Second-line chemotherapy FOLFIRINOX in unresectable cholangiocarcinoma

Published: 09-12-2015
Last updated: 19-04-2024

Pilot study:Primary objective: feasibilitySecondary objectives: response rate, time to progression, overall survival and quality of life.Phase II study:Primary objective: efficacy.Secondary objectives: toxicity, especially grade 3 and 4 toxicities,...

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

Summary

ID

NL-OMON42542

Source
ToetsingOnline

Brief title
4CC

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified

Synonym
Bile duct and gallbladder cancer; cholangiocarcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: biliary tract neoplasms, FOLFIRINOX, secondline, unresectable cholangiocarcinoma

Outcome measures

Primary outcome

Pilot study: toxicity

Phase II study: response rate.

Secondary outcome

Pilot study: response rate, time to progression, overall survival and quality

of life.

Phase II study: toxicity, especially grade 3 and 4 toxicities, time to

progression, overall survival and quality of life.

Study description

Background summary

Cholangiocarcinoma is a malignant gastrointestinal tumor of low incidence with a poor prognosis. Chemotherapy is the most common treatment for advanced disease. On the basis of a phase III clinical study, cisplatin plus gemcitabine is considered standard first-line treatment in advanced cholangiocarcinoma patients, but there is no established second-line therapy.
Since 5- fluorouracil (5-FU) and leucovorin combined with irinotecan and oxaliplatin (FOLFIRINOX) appears to be safe and demonstrated efficacy in clinical studies of advanced pancreatic cancer, colorectal cancer and cholangiocarcinoma patients participating in a phase I study of solid tumors, the combination could be an effective second-line treatment for patients with advanced cholangiocarcinoma.

Study objective

Pilot study:
Primary objective: feasibility
Secondary objectives: response rate, time to progression, overall survival and

quality of life.

Phase II study:
Primary objective: efficacy.
Secondary objectives: toxicity, especially grade 3 and 4 toxicities, time to progression, overall survival and quality of life.

Study design

Two steps design.
Step 1: pilot study, inclusion of 10 patients.
Step 2: phase II study, inclusion of 20 patients

Step 2 will be initiated if, :
1. at least 1 out of 10 patients in the pilot study show an objective response and/or if at least 2 out of 10 patients show stable disease.
2. within the first 42 days (6 weeks) of treatment with FOLFIRINOX, maximal 3 patients out of 10 are admitted to the hospital as a result of treatment or if maximal 3 patients out of 10 die or develop febrile neutropenia. Hospital admission for treatment of biliary tract complications (e.g. biliary tract obstruction) or death due to biliary tract complications will be not considered in this futility analysis.
3. If more than 4 out of 10 patients require a dose reduction as a result of toxicity within the first 42 days (6 weeks) and if there is enough response to FOLFIRINOX treatment (as described above in item 1), the step 2 of this study (phase II study) will be initiated with standard dose reduction (modified FOLFIRINOX).

Intervention

Oxaliplatin 85 ml/m2, irinotecan 180 mg/m2 and leucovorin 400 mg/m2 every 2 weeks. Fluorouracil 400 mg/m2 followed by a continuous infusion of 2400 mg/m2 over a 46-hour period will be administrated at cycle 1. Beginning with cycle 2, the 5-FU continuous-infusion dose will be adjusted based on 5-FU plasma concentrations until the therapeutic range (AUC 20-25 mg.h.L-1) will be reached.

Study burden and risks

The treatment applied has a high risk of side effects, but also a chance for response. A wide variety of possible side effects are mentioned in the protocol (page 27) and in the patient information sheet (page 8). Most side effects are temporary and recover after cessation of treatment or dose reduction. For the treatment, the patient will visit the hospital regularly. In order to avoid the unnecessary exposure to this treatment, patients undergo regular evaluation scans to assess the effect of the treatment. This allows a limitation of

unnecesarry exposure to the treatment and a limitation of possible sideeffects.
One of the drugs (5-FU) is given continuously during a 46 hours period,a central venous access (eg, a PICC line or a port-a-cath) is standardly placed. This is a small procedure with the advantage that patients do not have to stay in hospital.
Also, there is already a lot of experience with this treatment in large groups of patients (patients with pancreatic carcinoma), but there is little experience with this treatment in the group of cholangio- and glablaascarcinoom patients. Therefore, in a small group of patients (10) we will test the feasibility of the treatment before this treatment will be given in a larger group of patients (20 patients).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AX
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Histological or cytological diagnosis of cholangiocarcinoma. Histological diagnosis is needed if a patient wants to participate in the translational study (see section 11).
- Metastatic disease or unresectable locally advanced cholangiocarcinoma.
- Measurable disease according RECIST criteria version 1.1.
- Age from 18 up to 75 year.
- ECOG performance status 0-1.
- Patients who received at least 3 cycles of gemcitabine/cisplatin in the first-line.
- Adequate hematological function (WBC > 3.0 x 109/L, platelets > 100 x109/L)
- Adequate hepatic function (bilirubin * 1.5 x upper normal limit (ULN); ALAT or ASAT <5x ULN in case of liver metastases and < 2.5 x ULN in absence of liver metastases.
- Adequate renal function (creatinine clearance > 60 ml/min; creatinine <120 µmol/L)
- Absence of cardiac insufficiency, chest pain (not medically controlled) and myocardial infarction in the 12 months preceding study entry.
- Written informed consent.

Exclusion criteria

- Concurrent secondary malignancies or other malignancies within 3 years prior to enter this study with the exception of non-metastatic basal cell or squamous cell skin cancer or carcinoma in situ of the cervix treated by cone-biopsy or resection
- Presence of cerebral or meningeal metastases
- Hypersensitivity to the active substance of oxaliplatin, leucoverin,irinotecan and/ or 5-FU or to any of excipients used in these drugs as described in Summary of Product Characteristics (SPCs).
- History of chronic diarrhea or colorectal inflammatory conditions
- Active infection or other serious underlying conditions which may prevent the patient from receiving the planned treatment. For example: prolonged unresolved bacterial cholangitis with destruction of bile duct branches (e.g. after endoprothesis insertion) or two or more periods of cholangitis in the last 6 months. Patients with other active or uncontrolled severe infection, cirrhosis or chronic active hepatitis will be excluded.
- Presence of cardiac insufficiency, unstable angina pectoris, symptomatic congestive heart, failure myocardial infarction 6 months prior to randomization, serious uncontrolled cardiac arrhythmia.

- Patients with peripheral sensory neuropathy with functional impairment prior to the first cycle of FOLFIRINOX.
- Bone marrow depression after radiotherapy or treatment with other antineoplastic drugs, defined as baseline values neutrophils <2 x 109 / L and / or platelets <100 x 109 / L.
- Current iInclusion in another investigational clinical trial of cancer treatment.
- Patients who use Azole antifungals and/or anti-cancer medication at inclusion (see section 6.1.6). Patients who use brivudine, sorivudine and there analogs. Patiënt with concomitant use of St. John's wort preparations.
- Pernicious anemia or other anaemias due to vitamin B 12 deficiency.
- Males who wish to have children while receiving this chemotherapy or within 6 months after the end of participation in this study.
- Women who are pregnant, breast-feeding or not using adequate contraceptive
- Age younger than 18 or older than 75 years
- ECOG performance status >1.
- Incapacitated persons who are not able to provide consent.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5-fluorouracil
Generic name:	Adrucil
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Irinotecan
Generic name:	Camptosar
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Leucovorin
Generic name:	Metafolin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Eloxatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTRNL2015-001378--NL
ClinicalTrials.gov	NCT02456714
CCMO	NL53822.018.15