Real-time MR imaged treatment with holmium microspheres of patients with primary liver cancer; a single center, interventional, non-randomized, feasibility study

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To investigate the safety and feasibility of a personalized Ho-166-PLLA-MS TARE approach by using MRI guidance in inoperable patients with HCC.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON51293

Source
ToetsingOnline

Brief title
EMERITUS-2

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Hepatobiliary neoplasms malignant and unspecified

Synonym
Hepatocellular carcinoma, Liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Bedrijven,Terumo

Intervention

Keyword: holmium-166, radioembolization, TARE

Outcome measures

Primary outcome

To determine the safety and feasibility of MRI guided administration of

Ho-166-PLLA-MS in patients.

Secondary outcome

Secondary endpoints include response at 3, 6 and 12 months, and overall

survival.

Study description

Background summary

Each year, worldwide over 600,000 people develop hepatocellular carcinoma (HCC). In case surgical or systemic therapies are not feasible, (loco)regional therapies such as transarterial radioembolization (TARE) may be used. TARE is a technique where radioactive microspheres are injected in the hepatic artery, which mostly supplies the tumours contrary to the healthy liver tissue, which is mostly supplied by the portal vein. The microspheres lodge in the microvasculature, selectively irradiating the tumour tissue. Patient outcome after TARE has been variable due to lack of tumor targeting. The Dosipshere-1 and SARAH study show that personalised TARE leading to a high tumour dose leads to better patient outcome. In order to be able to better visualise the distribution of microspheres, TARE microspheres with gamma emission and paramagnetic properties were developed. By administering holmium-microspheres (Ho-166-PLLA-MS) inside an MRI-scanner, the clinician can verify the distribution of microspheres in the liver while administering the microspheres, and adjust microsphere administration during treatment, leading to a more personalised approach to traditional TARE, and possibly better patient outcome.

Study objective

To investigate the safety and feasibility of a personalized Ho-166-PLLA-MS TARE approach by using MRI guidance in inoperable patients with HCC.

Study design

This is a single centre, interventional treatment, non-randomized, open label, dose escalation study with an investigational medical device in at least 9 patients (financing for 15 patients).
Patients will undergo interventional radiological placement of an MR opaque catheter, after which the patient is moved to the MRI, where administration of microspheres is performed under MRI guidance. Microsphere distribution will be evaluated regularly, and administration will be stopped after the healthy liver dose has been reached (40-60-80 Gy) or tumours are saturated with microspheres.

Intervention

Ho-166-PLLA-MS will be administered using a medical device via a catheter during MR imaging.

Study burden and risks

It is anticipated that treatment with radioactive microspheres will reduce tumour size and will improve quality of life as known from literature from holmium-166 and yttrium-90 TARE. Patient treatment will be planned with a maximal healthy liver dose different to conventional treatment (40-60-80 Gy), which could lead to additional burden to the patient (liver toxicity) but is expected to have a potential benefit to patients, since the administered dose will be monitored over time during treatment, and both tumour and healthy liver dose will be optimized.

The additional burden for patients participating in the study consists of treatment taking place at the MRI-scanner instead of the angio suite, as a result of which treatment will take approximately 60-90 minutes longer than usual. For treatment within this study, a total of 9 visits (one is a telephone call) is required, most of which are part of regular patient care. Multiple diagnostic scans will be performed outside regular patient care.

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. Diagnosis of hepatocellular carcinoma
2. At least one lesion of 10 mm or more in the longest diameter on contrast-enhanced MRI/CT
3. Patient is eligible for TARE as determined by the tumour board (in Dutch: MDO)
4. Patient has a life expectancy of 12 weeks or longer
5. Patient has a WHO performance score of 0-2

Exclusion criteria

1. Extrahepatic disease that cannot be targeted during the TARE session (enlarged lymph nodes in the liver hilus are allowed)
2. Radiation therapy, chemotherapy or major surgery within 4 weeks before treatment
3. Serum bilirubin > 2.0 x the upper limit of normal
4. ALAT, ASAT, alkaline phosphatase (AF) > 5x the upper limit of normal
5. Glomerular filtration rate (GFR-MDRD) <35 ml/min

6. Leukocytes <4.0 * 109/L or platelet count <60 * 109/L
7. Significant heart disease that in the opinion of the physician increases the risk of ventricular arrhythmia.
8. Pregnancy or breast feeding
9. Disease with increased chance of liver toxicity, such as primary biliary cirrhosis or xeroderma pigmentosum
10. Patients ineligible to undergo MR-imaging (claustrophobia, metal implants, etc)
11. Portal vein thrombosis of the main branch (more distal branches are allowed)
12. Evidence of clinically relevant, untreated portal hypertension combined with grade 3 oesophageal varices
13. Untreated, active hepatitis
14. Body weight > 150 kg (because of maximum table load)
15. Severe allergy for i.v. contrast (Iomeron, Dotarem and/or Primovist)
16. Lung shunt > 30 Gy, as calculated using scout dose 166Ho SPECT/CT.
17. Uncorrectable extrahepatic deposition of scout dose activity. Activity in the falciform ligament, portal lymph nodes or gallbladder are accepted.
18. Unstable final catheter position due to hepatic artery anatomy, which might lead to dislocation of the catheter during transfer to the MRI.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	05-07-2023
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	Q-suite
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	17-01-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-10-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL81813.091.22