A phase III Trial of postoperative chemotherapy or no further treatment for patients with node-negative stage I-II intermediate or high risk endometrial cancer.

ENGOT-EN2-DGCG / EORTC-55102

Version 2.1

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Supported by

Danish Cancer Society

5-year survival - FIGO

Stage I	G1	G2	G3
Ia	93	91	80
Ib	92	93	82
Ic	91	86	75
Stage II			
IIa	90	84	68
IIb	81	77	65

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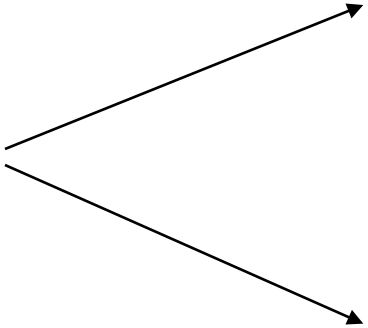
Creasman et al., IJGO, 2007

Design: 1:1 randomization

n=678

Endometrioid:
Stage I (Grade 3)
Stage II

Non-endometrioid:
Stage I-II



Chemotherapy

Carboplatin AUC5 IV q21d
Paclitaxel 175mg/m2 IV q21d
6 courses

+ Brachytherapy

Observation

+ Brachytherapy

Adjuvant vaginal brachytherapy is permitted in both arms.
In chemotherapy arm, timing of VBT should not cause delay in chemotherapy schedule.

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Stratifications

1: endometrioid versus non-endometrioid

2: stage 1a vs. 1b vs. 2 disease

3: para-aortic (≥10)and pelvic (≥20) LNE versus lesser LNE

4: Brachytherapy planned yes/no

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Inclusion Criteria
Prior Therapy

- Hysterectomy (total abdominal hysterectomy, radical hysterectomy, laparoscopic or robotic hysterectomy)

- Bilateral salpingo-oopherectomy (BSO)

- pelvic lymphadenectomy (LNE): minimum 12 pelvic nodes (minimum 6 from each side) should be removed. Para-aortic LNE is optional

- Omentectomy recommended in clear cell, serous or undifferentiated carcinoma

- Surgery performed within 10 weeks of randomization. If the dates for hysterectomy and lymph node dissection are different, 10 weeks are counted from the last surgery, and in that case the gap between two surgeries should not exceed 8 weeks.

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Treatment
Vaginal Brachytherapy

The investigator shall decide prior to informed consent and randomization, if VBT is planned for the patient.

In chemotherapy arm, timing of VBT should not cause delay in chemotherapy delivery.

Dose recommendation:

A dose equal to 7Gy weekly x 3 times (total dose 21 Gy) at 5 mm (upper vagina) to 0 mm (mid vagina) from the applicator at the upper half of vagina (HDR/PDR).

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Study End Points

Primary Endpoint

- Overall Survival

Secondary Endpoints

- Disease Specific Survival (DSS)
- Progression-Free Survival (PFS)
- Toxicity
- PRO: (QOL) EORTC QLQ-C30 and EORTC-QLQ-EN24
- Rate of isolated pelvic relapse (central and/or pelvic wall)
- Rate of isolated distant relapse
- Rate of mix local and distant relapse

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Statistical plan

To detect an overall absolute difference in five-year survival of 10%, from 72% to 82%, at the 2.5% level with 80% power, 135 deaths corresponding to 644 patients are needed.

In the **endometrioid subgroup** an absolute difference in five-year survival of 12%, from 74% to 86% is expected. Assuming this, 79 deaths corresponding to **438 patients** are needed to yield 80% power at the 2.5% level.

Assuming a dropout rate of 5%, **678 patients** have to be accrued, leaving 644 patients for the overall analysis and 75% of these, or 483 patients, for the analysis in the endometrioid subgroup.

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Initiation status

Group	Activation initiated	Total number of sites	Sites activated till date	Patients enrolled
DGCG (Denmark)	Dec 2011	6	6	15
NSGO (Sweden; Finland)	Dec 2012	10	5	5
EORTC (Belgium, Germany, Austria, Italy, Spain Portugal, UK, Nederlands)	May 2013	20-24	4	0
BGOG (Belgium)	April 2013	14	4	0
Total		**50-54**	**19**	**20**

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