Radioembolization with 166Ho-microspheres in elderly and/or fragile patients with previously untreated unresectable liver-only metastases of colorectal cancer, CAIRO7 study endorsed by the Dutch Colorectal Cancer Group (DCCG)

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

Summary

ID

NL-OMON56361

Source
ToetsingOnline

Brief title
CAIRO7

Condition

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

Synonym
liver metastases, primairy colorectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: veelbelovende zorg

Intervention

Keyword: efficacy, fragile, holmium radioembolisation, liver metastases

Outcome measures

Primary outcome

efficacy of RE in terms of PFS in CRC patients with liver-only metastases who

are candidates for palliative systemic treatment with capecitabine plus

bevacizumab.

Secondary outcome

•safety/toxicity.

•cost-effectiveness.

•quality of life (QoL).

•overall survival.

•PFS in the subgroups of patients with and without their primary tumour in situ

Study description

Background summary

In frail/elderly patients without curative treatment options the standard treatment is capecitabine plus an antibody against the vascular endothelial growth factor (VEGF, i.e. bevacizumab or biosimilar), given until disease

progression or unacceptable toxicity, resulting in a median progression free survival (PFS) of 8.5-9.2 months. Capecitabine-induced hand-foot syndrome and diarrhoea are the most commonly occurring toxicities. Prolonged exposure to CTC grade 2 toxicity in frail or elderly patients may already significantly impact quality of life and daily living. Therefore, treatments with less toxicity would be of great value for these patients.
Radioembolization (RE) is a minimally invasive treatment with administration of radioactive microspheres into the hepatic artery via a microcatheter. Since tumors are preferentially supplied by the hepatic artery, most microspheres get trapped in the tumor. RE has been shown a feasible and safe procedure for the late-line treatment of unresectable CRC liver metastases. These data compare favorably with the toxicity data of capecitabine plus bevacizumab, but this should be validated in a prospective study in first-line.
The proposed study investigates the efficacy of RE as an alternative, better tolerated and more cost-effective treatment option in elderly or frail patients compared to chronic systemic treatment with comparable progression-free survival.

Study objective

Primary objective:
The objective of this randomized phase 2 study is to demonstrate efficacy of RE in terms of PFS in colorectal cancer patients with liver-only metastases who are candidates for palliative systemic treatment with capecitabine plus bevacizumab.

Secondary objectives:
• To evaluate safety/toxicity.
• To evaluate cost-effectiveness.
• To evaluate quality of life (QoL).
• To evaluate overall survival.
• To evaluate PFS in the subgroups of patients with and without their primary tumour in situ

Study design

Multi-center, interventional, treatment, randomized phase 2, open label, comparative study. The study will be conducted within the network of the Dutch Colorectal Cancer Group (DCCG).

Intervention

Individualized 166Ho-RE will be performed via a catheter during angiography. Dosimetry-based treatment planning will be individualized using Q-Suite* software. The comparator, standard systemic treatment, will be given by the local investigator and will consist of capecitabine orally 1000 mg/m2 bid day

1-14 + anti-VEGF antibody i.v. 7.5 mg/kg day 1 at 3-weekly cycles, continued until disease progression or unacceptable toxicity.

Study burden and risks

It is hypothesized that treatment with radioactive microspheres will have comparable efficacy in terms of PFS and will reduce toxicity and improve quality of life relative to standard treatment. It is anticipated that the gamma (γ) emission of the radioactive holmium-166 (166Ho) will ensure the safety of the procedure by enabling pre-treatment distribution analysis after scout dose imaging and subsequent dosimetry-based individualized treatment planning.
In general, common adverse events after receiving radioactive microspheres to the liver are fever, abdominal pain, nausea, vomiting, and fatigue. These adverse events are all part of the so-called post-RE syndrome. An abnormality of liver function tests is also likely to occur, without direct clinical relevance. In general, these effects are transient.
Apart from the angiographic procedures and the RE related toxicity, standard radiological and nuclear procedures are also used, which may have inherent side effects.

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

4.2 Inclusion criteria
In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Patients must have given written informed consent.
2. Female or male patients aged >=18 years.
3. Metastatic colorectal cancer, with metastases confined to the liver, previously not systemically treated.
4. Elderly/frail patients, according to the local investigator not eligible for local treatments or intensive systemic regimens with combination chemotherapy.
5. ECOG Performance status 0-2
6. Eligible for systemic treatment with capecitabine + anti-VEGF antibody.
7. Adequate bone marrow (Hb >= 6 mmol/L, WBC >= 3x109/L, platelets >= 100x109/L), liver (serum bilirubin <= 1x upper limit of normal (ULN), Albumin >= 30 g/L, /ALAT <= 5x (ULN), and renal (GFR >= 40 ml/min) functions.

Exclusion criteria

4.3 Exclusion criteria
A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Previous systemic treatment for metastatic disease.
2. Previous adjuvant treatment completed within 6 months prior to randomization.
3. Symptoms of primary tumor, if in situ, that require intervention; prior treatment with (chemo)radiotherapy and/or resection of primary tumor is allowed.
4. Eligible for more intensive systemic regimens (i.e. doublet or triplet chemotherapy).
5. Eligible for other local treatment of liver metastases (e.g. surgical resection, ablation).
6. Presence of extrahepatic metastases; the presence of small (<= 1 cm) lesions outside the liver on CT scan that are not clearly suspicious for metastases and/or the presence of enlarged hilar lymph nodes in the liver up to a maximal diameter of 2 cm is allowed.
7. Non-correctable INR >2.0.
8. Any serious and/or chronic liver disease preventing the safe administration

of radioembolization
9. Any serious comorbidity preventing the safe administration of anti-VEGF antibody treatment. This includes uncontrolled hypertension or treatment with >=3 antihypertensive drugs, arterial (cerebro)vascular event within the past 12 months, history of bleeding, history of GI perforation, or presence of fistulae.
10. Pregnancy or breastfeeding.
11. Mental disorders that may compromise patient compliance.
12. Concurrent second malignancy or cancer diagnosed within two years, with the exception of tumors with low risk of systemic relapse (systemic relapse risk of <10% over 2 years, such as adequately treated basal cell carcinoma of skin and low risk prostate cancer). If patients have a second malignancy, liver metastases need histological confirmation of CRC origin.
13. Body weight over 150 kg (because of maximum table load).
14. Known severe allergy for intravenous contrast fluids.
15. Actual or planned participation to another investigational study which may compromise any endpoint of the study. This also applies to any intervention that may influence quality of life.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-06-2023
Enrollment:	220
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	01-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-02-2025
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

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT05092880
CCMO	NL77263.041.21