



FERTility Sparing Surgery in cervical cancer patients outside controlled trials (FERTISS)

Retrospective cohort study

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- STUDY DESIGN:** International, Multicentric, Retrospective Cohort

TABLE OF CONTENTS

RATIONALE	2
AIM OF THE TRIAL.....	3
INCLUSION CRITERIA	3
EXCLUSION CRITERIA	3
END-POINTS.....	4
ETHICAL COMMITTEE APPROVAL.....	4
MINIMUM REQUIREMENTS FOR CENTER PARTICIPATION	4
DATA HANDLING.....	5
MONITORING.....	5
FUNDING	5
PUBLICATION RULES.....	5
1. General	5
2. Additional publications of sub-projects or subgroup/institutional data.....	6
ABBREVIATIONS.....	6
REFERENCES.....	7

RATIONALE

- Generally accepted fertility-sparing treatment (FST) in patients with small cervical cancers includes vaginal radical trachelectomy and abdominal radical trachelectomy, combined with pelvic lymph node dissection.
- Recent development is toward less-radical procedures, including simple trachelectomy, conization, and sentinel lymph node biopsy.
- Although oncological outcomes are reported to be equal to or better than non-fertility sparing management, published groups are small, mostly from one institution; inclusion criteria vary; and treatment is not uniform.
- Pregnancy rates differ substantially, reflecting many aspects such as pre-treatment fertility potential assessment, radicality of the treatment, length and completeness of follow-up, and differences in fertility desire between the groups.

- Low risk of parametrial involvement is one of the key arguments for abandoning parametrectomy in small tumors, but standard pathology processing is not sufficient to detect small metastasis in parametrial lymph nodes. Oncological risk of less-radical FST according to the presence of prognostic risk factors (tumor size, LVSI) and particular management is unknown.
- Recently, a few publications showed a higher recurrence rate after FST than anticipated in the same cohort of patients after standard non-FST management.

AIM OF THE TRIAL

The aim of this study is to collect retrospective data on FST, subsequent follow-up, and pregnancies in patients with cervical cancer treated outside of clinical studies as the majority of published data comes from carefully selected single-institutional cohorts that may not reflect the situation in current clinical practice.

INCLUSION CRITERIA

- Age 18–40
- Any stage \geq IA1+LVSI
- Any grade
- Any histotype
- Any FST management: conization (any technique), vaginal trachelectomy, vaginal radical trachelectomy, abdominal trachelectomy, abdominal radical trachelectomy
- Any lymph-node staging
 - SLN and/or pelvic lymphadenectomy/paraaortic lymphadenectomy
- Neoadjuvant chemotherapy acceptable
- Follow-up of at least 6 months available

EXCLUSION CRITERIA

- Second-step hysterectomy as a part of primary treatment

END-POINTS

Primary end-points:

- Disease-free interval (DFS)
- Pregnancy rate

Secondary end-points:

- Pelvic DFS
- Pre-cancer recurrence rate
- Attempt-to-conceive rate
- Delivery rate (term/pre-term)
- Outcome according to stratification criteria (histology, stage, type of procedure, use of neoadjuvant chemotherapy)
- Diagnostic value of various methods used during follow-up

ETHICAL COMMITTEE APPROVAL

Participating institutions are responsible for receiving approval from the institutional ethical committee. Patient consent is not required. The study will be performed in accordance with the terms of the protocol and the generally accepted standards of Good Clinical Practice. Moreover, investigators will adhere to all applicable laws and regulations governing the conduct of clinical trials, including but not limited to the ICH Harmonized Tripartite Guidelines for Good Clinical Practice and the Declaration of Helsinki. The Investigator shall treat all information and data relating to the study as confidential and shall not disclose such information to any third parties or use such information for any purpose other than the performance of the study.

MINIMUM REQUIREMENTS FOR CENTER PARTICIPATION

- ≥ 1 case meeting the inclusion criteria
- Local ethical committee approval

DATA HANDLING

The trial will use a web-based electronic data capture FERTISS Information System (FIS) for all data collection (<https://trial4you.eu/fertiss-study/#/users>). Users will be able to access the FIS through major web browsers without additional software installation. Access to FIS will be restricted to authorized users only and communication between the server and users will be secured by an encrypted protocol HTTPS. Only non-identifiable data will be collected and a local identifier will be provided by the system for all patients. Each center will obtain a unique username and password for FIS after the submission of agreement to join the FERTISS Trial (ceegog@ceegog.eu).

MONITORING

Monitoring will be provided by the Trial office, which is responsible for checking the accuracy, completeness, and plausibility of all data and its compliance with the protocol and GCP requirements.

FUNDING

The FERTISS trial is a non-commercial retrospective trial that does not receive any support from the industry. **Participating institutions will not receive any financial compensation for participation in the study.** All expenses related to the trial (administrative center, statistics, electronic data capture system, monitoring) will be covered by research grants.

PUBLICATION RULES

1. General

- a) All calculations regarding the number and position of co-authors will be based on the numbers of patients recruited by institutions/groups, with positions guaranteed by the institution/group leading the specific project.
- b) Each institution/group is independent and free to fill in individual names according to its number and position of co-authorships.

Number of co-authors per group

- a) An institution/group receives a co-authorship position if it has recruited/submitted at least 5% of the total number of patients/cases. Every additional 5% = 1 additional co-author.
- b) Institutions that recruit <5% of patients can be co-authors of secondary publications.

2. Additional publications of sub-projects or subgroup/institutional data

- a) Each participating institution/group can receive a dataset of patients recruited by the respective study institution/group after the final analysis.
- b) Separate analyses by one participating institution/group on their included patients should not include primary or secondary end points, and the leading institution (Trial Chair) must be informed about any such project.
- c) All sub-publications or meta-analyses can only be published after the main manuscript of the study has been published.
- d) Any additional subgroup analysis of the whole population (usage of other institutions' data) done by a participating institution/group should be prospectively discussed among the whole group and agreed upon.
- e) Co-authors' number and position in sub-publications follows the same rules as for main publication.

ABBREVIATIONS

CEEGOG – Central and Eastern European Gynecologic Oncology Group

DFS – Disease-free interval

FERTISS – FERTility Sparing Surgery in cervical cancer patients outside controlled trials

FIS – FERTISS Information System

FST – Fertility-sparing treatment

HTTPS – Hypertext Transfer Protocol Secure

LVSI – lymphovascular space invasion

SLN – Sentinel lymph node

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