Validation and evaluation of a gene set classifier for late radiation toxicity in prostate cancer patients

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Prospective validation of a previously determined gene set expression classifier that allows assessment of late radiation toxicity risk in irradiated prostate cancer patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON32354

Source
ToetsingOnline

Brief title
Late radiation toxicity AMC & LUMC

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: KWF-Kankerbestrijding

Intervention

Keyword: DNA micro-array, Late effects, Prostate cancer, Radiation toxicity

Outcome measures

Primary outcome

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Secondary outcome

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Study description

Background summary

Most patients with prostate cancer can be cured by radiotherapy. Increasing the radiation dose improves tumour control, but will give more normal tissue complications. The availability of a test for late radiation toxicity with high predictive power enables patient-tailored therapy. Recently we obtained evidence that genetic factors are important for individual radiation toxicity. Gene set analysis of the radiation-induced transcriptional response in ex vivo cultured lymphocytes allowed discrimination between patients with and without severe late toxicity after radiotherapy (Svensson, 2006). A prospective study with a larger number of patients is required to validate this gene set classifier. In addition, we will assess *-H2AX foci: This simple assay determines the rate of disappearance of DNA-DSB associated *-H2AX foci after ionizing radiation. Combination of the two assays will provide insight in whether cellular or tissue responses determine late effects. Gene expression profiles reflect differences in overall tissue response to ionizing radiation; with the **H2AX test we wish to address a more specific cellular mechanism involved in radiation response.

Study objective

Prospective validation of a previously determined gene set expression classifier that allows assessment of late radiation toxicity risk in irradiated prostate cancer patients.

Study design

Following informed consent, 200 patients with newly diagnosed prostate cancer

who will have curative external beam radiotherapy will be entered in this study. The following data will be collected:
* 50 ml blood sample for gene expression profiling (according to Svensson, 2006) and determination of gamma-H2AX foci [Kato 2006, 2007].
* Radiation toxicity will be scored using a modified RTOG/SOMA LENT score before and at the end of radiotherapy, and 6, 12, and 24 months after radiotherapy [Peeters, 2006; Heemsbergen, 2006],
* Baseline clinical data (a.o. age, tumour stage, histology, PSA, co-morbidity, smoking),
* Treatment data: diagnostic surgery, hormonal treatment, radiotherapy (dose, fractionation, and volume data, particularly of prostate, bladder and rectum),
* Tumour follow-up data (PSA, secondary treatment)
Multivariate statistical methods, particularly correcting for the large amount of genetic data, will be used to validate the predictive value of the earlier assessed gene set classifier.

Intervention

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Study burden and risks

The combination of clinical and genetic risk factors could yield a screening test for treatment selection in prostate cancer patients, improving treatments by reducing side effects. The patient will give a single blood sample (50 ml) and will answer repeated questionnaires assessing side effects, but will further not impose anyy burden to the patients.

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

- Adult patients with prostate cancer who will have curative external beam radiotherapy,
- Proficient in Dutch
- Written informed consent

Exclusion criteria

- Patients who had prostatectomy, iodine-125 brachytherapy or radiotherapy for recurrent disease
- Patients with psychosocial or somatic disorders in the medical history, limiting the possibilities for adequate follow-up

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2008
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Amsterdam UMC

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	NL22628.018.08