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

Submission date
03/06/2016

Recruitment status
No longer recruiting

Registration date
24/06/2016

Overall study status
Ongoing

Last Edited
11/12/2024

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

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: extermal 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

Secondary identifying numbers
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 objectives
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

Health condition(s) or problem(s) studied
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

Completion date
31/12/2028

Eligibility

Key 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

Key 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

Date of first enrolment
01/06/2016

Date of final enrolment
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 Tubingen
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
Universitatsklinikum 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

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?
Results article	results	01/10/2018		Yes	No
Participant information sheet	Short patient information in English		17/08/2021	No	Yes
Participant information sheet	v2.2	09/04/2016	17/08/2021	No	Yes
Participant information sheet	v2.5.1	26/06/2020	17/08/2021	No	Yes
Protocol article		12/10/2020	17/08/2021	Yes	No
Results article	Brachytherapy quality assurance	05/11/2020	17/08/2021	Yes	No