A Multicenter, Open label, Phase III Extension Trial to Study the Long-term Safety and Efficacy in Participants with Advanced Tumors Who Are Currently on Treatment or in Follow-up in a Pembrolizumab Trial.

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This study has been transitioned to CTIS with ID 2022-501254-10-00 check the CTIS register for the current data. The purpose of this trial is to rollover participants who previously enrolled in MSD-sponsored pembrolizumab trials, including those who...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52613

Source
ToetsingOnline

Brief title
MK3475-587

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms
- Skin neoplasms malignant and unspecified

Synonym
advanced tumor, cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: advanced, pembrolizumab

Outcome measures

Primary outcome

To estimate the overall survival (OS)

Secondary outcome

1. To estimate the Duration of Response (DOR) and Duration of Complete Response (DOCR) per evaluation criteria used in the parent trial by investigator assessment for participants who have received or are receiving First Course Phase trial treatment with pembrolizumab or a pembrolizumab-based combination.

2. To evaluate the safety and tolerability of pembrolizumab or a pembrolizumab-based combination in subjects who receive it as First or Second Course Phase trial treatment.

Study description

Background summary

Pembrolizumab (also known as MK-3475, KEYTRUDA® and SCH900475) is a potenthumanized immunoglobulin G4 (IgG4) monoclonal antibody with high specificity of binding to the programmed cell death 1 (PD-1) receptor, thus inhibiting its interaction with programmed cell death ligand 1 (PD-L1) and programmed cell death ligand 2 (PD-L2). Based on preclinical in vitro data, pembrolizumab has high affinity and potent receptor blocking activity for PD-1.

Pembrolizumab has an acceptable preclinical safety profile and is in clinical development as an intravenous (IV) immunotherapy for advanced malignancies. Pembrolizumab is indicated for the treatment of patients across a number of indications. Refer to the Investigator*s Brochure (IB)/approved labeling for specific indications and detailed background information on pembrolizumab.

Study objective

This study has been transitioned to CTIS with ID 2022-501254-10-00 check the CTIS register for the current data.

The purpose of this trial is to rollover participants who previously enrolled in MSD-sponsored pembrolizumab trials, including those who received pembrolizumab, pembrolizumab-based combinations or control, into an extension trial to collect long-term efficacy and safety data.

Study design

A Multicenter, Open label, Phase III Extension Trial to Study the Long-term Safety and Efficacy in Participants with Advanced Tumors Who Are Currently on Treatment or in Follow-up in a Pembrolizumab Trial.

Intervention

1. Pembrolizumab 200 mg every 3 weeks (Q3W) or 400 mg every 6 weeks (Q6W)
2. Pembrolizumab-based combinations (per parent trial)
3. Control arm (per parent trial)

Study burden and risks

All participants that rollover into this extension trial will be from MSD pembrolizumab-based parent trials that have completed all regulatory requirements and submissions, if any, including completion of the final analysis database lock, or have fully addressed their primary endpoint(s). Each participant will enroll in the trial from the time the subject provides the informed consent through the final protocol-specified contact.

After consenting to enroll, each participant will roll-over to this extension trial in one of the following three phases, depending on the study phase they were in at the completion of the parent trial: 1) First Course Phase, 2) Survival Follow-up Phase or 3) Second Course Phase. Participants who were in the Follow-up Phase in the parent trial (posttreatment or Survival Follow-up Phase) will enter the Survival Follow-up Phase of this trial.

Participants who were in the First Course Phase of trial treatment in their parent trial will enter the First Course Phase of this trial and continue trial

treatment with pembrolizumab or a pembrolizumab-based combination until disease progression is documented by the investigator per the parent trial evaluation criteria, unacceptable adverse event(s) (AEs), intercurrent illness that prevents further administration of trial treatment, investigator*s or participant*s decision to withdraw the participant, noncompliance with trial treatment or procedure
requirements, or administrative reasons requiring cessation of trial treatment. In addition, for parent protocols where pembrolizumab dosing is without a defined treatment period (ie. Keynote 001 [KN001], Keynote 002 [KN002]),

participants who had confirmed stable disease (SD) or better in their parent trial may stop First Course Phase trial
treatment as long as they complete 35 doses of pembrolizumab (approximately 2 years). Participants who were allowed to continue trial treatment in their parent trial with pembrolizumab or with a pembrolizumab-based combination beyond disease progression at the investigator*s discretion (eg, KN001) will enter First Course Phase and continue trial treatment with pembrolizumab or with a pembrolizumab-based combination until unacceptable AEs, intercurrent illness that prevents further administration of trial treatment, investigator*s or participant*s decision to withdraw the participant, noncompliance with trial treatment or procedure requirements, or administrative reasons requiring cessation of trial treatment.

Participants who stopped First Course Phase trial treatment in their parent trial or while on KN587, after receiving 35 doses or more of pembrolizumab or a pembrolizumabbased combination for reasons other than disease progression or intolerability, or participants who attained a CR and stopped trial treatment may be eligible for 17 additional doses (approximately 1 year) of pembrolizumab or a pembrolizumab-based combination (if allowed in the parent trial) upon experiencing disease progression (Section 7.2.2). This will be considered the Second Course Phase.

Participants who were in the Second Course Phase in their parent trial will enter Second Course Phase of this trial and complete 17 doses of trial treatment with pembrolizumab or a pembrolizumab-based combination (if allowed in the parent trial), inclusive of the Second Course doses receive
in the parent trial. Under exceptional circumstances and upon Sponsor consultation, participants may be allowed to continue to receive pembrolizumab or a pembrolizumabbased combination beyond the 17 doses if the participant does not meet any criteria for trial treatment discontinuation (Section.8.1). After treatment discontinuation, participants will then be followed radiographically by the site per standard of care (SOC) and for OS until death, withdrawal of consent, start of a new antineoplastic therapy, or the end of the trial. This will be considered the Survival Follow-up Phase. If a participant in Survival Follow-up Phase has disease progression and is eligible for Second Course Phase in this
trial, the participant will enter into Second Course Phase following a

determination of eligibility (Section 7.2.2). Once Second Course Phase trial treatment is completed, participants will re-enter Survival Follow-up Phase.

Participants who were being treated in the First Course Phase in their parent trial with a control (eg, chemotherapy) will enter Survival Follow-up Phase of this trial and continue to be treated as per SOC. These participants will be followed radiographically by the site per SOC and for OS until death, withdrawal of consent, start of a new antineoplastic therapy, or the end of the trial. After the end of trial treatment, each participant will be followed for the occurrence of SAEs throughout 90 days and AEOSI and ECIs throughout 30 days following the discontinuation of trial treatment and for drug-related SAEs and spontaneously reported pregnancy as described under Section 9.3.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Participants that are currently enrolled in MSD-sponsored pembrolizumab trials and are receiving trial treatment or in a Follow-up Phase at the time KN587 is open. Participants must be from MSD-sponsored pembrolizumab parent trials established by the Sponsor as KN-587 transition ready.
2. The participant (or legally acceptable representative if applicable) provides informed consent for the trial and agrees to follow study procedures.

Exclusion criteria

There are no exclusion criteria to participate in KN587., Participants are excluded from entering Second Course trial treatment once they are enrolled on KN587 if any of the following criteria applies:
1. Woman of Childbearing Potential who has a positive urine pregnancy test within 72 hours prior to trial treatment allocation. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
2. Has severe hypersensitivity (>= Grade 3) to pembrolizumab and/or any of its excipients (the list of excipients is provided in the IB).
3. Has received a live vaccine within 30 days prior to the first dose of Second Course Phase trial treatment. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed.
4. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior to the Cycle 1 Day 1 of Second Course Phase.
5. Has a known additional malignancy that is progressing or requires active treatment. Exceptions include early stage cancers (carcinoma in situ or Stage 1) treated with curative intent, melanoma (non-ulcerated, thin primary), basal cell carcinoma of the skin, squamous cell carcinoma of the skin, in situ cervical cancer, or in situ breast cancer that has undergone potentially curative therapy.
6. Has known active central nervous system metastases and/or carcinomatous meningitis.
7. Has an active autoimmune disease that has required systemic treatment in the past 2 years (ie. use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (eg, thyroxine, insulin, or

physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.
8. Has a history of (non-infectious) pneumonitis that required steroids or has current pneumonitis.
9. NSCLC participants only: Has interstitial lung disease.
10. Has an active infection requiring systemic therapy.
11. Has a known history of human immunodeficiency virus infection.
12. Has a known history of or is positive for hepatitis B (hepatitis B surface antigen reactive) or hepatitis C (hepatitis C virus RNA [qualitative] is detected). Hepatitis C lab testing is allowed for eligibility purposes in countries where hepatitis C virus RNA is not part of SOC.
13. Is pregnant or breastfeeding or expecting to conceive or father children within the projected duration of the trial, starting with the Second Course Phase eligibility Visit through 120 days after the last dose of trial treatment.
14. Has severe cardiovascular disease, ie. arrhythmias, requiring chronic treatment, congestive heart failure (New York Heart Association Class III or IV) or symptomatic ischemic heart disease.
15. Has hepatic decompensation (Child-Pugh score > 6 [class B and C]).
16. Has uncontrolled thyroid dysfunction.
17. Has uncontrolled diabetes mellitus.
18. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the participant's enrollment for the full duration of the trial, or is not in the best interest of the participant to enroll, in the opinion of the treating investigator.
19. Has known psychiatric or substance abuse disorders that would interfere with cooperating with the requirements of the trial (specific testing is not required).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-12-2018
Enrollment:	18
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	28-06-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-10-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-01-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-09-2019
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-11-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-04-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2021
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:	17-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-07-2022
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	CTIS2022-501254-10-00
EudraCT	EUCTR2017-004417-42-NL
ClinicalTrials.gov	NCT03486873
CCMO	NL65996.056.18