The RALLY study: dose finding study for radiation lobectomy using holmium-166 microspheres to improve resectability in patients with HCC.

Published: 14-09-2021
Last updated: 04-04-2025

Primary Objective:To establish the maximum tolerated healthy liver-absorbed dose of 166Ho-microspheres in patients with HCC who receive RL as a bridge to resection.Secondary Objective(s): 1) To establish dose-response relationships between:a. The...

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

Summary

ID

NL-OMON54237

Source
ToetsingOnline

Brief title
RALLY

Condition

- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary neoplasms malignant and unspecified
- Hepatobiliary therapeutic procedures

Synonym
hepatocellular carcinoma, liver cancer (hepatoma)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,Quirem Medical BV,Quirem Medical BV verschaft de holmium microsferen voor zowel proefbehandeling (=scout) als therapeutische behandeling

Intervention

Keyword: Hepatocellulaire carcinoom, Holmium-166, radiation lobectomie

Outcome measures

Primary outcome

The maximum tolerated radiation dose will be determined using the CTCAE v5.0 methodology. Toxicities exceeding grade 3 that were deemed definitely, probably or possibly related to the administration of 166Ho-microspheres will be defined as a dose-limiting toxicity (DLT). Exceptions will be made for the expected lymphopenia, elevated liver enzymes and post-embolization syndrome. FLR response will be assessed using HBS.

Secondary outcome

Tumour response will be evaluated using the mRECIST criteria. QoL will be assessed using the questionnaire EORTC QLQ C30 and HCC18 as well as the BPI questionnaire.

Study description

Background summary

Radiation lobectomy (RL) as a means of controlling tumour growth while concomitantly inducing future liver remnant (FLR) hypertrophy has recently gained interest to convert unresectable hepatocellular carcinoma (HCC) patients. Dosimetry is of major importance here, since particularly healthy liver-absorbed dose drives FLR response. However, current techniques using

yttrium-90 (90Y) beta-radiation emitting microspheres, cannot be visualised properly. This makes it difficult to accurately predict healthy liver-absorbed dose. RL using holmium-166 (166Ho) offers a potentially more safe, effective and personal treatment modality, due to its variety of imaging options. However, the acceptable toxicity dose profile of 166Ho on healthy liver tissue in this setting is unknown.

Study objective

Primary Objective:
To establish the maximum tolerated healthy liver-absorbed dose of 166Ho-microspheres in patients with HCC who receive RL as a bridge to resection.

Secondary Objective(s):
1) To establish dose-response relationships between:
a. The perfused normal liver-absorbed dose and FLR response.
b. The tumour-absorbed dose and tumour response.
2) To establish the safety and feasibility of surgical resection of the irradiated lobe in converted patients.
3) To assess the quality of life of patients.
4) To generate a biobank of resected liver specimens and blood samples for future analyses of therapy surviving cancer cells.

Study design

Multicentre, interventional, non-randomized, open-label, non-comparative dose-escalation study. This study is a collaboration between UMC Utrecht, Erasmus MC Rotterdam, Amsterdam UMC, UMC Groningen, and MUMC The study will commence in the UMC Utrecht and will expand to other participating sites via amendments.

Intervention

Primary: RL with 166Ho microspheres administered via a catheter during angiography.
Secondary: (only if conversion to surgery) Surgical resection of the irradiated lobe, provided sufficient gain of function of the FLR has been attained and tumour anatomy still permits surgical resection.

Study burden and risks

Patients who enrol in the study will visit the hospital more frequently than standard care (portal venous embolization (PVE)). Patients will receive more scans and are asked to fill in questionnaire on QoL at every follow-up visit. RL as a means of inducing FLR growth is less well studied than PVE. Sufficient FLR growth cannot be guaranteed, and often takes longer than PVE. However,

patients included in this studied are in need of concomitant control of tumour burden. This makes RL an attractive alternative for these patients.

The most important side effects related of radioembolization are:
- Post-embolization syndrome (PES) is a common side effect of radioembolization. Its symptoms include nausea, vomiting, fever, right upper quadrant pain, and increased liver enzymes. PES is generally well tolerated and pain symptoms subside within 24 hours.
- Radioembolization-induced liver disease (REILD), occurs in 0-5% of radioembolization cases and can be life-threatening. Improved dosimetry and treatment planning using the newly developed 166Ho microspheres aims to prevent this. Treatment is symptomatic and mainly consists of high dose steroids.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study (including the biobank), a subject must meet all of the following criteria: 1) Patients must have given written informed consent. 2) Age >= 18 years. 3) ECOG Performance status 0-1 (Table 1). 4) Diagnosis of HCC, established according to the Netherlands HCC guideline criteria (in line with American AASLD criteria): nodule >1 cm in a patient at risk for HCC, with combination of arterial hypervascularity and venous or delayed phase wash-out on multiphase CT-scan or MRI-scan. 5) HCC with indication for major hepatectomy (i.e. >2 segments), as decided by multidisciplinary tumour board. 6) HBS > 1.5%/min/m2 and < 2.7 %/min/m2. 7) Negative pregnancy test for women of childbearing potential. Female patients of child- bearing potential should use an highly effective acceptable method of contraception (oral contraceptives, barrier methods, approved contraceptive implant, long-term injectable contraception, intrauterine device or tubal ligation) or should be more than one year postmenopausal or surgically sterile during their participation in this study (from the time they sign the consent form), to prevent pregnancy. 8) Patients with compensated Child-Pugh A and unilobar BCLC-B or less (without evidence of portal hypertension).

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study (including the biobank): 1) Evidence of extrahepatic disease (MRI-scan liver and multiphase abdominal CT as well as a thoracic CT are routinely performed at screening). 2) Any previous hepatic external beam radiation therapy before the start of study therapy. 3) Previous treatment with RE/RL. 4) Major surgery within 4 weeks or incompletely healed surgical incision before starting study therapy. 5) Glomerular filtration rate <35 ml/min, determined according to the Modification of Diet in Renal Disease formula. 6) Non correctable INR > 1.5. 7) Significant cardiac event (e.g. myocardial infarction, superior vena cava syndrome, New York Heart Association (NYHA) classification of heart disease >= 2 within 3 months before entry, or presence of cardiac disease that in the opinion of the investigator increases the risk of ventricular arrhythmia. 8) Pregnancy or breastfeeding. 9) Patients suffering from psychic disorders that make a comprehensive judgment impossible, such as psychosis, hallucinations and/or depression. 10) Patients who are declared incompetent. 11) Previous enrolment in the present study. 12) Patients who do not use an acceptable method of contraception during their participation in this study (from the time they sign the consent form) to prevent pregnancy. In case of female: are less than 1 year postmenopausal and not using an acceptable method of contraception. Patients who had surgical sterilization may be included. 13) Any contraindication precluding surgery, with the exception of insufficient FLR as defined by HBS. 14) Portal vein thrombosis (tumour and/or

bland) (diagnosed on contrast enhanced transaxial images). 15) Untreated active hepatitis. In case of detectable viral HBV hepatitis B virus load, treatment with a nucleos(t)ide analog such as entecavir or tenofovir should be instituted. 16) Transjugular intrahepatic portosystemic shunt. 17) Body weight over 150 kg (because of maximum table load). 18) Severe allergy for intravenous contrast (Visipaque®). 19) Lung shunt > 30 Gy, as calculated using 166Ho-microspheres scout dose using SPECT/CT. 20) Not correctable extrahepatic deposition of scout dose activity. Activity in the falciform ligament, portal lymph nodes and gallbladder is accepted. 21) Any systemic therapy (including transcatheter arterial chemoembolization) prior to the start of study therapy. RFA or previous resection (> 4 weeks) is accepted. 22) Leukocytes <2 109/L and/or platelet count <50 109/L. Serum bilirubin >34.2 micromol/L (2 mg/dL).

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-08-2022
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	Quirem Scout and QuiremSpheres
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	14-09-2021

Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	03-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-07-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2025
Application type:	Amendment
Review commission:	METC NedMec

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: 23909
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL75713.041.21
Other	NL8902