A Multicenter, Open-label, Phase 2 Basket Study of MK-7684A, a Co-formation of Vibostolimab (MK-7684) with Pembrolizumab (MK-3475), With or Without Other Anticancer Therapies in Participants with Selected Solid Tumors

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This study has been transitioned to CTIS with ID 2023-505284-36-00 check the CTIS register for the current data. Objective 1: To compare MK-7684A to pembrolizumab alone with respect to ORR in participants with cervical cancer whose tumors express PD…

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

Summary

ID

NL-OMON52069

Source
ToetsingOnline

Brief title
MK7684A-005 / KEYVIBE-005

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Biliary cancer, bladder cancer, Cervical cancer, endometrial cancer, esophageal cancer, gastric cancer, HCC, HNSCC, ovarian cancer, triple-negative breast cancer

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: phase 2, solid tumors, Vibostolimab with Pembrolizumab

Outcome measures

Primary outcome

Endpoint to objective 1: Objective response: A confirmed CR or PR

Endpoint to objective 2: PFS: The time from randomization to first documented disease progression or death due to any cause, whichever occurs first

Endpoint to objective 3: Objective response: A confirmed CR or PR

Endpoint to objective 4: PFS: The time from first dose of study intervention to first documented disease progression or death due to any cause, whichever occurs first

Secondary outcome

1) Overall survival (OS)

2) Progression free survival (PFS)

3) The duration of response (DOR)

4) Change from baseline in HRQoL

5) Safety and tolerability of MK-7684A alone or in combination with other

anticancer therapies (measured by Adverse Events)

6) Objective response (confirmed CR or PR)

Study description

Background summary

In 2020, there were approximately 1.7 million newly diagnosed solid tumors in the United States. About 25% of these patients were in stage IV disease at diagnosis. For this group of patients chemotherapy is the only available treatment option, while chemotherapy is associated with significant toxicities and low response rates. For this patient population, there is an unmet medical need for the development of alternative treatment options. Therefore, this study will investigate the effect of a combination of Pembrolizumab and Vibostolimab in various advanced solid tumors.

MK-7684A is a co-formulation of 200mg MK-3475 and 200mg MK-7684. Vibostolimab (MK-7684) is a human anti-TIGIT monoclonal antibody that can bind to the TIGIT receptors on the T cells of our immune system. Pembrolizumab (MK-3475) is a human anti-PD-1 monoclonal antibody that can bind to the PD-1 receptors on the T cells of our immune system. The PD-1 receptor and TIGIT-receptor ligand interactions are major pathways hijacked by tumors to suppress immune control. The normal function of PD-1 and TIGIT, expressed on the cell surface of activated T- cells under healthy conditions, is to down-modulate unwanted or excessive immune responses, including autoimmune reactions. As a consequence, the PD-1/PD-L1 and TIGIT pathways are attractive targets for therapeutic intervention in solid tumors.

Study objective

This study has been transitioned to CTIS with ID 2023-505284-36-00 check the CTIS register for the current data.

Objective 1: To compare MK-7684A to pembrolizumab alone with respect to ORR in participants with cervical cancer whose tumors express PD-L1 (CPS >=1)

Objective 2: To compare MK-7684A to pembrolizumab alone with respect to PFS in participants with cervical cancer whose tumors express PD-L1 (CPS >=1)

Objective 3: To evaluate MK-7684A alone or in combination with other anticancer therapies with respect to ORR in participants with selected solid tumors, excluding those with cervical cancer whose tumors express PD-L1 (CPS >=1)

Objective 4: To evaluate MK-7684A in combination with other anticancer therapies with respect to PFS per RECIST 1.1 at 9 months (PFS-9) and 12 months (PFS-12) as assessed by the investigator in participants with previously untreated BRCA1/2 nonmutated and HRD-negative advanced epithelial ovarian cancer enrolled in Cohort I

Study design

This is a non-randomised (with exception of cohort A, which will be 1:1 randomized), multicenter, multicohort, open-label, phase 2, basket-study with MK-7684A, a co-formulation of vibostolimab (MK-7684) with pembrolizumab (MK-3475), alone or in combination with other anticancer therapies in participants with selected solid tumors.
About 610 participants will be assigned to the study. Screening procedures must be completed within 28 (or 56) days prior to treatment. Eligible participants are randomly assigned in cohort A1 or cohort A2 to cohort G to one of the following study intervention groups, depending on the cancer type selected A safety-lead-in will be performed to determine the tolerability and RP2D of lenvatinib, 5 FU/cisplatin, and paclitaxel to be used in combination with MK 7684A. Additional dose levels are included in the safety lead-in only to complete dose-finding and identification of the RP2D. Enrollment may be expanded in the event intermediate dose levels are explored during the safety lead-in to identify the RP2D for lenvatinib, 5 FU/cisplatin, and paclitaxel to be used in combination with MK-7684A. Continued allocation into these cohorts will only occur if the starting dose (ie, Dose Level 0) is determined to be the RP2D.

With protocol amendement 05 new cohorts with different types of solid tumors are added to evaluate safety and efficacy of MK7684A.

Intervention

The intervention differs per cohort. This concerns both the study drugs as well as frequency, dose and duration. Potential study treatment consists of pembrolizumab or MK7684A (combination of pembrolizumab and vibostolimab), which could be combined with lenvatinib, chemotherapy (capecitabine, carboplatin, cisplatin, docetaxel, fluorouracil (5-FU), gemcitabine, oxaliplatin, paclitaxel) or bevacizumab. Refer to the protocol for a complete overview.

Study burden and risks

For this study, patients will be subjected to invasive procedures such as blood collection, biopsy, CT, MRI or bone scans, physical exams, possibly confrontational questionnaires, and patients will be asked to visit the hospital regularly. Patients will be administered with different combination therapies, during three-week cycles up to a maximum of 35 treatments. It cannot

be guaranteed that participants in clinical studies will directly benefit from study intervention during participation, as clinical studies are designed to provide information about the safety and effectiveness of an investigational medicine.

Pembrolizumab has been administered in a large number of cancer participants with a well characterized safety profile and has received regulatory approval for multiple malignancies. Overall, pembrolizumab is well tolerated at doses up to 10 mg/kg every 2 weeks (Q2W). Pembrolizumab has also demonstrated anticancer clinical activity and efficacy in a broad range of cancer indications.
Available clinical safety data indicated that vibostolimab is tolerable at doses up to and including 700 mg, both when used as monotherapy and in combination with pembrolizumab. No DLTs were observed at any of the vibostolimab doses tested either as monotherapy or in combination with pembrolizumab during the dose escalation and confirmation portion of Study MK-7684-001, and the MTD was not reached.

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

A participant will be eligible for inclusion in the study if the participant:
1. Has histologically or cytologically confirmed, advanced (locally recurrent unresectable or metastatic) solid tumor as follows:
• Squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix
• Endometrial cancer
• Head and neck squamous cell carcinoma (HNSCC)
• Unresectable biliary adenocarcinoma (gallbladder or biliary tree [intrahepatic or extrahepatic] cholangiocarcinoma)
• Adenocarcinoma or squamous cell carcinoma of the esophagus or advanced/metastatic Siewert type 1 adenocarcinoma of the gastroesophageal junction (GEJ)
• Triple-negative breast cancer (TNBC)
• Hepatocellular carcinoma (HCC)
• Urothelial carcinoma of the renal pelvis, ureter, bladder, or urethra
• Ovarian cancer
• Gastric cancer
2. Has measurable disease per RECIST 1.1 as assessed by the BICR (Cohort A1 only) or local site investigator/radiology (all other cohorts)
3. Can provide a newly obtained core or excisional biopsy of a tumor lesion (or archived tumor tissue sample)
4. Is male or female, who is at least 18 years of age at the time of signing the informed consent
5. Has an ECOG Performance Status of either 0 or 1 (ECOG PS of 2 allowed for Cohort H only), as assessed within 7 days before starting study intervention
6. Has a predicted life expectancy of at least 3 months
7. Male participants must agree to follow contraceptive guidance
8. Female participants are not pregnant or breastfeeding, not women of child-bearing potential (WOCBP) or are WOCBP and agree to follow contraceptive guidance
9. The participant has provided documented informed consent for the study
10. Has adequately controlled BP with or without antihypertensive medications. Note: this criterion only applies to participants who will receive lenvatinib
11. HIV-infected participants must have well controlled HIV on ART
12. Participants who are HbsAg positive are eligible if they have received HBV antiviral therapy for at least 4 weeks and have undetectable HBV viral load before randomization/allocation
13. Participants with history of HCV infection are eligible if HCV viral load is undetectable at Screening

14. Has adequate organ function

Exclusion criteria

Participant must be excluded from the study if the participant:
1. Has a history of a second malignancy, unless potentially curative treatment has been completed with no evidence of malignancy for 3 years
2. HIV-infected participants with a history of Kaposi's sarcoma and/or Multicentric Castleman's Disease
3. Has received prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, or anti-TIGIT agent
4. Has received prior systemic anticancer therapy including investigational agents within 4 weeks. Note: This does not include lead in chemotherapy in Cohort I
5. Has received prior radiotherapy within 2 weeks or radiation-related toxicities requiring corticosteroids
6. Has received a live or live-attenuated vaccine within 30 days
7. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days
8. Has known active CNS metastases and/or carcinomatous meningitis
9. Known severe hypersensitivity (>=Grade 3) to study medication or any of their excipients
10. Has an active autoimmune disease that has required systemic treatment in past 2 years
11. Has a history of (noninfectious) pneumonitis/interstitial lung disease that required steroids or has current pneumonitis/interstitial lung disease
12. Has an active infection requiring systemic therapy
13. Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the study, interfere with the participant's participation
14. Has present accumulation of pleural, ascitic, or pericardial fluid requiring drainage or diuretic drugs within 2 weeks
15. Has concurrent active hepatitis B and hepatitis C infection
16. Has not adequately recovered from major surgery
17. Participants unlikely to comply with the requirements of the study
18. Has had an allogenic organ transplant
19. Has received an investigational agent or has used an investigational device within 4 weeks before the first dose of study intervention
All Cohorts except B1:
20. Has known MSI-H or MMR deficient cancer
Cohort B1 and B2 only:
21. Greater than 1 prior systemic chemotherapy regimen
For participants who will receive Lenvatinib: Cohort B2 & G:
22. Has had major surgery within 3 weeks
23. Has current, clinically relevant >=Grade 3 fistula

24. Has urine protein >=1 g/24 hours
25. Has a LVEF below the normal range
26. Has radiographic evidence of encasement or invasion of a major blood vessel, or of intratumoral cavitation
27. Has prolongation of QTc interval to >480 ms
28. Has clinically significant cardiovascular disease within 12 months
29. Has serious nonhealing wound, ulcer, or bone fracture
30. Has GI malabsorption
31. Has active hemoptysis
32. Has had esophageal or gastric variceal bleeding within the last 6 months (G only)
Cohort D2:
33. Has had previous systemic therapy for advanced or unresectable biliary tract cancer
Cohort F:
34. Has a history of class II-IV congestive heart failure or myocardial infarction within 6 months
Cohort H:
35. Has disease suitable for local therapy administered with curative intent
36. Is receiving hemodialysis
Cohort I:
37. Has mucinous, germ cell, or borderline tumor of the ovary
38. Has ongoing Grade 3 or 4 toxicity, excluding alopecia, following chemotherapy administered during the Lead-in Period
39. Has received colony-stimulating factors within 4 weeks prior to receiving chemotherapy during the Lead-in Period
40. Is considered to be of poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection
41. Has had surgery <6 months prior to screening to treat borderline tumors, early stage EOC or early stage fallopian tube cancer
42. Has uncontrolled hypertension
43. Has current, clinically relevant bowel obstruction (incl. subocclusive disease), abdominal fistula or gastrointestinal perforation, related to underlying EOC
44. Has a history of hemorrhage, hemoptysis or active gastrointestinal bleeding within 6 months prior to allocation
45. Has received prior treatment for any stage of OC
46. Is a participant for whom intraperitoneal chemotherapy is planned or has been administered as 1L therapy
47. Has severe hypersensitivity (>=Grade 3) to pembrolizumab, carboplatin, paclitaxel, or bevacizumab and/or any of their excipients
48. Has resting ECG indicating uncontrolled, potentially reversible cardiac conditions, as judged by the investigator or participant has congenital long QT syndrome
49. Had either major surgery within 3 weeks of allocation or has not recovered from major surgery

Cohort J:
50. Has squamous cell or undifferentiated gastric cancer
51. Has preexisting peripheral neuropathy >Grade 1
52. Has had previous therapy for locally advanced, unresectable or metastatic gastric cancer
53. Has received prior therapy with an agent directed to a stimulatory or co-inhibitory T-cell receptor

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-12-2021
Enrollment:	12
Type:	Actual

Medical products/devices used

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

Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	N/A
Generic name:	Vibostolimab/Pembrolizumab co-formation

Ethics review

Approved WMO Date:	28-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-12-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	29-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2023
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	CTIS2023-505284-36-00
EudraCT	EUCTR2021-001009-56-NL
ClinicalTrials.gov	NCT05007106
CCMO	NL77693.056.21