Hypofractionated Focal Lesion Ablative Microboost in prostatE cancer (Hypo-FLAME)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44816

Source
ToetsingOnline

Brief title
Hypo-FLAME

Condition

- Reproductive neoplasms male malignant and unspecified
- Male genital tract therapeutic procedures

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Hypofractionation, MRI, Prostate cancer, Toxicity

Outcome measures

Primary outcome

The primary endpoints of this study are acute gastrointestinal (GI) and genitourinary (GU) toxicity using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

Secondary outcome

Secondary endpoints are late GI and GU toxicity, QoL, and bDFS. Simultaneously, two side-studies will be performed, i.e. to prepare for MRI-guided radiotherapy (except for Radboudumc and UZ Leuven) and blood sampling for translational research (radiogenomics) and Biobank purposes (except for Radboudumc).

Study description

Background summary

Hypofractionation with a stereotactic body radiotherapy (SBRT) technique for prostate cancer produces excellent treatment outcome in terms of survival and toxicity and is much more convenient than the current fractionation scheme. Local recurrence occurs most frequently at the site of the primary or dominant tumor location prior to treatment. Therefore dose escalation at the site of the primary tumor may improve disease control.

Study objective

The main goal of this phase II study is to investigate whether a focal ablative SBRT boost to the macroscopic tumor is feasible and associated with acceptable toxicity in addition to whole gland prostate SBRT. Based on the present study, a phase III study will be designed to compare whole gland SBRT prostate and whole gland SBRT prostate with an additional focal boost. The secondary objectives of this study are: late toxicity, quality of life (QoL) and biochemical disease free survival (bDFS).

Furthermore, two side-studies are incorporated in this phase II study: 1) a weekly MRI will be performed to prepare for future MRI-guided (MR-linac) treatment without gold fiducial markers (except for Radboudumc and UZ Leuven) and 2) blood sampling for translational research (radiogenomics) and Biobank purposes (except for Radboudumc).

Study design

Prospective interventional study on whole gland prostate SBRT using MRI for focal boost in 100 consecutive intermediate or high risk prostate cancer patients.

Intervention

Patients will be treated by external beam radiotherapy with a SBRT technique with 35 Gy in 5 weekly fractions and an additional simultaneously integrated focal boost to the tumor nodule(s) visible on MRI up to 50 Gy. In addition, patients will be asked to undergo 5 additional MRI scans (~15 min/scan) without contrast enhancement prior to or after each radiation session (except for Radboudumc and UZ Leuven) as well as blood sampling for translational research (radiogenomics) and Biobank purposes (except for Radboudumc).

Study burden and risks

Standard of care: Prior to radiation, patients in general visit the hospital 3 times for radiotherapy preparation; a first consultation visit with their physician, gold fiducial marker implantation and pre-treatment imaging (planning computed tomography (CT)-scan and magnetic resonance imaging (MRI)-scan). Follow-up takes place according to standard of care. Patients will be seen regularly for 10 years by their radiation oncologist and/or urologist.
Study procedures: The present study requires the same preparation for radiotherapy treatment, but the radiation treatment involves only 5 fractions in 5 weeks instead of the standard 28 to 35 fractions and is therefore much more convenient.
Compelling data with sufficient follow-up are available on biochemical control and toxicity for the SBRT protocol for 35-40 Gy in 5 fractions. In the present study the macroscopic tumor will receive an additional radiation dose. Doses up to 50 Gy in 5 fractions to the whole prostate have already been administered in a phase II study with acceptable acute toxicity, but higher than acceptable late rectal toxicity. Since in the current protocol only a small part of the prostate volume receives an increased dose, unacceptable higher toxicity to the organs at risk is not expected. This was confirmed in a phase II study using Cyberknife. Furthermore, the dose constraints for the bladder and rectum will be maintained as in the Canadian SBRT PATRIOT protocol (which were proven safe and were associated with a very low rate of severe toxicity). To achieve equal or less toxicity compared to the current radiotherapy protocols, the organs at

risk dose will be prioritised (i.e. the gross tumor volume (GTV) boost dose of 50 Gy will be adjusted to a lower dose if the dose constraints to organs at risk are at risk). Toxicity and thus safety will be the primary endpoint of this phase II study. Besides the standard toxicity assessments an additional toxicity assessment will take place 3 months (± 1 maand) after the first radiation treatment (by telephone or outpatient visit). QoL questionnaires will be sent and returned by mail at baseline, at week 5 during treatment, at 1 month (± 2 weeks) and at 6 months (± 1 month) after the last radiation treatment and every year (± 1 month) up to 5 year after the last radiation treatment. Participating patients may benefit from this study since a reduced number of 5 treatment fractions will be less disruptive to daily life than the current 28 to 35 treatments.
For this study patients will also be asked to undergo 5 additional MRI scans (~15min/scan) without contrast enhancement prior to or after each radiation session (except for Radboudumc and UZ Leuven) as well as blood sampling for translational research (radiogenomics) and Biobank purposes (except for Radboudumc).

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

- Men >= 18 years with histologically confirmed prostate adenocarcinoma;
- Intermediate-risk prostate cancer or high-risk prostate cancer, defined as at least one of the following risk criteria:
* Clinical T-stage T2b, T2c or T3a (defined on MRI) or T3b with less than 5 mm invasion in the seminal vesicle.
* Gleason sum score >= 7.
* Prostate specific antigen (PSA) >= 10 ng/mL.
- Prostate tumor nodule visible on MRI;
- Ability to give written informed consent and willingness to return for follow-up.

Exclusion criteria

- Prior pelvic radiotherapy, transurethral prostate resection or prostatectomy;
- Unsafe to have gold fiducial marker implantation;
- Contraindications to MRI according to the Radiology Department guidelines (metal implants, non-compatible cardiac device, allergy to Gadolinium, severe renal dysfunction or severe claustrophobia);
- Evidence of lymph node involvement or distant metastatic disease;
- Clinical T-stage > T3b with >= 5 mm invasion in theseminal vesicle;
- World Health Organization (WHO) performance score > 2;
- International prostate symptoms score (IPSS) >= 15;
- PSA >30 ng/mL.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-04-2016
Enrollment:	85
Type:	Actual

Ethics review

Approved WMO Date:	16-03-2016
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	04-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-11-2017
Application type:	Amendment
Review commission:	METC NedMec

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
ClinicalTrials.gov	NCT02853110
CCMO	NL53719.041.15