Radioactive holmium microspheres for the treatment of patients with non-resectable liver metastases of mixed origin; a single center, interventional, non-randomized, open label, safety study.

Published: 04-08-2009
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Primary objective:To establish the safety and toxicity profile of treatment with Ho-166-PLLA-MS.Secondary objectives:• To evaluate tumor response. • To evaluate patient dosimetry. • To evaluate performance status.• To evaluate Quality of Life (QOL...

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

Summary

ID

NL-OMON35649

Source
ToetsingOnline

Brief title
HEPAR-trial

Condition

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

Synonym
liver metastases of mixed origines

Research involving
Human

Sponsors and support

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

Intervention

Keyword: holmium, liver metastases, microspheres, radio-embolisation

Outcome measures

Primary outcome

Safety and toxicity profile of treatment with Ho-166-PLLA-MS.

Secondary outcome

• Tumor response.

• Patient dosimetry.

• Performance status.

• Quality of Life.

• Comparison of Tc-MAA-scan and Ho-166-PLLA-MS safety dose scan.

Study description

Background summary

A significant need for new treatment options for dominant liver metastases is recognized, because survival of patients with unresectable liver disease is poor. The preclinical phase of studies with Ho-166-PLLA-MS has been successfully completed and now clinical studies for evaluation of safety and efficacy are warranted.

Study objective

Primary objective:
To establish the safety and toxicity profile of treatment with Ho-166-PLLA-MS.

Secondary objectives:
• To evaluate tumor response.
• To evaluate patient dosimetry.
• To evaluate performance status.
• To evaluate Quality of Life (QOL).
• To compare Tc-MAA-scan with Ho-166-PLLA-MS safety dose scan.

Study design

Interventional, treatment, non-randomized, open label uncontrolled, safety study.

Intervention

Ho-166-PLLA-MS will be administered via a catheter (type Cobra glide-catheter (Cook) 5 French) during angiography.

Study burden and risks

The burden for the patient consits of:
1 screening visite, 1 hospital admission for 24 hours, 1 hospital admission for 48 hours, 12 outpatient visits, 15 blood samples for safety, 3 HRQOL questionnaires. Physical examination at every visit. 2 angiographies, CT-scans, PET-scans and MRI-scans. 1 technetiumscan, 1 non-contrast enhanced MRI of limited duration and 2 holmiumscans. 1 time 48-hours and 2 times 24-hours urine collection.

Risks
Apart from the angiographic procedures and device related toxicity as described in chapter 7, standard radiological and nuclear procedures are also used that may have their inherent side effects. For the frequent blood sampling 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. After initial irritation, the presence of an indwelling cannula is usually painless and hardly noticeable. 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).

Benefits
It is anticipated that treatment with radioactive microspheres will reduce tumor size and will improve quality of life as known from literature from yttrium-90. It is anticipated that the gamma emission of the radioactive Holmium will improve the safety of the procedure. Also the difference in specific activity of Ho-166-PLLA-MS compared to the currently available yttrium-90 may improve therapeutic results.

Participation in this study may possibly produce useful scientific data for the future. Regular medical check-ups during the study can be seen as an additional benefit. The number of visits (15) is comparable to a standard chemotherapy protocol. However, the scheduling is different.

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

- Patients must have given written informed consent.
- Female or male aged 18 years and over.
- Confirmed histological diagnosis of metastatic malignancy with dominant liver metastases without standard therapeutic options for treatment including chemotherapy or surgery.
- Life expectancy of 12 weeks or longer.
- World Health Organisation (WHO) Performance status 0-2.

- One or more measurable lesions at least 10 mm in the longest diameter by spiral Computed Tomography (CT) scan.
- Negative pregnancy test for women of childbearing potential.

Exclusion criteria

- Brain metastases or spinal cord compression, unless irradiated at least 4 weeks prior to the date of the experimental treatment and stable without steroid treatment for at least 1 week.
- Radiation therapy or the last dose of prior chemotherapie within the last 4 weeks before the start of study therapy.
- Major surgery within 4 weeks, or incompletely healed surgical incision before starting study therapy.
- Serum bilirubin > 1.5 x Upper Limit of Normal (ULN).
- Serum creatinine > 185 µmol/L.
- Alanine aminotransferase (ALT), aspartate aminotransferase (AST), or alkaline phosphatase (ALP) > 5 x ULN.
- Leukocytes < 4.0 10EXP9/l and/or platelet count < 150 10EXP9/l.
- Significant cardiac event or presence of cardiac disease that in the opinion of the Investigator increases the risk of ventricular arrhythmia.
- comorbidity with a grave prognosis (estimated survival <3 months) and/or worse then the basic disease for which the patients will be included in the study.
- patients with abnormalities of the bile ducts (such as stents) with a increased chance of infections of the bile ducts.
- patients suffering from diseases with a increased chance of liver toxicity, such as primary biliairy cirrhosis or xeroderma pigmentosum.
- patients suffering from psychic disorders that make a comprehensive judgement impossible, such as psychosis, hallucinations and/or depression.
- patients who are declared incompetent.
- Treated with an investigational agent within 42 days prior to starting study treatment.
- Evidence of portal hypertension, splenomegaly or ascites.
- Active hepatitis (B and/or C).
- Liver weight > 3 kg.
- Patients who have arterial variations that will not allow whole liver treatment by a single administration via the hepatic artery

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-11-2009
Enrollment:	24
Type:	Actual

Medical products/devices used

Generic name:	holium microspheres
Registration:	No

Ethics review

Approved WMO Date:	04-08-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	10-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-06-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-01-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-03-2011
Application type:	Amendment

Review commission: METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL25956.041.08