Individualized dosimetry for holmium-166-radioembolization in patients with unresectable hepatocellular carcinoma; a multi-center, interventional, non-randomized, non-comparative, open label, early phase II study: iHEPAR

Published: 16-12-2021
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Primary objective:To establish the safety and toxicity profile of individualized 166Ho-RE in patients with hepatocellular carcinoma. Secondary objectives:• To evaluate efficacy of individualized 166Ho-RE.• To evaluate biodistribution / dosimetry.•...

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

Summary

ID

NL-OMON55061

Source
ToetsingOnline

Brief title
iHEPAR

Condition

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

Synonym
hepatocellular carcinoma, primary liver cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Quirem Medical B.V. verschaft de holmium microsferen voor zowel proefbehandeling (=scout) als therapeutische behandeling,Terumo Quirem Medical B.V.

Intervention

Keyword: hepatocellular carcinoma, holmium, individualized dosimetry, radioembolization

Outcome measures

Primary outcome

Safety, expressed as the rate of unacceptable toxicity.

Secondary outcome

• Tumor response.

• Biodistribution / Dosimetry.

• Changes in tumor marker alpha-fetoprotein (AFP).

• Quality of Life (QoL).

• Changes in hepatic function as determined by hepatobiliary scintigraphy.

• Changes in Child Pugh score.

• To compare study results with HEPAR Primary study results.

Study description

Background summary

Patients with hepatocellular carcinoma often die from intrahepatic disease

because current treatment options are limited. Local treatment using 166Ho-radioembolization (166Ho-RE) offers a safe and effective treatment. Because 166Ho-microspheres are used as a scout dose for treatment simulaton and for the actual treatment itself, a tailored approach can be used. This concept has proven to be more predictive than the 90Y-radioembolization concept (current standard-of-care), which is a based on a surrogate scout dose (i.e. 99mTc-MAA). A personal treatment plan may be used for 166Ho-radioembolization to optimize efficacy, based on scout dose distribution. However, individualized treatment planning inherently leads to treatment doses that deviate from the currently approved 'one-size-fits-all' approach (i.e. 60 Gy average absorbed dose for all patients). Therefore, safety of individualized 166Ho-RE will be evaluated first to validate safety and confirm safety thresholds. These thresholds will be used in subsequent randomized controlled studies.

Study objective

Primary objective:
To establish the safety and toxicity profile of individualized 166Ho-RE in patients with hepatocellular carcinoma.
Secondary objectives:
• To evaluate efficacy of individualized 166Ho-RE.
• To evaluate biodistribution / dosimetry.
• To evaluate tumor marker response.
• To evaluate quality of life.
• To evaluate hepatic function.
• To evaluate (de)compensation of the liver.
• To compare study results with HEPAR Primary study results (i.e. non-individualized 166Ho-RE).

Study design

Multi-center, interventional, treatment, non-randomized, open label, non-comparative, early clinical safety study. The study is a collaboration between UMC Utrecht and Erasmus MC Rotterdam. Recruitment and treatment of patients will take place in both centers.

Intervention

Individualized 166Ho-RE will be performed via a catheter during angiography. Dosimetry-based treatment planning will be individualized based on Q-Suite* software.

Study burden and risks

It is anticipated that treatment with radioactive microspheres will reduce tumor size and will improve quality of life. It is anticipated that the γ-

emission of the radioactive 166Ho will improve the safety of the procedure by enabling pre-treatment distribution analysis after scout dose imaging and subsequent dosimetry-based individualized treatment planning. Also the differences in specific activity of 166Ho-microspheres and the dose rate compared to the currently available 90Y-microspheres may theoretically improve tumor response and accordingly, liver specific progression-free survival. Regular medical check-ups during the study can be seen as an additional benefit.

Apart from the angiographic procedures and device-related toxicity, standard radiological and nuclear procedures are also used, which may have inherent side effects. For the frequent blood sampling and/or pre- and post-hydration, an indwelling cannula may be used and this may be accompanied by mild bruising and also, in rare cases, by transient inflammation of the vessel wall (phlebitis). The same applies to single vein punctures for blood sampling. When needed, the use of a urethral catheter may also cause infection. The total amount of blood withdrawn during the study will be up to 100 ml (normal blood donation: 500 ml).

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Patients must have given written informed consent.
2. Female or male aged 18 years and over.
3. 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.2, 4 LR-5 and LR- 4 based on Liver Imaging Reporting and Data System can be included.
4. No curative treatment options (resection, transplant, or in case of solitary tumor <5 cm, RFA).
5. Life expectancy of at least 6 months.
6. ECOG Performance status 0-1.
7. Liver-dominant disease (maximum 5 lung nodules all <=1.0 cm, solitary clinically stable adrenal metastasis, and mesenteric or portal lymph nodes all <=2.0 cm are accepted).
8. Child-Pugh class A5-6 or B7 (only for patients with known cirrhosis).
9. At least one measurable liver lesion according to the modified RECIST criteria.
10. Negative pregnancy test for women of childbearing potential. Female patients of childbearing potential should use a 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 1 year postmenopausal or surgically sterile during their participation in this study (from the time they sign the consent form), to prevent pregnancy

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Evidence of significant extrahepatic disease (MRI-scan liver and multiphase abdominal CT as well as a thoracic CT are routinely performed at screening).
2. Hepatic radiation therapy within the last 4 weeks before the start of study therapy.
3. Previous or current treatment with RE. Previous treatment with TACE, surgery, RFA, and previous or current treatment with sorafenib are allowed.
4. Major surgery within 4 weeks or incompletely healed surgical incision before

starting study therapy.
5. Serum bilirubin >34.2 micromole/L (2 mg/dL).
6. Glomerular filtration rate <35 ml/min.
7. Non-correctable INR >1.5 in case of femoral approach (as opposed to radial).
8. Leukocytes <2 109/l and/or platelet count <50 109/l.
9. Significant cardiac event (e.g. myocardial infarction, superior vena cava (SVC) 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.
10. Pregnancy or breastfeeding.
11. Patients suffering from psychic disorders that make a comprehensive judgment impossible, such as psychosis, hallucinations and/or depression.
12. Patients who are declared incapacitated.
13. Previous enrollment in the present study.
14. Male patients who are not surgically sterile or 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 a partner.
15. Evidence of untreated, clinically significant grade 3 portal hypertension (i.e. large varices at oesophago-gastro-duodenoscopy). In these cases, therapy with non-selective beta-blocker (propranolol) or rubber band ligation should be instituted according to accepted guidelines. In case of small varices, prophylactic propranolol is advised.
16. Portal vein thrombosis (tumor and/or bland) of the main branch (diagnosed on contrast enhanced transaxial images). Involvement of the right or left portal vein branches and more distal is accepted.
17. Untreated active hepatitis. In case of detectable viral HBV load, appropriate treatment should be instituted.
18. Transjugular intrahepatic portosystemic shunt (TIPS).
19. Body weight over 150 kg (because of maximum table load).
20. Severe allergy for intravenous contrast used (Visipaque®)(because of CT evaluation, pre-treatment angiography and treatment angiography).
21. Lung shunt >30 Gy, as calculated using scout dose SPECT/CT.
22. Uncorrectable extrahepatic deposition of scout dose activity. Activity in the falciform ligament, portal lymph nodes and gallbladder is accepted.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-02-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	QuiremScout and QuiremSpheres
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	16-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	31-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-02-2024
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

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT03379844
CCMO	NL74751.041.21