

PORTEC-2: Postoperative Radiation Therapy for Endometrial Carcinoma - a multicenter randomised phase III trial comparing external beam radiation and vaginal brachytherapy.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25442

Source

Nationaal Trial Register

Brief title

PORTEC-2

Health condition

Endometrial carcinoma; indication for postoperative radiation therapy.

Sponsors and support

Primary sponsor: Leiden University Medical Center,
Department of Clinical Oncology

Source(s) of monetary or material Support: Dutch Cancer Society (KWF
Kankerbestrijding): CKTO 2001-04

Intervention

Outcome measures

Primary outcome

5-year actuarial vaginal relapse.

Secondary outcome

1. 5-year overall survival and cancer-specific survival;
2. quality of life and treatment related morbidity;
3. 5-year rates of pelvic and distant relapse;
4. Local control and survival after relapse.

Study description

Background summary

Background and aim of the study:

The PORTEC-1 trial has demonstrated that postoperative external beam radiotherapy for stage 1 endometrial cancer significantly increases local control (from 85 to 96%), but has no impact on survival. Salvage therapy for isolated vaginal recurrence, the main site of recurrence in the control group, was effective with a complete remission rate of 89% and actuarial 5-year survival of 65% in the control group. The use of postoperative RT should therefore be limited to the group of patients at sufficiently high risk of locoregional recurrence (15% or over) to warrant the risk of treatment associated morbidity in order to maximize initial local control and relapse-free survival.

It was concluded that RT should be limited to those subgroups of stage 1 endometrial cancer with at least 2 of the following 3 major risk factors: grade 3, age 60 and over, outer 50% myometrial invasion.

For these subgroups (2 of the 3 risk factors) combined, the rate of locoregional relapse in the control arm of the PORTEC trial was 19%. Omitting RT in these subgroups would leave these patients at a significant risk of vaginal and pelvic relapse.

Recent studies have reported that vaginal brachytherapy provides high vaginal control rates (95% and over), comparable to external beam pelvic radiotherapy, with very low morbidity rates. These studies included, however, mainly low-risk patients.

The PORTEC -2 trial was designed to investigate whether vaginal brachytherapy may be used in intermediate-risk endometrial carcinoma patients to obtain equally high vaginal control and 5-year survival rates with less side effects and better quality of life.

Population, study design, intervention:

Patients with endometrial carcinoma stages IB-2A will after surgery be randomized to receive postoperative external beam pelvic radiotherapy (46 Gy in 2 Gy fractions in 5 weeks; standard arm) or vaginal brachytherapy (HDR 21 Gy in 3 fractions of 7 Gy, each 1 week apart; or MDR 28 Gy or LDR 30 Gy in one session; study arm). Patients are stratified by FIGO stage (IB, IC or 2A), RT center, brachytherapy dose rate (LDR or HDR), and patient age (below 60 or 60 and over) using a minimisation procedure.

Endpoints and statistics:

The primary study endpoint is 5-year actuarial vaginal relapse. Secondary endpoints are 5-year overall survival and cancer-specific survival; quality of life and treatment related morbidity; 5-year rates of pelvic and distant relapse; and local control and survival after relapse.

To estimate the difference in vaginal relapse rate (competing risk) with sufficient precision (based on a rate of vaginal relapse of 2% in the ERT group) 200 patients will be recruited in each treatment arm.

The study has sufficient power (>80%) for detecting a difference of 6% (8% vs 2%) or more in vaginal relapse between the study arms.

The repeated measures of the QLQ-C30 functional and symptom scales and of the global health index will be analysed to evaluate the differences between the treatment groups with respect to quality of life during treatment and up to 5 years thereafter.

Side studies:

Tumour samples will be collected and saved in a dedicated tissue bank for immunohistochemical studies and/or molecular genetic studies studies of new prognostic factors and factors predicting response to radiotherapy.

Study objective

Vaginal brachytherapy, as compared to external beam pelvic radiotherapy, will provide equal 5-year vaginal control and overall survival, with less treatment related morbidity and better quality of life.

Study design

N/A

Intervention

Patients are randomized to receive external beam pelvic radiotherapy (standard arm: 46 Gy in 2 Gy fractions in 5 weeks) or vaginal brachytherapy (study arm: HDR 21 Gy in 3 fractions of 7 Gy, each 1 week apart; or MDR 28 Gy in one session; or LDR 30 Gy in one session).

Contacts

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Eligibility criteria

Inclusion criteria

1. Endometrial carcinoma, with one of the following combinations of postoperative FIGO stage and age:
 - a. Stage 1C grade 1 or 2 and age 60 or over;
 - b. Stage 1B grade 3 and age 60 or over;
 - c. Stage 2A, any age, grade 1 or 2;

- d. Stage 2A, any age, grade 3 with $< \frac{1}{2}$ myometrial invasion;
- 2. Surgery consisted of a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO);
- 3. Histologically proven adenocarcinoma; grade of differentiation determined according to the FIGO/AFIP criteria; depth of myometrial invasion documented;
- 4. WHO-performance status 0-2;
- 5. Written informed consent.

Exclusion criteria

- 1. One of the following combinations of FIGO stage and age:
 - a. Stage 2B, 3 or 4;
 - b. Stage 2A and grade 3 with 50% or greater myometrial invasion;
 - c. Stage 1A or 1B grade 1 or 2;
 - d. Stage 1B grade 3 and age below 60;
 - e. Stage 1C grade 1 or 2 and age below 60;
 - f. Stage 1C grade 3, any age;
- 2. Histological subtypes papillary serous carcinoma or clear cell carcinoma;
- 3. Routine staging lymphadenectomy;
- 4. Interval between the operation and start of radiotherapy exceeding 8 weeks;
- 5. History of any previous malignancy, except for basal cell carcinoma of the skin;
- 6. Previous pelvic radiotherapy;
- 7. Hormonal therapy or chemotherapy for this tumour;
- 8. Prior diagnosis of Crohn's disease or ulcerative colitis.

Study design

Design

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

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2002
Enrollment:	400
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Plan description

IPD will be shared after a scientific request and approval by the study group (e.g., for meta-analysis)

Ethics review

Positive opinion	
Date:	09-09-2005
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	NL294
NTR-old	NTR332
Other	METC Leiden-Den Haag-Delft : METC LUMC P01.146
ISRCTN	ISRCTN16228756

Study results

Summary results

Wortman BG, Creutzberg CL, Putter H, et al:

Ten-year results of the PORTEC-2 trial for high-intermediate risk endometrial carcinoma: improving patient selection for adjuvant therapy.

Br J Cancer. 2018 Oct;119(9):1067-1074. doi: 10.1038/s41416-018-0310-8. Epub 2018 Oct 25.

Nout RA, Putter H, Jurgenliemk-Schulz IM, et al:

Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data.

Eur J Cancer.2012 Jul;48(11):1638-48. doi: 10.1016/j.ejca.2011.11.014. Epub 2011 Dec 14

Nout RA, Smit VTHB, Putter H, et al:

Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial carcinoma of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial.

Lancet 375:816-823, 2010.

Nout RA, Putter H, Jurgenliemk-Schulz IM, et al:

Quality of life after pelvic radiotherapy or vaginal brachytherapy for endometrial cancer: first results of the randomized PORTEC-2 trial.

J Clin Oncol 27:3547-3556, 2009.