Comparing tumour heterogeneity in primary tumour, circulating tumour cells and its metastases

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- Comparing the heterogeneity of the original tumour and its metastases.- Comparing the mutations in CTC*s to those of both the original tumour and the metastatic processes.- Assessing whether certain mutations precede the others (so called trunk...

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON45251

Source
ToetsingOnline

Brief title
CTC Autopsy study

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: het innovative Medicine initiative van de europese unie heeft betaald voor de PhD student (M. Tamminga). zij hebben het UMCG 300.00 toegekend. De overige kosten worden gedragen door de afdeling longziekten van het UMCG.

Intervention

Keyword: lung cancer, NSCLC, SCLC, tumour heterogeneity

Outcome measures

Primary outcome

immunohistochemistry and genome sequencing with specific mutations and

mutational load.

Secondary outcome

not applicable

Study description

Background summary

Therapeutic decisions in lung cancer are increasingly dependent on adequate tumour tissue biopsies. However, amongst others, tumour heterogeneity and technical issues with the handling of tissue allow adequate diagnosis in only part of patients(1,2). We are interested in the tumour heterogeneity, as it provides crucial information regarding the metastatic processes of tumours and the response to treatment.
To study the tumour heterogeneity adequately, we plan to obtain material from all accessible metastatic tumour sites and the primary tumour from patients with metastasized lung cancer ([N]SCLC) after they have passed away, by an autopsy.
As CTC*s are an important prognostic factor, and play an important role in the metastatic process, all subjects that participate in this study will have 15mL blood drawn at a regular outpatient visit, in order to obtain CTC*s. These CTC*s will be studied for their genetical characteristics and will be compared to both the original tumour and its metastases. We think it is important to incorporate CTC*s as liquid biopsies in the project as they may help to bypass the problems of normal biopsies: CTCs do not have the issue of contamination with normal cells and DNA/RNA from leukocytes that come with this technique can be harvested in the same run(3).

Therefore, CTCs may replace current tumour biopsy practices when an adequate number of tumour cells can be detected, while also giving the option for further mutation analysis(4,5). But while specific mutations have been assessed, it is unknown whether CTC*s accurately reflect the heterogeneity of the malignancies.
In this study we can assess whether the CTC*s do reflect the heterogeneity by comparing them to the original tumour. At the same time we are able to assess the differences between original tumour and metastases and the differences in the heterogeneity by comparing SNP, mutations and DNA instability. Our hypothesis is twofold: Firstly, that the metastatic processes will have less heterogenicity than the primary tumour. Secondly, that the CTC*s will mimic original tumour heterogeneity, but are more closely related to the metastases and that this is visible in the mutations and genetic profile.

Study objective

- Comparing the heterogeneity of the original tumour and its metastases.
- Comparing the mutations in CTC*s to those of both the original tumour and the metastatic processes.
- Assessing whether certain mutations precede the others (so called trunk and branch mutations).
- Analyzing whether mutations in metastases all originated from the primary tumour.

Study design

Terminal patiënts with proven lung cancer (NSCLC or SCLC, cytological or pathological proven) will be asked to participate. The treating physician will assess wether he can bring this research up with the patient. If he deems the patient can't discuss it, he will abstain from doing so, but otherwise he will give the patient an introduction and the written information.
If the patient approves, we will draw some blood from which we can obtain CTCs. After the participants death, the family will be asked to consent with an obduction, which will be recorded in the patients file according to common practice. A warm obduction will be performed during which biopsies will be taken. These biopsies will be processed by the pathological department of the UMCG as patient material. The biopsies will be used for genetic testing on heterogeneity and mutational load and specific mutations. The different biopsies will be compared to one another using paired statistics

Study burden and risks

While the risk associated with the study is inherently low (it mostly takes places after the participant has deceased), we do believe there could be an emotional strain considering the nature of participating in this study. The question of autopsy is not always easy for a patient, but we believe that the

insights we could gain by this research could be important in the future. Ofcourse it goes without saying that physicians will bring up the subject only with patients they deem capable of handling this topic. And they will bring the subject as tactfully as possible.

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

1. Patients with a histologically/cytologically proven lung cancer.
2. Patients have to have a non-curable disease state, without curative treatment options
3. Signed informed consent of patient
4. Patients family has asserted their acceptance of the patients participation

Exclusion criteria

none

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2017
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

Date:	30-08-2017
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

ID: 29203
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL59037.042.16
OMON	NL-OMON29203