PRophylactic cerebral Irradiation or active MAgnetic resonance imaging surveillance in small-cell Lung cancer patients

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The primary objective is to show that brain MRI surveillance alone is non-inferior in terms of overall survival (OS) to brain MRI surveillance combined with prophylactic cranial irradiation (PCI) for the treatment of small cell lung cancer (SCLC).

Ethical review	Approved WMO
Status	Pending
Health condition type	Metastases
Study type	Interventional

Summary

ID

NL-OMON57223

Source
ToetsingOnline

Brief title
PRIMALung

Condition

- Metastases
- Respiratory tract neoplasms

Synonym
matastasis in the brain

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: Astra Zeneca,Lung Cancer Group; Belgian Government Association; La Ligue Contre le Cancer; Unicancer; Swiss Canver League

Intervention

Keyword: brain metastases, MRI surveillance, prophylactic cranial irradiation, Small- cell Lung cancer

Outcome measures

Primary outcome

In this phase III study, the primary objective is to show that overall survival

(OS) with brain MRI surveillance alone is non-inferior to brain MRI

surveillance combined with prophylactic cranial irradiation (PCI) for the

treatment of small cell lung cancer (SCLC).

The primary endpoint in this study is overall survival (OS).

Secondary outcome

The secondary objectives are:

• To show that brain MRI surveillance is superior in terms of cognitive failure

free survival (CFFS) compared to prophylactic cranial irradiation (PCI)

combined with brain MRI surveillance.

• To show that brain MRI surveillance is superior in terms of global health

status/QoL and cognitive functioning according to EORTC QLQ-C30 questionnaire

compared to prophylactic cranial irradiation (PCI) combined with brain MRI

surveillance.

• To evaluate the frequency and severity of toxicities according to CTCAE v5.0

in the two arms.

• Cognitive failure free survival (CFFS) as measured by the study cognitive functioning tests (HVLT-R, COWA, and Trail-making Test) (see chapter 8 on Criteria of evaluation for the exact definition of this endpoint).

• Global health status/QoL and cognitive functioning according to QLQ-C30 questionnaire.

• Safety according to the CTCAE (NCI Common Terminology Criteria for Adverse Events) Version 5.0 for toxicity and Serious Adverse Event reporting.

Study description

Background summary

Small-cell lung cancer (SCLC) is characterised by a rapid doubling time and early dissemination, including to the brain. Patients with SCLC are typically divided into those with limited-stage (LS) versus extensive-stage (ES) disease. LS is defined as disease confined to one hemithorax (i.e., disease which can be included in a "tolerable" radiation field). ES consists of the remainder cases that could not be safely treated with radiotherapy initially.
About one-third of patients present with LS disease, although many of these patients probably already have subclinical metastatic disease. Concurrent thoracic chemoradiotherapy (CTRT) is the mainstay of the treatment of patients with LS-SCLC because of the high likelihood of early dissemination, both locally and distantly.
Initial platinum-based chemotherapy-immunotherapy with anti PD-L1 (atezolizumab or durvalumab) has recently become the standard first-line treatment in ES-SCLC. As brain metastases (BM) develop in more than 50% of ES patients, prophylactic cranial irradiation (PCI) has been offered to SCLC patients who respond to initial treatments to decrease the frequency of subsequent intracranial relapse and improve survival.
While PCI is accepted as the standard of care in LS-SCLC and optional in guidelines for ES-SCLC, recent concerns with regards to neurotoxicity and the availability of brain MRI active surveillance have challenged the routine use of PCI, particularly in ES SCLC. Furthermore, there are questions about the role and sequencing of PCI in the era of immunotherapy, particularly in ES SCLC.

In order to evaluate active brain MRI surveillance in SCLC patients, we propose to perform a randomized phase III trial comparing active brain MRI surveillance alone (experimental arm) to brain MRI surveillance combined with PCI (control arm) in patients with any stage SCLC.

Study objective

The primary objective is to show that brain MRI surveillance alone is non-inferior in terms of overall survival (OS) to brain MRI surveillance combined with prophylactic cranial irradiation (PCI) for the treatment of small cell lung cancer (SCLC).

Study design

Patients will be treated with Standard of Care treatment. patients with any response and no brain metastases on baseline MRI brain will be randomized betwee intervention arm (no PCI and surveillance with MRI every three months) and control group (PCI followed by MRI every three months)

patients will be randomized in a 1:1 ratio between the 2 arms, and stratified by country, stage of disease (limited versus extensive), use of immunotherapy as part of the first-line treatment (yes/no), and ECOG Performance Status (0 or 1 versus 2).

Brain MRI will be performed every 3 months until month 12 and thereafter every 6 months until month 24, from randomization, regardless of delayed or interrupted treatment.
Chest-abdomen-pelvis contrast CT scan or MRI shall be performed per institutional standards at the discretion of the treating physician. However, it is recommended to perform an assessment every 3 months until month 12 and thereafter every 6 months until month 24.

Intervention

Prophylactic cranial irradiation will be delivered at the dose of 25 Gy in 10 fractions to the whole brain. PCI should be initiated at the latest 14 days post randomization.
Patients must have a brain MRI performed within 28 days before randomization and at 3, 6, 9, 12, 18 and 24 months after randomization (see brain MRI guidelines).
Clinical evaluation will be performed every 3 months up to month 12.
Extracranial imaging is recommended and will be performed per institutional standards at the discretion of the treating physician.

Study burden and risks

Both groups will have brain MRI's and Quality of Life forms.
Control group will have prophylactic cranial irridiation.
Intervention group will only receive brain irridiation when brain metastases develop. Not receiving brain irridiation when there are no brain metastases present will result in longer cognitive failure free 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

• Age >= 18 years
• Histologically/cytologically proven diagnosis of SCLC
• Absence of progressive disease after completed standard therapy on systemic imaging (computed tomography (CT) or magnetic resonance imaging (MRI) of Chest/Abdomen/Pelvis), 42 days before randomization.

• Absence of brain metastases or leptomeningeal disease after completed standard therapy on systemic imaging (brain MRI), within 28 days before randomization.
Limited and extensive stage:
• LS SCLC: Stage I-III (T any, N any, M0, according to UICC TNM staging v8.0) that can be safely treated with definitive radiation doses.
• ES SCLC: Stage IV (T any, N any, M 1a/b/c), or T3-4 due to multiple lung nodules that are too extensive or have tumour/nodal volume that is too large to be encompassed in a tolerable radiation plan.

Exclusion criteria

• Prior radiotherapy to the brain or whole brain radiotherapy.

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:	Pending
Start date (anticipated):	01-01-2025
Enrollment:	9
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	19-11-2024
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NCT04790253
CCMO	NL85190.042.23