Validation of circulating tumor cells (CTC) detection techniques in patients with advanced solid tumors

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

Summary

ID

NL-OMON33920

Source
ToetsingOnline

Brief title
CTC detection in advanced solid tumors

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Advanced cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Eisai,Farmaceutisch bedrijf

Intervention

Keyword: cancer, circulating tumor cells, CTC, solid

Outcome measures

Primary outcome

Primary objective

To optimize CTC detection assay sensitivity and specificity in different types of advanced solid tumors by comparison of enrichment techniques and expression level of a panel of selected marker genes.

Amendment:

To compare CTC detection results of the FAST cytometry method to the qRT-PCR method.

Secondary outcome

Secondary objectives

To determine intra-patient variation of CTC detection assay outcome.

To assess inter-patient variation in CTC detection assay outcome.

To determine which CTC detection assay is best suitable in the population of patients that participate in clinical trials.

Study description

Background summary

The development of metastasis in cancer reduces prognosis, increases morbidity and marks a change in the focus of treatment since this is no longer aimed at curation but at palliation. The pathophysiology of metastasis therefore is the subject of extensive research. The process of metastasis involves different

stages: outgrowth of the primary tumor, angiogenesis, intravasation of tumor cells into circulation, extravasation of tumor cells at distant organs, proliferation into micrometastasis and outgrowth of metastasis.
Although they are rare, intravasated circulating tumor cells (CTC) can be identified in whole blood and bone marrow of a cancer patient. In prospective trials of breast cancer patients, the number of CTCs at baseline was found to be a predictor of progression-free survival and overall survival and an increase in number of CTCs during treatment indicated a deterioration of prognosis. CTC detection assays could be used to monitor efficacy of therapy and to detect disease progression in an early stage. Currently, CTC detection techniques are being developed to serve in the clinic to improve diagnostics and to predict prognosis.
Because CTCs are rare, isolation is mainly based on combined enrichment and subsequent detection of cell-specific markers by, for example, immunocytochemistry or semi-quantitative RT-PCR. Current enrichment techniques include both immunomagnetic enrichment and depletion, filtration by size and a recently described adapted flow chamber. Quantification techniques include immunocytochemistry, immunofluorescence and semi-quantitative RT-PCR.
For breast cancer, by group van*t Veer, already a highly sensitive and specific assay for whole blood was developed and optimized. CTCs were found in 87,5% of patients with advanced breast cancer. This assay uses an immunomagnetic column with both ErbB2 and CD326 antibodies followed by semi-quantitative RT-PCR with selected multiple marker genes.

Study objective

In our opinion, CTCs could serve as a pharmacodynamic marker to monitor anti-cancer therapy in clinical trials. Encouraging results, that show that CTCs have pharmacodynamic properties, were recently found in a prospective trial in which CTC number was studied in whole blood in patients with adjuvant chemotherapy for breast cancer. An increase or decrease in CTC number after starting chemotherapy was associated with respectively a worsened and improved prognosis (Pachmann et al 2008).
Such biomarkers are very much needed in developing drugs to assess anti-tumor activity in an early stage of treatment, to identify patients that could benefit from treatment and to target proper dosing. For example, for specific anti-angiogenic therapy, circulating endothelial cells (CECs) is being studied as such in (Bertolini et al 2006).
The focus of this study is to further optimize and to validate enrichment and detection techniques for CTCs in whole blood. For this, CTC assays need to be optimized in a well defined but heterogenic group of patients with metastasized solid tumors.

Study design

Observational, laboratory experimental.

Written informed consent will be obtained from all patients and normal volunteers. For every selected type of tumor, we will investigate a group of a minimum of 5 patients and a maximum of 20 patients that are being treated at the NKI-AVL. Normal volunteers will serve as control group.
From every patient, per visit, 3x8 ml of whole blood will be drawn simultaneously. With these samples, 2 different techniques will be compared (2x8 ml). The third (1x8 ml) will serve as duplicate or, in later analysis, for storage analysis.
From every patient, sampling will be repeated with a total maximum of 6 times. The inclusion period will be the same as the overall study time. This will be 5 months.

Study burden and risks

The burden of sampling includes veni-puncture under the skin and could consist of well-known side-effects: discomfort, bruising and hematoma, infection.

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

Patients who are treated for advanced solid tumors;
Age of 18 years or older;
Able and willing to give written informed consent;
Able and willing to undergo veni-puncture;
Life expectancy of 3 months or more;
WHO performance status of 0, 1 or 2;

Exclusion criteria

Any condition that may interfere with the study protocol

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-06-2008
Enrollment:	200
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
CCMO	NL22872.031.08