Cell-derived vesicles as diagnostic instrument for prostate cancer.

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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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON28556

Bron
NTR

Aandoening

prostate cancer

Ondersteuning

Primaire sponsor: Academisch Medisch Centrum Amsterdam
Overige ondersteuning: NWO

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

n.a.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland
Status: Werving nog niet gestart

(Verwachte) startdatum:	01-08-2018
Aantal proefpersonen:	60
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	08-06-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 46711
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten