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Isolation of circulating tumor cells from the blood of prostate cancer patients using an antibody-coated nanodetector

Submission date 23/01/2012	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 06/02/2012	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 02/11/2012	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims.
Prostate cancer is the most common type of tumour and the second leading cause of all cancer-related deaths in men. Prostate cancer in advanced stages develops metastasis- most often in bones. In the clinical course, the cancer is very often resistant to hormone therapy (androgen resistance), which is associated with a poor outcome. For 20 - 40% of patients, those with advanced disease at the time of diagnosis there is currently no effective treatment. Basis in the current diagnosis of prostate cancer are digital rectal examination (DRE), the determination of prostate specific antigen (PSA) levels, transrectal ultrasonography (TRUS) and prostate biopsy. PSA is currently the most specific tumour marker for diagnosis, screening and monitoring of prostate cancer. PSA is not a disease-specific marker, since it is also increased in a condition called benign prostate hyperplasia (BPH) and in infected/inflamed prostate glands, conditions which are rather common (they can occur in 25-86% of prostate cancer patients). Also PSA levels may be raised in other non-cancerous diseases, and may even be raised in healthy individuals and there is also the possibility that prostate cancer may be missed in a significant number of patients. The limitations of the PSA assay reflect the lack of reliable measures for predicting the transition from local to metastatic cancer stages. New methods are needed to help doctors in their diagnosis.
The GILUPI GmbH developed a medical device for the isolation of circulating tumour cells (CTCs) directly from the bloodstream. This method has the advantage of capturing the limited number of CTCs directly, instead of using a small blood sample. A thin medical wire, also called nanodetector, is inserted through a conventional venous cannula routinely placed in a vein in the elbow area, so that about 2 cm of the wire reach into the bloodstream. The nanodetector has a special coating which has the ability to bind cancer cells, which after removal of the wire can be counted under the microscope, thus estimating the number of circulating tumour cells in the patients blood. This in vivo method has the advantage of fishing for tumour cells in a much larger volume instead of using only a small blood sample from the patient. Using the fishing analogy, a blood draw would resemble a person going to a river with a bucket and hoping to have a fish in a bucket full of water, whilst the nanodetector resembles a fishing rod placed into the river.
With this study we want to evaluate the sensitivity and specificity of the nanodetector regarding

the isolation of EpCAM-positive tumour cells in prostate cancer patients compared to benign prostate disease and healthy individuals. Secondary objectives are to compare the nanodetector method with the reference system CellSearch, and to see if the isolated tumour cells can be used for the analysis of certain cancer related proteins.

Who can participate?
Requirements to participate in the study:
Group A: prostate cancer patients, confirmed diagnosis of prostate cancer of any stage
Group B: BPH control group, Confirmed diagnosis of any stage of BPH
Group C: Healthy control subjects, female

What does the study involve?
If you take part in the study, first of all, you will be asked to give a small sample of blood to test blood values for inclusion and exclusion criteria. Should you be eligible to participate, the nanodetector will be inserted in an elbow vein. The procedure of the insertion of the nanodetector is similar to inserting a small tube for blood collection and takes 30 min. This is a standard procedure in hospitals and medical practices. All patients in the study are treated in the same way. Afterwards you will be asked again to give a small sample of blood to check if blood values change after the insertion of the nanodetector, and to have a sample for the control method Cell Search.
If you are in group A with prostate cancer and with metastases, you will have 8 applications with the nanodetector (every month in for the first six months, 7th application in the 9th month, 8th application in the 12th month). If you are in group A with prostate cancer without metastases, you will have 3 applications (before surgery, 6 months after surgery and one year after operation). If you are in group B (BPH) you will have 3 applications (1st month, 6th month, 12th month). If you belong to group C (healthy subjects) you will have one application.

What are the possible benefits and risks of participating?
The cancer patients participating benefit from increased regular medical care, ranging from the provision of additional, non-routine measurement of certain blood parameters (cytokines, and the results of clinical examination (results of downstream diagnostics: ability to distinguish between a localized and metastatic prostate cancer).
The application with the nanodetector is similar to a normal blood collection. Therefore the risk for the participants is comparable to the risk of a normal blood collection. All insertions of the nanodetector will be carried out by trained physicians.

Where is the study taking place?
The study takes place at the university hospital and health care centre of Urology and Kidney transplantation centre of the Martin-Luther University Halle-Wittenberg, Germany.

When is the study starting and how long is it expected to run for?
Patients have been enrolled since December 2010, and the study will end 1 year after inclusion of the last cancer or BPH patient. By that time 105 patients should have been enrolled.

Who is funding the study?
The study is being funded by the GILUPI company (Potsdam, Germany)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CIP FSMW EpCAM-Prostata-M000

Study information

Scientific Title
Isolation of circulating tumor cells from the blood of prostate cancer patients using an antibody-coated nanodetector: An explorative mono-center non-randomized blinded trial

Study objectives
This is a single-center exploratory study in which an antibody coated nanodetector called the Functionalized Structured Medical Wire (FSMW) is evaluated in vivo as a medical device. The performance of the FSMW will be estimated by counting the number of circulating tumor cells isolated in vivo. The specificity is determined by a single application in healthy subjects.

The CellSearch system, using a similar antibody-based extraction technique for circulating tumor cells in a single blood sample in vitro, will be used as a reference system. Furthermore the CEER-Assay (Prometheus Labs) will be used for an explorative analysis of certain tumor relevant protein pathways on the isolated circulating tumor cells (CTCs).

Please note that as of 02/11/2012, the following changes were made to the record:
1. The target number of participants was updated from 80 to 105
2. The anticipated end date was updated from 28/02/2013 to 31/03/2014

Ethics approval required
Old ethics approval format

Ethics approval(s)

The Committee on Ethics at the Medical Faculty of the Martin-Luther University in Halle,13th April 2010 (ref: FSMW EpCAM-Prostata-M000); amendment 1 approved on 16th June 2011, amendment 2 on 24th July 2011 , amendment 3 on 20th April 2012 and amendment 4 on 20th July 2012.

Primary study design
Interventional

Study design
Explorative mono-center non-randomised blinded trial

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Prostate cancer (all stages), Benign prostatic hyperplasia (all stages)

Interventions
The nanodetector will be inserted in all patients from all groups (A, B and C) for 30 min. With this study we want to compare different methods to detect CTCs. Within the groups there are different sets of downstreaming diagnostics.
Group A: 50 % of all patients from this group the nanodetector will be analysed with immunocytochemistry. From the same patients a blood sample will be taken and analysed with the CellSearch method. From 50 % the nanodetector will be analysed with the CEER-Assay.
Group B: : 75 % of all patients from this group the nanodetector will be analysed with immunocytochemistry. From 50 % of the patients a blood sample will be taken and analysed with the CellSearch method. From 25 % the nanodetector will be analysed with the CEER-Assay.
Group C: 75 % of all patients from this group the nanodetector will be analysed with immunocytochemistry. From 25 % of the patients a blood sample will be taken and analysed with the CellSearch method. From 25 % the nanodetector will be analysed with the CEER-Assay.

All methods for detecting circulating tumor cells will be compared at the end of the trial.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Positive isolation of circulating tumor cells from peripheral blood of patients with prostate cancer by using the nanodetector (proof of concept) in comparision to patiens with BPH and healthy volonteers
2. Investigation of the specificity of the device

Key secondary outcome(s)
1. Review of product-application-procedures
2. Comparison of the results with the CellSearch® method
3. Explorative analysis of cancer related cell pathway proteins by using the CEER-Assay (Prometheus Labs)

Completion date
31/03/2014

Eligibility

Key inclusion criteria
Group A
1. Confirmed diagnosis of prostate cancer of any stage
2. Written informed consent of the patient after explanation by the investigator

Group B
1. Are patients which must have the diagnosis of any stages of Benign prostatic hyperplasia (BPH). But apart from this diagnosis, the patients are healthy.
2. Written informed consent of the patient after explanation by the investigator

Group C:
1. Healthy female probands according to anamnestic and clinical criteria
2. Written informed consent of the patient after explanation by the investigator

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Male

Key exclusion criteria
For all groups
1. Age > 18 years
2. Known anaphylaxis
3. Auto immunological diseases: Anti-phospholipid antibody syndrome (lupus anticoagulant), Goodpasture's syndrome, lupus erythematosus, relapsing polychondritis, rheumatoid arthritis, sarcoidosis, scleroderma, Sjogren's syndrome, antineutrophilic cytoplasmic antibody (ANCA); Immuno deficiencies: X-linked aggamaglobulinaemia (XLA), severe combined immunodeficiency (SCID), common variable immunodeficiency (CVID), selective IgA deficiency
3. Known infection with: Hepatitis A, B and C, human immunodeficiency virus (HIV), herpes simplex virus (HSV), cytomegalovirus (CMV), syphilis, toxoplasmosis, tuberculosis
4. Not allowed concomitant medication: oral anticoagulants (Phenprocoumon, Coumadin), Platelet aggregation inhibitors (clopidogrel, prasugrel, ASS); recurrent thrombosis and pulmonary embolism
In addition for:
Group A: heart rhythm disturbances, clinically significant hypotension or hypovolemia
Group B:diagnosis prostate cancer
Group C: pregnancy and lactation, malignant tumour

Date of first enrolment
01/12/2010

Date of final enrolment
31/03/2014

Locations

Countries of recruitment
Germany

Study participating centre
Klinik und Poliklinik für Urologie und Nierentransplantationszentrum der Universität Halle-Wittenberg
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Sponsor information

Organisation
GILUPI GmbH (Germany)

ROR
https://ror.org/03fs77m09

Funder(s)

Funder type
Industry

Funder Name
GILUPI GmbH (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration