Short-term Testosterone replacement in testicular cancer survivors to treat overweight and improve cardiometabolic risk: a pilot study

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To assess the effects of testosterone replacement therapy on fat mass and other components of the metabolic syndrome.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Endocrine disorders of gonadal function
Study type	Interventional

Summary

ID

NL-OMON50478

Source
ToetsingOnline

Brief title
Short-term Testosterone Replacement in Testicular Cancer Survivors

Condition

- Endocrine disorders of gonadal function
- Reproductive neoplasms male malignant and unspecified

Synonym
testicular cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W,Besins Healthcare Benelux

Intervention

Keyword: cardiometabolic risk, overweight, testicular cancer, testosterone

Outcome measures

Primary outcome

Primary endpoint is the change in fat mass as measured by Dual-Energy X-ray

Absorption (DEXA) scan after 20 weeks of Androgel compared to placebo.

Secondary outcome

Secondary endpoints are changes in fat mass between 20 and 40 weeks, and

changes in abdominal visceral fat, BMI, adipocytokines, metabolic syndrome

parameters, bone mass density, semen quality, sexual function, and quality of

life between Androgel and placebotreated

patients.

Study description

Background summary

Testicular cancer (TC) survivors have an increased risk of hypogonadism (decreased testosterone and/or increased luteinizing hormone levels) and cardiovascular disease (CVD). Metabolic syndrome develops early after chemotherapy in 20-30% of longterm TC survivors and is associated with an increased risk of atherosclerotic disease in the general population. TC survivors who develop the metabolic syndrome have a higher body mass index (BMI) pretreatment, a larger BMI increase during follow-up, and lower total testosterone levels than patients without the metabolic syndrome. Testosterone replacement therapy as a short-term intervention during a limited time period may be an important
strategy to reduce body weight and fat mass, restore cardiometabolic balance, and decrease the prevalence of the metabolic syndrome in TC survivors.

Study objective

To assess the effects of testosterone replacement therapy on fat mass and other components of the metabolic syndrome.

Study design

Randomized double-blind placebo controlled intervention study, followed by an open-label treatment phase. Results of this pilot study will be used to design a multicenter randomized controlled study in a large group of TC survivors.

Intervention

Patients will be randomized to treatment with transdermal testosterone gel (Androgel) or placebo gel once daily during 20 weeks, followed by 20 weeks of active Androgel treatment in all participants. The treatment dose will be 50 mg daily, adjusted to 25 mg in case of increased testosterone concentrations (average of 2 measurements >25 nmol/L) or signs of overdosing. Patients will be stratified according to testosterone level (8-12 nmol/L versus <8 nmol/L) and BMI (25-30 kg/m2 versus 30-35 kg/m2).

Study burden and risks

The study will provide an answer to the question whether testosterone replacement therapy as a short-term intervention has significant effects on obesity and fat metabolism and may, thus, reduce the prevalence of the metabolic syndrome in this population of young men with excellent long-term cancer-related prognosis, but an increased CVD risk. At various time points during the intervention, patients will be subjected to history taking and physical examination. Furthermore, blood will be drawn to: measure hormone levels, adipocytokines, lipids, glucose, insulin, bone and senescence markers; to extract DNA for determination of gene polymorphisms; and to measure hematocrit and PSA as safety parameters. Semen analysis and a full body DEXA scan will be performed at 0, 20 and 40 weeks only. Patients will be asked to fill out questionnaires
regarding quality of life, sexual health, and androgen deficiency symptoms at various time points during the intervention.

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

We will include patients with metastatic testicular cancer after chemotherapy, at least 12 months after completion of last treatment and without evidence of disease. Combination chemotherapy should have contained a platinum compound, either cisplatin or carboplatin. In TC survivors, testosterone levels are routinely measured in blood during follow-up once every two years. Patients are eligible for screening if they are between 18 and 55 years of age, and have a documented low or low-normal total testosterone level <=14 nmol/L, as measured during any of the follow-up visits, irrespective of signs and symptoms of androgen deficiency. Eligible for actual study participation and randomization between Androgel and placebo will be: survivors of TC not using testosterone supplements, having biochemical evidence of hypogonadism (defined as a serum total testosterone
concentration <= 12 nmol/L (345 ng/dL) measured after an overnight fast between 8:00 and 10:00
AM), and being overweight (as defined by a BMI >= 25 and <35 kg/m2). Patients should be able
to understand and abide to the study protocol and sign written informed consent.

Exclusion criteria

We will exclude: patients planning to father children within the next 12 months; patients already treated for hypogonadism, patients taking corticosteroids or hormone replacement other than testosterone with dose-adjusments within the last 3 months prior to randomization; patients taking medication with any antiandrogenic effects (e.g. spironolactone); patients with signs or history of hormone-dependent cancer (prostate or breast cancer); patients with severe lower
urinary tract symptoms (as defined by International Prostate Symptom Score >19); patients
with a history of coronary artery disease (angina pectoris, myocardial infarction) or heart
failure; patients with hematocrit >50%; patients with untreated severe obstructive sleep apnea;
patients with uncontrolled hypertension; patients with a BMI > 35 kg/m2; patients with a history of
epilepsy; patients with debilitating psychiatric illness or inability to understand the study protocol,
according to the opinion of the investigator.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-12-2018
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Androgel
Generic name:	Testosterone gel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	29-08-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-12-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-02-2021
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2015-004430-96-NL
ClinicalTrials.gov	NCT03339635
CCMO	NL57224.042.17