







# PORTEC-4a: Randomised trial of standard or molecular profile-based recommendation for radiotherapy after surgery for women with early stage endometrial cancer

<b>Submission date</b> 03/06/2016	<b>Recruitment status</b> No longer recruiting	 Retrospectively registered
		 Protocol added
<b>Registration date</b> 24/06/2016	<b>Overall study status</b> Ongoing	 SAP not yet added
		 Results added
<b>Last Edited</b> 13/12/2021	<b>Condition category</b> Cancer	 Raw data not yet added
		 Study ongoing and record not updated in last year

## Plain English Summary

### Background and study aims

For women with early stage endometrial (womb) cancer, current standard treatment is surgery (removal of the uterus and ovaries) followed by vaginal brachytherapy. Vaginal brachytherapy is a type of radiotherapy where a special applicator is placed in the vagina in which a small pellet of radioactive material is placed to give radiation treatment to the inner part of the vagina. With brachytherapy, the risk of local recurrence (that is, the tumour coming back) is very low and there are very few side effects. However, many women are treated with vaginal brachytherapy, while only few really need this. About 10 women have to be treated to prevent 1 vaginal recurrence. If local recurrence is found, this can be effectively treated at that time. Therefore, treating all women considered to be at risk seems unnecessary. If a better way of predicting which women are likely to suffer a relapse (vaginal recurrence) can be developed then not so many women have to undergo vaginal brachytherapy. This, in turn, will reduce health care costs. In recent years, scientific studies have shown that there are specific alterations in the genes of tumor cells which enable recurrence and the spread of cancer. For endometrial cancer, a better individual risk prediction has been obtained by combining known risk factors with individual alterations in the genes of their tumor. By determining this risk profile on the tumor tissue which has been removed at surgery, a better recommendation can be obtained as to what treatment should be performed, including whether or not vaginal brachytherapy is required

### Objectives and design:

In the PORTEC-4a trial, the standard vaginal brachytherapy (standard treatment) will be compared to the use of the individual risk profile to determine adjuvant treatment (favorable: observation; intermediate: vaginal brachytherapy; unfavorable: external beam radiotherapy). The aim is to evaluate if the use of the individual risk profile saves many women unnecessary vaginal brachytherapy with similarly high recurrence-free survival and local control, and reduced health costs.

This is a randomised trial, and eligible and consenting women will be randomly assigned (1:2) to vaginal brachytherapy (standard arm) or molecular profile-based recommendations for either observation, vaginal brachytherapy or external beam radiotherapy (investigational arm).

Who can participate?

Women of any age (above 18) who have had surgery (removal of uterus and ovaries) for early stage endometrial cancer.

What does the study involve?

Participants are randomly allocated to one of two groups. Those in group 1 (control group) have vaginal brachytherapy as usual. Those in group 2 (intervention group) either have no further treatment after surgery, vaginal brachytherapy or external beam radiation therapy, depending upon their molecular profile (that is, the type of alterations in the genes of the tumor cells). All participants are then followed up for at least 5 years to check for recurrence of the tumor, quality of life and any side effects.

What are the possible benefits and risks of participating?

Possible benefits include being spared from further treatment after surgery and have a better understanding what the individual risk of recurrence is.

Where is the study run from?

Lead center is Leiden University Medical Center in the Netherlands. Participating centres are found in all regions of the Netherlands.

When is study starting and how long is it expected to run for?

June 2016 to December 2028

Who is funding the study?

Dutch Cancer Society.

Who is the main contact?

Professor Carien Creutzberg

**Study website**

<https://www.msbi.nl/portec4>

## Contact information

**Type(s)**

Scientific

**Contact name**

Prof Carien Creutzberg

**ORCID ID**

<http://orcid.org/0000-0002-7008-4321>

**Contact details**

Leiden University Medical Centre,  
Dept of Radiation Oncology, K1-P,  
Albinusdreef 2,

Leiden  
Netherlands  
2333 ZA  
+31.71.526.5120  
c.l.creutzberg@lumc.nl

**Type(s)**  
Scientific

**Contact name**  
Dr Anne-Sophie V.M. van den Heerik

**ORCID ID**  
<http://orcid.org/0000-0001-6403-0143>

**Contact details**  
Leiden University Medical Center, Dept of Radiation Oncology  
Albinusdreef 2  
Leiden  
Netherlands  
2333 ZA  
+31 (0)71 526 5539  
a.v.m.van\_den\_heerik@lumc.nl

## **Additional identifiers**

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**  
NCT03469674

**Protocol/serial number**  
UL2011-5336; P16.054; NL56828.058.16

## **Study information**

**Scientific Title**  
PORTEC-4a: Randomised Phase III Trial of molecular profile-based versus standard recommendations for adjuvant radiotherapy for women with early stage endometrial cancer

**Acronym**  
PORTEC-4a

**Study hypothesis**  
Molecular risk profile-based recommendations for no additional treatment (55%), vaginal brachytherapy (40%) or external beam radiotherapy (5%) will lead to similar vaginal control for women with early stage endometrial cancer with high-intermediate risk features, while sparing about 50% of these women vaginal brachytherapy and reducing health care usage.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Committee for Medical Ethics, Leiden University Medical Center, Leiden, The Netherlands, 10/05/2016, ref: P16.054

**Study design**

Randomised multicenter phase III trial

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

<https://msbi.nl/promise/LinkClick.aspx?fileticket=IYQIkIT4IHw%3d&tabid=125&portalid=0&mid=581>

**Condition**

Endometrial cancer

**Interventions**

Participants are randomly allocated to one of two arms:

**1. Standard arm:**

Vaginal brachytherapy (3 short outpatient internal radiation treatments over 2 weeks to the vaginal cuff), based on PORTEC-2 trial.

**2. Investigational arm:**

Based on the molecular profile, either no further treatment after surgery (for favourable profile), or vaginal brachytherapy (as above, for intermediate profile) or external beam radiation therapy (5 weeks of daily out-patient external radiation treatments to the pelvic area, for unfavourable profile).

After completion of patient recruitment, follow-up will continue until the time of final analysis is reached and until at least 5 years after inclusion of each patient.

**Intervention Type**

Other

**Primary outcome measure**

Vaginal recurrence, measured during each follow-up visit by vaginal inspection and pelvic examinations (3 monthly first 2 years, 6 monthly until 5th year) and confirmation by histology in case of suspected recurrence

### **Secondary outcome measures**

1. Recurrence-free survival - regular follow-up visits (3 monthly first 2 years, 6 monthly until 5th year) with history focused on symptoms and side effects and pelvic examination; further evaluation in case of suspected recurrence locally or at distant sites by (PET)-CT and/or MRI scanning and histological confirmation. In case of death, information on date and cause of death are recorded
2. 5-year vaginal control - local recurrence free at 5 years either without any evidence of recurrence or after treatment for vaginal recurrence
3. Quality of life- Patients receive a QoL questionnaire consisting of EORTC QLQ-C30 and EN24 at baseline (after surgery, before study treatment or observation), at 6 weeks after randomisation, and at 6, 12, 18, 24, 36 and 60 months after randomisation
4. Side effects- Regular follow-up visits (3 monthly first 2 years, 6 monthly until 5th year) with history focused on symptoms and side effects – recording of adverse events according to CTCAEv 4.0
5. Health care costs - EC-related healthcare costs will include the costs of the randomised care and care associated with (serious) adverse events. Healthcare use over the follow-up period will be converted to costs using standard prices, discounted over time. Costs will be evaluated at each follow-up and at recurrence by recording hospital admissions, surgeries, etc over the past follow-up period

### **Overall study start date**

01/06/2016

### **Overall study end date**

31/12/2028

## **Eligibility**

### **Participant inclusion criteria**

Histologically confirmed endometrioid type endometrial carcinoma, FIGO 2009 stage I, with one of the following combinations of stage, grade, age, and LVSI:

1. Stage IA, grade 3 (any age, with or without LVSI)
2. Stage IB, grade 1 or 2 and age >60 years
3. Stage IB, grade 1-2 with documented LVSI
4. Stage IB, grade 3 without LVSI
5. Stage II (microscopic), grade 1

WHO-performance status 0-2

Written informed consent

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Female

**Target number of participants**

550

**Participant exclusion criteria**

1. Any other stage and type of endometrial carcinoma
2. Histological types papillary serous carcinoma or clear cell carcinoma (at least 10% if mixed type)
3. Undifferentiated or neuroendocrine carcinoma
4. Uterine sarcoma (including carcinosarcoma)
5. Previous malignancy (except for non-melanomatous skin cancer) < 5 yrs
6. Previous pelvic radiotherapy
7. Interval between the operation and start of radiotherapy exceeding 8 weeks

Updated 17/08/2021:

7. Expected interval between the operation and start of radiotherapy exceeding 8 weeks

**Recruitment start date**

01/06/2016

**Recruitment end date**

24/12/2021

## **Locations**

**Countries of recruitment**

Austria

Belgium

Czech Republic

France

Germany

Ireland

Netherlands

Switzerland

**Study participating centre**

**Leiden University Medical Center (lead center)**

Netherlands

2333 ZA Leiden

**Study participating centre**  
**Academic Medical Center**  
Amsterdam  
Netherlands

-

**Study participating centre**  
**Catharina Hospital**  
Eindhoven  
Netherlands

-

**Study participating centre**  
**Erasmus Medical Center**  
Rotterdam  
Netherlands

-

**Study participating centre**  
**Institute Verbeeten**  
Tilburg  
Netherlands

-

**Study participating centre**  
**Isala Clinics**  
Zwolle  
Netherlands

-

**Study participating centre**  
**Maastricht Radiation Oncology Clinic**  
Maastricht  
Netherlands

-

**Study participating centre**

**Medical Centre Haaglanden**

Den Haag  
Netherlands

-

**Study participating centre**

**NKI/Antoni v. Leeuwenhoekhuis (The Netherlands Cancer Institute)**

Amsterdam  
Netherlands

-

**Study participating centre**

**Radiotherapy Group, Arnhem**

Arnhem  
Netherlands

-

**Study participating centre**

**Radiotherapy Institute Friesland, Leeuwarden**

Leeuwarden  
Netherlands

-

**Study participating centre**

**University Medical Center Groningen**

Groningen  
Netherlands

-

**Study participating centre**

**University Medical Center Radboud**

Nijmegen  
Netherlands

-

**Study participating centre**



**University Medical Center Utrecht**

Utrecht  
Netherlands

-

**Study participating centre**

**Zuidwest Radiotherapy Institute**

Vlissingen  
Netherlands

-

**Study participating centre**

**University Hospital Gent**

Corneel Heymanslaan 10  
Gent  
Belgium  
9000

**Study participating centre**

**University Hospital Tübingen**

Hoppe-Seyler-Straße 3  
Tübingen  
Germany  
72076

**Study participating centre**

**Rotkreuzklinikum München**

Rotkreuzpl. 8  
München  
Germany  
80634

**Study participating centre**

**Kliniken Essen-Mitte**

Henricistraße 92  
Essen  
Germany  
45136

**Study participating centre**  
**Universitätsklinikum Schleswig-Holstein**  
Campus Lübeck  
Ratzeburger Allee 160  
Lübeck  
Germany  
23562

**Study participating centre**  
**Kaiserswerther Diakonie Düsseldorf**  
Kreuzbergstraße 79  
Düsseldorf  
Germany  
40489

**Study participating centre**  
**Universitätsklinikum Heidelberg**  
Im Neuenheimer Feld 672  
Heidelberg  
Germany  
69120

**Study participating centre**  
**Sankt Gertrauden Krankenhaus Berlin**  
Paretzer Straße 12  
Berlin  
Germany  
10713

**Study participating centre**  
**Kantonsspital Frauenklinik Lucerne**  
Spitalstrasse  
PO Box 6000  
Luzern  
Switzerland  
16

**Study participating centre**  
**Saint Luke's Radiation Oncology Network (SLRON), Dublin**  
Oakland Drive  
Highfield Road

Dublin  
Ireland  
6

**Study participating centre**  
**St James's Hospital (SJH), Dublin**  
James Street  
Dublin  
Ireland  
8

**Study participating centre**  
**University Hospital Prague**  
U Nemocnice 499/2  
Prague  
Czech Republic  
128 08

**Study participating centre**  
**Institut Gustave-Roussy, Paris**  
114, rue Édouard-Vaillant  
Villejuif Cedex  
France  
94805

**Study participating centre**  
**Hôpital Européen Georges-Pompidou, Paris**  
20 Rue Leblanc  
Paris  
France  
75015

**Study participating centre**  
**Hôpital Tenon, Paris**  
4 Rue de la Chine  
Paris  
France  
75020

**Study participating centre**  
**Medical University, Vienna**  
Spitalgasse 23  
Wien  
Austria  
1090

## Sponsor information

### Organisation

Leiden University Medical Center

### Sponsor details

Albinusdreef 2  
Leiden  
Netherlands  
2333 ZA

### Sponsor type

Hospital/treatment centre

### Website

[www.lumc.nl](http://www.lumc.nl)

### ROR

<https://ror.org/05xvt9f17>

## Funder(s)

### Funder type

Charity

### Funder Name

KWF Kankerbestrijding

## Results and Publications

### Publication and dissemination plan

To be confirmed at later date

Protocol is available online. Publication of the trial results after we have completed the trial.

We may publish the trial background and design in a Dutch oncology and possibly later on also in the UK when international participation is getting started.

## Intention to publish date

31/12/2024

## Individual participant data (IPD) sharing plan

After publication of the full results (including long-term results) the de-identified data will be available for relevant scientific studies, upon request and submission of a research proposal, and after evaluation of the PORTEC-group.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/10/2018		Yes	No
<a href="#">Participant information sheet</a>	Short patient information in English		17/08/2021	No	Yes
<a href="#">Participant information sheet</a>	v2.2	09/04/2016	17/08/2021	No	Yes
<a href="#">Participant information sheet</a>	v2.5.1	26/06/2020	17/08/2021	No	Yes
<a href="#">Protocol article</a>		12/10/2020	17/08/2021	Yes	No
<a href="#">Results article</a>	Brachytherapy quality assurance	05/11/2020	17/08/2021	Yes	No