

CERVANTES (CERVical cancer AdjuvaNt Treatment Study)

An international randomized trial of radical surgery followed by adjuvant therapy versus no further treatment in patients with early-stage, intermediate-risk cervical cancer

ENGOT-cx16/CEEGOG/CERVANTES; CEEGOG CX-05

ENGOT model: A

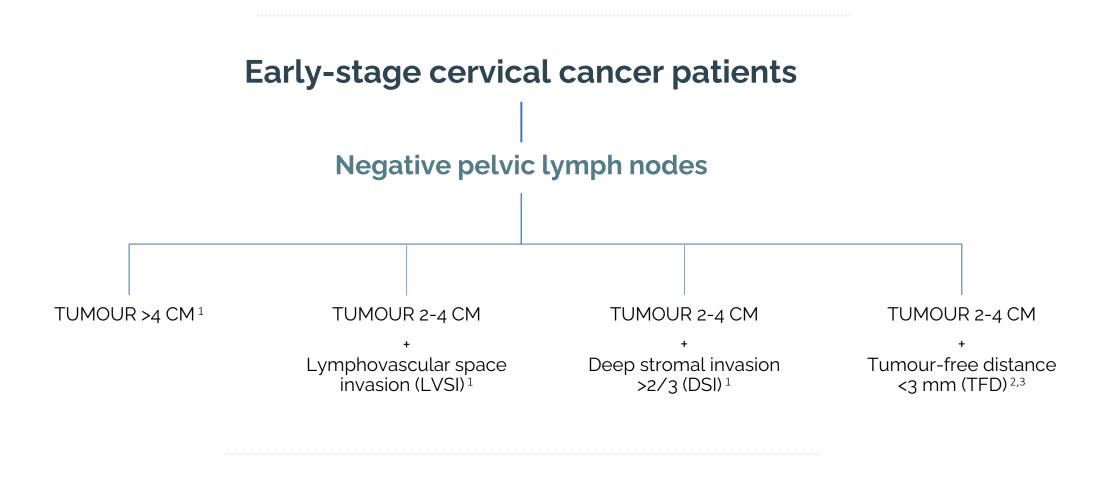
Sponsor: CEEGOG

Planned no. of patients: 514

Status: initiated/recruiting

Trial chair: David Cibula

Intermediate-risk (IR) group



Rationale

- Management of intermediate risk (IR) cervical cancer patients is not harmonized and both types of treatment are currently used as a standard of care:
 - i. Radical surgery alone
 - ii. Radical surgery followed by adjuvant (chemo)radiation
- Criteria for definition of IR group vary (variations of GOG criteria).¹
- Besides excellent outcome of radical surgical treatment,² the increasing proportion of patients with early-stage disease:
 - i. has been referred to primary chemoradiation, OR
 - ii. has been receiving combination treatment associated with higher treatment morbidity.
- Available evidence for combination treatment benefit is based on a single prospective randomize study which was conducted more than 20 years ago.¹
- Recently, number of retrospective studies showed in IR group an excellent local control after radical surgery
 without adjuvant treatment.^{3,4}
- More precise pre-operative clinical staging, improved standards of pathologic assessment, and SLN pathological
 ultrastaging currently contribute to the exclusion of cases with high-risk features and much better selection of IR
 group than at the time of GOG trial.

¹Sedlis et al. 1999. doi: 10.1006/gyno.1999.5387; ²Ramirez PT et al. 2018. doi: 10.1056/NEJMoa1806395; ³Cibula et al. 2018. doi:10.1016/j.ygyno.2018.10.018; ⁴van der Velden 2019. doi: 10.1136/jjgc-2019-000445

Main objective

- The purpose of the trial is to evaluate if adjuvant treatment is associated with disease free survival benefit after radical surgery in patients with intermediate-risk cervical cancer.
- The key secondary objective is to compare the overall survival benefit between trial arms.

Primary endpoint

Disease-free survival (DFS)

Calculated as an interval from the day of randomization until diagnosis of recurrence.

Key secondary endpoint

Overall survival (OS)

Other secondary endpoints

- Pelvic disease-free survival
- Health-related quality of life (HR-QoL)
- Treatment-related adverse events



Trial design



Patient enrolment after surgery

Once all the inclusion criteria are confirmed from the pathological assessment

Minimum standard for adjuvant therapy

Mandatory minimal and the internationally recognized standard for adjuvant therapy was set to

pelvic external beam radiotherapy (EBRT)

Adjuvant therapy could be modified according to the institutional or regulatory guidelines only if the minimal requirement is fulfilled consistently on the protocol.

Preceding trial treatment AC: adenocarcinoma; CCR: complete cytogenetic response; CTQAC: Quality assurance committee; DSI: deep stromal invasion; ECOG: Eastern Cooperative Oncology Group; EUS: expert ultrasound; IR: intermediate-risk; LN: lymph node; LVSI: lymphovascular space invasion; MO: no distant metastasis; M1: Cancer has spread to other parts of the body; MAC: macrometastasis; MIC: micrometastasis; MIS: minimally invasive surgery; MRI: magnetic resonance imaging; NO: no lymph node involvement; N1: lymph node involvement, NACT: neoadjuvant chemotherapy; PLND: pelvic lymphadenectomy; R1: Positive surgical margins; RH: radical hysterectomy; SC: CLINICAL STAGING BY IMAGING Squamous cell cancer; (S)LN: (sentinel) lymph node; TFD: tumour free distance. MRI or expert ultrasound examination **EXCLUDED** INCLUSION CRITERIA (BASED ON FINAL PATHOLOGY) SURGERY – RECOMMENDED 1. FIGO <IB2 / >IIA **STANDARDS** 2. Other histological types, unusual type FIGO IB2-IIA; pN0; SC or HPV-related AC; M0 in (laparotomy, MIS acceptable only for LN AC (HPV unrelated) combination with staging) 3. N1 (ITC, MAC or MIC) 1. tumour ≥4 cm OR 4. M1 RH (C1 in 2-4 cm; C2 in ≥4 cm or 2-4 2. tumour > 2 cm < 4 cm and LVSI OR 5. R1: either parametrial or vaginal cuff cm + TFD <3 mm) tumour >2 cm <4 cm and TFD <3 mm OR margins positive SLN biopsy ± systematic PLND[£] tumour >2 cm <4 cm and DSI >2/3 6. Adequate type of surgery not performed (type of RH; adequate LN staging) SLN detected bilaterally Previous pelvic malignancy **REGISTRATION AND** Previous pelvic radiotherapy RANDOMISATION History of second primary cancer Arm A Arm B outside pelvis if ≤ 3 years CCR Adjuvant therapy No adjuvant 10. Immunosuppressive medication if (EBRT) treatment cannot be terminated for the trial duration 11. NACT prior to surgical treatment INITIAL VISIT 12. Low likelihood of patient's compliance Post-surgery visit: 4-6 weeks after surgery (both ARMs) to the follow-up 13. Lactating patients not willing to stop POST-THERAPY VISIT before the trial treatment. Post-adjuvant therapy visit: 4 weeks after the end of 14. Not suitable for adjuvant external beam adjuvant treatment (ARM B only) radiotherapy 15. HIV positive **FOLLOW UP VISITS** 1st follow-up visit: 6 months after randomisation. Frequency of further follow-up visits:

1st – 3rd year: every 6 months

every 12 months

≥4th year:

Contact information

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Further groups/sites welcome to join the trial



