INTense Exercise foR surVivAL among men with Metastatic Castrate-Resistant Prostate Cancer (INTERVAL - MCRPC): A Multicentre, Randomised, Controlled, Phase III Study

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Primary Objective is to determine if high intensity aerobic and resistance training plus psychosocial support increases overall survival compared to psychosocial support alone in patients with metastatic castrate-resistant prostate cancer.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON47400

Source
ToetsingOnline

Brief title
INTERVAL - MCRPC

Condition

- Other condition

Synonym
prostate cancer, prostate carcinoma

Health condition

urologische aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: The Movember Foundation
Source(s) of monetary or material Support: Movember Foundation

Intervention

Keyword: Exercise, Prostate cancer, RCT, Survival

Outcome measures

Primary outcome

Overall survival

Secondary outcome

Secondary endpoints

Progression-free survival, symptomatic skeletal-related events, pain, opiate

use, cancer-related fatigue, metabolic biomarkers, physical function,

quality-of-life (QOL) and QOL-adjusted survival

Study description

Background summary

Exercise has been established to be safe and result in improved physical function and quality of life for most individuals with cancer. However, little information exists regarding whether exercise can increase overall survival and reduce disease progression, skeletal-related events, and pain in patients with metastatic castrate-resistant prostate cancer.

Study objective

Primary Objective is to determine if high intensity aerobic and resistance training plus psychosocial support increases overall survival compared to psychosocial support alone in patients with metastatic castrate-resistant

prostate cancer.

Study design

1:1 Randomized Controlled Trial

Intervention

A 1 year supervised aerobic and resistance exercise program. After the completion of the supervised exercise program, the respondent will complete a 1 year self-managed exercise program. Over the course of the trial the respondent will receive behavioral and psychosocial support.

Study burden and risks

Rare risks for all patients

Blood Collection - There are minor risks associated with blood draw (i.e., bruising, infection, discomfort, light-headedness). However, this procedure is considered to be of minimal risk and will be performed by a trained phlebotomist with extensive experience. No syringes, lancets, needles or other devices capable of transmitting infection from one person to another shall be reused. All of these items will be destroyed after each use.

Likely, Minimal risks for patients randomized to the intervention group

Exercise may result in mild discomfort and muscle soreness. There is also the possibility of muscle pulls or strains. During exercise, it is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, muscle cramps or strain, and nausea. In order to minimize these risks, participants will perform a warm-up and cool-down before and after each exercise session, thoroughly familiarized with the movements involved, comprehensively instructed on the correct technique, and highly supervised at the beginning of the program by qualified professionals. These potential risks are common to any form of physical activity.

Rare, but Serious, risks for patients randomized to the intervention group

Exercise may cause temporary risks of an adverse cardiovascular event, such as a heart attack. The screening procedures for this study, including our screening questions, medical record review, doctor*s clearance, and the baseline symptom-limited exercise testing, are designed to tell us whether or not you are healthy enough for exercise. Only men who are determined to be healthy enough will be eligible to continue with the study. Nevertheless, there is a small risk of an adverse cardiovascular event even among men who pass these screening procedures. There is also a risk of skeletal fracture while

exercising. However, participants will be closely supervised at the beginning of the exercise program and instructed on proper technique to reduce the risk of a fracture occurring.

The researchers recognize patients with bone metastases are at an increased risk of bone pain, skeletal fractures, spinal cord compressions, and hypercalcemia (i.e. elevated levels of calcium in the blood). The exercise intervention in this study will be highly supervised and targeted to patient*s specific needs using a modular prescription exercise approach (e.g. targeting non bone lesion areas) to minimize such risks during exercise.

Randomization risks - You will be randomly assigned to one of two groups (resistance and aerobic exercise, or usual care). It is unknown if exercise affects cancer progression in advanced prostate cancer patients or will have more side effects than usual care.

Unknown Risks - The exercise program may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

Contacts

Public
The Movember Foundation

PO Box 60
East Melbourne VIC 8002
AU
Scientific
The Movember Foundation

PO Box 60
East Melbourne VIC 8002
AU

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Patients must be mCRPC. This is defined as adenocarcinoma of the prostate with systemic metastatic disease despite castrate levels of testosterone (<50 ng/dL) due to orchiectomy or LHRH agonist.
o Patients must have one or more of the following to be considered mCRPC
* Metastatic Disease Progression: >20% increase in the sum of diameters of measurable lesions from the time of maximal regression or appearance of one or more new lesions.
* Bone Scan Progression: Appearance of one or more new lesions on bone scan attributable to prostate cancer.
* PSA Progression: PSA >=2 ng/ml that has risen serially on at least two occasions, each at least one week apart (PSA1 < PSA2 < PSA3).
* Castrate levels of testosterone must be maintained while on study. Be on androgen deprivation therapy (ADT) with a GnRH agonist/antagonist or prior bilateral orchiectomy. All patients will be required to be on ADT during the study period or have had a prior bilateral orchiectomy. Men with small cell neuroendocrine tumours or features of small cell disease are not eligible.
* At enrolment, patients must fit into one of the following 5 categories:;1. Treatment naïve for mCRPC (have not yet started approved therapies for CRPC ie: Abiraterone/Enzalutamide/ Apalutamide/Docetaxel; less than 4 weeks on approved therapies is still considered to be treatment naïve)
Or
2. Receiving Abi/Enza/Apa for mCRPC AND responding or stable (PSA values must be stable or declining after at least 4 weeks since starting Abi/Enza/Apa for mCRPC)
Or
3. Patients with PSA progression while on Abi/Enza/Apa are eligible as long as they are asymptomatic AND there is no intent on starting chemotherapy within 6 months
Or;4. Patients treated with Docetaxel as first line therapy for mCRPC who are asymptomatic without ANY evidence of progression
Or
5. Patients may have progressed following Docetaxel first line and are now receiving treatment with Abi/Enza/Apa. These patients must absolutely be responding or stable (PSA values must be stable or declining after starting Abi/Enza/Apa treatment) and have an expected life expectancy of more than 1 year. ;* >=4 weeks since last major surgery and fully recovered.
* No known contraindications to high intensity exercise, including, but not limited to: brain metastases; current congestive heart failure (New York Heart Association Class II, III or IV); serious or non-healing wound, ulcer, or bone fracture; spinal cord compromise or instrumentation due to metastatic disease; peripheral neuropathy >=grade 3. No serious

cardiovascular events within 12 months including, but not limited to, transient ischemic attack (TIA), cerebrovascular accident (CVA), or myocardial infarction (MI). Patients with a history of hypertension must be well-controlled (< 160/90) on anti-hypertensive therapy.
* Halabi Nomogram score <1951 (Risk Category rated as low or intermediate risk)
* Age >=18 years
* Required Baseline Laboratory Values: ANC >= 1500/uL; Platelet count >= 100,000/uL; Creatinine <= 1.5 x upper limits of normal; Bilirubin <= 1.5 x upper limits of normal; AST <= 1.5 x upper limits of normal; Serum testosterone <= 50 ng/dL
* ECOG performance status 0-1
* Medical clearance by treating physician to undergo a symptom-limited cardiopulmonary exercise test and vigorous aerobic and resistance exercise training, and able to complete an acceptable cardiopulmonary exercise test.
* Exercise Coordination Centre (ECC) review and approval of subject*s screening bone scan / areas with bone metastases.
* Men participating in vigorous aerobic exercise for >60 min/week or structured resistance exercise >=2 days/week, are not eligible.
* Subject is willing and able to use technological aspects of the trial.;* The subject is fluent in the language as designated by the institution at which he would be enrolled.

Exclusion criteria

* Previous radiographic or clinical progression (PSA progression is permitted) while on treatment with abiraterone, enzalutamide, apalutamide, or a combination.
* Previously identified small cell neuroendocrine tumours or pure small cell carcinoma of the prostate, based on a prior biopsy of the prostate.
* Brain metastases (brain imaging is not required)
* Previous and/or concurrent treatment with other anti-cancer treatments is permitted. Patients are allowed to be treated with chemotherapy during the duration of the trial. Patients who have received chemotherapy as part of initial androgen deprivation therapy for metastatic castration sensitive disease are eligible.
* Currently receiving experimental treatment with non-approved drugs at the time of enrolment. Patients must undergo a 28-day washout between last dose and screening CPET.
* Poorly controlled hypertension. During screening >=2/3 of readings must be < 160/90, regardless of whether on a regimen of anti-hypertensive therapy or not.
o If patient is currently taking hypertensive medication(s)/therapy, please indicate medication and include in the Treatment and Concomitant Medications Log (SOM: Appendix 11).
* Current congestive heart failure (New York Heart Association Class II, III or IV)
* Recent serious cardiovascular events (within 12 months) including, but not limited to, transient ischemic attack (TIA), cerebrovascular accident (CVA), or myocardial infarction (MI).
* Medical condition such as uncontrolled infection or cardiac disease that, in the opinion of the physician, would make this protocol unreasonably hazardous for the patient.
* Patients with a currently active second malignancy other than non-melanoma skin cancer. Patients are not considered to have a currently active malignancy if they have completed necessary therapy and are considered by their physician to be at <30% risk of relapse at time of assessment.

* Psychiatric illness, which would prevent the patient from giving informed consent or adhering to the study protocol.
* Serious or non-healing wound, ulcer, or bone fracture.
* Known spinal cord compromise or instrumentation due to metastatic disease in the mCRPC state. Radiation therapy for metastatic disease is allowed.
* Peripheral neuropathy >=grade 3.
* Men participating in vigorous aerobic exercise for more than 60 minutes per week or structured resistance exercise two or more days per week (seek ECC approval before exclusion).
* Experiences shortness of breath, chest discomfort, or palpitations when performing activities of daily living (patient with these symptoms can participate in the study with cardiologist clearance)
* Ongoing restriction of physical activity with physician documentation
* Has chest pain brought on by physical activity (patient can participate in the study with cardiologist clearance)
* Has developed chest pain in the past month (patient can participate in the study with cardiologist clearance)
* Moderate-to-severe bone pain (i.e., National Cancer Institute*s Common Terminology Criteria for Adverse Events grade 2-3 bone pain).
* Men who do not complete the baseline lifestyle and quality-of-life questionnaires and 3-days of diet diaries or country-specific FFQ will not be eligible

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-12-2018
Enrollment:	46
Type:	Actual

Ethics review

Approved WMO Date:	01-09-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NCT02730338
CCMO	NL57000.078.17