Prostate cancer Immune profiling before, during and after HDR-brachytherapy in local relapsed prostate cancer.

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To investigate that low-dose HDR-brachytherapy of prostate cancer will make from an immunologically *cold* (no T-cell infiltrations) prostate cancer an immunologically *hot* (CD4 and CD8-cell infiltrations) tumor.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Prostatic disorders (excl infections and inflammations)
Study type	Observational invasive

Summary

ID

NL-OMON48348

Source
ToetsingOnline

Brief title
PRIMUS

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
Expression of PD-(L)-1, prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic
Source(s) of monetary or material Support: Varian,Varian Medical Systems

Intervention

Keyword: HDR-brachytherapy, Immunotherapy (IO), Prostate cancer

Outcome measures

Primary outcome

Primary endpoint: expression of PD-(L)-1 in the tumor.

Secondary outcome

Secondary endpoints: presence of CXCL12, IL-23 receptor in the tumor at 4

different time points (before and after the 1st fraction; before the 2nd and

3rd fraction of the salvage treatment). Furthermore, increase of T cell

infiltration, and HLA class I-A,B,C expressive lymphocytes will be detected.

Study description

Background summary

Immunotherapy (IO) is currently revolutionizing the field in oncology. However, prostate cancer until now fails to respond to classical IO, like PD-1 and CTLA-4 inhibitors.
Several reasons are mentioned:
Firstly, the tumor micro-environment consist of a whole series of normal immune cells, together with endothelia, and eventually cancer cells. This is a dynamic immunosuppressive network: a lack of this network could be form a major obstacle to immunotherapeutic interventions in prostate cancer.
Secondly, the expression of the programmed death 1 (PD-1) receptor and its ligand, PD-(L)-1, are detected at extremely low levels (> 1%), suggesting low anti-tumor T-cell activity in combination with low mutational indices as the most probable explanation for failed therapy.
Thirdly, a possible resistance mechanism is upregulation of different immune regulation mechanisms involved in carcinogenesis (like CXCL12 also known as stromal-cell derived factor-1*, SDF-1*)
Fourthly, other processes are identified like IL-23, CXCL12 produced by the myeloid derived suppressor cells acting as a driver of metastatic potency which is proven in animal models.

Radiotherapy (RT) delivered to the primary tumor impacts both tumor cells and

surrounding stromal cells. RT-induced cancer cell damage exposes tumor-specific antigens that make them visible to the immune system and leads to improved priming and activation of cytotoxic T cells. RT-induced modulation of the tumor microenvironment may also facilitate the recruitment and infiltration of immune cells.

The main-hypothesis: is that low-dose HDR-brachytherapy of prostate cancer will make from an immunologically *cold* (no T-cell infiltrations) prostate cancer an immunologically *hot* (CD4 and CD8-cell infiltrations) tumor.

It is obvious that more research is needed to clarify all these underlying mechanisms. Consequently methods of enriching the pool of prostate cancer recognizing T-cells infiltrating the tumor will likely enhance the efficacy of checkpoint inhibitors. RT can alter the tumor microenvironment by 1/ attracting T-cells through the release of chemokines and 2/ broadening up the immune repertoire.

The aim of this small pilot study is to explore the immunostimulary effects of RT in the context patients having a solitary local tumor relapse within the prostate after previous RT. Moreover to look at PD-(L)-1, CXCL12, IL-23 receptor and T-cell infiltration in biopsies of local relapses of prostate cancer patients.

Study objective

To investigate that low-dose HDR-brachytherapy of prostate cancer will make from an immunologically *cold* (no T-cell infiltrations) prostate cancer an immunologically *hot* (CD4 and CD8-cell infiltrations) tumor.

Study design

This will be a prospective analysis of repeated biopsies from 10 patients.

Study burden and risks

Very low risk: it is an unique opportunity to take biopsies in this setting. The therapeutic context of 3 consecutive treatment sessions allows us to repeatedly (before and multiple points following RT) sample tumor histology from these patients without causing any additional burden. This extremely increase the feasibility of the project. Furthermore a blood sample taking during the anesthesia is of no additional burden.

It is an unique opportunity to study molecular interactions of radiation and the immune system within human cancer histology.

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

- Local relapse of prostate cancer, who is candidate for a salvage HDR treatment.
- 18 years or older
- Willing and able to comply with the study prescriptions.
- Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

- Not eligible for proposed (HDR brachytherapy) treatment.

- No compliance

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):	20-02-2020
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	13-01-2020
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	03-03-2020
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	NL69713.096.19