Preventing liver recurrence after partial hepatectomy for intrahepatic cholangiocarcinoma using adjuvant hepatic arterial infusion pump chemotherapy - PUMP IV trial

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

Summary

ID

NL-OMON57237

Source
ToetsingOnline

Brief title
PUMP IV trial

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
bile duct cancer, Intrahepatic cholangiocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: het KWF kankerfonds

Intervention

Keyword: HAIP chemotherapy, Intrahepatic cholangiocarcinoma

Outcome measures

Primary outcome

The main trial endpoint is the rate of recurrence of iCCA in the liver after

two years.

Secondary outcome

Secondary endpoints will be: complications after the surgery to remove the

iCCA, complications from the chemotherapy (FUDR), the rate of recurrence of the

cancer in general, quality of life, cost-effectiveness of HAIP chemotherapy,

and biomarkers in the blood to predict effectivity of HAIP chemotherapy.

Study description

Background summary

Intrahepatic cholangiocarcinoma (iCCA), a type of liver cancer in the bile ducts of the liver, has a 30% survival rate after resection, and about two-thirds of patients face a recurrence, often (approx. 80%) in the liver. Hepatic arterial infusion pump (HAIP) chemotherapy, delivering a drug called floxuridine (FUDR) directly to the liver, has shown a 60% success rate in controlling unresectable iCCA . This method aims to reduce liver recurrence by targeting occult micrometastases left after resection. FUDR, administered this way, reaches very high concentrations in the tumour without causing widespread side effects. The hypothesis of this trial is that the hepatic recurrence free survival time will increase in patient treated with HAIP chemotherapy.

Study objective

The aim of this study is to find out whether the addition of HAIP chemotherapy with floxuridin in patients with operable iCCA is effective, i.e. the time to recurrence is longer than with standard care.

Study design

A prospective multicentre single arm phase II trial, where patients receive surgery and as an addition HAIP chemotherapy.

Intervention

During the resection of iCCA, there will be a subcutaneous chemopump implanted. By means of this chemopump, a chemotherapeutical agent called Floxuridin will be administered to the liver tumour through a small catheter. A maximum of 4 cycles of floxuridin will be given to a trial subject (=16 weeks of treatment).

Study burden and risks

The intervention (HAIP chemotherapy) is an addition to the standard care.

Burden related to surgery:
During the liver resection a subcutaneous pump will be implanted. Surgical complications related to HAIP pump placement are uncommon (+/-10%), and include hepatic artery thrombosis, hepatic artery dissection, and bleeding at the site of catheter insertion, catheter dislocation, pump dysfunction, pump migration (flipping), pump pocket infection, pump pocket seroma, and pump pocket hematoma.

Burden related to imaging:
Prior to the first administration of HAIP chemotherapy, a nuclear scan is performed to confirm adequate blood flow in the liver and rule out leakage of chemotherapy outside of the liver. The radiation dose of the scan is low.
CT-scans of the chest and abdomen during treatment and follow-up are performed every 6 months after operation in the first and second year and every year thereafter until the end of follow-up after 5 years.

Burden related to HAIP chemotherapy administration:
Two additional hospital visits per cycle are required for HAIP chemotherapy. A maximum number of 4 cycles will be administered with a maximum of 8 additional visits. At each visit a blood sample of 50 mL will be taken to evaluate toxicity. HAIP chemotherapy toxicity is mainly biliary sclerosis (5.5%), which is largely avoided by monitoring of liver tests and dosages adjustments. In case of increased liver function test that may reflect impending biliary obstruction, high dose of dexamethasone is administered through the pump. Systemic side effects with HAIP chemotherapy of floxuridin are rare (<1%).

Burden related to Quality of Life questionnaires:
All patients will be asked to complete Quality of Life (QoL) questionnaires questionnaire at five time points (baseline, 3, 6, 9 and 12 months (+/- 30 days)) during the first year of this trial. After 1 year of follow up the questionnaires will be taken annually.

Burden related to biomarker assessments:
Five blood samples are scheduled with a total volume of 150 ml. The time points of the biomarker assessments are:
• The day of surgery before incision
• During surgery directly drawn from the hepatic vein
• At the start of HAIP chemotherapy
• After the last cycle of HAIP chemotherapy
• At one year after surgery or once recurrence of iCCA occurs

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

- Age >= 18 years.
- ECOG performance status 0 or 1
- Diagnosis of resectable iCCA on imaging. No histological confirmation is needed before surgery, according to standard of care.
- Patient is able to undergo a laparotomy.
- Positioning of a catheter for HAIP chemotherapy is technically feasible based on a CT-scan with early arterial phase with 1mm cuts. The default site for the catheter insertion is the GDA. Accessory or aberrant hepatic arteries are no contraindication for catheter placement.

- Adequate bone marrow, liver, and renal function as assessed by the following laboratory requirements to be conducted within 30 days prior to inclusion:

+ Absolute neutrophil count (ANC) >= 1.5 x 109/L
+ White blood cell count (WBC) >= 2.5 x 109/L
+ Platelets >= 100 x 109/L
+ Glomerular filtration rate (GFR) >= 30 ml/min
+ Haemoglobin (Hb) >= 5.5 mmol/L
+ Total bilirubin <= 25 µmol/L

- Written informed consent must be given according to ICH/good clinical practice (GCP), and national/local regulations.

Exclusion criteria

- Presence of extrahepatic disease at the time of first presentation. Patients with locoregional lymph node disease or with small (<= 1 cm) extrahepatic lesions that are too small to characterise are eligible.
- Second primary malignancy, except for adequately treated non-melanoma skin cancer, or other malignancy treated at least 3 years previously without evidence of recurrence or with a life expectancy longer than 5 years.
- Known homozygous dihydropyrimidine dehydrogenase (DPYD) deficiency.
- Prior hepatic radiation, ablation, or resection for iCCA.
- Clinical evidence of portal hypertension (ascites, gastroesophageal varices, or portal vein thrombosis). Some postoperative ascites is allowed.
- (Partial) portal vein thrombosis in future liver remnant.
- Pregnant or lactating women.
- History of psychiatric disability judged by the investigator to be clinically significant, precluding informed consent or interfering with compliance for HAIP chemotherapy.
- Serious concomitant systemic disorders that would compromise the safety of

the patient or his/her ability to complete the study, at the discretion of the investigator.
- Organ allografts requiring immunosuppressive therapy.
- Chronic treatment with corticosteroids (dose of >=10 mg/day methylprednisolone equivalent excluding inhaled steroids).
- Serious infections (uncontrolled or requiring treatment).
- Participation in another interventional study for iCCA with survival as outcome.
- Participation in another prospective study with an interventional medical product.
- Any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	40
Type:	Anticipated

Medical products/devices used

Generic name:	IP2000V
Registration:	No

Ethics review

Approved WMO Date:	27-08-2024
Application type:	First submission
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
CCMO	NL86208.078.24