# Systemic and local estrogen metabolism in healthy women compared to endometrial cancer patients

Gepubliceerd: 20-03-2016 Laatst bijgewerkt: 18-08-2022

This study is a pilot study to obtain an idea of the complete estrogen metabolism in pre- and post menopausal healthy women, compared to endometrial cancer patients. The complete estrogen metabolism is defined as the serum steroid levels and the...

Ethische beoordeling Status	Positief advies Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

# Samenvatting

#### ID

NL-OMON25168

Bron

NTR

Verkorte titel

TEC study

#### Aandoening

endometrial cancer estrogen metabolism estrone 17beta-estradiol 17beta-hydroxysteroid dehydrogenase steroid sulfatase steroid sulfotransferase aromatase serum hormone levels endometrial tissue

### Ondersteuning

Primaire sponsor: Maxima Medisch Centrum, Veldhoven

1 - Systemic and local estrogen metabolism in healthy women compared to endometrial ... 12-05-2025

**Overige ondersteuning:** Maxima Medisch Centrum, Veldhoven KWF grant

#### **Onderzoeksproduct en/of interventie**

### Uitkomstmaten

#### Primaire uitkomstmaten

The primary outcome will be the difference between premenopausal, postmenopausal and endometrial cancer patients in the local tissue enzyme mRNA levels analysed by rt-PCR and described as fold change compared to housekeeping genes. Enzyme activity levels analysed by LCMS for HSD17B1, HSD17B2, STS, SULT1E1, ARO will be described in pmol/mg/hour. Systemic serum steroid levels (see for specification section 5.3 study procedures).will be measured and described in ng/ml or pg/ml.

# **Toelichting onderzoek**

#### Achtergrond van het onderzoek

Rationale: Endometrial cancer is the most common gynaecological malignancy in the western world with over 320.00 new patients a year worldwide (1). Although good 5 year survival ranging between 74% to 91%, 20-30% will develop recurrence or are diagnosed at high stage (1). For those patients besides chemotherapy and/or hormonal therapy (which is only successful in 30% of the cases) no other options are available.

It is well known that exposure to estrogens increases the risk of the development of endometrial cancer. However, little is known about the complete estrogen metabolism, i.e. the way estrogens are supplied to endometrial cancer, which can occur via the circulation, or through the local generation of steroids.

Objective: To investigate the complete estrogen metabolism in pre- and postmenopausal healthy women compared with endometrial cancer patients.

Our secondary objective is the detection of possible serum and/or endometrium specific risk factors in the development of endometrial cancer, patients' prognosis in relation to specific serum and/or endometrium markers, novel interesting biomarkers for future therapeutic target.

Study design: We aim to conduct a prospective pilot cohort study investigating the estrogen metabolism in blood serum and endometrial (cancer) tissue.

Study population: Pre- and postmenopausal healthy women and endometrial cancer patients who underwent hysterectomy in our hospital can be included. An endometrial tissue sample

and blood sample will be taken to investigate or objective.

Main study parameters/endpoints:

The main parameters are: the levels of enzymes involved in the local estrogen synthesis (HSD17B1, HSD17B2, STS, SULT1E1, ARO) in endometrial tissue and the systemic serum steroid levels. Premenopausal, postmenopausal women and endometrial cancer patients will be compared.

#### Doel van het onderzoek

This study is a pilot study to obtain an idea of the complete estrogen metabolism in pre- and post menopausal healthy women, compared to endometrial cancer patients. The complete estrogen metabolism is defined as the serum steroid levels and the local estrogen metabolism in endometrial (cancer) tissue. This will result in an overview of patients' specific estrogen metabolism; furthermore, the level of each individual serum steroid and endometrial tissue enzyme levels per group will be compared to indicate if there are any differences

#### Onderzoeksopzet

Endpoint all inclusions01-11-2017, after all inclusions the analyses will be preformed.

#### **Onderzoeksproduct en/of interventie**

Endometrial tissue analysis

mRNA analyses will be preformed using real-time PCR.

RNA will be isolated with Trizol reagent and assesses spectrophotmetrically for quantity and purity and c DNA will be synthesized. Primers for PCR amplification for HSD17B1, HSD17B2, STS, SULTE1 and Aromatase are commercially available and will be used.

Enzyme activity levels will be measured using our recently developed method by Liquid chromatography-mass spectrometry (LCMS).

Method; frozen samples will be homogenized with a blender in a radioimmunoprecipitation assay buffer, debris will be removed by centrifugation and protein concentration will be determined. The activity of enzymes will be determined using a LCMS-based method.

The following mRNA and enzyme activity levels of the proteins controlling the local estrogen metabolism will be assessed;

- 17beta-hydroxysteroid dehydrogenase type 1 (HSD17B1)

- 17beta-hydroxysteroid dehydrogenase type 2 (HSD17B2)

3 - Systemic and local estrogen metabolism in healthy women compared to endometrial ... 12-05-2025

- Steroid sulphatase (STS)
- Estrogen sulphotransferase (SULT1E1)
- Aromatase (ARO)

Blood analysis

Blood analyses will be assessed in collaboration with prof. Auriola of the Eastern University Finland (34).

The most recently developed Multiplex steroid analyse protocol allows the identification and quantification of the following steroids; estradiol, cortisol, cortisone, estriol, aldosterone, 17OH-pregnenolone, 11deoxycortisol, estrone, DHEA, testosterone, 17OH-progesterone, androstrome, etiocholanolone, dht, androstenedione, pregnenolone, 21OH-progestreone, progesterone.

Additional steroids will be analysed at the laboratory at the Maastricht University Medical Center (MUMC) by LCMS.

- Adiol

- Estrone sulphate (E1S)

In case of specific new research questions or interest on the analyses of other parameters and metabolites, separate METC protocol or appropriate amendments will by applied.

# Contactpersonen

#### **Publiek**

Karlijn Cornel Maastricht The Netherlands

### Wetenschappelijk

Karlijn Cornel Maastricht The Netherlands

# **Deelname eisen**

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

#### Patients with;

- Hysterectomy needs to be preformed because of endometrial cancer or benign indication (like prolapse, menorrhagia, uterus myomatosis)

- Menopausal status is known
- Blood collection need to be allowed
- Informed consent is given
- No history of malignancies in the previous 5 years
- Minimum age: 18 years

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

Patients with;

- Neoadjuvant treatment defined as chemotherapy and/or radiotherapy
- Aged under 18 years

# Onderzoeksopzet

#### **Opzet**

Туре:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

5 - Systemic and local estrogen metabolism in healthy women compared to endometrial ... 12-05-2025

### Deelname

Nederland	
Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-05-2016
Aantal proefpersonen:	90
Туре:	Verwachte startdatum

# **Ethische beoordeling**

Positief advies
Datum:
Soort:

20-03-2016 Eerste indiening

# 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

ID
NL5007
NTR5780
NL55799.015.15

# Resultaten