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

Gepubliceerd: 09-12-2015 Laatst bijgewerkt: 15-05-2024

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Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON19904

Bron
NTR

Verkorte titel
CANCER-ID CTC-DLA

Aandoening

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

Ondersteuning

Primaire sponsor: Sponsor: Innovative Medicine initiative

performer: UMCG
Overige ondersteuning: Innovative Medicine initiative

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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).

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd

Controle: N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-01-2016
Aantal proefpersonen:	80
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 43511
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL5423
NTR-old	NTR5540
CCMO	NL55754.042.15
OMON	NL-OMON43511

Resultaten