Prophylactic Cranial Irradiation with or without hippocampal avoidance in SCLC: a randomized phase III study

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To assess memory function at 4 months after Hippocampus Avoidance-PCI versus standard whole brain PCI

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45142

Source
ToetsingOnline

Brief title
HA-PCI

Condition

- Other condition
- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
memory function, small cell lung cancer

Health condition

cognitieve functies

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: IWT Agentschap voor Innovatie door Wetenschap en Technologie (Belgie) onder n ummer 130262,KWF-CKS onder nummer NKI 2013-6096 en Vlaamse Liga tegen Kanker (

Intervention

Keyword: brain irradiation, Hopkins Verbal Learning Test-Revised, memory function, radiotherapy

Outcome measures

Primary outcome

To assess memory function at 4 months after PCI versus HA-PCI. A decline of 5

points in the total recall score will be considered as a failure.

Secondary outcome

* To assess early and late neurotoxicity and quality of life following PCI with

or without hippocampal sparing.

* To assess structural brain damage from PCI on MRI with and without sparing of

the hippocampus.

* To assess the incidence and location of brain metastases after PCI with or

without hippocampal sparing.

* Overall survival.

Study description

Background summary

The high incidence of brain metastases is a major problem in lung cancer patients because of serious impairment in patients* quality of life, shortened survival and life-threatening symptoms. Systemic treatment options to treat brain metastases are limited. If brain metastases become symptomatic

radiotherapy is often inadequate to diminish the neurological symptoms. PCI proved to reduce the incidence of brain metastases significantly in patients with limited and extensive SCLC in remission after treatment of the primary tumor, and increased the patient*s overall survival. Cognitive deficits after Prophylactic Cranial Irradiation (PCI) play an important role in the neurological morbidity after radiotherapy.

The reduction in the incidence of brain metastases after prophylactic whole brain irradiation should be counterbalanced with the radiotherapy associated neurological complications. Observed symptoms after PCI include predominantly mental slowing, loss of concentration, short memory problems and fatigue. It is described that blocking of the hippocampi (a centrally located structure) during PCI may diminish cognitive side effects. Modern radiotherapy techniques makes the relative sparing of this hippocampal area achievable. Recent attempts to reduce cognitive side effects of PCI by introducing hippocampi avoidance PCI (HA-PCI) have not been fully investigated yet. Patients with small cell lung cancer will be randomized between conventional whole brain PCI and HA-PCI. Cognitive functioning will be evaluated with specific neuropsychological tests 5 times from baseline until 2 years after PCI. Also pre and post PCI Magnetic Imaging (MRI) scans of the brain will be compared to evaluate brain metastases, white matter lesions and to measure and compare the hippocampi volumes before and after treatment.

At three time points blood will be drawn for biomarkers (Placental Growth Factor and neuro-inflammatory markers) as predictors of the incidence of brain metastases and neuro-inflammation

Study objective

To assess memory function at 4 months after Hippocampus Avoidance-PCI versus standard whole brain PCI

Study design

It is a randomised Phase III study in which SLCL patients will receive Prophylactic Cranial Irradiation with or without Hippocampal avoidance.
Since concurrent use of systemic therapy may influence the risk on memory function and other neurocognitive functioning and influence quality of live, concurrent systemic treatment is not allowed until three weeks prior to PCI
Patient will have prophylactic whole brain irradiation in 10 fractions with a total dose of 25Gy.
Study duration is 4 years but two years for the individual patient.

Intervention

Patient will receive prophylactic brain irradiation in 10 fractions

Study burden and risks

Patient will receive a prophylactic PCI versus a HA-PCI in 10 fractions of radiotherapy. Neurocognitive functions will be tested a 6 time points. Also MRI scans of the brain will be processed to measure and compare the hippocampal volumes. And biomarkers will be drawn to analyse predictors

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

* SCLC patients (stage I-III or stage IV without clinical or radiological evidence of brain metastases) candidate for PCI, i.e. without progressive disease after chemo-radiotherapy in stage I-III or after a remission after chemotherapy in stage IV

* WHO-performance status * 2(see Appendix IV).
* Sufficient proficiency in Dutch language
* Written informed consent must be given according to ICH/GCP, national and local regulations

Exclusion criteria

* Prior radiotherapy to the brain
* clinical evidenceof brain metastases or primary brain tumors
* Evidence of progressive extracranial metastatic disease
* Previous malignancy < 2 years ago except for adequately treated basal cell carcinoma of the skin and carcinoma in situ of the cervix
* Any systemic anticancer treatment during PCI or within 3 weeks before start PCI.
* Pregnancy or lactation

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:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-04-2013
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO Date:	27-02-2013
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-11-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-01-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-01-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-02-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-03-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-07-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-10-2014

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-08-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-01-2017
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
CCMO	NL41178.031.12