Hepatic arterial infusion pump chemotherapy in patients with unresectable intrahepatic cholangiocarcinoma

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The aim of the study is to demonstrate that HAIP chemotherapy is an effective treatment for unresectable intrahepatic cholangiocarcinomas.

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

Summary

ID

NL-OMON52590

Source
ToetsingOnline

Brief title
Hepatic Arterial Infusion Pump chemotherapy for unresectable ICC.

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
Unresectable intrahepatic cholangiocarcinoma; unresectable bileduct cancer in the liver.

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Dutch Cancer Society (KWF)

Intervention

Keyword: Hepatic arterial infusion pump chemotherapy, Intrahepatic cholangiocarcinoma, Phase II study, Unresectable

Outcome measures

Primary outcome

The primary objective of this study is to evaluate efficacy, expressed by OS, of HAIP chemotherapy and concurrent systemic chemotherapy in patient with unresectable ICC in the Netherlands

Secondary outcome

Secondary objectives include postoperative complications, chemotherapy related adverse events, 2-, 3- and 5-years OS, progression free survival (PFS), response rate, conversion to resection rate, quality of life, and cost-effectiveness. The accuracy of CT angiography to detect extrahepatic perfusion will be measured. Next, we aim to identify predictive biomarkers for the efficacy of HAIP chemotherapy.

In 5 patients at Erasmus MC, we aim to perform a PSMA PET-CT/MRI to measure PSMA expression in ICC tumours.

Study description

Background summary

Intrahepatic cholangiocarcinoma (ICC) is the second most prevalent primary liver cancer after hepatocellular carcinoma, and is increasing in incidence. ICC makes up about 10% of all cholangiocarcinomas. It is an aggressive malignancy that arises from the epithelium of bile ducts. ICC is most prevalent in East Asian, with incidences ranging from 10 to 71 per 100.000 persons.(2, 3)

A correlation with diseases causing biliary inflammation, such as primary sclerosing cholangitis has been noted. The incidence of ICC in the western world countries is approximately 1 per 100.000.

Complete resection remains the only curative option, which is only feasible in the minority of patients (15%). Resection results in a median survival of less than 3 years. Most of ICCs, however, present at an advanced unresectable stage with limited treatment options due to the usually clinically silent progression, and consequently its late manifestation. Overall survival (OS) of patient with unresectable ICCs is reported to be 5 months without treatment and approximately 1 year with systemic chemotherapy. The five year survival rate is approximately 5%. Currently used treatment regimens consist of gemcitabine and cisplatin, which offers minimal OS benefit over gemcitabine monotherapy (11.7 versus 8.1 months, respectively). Another trial found similar results of 11.2 and 7.7 respectively (not significant, however, due to lack of power). Previous results are similar to other gemcitabine-based regimes, such as gemcitabine and oxaliplatin. A post-hoc analysis of 34 patients with unresectable liver only ICC, treated with gemcitabine and cisplatin, showed 3-years OS of 0%. More effective therapies are needed to improve survival.

Study objective

The aim of the study is to demonstrate that HAIP chemotherapy is an effective treatment for unresectable intrahepatic cholangiocarcinomas.

Study design

Patients with an unresectable intrahepatic cholangiocarcinoma are included in the study, provided they give oral and written consent. In addition to the regular systemic chemotherapy, the study subjects will receive an operation for the placement of the infusion pump and will subsequenty undergo 6 consecutive cycles (4 weeks per cycle) of chemotherapy via the infusion pump.

Intervention

Operation for placement of the infusion pump. 2 to 4 weeks later, patients with 6 consecutive cycles (4 weeks per cycle) of chemotherapy via the pump.

Study burden and risks

Patients will be hospitalised for 4 days to surgically place the pump and to provide the technetium99-labeled macoaggreted albumin scan. After the operation, 6 cycles of chemotherapy are administered subcutaneously into pump. This regimen will be followe in conjunction to the regular chemotherapy. For these 6 cycles 12 outpatient appointments are necessary, which are combined

with the regular appointments for systemic chemotherapy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age >= 18 years.
• ECOG performance status 0 or 1
• Histologically confirmed diagnosis of intrahepatic cholangiocarcinoma (ICC).
• Unresectable ICC confined to the liver (<70% of the liver involved) with or without limited regional lymph node disease (portal) at initial presentation, as confirmed by HPB surgeons. Regional lymph nodes will be allowed, provided it is potentially amenable to resection.
Unresectability confirmed:
o Radiologically
o Or during surgical exploration in patients initially considered candidates

for resection
• Patient is able to undergo a laparotomy or minimal-invasive surgery for pump placement.
• Positioning of a catheter for HAIP chemotherapy is technically feasible (see chapter 5) based on a CT with excellent arterial phase. The default site for the catheter insertion is the gastroduodenal artery (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:
o Absolute neutrophil count (ANC) >= 1.5 x 109/L
o White blood cell count (WBC) >= 2.5 x 109/L
o Platelets >= 100 x 109/L
o Glomerular filtration rate (GFR) >= 50 ml/min
o Haemoglobin (HB) >= 5.5 mmol/L
o Total bilirubin <= 25 µmol/L

Exclusion criteria

•Presence of extrahepatic disease at the time of first presentation. Patients with limited (portal) lymph node disease, patients with small (<= 1 cm) extrahepatic lesions that are too small to characterize 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 DPYD deficiency. Patients with intermediate DPYD metabolism (DPD activity score: 1.5) are eligible and a 50% reduced starting dose of floxuridine will be administered by discretion of the medical oncologist.
• Prior hepatic radiation, ablation, or resection for cholangiocarcinoma.
• Life expectancy of less than 12 weeks.
• Clinical evidence of portal hypertension (ascites, gastroesophageal varices, or portal vein thrombosis). Surgically related ascites is allowed.
• (Partial) portal vein thrombosis.
• 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.
• Serious, non-healing wound, ulcer, or bone fracture.
• 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 ICC 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:	Recruiting
Start date (anticipated):	17-12-2019
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	FUDR
Generic name:	Floxuridine

Ethics review

Approved WMO

Date:	15-08-2019
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-11-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-02-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2022
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

ID: 23810
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-004013-41-NL
CCMO	NL70452.078.19
OMON	NL-OMON23810