Generation of circulating tumor cell derived organoids through enrichment by leukapheresis - A novel drug screening system in metastatic prostate cancer

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON46104

Source
ToetsingOnline

Brief title
Circle study

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Gelden van de afdeling Interne Oncologie en Alpe d'HuZes/KWF fonds

Intervention

Keyword: circulating tumor cells, leukapheresis, organoids, prostate cancer

Outcome measures

Primary outcome

The primary endpoint is the success rate of culturing organoids from CTCs

obtained by LA.

Secondary outcome

Secondary endpoints include the fraction of metastatic PCa patients who have *

300 viable CTCs obtained by LA and the exploratory analysis comparing drug

sensitivity in organoids to therapy response of the matching patient in the

clinic.

Study description

Background summary

Prostate cancer (PCa) is the most common malignancy in men worldwide. 20-40% of patients will have recurrent (metastatic) disease within 10 years after primary treatment. The last decade many novel treatment options have been developed for patients with metastatic PCa. At this moment selecting the best treatment and determining the optimal treatment sequence for individual metastatic PCa patients remains an important issue as few biomarkers exist that predict treatment response. Therefore, our search for novel predictive biomarkers needs to continue. A potential advance would be culturing tumor cell using so-called *organoids* as these could be used to perform *ex vivo* drug screening for individual patients potentially enabling more tailored treatment choices. Moreover, systematic exploration of ex vivo drug sensitivity enables the search for novel biomarkers which is essential for further realization of more tailored patient management. Obtaining such cultures in metastatic PCa patients is challenging as metastases are frequently confined to bone, making it hard to retrieve sufficient material. Circulating tumor cells (CTCs) could

potentially serve as a more accessible source which can be even obtained repeatedly at different stages during disease progression. Recently, investigators have determined that the number of input cells is the main driver of successfully culturing organoids and that at least 300 CTCs are needed. However, CTCs have a low abundance in blood of generally 1 CTC/ml. To obtain the minimally required number of 300 CTCs for organoid generation, leukapheresis (LA) is a conceivable method to increase the CTC yield from blood. In this study we aim to generate CTC-derived organoids using CTC enrichment by leukapheresis in metastatic PCa patients. Organoid cultures from CTCs have the ability to transform the treatment of metastatic PCa patients and could help to decipher the biology of this complex disease.

Study objective

The primary objective of this study is to establish the success rate of culturing organoids from CTCs obtained by LA. Secondary objectives include to assess the fraction of metastatic PCa patients who have * 300 viable CTCs obtained by LA, the exploration of the potential of cultured organoids to represent realistic disease models, the exploration of the presence of novel molecular biomarker predictive of response and exploration of drug sensitivity in organoids compared to therapy response of the matching patient in the clinic.

Study design

Prospective, observational study

Study burden and risks

All patients are asked to undergo a single LA procedure which will take 3-5 hours. A volume of 10 L peripheral blood will be processed with the use of an Optia Spectra Cell Separator. Patients do not benefit from this study. The most common adverse events to be expected are pain or bruising at the venipuncture site (1-5%), apprehension or fainting associated with venipuncture (1-5%), fluid imbalance (0.01-0.1%) and citrate anticoagulant infusion-related symptoms resulting in tingling or buzzing around the mouth or fingers (20-50%). All patients will receive intravenous calcium to prevent this. The risk of adverse events associated with LA is considered negligible.

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

- metastasized prostate cancer
- age * 18 years
- Written informed consent of the patient
- * 2 adequate peripheral veins as access point for leukapheresis

Exclusion criteria

- CTC count of < 5 CTCs/7.5 mL of blood
- Patients with a known hypersensitivity to the used LA-anticoagulant
- mHSPC patients with current ADT
- Hemorrhage disease and/or coagulation disorder
- Inadequate liver and/or renal function
- Inadequate hematology and coagulation status
- Chronic viral infections

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-12-2016
Enrollment:	79
Type:	Actual

Ethics review

Approved WMO Date:	16-09-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL57710.078.16