Senescence and the early ageing phenotype after chemotherapy for testicular cancer: the SEA-CAT study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON52734

Source
ToetsingOnline

Brief title
SEA-CAT study

Condition

- Renal and urinary tract neoplasms 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: KWF Kankerbestrijding

Intervention

Keyword: ageing, late effects, Senescence, testicular cancer

Outcome measures

Primary outcome

In the cross-sectional part of this study the primary endpoint is correlation between senescence and the early ageing phenotype. The amount of senescent cells in skin and fat tissue will be correlated with the early ageing phenotype defined as

a) vascular stiffness (pulse wave velocity, PWV), the gold standard measurement for vascular age and

b) the metabolic syndrome.

In the longitudinal part of the study the primary endpoint will be to investigate the development of senescent burden during cisplatin-combination chemotherapy. The percentage, and -if any- upregulation of senescent cells in skin and fat tissue will be measured and compared between pre-chemotherapy measurements and the different time points afterwards and compared between the chemotherapy group, the stage I control group and the healthy control group.

Secondary outcome

- Senescence-associated secretory phenotype (SASP): Defined as elevated levels of the cytokines IL-6, IL-8 or VEGF.

- (Sub)clinical features of the early ageing phenotype: Presence or development of the early ageing phenotype will be assessed measuring vascular damage (vascular stiffness (pulse-wave velocity, PWV), biomarkers, intima-media

thickness (IMT), peripheral digital ischaemia, systolic and diastolic cardiac function, global longitudinal strain (GLS), and advanced glycation end products (AGEs) as measure for metabolic memory). Presence or development of cardiovascular risk factors will be assessed (body mass index, waist-hip ratio, blood pressure, lipid profile, fasting glucose and presence of the metabolic syndrome.

- Platinum levels: Both circulating platinum levels and the amount of platinum depositions in skin and fat tissue will be assessed (ICP-MS).

- Fat tissue metabolism and metabolic state: The adipocytokines (leptin, adiponectin, IL-6, PAI-1, TNF-α), p53 activation and microRNA regulation of insulin signaling in adipose tissue: miR-103, miR-107, miR-29) will be measured.

Study description

Background summary

Cisplatin-combination chemotherapy causes inevitably DNA damage by platinum-DNA adduct formation of both tumor cells but also healthy cells. It therefore stands to reason that testicular cancer treatment causes an increased burden of senescent cells, which causes upregulation of the SASP resulting in a pro-inflammatory phenotype. We hypothesize that this may be an important mechanism behind development of late effects and an early ageing phenotype after treatment for testicular cancer.

Study objective

The aim of this study is to improve our understanding of the development of late effects after cancer treatment and reveal potential targets for intervention/prevention. Therefore we will investigate mechanisms behind the early ageing phenotype emerging after cisplatin-combination treatment for testicular cancer.

Study design

A study will be performed consisting of a cross-sectional part and a longitudinal part with two cohorts.
Cross-sectional study:
1. Testicular cancer survivors who were treated between 2000 and 2005 or between 2006 and 2012 with cisplatin-combination chemotherapy and who were extensively phenotypically mapped within two longitudinal trials (15,16) will be invited to participate in a single cross-sectional follow-up study visit 5-20 years after chemotherapy.
2. Testicular cancer survivors who were treated between 2013 and 2019 with cisplatin-combination chemotherapy and who were extensively phenotypically mapped within the ACT trial, (Optimal Timing of a Tailored Physical Activity Program During Chemotherapeutic Cancer Treatment to Reduce Long-term Cardiovascular Morbidity; clinicaltrails.gov: NCT01642680), will also be invited to participate in a single cross-sectional follow-up study visit 1.5-10 years after chemotherapy.
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Longitudinal study:
Patients with metastasized testicular cancer who are about to start with cisplatin-combination chemotherapy will be invited in the longitudinal part of this study. Study participation involves four study visits:
Visit 1: before start of chemotherapy
Visit 2: before third cycle of chemotherapy
Visit 3: one month after completion of chemotherapy
Visit 4: one year after start of chemotherapy
Patients with stage I testicular cancer will serve as control group with two study visits:
Visit 1:one to two months after orchidectomy
Visit 2: one year after orchidectomy.
Healthy male volunteers who were not treated for any type of cancer will serve as a second control group. Study participation involves one study visit.

Study burden and risks

In case of participation in the cross-sectional part of this study one visit during one morning will be planned. In case of participation in the longitudinal part of this study four (chemotherapy-group) or two (stage I control-group) visits , or one visit (healthy control-group) during one morning per visit will be planned. Invasive procedures are the skin and fat biopsy and a venapuncture. All three procedures have a low risk of adverse effects.

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

Cross-sectional part of this study:
- Diagnosed with metastatic testicular cancer in 1999-2019 and participated in the above mentioned longitudinal studies (stage II or higher)
- Received first-line cisplatin-based chemotherapy
- Was younger than 50 years of age at start of chemotherapy, Longitudinal part of this study:
Chemotherapy-group:
- Diagnosis of metastatic testicular cancer (stage II or higher)
- Is about to start with first-line cisplatin-based chemotherapy
- Younger than 50 years of age at diagnosis of metastatic testicular cancer,
Stage I control-group:
- Diagnosis of testicular cancer stage I disease

- Younger than 50 years of age at diagnosis of testicular cancer

In order to be eligible to participate in the control group of this study, a subject must meet all of the following criteria:
Healthy control-group:
- Male younger than 60 years of age

Exclusion criteria

- Earlier diagnosis with another malignancy except from successfully treated squamous cell carcinoma of the skin.
- Not able to provide informed consent (in example in case of mental or psychiatric disability)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-02-2019
Enrollment:	192
Type:	Actual

Ethics review

Approved WMO

Date:	31-08-2018

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-08-2022
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
ClinicalTrials.gov	NCT04113122
CCMO	NL63331.042.17