Protein and calorie restriction as treatment for prevention of cardiotoxicity in women receiving chemotherapy.

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To investigate the effects of a 5-day diet with 30% caloric and 70% protein restriction on cardiotoxicity induced by anthracycline treatment in women with triple negative or hormone receptor-positive breast cancer. The biomarker high-sensitivity...

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

Summary

ID

NL-OMON53779

Source
ToetsingOnline

Brief title
The PROTECT-COR trial

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, Mammacarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Stichting VIOZ (Vrienden Integrale Oncologische Zorg)

Intervention

Keyword: Anthracyclines, Breast cancer, Cardiotoxicity, Dietary restriction

Outcome measures

Primary outcome

The primary outcome measure is to investigate the effectiveness of a diet with 30% caloric and 70% protein restriction on cardiotoxicity due to treatment with anthracyclines. The primary study variable is cardiotoxicity, as measured by high-sensitivity troponin T (hsTnT) concentrations.

Secondary outcome

Secondary outcome measures are:

- Difference in troponin levels, before and after each chemotherapy cycle, Δ HsTnT.

- Brain natriuretic peptide, creatine kinase, electrocardiograms and ultrasounds of the left ventricular ejection fraction (LVEF) and global longitudinal strain.

- Other anthracycline-related toxicity, which will be measured by CTCAE-grading.

- Pharmacokinetics of anthracycline chemotherapy, following dietary restriction. This is measured as concentrations of anthracyclines and the active metabolites.

- Well-being of patients after dietary restriction and chemotherapy, to be measured by means of questionnaires.

- Metabolic parameters to assess dietary adherence: retinol binding protein,

albumin, insulin and lipid profile.

- Effects of dietary restriction on tumor progression and tumor size by radiographic response before, during and after treatment. This is presented as Complete Response / Partial Response / Stable Disease / Progression of disease, using the RECIST method. This response is also used as standard of care and has therefore already been validated.

Study description

Background summary

Breast cancer is the leading cancer in women around the world. A cornerstone in the treatment of breast cancer are anthracyclines. This is a group of medicines that are given for, among other things, breast cancer. Anthracyclines are very effective, but the biggest limiting factor for optimal use of this treatment is cardiotoxicity. Cardiotoxicity can cause cardiac arrhythmias or even lead to heart failure. This side effect can occur in any patient and is therefore the reason why anthracyclines cannot be dosed optimally. In practice, the dose is cumulative: for each patient, meaning there is a maximum amount of anthracyclines that they may receive throughout their life.

In previous studies, we have shown that dietary restriction improved resistance to oxidative stress. This was reflected in better recovery of patients after kidney donation and kidney transplantation. In patients treated with the chemotherapy drug irinotecan, dietary restriction increased active concentrations of the drug without change in toxicity or side effects. In this study we want to show whether a short-term calorie-restricted and low-protein diet has the same positive effect as chemotherapy with anthracyclines. This diet will be followed in patients diagnosed with early invasive breast cancer prior to each chemotherapy regimen. The effects of this are compared with a group that receives the same chemotherapy regimen without a diet.

Study objective

To investigate the effects of a 5-day diet with 30% caloric and 70% protein restriction on cardiotoxicity induced by anthracycline treatment in women with triple negative or hormone receptor-positive breast cancer. The biomarker high-sensitivity troponin T (hsTnT) will primarily be used to measure cardiotoxicity. Secondary, changes at the ultrasound level are also examined.

Furthermore, the effects of this diet on other anthracycline-related toxicity and the effect on tumor progression will be investigated. Patient well-being will be tracked through questionnaires.

Study design

A randomized controlled trial, in which the patients are divided into two groups. Both groups will receive the same chemotherapy regimen. Group 1 follows a diet with approximately 30% calorie and 70% protein restriction for 5 days prior to each chemo cycle. To make the diet as homogeneous as possible, synthetic nutrition will be given, based on the individual daily calorie requirement. The outcome measures are compared with a control group to investigate whether such a diet influences the cardiotoxicity of anthracyclines. The control group will be called by an experienced dietician before each anthracycline chemotherapy. They will be asked about all the food eaten in the last 24 hours, which will be analyzed by the dietician.

Blood will be taken from patients for analysis and an electrocardiogram and ultrasound will be performed a number of times. In addition, patients will be asked to complete questionnaires regarding quality of life, pain, fatigue and nausea.

Intervention

After consent has been given by the patients, they will be divided into 2 groups:

1) The intervention group. This group follows a prescribed diet 5 days prior to each chemotherapy cycle, for a maximum of 4 cycles. This diet consists of 30% caloric and 70% protein restriction, based on the individual daily energy requirement.

2) The control group. He is not prescribed a diet, but is called by a dietitian just before each anthracycline chemotherapy to ask what has been eaten in the past 24 hours. Based on this, the calorie and macronutrient intake is calculated.

Study burden and risks

For this study, 7 additional blood draws are taken during the routine blood draws. Patients will have to complete standardized questionnaires before, during and after each diet cycle to measure side effects and quality of life, these will take approximately a few minutes each. In addition, an electrocardiogram and ultrasound will be performed. The electrocardiogram will be performed before each cycle, the ultrasound will be performed a total of 3 times during the study period (up to 12 months after the end of the study at

the latest).
The synthetic diet can cause a feeling of hunger, mild headache and slight weight loss.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Women with newly diagnosed triple negative or hormone receptor-positive breast cancer with an indication for (neo-)adjuvant anthracycline-based chemotherapy and of intent to start anticancer treatment
2. Age between 18 and 75 years
3. Written informed consent

4. Body mass index >= 19.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Allergic to any of the ingredients of the diet
2. Known history of cardiac dysfunction
3. Severe morbidity with the inability to receive anticancer treatment.
4. Participation in another clinical trial with an intervention arm (database and/or biobank studies excluded)
5. Pregnant women
6. Previous treatment with anthracycline

Study design

Design

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

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-10-2023
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	13-03-2023
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2024
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
CCMO	NL83401.078.22