A Phase 2, Multicenter, Multi Arm, Study to Evaluate MK-1308A (Coformulated quavonlimab (MK-1308)/pembrolizumab) Versus Other Treatments in Participants with Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Stage IV Colorectal Cancer: (MK-1308A-008)

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This study has been transitioned to CTIS with ID 2022-502100-70-00 check the CTIS register for the current data. The aim of this research is:1. To test the safety of MK-1308A, MK-4280A, MK-7684A and MK 4830 + pembrolizumab against pembrolizumab as...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53742

Source
ToetsingOnline

Brief title
MK1308A-008

Condition

- Other condition
- Miscellaneous and site unspecified neoplasms benign

Synonym
dMMR (Mismatch Repair Deficient) colorectal cancer, metastatic colorectal cancer

Health condition

darmkanker

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Colorectal cancer, MK-1308A, Phase 2

Outcome measures

Primary outcome

Objective (Cohort B): To compare MK-1308A, MK-4280A, MK-7684A,

MK-4830+Pembrolizumab, and pembrolizumab mono-therapy with respect to Objective

Response Rate per RECIST 1.1 as assessed by Blinded Independent Central Review

Secondary outcome

To evaluate Duration of Response

To compare MK-1308A, MK-4280A, MK-7684A, MK-4830+Pembrolizumab, and

pembrolizumab monotherapy with respect to Progression-Free Survival

To compare MK-1308A, MK-4280A, MK-7684A,MK-4830+Pembrolizumab, and

pembrolizumab monotherapy with respect to Objective Response Rate

To compare MK-1308A, MK-4280A, MK-7684A, MK-4830+Pembrolizumab, and

pembrolizumab monotherapy with respectt o Overall Survival

To evaluate the safety and tolerability of MK-1308A, MK-4280A, MK-7684A,

MK-4830+Pembrolizumab, and compared to pembrolizumab

monotherapy

Study description

Background summary

CRC is a serious, life-threatening condition. he incidence of CRC reported in 2018 was ~1.8M (~10% of all cancers), and the number of worldwide cancer-related deaths due to CRC was ~881,000, making it the second leading cause of cancer death worldwide. Stage at diagnosis is the most important predictor of survival. The 5-year relative survival rate for CRC was approximately 64% with only 14% for distant disease (22% of CRC patients at diagnosis). Mismatch repair deficient or MSI-H CRC comprises approximately 15% of CRC. While dMMR/MSI-H CRC has a prognostic advantage in earlier stage disease, this advantage is less pronounced upon disease recurrence (worse PFS and OS). In previous studies, pembrolizumab monotherapy showed significant efficacy in 1L or 2L+, however, even with this improvement in outcomes, there remains a need for
still more progress. Another unmet need is treatment options for patients who initially respond to pembrolizumab monotherapy, but whose disease subsequently progresses despite continued treatment.

Therefore, it might be beneficial to make use of different effects on the immune system from different pathways by adding a second checkpoint inhibitor. This study investigates the potential benefit of the combination of pembrolizumab with Quavonlimab, Favezelimab, Vibostolimab and MK-4830 (coformulations)

Study objective

This study has been transitioned to CTIS with ID 2022-502100-70-00 check the CTIS register for the current data.

The aim of this research is:
1. To test the safety of MK-1308A, MK-4280A, MK-7684A and MK 4830 + pembrolizumab against pembrolizumab as the single agent.
2. To test how well MK-1308A, MK-4280A, MK-7684A and MK-4830 + pembrolizumab are tolerated by participants versus pembrolizumab alone.
3. To test how well MK-1308A, MK-4280A, MK-7684A and MK-4830 + pembrolizumab work against pembrolizumab alone.
4. See if participants receiving MK-1308A, MK-4280A, MK-7684A, or MK-4830 + pembrolizumab live longer compared to participants receiving pembrolizumab alone.
5. See if participants receiving MK-1308A, MK-4280A, MK-7684A, or MK-4830 + pembrolizumab have a better quality of life compared to participants receiving pembrolizumab alone.
6. Measure what happens as the study drugs pass through the body.
7. Seeing how the immune system responds to the study drugs.

Study design

This is a randomized, multicenter, open-label, phase 2 trial of multiple investigational agents for the treatment of patients with chemotherapy-naïve chemotherapy-naïve colorectal cancer with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) stage IV colorectal cancer .

After a screening period of up to 28 days, participants will be randomized 1:5 to 1 of the following groups from Cohort B. (The Netherlands does not participate in Cohort A). In the Netherlands approximately 3 participants will participate in the study.

• Group 1. The people in this group receive only pembrolizumab every 6 weeks.
• Group 2. The people in this group receive the study drug MK-1308A (quavonlimab + pembrolizumab) every 6 weeks
• Group 3. The people in this group receive the study drug MK-4280A (favezelimab + pembrolizumab) every 3 weeks.
• Group 4. The people in this group receive the study drug MK-7684A (vibostolimab + pembrolizumab) every 3 weeks.
• Group 5. The people in this group receive the study drug MK-4830 together with pembrolizumab every 3 weeks.

All study drugs will be administered through an IV. MK-4830 and pembrolizumab are administered via a separate infusion. Pembrolizumab is given first. After this, about 30 minutes later, MK-4830 is given. All other study drugs will be given through a single infusion. Treatment with pembrolizumab alone and MK-1308A is given up to 17 times. Treatment with MK-4280A, MK-7684A and MK-4830+pembrolizumab is given up to 35 times.

Adverse reactions will be monitored throughout the study and graded in severity according to the guidelines outlined in the NCI CTCAE v5.0. Each participant will be checked for AE's and SAE'

Intervention

Cohort B:
- Pembro monotherapy: 400 mg - IV -Q6W up to 17 doses

- MK1308A - 25 mg/400 mg - IV - Q6W up to 17 doses

- MK4280A - 800 mg MK- 4280 + 200 mg MK- 3475 ; IV ; Q3W up to 35 doses

- MK7684A - 200 mg MK- 7684 + 200 mg MK- 3475 ; IV ; Q3W up to 35 doses

- MK4830 + Pembro; 800 mg MK- 4830 + 200 mg MK- 3475 ; IV ; Q3W up to 35 doses

Study burden and risks

For this study, patients will be subjected to invasive procedures such as blood collection, Biopsy, CT-MRI or bone scans, physicalexams, 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. It cannot be guaranteed that participants in clinicalstudies will directly benefit from study intervention during participation, as clinical studies are designed to provide information aboutthe safety and effectiveness of an investigational medicine.

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. Has a histologically confirmed diagnosis of Stage IV CRCadenocarcinoma
2. Has locally confirmed dMMR/MSI-H.
3. Has untreated Stage IV dMMR/MSI-H CRC with no prior chemotherapy or immunotherapy for this disease.
4. Is male or female and at least 18 years of age at the time of providing documented informed consent.
5. Has a life expectancy of at least 3 months.
6. Has ECOG Performance Status of 0 to 1 at Screening and within 3 days before Cycle 1 Day 1 treatment.
7. A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies:
• Not a WOCBP
OR
• A WOCBP and uses a contraceptive method that is highly effective, or be abstinent from heterosexual intercourse as their preferred and usual lifestyle
9. The participant (or legally acceptable representative) has provided documented informed consent/assent for the study. The participant may also provide consent/assent for FBR. However, the participant may participate in the study without participating in FBR.
10. Have measurable disease per RECIST 1.1 as assessed by the site and verified by BICR. Lesions situated in a previously irradiated area are considered measurable if progression has been shown in such lesions.
11. Submit an archival (within 5 years of Screening) or newly obtained tumor tissue sample that has not been previously irradiated;
12. Have adequate organ function.

Exclusion criteria

1. Has received prior therapy with an agent directed to another stimulatory or coinhibitory T-cell receptor (eg, PD 1, CTLA-4, OX-40, CD137, PD-L1, ILT-4, LAG-3, TIGIT).
2. Has received prior systemic anticancer therapy including investigational agents within 4 weeks before the first dose of study intervention.
3. If the participant had a surgery and they have not recovered adequately from the procedure and/or any complications from the surgery before starting study intervention.
4. Has received prior radiotherapy within 2 weeks of start of study intervention.
5. Has received a live or live-attenuated vaccine within 30 days before the first dose of study intervention.
6. Is currently participating in or has participated in a study of an investigational agent or has used an investigational device within 4 weeks before the first dose of study intervention.
7. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the first dose of study medication.
8. Has a known additional malignancy that is progressing or has required active treatment within the past 2 years.
9. Has known active CNS metastases and/or carcinomatous meningitis. Participants with previously treated brain metastases may participate provided they are radiologically stable, (ie, without evidence of progression) for at least 4 weeks by repeat imaging
10. Has severe hypersensitivity (>=Grade 3) to pembrolizumab, quavonlimab, favezelimab, vibostolimab, MK-4830, and/or any of their excipients.
11. Has an active autoimmune disease that has required systemic treatment in past 2 years
12. Has a history of (noninfectious) pneumonitis that required steroids or has current pneumonitis.
13. Has a history of acute or chronic pancreatitis.
14. Has neuromuscular disorders associated with an elevated creatine
15. Has urine protein >=1 g/24h.
16. Has an active infection requiring systemic therapy (eg, tuberculosis, known viral or bacterial infections, etc.).
17. Has a known history of HIV infection.
18. Concurrent active Hepatitis B and Hepatitis C virus infection.
19. Has clinically significant cardiac disease, including unstable angina, acute myocardial infarction within 6 months from Day 1 of study intervention administration.
20. Has present or progressive accumulation of pleural, ascitic, or pericardial fluid requiring drainage or diuretic drugs within 2 weeks before randomization/allocation.
21. 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 for the full duration of the study, or is not in the best interest of the participant to participate, in the opinion of the treating investigator.
22. Has a known psychiatric or substance abuse disorder that would interfere with the participant's ability to cooperate with the requirements of the study.
23. Has had an allogenic tissue/solid organ transplant.

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):	14-04-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	KEYTRUDA
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	N/A
Generic name:	Favezelimab /Pemrbolizumab co-formulation

Product type:	Medicine
Brand name:	N/A
Generic name:	Quavonlimab /Pemrbolizumab co-formulation
Product type:	Medicine
Brand name:	N/A
Generic name:	Vibostolimab/Pemrbolizumab co-formulation

Ethics review

Approved WMO Date:	16-01-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	14-04-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-05-2023
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2022-502100-70-00
EudraCT	EUCTR2020-005114-18-NL
ClinicalTrials.gov	NCT04895722
CCMO	NL82990.041.22