE FROM THE SAME SINGLE TUMOR SPECIMEN.
4.If enrollment in Groups A-J has moved to biomarker enrichment, have a tumor that is positive for one or more of the pre-specified primary biomarker(s), as assessed by the central laboratory. These enrichment biomarkers may be PD-L1 expression by IHC (at a percentage to be prespecified), a positive tumor RNA GEP score (at a prespecified cut-off), and/or tumor MSI-H.
5.Have radiologically measurable disease based on RECIST 1.1. Independent central radiologic review must confirm the presence of radiologically measureable disease based on RECIST 1.1 for the subject to be eligible to participate in the trial (see Site Imaging Manual for detailed instructions). 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. This performance status must be confirmed within 3 days prior to the first dose of pembrolizumab or the subject must be excluded.
7. Life expectancy of at least 3 months.
8. Adequate Organ Function Laboratory Values: Hemoglobin (Hgb) > or = 9.0 g/dL or > = 5.6 mmol/L, without recent transfusion (defined as a transfusion that has occurred within 2 weeks of the Hgb measurement)., Refer to protocol for complete list

Exclusion criteria

- Is currently participating and receiveing study therapy or has been within 4 weeks of the first dose of treatment

-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., -Has an active autoimmune disease that has required systemic treatment in the past 2 years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) or treatment with drugs (e.g. neomercazol, carbamazole, etc.) that function to decrease the generation of thyroid hormone by a hyperfunctioning thyroid gland (e.g. in Graves' disease) is not considered a form of systemic treatment of an autoimmune disease. , -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., - Has a known additional malignancy within 2 years prior to enrollment with the execption of curatively treated basal cell carcinoma of the skin, squamous cell carcinoma of the skin, and/or curatively resected in situ cancers. , - Has known active central nervous system (CNS) metastases and/or carcinomatous
meningitis., - Has known glioblastoma multiforme of the brainstem., - Has evidence history of active (non-infectious) pneumonitis that required steroids or current pneumonitis., Refer to protocol for complete list.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-12-2015
Enrollment:	47
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pembrolizumab
Generic name:	Keytruda
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-01-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-05-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2016
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-06-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-11-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-11-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-07-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	13-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-08-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	28-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EU-CTR	CTIS2022-501253-37-00
EudraCT	EUCTR2015-002067-41-NL
CCMO	NL55404.056.15