A Randomized Phase II Study of Systemic Chemotherapy with or without HAI FUDR/Dexamethasone in Patients with Unresectable Intrahepatic Cholangiocarcinoma

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This study has been transitioned to CTIS with ID 2024-518065-10-00 check the CTIS register for the current data. The aim of the study is to demonstrate that HAI P chemotherapy is an effective treatment for unresectable intrahepatic...

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

Summary

ID

NL-OMON56819

Source
ToetsingOnline

Brief title
PUMP RCT

Condition

- Hepatobiliary neoplasms malignant and unspecified
- 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: Memorial Sloan Kettering Cancer Center
Source(s) of monetary or material Support: Ministerie van OC&W,Grant vanuit National Institutes of Health (NIH)

Intervention

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

Outcome measures

Primary outcome

Compare the progression-free survival (PFS) of HAI FUDR/Dex in combination with

systemic GemOx versus systemic GemOx only.

Secondary outcome

1. Compare the overall survival in first-line HAI FUDR/Dex in combination with

GemOx versus systemic GemOx only.

2. Estimate the overall response rate (CR+PR) between treatment groups.

3. Estimate the time to first recurrence patterns between treatment groups.

4. Describe the toxicity rates separately for each treatment groups.

5. Define the mutational pattern of IHC and determine the extent to which

genomic features and intratumoral heterogeneity correlate with treatment

response and survival.

6. Assess cfDNA and correlate with treatment response and survival outcomes.

7. Assess tumor heterogeneity and correlation with treatment response using

quantitative imaging techniques (radiomics).

8. Assess the correlation between texture features and intratumoral

heterogeneity

Study description

Background summary

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy 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 the biliary tract. ICC is most common in East Asia, with incidences ranging from 10 to 71 per 100,000 people. An association has been established with diseases that cause biliary inflammation, such as primary sclerosing cholangitis. The incidence of ICC in the western world countries is about 1 per 100,000.
Complete resection remains the only curative option, but is feasible in a minority of patients (15%). Resection results in a median survival of less than 3 years. However, most patients with ICCs present with an ICC in an advanced unresectable stage because of the usually clinically silent progression of the disease. For unresectable ICCs, treatment options are limited. The overall survival (AO) of a patient with an unresectable ICC is 5 months without treatment and approximately 1 year with systemic chemotherapy. The 5-year survival is about 5%. The current treatment regimens used consist of gemcitabine and cisplatin, which offer minimal AO advantage over gemcitabine monotherapy (11.7 vs 8.1 months, respectively). Another study found comparable results of 11.2 and 7.7 respectively (not significant, however due to lack of power). Previous results are comparable to other gemcitabine-based regimens, such as gemcitabine and oxaliplatin. A post-hoc analysis of 34 patients with unresectable
(liver only) ICC treated with gemcitabine and cisplatin showed a 3-year survival of 0%. More effective therapies are needed to improve survival.

Study objective

This study has been transitioned to CTIS with ID 2024-518065-10-00 check the CTIS register for the current data.

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

Study design

Multicenter, prospective randomized controlled phase II trial

Intervention

Chemo pump placement surgery. 2 to 4 weeks later, patients start with 6 consecutive courses (4 weeks per course) of chemotherapy via the pump.

Study burden and risks

Patients will be hospitalized for 4 days to surgically place the pump and to provide the technetium99-labeled albumin scan. After the operation, 6 cycles of chemotherapy are administered subcutaneously into pump. This regimen will be followed 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)
Elderly (65 years and older)

Inclusion criteria

1. Age >=18 years.
2. ECOG 0-1.
3. Histologically confirmed intrahepatic cholangiocarcinoma (also variously reported as peripheral cholangiocarcinoma, cholangiolar carcinoma or cholangiocellular carcinoma) (IHC). Confirmation of the diagnosis at MSKCC or at the enrolling institution must be obtained prior to randomization.
4. Clinical or radiographic evidence of metastatic disease confined to the liver. Note: presence of regional (porta hepatis) lymph node metastases will be allowed, provided they are amenable to resection. (Note: If peritoneal or other extrahepatic disease is found at time of pump placement, the pump will not be implanted. The patient will be removed from study, deemed nonevaluable and will not count toward the overall study accrual.)
5. Radiographically measurable disease. Measurable disease is defined as disease that can be assessed with 2-dimensional measurements on a cross-sectional imaging. Minimum lesion size is 2 cm in greatest diameter as per RECIST criteria.
6. Disease must be considered unresectable at the time of preoperative evaluation.*
7. Considered candidate for general anesthesia, abdominal exploration and hepatic artery pump placement.
8. Patients with chronic hepatitis and/or cirrhosis are eligible, but must be Child-Pugh class A.
9. WBC >= 2,000/mcL , ANC >= 1000/mcL
10. Platelet count >= 75,000/mcL
11. Creatinine <= 1.8 mg/dL
12. Total bilirubin < 1.5 mg/dL
13. Hgb > 7 g/dL

Exclusion criteria

1. Presence of distant metastatic disease. Patients will undergo radiographic evaluation to exclude the possibility of distant metastatic disease. For patients who have undergone pre- or post-operative biopsies that definitively diagnose IHC, the diagnostic studies may be modified at the discretion of the MSKCC Principal Investigator. Clinical or radiographic evidence of metastatic disease to regional lymph nodes will be allowed, provided it is amenable to resection.
2. Patients previously treated with systemic chemotherapy for IHC will be non-eligible.
3. Prior treatment with FUDR.
4. Prior external beam radiation therapy to the liver.
5. Prior ablative therapy to the liver.

6. Diagnosis of sclerosing cholangitis.
7. Clinical evidence or portal hypertension (ascites, gastroesophageal varices, or portal vein thrombosis; surgically related ascites does not exclude the patient).
8. Active infection within one week prior to HAI placement.
9. Pregnant or lactating women.
10. History of other malignancy within the past 3 years except with early stage/localized cancer that was surgically resected or radiation treatment that would yield the same result as surgery within the past 3 years.
11. Life expectancy <12 weeks.
12. Inability to comply with study and/or follow-up procedures.
13. History of peripheral neuropathy.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2024
Enrollment:	60
Type:	Anticipated

Medical products/devices used

Generic name:	IP2000V implantable infusion pump
Registration:	No
Product type:	Medicine
Brand name:	FUDR

Generic name:	Floxuridine

Ethics review

Approved WMO Date:	10-01-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-06-2024
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
EU-CTR	CTIS2024-518065-10-00
EudraCT	EUCTR2022-002851-21-NL
ClinicalTrials.gov	NCT04891289
CCMO	NL82386.078.24