A multicenter phase II randomized trial to evaluate systemic therapy versus systemic therapy in combination with stereotactic radiotherapy in patients with metastatic colorectal cancer

Published: 17-02-2022
Last updated: 04-04-2024

To assess the impact of SBRT in combination with systemic therapy compared to systemic therapy alone on safety and efficacy in patients with mCRC.

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

Summary

ID

NL-OMON52282

Source
ToetsingOnline

Brief title
SIRIUS

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Bowel cancer, colon cancer, rectum cancer

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: Colorectal cancer, Image guided radiation, MR guided therapy, Oligometastatic/polymetastatic cancer

Outcome measures

Primary outcome

Lead-in:

Feasibility, based on technical feasibility, logistical feasibility and patient

acceptance (details are provided in the protocol)

Phase II:

Progression free survival. Defined as the time from randomization until

progression of disease or death, whichever occurs first.

Secondary outcome

Lead-in:

Secondary outcome: Grade II adverse events of specific interest and grade

III/IV adverse events.

Phase II:

Overall survival, objective response rate of SBRT, time to disease related

treatment failure, health related quality of life, depth of response, pattern

of recurrence, treatment success rate, grade II adverse events of specific

interest and grade III/IV adverse events of SBRT and fatigue measurements by

MFI-20.

Study description

Background summary

In the Netherlands approximately 12.000 people per year are diagnosed with colorectal cancer (CRC) of which 50% will develop distant metastases (mCRC). A small number of CRC patients with limited metastases may be candidates for local treatment of metastases (e.g., resection, ablation) with curative intent. However, the majority of mCRC patients will not have this treatment option. The standard treatment for these patients is palliative systemic treatment, of which a benefit in overall survival has been demonstrated. The addition of stereotactic body radiation therapy (SBRT) to metastases in a limited unresectable metastatic setting might improve progression-free survival (PFS), however is controversial. Two small proof of concept trials have demonstrated positive effects in terms of survival and quality of life.
The success of the addition of local treatments in mCRC patients depends largely on: control of microscopic disease, diagnostic accuracy of macroscopic disease and effective treatment of all detected metastases with limited additional toxicity to surrounding tissues. Until shortly, the use of SBRT was possible to a limited number of locations due to target movement or toxicity to surrounding radiosensitive structures. With the introduction of MRI-guided radiotherapy these limitations have largely disappeared due to the possibility to make a daily new treatment plan based on MRI-visualized anatomy. This allows the use of smaller margins for uncertainty with less healthy tissues in the radiation field. Thereby, a broader application of SBRT to add local control to metastases became possible.

Study objective

To assess the impact of SBRT in combination with systemic therapy compared to systemic therapy alone on safety and efficacy in patients with mCRC.

Study design

This study is an open-label, multicenter, randomized phase II screening trial with a lead-in.

Intervention

SBRT on all metastatic sites followed by maintenance treatment.

Study burden and risks

It is hypothesized that systemic therapy and SBRT (experimental arm) significantly improve the PFS of mCRC patients with locally untreatable metastases compared to the current standard treatment of systemic therapy alone (control arm). The most important potential burden/risks for patients allocated in the experimental arm are: additional hospital visits for SBRT, which are one preparation visit and one to four visits for treatment (dependent on locations of metastases) and increased chance of adverse effects after SBRT. The investigators expect that the potential overall PFS 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

- Histological proof of colorectal carcinoma (CRC)
- Colorectal metastatic disease
- Ten or less metastases as determined by the UCMU central review
- Stable disease or partial response after induction chemotherapy according to RECIST 1.1 criteria
- Written informed consent
For all in- and exclusion criteria we want to refer to chapter 4 of the protocol.

Exclusion criteria

- Possible treatment with curative intent according to local tumor board
- Substantial overlap with a previously treated radiation volume. Previous radiotherapy is allowed as long as the composite plan meets dose constraints herein.
- Contra-indication MR-LINAC (pacemaker or implantable cardioverter-defibrillator)
For all in- and exclusion criteria we want to refer to chapter 4 of the protocol.

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-03-2022
Enrollment:	105

Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	17-02-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-01-2024
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
ClinicalTrials.gov	NCT05375708
CCMO	NL76444.041.21