Supervised exercise to PRomote Infiltration of NK-cells into the Tumor (SPRINT): a randomized feasibility-trial.

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Primary Objective: To study trial feasibility in terms of patient enrollment and the percentage of tumor biopsies that can be assessed successfully.Secondary Objective(s): To study preliminary effects of exercise on immune function and generate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON49331

Source
ToetsingOnline

Brief title
SPRINT

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breastcancer, breastcarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Cancer Center Amsterdam

Intervention

Keyword: Breast cancer, Exercise, Immune function, NK-cells

Outcome measures

Primary outcome

Feasibility is the primary outcome measure of this study:

1) Recruitment

What is the proportion of eligible patients who are willing to participate in

this study and undergo an additional tumor biopsy?

2) Quality of tumor material

What is the percentage of tumor biopsies that can be assessed successfully from

all planned measurements both at baseline and after 6 weeks of neo-adjuvant

treatment?

We conclude that our pilot-study is feasible if:

1. We achieve a recruitmentrate of at least 20%.

2. At least 50% of the total number of biopsies (both T0 and T1) can be

examined successfully on infiltration of NK-cells.

Secondary outcome

Preliminary effects on immune function, IL-6 levels before and after an

exercise session and physical fitness. Primary end-point for the preliminary

effects is the alteration in number of NK-cells per total number of lymphocytes

and in NK-phenotype measured from biopsy tissue. In addition, immune function

will be measured from blood.

Study description

Background summary

Observational studies showed that higher levels of physical physical activity compared to lower levels are associated with a 38% reduction in risk of breast cancer-specific mortality (McTiernan, 2019). However, the causality and un-derlying mechanisms have not been elucidated. Recent studies in rodents have shown that exercise can directly affect cancer outcomes. Exercise training (voluntary wheel running) in mice results in an increase in intratumoral Natural Killer (NK) and T-cells, which contributed to a 50-60% reduction in tumor growth. Further analyses showed that exercise induced an in-crease in epinephrine which resulted in mobilization of NK-cells into the circulation which were then activated and redistributed to the tumor as a result of the production of IL-6 released by contracting muscles (Pedersen, 2016).
It is unclear whether a physical exercise program that has been proven feasible and effective for improving physical fitness, fatigue, quality of life and chemotherapy completion in patients with breast cancer receiving (neo)adjuvant chemotherapy can yield similar results on tumor responses in patients. A randomized controlled trial (RCT) in patients with breast cancer receiving neoadjuvant chemotherapy is needed to formally assess whether physical exercise would improve antitumor responses and patient outcome and such a study would provide an opportunity to directly assess the effects of exercise on the tumor in situ. However, the latter requires an additional tumor biopsy which might be a great barrier for patients to participate in such a study. Therefore, a pilot study is needed to determine the feasibility of conducting a sufficiently powered RCT.

Study objective

Primary Objective: To study trial feasibility in terms of patient enrollment and the percentage of tumor biopsies that can be assessed successfully.
Secondary Objective(s): To study preliminary effects of exercise on immune function and generate preliminary data on the potential effects of exercise on immune function.

Study design

This is a multicenter randomized controlled feasibility trial. After baseline measurements participants will be randomized in either the intervention or control group. Study parameters will be assessed before start of chemotherapy (T0) and after 6 weeks (T1).

Intervention

The intervention group will receive a supervised exercise intervention during neoadjuvant chemotherapy (6 weeks). Supervised one-hour exercise sessions include aerobic and resistance exercises and will be given twice a week. Additionally, patients are encouraged to be physically active for at least 30 minutes per day at Borg level 12-14. Patients in the control group will receive care as usual and are requested to maintain their usual daily physical activities.In order to limit contamination (increase of exercise in the control group), non-participation and pre-vent dropout, the control group will be offered the same 6-week exercise intervention after the tumor biopsy has been taken after 6 weeks.

Study burden and risks

Patients randomized to the exercise group will be guided by an physical therapist that is educated specifically on the exercise protocol for this study and are used to working with oncology patients. Therefore we expect a negligible risk for participants with regard to the exercises. In addition, evidence from randomized controlled trials, including our own, shows that exercise during cancer treatment benefits physical fitness, fatigue and quality of life (Buffart 2014 en 2018). Additionally, women with breast cancer who exercised during chemotherapy appeared to have fewer dose adjustments (van Waart, 2015 en Courneya, 2007). For this reason, the control group will be offered the same intervention after 6 weeks. Even though this evidence exists, referral to an physical therapist during chemotherapy is still not standard care, which might be due to the financial limitations.

The risk of participating in the endurance and strength tests is considered as minimal as participants will be supervised by a trained professional. Venepuncture can cause hemorrhage. The risk of clinically relevant complications of a breast biopsy was around 0,2% in a multi-institutional study in 1994 (Parker et al). Nowadays, the risk of complications is even lower, due to technological improvements that are implemented. The biopsies are very important to study the effect of an exercise intervention on tumour cells.

Measurements for study outcomes will be conducted in the hospital. Participants will visit the hospital 2 times over the course of 6 weeks, one visit will take about 75 minutes. At baseline (T0) this visit consists of blood collection and physical fitness tests. After 6 weeks (T1) the first visit consists of the blood collection and biopsy and wiil take around 75 minutes. The second visit consists of physical fitness tests and will be conducted, if possible, the same day as the start of the 3th or 4th cycle of chemotherapy.

Participants in the intervention group will visit the physical therapist twice a week for 6 weeks.

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

* Stage I-III breast cancer
* scheduled for neoadjuvant chemotherapy with 2 or 3-weekly Adriamycin/Cyclofosfamide, followed by Paclitaxel weekly +/- trastuzumab, for early (stage I-III) breast cancer
* willing to undergo an additional ultrasound guided biopsy
* ECOG-performance score * 2 (able to perform basic activities of daily living such as walking or biking)

Exclusion criteria

* addition of immuno- or targeted therapy at start neoadjuvant chemotherapy

* currently participating in structured vigorous aerobic exercise and/or resistance exercise (*2 days per week).
* cognitive disorder or severe emotional instability
* presence of other disabling co-morbidity that might hamper physical exercise e.g. heart failure (NYHA classes 3 and 4), chronic obstructive pulmonary disease (COPD, gold 3 and 4), orthopaedic conditions and neurological disorders (e.g., hernia, paresis, amputation, active rheumatoid arthritis);
* immunosuppressive medication (e.g. corticosteroids (other than used as part of standard chemotherapy premedication protocol), cyclosporine)
* immunodeficiency (primary or secondary)
* impossibility to perform an ultrasound-guided biopsy of the tumor

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-05-2021
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	19-10-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-03-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL72539.029.20