Cell-derived vesicles as diagnostic instrument for prostate cancer.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28556

Source
NTR

Health condition

prostate cancer

Sponsors and support

Primary sponsor: Academisch Medisch Centrum Amsterdam
Source(s) of monetary or material Support: NWO

Intervention

Outcome measures

Primary outcome

To determine the concentration of tdEVs in plasma and urine in PCa patients and assess whether a relationship exists to disease state.

Secondary outcome

1. To determine whether (elevated levels of) prostate-derived EVs are detectable in plasma and/or urine samples from mCRPC patients compared to both healthy controls as well as controls with elevated PSA.

2. To determine whether (elevated levels of) prostate-derived EVs are detectable in plasma and/or urine samples from early stage PCa patients to both healthy controls as well as controls with elevated PSA.

3. To identify mRNAs that differentiate PCa from controls

4. To assess whether a correlation exists between ctDNA, tdEV, mRNA.

5. To verify that any PCa associated markers from secondary objectives 1-4 are reduced to approximately the control level after prostatectomy.

Study description

Background summary

Prostate cancer (PCa) is the second most frequently diagnosed cancer and the sixth cause of cancer-related death in men worldwide [1]. Prognosis and monitoring of therapy efficacy in metastatic castrate resistant prostate cancer (PCa) is possible using circulating tumor cells (CTCs) in whole blood [1-3]. In castration resistant PCa patients (CRPC) the median concentration is 5 CTC's/7.5 mL whole blood [2]. This low number results in a large uncertainty on the actual concentration of CTCs, which in turn limits the application of CTCs in clinical practice. To detect more CTCs one would either require substantially larger blood samples, or the adjustment of the CTC definition to also include CTC derived particles [4]. A larger blood volume is undesirable due to the burden for the patient. Large (2-4 µm) tumor derived extracellular vesicles (tdEVs) are equally prognostic to CTC, with a 30-fold higher concentration [5]. This result is remarkable because these tdEVs were measured in the cell fraction (red blood cell + buffy coat), while we expect to find the majority in blood plasma. Furthermore, we also expect to find tdEVs in urine. At present, the concentration of tdEVs in plasma and urine are unknown.

Furthermore, the presence of at least one CTC/30 mL blood was prognostic for reduced survival in early stage breast and colorectal cancer [6, 7]. A low number of CTC's were found in locally advanced PCa patients, but not evaluated for prognostic value [10]. Because the number of CTC's correlates to disease stage, and tdEVs are more numerous, we expect to find tdEVs in earlier stage PCa patients, albeit at a lower concentration than in mCRPC patients. Thus, the concentration of tdEVs might be a prognostic indicator for all stages of PCa.

A radical prostatectomy is expected to greatly reduce the number of tdEVs, and thus is expected to prove that the detected tdEVs are prostate specific.

The composition of the selected population is aimed at a first determination of the number of tdEVs in plasma and urine in PCa patients at different stages, together with appropriate controls.

1. Metastatic Castration-Resistant Prostate Cancer. Clinical Cancer Research, 2008. 14(19): p. 6302-6309.

2. Scher, H.I., et al., Circulating tumour cells as prognostic markers in progressive, castration-resistant prostate cancer: a reanalysis of IMMC38 trial data. Lancet Oncology, 2009. 10(3): p. 233-239.

3. Coumans, F.A., S.T. Ligthart, and L.W. Terstappen, Interpretation of changes in circulating tumor cell counts. Translational oncology, 2012. 5(6): p. 486.

4. Coumans, F.A., et al., Challenges in the Enumeration and Phenotyping of CTC. Clinical Cancer Research, 2012.

5. Coumans, F.A.W., et al., All circulating EpCAM+CK+CD45- objects predict overall survival in castration-resistant prostate cancer. Annals of Oncology, 2010. 21(9): p. 1851-1857.

6. Franken, B., et al., Circulating tumor cells, disease recurrence and survival in newly diagnosed breast cancer. Breast Cancer Research, 2012. 14(5): p. R133.

7. van Dalum, G., et al., Importance of circulating tumor cells in newly diagnosed colorectal cancer. International Journal of Oncology, 2015. 46(3): p. 1361-1368.

8. Cristofanilli, M., et al., Circulating tumor cells, disease progression, and survival in metastatic breast cancer. N Engl J Med, 2004. 351(8): p. 781-91.

9. Cohen, S.J., et al., Prognostic significance of circulating tumor cells in patients with metastatic colorectal cancer. Annals of Oncology, 2009. 20(7): p. 1223-1229.

10. Thalgott, M., et al., Detection of circulating tumor cells in different stages of prostate cancer. Journal of cancer research and clinical oncology, 2013. 139(5): p. 755-763.

Study objective

Tumor derived extracellular vesicles (tdEVs) in plasma and urine can be used as a diagnostic instrument for prostate cancer. To determine the concentration of tdEVs in plasma and urine in PCa patients and assess whether a relationship to disease state exists.

Study design

Max. 3 times blood collection and urine. Once at determination PSA value, possibly once before and once after 12 weeks after removal of prostate.

Intervention

n.a.

Contacts

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Eligibility criteria

Inclusion criteria

Healthy volunteers:

Adult male not related to the Urology department ≤ 40 years old. Informed consent signed.

Elevated PSA level:

Patients presenting with a PSA level ≥ 3.0 ng/mL

Informed consent signed.

Before/after prostatectomy:

Patients with localized PCa after prostate biopsy, who are planned for radical prostatectomy.

Informed consent signed.

mCRPC:

Patients with histologically confirmed prostate cancer that is metastatic and progressing despite castrate levels of testosterone (<50 ng/mL).
Informed consent signed.

Exclusion criteria

Healthy volunteers:

Clinical signs of prostate diseases, medical or surgical therapy for prostate disease.

Elevated PSA level:

No history or presence of cancers, or non-prostate urological disorders.

Before/after prostatectomy:

None.

mCRPC:

None.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2018
Enrollment:	60
Type:	Anticipated

Ethics review

Positive opinion

Date:	08-06-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 46711
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL7106
NTR-old	NTR7311
CCMO	NL64623.018.18
OMON	NL-OMON46711

Study results