A PHASE II, RANDOMIZED, ACTIVE-CONTROLLED, MULTI-CENTER STUDY COMPARING THE EFFICACY AND SAFETY OF TARGETED THERAPY OR CANCER IMMUNOTHERAPY GUIDED BY GENOMIC PROFILING VERSUS PLATINUM-BASED CHEMOTHERAPY IN PATIENTS WITH CANCER OF UNKNOWN PRIMARY SITE WHO HAVE RECEIVED THREE CYCLES OF PLATINUM DOUBLET CHEMOTHERAPY

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Study MX39795 will compare the efficacy and safety of molecularly-guided therapy versusstandard platinum-containing chemotherapy in patients with poor prognosis cancer of unknown primary site(CUP; non-specific subset) who have achieved disease...

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

Summary

ID

NL-OMON55349

Source
ToetsingOnline

Brief title
MX39795 CUPISCO

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer, solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: Sponsor

Intervention

Keyword: CUP, Genomic profiling, Phase II

Outcome measures

Primary outcome

To evaluate the efficacy of molecularlyguided therapy versus platinum

chemotherapy in term of Progressionfree survival in patients with CUP

whose best response to 3 cycles of platinum induction chemotherapy was assessed

CR, PR or SD

Secondary outcome

To evaluate the efficacy of molecularly guided therapy versus platinum

chemotherapy in terms of overall survival, objective response rate, duration of

response and disease control rate.

For further objectives and details see: Synopsis Table 1

Study description

Background summary

Cancer of unknown primary site (CUP) is defined as a histologically-confirmed metastatic cancer for which a standardized diagnostic work-up fails to identify the site of origin at the time of diagnosis.
A standardized diagnostic work-up in this context includes mainly:
•*A histopathological review of biopsy material using immunohistochemistry (IHC)
•*A detailed medical history of the patient
•*A complete physical examination (including pelvic and rectal examination)
•*A full blood count and biochemistry analysis
•*Urinalysis and stool occult blood tests
•*A computed tomography (CT) scan of the thorax, abdomen and pelvis
•*A mammography scan and breast MRI (in certain cases)
CUP accounts for 3% to 5% of all malignancies. The disease has a median age of occurrence of approximately 60 years, is rare in children, and is marginally more frequentin males. Survival of patients with CUP is poor, with a median overall survival (OS) of 8-11 months and a one-year survival rate of 25%.

For more information about the background see section 1 of the protocol

Study objective

Study MX39795 will compare the efficacy and safety of molecularly-guided therapy versus
standard platinum-containing chemotherapy in patients with poor prognosis cancer of unknown primary site
(CUP; non-specific subset) who have achieved disease control (CR, PR or SD) after 3 cycles of first-line platinum based induction chemotherapy.
Molecularly-guided therapies will include 8 targeted cancer therapy regimens and 2 cancer immunotherapy regimens, and will be chosen based on each patient*s comprehensive genomic profile (see below for further details).

For specific information about the objectives zie table 4 of the protocol

Study design

Study MX39795 is a phase II, randomized, open-label, active-controlled, multi-center trial. The study will consist of a Screening Period, an Induction Period including an End of Induction Workup, a Pre-Treatment Work-up, a Treatment Period, an End of Treatment Visit occurring 30 (± 7) days from last treatment or at initiation of other anti-cancer therapy (whichever occurs first), and a Follow-Up Period. The first day of treatment during the Induction Period will be Day 1 (baseline) of the study.

For a schematic overview of the study design see figure 2 of the protocol

Intervention

Patients will be treated with 3 cycles of chemotherapy in the induction phase of the study. In the treatment phase subjects will be treated with either chemotherapy or one of the targeted therapies. Depending on results from the induction phase, randomization and genomic profiling.

Study burden and risks

The general burden for the patiënt consists, a.o., of bloodsamples (every cycle), possible collection of a tumorsample, and the administration of chemotherapy and specific investigational products (every cycle, depending on the phase of the study the patient is in) that may lead to various adverse events.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age >=18 years
• Histologically-confirmed unresectable CUP
• At least one lesion that is measurable according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1)
• Availability of a tumor Formalin-fixed paraffin-embedded(FFPE) block <=4 months old at Screening that is expected to be sufficient and suitable (in quantity and quality) for generation of a Foundation medicine tissue biopsy assay comprehensive genomic profile at a central reference pathology laboratory
• Availability of test reports confirming local CUP diagnosis If test reports confirming local CUP diagnosis are not available, an FFPE block must be submitted that is sufficient to allow for central confirmation of CUP diagnosis
• No prior systemic therapy for the treatment of CUP
• Prior local intratumoral therapy may be accepted. If prior local intratumoral therapy, at least one of the measurable lesion(s) must have not benefited from local intratumoral therapy
• ECOG performance status of 0 or 1
• Life expectancy >=12 weeks
• Eligible for platinum-based chemotherapy
• Adequate hematologic and end-organ function
• Use of appropriate contraceptive methods

Exclusion criteria

- Squamous cell CUP
- Patients with histology and immunohistology profiles (per 2015 ESMO guidelines) that are not adenocarcinoma or poorly differentiated carcinoma / adenocarcinoma)
- Patient with an immunohistochemistry profile that provides a definitive clinical indication of a primary cancer with a specific treatment
-Patients who can be assigned to a specific subset of CUP for which a specific treatment is recommended by the 2015 ESMO Clinical Practice Guidelines for CUP or with a clinical and IHC profile indicative of a specific primary tumor are also excluded. These are:
- Poorly differentiated carcinoma with midline distribution
- Women with papillary adenocarcinoma of the peritoneal cavity
- Women with adenocarcinoma involving only the axillary lymph nodes
- Squamous cell carcinoma of the cervical lymph nodes
- Poorly differentiated neuroendocrine tumors

- Men with blastic bone metastases and elevated PSA
- Patients with a single, small, potentially resectable tumor
- Colon cancer-type CUP
- CK7 positive, CK20 negative and TTF-1 positive tumors in a context suggestive of lung adenocarcinoma or thyroid cancer, IHC profile definitely indicative of breast cancer OR an IHC profile indicative of breast cancer and either a history of breast cancer or lymph nodes in the drainage areas of the breast, high-grade serious carcinoma histology and elevated CA125 tumor marker and/or a mass in the gynecological tract or any tumor mass or lymph node in the abdominal cavity, IHC profile suggestive of renal cell carcinoma and renal lesions, with a Bosniak classification higher than IIF, IHC profile compatible with cholangiocarcinoma or pancreatobiliary and 1 or 2 liver lesions without extrahepatic disease or with only pulmonary metastases and/or lymph nodes in the drainage areas of the liver

-Known presence of brain or spinal cord metastasis (including metastases that have been
irradiated only), as determined by CT or magnetic resonance imaging (MRI) evaluation during screening

-History or known presence of leptomeningeal disease

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):	25-02-2020
Enrollment:	20

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alecensa
Generic name:	Alectinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Avastin
Generic name:	Bevacizumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cotellic
Generic name:	Cobimetinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tarceva
Generic name:	Erlotinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-08-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-10-2019
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-10-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	23-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2020
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:	28-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	25-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-11-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-04-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-09-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	26-03-2023
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Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-04-2023
Application type:	Amendment
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Application type:	Amendment
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Application type:	Amendment
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Approved WMO Date:	23-10-2023
Application type:	Amendment
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Approved WMO Date:	08-11-2023
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
EudraCT	EUCTR 2017-003040-2-NL
ClinicalTrials.gov	NCT03498521
CCMO	NL69436.056.19