COLLISION-XL trial: Unresectable colorectal liver metastases: stereotactic body radiotherapy versus microwave ablation - a phase II prospective randomized controlled trial for CRLM 3-5 cm

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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-OMON52908

Source
ToetsingOnline

Brief title
COLLISION XL - SBRT vs MWA for unresectable CRLM 3-5 cm

Condition

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

Synonym
colorectal liver metastases; large bowel cancer liver metastases

Research involving
Human

Sponsors and support

Primary sponsor: Radiologie en nucleaire geneeskunde
Source(s) of monetary or material Support: grant van Ethicon;Johnson & Johnson voor arts-onderzoeker; beide behandelingen zijn standaardzorg,Johnson & Johnson

Intervention

Keyword: Colorectal cancer, Colorectal liver metastases, Microwave ablation, Stereotactic body radiotherapy

Outcome measures

Primary outcome

Primary endpoint is local tumour progression free survival (LTPFS) at 1 year.

Secondary outcome

Secondary endpoints are overall survival (OS), Local tumour progression free survival time, disease-free survival (DFS), time to progression (TTP), distant progression free survival (DPFS), procedural morbidity/toxicity and mortality, assessment of pain and quality of life (QoL) and cost-effectiveness ratio (ICER).

Study description

Background summary

Colorectal carcinoma is one of the most common malignancies in the Western world. In the course of the disease 40-60% of patients develop colorectal liver metastases (CRLM). Without treatment, survival for these patients is cumbersome with a median overall survival (OS) of 7.4 - 11 months. Although chemotherapeutic regimens are slowly improving, local therapy for CRLM remains the only option associated with a realistic chance of long-term disease control or in selected cases even full cure. Surgical resection represents the historical standard and treatment of first choice with 5-year OS reaching

35-60%. However only a minority of the patients (i.e. 10-20%) is eligible for surgery due to size, number or location of the metastases, or relevant co-morbidities. To eliminate unresectable metastases, several ablative strategies have emerged.

Thermal ablation techniques employing radiofrequency ablation (RFA) and microwave ablation (MWA) have slowly worked their way into common clinical practice and international guidelines. Thermal ablation for small liver lesions has an excellent safety profile with a low complication rate for smaller liver tumours. However, the issue of local site recurrence after thermal ablation has prohibited widespread adoption of the technique for resectable lesions. In the last few years, thermal ablation techniques have substantially improved with primary efficacy rates (complete ablation after the first procedure) for lesions <=3cm now reaching 92-100%. These results are comparable to recurrences after surgical resection for similar-sized lesions. The relative ease to percutaneously re-ablate potential site recurrences, nowadays often in the setting of a one-day admission under conscious sedation, has downgraded the relevance of local site recurrence (LSR) with local control rates (assisted technique effectiveness) approaching 100% for lesions <=3cm. The recently presented long-term results from the EORTC CLOCC-trial (ASCO 2015) show a clear survival benefit of RFA plus systemic chemotherapy over chemotherapy alone for unresectable CRLM: 8-year OS 36% vs 8.9% (p=0.01; HR 0.58; 95%CI 0.38-0.88). Numerous studies have demonstrated a superior safety profile in addition to lower direct and indirect costs of thermal ablation over surgical resection.

Stereotactic body radiotherapy (SBRT) is gaining interest as a potential means to treat CRLM. Especially for solitary or a limited number of CRLM the potential to induce long-term local tumour control has been established with acceptable toxicity. Several recent propensity matched comparisons from the radiation oncology community seem to favour SBRT over thermal ablation for lesions >3cm, substantiated by a superior long-term freedom from local recurrence rate following the initial treatment.

In their response, the interventional oncology communities state that simply comparing local control rates following an ablative procedure seems unjust when comparing an easily repeatable technique with a one-shot treatment method. Furthermore, the claim that SBRT is less-invasive because it is a no-needle technique seems unsubstantiated and may well be prejudiced given the unquestionably larger area of collateral damage following SBRT.

Given the results from the EORTC-CLOCC trial, the comparable survival for ablation*+*surgery versus surgery alone, the potential to induce long-term disease control and the very low complication rate following percutaneous ablations for CRLM <= 3 cm and given the fact that the local control rate has approached 100% for smaller CRLM, we believe SBRT is currently not indicated for thermally ablatable CRLM <= 3 cm.

However, thermal ablation local control rates clearly descent with increasing tumour-size and the number of complications will rise. Hence, we believe clinical and oncological equipoise for CRLM 3 - 5 cm has been reached for unresectable CRLM treated with either MWA versus SBRT.

Study objective

The primary objective is to compare efficacy of MWA to the efficacy of SBRT with regards to the primary endpoint (local tumour progression free survival at 1 year [1-year LTPFS]) in patients with unresectable CRLM (3 - 5 cm) that are unsuitable for surgery due to either comorbidities, a history of extensive abdominal surgery, a poor performance status or due to a certain unfavourable anatomical location of the tumour.

Study design

COLLISION XL is a prospective multi-centre phase-II randomized controlled trial.

Intervention

SBRT or MWA. The expert panel, consisting of at least two interventional radiologists, two hepatobiliary surgeons and two radiation oncologists, will appoint lesions of 3-5cm, that are unresectable and suitable for both MWA and SBRT, as target lesions.

Study burden and risks

Over the last decades, technical developments made it possible to deliver high radiation doses per treatment fraction more precisely to the tumour, called stereotactic body radiotherapy (SBRT). Furthermore, in some hospitals it is possible to visualize the tumour during radiation treatment to deliver gated treatment (beam-on only when the tumour is in the predetermined position) using small uncertainty margins and thereby limiting the dose delivered to surrounding normal organs, likely resulting in decreased toxicity.
Disadvantages include the need to be positioned within the MRI bore during radiation delivery, and a prolonged time per treatment fraction. Local tumour control of SBRT for liver malignancies ranges between 50-95% after one year. A recent systematic review showed a one-year local control rate of 67% and a two-year local control rate of 59.3%; however, this systematic review also included older studies and in the last few years SBRT techniques have substantially improved. Grade I-II toxicity occurred in 23-78% of patients receiving SBRT, grade III toxicity or higher only occurred in 0-10% of patients.
Reported outcomes after thermal ablation for CRLM are improving. Survival results after thermal ablation for non-surgical candidates for lesions <3cm

have approached the results achievable with surgery for resectable disease. However for lesions >3cm the local control rate decreases significantly. In a study from Tanis et al local recurrence rate was 21.4% after RFA for lesions >3cm, this is in accordance with the findings of Mulier et al where the local recurrence rate after surgical RFA for liver tumours of 3-5cm was 21.7%. Local recurrence after MWA for liver tumours >3cm showed a similar rate of 23%. Major complications occur in 2-4% of patients receiving MWA.
By participating in the study, patients agree to undergo either SBRT or MWA. For each participant, the method of treatment will be decided upon by randomization. Pre-treatment screening will not be different from the standard screening for these techniques and will not be an extra burden. Both SBRT and MWA are considered safe and established treatment options for the target population.
At the moment it is uncertain whether SBRT or thermal ablation is preferable for intermediate size unresectable CRLM. No randomized controlled trials comparing SBRT to MWA in CRLM have been conducted so far. If this study shows that the efficacy of one technique is superior over the other this could lead to a prolonged LTPFS for patients with CRLM, reducing the number of required repeat procedures and potentially improving disease free and overall survival.

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 documentation of primary colorectal tumour;
• 1-3 unresectable CRLM size 3-5 cm eligible for both MWA and SBRT (target lesions);
• Additional unresectable CRLM < 3 cm should be ablatable;
• Additional unablatable CRLM should be resectable;
• No or limited extrahepatic disease (1 extrahepatic lesion is allowed, not including positive para-aortal lymph nodes, celiac lymph nodes, adrenal metastases, pleural carcinomatosis or peritoneal carcinomatosis);
• Maximum number of total CRLM is 5 if there is extrahepatic disease and 10 if there is no extrahepatic disease;
• Unsuitable for (further) chemotherapy regimens
• Resection for resectable lesions considered possible obtaining negative resection margins (R0) and preserving adequate liver reserve
• Previous radiotherapy, surgical resection or focal ablative therapy for CRLM prior to inclusion are allowed;
• Age >18 years;
• Written informed consent

Exclusion criteria

• Pregnant or breast-feeding subjects;
• Immunotherapy <= 6 weeks prior to the procedure;
• Chemotherapy <= 6 weeks prior to the procedure;
• Severe allergy to contrast media not controlled with premedication;

Study design

Design

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

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-10-2020
Enrollment:	68
Type:	Actual

Medical products/devices used

Generic name:	Stereotactic body radiotherapy (SBRT) and Microwave ablation (MWA)
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	06-08-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-01-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL68326.029.19