Single-arm, phase II trial of trifluridine/tipiracil (FTD-TPI), bevacizumab, and individualized radioembolization with 166Ho-microspheres in refractory metastatic colorectal cancer.

Published: 31-05-2024
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To determine safety, tolerability, and activity of individualized radioembolization with 166Ho-microspheres combined with FTD-TPI and bevacizumab.

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

Summary

ID

NL-OMON56792

Source
ToetsingOnline

Brief title
STARLIGHT

Condition

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

Synonym
colorectal cancer, liver metastases

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Servier,Terumo,Terumo;Servier

Intervention

Keyword: Colorectal cancer, Holmium radioembolization, Liver metastases, Safety and feasibility

Outcome measures

Primary outcome

To assess activity of radioembolization, FTD-TPI, and bevacizumab in terms of

hepatic objective tumor response (hORR) determined by PERCIST 1.0

Secondary outcome

Activity

• Hepatic objective response rate (hORR) (RECIST 1.1)

• Overall and extra-hepatic ORR (RECIST 1.1, PERCIST 1.0)

Safety

• SAE*s

• Grade >=3 adverse events (CTCAE 5.0)

• Occurrence of REILD (see 8.1.2)

• Radioembolization related vascular events

Tolerability

• Dose reductions, dose delays of FTD-TPI

• Radioembolization completion rate

Efficacy

• Progression-free survival

• Overall survival

Study description

Background summary

Extrahepatic disease progression limits clinical efficacy of individualized radioembolization for patients with refractory metastatic colorectal cancer (mCRC). In the same patient population, trifluridine/tipiracil (FTD-TPI) and bevacizumab lead to disease control and overall survival benefit and may be a radiosensitizer.(Prager et al., 2023)
There is no clear treatment preference, therefore individual treatment goals dictate the choice of extra-hepatic tumor stabilization with FTD-TPI and bevacizumab or intra-hepatic tumor reduction with radioembolization. However, in most patients with liver-dominant, chemotherapy-refractory mCRC both treatment goals overlap. The combination of radioembolization, FTD-TPI, and bevacizumab could potentially be preferable, if this is a safe and effective alternative.

Study objective

To determine safety, tolerability, and activity of individualized radioembolization with 166Ho-microspheres combined with FTD-TPI and bevacizumab.

Study design

Single-arm, open label, phase II trial.

Intervention

• Individualized 166Ho radioembolization combined with:
• 35 mg/m2 FTD-TPI day 1-5 and 8-12, every 4 weeks
• 5 mg/kg bevacizumab iv. on day 1 and 15, every 4 weeks

Study burden and risks

It is hypothesized that systemic therapy and radioembolization improve hepatic objective response rate of mCRC patients with liver dominant metastases compared to the current standard treatment of systemic therapy alone. This potential benefit should be weighed against the burden and risks of the experimental treatment. The most important potential burden/risks are: additional hospital visits, a small but increased risk for complications and an intensified and prolonged initial treatment that could decrease health-related quality of life. Taken into the account the severity of impact and likelihood of occurrence of the potential risks, the investigators have classified this study as medium risk. The investigators feel that the potential response rate benefit of the experimental arm outweighs the burden and risks of participation.

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

• Unresectable liver dominant mCRC
• Prior therapy with fluoropyrimidine, oxaliplatin, and irinotecan for the treatment of advanced colorectal cancer and had demonstrated progressive disease or intolerance to their last regimen
• Written informed consent
• Age >=18 years
• Estimated hepatic tumor replacement >= 10% and <= 50% of total liver volume
• ECOG performance status 0-1
• Adequate organ function as measured by:
o WBC >= 3.0 x 109/L, platelets >= 100 x 109/L, absolute neutrophil count > 1.5 x 109/L, Hemoglobin > 5 mmol/L (>8.1 g/dL)
o eGFR >= 35 ml/min
o Serum transaminases (AST & ALT) <= 5 x ULN
o Total bilirubin <= ULN
o Albumin > 3 g/dL
• At least one measurable liver lesion according to the PERCIST 1.0
• Included in PLCRC

Exclusion criteria

• Significant extrahepatic disease, defined as symptomatic extrahepatic disease, greater than 10 pulmonary nodules (maximum diameter of each lung metastasis <20mm), and/or peritoneal carcinomatosis. (Definition of liver dominant disease)(Fidelman et al., 2022)
• Eligible for local treatment of liver metastases (e.g. surgical resection, ablation)
• Lung shunt >20 Gy, as calculated using scout dose SPECT/CT
• Absorbed tumor dose <90 Gy when dosing at a maximum average absorbed normal liver dose
• Other malignancy confounding prognosis
• Receipt of chemotherapy within 28*days prior to study treatment
• Previous or current treatment with radioembolization
• Major surgery within 28 days or incompletely healed surgical incision before starting study therapy
• 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 6 months, history of severe bleeding, history of GI perforation, or presence of fistulae
• Any serious and/or chronic liver disease preventing the safe administration of radioembolization

• Uncorrectable extrahepatic deposition of scout dose activity; activity in the falciform ligament, portal lymph nodes and gallbladder is accepted
• Pregnancy or breastfeeding
• Body weight over 150 kg (because of maximum table load)
• Known severe allergy for intravenous contrast fluids
• Participation to another investigational study which may compromise any endpoint of the study

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-09-2024
Enrollment:	40
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	31-05-2024
Application type:	First submission
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
CCMO	NL85987.041.24