Adjuvant dendritic cell based immunotherapy (DCBI) after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal mesothelioma

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To assess the feasibility of administering DCBI after CRS-HIPEC in patients with malignant peritoneal mesothelioma.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mesotheliomas
Study type	Interventional

Summary

ID

NL-OMON48572

Source
ToetsingOnline

Brief title
MESOPEC

Condition

- Mesotheliomas

Synonym
asbestos cancer, peritoneal mesenthelioma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,KWF Kankerbestrijding;Stichting Coolsingel

Intervention

Keyword: dendritic cell, immunotherapy, malignant peritoneal mesothelioma

Outcome measures

Primary outcome

The aim of this phase II study is to determine the feasibility of adjuvant DCBI

with injection of MesoPher in patients with MPM after CRS-HIPEC.

Secondary outcome

Secondary endpoint of this study is safety of this therapy, which has already

been proven in patients with pleural mesothelioma. Another secondary endpoint

is the determination of an immunological response against the tumor as result

of the adjuvant therapy.

Study description

Background summary

Malignant peritoneal mesothelioma (MPM) is an uncommon but aggressive neoplasm, related to asbestos exposure. MPM has low survival rates of approximately one year, even after palliative surgery and/or systemic chemotherapy. Recent advancement in treatment strategies that focus on cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have resulted in improved median survival of 53 months and a 5-year survival of nearly 50%. However, recurrence rates are high. Current systemic chemotherapy in the adjuvant setting is of limited efficacy, while immunotherapy with dendritic cell based immunotherapy (DCBI) has yielded promising results in murine models with peritoneal mesothelioma and in patients with pleural mesothelioma.

Study objective

To assess the feasibility of administering DCBI after CRS-HIPEC in patients with malignant peritoneal mesothelioma.

Study design

An open-label single-centre phase II study.

Intervention

4 to 6 weeks before CRS-HIPEC a leukapheresis is performed of which the monocytes are used for differentiation to dendritic cells (DCs) using specific cytokines. Pulsed autologous DCs (MesoPher) are re-injected 8-10 weeks after surgery, 3 times every two weeks. After the third injection with MesoPher, revaccinations to boost the immune system are given after 3 and 6 months.

Study burden and risks

Patients have to undergo extra outpatient visits for this study and extra invasive procedures especially for this trial, like an intravenous catheter. These are invasive procedures but risks are limited. This IV entrance is necessary, for the leukapheresis, for blood samples and for the injection of the DCs. A leukapheresis is a standard procedure and will be performed according to standard procedures. There is a limited risk for transient thrombocytopenia and leukopenia. During the leukapheresis patients can experience palpitations, increased heartrate, a decrease in blood pressure and dizziness. All of these complaints are transient. In addition, there is a low risk of a calcium reduction. If patients experience complaints, extra calcium may be administered to the patient.
The administration of autologous cells, that have been loaded with allogeneic human materials, is a potential risk and that is one subject of the study. Because not the lysate itself is administered to the patients but only when it is processed by the dendritic cells of the patient we expect these risks to be limited. Pervious clinical studies showed that injection with tumor lysate-pulsed autologous DCs was overall well tolerated without systemic toxicity, with the exception of a low-grade flu-like symptoms like fever and rigors.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Patients with a histologically confirmed diagnosis of malignant peritoneal mesothelioma
• Patients must be at least 18 years old and must be able to give written informed consent
• Patients must be ambulatory (WHO-ECOG performance status 0 or 1) and in stable medical condition
• Patients must have normal organ function and adequate bone marrow reserve: absolute neutrophil count >1.0 *109/l, platelet count >100*109/l and Hb >6.0mmol/l
• Ability to return to the study center for adequate follow-up and vaccinations
• Positive DTH skin test (induration > 2mm after 48 hrs) against at least one positive control antigen tetanus toxoid.
• Written informed consent according to the ICH-GCP
• Planned start date of vaccination within 8-10 weeks after CRS-HIPEC
• The expected survival must be at least 6 months
• Ability to return to the Erasmus MC for adequate follow-up as required by this protocol

Exclusion criteria

4.3 Exclusion criteria A potential participant who meets any of the following criteria will be excluded from participation in the study: • Extra-abdominal disease/ metastatic disease • Medical or psychological impediment to probable compliance with the protocol • Current use of steroids or other immunosuppressive agents. Patients must have had six weeks of discontinuation before the first vaccination and must stop any such treatment during the time of the study on the basis of potential immune suppression. Prophylactic usage of dexamethasone during chemotherapy is excluded from that 6 weeks interval. • Prior cytoreductive surgery • Subject with any previous malignancy except adequately treated basal cell or squamous cell skin cancer, superficial or in-situ cancer of the bladder or other cancer for which the subject has been disease-free for at least 3 years or a malignancy that requires no active treatment. • Serious concomitant disease or active infections • History of auto-immune disease or organ allografts, or with active or chronic infection, including HIV and viral hepatitis • Serious intercurrent chronic or acute illness such as pulmonary (COPD or asthma) or cardiac (NYHA class III or IV) or hepatic disease or other illness considered by the study coordinator to constitute an unwarranted high risk for CRS-HIPEC or investigational DC treatment • Pregnant or lactating women • Inadequate peripheral vein access to perform leukapheresis • Concomitant participation in another clinical trial • An organic brain syndrome or other significant psychiatric abnormality which would comprise the ability to give informed consent, and preclude participation in the full protocol and follow-up • Absence of assurance of compliance with the protocol • Patients with a known allergy to shell fish (may contain KLH)

Study design

Design

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

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	28-03-2018
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	08-02-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2017-000897-12-NL

Register	ID
ClinicalTrials.gov	NCT02395679
CCMO	NL60856.000.17

Study results

Date completed:	24-05-2023
Actual enrolment:	18