A Prospective Randomized Study to Compare Neurocognitive Outcome after Gamma Knife Radiosurgery or Whole Brain Radiation Therapy for the Treatment of Multiple Brain Metastases

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28765

Source
Nationaal Trial Register

Brief title
The CAR study

Health condition

Brain metastases

Sponsors and support

Primary sponsor: St Elisabeth Hospital, Tilburg and Tilburg University
Source(s) of monetary or material Support: ZonMw (The Dutch Organisation for Health Research and Development)

Intervention

Outcome measures

Primary outcome

The definition of the primary endpoint is the statistically significant difference in the percentage of patients with significant cognitive decline at three months between treatment groups. Decline is defined as a 5-point decrease from baseline based on the reliable change index (with correction for practice effects) in HVLT-R Total Recall score.

Secondary outcome

• Differences in percentage of patients with a 5 or more point decrease in HVLT-R between treatment arms will be assessed at 6, 9, 12, and 15 months as is done for 3 months for the primary endpoint. We will assess both proportions at each time and the overall trend of change over time.

• Group mean scores for all neuropsychological tests will be determined for both treatment arms at baseline, 3, 6, 9, 12, and 15 months. We will assess both proportions at each time and the overall trend of change over time.

• Overall survival will be measured from the first day of treatment to date of death or last study follow-up (15 months).

• Local and distant brain tumor control of the initial GKRS- or WBRT-treated lesions is defined according to the RECIST Response Criteria.
• Depression, anxiety, health related QOL and fatigue.

• Type and duration of systemic therapy and medication use will be recorded. The total number of cycles of systemic therapy will be calculated from either the day of treatment with GKRS or from the first day of WBRT.

• Treatment side effects (e.g. toxicity due to chemotherapy) for both arms will be recorded at 3, 6, 9, 12, and 15 months according to the EORTC Common Toxicity Criteria (CTC AE version 4).

Study description

Background summary

Effective treatment for patients with BM without negative cognitive side effects is increasingly becoming more important, since more patients survive and live longer after treatment. This study aims to examine cognitive outcome and therefore quality of life in patients with BM after GKRS or WBRT.

The proposed study is a prospective randomized trial, designed to evaluate cognitive functioning over time after treatment with either GKRS or WBRT in adult patients with multiple (11-20) brain metastases in the Netherlands.

Neuropsychological assessment will be performed at baseline. Follow-up at 3, 6, 9, 12, and 15 months (cognitive testing) and 3-monthly MRI scan. Ultimately, the purpose of this line of research is to inform individual patients with BM more precisely about the (long-term) cognitive effects and the consequences they can expect from treatment with either GKRS or WBRT. This will enable patients and doctors to make a better-informed treatment decision grounded on scientific evidence.

Study objective

Effective treatment for patients with brain metastases (BM) without negative cognitive side effects is increasingly becoming more important, since more patients survive and live longer after treatment. Ultimately, the purpose of this line of research is to inform individual patients with BM more precisely about the (long-term) cognitive effects and the consequences they can expect from treatment with either whole brain radiation therapy (WBRT) or Gamma Knife Radiosurgery (GKRS). This will enable patients and doctors to make a better informed treatment decision grounded on scientific evidence. This study aims to examine cognitive outcome and therefore QOL in patients with BM after WBRT or GKRS.

Study design

The neuropsychological test battery, including the questionnaires, will be administered at baseline (before GKRS or WBRT) and 3, 6, 9, 12, and 15 months after treatment.

Intervention

Patients will complete a standardized battery of neuropsychological test both at baseline and 3, 6, 9, 12, and 15 months post GKRS or WBRT. Patients in the WBRT group will receive 4 Gy x 5 fractions (total of 20 Gy) in one week, which is a commonly utilized treatment schedule according to Dutch guidelines. GKRS will be performed with a (fully robotic) Leksell Gamma Knife® Perfexion, Elekta Instruments, AB. Depending upon the volume, a dose of 18-25 Gy will be prescribed with 99-100% coverage of the target.

Contacts

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Eligibility criteria

Inclusion criteria

• Histologically proven malignant cancer

• Imaging and clinical presentation consistent with BM; contrast enhanced volumetric MRI used for treatment planning showing 11-20 newly diagnosed BM with a maximum total tumor volume of 30 cm3

• Lesion >3mm from brainstem or optic apparatus

• Patient age >/=18 years

• Karnofsky Performance Status >/=70

• WHO performance status ≤2

• Anticipated survival (independent of the BM) greater than 3 months

• Patient informed consent obtained (verifying that patients are aware of the investigational nature of this study).

Exclusion criteria

• No prior histologic confirmation of malignancy

• Primary brain tumor, a second (active) primary tumor

• Small cell lung cancer

• Leukemia

• Meningeal disease

• Lymphoma

• Progressive, symptomatic systemic disease without further treatment options

• Prior brain radiation

• Prior surgical resection of BM

• Additional history of a significant neurological or psychiatric disorder

• Participation in a concurrent study in which neuropsychological testing and/or health-related QOL assessments are involved

• Contra indications to MRI or gadolinium contrast

• Underlying medical condition precluding adequate follow-up

• Lack of informed consent

• Patients unable to complete test battery and/or study questionnaires due to any of the following reasons: lack of basic proficiency in Dutch, IQ below 85, severe aphasia, paralysis grade 0-3 according to MRC scale (Medical Research Council)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2015
Enrollment:	80
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion Date:	14-09-2015
Application type:	First submission

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
NTR-new	NL5353
NTR-old	NTR5463
Other	Project number ZonMw; Protocol ID MEC : 842003006; P1516

Study results