Chloroquine as an anti-autophagic radiosensitizing drug in stage I-III small cell lung cancer (SCLC) patients: A phase I trial.

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To determine the toxicity of adding chloroquine in escalating doses in patients with small cell lung cancer to standard therapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON41612

Source
ToetsingOnline

Brief title
Chloroquine I-III

Condition

- Respiratory tract neoplasms

Synonym
small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic
Source(s) of monetary or material Support: METOXIA en MAASTRO

Intervention

Keyword: autophagy, chloroquine, phase I trial, small cell lung cancer

Outcome measures

Primary outcome

Toxicity

Secondary outcome

- Tumor response

- Overall survival

Study description

Background summary

Tumor hypoxia is al well-known factor negatively influencing the outcome in many solid tumors, including small cell lung cancer. Hypoxic cells are more radio-resistant, more chemo-resistant and more prone to develop distant metastases than normoxic cells. One of the mechanisms responsible for survival of these therapy-resistant hypoxic cells is (macro-)autophagy: a phenomenon in which cells provide themselves with energy (ATP) by digesting their own cell-organelles. Chloroquine is a potent blocker of autophagy and has been demonstrated in a lab setting to dramatically enhance tumor response to radiotherapy, chemotherapy and evenanti-hormonal therapy.
Thus, chloroquine might very well be able to increase overall survival in small cell lung cancer by sensitizing cells reistant to chemotherapy and radiotherapy.

Study objective

To determine the toxicity of adding chloroquine in escalating doses in patients with small cell lung cancer to standard therapy.

Study design

Phase I study

Intervention

Addition of chloroquine to (chemo)radiotherapy

Study burden and risks

The examinations that take place for this study are done while patient is hospitalized for the standard chemotherapy. This decreases the burden for the patient to a minimum. Patients are submitted to a hearing and eye-test and lungfunction. Furthermore, they are asked to note the intake of chloquine.

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 or cytologically confirmed ``stage I-III`` ie stage T0-4 N0-3 M0 small cell lung

cancer, excluding malignant pleural/pericardial effusion.
. WHO performance status 0-2
. Absolute neutrophil count at least 1800/µl and platelets at least 100000/µl and hemoglobin at least 6.2 mmol/l.
. Adequate renal function: calculated creatinine clearance at least 60 ml/min
. Adequate hepatic function: Total bilirubin * 1.5 x upper limit of normal (ULN) for the institution; ALT, AST, and alkaline phosphatase * 2.5 x ULN for the institution (in case of liver metastases * 5 x ULN for the institution)
. No previous platinum chemotherapy or topo-isomerase-inhibitors for SCLC.
. Lung function: FEV1 at least 30 % and DLCO at least 30 % of the age predicted value
. No history of prior chest radiotherapy
. Life expectancy more than 6 months
. Willing and able to comply with the study prescriptions
. 18 years or older
. Not pregnant or breast feeding and willing to take adequate contraceptive measures during the study
. Ability to give and having given written informed consent before patient registration
. No mixed pathology, e.g. non-small cell plus small cell cancer
* No recent (< 3 months) severe cardiac disease (NYHA class >1) (congestive heart failure, infarction)
. No history of cardiac arrythmia (multifocal premature ventricular contractions, uncontrolled atrial fibrillation, bigeminy, trigeminy, ventricular tachycardia) which is symptomatic and requiring treatment (CTC AE 3.0), or asymptomatic sustained ventricular tachycardia. Asymptomatic atrial fibrillation controlled on medication is allowed.;. No cardiac conduction disturbances or medication potentially causing them:;- QTc interval prolongation with other medications that required discontinuation of the treatment
- Congenital long QT-syndrome or unexplained sudden death of first degree relative under 40 years of age
- QT interval > 480 msec (note: when this is the case on screening ECG, the ECG may be repeated twice. If the average QT-interval of these 3 measurements remains below 480 msec, patient is eligible)
- Patients on medication potentially prolongating the QT-interval are excluded if the QT-interval is > 460 msec (Appendix, table 2).
- Medication that might cause QT-prolongation or Torsades de pointes tachycardia is not allowed (Appendix, Table 1). Drugs with a risk of prolongating the QT-interval that cannot be discontinued are allowed, however, under close monitoring by the treating phtysician (Appendix, table 2).
- complete left bundle branch block;* No uncontrolled infectious disease
. No other active malignancy
. No major surgery (excluding diagnostic procedures like e.g. mediastinoscopy) in previous 4 weeks
. No treatment with investigational drugs in 4 weeks prior to or during this study
. No chronic systemic immune therapy
. No known G6PD deficiency
. Patients must not have psoriasis or porphyria.
. No known hypersensitivity to 4-aminoquinoline compound.
. Patients must not have retinal or visual field changes from prior 4-aminoquinoline

compound use.
. No known prior hypersensitivity to cisplatin, etoposide or chloroquine or any of their components.

Exclusion criteria

The opposite of the inclusion criteria

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-02-2013
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	A-CQ 100
Generic name:	Chloroquine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	27-02-2014

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-05-2014
Application type:	First submission
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
EudraCT	EUCTR2012-001774-28-NL
ClinicalTrials.gov	NCT01575782
CCMO	NL40391.068.12