Probach.

Gepubliceerd: 12-03-2013 Laatst bijgewerkt: 18-08-2022

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28094

Bron
Nationaal Trial Register

Aandoening

prostate cancer
radiotherapie
HDR
Brachytherapy
intermediate risk

Ondersteuning

Primaire sponsor: Erasmus MC, Dept. Of Radiation Oncology
Erasmus MC
Groene Hilledijk 301
3075 EA Rotterdam
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Overige ondersteuning: KWF commission clinical studies

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The incidence of late gastro-intestinal and genito-urinary toxicity (grade ≥ 2 RTOG) during 3 years of follow-up after treatment completion.

Toelichting onderzoek

Achtergrond van het onderzoek

There is by now accumulating evidence that high radiation dose (≥ 75 Gy) is necessary for tumour control when treating intermediate and high risk prostate cancer. To treat safely at high doses with external beam therapy, 3-Dimensional Conformal Radiotherapy (3D-CRT) or Intensity Modulated Radiotherapy (IMRT) techniques must be used. In this way using the IMRT with a validated position verification protocol as standard of care, the toxicity can be limited while the dose to the prostate is escalated. However, despite the use of IMRT the incidence rates for GI and GU toxicity are still high and the adverse effect of IMRT dose distribution pattern on the long term has to be evaluated. Another way of delivering high dose to the prostate, but limiting the dose to the neighbouring organs is with brachytherapy. For treating intermediate risk prostate cancer with brachytherapy, brachytherapy and IMRT are combined. IMRT is used to deliver an elective dose to the prostate and seminal vesicles. Brachytherapy is used as a boost (IMRT+BRACHY). The main advantage of brachytherapy is the limited dose in neighbouring organs and potentially causing less toxicity. In this study, differences in outcome of treatment between IMRT only and IMRT+BRACHY will be investigated in a prospective randomized setting. It is hypothesized that the incidence of grade ≥ 2 RTOG long-term genitourinary (GU) and gastrointestinal (GI) toxicity of IMRT+BRACHY is half of IMRT only (3 year incidence is 15% vs. 30%). Because less long-term toxicity is expected with IMRT+BRACHY differences in qualityof-life need to be assessed with validated questionnaires.
Because the dose to the prostate is similar for both groups, no difference in tumour control, expressed as Biochemical Disease Free Survival (bDFS) and relapse free survival (RFS), is anticipated.
Study objectives The primary study objective is to show a 50% reduction of the

incidence of long-term gastrointestinal and genito-urinary toxicity in the treatment of prostate cancer in the intermediate and high risk group, by treatment with IMRT followed by brachytherapy (IMRT+BRACHY), compared to treatment with IMRT alone (IMRT). Secondary objectives are to investigate the effect of this combined treatment on acute toxicity, tumour control, Quality of Life (QOL), overall survival, costs and cost-effectiveness compared to standard treatment with IMRT alone.

Study design Randomized, prospective, phase III study

Patient population Patients with prostate cancer, belonging to the intermediate- and partially high-risk profile are candidates for the study, provided brachytherapy can be performed.

Intervention Patients will be randomized into two groups. One group will be treated with high dose external beam radiotherapy using the IMRT technique (standard treatment). The other group will be treated with external beam radiotherapy (IMRT) combined with HDR or PDR brachytherapy as boost.

Duration of treatment For both arms the total equivalent dose in 2-Gy fractions (EQD2) is 79 Gy. For the IMRT arm the dose is delivered in 35 fractions of 2.20 Gy, resulting in an EQD2 dose of 79.2 Gy.

Total treatment duration will be 7 weeks. The IMRT+BRACHY group is treated up to 44 Gy in 2.20 Gy daily fractions (EQD2 = 45.3Gy) with IMRT and a High Dose Rate (HDR) or Pulsed Dose Rate (PDR) brachytherapy treatment is applied for the boost. The HDR dose is equivalent (EQD2) to 33.4 Gy calculated with an alpha/beta ratio for prostate of 5 Gy, given in a single fraction of 13 Gy. The PDR dose is 24 times 1.27 Gy (EQD2 33.8 Gy). Total treatment duration will be 6 weeks. Subsequently, patients will be followed for evaluation of acute and late toxicity, bDFS, RFS, OS, Quality of Life and costs.

Target number of patients

240

Expected duration of accrual

3 years

Main study endpoints Primary endpoint: the incidence of late gastro-intestinal and genito-urinary toxicity (grade ¡Ý 2 RTOG) during 3 years of follow-up after treatment completion.

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Secondary endpoints: Incidence of acute toxicity, bDFS, RFS, OS, QOL, costs and cost-effectiveness (all costs of treatment and during 5 years of FU after treatment completion).

Benefit and nature and extent of the burden and risks associated with

participation
Patients who will participate in the study and randomize for arm 2 (IMRT+brachytherapy) will visit the hospital less frequently during the treatment phase (21 times), compared to standard treatment (35 times). However, for brachytherapy catheters/needles need to be placed inside the prostate gland under general or spinal anaesthesia. The HDR brachytherapy will be given in one fraction without the need of hospital admission, and for PDR brachytherapy the fractions are administered in a hospital stay of 2 days. It is expected that in arm 2 the incidence of acute and late GI and GU toxicity will be lower than in arm 1 (standard treatment). Unlike non-study patients, all patients participating in the study will complete Quality of Life questionnaires (QLQ-C30, QLQ-PR25, IPSS, and IIEF) at baseline and then every 6 months until 3 years after treatment completion and yearly thereafter until 5 years after treatment completion.
Planned interim analysis
and DSMB (if applicable)
No interim analysis is planned for this study. No DSMB will be installed due to the minimal risk involved in participation in the study.

Doel van het onderzoek

The primary study objective is to show a 50% reduction of the incidence of long-term gastrointestinal and genito-urinary toxicity in the treatment of prostate cancer in the intermediate and high risk group, by treatment with IMRT followed by brachytherapy (IMRT+BRACHY), compared to treatment with IMRT alone (IMRT). Secondary objectives are to investigate the effect of this combined treatment on acute toxicity, tumour control, Quality of Life (QOL), overall survival, costs and cost-effectiveness compared to standard treatment with IMRT alone.

Onderzoeksopzet

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Onderzoeksproduct en/of interventie

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treated with high dose external beam radiotherapy using the IMRT technique (standard treatment). The other group will be treated with external beam radiotherapy (IMRT) combined with HDR or PDR brachytherapy as boost.

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Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Patients ≤ 80 years with histologically proven adenocarcinoma of the prostate;

2. The following disease extensions are eligible:

A. T1c-T2b with Gleason ≤ 6 and PSA 15-40 ng/ml, Nx, Mx*;

B. T1c-T2b with Gleason 7 and PSA 10-30 ng/ml, Nx, Mx;

C. T1c-T2b with Gleason 8 and PSA ¡Ü 10 ng/ml, Nx, Mx;

D. T2c-T3a with Gleason ¡Ü 7 and PSA ¡Ü 15 ng/ml, Nx, Mx.

*For patients with T3a, PSA > 20 and/or Gleason-score of 8 an evaluation of lymph node status and distant metastases have to be done before randomisation.
These patients will be divided to 2 groups for stratification endpoints:

i. Intermediate risk: T1c-T2c, G ≤7 and PSA <20 ng/ml;

ii. (low) High risk: any of the following factors: T3, G 8, PSA ≥20.

3. Accessible for brachytherapy;

4. WHO performance status ≤ 2;

5. International Prostate Symptom Score (IPSS) ≤ 20;

6. Maximal urinary flow ≥ 10 ml/sec;

7. Post voiding residual bladder volume ≤ 200 ml;

8. Written informed consent;

9. Able to comply with follow-up;

10. Willing and able to complete the QOL questionnaires during follow-up.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1. Other malignancy (except adequately treated basal cell carcinoma of the skin or other malignancy from which the patient has been cured for at least 5 years);

2. Metallic hip prosthesis;

3. Inflammatory bowel diseases such as colitis ulcerosa or M. Crohn in medical history;

4. Prior radiotherapy on prostate or pelvic area;

5. TURP;

6. Co-morbidity preventing general or spinal anaesthesia;

7. Very high risk patients (PSA>40, G >8, T-stadium >T3a) beyond the above mentioned group;

8. T1-3, N+ M+.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	20-03-2013
Aantal proefpersonen:	240
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	12-03-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3734
NTR-old	NTR3897
Ander register	KWF : EMCR-2012-5527
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
Publications resulting from this study will be submitted to peer-reviewed journals. Authorship will be: first or second or last, S. Aluwini and/or B. Pieters. The other coauthors will be investigators who have included at least 5% of the evaluable patients by order of inclusion, the statistician and central data manager. Any publication, abstract or preservation based on patients included in this study must be approved by the primary investigators and the study coordinators. This is applicable to any individual patient registered in the trial, or any subgroup of the trial patients. Such a publication cannot include any comparisons between randomized treatment arms or an analysis of any of the study end-points unless the final results of the trial have already been published.