Randomized phase II study of amrubicin as single agent or in combination with cisplatin versus etoposide-cisplatin as first-line treatment in patients with extensive stage SCLC (ES).

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Investigate the activity and safety of amrubicin alone versus amrubicin incombination with cisplatin versus standard treatment for extensive disease(ED) small-cell lung cancer in the first line setting.

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON30640

Source
ToetsingOnline

Brief title
amrubicin, amrubicin-cisplatin versus etoposide-cisplatin in SCLC

Condition

- Respiratory disorders NEC

Synonym
lung cancer; small cell lung cancer extensive disease

Research involving
Human

Sponsors and support

Primary sponsor: European Organisation for Research in Treatment of Cancer (EORTC)
Source(s) of monetary or material Support: Ministerie van OC&W,Cabrellis Pharmaceutical Cooperation,Cabrellis Pharmaceutical Cooperation / 9393 Towne Centre Drive / 92121 San Diego - California USA

Intervention

Keyword: activity and safety, amrubicin, first-line treatment, small cell lung cancer

Outcome measures

Primary outcome

Objective tumor response, measured according to the RECIST criteria, will

be used as the principal endpoint in this trial. Disease assessments will be

preformed every 2 cycles.

Secondary outcome

Safety: This study will use the International Common Toxicity Criteria (CTCAE),

version 3.0, for toxicity and adverse event reporting.

progression-free survival (PFS)

overall survival (OS).

Study description

Background summary

The standard for treatment is Cisplatin with Etoposide. In Europe, platinum-based combination chemotherapy has become the standard for the treatment of extensive disease SCLC (ED SCLC). Results of treatment remain far from satisfactory since virtually all patients die of disease and long term survivors are very few (under 10%). One way to improve upon these results is

the incorporation of new agents into existing combinations.
The combination of amrubicin and cisplatin has demonstrated an impressive response rate (87.8%) and MST (13.6 months) in Japanese patients with previously untreated ED-SCLC while amrubicin single agent produced the response rate of 76%. The majority of patients receiving the amrubicin regimen developed neutropenia, but cardiotoxicity typical for anthracyclines was not common. Therefore, a confirmation of these results in a non-Japanese population is of interest. The single agent data, if confirmed, would make this a preferable agent to a cisplatin combination in a significant number of patients.

Study objective

Investigate the activity and safety of amrubicin alone versus amrubicin in combination with cisplatin versus standard treatment for extensive disease (ED) small-cell lung cancer in the first line setting.

Study design

This is an open randomized 3-arm multicenter late phase II study. Patients will be stratified by WHO status, sex and institution. The primary endpoint is response rate. A one-stage Fleming design has been used to design the study.

Intervention

ARM 1: 3-weekly cycles of amrubicin (45 mg/m², days 1-3);
ARM 2: 3-weekly cycles of amrubicin (40 mg/m² days 1-3) + cisplatin (60 mg/m², day 1);
ARM 3: 3-weekly cycles of cisplatin (75mg/m², day 1) + etoposide (intravenous injection 100 mg/m² on day 1, oral administration 200mg/m² on days 2-3).
Treatment should start within 7 days of randomization.

Study burden and risks

At start of the study: anamnese (including medication intake), general condition, medical history and physical examintaion. Before start of treatment a CT of the head, thorax and abdomen are made. During treatment this will be repeated every 6 weeks.
Before each chemotherapy treatment: blood sample, physical examination, adverse events and concomitant medication.
An ECG and echocardiogram will be carried out before and at the end of treatment. At the last visit:a physical examination, which may include an assessment of sensory neurological clinical symptoms.

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

-Histologically/cytologically proven small cell lung cancer
-WHO performance status 0-2
-Measurable disease according to RECIST criteria
-Age > 18 years
-Normal baseline cardiac function
-Adequate haematological function (WBC >1.5 x 10 9/L, platelets >100 x 10 9/L, Hb >9 g/dL)
-Creatinine clearance: > 60 ml/min (Cockcroft and Gault)
-Adequate hepatobiliary function (ALAT/AST <2.5 x Upper Limit of Normal)
-Written informed consent before randomization, according to ICH/EU GCP and national/local regulations

Exclusion criteria

-No prior systemic chemotherapy for small cell lung cancer
-No history of interstitial lung disease or pulmonary fibrosis
-No history of prior malignancy unless patient has been disease free for >5 years, or the tumour was a non-melanoma skin cancer or in-situ carcinoma of the cervix
-Absence of pre-existing peripheral neuropathy (CTCAE version 3.0 grade >1)
-Absence of uncontrolled or severe cardiovascular disease including myocardial infarction within 6 months of enrollment, New York Heart Association Class III or IV heart failure, uncontrolled angina, clinical significant pericardial disease or cardiac amyloidosis
-No pregnancy or breast feeding. Men and women of child bearing potential must use an appropriate method of contraception if the risk of conception exists

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2006
Enrollment:	14
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	amrubicin
Generic name:	amrubicin

Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Etopophos
Generic name:	Etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vepesid
Generic name:	Etoposide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Application type:	First submission
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
EudraCT	EUCTR2006-001956-11-NL
CCMO	NL14506.018.06