Een onderzoek naar de veiligheid van het gebruik van oestradiol als hormoontherapie bij patiënten met lokaal gevorderde prostaatkanker die worden behandeld met uitwendige bestraling in combinatie met hormoontherapie

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20250

Source
Nationaal Trial Register

Brief title
Oestradiol Adjuvant Trial (OAT)

Health condition

Locally extended prostate cancer.

Sponsors and support

Primary sponsor: Erasmus MC, Dept. Urology
Source(s) of monetary or material Support: Stichting Achmea Gezondheidszorg

Intervention

Outcome measures

Primary outcome

Incidence of cardiovascular events (number of cardiovascular events per 100 person years).

Secondary outcome

1) Compliance to the study intervention (measured by oestradiol serum levels at every visit).

2) Incidence of endocrine related side effects.

3) Changes of metabolic serum parameters (liver function (SGOT, SGPT, bilirubin), endocrine (oestradiol, testosterone, PSA), lipid profile (HbA1c, cholesterol, HDL).

4) Time to reach testosterone castration levels (during run-in period, T ¡Ü 1.7 nmol/L).

5) Quality of Life (EORTC QC 30, PR25 potency, overall).

Study description

Background summary

Endocrine treatment is the mainstay for metastatic prostate cancer. During the last three decades, medical castration has been chosen above surgical castration by orchidectomy. Current options involve predominantly the use of relatively expensive Luteinizing-hormone-releasing hormone (LHRH) agonists because of their reported preference with regard to the incidence of thromboembolic events when compared to oestrogens. [1] However, LHRH agonists (LHRHa) are associated with long-term toxic effects, including osteoporosis, and adverse metabolic changes. The use of parenteral oestrogen is under trial in the PATCH-trial that reported recently on the intermediate long term effects of transdermal oestradiol application in men who require permanent androgen deprivation. The thromboembolic complications associated with transdermal oestrogen appear similar to that of LHRH agonists in this randomised study. [1] As parenteral oestrogen administration avoids the entero-hepatic circulation (first pass hepatic metabolism) it is associated with a reduced incidence of cardiovascular toxicity compared with oral oestrogen. [2] The recently updated prostate cancer guideline of the Dutch Urological Society, stated that though parenteral oestrogen treatment could be safe in patients without cardiovascular risk factors, further study is needed before this therapy might become standard care. [3] However, oestrogen treatment is already regularly prescribed by a lot of Dutch urologists (amongst which the urologists participating in the current trial) for androgen deprivation in patients with prostate cancer,

also in the earlier phase of the disease. Treatment with oestrogens is reimbursed by the health care insurances.

During this study it will be analysed whether transdermal applied oestrogens in the earlier phase of the disease, that is during the adjuvant endocrine setting during curative treatment for locally extended prostate cancer, might even be less toxic compared to the standard medical castration therapy.

The burden related to participation in this study are the two extra visits at week 0 and 4 (run in period), filling in questionnaires at 7 visits, and the extra blood/serum withdrawal for analysis of hormones and related metabolites and/or safety measurements (8.5 ¨C 25 ml per withdrawal, 8 times). Weight and blood pressure (BP) are measured 7 times, otherwise no physical exams or tests will be done. Therefore the risks for this study with regard to extra tests are negligible.

Side effects expected based on information of the PATCH trial are:

- Cardiovascular (thromboembolism): 5% (in the PATCH trial 10.1 % was observed in the oestrogen-patch group of which 50% after crossover to LHRH-agonists due to disease progression which is unlikely in the presented trial of men in earlier stages of the disease).

- Gynaecomastia: 75% in several undescribed grades of severity. Personal communication with the PI of the PATCH trial (urologist prof. N. Clark, Leeds, UK) showed that in a very small number of men Tamoxifen was given as treatment for this side effect.

- Hot flushes in 25%, for which antiandrogens are sometimes effective.

- Dermatological problems of undetermined nature in 42%.

Overall only the cardiovascular effects might be of serious health risk, however as reported they are equal or less in frequency when compared to LHRH-agonists (reported incidence in the PATCH trial 7%).

[1] Langley, R.E., et al., Cardiovascular outcomes in patients with locally advanced and metastatic prostate cancer treated with luteinising-hormone-releasing-hormone agonists or transdermal oestrogen: the randomised, phase 2 MRC PATCH trial (PR09). Lancet Oncol, 2013. 14(4): p. 306-16.

[2] Turgeon, J.L., et al., Hormone therapy: physiological complexity belies therapeutic

simplicity. Science, 2004. 304(5675): p. 1269-73.

[3] Reijke, T.M.d., Richtlijn Prostaatcarcinoom, 2013: Oncoline.

Study objective

It is safe to give oestradiol in the setting of endocrine treatment for locally extended prostate cancer adjuvant to radiotherapy.

Study design

24 months (primary outcome) and continuous (secondary outcomes)

Intervention

During a run¨Cin period of approximately 3 months subjects will self-administer four skin patches for transdermal application of oestradiol (100 mcg per 24 h) per time, which will be changed twice weekly. After the run-in period, a regimen of three oestradiol patches changed twice weekly will be given as soon as castrate testosterone concentrations (1.7 nmol/L or lower) have been reached. Subjects will be treated with oestradiol patches for a period of two years.

Contacts

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Eligibility criteria

Inclusion criteria

1) Men > 18 years.

2) Locally advanced prostate cancer.

3) Selected for at least two years of adjuvant endocrine therapy and EBRT.

4) Signed informed consent.

5) Testosterone serum level > 6 nmol/l.

Exclusion criteria

1) Current endocrine treatment or previous therapy within 6 months (5-alpha reductase inhibitors are permitted).

2) Previous radiological confirmed deep venous thrombosis or pulmonary embolus.

3) Cerebrovascular event (TIA or CVA) within 6 months

4) Coronary heart disease within 6 months.

5) Instable angina pectoris within 6 months.

6) Congenital thrombofilic diseases.

7) Thrombolic disease within 6 months.

8) Heart failure as defined by NYHA class >2.

9) Hypertension (not corrected by medication) >160/100 mmHg. If either systolic or diastolic value is higher than these values the patient is not eligible.

10) Suboptimal regulated diabetes mellitus or de novo diabetes mellitus as defined by HbA1c of over 6,5% (48 mmol/mol).

11) Rheumatoid arthritis.

12) Impaired renal function as defined by a GFR < 30 ml/ min/1,73 m2

13) Acute liver failure or reduced liver function showing as increased serum parameters (SGOT, SGPT, bilirubine > 2.5 times normal).

14) Porfyria.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-09-2014
Enrollment:	200
Type:	Anticipated

Ethics review

Positive opinion

Date:	09-09-2014
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50312
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4625
NTR-old	NTR4776
CCMO	NL47698.078.14
OMON	NL-OMON50312

Study results