Whole Brain Radiotherapy (WBRT) versus Stereotactic Radiosurgery (SRS) for 4 up to 10 brain metastases: a phase III randomized multicenter trial

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To determine if SRS is a better palliative treatment than WBRT for patients with 4 up to 10 BM in terms of QOL at 3 months post-radiotherapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON47148

Source
ToetsingOnline

Brief title
WBRT versus SRS for patients with 4 up to 10 brain metastases

Condition

- Metastases

Synonym
brain metastases

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO Clinic
Source(s) of monetary or material Support: Ministerie van OC&W,Varian Medical

Systems

Intervention

Keyword: brain, metastases, radiosurgery, radiotherapy

Outcome measures

Primary outcome

Difference in quality of life (EQ-5D EUROQOL score) at 3 months post-radiotherapy with respect to baseline

Secondary outcome

Difference in quality of life (EQ5D EUROQOL score) at 6, 9, and 12 months post-radiotherapy with respect to baseline. At 3, 6, 9, and 12 months after radiotherapy survival, Karnovsky*70, WHO performance status, steroid use (mg), toxicity according CTCAE V4.0 including hair loss, fatigue, neurocognition question, and brain salvage during follow-up, type of salvage, time to salvage after randomization, and Barthel index.

Facultative secondary endpoints are neurocognition with the Hopkins Verbal Learning Test, quality of life EORTC QLQ-C30, quality of life EORTC BN20 brain module, and fatigue scale EORTC QLQ-FA13.

Study description

Background summary

In the Dutch guideline the advice is stereotactic radiosurgery (SRS) for patients with 1 up to 3 brain metastases (BM) and whole brain radiotherapy (WBRT) for patients with 4 or more BM. An interim analysis of the QUARTZ study showed that WBRT did not provide benefit in quality of life (EQ5D EUROQOL

score) nor survival over best supportive care. WBRT has significant side effects, such as hair loss, fatigue, and cognitive dysfunction which may result in decreased quality of life (QOL). A recently published study showed that SRS in patients with 5 up to 10 BM results in comparable survival as SRS in patients with 2 up to 4 BM. Many systemic therapies do not have a satisfactory intracranial response, because of the blood-brain barrier. There are potential advantages of SRS over WBRT, i.e, limiting radiation doses to the uninvolved brain and a high rate of local tumor control by just a one tot three treatments. The next logic step would be to compare WBRT with SRS alone in patients with 4-10 BM and evaluate whether SRS is superior to WBRT with regard to QOL.

Study objective

To determine if SRS is a better palliative treatment than WBRT for patients with 4 up to 10 BM in terms of QOL at 3 months post-radiotherapy.

Study design

Prospective randomized multicenter phase III trial

Intervention

Patients will be randomized between WBRT in 5 fractions of 4 Gy to a total dose of 20 Gy. (standard arm) and one to three dosisse SRS to the BM (study arm). The largest BM or a localization in the brainstem will determine the prescribed dose for all BM. According to the volume criteria presented in the Dutch National Platform Radiotherapy and Neuro-oncology (LPRNO) consensus (November 2014 Eekers, Hurkmans) SRS for BM, the prescribed dose will be determined in the range of one tot three fractions of 15Gy up to 24Gy dependent on Planning Target Volume (PTV).

Study burden and risks

For patients in a good physical shape with one to three BM, SRS is the preferred treatment. For patients with 4 or more BM current Dutch guidelines advise WBRT. This study is performed in patients with 4 up to 10 BM referred for radiotherapy. The aim of this study is to compare the standard of care, WBRT, with the experimental arm SRS, and determine which arm provides best palliation treatment in terms of QOL. SRS requires an extra MRI, but is delivered in less fractions than WBRT, and there is globally broad experience with SRS. WBRT is a fast treatment, which takes 5-10 minutes per visit. With recent technical advances, the beam-on time during treatment with SRS for patients with multiple BM, is in the range of several minutes to 45 minutes, a high rate of local tumor control by just one to three treatments and the avoidance of complete hair

loss. For this study, no standard imaging during follow-up is performed outside institutional standards, except when indicated on clinical grounds. The baseline and follow-up scores of the EQ5D questionnaires will be collected in patients treated with WBRT or SRS followed by telephone contact at several time-points post-treatment and will take less than 10 minutes. In case a patient refuses participation in the study, patient will be treated according to the institutional standard, which most often will be WBRT, in agreement with Dutch guidelines. For centres that have the logistic capacity extra neurocognitive tests and more extensive QOL tests will be done before treatment and only at 3 months after treatment.

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

* Age*18 years
* Minimal 4 up to a maximum of 10 brain metastases (BM) on diagnostic MRI scan
* Maximum PTV of the largest BM of 65 cm3
* Karnofsky performance status * 70
* Any solid primary tumour. Small cell lung cancer, germinoma, and lymphoma are excluded
* Ability to provide written informed consent

Exclusion criteria

* Contra-indication for MRI
* Prior treatment for brain metastases (i.e. surgery, SRS or WBRT)
* Concurrent use of systemic therapy
* More than 10 BM on plannings-MRI
* A brainstem metastasis with a PTV of more than 20 cm3

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-07-2016
Enrollment:	230
Type:	Actual

Ethics review

Approved WMO Date:	02-05-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-03-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-09-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-03-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NCT02353000
CCMO	NL53852.068.15

Study results

Date completed:	05-04-2019
Actual enrolment:	30

Summary results
Trial ended prematurely