Intraperitoneal Paclitaxel for Patients with Primary Malignant Peritoneal Mesothelioma - a Phase I/II Dose Escalation and Safety Study

Published: 21-09-2021
Last updated: 09-11-2024

This study has been transitioned to CTIS with ID 2024-516738-36-00 check the CTIS register for the current data. The primary purpose of this study is to determine the maximum tolerable dose (MTD) of IP monotherapy with paclitaxel for patients with...

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

Summary

ID

NL-OMON56619

Source
ToetsingOnline

Brief title
INTERACT MESO

Condition

- Mesotheliomas

Synonym
asbestos cancer, Peritoneal mesothelioma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Erasmus Foundation

Intervention

Keyword: Dose-escalation study, Intraperitoneal chemotherapy, Malignant Peritoneal Mesothelioma

Outcome measures

Primary outcome

The primary endpoint of the study is to determine the maximum tolerable dose (MTD) of intraperitoneal (IP) paclitaxel monotherapy, for patients with malignant peritoneal mesothelioma (MPM) who are not eligible to undergo CRS-HIPEC.

Secondary outcome

- Safety: toxicity assessment according to CTCAE version 5.0

- Feasibility: the treatment will be considered feasible if at least 50% of patients are able to finish 75% (i.e. 6) of total planned cycles (i.e. 8).

- Pharmacokinetic profile: intraperitoneal and systemic pharmacokinetic measurements will be obtained during the first and fourth treatment cycle, at time points prior to infusion, at the end of peritoneal infusion as well as every hour up to patients discharge.

Study description

Background summary

Malignant Peritoneal Mesothelioma (MPM) is a rare, but unfortunately very aggressive cancer with a poor prognosis. Currently, the only possibly curative treatment is cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC). However, the majority of patients are not eligible to undergo this treatment, mainly due to extensive local disease. Currently, a

palliative treatment with low morbidity is not available. Overall response rates to systemic chemotherapy are low, though morbidity rates are high. Immunotherapy presents similar shortcomings, as the morbidity rate is comparable to that of systemic chemotherapy, while its benefit for MPM patients is not proven. Especially given the high morbidity rate, and the limited effectiveness of systemic treatment with either immunotherapy or chemotherapy, there is lack of treatments suitable as palliative treatment for patients with MPM. Thereby, the majority of MPM patients currently receive no anti-tumor treatment.
As MPM very rarely disseminates outside the abdominal-cavity, the use of intraperitoneal (IP) chemotherapy seems a logical and promising step. This therapy can be delivered through an IP port-a-cath (PAC), and potentially has major advantages over systemic treatment. A higher, more effective dose of chemotherapy can directly be delivered at the site of disease, while systemic uptake is limited likely resulting in fewer toxicity. In rare cases where metastases do develop, a switch can be made to systemic treatment. By first applying local treatment, most patients will be spared a toxic and often ineffective systemic therapy. Another major advantage of the suggested approach is that ascites, a common MPM-symptom that causes major morbidity, can be drained through the same PAC-system. Paclitaxel is a well-known chemotherapeutic agent and is considered extremely favorable for IP use. To date, there are no studies investigating IP chemotherapy in MPM patients.

Study objective

This study has been transitioned to CTIS with ID 2024-516738-36-00 check the CTIS register for the current data.

The primary purpose of this study is to determine the maximum tolerable dose (MTD) of IP monotherapy with paclitaxel for patients with MPM. Secondary objectives are to assess safety and feasibility of this strategy, and to study the pharmacokinetics of paclitaxel in this setting. The broader, long-term aim of this research, is to provide a better palliative treatment for patients with MPM, resulting in less toxicity, improved quality of life, and possibly prolonged survival.

Study design

We will conduct a classic three-plus-three dose escalation study with three dose levels. In short: Three patients are initially enrolled into a given dose cohort. If there is no dose limiting toxicity (DLT) observed in any of these patients, the trial proceeds to enroll additional patients to the next higher dose cohort. If one patient develops a DLT at a specific dose level, three additional subjects are enrolled into that same dose cohort. Development of a DLT in more than 1 patient in a specific dose cohort (>=33%) suggests that the MTD has been exceeded, and further dose escalation is not pursued. The previous

dose is considered the MTD. When the MTD is found, an expansion of 3-6 more patients in that dose cohort will be performed, to achieve a total number of 9 patients treated at the MTD-level.

Intervention

Patiënts undergo a diagnostic laparoscopy (DLS) according to standard work-up for CRS-HIPEC. If the disease is considered not resectable, a peritoneal PAC will be placed during DLS. Through this PAC intraperitoneal paclitaxel will be administered weekly (dosage according to dose-escalation schedule). The number of cycles depends on toxicity and response to the treatment. The first response evaluation is scheduled after 8 cycles. There is no limit to the number of cycles, in case of continuing response to treatment. During the first and the fourth cycle, additional blood samples and IP-fluid samples will be collected for pharmacokinetic analysis.

Study burden and risks

The intervention is an alternative for the standard of care with systemic chemotherapy. Patients who participate will receive a peritoneal access port, that will be implanted subcutaneously. This will be done during diagnostic laparoscopy, which is part of standard of care. Patients do not have to undergo extra surgery. There is a small chance of complications due to the peritoneal port, like (wound)infection or obstruction. However, experience from an ongoing study with the same type of peritoneal access port (INTERACT study) shows that there are no or few complications of the peritoneal port. The most important risk of participation is the occurrence of toxicity due to the administration of intraperitoneal chemotherapy. However, administration of intraperitoneal chemotherapy is expected to cause less toxicity than the current systemic chemotherapy. The current systemic treatment consists of cycles of 3 weeks, with a maximum of 6 cycles. Patients who participate in this study will have additional hospital visits. Also, they will have to undergo additional invasive procedures, like venapunction or intravenous catheter. The risks of these procedures are limited.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL
Scientific

Erasmus MC, Universitair Medisch Centrum Rotterdam

Dr. Molewaterplein 40
Rotterdam 3015 GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Histological confirmed diagnosis of malignant peritoneal mesothelioma • Patients that are not eligible (or willing) to undergo cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) • Age >= 18 years old • Written informed consent according to the ICH-GCP and national/local regulations • Patients must be ambulatory (WHO-ECOG performance status 0 or 1) • Ability to return to the Erasmus MC for adequate follow-up as required by this protocol • Patients must have normal organ function and adequate bone marrow reserve as assessed by the following laboratory requirements; absolute neutrophil count >1.5 * 10^9/l, platelet count >100*10^9/l and Hemoglobin >6.0mmol /l. Patients must have a Bilirubin < 1* x upper limit of normal (ULN), Serum AST and ALT < 2.5 x ULN

Exclusion criteria

• Extra-abdominal disease/metastatic disease established by preoperative CT-scan of thorax-abdomen and/or PET-scan. Imaging not older than two months at time of surgery
• Medical or psychological impediment to probable compliance with the protocol
• 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 participation in this study
• Pregnant or lactating women; for all women of child-bearing potential a negative urine pregnancy test will be required as well as the willingness to use adequate contraception during the study until 4 weeks after finishing treatment
• Absence of assurance of compliance with the protocol
• 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

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-03-2022
Enrollment:	21
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	21-09-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-11-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-11-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	CTIS2024-516738-36-00
EudraCT	EUCTR2021-003637-11-NL
CCMO	NL78373.078.21
Other	NL9718