PORTEC-4a, een onderzoek naar de waarde van een individueel moleculaire risicoprofiel om de nabehandeling na operatie voor vroeg stadium baarmoederkanker (endometriumcarcinoom) te bepalen.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25791

Source
Nationaal Trial Register

Brief title
PORTEC-4a

Health condition

Endometrial cancer
Uterine cancer
Endometrial carcinoma
Endometriumcarcinoom
Baarmoederkanker

Sponsors and support

Primary sponsor: Leiden University Medical Center (LUMC)
Source(s) of monetary or material Support: Dutch Cancer Society (UL2011-5336)

Intervention

Outcome measures

Primary outcome

vaginal recurrence

Secondary outcome

recurrence-free survival

pelvic and distant recurrence

patient-reported quality of life

adverse events

health care costs

Study description

Background summary

Current standard postoperative treatment for women with early stage, high-intermediat risk endometrial cancer is vaginal brachytherapy, which provides excellent local control with minimal side effects. However, as there is no difference in survival, as 7-8 women have to be treated to prevent 1 vaginal recurrence, and as patients with local recurrence can be effectively salvaged, the question is if this is overtreatment and more effective prediction of the risk of relapse can save many women vaginal brachytherapy and reduce health care costs.

In recent years, the genomic characterisation of endometrial cancer as published by The Cancer Genome Atlas and subsequent independent studies of molecular risk factors such as POLE, L1CAM, MSI, p53 have provided insight into the mutations underlying endometrial cancer development and progression, and have shown strong prognostic impact. In the translational research of PORTEC1- and 2 trials (900 pts) an integrated molecular risk profile has been determined which subclassifies patients with early stage, high-intermiadate risk endometrial cancer as favorable, intermediate or unfavorable, with significantly better prognostic power than the clinicopathologic risk assessment. In the PORTEC-4a trial, this integrated molecular risk profile will be used to evaluate the patient's individual risk and determine adjuvant treatment (favorable: observation; intermediate: vaginal brachytherapy; unfavorable: extermal beam radiotherapy) and compared to standard indication for vagial

brachytherapy for all patiente with early stage, high-intermediate risk features.

Objectives and design:

Patient with early stage, high-intermediate risk endometrial carcinoma 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).

The first cohort of 50 patients were included in a pilot phase of the study, which tested the acceptability and logistics of this multicentre study. Results were positive, and the trial has continued and will include 550 evaluable patients, with international participating groups.

Study objective

Molecular risk profile-based recommendations for adjuvant treatment will, in comparison to standard vaginal brachytherapy, lead to similar vaginal recurrence and recurrence-free survival in patients with high-intermediate risk endometrial carcinoma,while sparing about 50% of women postoperative vaginal brachytherapy and saving health care costs

Study design

5-year rates of vaginal control, survival, adverse events, quality of life, health care costs

Evaluation of outcomes and quality of life at 6 month intervals
Long-term outcomes at 7 years after randomisation

Publications:

Wortman BG, et al: Molecular-integrated risk profile to determine adjuvant radiotherapy in endometrial cancer: Evaluation of the pilot phase of the PORTEC-4a trial.Gynecol Oncol. 2018 Oct;151(1):69-75. doi: 10.1016/j.ygyno.2018.07.020. Epub 2018 Aug 3

Van den Heerik ASVM et al: PORTEC-4a: international randomized trial of molecular profile-based adjuvant treatment for women with high-intermediate risk endometrial cancer. Int J Gynecol Cancer. 2020 Dec;30(12):2002-2007. doi: 10.1136/ijgc-2020-001929. Epub 2020 Oct 12. PMID: 33046573

Wortman BG, et al: Brachytherapy quality assurance in the PORTEC-4a trial for molecular-integrated risk profile guided adjuvant treatment of endometrial cancer. Radiother Oncol. 2021 Feb;155:160-166. doi: 10.1016/j.radonc.2020.10.038. Epub 2020 Nov 5

Intervention

Arm 1 (standard): vaginal brachytherapy

Arm 2 (molecular profile based recommendations for adjuvant treatment): observation,

vaginal brachytherapy or external beam radiotherapy

Contacts

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Eligibility criteria

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

Exclusion criteria

Any other stage and type of endometrial carcinoma

Histological types papillary serous carcinoma or clear cell carcinoma (at least 10% if mixed type), or undifferentiated or neuroendocrine carcinoma

Uterine sarcoma (including carcinosarcoma)

Previous malignancy (except for non-melanomatous skin cancer) < 5 yrs

Previous pelvic radiotherapy

Interval between the operation and start of radiotherapy exceeding 8 weeks

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2016
Enrollment:	550
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
After publication of final results with long-term FU, IPD will be provided after submission and approval of a research request and plan.

Ethics review

Positive opinion

Date:	01-06-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL5602
NTR-old	NTR5841
Other	METC Leiden-Den Haag-Delft : METC P16.054; CCMO NL56828.058.16

Study results

Summary results
Molecular profile data based on combined PORTEC-1 and PORTEC-2 trial cohort:
Stelloo et al, Clinical Cancer Research 2016
PORTEC-2 trial results: Nout et al, Lancet 2010.