Development of a more sensitive method to predict breast cancer recurrence after 5-years of endocrine treatment making use of diagnostic leukapheresis to detect circulating tumor cells

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We hypothesize that CTC detection through diagnostic leukapheresis improves the detection rate among ER+, N+ primary breast cancer who have received 5 years of adjuvant endocrine therapy and will be a promising technique for risk classification in...

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	Breast disorders
Study type	Observational non invasive

Summary

ID

NL-OMON23853

Source
NTR

Brief title
SIBYLLA

Condition

- Breast disorders

Synonym
Breast cancer

Health condition

ER+, HER2 negative breast cancer, positive lymph nodes at diagnosis

Research involving
Human

Sponsors and support

Primary sponsor: KWF
Source(s) of monetary or material Support: Dutch Cancer Society (KWF Kankerbestrijding)

Intervention

Outcome measures

Primary outcome

The primary endpoint is a CTC detection rate through the DLA method of 15% in the 1-3 PLN group and 30% in the ≥4 PLN group.

Secondary outcome

Secondary outcome measures are - The concordance of the CTC detection rate in DLA product vs the CTC detection rate in 7.5mL and in 30mL blood samples per patient - The detection rate of CTCs compared to the detection rate of circulating tumor (ct)DNA per patient. - To assess the incidence of lymphedema following DLA using the Lymph-ICF questionnaire and arm circumference measure.

Study description

Background summary

Rationale: Adjuvant endocrine treatment (ET) for 5 years is standard for patients with primary hormone receptor positive (ER+) breast cancer. However, recurrences still occur, of which more than 50% occur after 5 years ET. Extended adjuvant endocrine therapy (EET), up to 10-15 years, increases disease free survival (DFS). However, there is no robust biomarker predicting late recurrence risk after 5-years ET. The measurement of circulating tumor cells (CTCs) as a reflection of residual disease could possibly serve as such a biomarker. Recent studies showed the prognostic value of CTC enumeration in ER+ lymph node positive (N+) primary breast cancer patients during and after ET. Unfortunately, the classic CTC enumeration method using 7.5 mL of blood is not sensitive enough as disease recurrence also occurred in patients without detectable CTCs. To measure residual disease through more sensitive CTC detection, screening of a larger blood volume is desired. CTC enumeration in 30 mL of blood yielded a higher percentage of patients who had ≥1 CTC than in 7.5 mL of blood, which increases sensitivity and specificity. However, the robustness of this test is weak

due to stochastic variation inherent to the low CTC numbers found. A technique to greatly increase the screened blood volume is called Diagnostic Leukapheresis (DLA). During DLA, 2.5-5L of blood is passed through a centrifuge, which isolates peripheral blood mononuclear cells (PBMCs) as well as CTCs from the blood, which is returned to the patient. Preliminary results have shown that this procedure increases the sensitivity of CTC detection substantially by 500-1000. We therefore hypothesize that CTC detection through DLA improves the detection rate among ER+, N+ primary breast cancer who have received 5 years of adjuvant endocrine therapy and will be a promising technique for risk classification in this patient group. Objective: The primary objective of this study is to demonstrate that our DLA-based method is promising enough to detect CTCs in ER+, N+ primary breast cancer patients after 5 years ET. Simultaneously, other methods (CTC detection in 7.5 ml and 30 ml of blood as well as ctDNA detection) will be assessed in this study population and explored how they compare with our DLA-based approach in terms of tumor load detection.

Study objective

We hypothesize that CTC detection through diagnostic leukapheresis improves the detection rate among ER+, N+ primary breast cancer who have received 5 years of adjuvant endocrine therapy and will be a promising technique for risk classification in this patient group.

Study design

Enrollment should be completed within 2.5 years

Contacts

Public
Erasmus MC
Noortje Verschoor

0107044375
Scientific
Erasmus MC
Noortje Verschoor

0107044375

Eligibility criteria

Age

Adults (18-64 years)
Adults (18-64 years)

Elderly (65 years and older)
Elderly (65 years and older)

Inclusion criteria

1. Female 2. Age >18 years 3. Diagnosed with ER+ Her2-negative lymph node positive, primary breast cancer 4. Received at least 4.5 - 5.5 years of adjuvant ET for breast cancer including those who are <6 months after finishing endocrine therapy. 5. No clinical signs of locoregional or distant recurrence. 6. At least one adequate peripheral vein in both arms as access for leukapheresis. 7. Provided written informed consent.

Exclusion criteria

1. Prior non-breast malignancies <5 years of inclusion, except for basal or squamous cell carcinoma of the skin 2. Pre-existing lymphedema, quantified by specialist 3. Known hypersensitivity to the used anticoagulant (ACD) 4. Inadequate cardiac function or severe cardiovascular comorbidity (heart failure NYHA class III/IV) 5. Coagulation disorders as defined by one of the following: NOTE: the use of all types of anticoagulant therapy is permitted o Coagulation disorder in medical history o Platelet count < 40 x 109/L; Patients not on anticoagulant therapy which affects PT or APTT if: o PT > 1.5 x ULN or PT-INR > 1.5 x ULN o APTT > 1.5 x ULN Patients who take anticoagulant therapy which affects PT or APTT if: o PT or APTT > 1.5 x the upper limit of the desired therapeutic window o Total bilirubin > 2.5 x ULN 6. BMI ≥ 35 kg/m2

Study design

Design

Study phase:	N/A
Study type:	Observational non invasive
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2020
Enrollment:	87
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion Date:	18-05-2020
Application type:	First submission
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
NTR-new	NL8597
Other	METC Erasmus MC : MEC 2020-0384

Study results