# DNA damage response in tumours of patients with endometrial cancer

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

# Samenvatting

## ID

NL-OMON23000

Bron NTR

Verkorte titel DNA damage

#### Aandoening

Endometrial cancer

## Ondersteuning

Primaire sponsor: ErasmusMC

**Overige ondersteuning:** Erasmus MC, Department of Gynaecologic Oncology, department of Molecular Genetics, department of Pathology, Erasmus MC.

# **Onderzoeksproduct en/of interventie**

## **Uitkomstmaten**

#### Primaire uitkomstmaten

We hope to find a way to perform ex- vivo testing of the respons to several therapies in fresh

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# **Toelichting onderzoek**

#### Achtergrond van het onderzoek

Endometrial cancer is the most common gynaecological malignancy, with an incidence of 1900 cases in The Netherlands each year. It is a heterogeneous group of tumours, consisting of carcinomas with endometrioid (87%), adenosquamous (4%), serous (4%), mucinous (1%), clear cell (1%), small cell neuro-endocrine (1%), and mixed (carcinosarcomas) (2%) histology. A large group of patients has low grade endometrioid histology, present with early stage disease and have a good prognosis. However, advanced disease and high grade endometrioid as well as serous, clear cell and the mixed subtypes are more aggressive and have a poor prognosis. Treatment options are limited to surgical staging or debulking followed by adjuvant platinum-based chemotherapy and/or adjuvant radiotherapy. Little progress in survival benefit has been achieved in the last decades.

Synthetic lethality is an exciting new avenue to disrupt cancer cells for targeted treatment. Two genes are said to be synthetic lethal if mutations in both genes cause cell death but a mutation in either of them alone is not lethal. In applying synthetic lethality to the discovery of cancer drugs, the goal would be to identify a target gene that when mutated or chemically inhibited, kills cells that harbour a specific cancer-related alteration, but spares otherwise identical cells lacking the cancer-related alteration. Thereby, the chance of negative side effects is limited. PARP inhibition in patients with high grade serous ovarian cancer is an important example.

We expect far more gynaecological cancer patients than only those with germ line and somatic BRCA mutated ovarian cancer to have potential benefit from targeted therapies including PARP inhibitors. Several endometrial cancers, especially serous endometrial cancers, yield a homologous recombination deficiency phenotype and may respond to PARP inhibition. Understanding underlying DNA damage mechanisms and potential targets in these cancers can further improve therapeutic strategies. PARP inhibition is only one of the potential new therapeutic strategies that can be tested; with the endometrial tumour material collected within this project we aim to expand our research to other new combinations of synthetic lethality as well. Detection of the presence of HRD might be a viable strategy to select patients for DNA repair inhibitor trials.

This is a preclinical study including the following steps:

- 1, Development of a method to use fresh tumour tissue for genetic analysis
- 2 Development of a method to measure DNA damage response in fresh tumour tissue.
- 3 Measure DNA damage response in tumour tissue
- 4.Ex vivo testing of the response to several therapies in fresh tumour tissue.

The final step is the ultimate goal of this study.

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#### Doel van het onderzoek

Ideally in the future, after a preclinical test on a tumour sample of an individual patient, a patient-tailored therapy will be chosen with the best perspectives thereby avoiding non-active therapies. An important advantage would be a less toxic treatment with fewer side effects for the patient, which could potentially be repeated depending on specific biological targets.

#### Onderzoeksopzet

We expect to answer Q1 within 12 months. When this is not possible the project ends

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

We will collect fresh tumour tissue from patients with endometrial cancer. Patients who received neo-adjuvant chemotherapy will be excluded from the study. We will use only leftover tissue after pathological review, and the material is collected during routine patient care i.e. hysterectomy and bilateral salpingo-oophorectomy, or debulking surgery.

# Contactpersonen

#### **Publiek**

ErasmusMC Cancer Institute Lena van Doorn

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#### Wetenschappelijk

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# **Deelname eisen**

## Belangrijkste voorwaarden om deel te mogen nemen

# (Inclusiecriteria)

Patients with all subtypes of endometrial cancer

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

Patients will be informed upfront that any relevant findings in this study will be reported back to themselves and to their attending physicians. They cannot participate in the study when they do not consent to these criteria.

# Onderzoeksopzet

## Opzet

Туре:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

#### Deelname

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	03-02-2019
Aantal proefpersonen:	50
Туре:	Verwachte startdatum

# Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

# **Ethische beoordeling**

Positief advies Datum:

03-02-2019

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# 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	NL7518
Ander register	METC Erasmus MC : MEC-2018-1653

# Resultaten