Circulating tumour cells by diagnostic leukapheresis mirror primary tumour heterogeneity in non-small cell lung cancer

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON19904

Source
NTR

Brief title
CANCER-ID CTC-DLA

Health condition

circulating tumour cells (CTC)
Non small cell lung carcinoma (NSCLC)
Diagnostic leukapheresis (DLA)
tumour heterogeneity
circulerende tumor cellen (CTC)
niet kleincellig long carcinoom (NSCLC)
diagnostische leukopherese (DLA)
tumor heterogeniteit

Sponsors and support

Primary sponsor: Sponsor: Innovative Medicine initiative
performer: UMCG
Source(s) of monetary or material Support: Innovative Medicine initiative

Intervention

Outcome measures

Primary outcome

Number of CTC's and percentage of patients who had CTC's detected. And comparing the CTC detection percentage per disease stage (stage I-IV).

Secondary outcome

survival and mutations measured in the CTC's and the original tumour.

Study description

Background summary

Circulating tumour cells (CTCs) are a strong predictor of prognosis and can be used as a biomarker for early detection of systemic cancer spread, therapy monitoring, and nowadays also for single cell genomics. Obtaining relevant information from blood by so called “liquid biopsies” is thus a simple method to detect tumour cells. Therapeutic decisions in lung cancer are increasingly dependent on adequate tumor tissue biopsies. However, amongst others, tumour heterogeneity and technical issues with the handling of tissue allow adequate diagnosis in only part of patients. CTCs may help to bypass these problems: 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.

Therefore, CTCs may replace current tumour biopsy practices when an adequate numbers of tumour cells can be detected, while also giving the option for further mutation analysis. Immunomagnetic enrichment of cancer cells from blood samples expressing membranous epithelial cell adhesion molecule (EpCAM) protein led to the development of the FDA approved CellSearch system, nowadays the most widely used standard for CTC detection. The relevant detection rate is set on >2 or >5 CTCs per 7.5 ml blood sample. Clinical use of CTCs is currently limited in NSCLC because all systems fail to detect CTCs at an acceptable rate and at a sufficient high yield (for mutation analysis) in a large fraction of patients. For NSLC, CTCs are observed in 26 to 49% of patients with metastatic disease. In nonmetastatic disease one CTC per 7.5 ml is observed in only 5 to 24% of patients. Extrapolation of CTC frequency distribution in 7.5 ml of blood from patients with metastatic breast, colon and prostate cancer showed that probably all these patients had CTCs in circulation, but the sample volume was not sufficient to detect them in all patients. A possible solution for this problem would be to significantly increase the blood volume. This can be achieved with leukapheresis that has been specified to increase CTC detection by means of a filter (e.g. Vycap). We hope this would provide a more reliable detection of CTCs at a higher frequency,

and that by using this technique CTC’s can be found in sufficient high yield, even in nonmetastatic disease. We will study these issues within the European CANCER-ID consortium, a public-private partnership supported by Europe’s Innovative Medicines Initiative (IMI) with currently 38 partners aiming at clinical validation of blood borne biomarkers and establishing standard protocols for these. Leukapheresis, a standard clinical method to isolate mononuclear cells (MNCs) from blood, is currently used as routine practice in hematological diseases. Usually one to five liters of blood is processed in adults. Diagnostic leukapheresis (DLA) has previously been studied in solid cancer patients. Median total processed blood volume for lung cancer was 2,6 l (1,4 – 11,0). This resulted in 56 mL (40 – 156) volume of DLA product with 40.108 MNCs. The detection rate of CTCs in peripheral blood was 22% versus 56% in DLA. The procedure took one hour without adverse events.

In this study we will first explore the frequency and number of CTCs in all stages of NSCLC. Our hypothesis is that CTCs mirror the primary tumour heterogeneity at different stages of disease. Therefore, we will combine diagnostic leukapheresis with single cell genetics to study tumour heterogeneity for the prediction of therapy response in different stages of NSCLC patient groups.

Study objective

Circulating tumour cells can help to diagnose Non small cell lung cancer (NSCLC), making the painful and invasive procedure of a lungbiopsy and bronchoscopy unnecesary. However, for this, we need to harvest higher amounts of CTC's and in more patients then we do using the current methods. Using diagnostic hemopharesis, we hope to obtain larger amount of cells in a larger percentage of the lung cancer patients.

Study design

Patients will be followed untill the end of the study to measure survival. Otherwise they will have two measurements: one at diagnosis and one 3 weeks after their first treatment regimen or operation.

Intervention

All patients will undergo apharesis: A procedure regularly used by the hematological department in the treatment of leukemia patients to isolate mononuclear cells (MNCs) from blood. We use this method because we can isolate circulating tumour cells (CTC's) from the apharesis product.

Contacts

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Eligibility criteria

Inclusion criteria

Patients with a histologically proven pulmonary malignancy (all disease stages)

Performance status 0-2

Patients using anticoagulants such as fraxodi or acenocoumarol are allowed, unless they have hemorrhagic events

Signed informed consent

Exclusion criteria

Patients with insufficient peripheral venes to undergo leukapheresis

Haemorrhagic diathesis: recent CVA, major bleeding, ulcus duodeni

Cardiac failure, LVEF<40%

No growth factors are allowed

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial

Control: N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2016
Enrollment:	80
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 43511
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL5423
NTR-old	NTR5540
CCMO	NL55754.042.15

Register	ID
OMON	NL-OMON43511

Study results