Combining drug-eluting bead transarterial chemoembolisation and radioembolization for treatment of colorectal liver metastases: DEBIR90Y study

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This study has been transitioned to CTIS with ID 2024-514767-26-00 check the CTIS register for the current data. To find the maximum tolerated dose of glass yttrium-90 (90Y) microspheres (TheraSphere®), when combined with DEBIRI in patients with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON48751

Source
ToetsingOnline

Brief title
DEBIR90Y

Condition

- Metastases
- Hepatobiliary therapeutic procedures

Synonym
Colorectal liver metastases, liver metastases from colon and rectal cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Colorectal liver metastases, DEBIRI, Phase 1, Radioembolization

Outcome measures

Primary outcome

The maximum tolerated absorbed dose of 90Y-microspheres (TheraSphere®, BTG international) when combined with DEBIRI for liver dominant mCRC.

Secondary outcome

Secondary endpoints:

- Adverse events (AEs) and serious adverse events (SAEs), up to 2 months after the second and final treatment cycle. AEs and SAEs are defined by the study protocol (NCI Common Toxicity Criteria for Adverse Events; CTCAE v 5.0).

- Overall response rate (ORR, every 3 months up to progression) of the CRLM from the first treatment cycle by RECIST v1.1 and PERCIST, according to index lesions, hepatic response and overall response.

- Overall Survival (OS), evaluated 12 months after enrolment of the last patient.

- Conversion from non-resectable to resectable CRLM.

- Tumor marker (CEA) at 2 months after the second and final treatment cycle

- Circulating tumor DNA levels before and after treatment.

- Amount of drug-eluting beads (DEB) delivered.

- Post-treatment dosimetry, related to pre-treatment dosimetry, as assessed by

Simplict90Y* software.

Study description

Background summary

Drug eluting beads preloaded with irinotecan (DEBIRI) is a promising method of treating patients with liver-dominant metastatic colorectal carcinoma (mCRC), and is a reimbursed procedure in several European countries. Although tumor response is generally good after DEBIRI (68.6% overall response rate), all patients eventually have progressive disease. A large proportion of those patients has progression in the liver (54%). Another increasingly used minimally invasive treatment for patients with liver-dominant mCRC is radioembolization, which irradiates tumors from the inside out. Radioembolization has proven to prolong the time to progression. However, almost all patients eventually have progressive disease, and an overall survival benefit was not yet proven. Due to their differing mechanisms of action, combining DEBIRI with radioembolization is expected to provide double coverage and improve progression free survival, as well as overall outcome.

Study objective

This study has been transitioned to CTIS with ID 2024-514767-26-00 check the CTIS register for the current data.

To find the maximum tolerated dose of glass yttrium-90 (90Y) microspheres (TheraSphere®), when combined with DEBIRI in patients with liver-dominant colorectal liver metastases (CRLM).

Study design

Phase I dose-escalation study.

Intervention

Injection of escalating doses of 90Y-microspheres followed by DEBIRI via a catheter in the hepatic arteries.

Study burden and risks

Anticipation of benefits:
We expect that patients treated with radioembolization and DEBIRI will have a more effective treatment of the CRLM compared to i.v. chemotherapy alone. This

may lead to a prolonged progression free survival and a better QoL. We also expect the incidence and severity of systemic side effects of irinotecan to be lower in DEBIRI compared to intravenous irinotecan based regimens.

Anticipation of the risks:
The risks associated with participation in this study mainly consist of the side-effects of the individual treatments, and the combination of both. The added risk of the combination lies in the fact that we have to find the maximum tolerated dose. As both radioembolization and DEBIRI have hepatotoxic effects, dose limiting toxicity (DLT) is expected to occur at some point during this study. Hepatotoxicity must be treated symptomatically as radioembolization and DEBIRI are permanent devices.

Side effects of radioembolization and DEBIRI
The most important side-effects related to radioembolization and DEBIRI include:

• Post-embolization syndrome (PES) is a common side effect of both radioembolization and DEBIRI, its symptoms include nausea, 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 1-5% of radioembolization cases and is a serious life-threatening side-effect. Improved dosimetry and treatment planning aims to prevent this. Treatment is symptomatic and mainly consists of high dose steroids.

Other side effects are with relatively low incidence or less significant clinical impact are listed in the answer to question E9 or in paragraphs 6.4 and 7.4 of the protocol

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. Written informed consent.
2. >=18 years old with confirmed unresectable liver metastases from CRC
3. The primary tumor should be clinically stable.
4. Bilobar (to avoid bias in toxicity analysis), unresectable liver dominant mCRC (i.e. up to 2 lesions limited to one extra-hepatic organ with a maximum size of 1 cm and 2 cm for lymph nodes), with disease progression after first line systemic treatment.
5. Eligible to receive second-line standard-of-care chemotherapy with an irinotecan-based chemotherapy regimen.
6. Measurable (target) liver lesions on contrast-enhanced CT, according to RECIST 1.1.
7. Contrast-enhanced CT and FDG-PET-CT maximum 4 weeks prior to enrolment.
8. Tumor replacement >= 5% and <= 50% of total liver volume.
9. Started the last cycle of the first line chemotherapy (without irinotecan) at least 28 days prior to the initiation of second line chemotherapy under the protocol.
10. Eastern Cooperative Oncology Group performance status 0-1.
11. Life expectancy of >= 12 weeks.
12. Hematologic function: WBC >= 3.0 x 10^9/L, platelets >= 100 x 10^9/L, absolute neutrophil count ; 1.5 x 10^9/L, Hemoglobin; 5 mmol/L.
13. Adequate organ function as measured by:
o GFR >= 35 ml/min.
o Serum transaminases (AST; ALT) <= 5 x ULN.
o Total bilirubin <= 1 x ULN
o Albumin > 3 g/dL.

Exclusion criteria

1. History of hepatic encephalopathy.
2. Contraindications to angiography.
3. Known severe allergy or intolerance to contrast agents, that cannot be managed medically.
4. Pulmonary insufficiency or clinically evident chronic obstructive pulmonary disease.
5. Cirrhosis or portal hypertension.
6. Prior liver-directed therapy (i.e. EBRT, chemoembolization, radioembolization, hepatic segmentectomies, radiofrequency ablation spanning >2 segments).
7. Treatment with VEGF inhibitors within 28 days prior to receiving 90Y glass microspheres.
8. Prior intervention for, or compromise of, the Ampulla of Vater.
9. Presence of clinically evident ascites (trace ascites on imaging is acceptable), or Child-Pugh score B/C.
10. Toxicities due to prior cancer therapy that have not resolved before the initiation of study treatment, if the investigator determines that the continuing complication will compromise the safe treatment of the patient.
11. Significant life-threatening extra-hepatic disease, including patients who have unresolved diarrhea or serious unresolved infections (e.g. patients who are known to be HIV positive or have acute HBV or HCV).
12. Contraindications to the planned second line standard-of-care chemotherapy regimen.
13. Pregnancy and/or breastfeeding.
14. Patients suffering from psychic disorders that make a comprehensive judgment impossible, such as psychosis, hallucinations and/or depression.
15. Patients who are declared incapacitated.
16. Participation in a clinical trial with an investigational therapy within 30 days prior to enrolment.
17. Any co-morbid disease or condition that would place the patient at undue risk.
18. Contraindications to TACE (e.g. porto-systemic shunt, portal vein thrombosis, hepatofugal blood flow, severe atherosclerosis precluding arterial access).
19. Contraindications to irinotecan (concomitant use with St John*s wort).

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-10-2019
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	Yttrium-90 glass microspheres (Therasphere®)
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Irinotecan generic
Generic name:	Irinotecan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-04-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	08-05-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-10-2019

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-06-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-07-2024
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
EU-CTR	CTIS2024-514767-26-00
EudraCT	EUCTR2018-002940-97-NL
CCMO	NL66938.041.19