Fase I/II trial with melphalan for percutaneous chemosaturation (CS-PHP-Mephalan) in treating irresectable liver metastases

Published: 26-11-2013
Last updated: 15-05-2024

Primary objective * To determine the overall response rate of two PHP with an interval of at least 6 weeks and 3 mg/kg melphalan in irresectable liver metastases patients.* To determine the percentage of patients qualifying for resection. Secondary…

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

Summary

ID

NL-OMON41379

Source
ToetsingOnline

Brief title
CS-PHP-Melphalan

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Metastases
- Hepatobiliary therapeutic procedures

Synonym
irresectable hepatic metastases, liver metastases

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: chemosaturation, hepatic perfusion, percutaneous

Outcome measures

Primary outcome

Primary endpoints

* Response rate expressed by RECIST criteria, after two percutaneous liver

perfusions with melphalan and a six week interval

* Number of curative resections after percutaneous perfusion

Secondary outcome

Secondary endpoints

* Safety of percutaneous liver perfusions with the Delcath 2nd generation system

* Overall survival and overall progression free survival

* Duration of response and duration of stable disease

* Quality of life

Study description

Background summary

Malignancies of the liver are the third most important cause of cancer-related deaths in the world. This kind of cancer can be primary (origin in the liver) of secondary (metastases from another part of the body). The most common form of primary liver cancer is the hepatocellular carcinoma (HCC) en the most common form of secondary liver cancer are metastases of colorectal carcinoma (CRCLM). About 30-50% of all patients with colorectal cancer, develop liver metastases synchronous: 14.5-25%, metachronous: 14.5-25%).

Patients with liver metastases of colorectal carcinoma often have a bad prognosis, and for these patients surgical resection is the only curative option, despite the constant innovations in chemotherapy. The surgical treatment offers an acceptable morbidity, mortality and the 5-year survival is around 40-50%. Unfortunately only 20-25% of the patients with CRCLM qualify for surgery. The other patients can only be treated with chemotherapy. A part of the patients treated with chemotherapy and with initially irresectable metastases, become operable because of the response to chemotherapy. The disadvantage of systemic administration of chemotherapy in the treatment of liver metastases is that, because of systemic toxicity, the maximum tolerated dose is reached earlier than the minimum effective dose. To accomplish better results with patients with irresectable metastases confined to the liver, isolated hepatic perfusion (IHP) has been developed. The principle of IHP is to shut the liver off of the systemic circulation by performing an operation. Subsequently the liver is flushed for an hour with a very high dose of chemotherapy, which would be toxic and lead to fatal complications when administered systemic. Then the liver is connected to the systemic circulation again. Because this procedure is associated with considerable morbidity (20%) and mortality (7%), a new procedure was developed by Delcath in which the hepatic perfusion can be performed percutaneous. Expected is that both morbidity and mortality will decrease significantly. In addition, this procedure can be performed several times.

Study objective

Primary objective
* To determine the overall response rate of two PHP with an interval of at least 6 weeks and 3 mg/kg melphalan in irresectable liver metastases patients.
* To determine the percentage of patients qualifying for resection.
Secondary Objective
* To assess safety of PHP using the Generation 2nd Delcath system in patients with irresectable liver metastases.
* To determine the overall survival and overall progression free survival
* To determine the duration of response and duration of stable disease
* To determine the quality of life after two percutaneous liver perfusions.

Study design

When all inclusion and exclusion criteria are met, a percutaneous hepatic perfusion will be performed twice, with a at least 6 week interval between the first and the second procedure.

Intervention

When all inclusion and exclusion criteria are met, a percutaneous hepatic perfusion will be performed twice, with an at least 6 week interval between the

first and the second procedure. The perfusion procedure is extensively described in the protocol.

Study burden and risks

Instead of systemic chemotherapeutics, the patients receives isolated hepatic perfusion twice, and one angiography.
This treamtent constists of less day admited in hospital, and no systemic effect of chemotherapeutics.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Liver metastases of histologically confirmed primary colorectal adenocarcinoma
- Resection of primary tumor > 1 month before IHP
- Irresectable metastases confined to the liver based on CT-Thorax/abdomen and PET imaging
- Metastases measurable on CT-scan
- Informed consent
- Life expectancy > 4 months
- Leukocytes * 3.0 X 10^9/L
- Thrombocytes * 100 X 10^9/L
- Creatinine clearance * 40 ml/min
- Bilirubin <17 µmol/L
- APTT < 32.5 sec
- PT < 13.7 sec

Exclusion criteria

- Biological age <18 and >75 years
- WHO performance status * 2 (Appendix A)
- < 40% healthy liver tissue
- Aberrant vascular anatomy, which impedes IHP (e.g. aberrant right or left hepatic artery, severe atherosclerosis, vascular dissections)
- Severe comorbidity (e.g. cardiovascular disease, diabetes with nephropathy, active infections, other liver disease)
- Incompetent / Mentally disabled
- Pregnancy, inadequate anticonception

Study design

Design

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

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	05-03-2014
Enrollment:	36
Type:	Actual

Medical products/devices used

Generic name:	Delcath generation 2 system
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-11-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-06-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28533
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL45013.058.13
OMON	NL-OMON28533