Ablation with irreversible electroporation in patients with advanced perihilar cholangiocarcinoma - a multicenter phase I/II safety study

Published: 19-04-2016
Last updated: 15-05-2024

This study is primarily set up to investigate the safety and feasibility of IRE for the treatment of unresectable, locally advanced or nodal metastasized PHC. The efficacy of IRE will also be studied.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON50469

Source
ToetsingOnline

Brief title
ALPACA study

Condition

- Hepatic and hepatobiliary disorders

Synonym
Klatskin tumor, perihilar bile duct tumor, Perihilar cholangiocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,AngioDynamics, het bedrijf dat de NanoKnife heeft ontwikkeld, stelt de elektrodenaalden voor de IRE procedures ter beschikking.

Intervention

Keyword: Ablation, Advanced, Irreversible electroporation, Perihilar cholangiocarcinoma

Outcome measures

Primary outcome

The primary outcome is safety, defined as the total number of clinically relevant complications (Common Terminology Criteria for Adverse Events [CTCAE], score of 3 or higher) within 90 days post-IRE.

Secondary outcome

Secondary outcomes are the success rate of completing IRE, intra-procedural complications related to IRE, duration of hospital stay, quality of life, impact of IRE on post-procedural CT imaging and blood biomarker response, time between IRE and start of palliative chemotherapy, metal stent patency, progression-free and overall survival.

Study description

Background summary

The majority of patients with perihilar cholangiocarcinoma (PHC) have locally advanced disease or lymph node metastases upon presentation or exploratory laparotomy, which makes resection not amenable. As the prognosis of patients with locally advanced PHC (LAPHC) or PHC with lymph node metastases in the palliative setting is significantly better compared to patients with organ metastases, ablative therapies may be beneficial.
Unfortunately, current ablative techniques are limited. Photodynamic therapy causes skin phototoxicity and thermal ablative methods, such as stereotactic body radiation therapy and radiofrequency ablation, are affected by a heat/cold-sink effect when tumors are located close to vascular structures,

such as the liver hilum. These limitations may be overcome by irreversible electroporation (IRE), which is a relatively new, non-thermal ablative method that is currently being studied in several other soft tissue tumors, such as pancreatic adenocarcinoma.

Study objective

This study is primarily set up to investigate the safety and feasibility of IRE for the treatment of unresectable, locally advanced or nodal metastasized PHC. The efficacy of IRE will also be studied.

Study design

A multicenter phase I/II safety study.

Intervention

Computed tomography-guided percutaneous IRE (N=11)
Open IRE (N=1), inclusion in this group closed

Study burden and risks

The risks associated with participation in this study are the adverse events of the procedure (i.e. cardiac arrhythmias, perforation, bile leakage, portal vein thrombosis, bleeding, intra-abdominal abscess, infections). The risk of this study is classified as 'high'. A potential benefit can be that patients will have an improvement of several months in progression-free and potentially overall survival. The second potential benefit can be that biliary stents will be patent for a longer period of time.

The potential risks associated with NanoKnife treatment are considered acceptable in this selected group of unresectable patients. Previous analysis of patients with unresectable PHC at the AMC has shown a median overall survival of 14 and 16 months for lymph node metastasized and locally advanced disease, respectively. Some of these patients had long-term survival of more than 36 months. Compared to a median overall survival of 3 and 5 months for patients who receive palliative chemotherapy for liver- and extrahepatic metastases, respectively, patients with earlier stages seem to have biologically more favorable tumors with indolent growth. When these patients are no candidates for liver transplantation, they may potentially benefit from local ablative therapies in combination with palliative chemotherapy.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Age 18 years or older
* Capable of providing written and oral informed consent
* WHO *2
* Meets criteria for advanced PHC
o Local recurrent disease localized on the distal bile duct remnant, hepatico-jejunostomy or in the liver hilum without N2 lymph nodes or distant metastases .
* Diagnosis of PHC or lymph node metastases must be confirmed with endoscopic brush, percutaneous- or laparoscopic biopsy, whichever is suitable, o Vascular or lymph node (N2) involvement on imaging or during staging laparoscopy
Diagnosis of PHC or lymph node metastases beyond N2 stations must be confirmed with endoscopic brush,

percutaneous- or laparoscopic biopsy, whichever is suitable
o Vascular or lymph node (N2) involvement during exploratory laparotomy
Must be confirmed with intra-operative frozen section

Exclusion criteria

* Resectable PHC upon exploratory laparotomy
* Locally advanced PHC eligible for liver transplantation (Appendix 3)
* PHC with > 5 cm extension along the common hepatic duct or common bile duct
* Metastases to peritoneum, liver or other organs confirmed by percutaneous biopsy, staging laparoscopy or intraoperative frozen section
* Lymph node metastases beyond N2 stations (e.g. inguinal, mediastinal)
* History of cardiac arrhythmia*s (any of the following)
o Sinus tachycardia (BPM>100)
o Sick sinus syndrome
o Sinoatrial exit block
o AV block
o Sinus node reentry
o Presence of a pacemaker or defibrillator
* Recent history of myocardial infarction (<6 maanden)
* Uncontrolled hypertension (blood pressure must be *160/95 mmHg at the time of screening on a stable antihypertensive regimen
* Uncontrolled infections (> grade 2 NCI-CTC, version 3.0)
* Epilepsy
* Both narrowing (sclerosis) of the portal vein and a reduced diameter of either the common hepatic artery, celiac trunk or superior mesenteric artery of >50%
* Any condition that is unstable or that could jeopardize the safety of the subject and their compliance in the study

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):	31-01-2017
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	19-04-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-06-2019
Application type:	Amendment
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

ID: 25184
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL56231.018.15
OMON	NL-OMON25184