# 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...

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|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestopt |
| **Type aandoening** | Borstaandoeningen |
| **Onderzoekstype** | Observationeel onderzoek, zonder invasieve metingen |

## Samenvatting

### ID

NL-OMON23853

**Bron**
NTR

**Verkorte titel**
SIBYLLA

### Aandoening

- Borstaandoeningen

**Aandoening**

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

**Betreft onderzoek met**
Mensen

## Ondersteuning

**Primaire sponsor:** KWF
**Overige ondersteuning:** Dutch Cancer Society (KWF Kankerbestrijding)

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

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.

# Toelichting onderzoek

### Achtergrond van het onderzoek

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.

**Doel van het onderzoek**

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.

**Onderzoeksopzet**

Enrollment should be completed within 2.5 years

# Contactpersonen

## Publiek

Erasmus MC
Noortje Verschoor

0107044375

## Wetenschappelijk

Erasmus MC
Noortje Verschoor

0107044375

# Deelname eisen

**Leeftijd**
Volwassenen (18-64 jaar)
Volwassenen (18-64 jaar)
65 jaar en ouder
65 jaar en ouder

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Fase onderzoek: | N.V.T. |
| Type: | Observationeel onderzoek, zonder invasieve metingen |
| Onderzoeksmodel: | Enkelvoudig |
| Toewijzing: | N.v.t. / één studie arm |
| Blindering: | Open / niet geblindeerd |
| Controle: | N.v.t. / onbekend |
| Doel: | Diagnostiek |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestopt |
| (Verwachte) startdatum: | 03-11-2020 |
| Aantal proefpersonen: | 87 |
| Type: | Werkelijke startdatum |

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nee

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 18-05-2020 |
| Soort: | Eerste indiening |
| Toetsingscommissie: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL8597 |
| Ander register | METC Erasmus MC : MEC 2020-0384 |

## Resultaten