STATISTICAL ANALYSIS PLAN

A RANDOMIZED PHASE III TRIAL COMPARING RADICAL HYSTERECTOMY AND PELVIC NODE DISSECTION VS SIMPLE HYSTERECTOMY AND PELVIC NODE DISSECTION IN PATIENTS WITH LOW-RISK EARLY-STAGE CERVICAL CANCER

CCTG Protocol Number: CX.5

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ABBREVIATIONS

AE	Adverse Event
AGO	Arbeitsgemeinschaft Gynakologische Onkologie
BGOG	Belgium and Luxembourg Gynaecological Oncology Group
BMI	Body Mass Index
C. I.	Confidence Interval
CRF	Case Report Form
CTCAE	Common Toxicity Criteria for Adverse Events
CCTG	Canadian Cancer Trials Group
DGOG	Dutch Gynaecological Oncology Group
DSMC	Data and Safety Monitoring Committee
ECOG	Eastern Cooperative Cancer Group
EPRFS	Extra-pelvic Relapse Free Survival
EORTC	European Organization for Research and Treatment of Cancer
FIGO	International Federation of Gynecology and Obstetrics
FSDS-R	Female Sexual Distress Scale
FSFI	Female Sexual Function Index
GINECO	Group of National Investigators for Ovarian and Breast Cancer Studies
ICORG	Cancer Research Ireland
KGOG	Korean Cooperative Cancer Group
LEEP	Loop Electrosurgical Excision Procedure
LKA	Last day the patient is Known Alive
MPV	Major Protocol Violation
NCRI	National Cancer Research Institute
OS	Overall Survival
PRFS	Pelvic Relapse Free Survival
PRO	Patient Reported Outcomes
QLQ	Quality of Life Questionnaire
QoL	Quality of Life
RFS	Relapse Free Survival
SAS	Statistical Analysis System
SN	Sentinel Node
STD	Standard Deviation

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1. Introduction

This analysis plan is to describe the final analysis performed by the Canadian Cancer Trials Group (CCTG) for the CX.5 trial. It will be used for the writing of the CCTG study report.

2. Study Description

2.1 Study Design

CX.5 is a multi-centre, international, prospective, randomized phase III trial of radical hysterectomy and pelvic node dissection versus simple hysterectomy and pelvic node dissection in patients with previously untreated, low-risk cervical cancer. The study is being conducted by the Canadian Cancer Trials Group.

This study opened to accrue patients on August 3, 2012 and the accrual to the study was closed on November 29, 2019 after required 750 patients were randomized.

The original statistical plan estimated that 49 pelvic relapses would have to be observed at the time of final analysis to demonstrate non-inferiority of a simple hysterectomy compared to a radical hysterectomy with pelvic relapse free survival being the primary end point. An interim analysis was planned at 25 events, which was predicted to be observed approximately at the end of accrual based on the assumptions in the original protocol. But only 14 pelvic recurrences were observed after 2 years of accrual completion. With the approval by the CCTG Data and Safety Monitoring Committee (DSMC), the protocol was amended in June of 2022 which changed the primary endpoint from pelvic relapse free survival to the pelvic recurrence rate at 3 years, since it is a timepoint of clinical interest and was used to derive the non-inferior limit for the hazard ratio of pelvic relapse free survival and sample size. The timing of final analysis was also changed to the time when the last recruited patients have been followed for three years. The planned interim analysis was also cancelled.

Since the last patient was enrolled on November 29, 2019, it was decided that November 29, 2022 will be the date of clinical data cut-off and the final analysis will be performed on a database which will be locked after all data observed before this clinical data cut-off date are received and cleaned. This analysis plan describes the analyses performed on this database.

The CCTG DSMC has been reviewing safety data annually and as otherwise required. These analyses have been prepared by a CCTG/Queen's Senior Biostatistician.

2.2 Treatment Allocation

A total of 700 patients would be enrolled. Eligible patients would be randomized in a 1:1 ratio to receive simple hysterectomy and pelvic node dissection or radical hysterectomy and pelvic node using the minimization method after stratified by cooperative group, intended use of SN mapping (yes vs. no), stage (IA2 vs. IB1), histological type (squamous vs. adenocarcinoma/adenosquamous), and tumour grade (1-2 vs. 3 vs. not assessable). A centralized system was used to randomize all patients in this study.

3. Objectives

3.1 Primary

The primary objective of this study is to evaluate whether treatment with simple hysterectomy and pelvic node dissection is non-inferior to treatment with radical hysterectomy and pelvic node dissection in terms of pelvic recurrence rate at 3 years.

3.2 Secondary

Secondary objectives are to compare the following endpoints between two treatment arms:

- Pelvic relapse free survival (PRFS)
- Extra-pelvic relapse free survival (EPRFS)
- Relapse free survival (RFS)
- Overall survival (OS)
- Rate of sentinel node detection
- Rate of parametrial involvement
- Rate of surgical margin involvement
- Rate of pelvic nodes involvement
- Treatment-related adverse events
- Patient report outcomes including quality of life and measures of sexual health
- Cost-effectiveness and cost-utility

Note: The analysis plan to address the last objective, i.e., evaluation of cost-effectiveness and cost-utility will be developed at a later date.

4. Endpoints

4.1 Primary Efficacy

The primary efficacy endpoint is pelvic recurrence rate at 3 years.

4.2 Secondary Efficacy

The secondary efficacy endpoints are:

- Pelvic relapse free survival (PRFS)
- Extra-pelvic relapse free survival (EPRFS)
- Relapse free survival (RFS)
- Overall survival (OS)
- Rate of sentinel node detection
- Rate of parametrial involvement
- Rate of surgical margins involvement
- Rate of pelvic nodes involvement
- Patient reported outcomes (using EORTC QLQ-C30 with module QLQ-CX24, FSFI and FSDS-R)

4.3 Safety

The safety endpoints are serious and non-serious adverse events, other safety events during the surgeries and follow-up.

5. Sample Size and Power

It was estimated that 3-year pelvic recurrence rate for the radical hysterectomy is around 4% and the non-inferiority of the simple hysterectomy to radical hysterectomy would be claimed if its 3-year pelvic recurrence rate is 8% or lower. In the original protocol with pelvic relapse free survival (PRFS) as the primary endpoint, this is equivalent to claim the non-inferiority of the simple hysterectomy to radical hysterectomy when a hazard ratio in PRFS of simple hysterectomy to radical hysterectomy is less than or equal to 2.04. In order to conclude the non-inferiority at 0.05 level with 80% power when PRFS is the same in the two arms, a total of 49 pelvic relapses would be required before the final analysis is performed. Assuming that enrollment rate is 200 patients/year and all patients would be followed for additional 3.5 years after the last patient randomized, enrollment of 700 patients in 3.5 years was required to observe the required number of pelvic relapses at the time of final analysis.

With 350 patients enrolled in each arm, the study would have 85% power to conclude the non-inferiority based on a margin of 4% in the revised primary endpoint, i.e., 3-year pelvic recurrence rate, at α=0.05 when the pelvic recurrence rate at 3 years is assumed the same in the two arms.

6. Data Set Descriptions

Three types of analysis samples will be used:

Intention-to-treat Patients:

All patients who have been randomized in the study with the treatment arm being as randomized.

Per-protocol Patients:

All eligible patients who have received hysterectomy, except those who were found to have more advanced stages of cervical cancer on sentinel node mapping, pelvic node dissection or other intraoperative findings consistent with pelvic disease, with the treatment arm being as actually treated.

All Treated Patients:

All patients who have been have received hysterectomy with the treatment arm being as actually treated.

7. Statistical Analysis

7.1 General Methods

Continuous and ordinal categorical variables are summarized using the mean with standard deviation or median with minimum and maximum values and, when appropriate, compared using the Wilcoxon test. Discrete variables are summarized with the number of proportion of subjects falling into each category and compared using Fisher's exact test when appropriate. Time to event variables are summarized using Kaplan-Meier plots. Primary estimates of the treatment differences are obtained with the hazard ratios and confidence intervals from stratified Cox regression models using treatment arm as the single factor. All confidence intervals are computed based on normal approximations except those for rates, which will be computed based on the exact method.

Percentages given in the summary tables will be rounded and may therefore not always add up to exactly 100%. Listings, tabulations, and statistical analyses will be carried out using the SAS (Statistical Analysis System, SAS Institute, North Carolina, USA) software.

Unless otherwise specified, date of randomization and stratification factors will be taken from the Centralized Randomization File.

Baseline evaluations will be those collected on CRF ELIGIBILITY WORKSHEET and BASELINE REPORT and closest to, but no later than, the first day of study treatment for treated subjects and closest to, but no later than, the date of randomization, for subjects who were randomized but who never received treatment.

Laboratory results, adverse events, and other symptoms are coded and graded using the NCI CTCAE when available.

When converting a number of days to other units, the following conversion factors will be used:

1 year = 365.25 days

1 month = 30.4375 days

When either day or month of a date is missing, the missing day and/or month will be imputed by the midpoint within the smallest known interval. For example, if the day of the month is missing for any date used in a calculation, the 15th of the month will be used to replace the missing day. If the month and day of the year are missing for any date used in a calculation, the first of July of the year will be used to replace the missing date.

7.2 Study Conduct

All intention-to-treat patients are included in the analysis of study conduct. Information will be tabulated by randomized treatment and pooled treatment.

7.2.1 Patient Disposition and Follow-up

- Number of patients randomized, treated with surgery, not treated with surgery, reason for not treated with surgery **(Table 1)**
- Number of alive patients **(Table 2)**
- Median (estimated by Kaplan-Meier method) and range (minimum and maximum) **(Table 2)** of the follow-up time (months) defined as time from the day of randomization (as recorded in centralized randomization file) to the last day the patient is known alive (LKA) as the last recorded date known alive or censored at the time of death and calculated as

  [(date of death or LKA – date of randomization) + 1)]/30.4375.

7.2.2 Accrual Patterns

- Number of patients randomized by cooperative group and center **(Table 3)**
- Number of patients by stratification factors at randomization **(Table 4)**
- Accrual of patients by calendar time pooled across two treatment arms **(Figure 1)**

7.2.3 Eligibility Violations/Protocol Deviations

Eligibility violations of inclusion or exclusion criteria are centrally reviewed by CCTG; a field (y/n) for eligibility status and reason for ineligibility is entered in the database. A major protocol violation (MPV) is defined as a deviation from the protocol, initiated by the center or the investigator, serious enough to mean that the patient's data contributes little, if any, information on the efficacy or toxicity of the regimen under study. MPVs are coded by CCTG based on its standard codes.

- Number of patients eligible, not eligible **(Table 5)**
- Reasons for ineligibility **(Table 5)**
- Major protocol violations: % for each type of violations **(Table 5)**

Deviations from randomization will be summarized as follows:

- Treatment as randomized versus as treated **(**Table 6**)**

7.3 Study Population

All intention-to-treat patients are included in the study population analyses. Information will be tabulated by randomized treatment and pooled treatments.

7.3.1 Patient Pretreatment Characteristics

- Age: median, minimum, maximum values**;** <65, ≥65 **(Table 7)**
- Race: White, Black or African American, Native Hawaiian or other Pacific Islander, Asian, Not reported (or refused), Unknown **(Table 7)**
- Body mass index (BMI): median, minimum, maximum values **(Table 7)**
- ECOG Performance Status: 0, 1, 2, 3, 4 **(Table 7)**

7.3.2 Pre-Treatment Pathological Diagnosis of Tumor

- Months from initial pathological diagnosis of cervical cancer to randomizaton: median, minimum, maximum values **(Table 8)**
- Diagnostic Procedure: LEEP, cone, cervical biopsy **(Table 8)**
- Histological type: squamous, adenocarcinoma, adenosquamous **(Table 8)**
- FIGO stage: IA2, IB1 **(Table 8)**
- Histologic grade: 1, 2, 3, not assessable **(Table 8)**

7.3.3 Tumor Description at Baseline

- Diagnostic Procedure: cervical biopsy, LEEP/cone (**Table 9**)
- Clinic visibility of lesion: yes, no **(Table 9)**
- Tumour thickness: median, min - max **(Table 9)**
- Depth of stromal invasion: median, min - max **(Table 9)**
- Lateral extension: ≤7.0mm, >7.0mm, not stated in report **(Table 9)**
- Presence of lymphovascular invasion: yes, no, not stated in report **(Table 9)**
- Resected margin involvement: yes, no, not stated in the report **(Table 9)**
- Margin(s) involved: exocervical, endocercical, deep, unknown
- Presence of intra-epithelial lesion: yes, no, not stated in report **(Table 9)**

7.3.4 Results of Pelvic Exam and Imaging Tumor at Baseline

- Pelvic exam results: normal, abnormal-not malignant, abnormal-malignant (**Table 10**)
- Maximum dimension for malignant tumor: median, min-max values (**Table 10**)

- Detection of disease in pelvic imaging: yes, no, not applicable **(Table 10)**
- Location of tumour: cervix, lymph node, other **(Table 10)**
- Percentage of stroma involved: <50%, ≥50% **(Table 10)**
- Maximum tumour dimension: ≤20mm, >20mm **(Table 10)**

7.3.5 Baseline Symptoms and Major Medical Problems

- Baseline symptom status **(Table 11)**
- Number of patients with past or current major medical problems ongoing at baseline **(Table 12)**
- Type of major medical problem (**Table 12**)

7.3.6 Tobacco Smoking History

- Ever smoked any tobacco product: yes, no (**Table 13**)
- Current smoker: yes, no **(Table 13)**
- Current average cigarettes per day: median, min-max **(Table 13)**
- Time from quitting smoking to randomization: median, min-max **(Table 13)**
- Smoking history: pipe or cigar smoker only, 100 or fewer cigarettes during lifetime, greater than 100 cigarettes during lifetime (**Table 13)**
- Time from beginning of smoking cigarettes to randomization: median, min-max **(Table 13)**
- Total number of years smoked cigarette: median, min-max **(Table 13)**
- Average number of cigarettes smoked per day: median, min-max (**Table 13)**
- Pack years: median, min-max **(Table 13)**

7.4 Treatment Information

All treated patients as defined in Section 6 will be included in the analysis based on the type of surgery received by the patients.

7.4.1 Hysterectomy Procedure

- Procedure performed: hysterectomy with parametrium, hysterectomy with no parametrium, unilateral/bilateral salpingectomy, unilateral/bilateral oophorectomy, vaginal cuff **(Table 14)**
- Length of vaginal cuff: median, min-max **(Table 14)**
- Type of surgical approach: abdominal, laparoscopic, vaginal, robotic **(Table 14)**
- Total time of hysterectomy: median, minimum and maximum values **(Table 14)**

7.4.2 Prophylactic Medications

- Prophylactic antibiotics used pre-operatively: yes, no **(Table 15)**
- Prophylactic antibiotics used post-operatively: yes, no **(Table 15)**
- Prophylactic anticoagulation used pre-operatively: yes, no **(Table 15)**
- Prophylactic anticoagulation used post-operatively: yes, no **(Table 15)**

7.4.3 Transfusion or Blood Products

- Estimated amount of blood loss during surgery: <500cc, 500-1000cc, >1000cc **(Table 16)**
- Transfusions or blood products during surgery and/or in the 4 weeks following surgery: yes, no **(Table 16)**
- Hemoglobin used pre-operatively: median, min-max **(Table 16)**

- Hemoglobin used post-operatively: median, min-max **(Table 16)**
- Type of transfusion: red cell concentrations, platelets, other **(Table 16)**
- Total number of units of transfusion of red cell concentrations: median, min-max **(Table 16)**
- Total number of units of transfusion of platelets: median, min-max **(Table 16)**
- Total number of units of other transfusions: median, min-max **(Table 16)**

7.4.4 Surgical Complications

- Intraoperative injury: yes, no **(Table 17)**
- Location of intraoperative injury: bladder, ureter, vein, artery, large bowel, small bowel, nerve injury, other **(Table 17)**
- Admission to hospital for the hysterectomy: yes, no **(Table 17)**
- Admission to intensive care for the hysterectomy: yes, no **(Table 17)**
- Days in intensive care for the hysterectomy: median, min-max **(Table 17)**
- Days from admission to hospital for the hysterectomy to discharge: median, min-max **(Table 17)**
- Destination of discharge: home, etc. **(Table 17)**

7.4.5 Results of Tumor Assessment after Hysterectomy

- Cervical cancer detected in hysterectomy specimen: yes, no **(Table 18)**
- Histologic tumour type: squamous, adenocarcinoma, adenosquamous **(Table 18)**
- Histologic grade: 1, 2, 3, not assessable **(Table 18)**
- Depth of stromal invasion: median, min-max **(Table 18)**
- Location of stromal invasion: inner half cervical wall, outer half cervical wall **(Table 18)**
- Horizontal spread/greatest diameter: median, min-max **(Table 18)**
- Lymphovascular invasion: yes, no, undetermined **(Table 18)**
- Resection margins involved: yes, no **(Table 18)**
- Presence of associated intra-epithelial lesion: yes, no **(Table 18)**
- Presence of tumour in the parametrium: yes, no, not applicable **(Table 18)**
- Location of tumour in the parametrium: in continuity with tumour, in lymphovascular space, in parametrial lymph node **(Table 18)**

7.4.6 Sentinel Node Mapping and Lymph Node Dissection

- Success of protocol-defined sentinel node mapping: yes, no, not applicable **(Table 19)**
- Reason for unsuccessful protocol-defined sentinel node mapping: technical reasons, patient refusal, allergy to blue dye, other reason **(Table 19)**
- Technique for sentinel node mapping: laparoscopic, open **(Table 19)**
- Pelvic node dissection done: yes, no **(Table 19)**
- Technique of pelvic node dissection: laparoscopic, open **(Table 19)**
- Para aortic lymph node dissection done: yes, no **(Table 19)**
- Technique of para aortic lymph node dissection: laparoscopic, open **(Table 19)**

7.4.7 Results of Sentinel Lymph Nodes Assessment and Non-Sentinel Lymph Nodes Assessment

For each of the lymph node sites assessed, the following information will be summarized for both sentinel and non-sentinel assessment:

- Number of nodes removed: median, min-max **(Table 20)**
- Number of metastatic nodes detected: median, min-max **(Table 20)**
- Size of largest metastasis: <0.2 mm, 0.2-2.0 mm, >2.0 mm **(Table 20)**
- Presence of extracapsular invasion: yes, no **(Table 20)**

7.4.8 Results of Assessment of Extrauterine Tissue Other Than Lymph Node and Extra-Pelvic Tissue

- Disease in extrauterine tissue other than lymph nodes: yes, no **(Table 21)**
- Location of disease in other extrauterine tissue: fallopian tube, parametrium, ovary, peritoneum, vagina, other **(Table 21)**
- Disease in extra-pelvic tissue: yes, no **(Table 21)**
- Location of disease in extra-pelvic tissue: omentum, abdominal organs, peritoneal disease, lung, other **(Table 21)**

7.4.9 Adjuvant Treatment within 4 Weeks after the Hysterectomy

- Patients planned to receive adjuvant radiation/chemotherapy therapy: yes, no **(Table 22)**
- Reason for the plan of adjuvant radiation/chemotherapy treatment: lesion size>2cm, positive margins in the hysterectomy specimen, etc. **(Table 22)**
- Patient received chemotherapy therapy: yes, no **(Table 22)**
- Drug name and dose for each chemotherapy **(Table 22)**
- Patient received radiotherapy Assessment **(Table 22)**
- Type of radiotherapy: external radiotherapy, boost radiotherapy, brachytherapy **(Table 22)**
- Total number of fractions and total dose for each type of radiotherapy **(Table 22)**

7.4.10 Other Surgeries/Procedures within 4 Weeks after the Hysterectomy

- Patients received other surgeries/procedures within 4 weeks after the hysterectomy: yes, no **(Table 23)**
- Type of the surgery/procedure and reason of surgery/procedure **(Table 23)**

7.5 Efficacy

7.5.1 Pelvic Recurrence Rate at 3 Years

The pelvic recurrence rate at 3 years, the primary endpoint of the study, will be estimated by 1-the Kaplan-Meier estimate for the probability of pelvic relapse free survival (PRFS) at 3 years, where PRFS is defined as the time from randomization (as recorded in Centralized Randomization File) to the time when a recurrence within the pelvic field was first documented (as recorded in Pelvic Recurrence Section in Recurrence Report). Patients found to have more advanced stages of cervical cancer on sentinel node mapping, pelvic node dissection or other intraoperative findings consistent with pelvic disease will be considered to have pelvic disease relapse as of the date of the surgical procedure. Patients who have a relapse outside of the pelvic

field documented or die before the documentation of a pelvic relapse will be censored at the time of first documented extra-pelvic relapse (as recorded in Extra-pelvic Recurrence Section in Recurrence Report) or death (as recorded in Death Report). The pelvic relapse free survival of patients who are alive without any relapse will be censored at the last disease assessment (randomization date, date of surgery in Surgery Report, date of physical exam in Surgery Report, date of last contact in Adjuvant Treatment Report, date of Attendance/Last Contact in Follow-up Report and Short Follow-up Report, date of last patient contact in Lost to Follow Up Report, date of consent withdrawal in Withdrawal of Consent Report, whichever comes the last).

A summary of patients who have pelvic recurrence and sites of the pelvic recurrence will be provided **(Table 24)**.

The pelvic recurrence rate at 3 years will be calculated for each arm as well as the difference in pelvic recurrence rates at 3 years between simple hysterectomy to radical hysterectomy. The upper limit of a one-sided 95% confidence interval for the difference will be calculated based on the Greenwood estimate for the variance of the estimated 3-year PRFS **(Table 25)**. The non-inferiority of simple hysterectomy to radical hysterectomy will be claimed when this upper limit is lower than or equal to 4%.

The primary analysis will be performed on all intention-to-treat patients and a sensitive analysis will additionally be conducted for all per-protocol patients defined in Section 6 based on arms they are treated **(Table 25)**.

7.5.2 Pelvic Recurrence Rate at 3 Years by Subsets

For each level of the following baseline factors baseline factors, the pelvic recurrence rate at 3 years in each of the treatment arms and the difference of 3-year recurrence rate between two arms with one-sided 95% C.I. will be displayed **(Table 25)**.

- Age: ≤65, >65
- Race: White, Asian, Others
- Intended use of SN mapping: yes, no
- Histological stage: IA2, IB1
- Histological type: squamous, adenocarcinoma/adenosquamous
- Tumour grade: 1-2, 3, not assessable

7.5.3 Pelvic Relapse Free Survival (PRFS)

All intention-to-treat patients will be included in the analysis of pelvic relapse-free survival as defined in Section 7.5.1.

A frequency table for the summary of patients with pelvic recurrence, sites of recurrence, censoring and causes of censoring will be provided (**Table 24**). The Kaplan-Meier curve for the PRFS in each treatment arm will be displayed **(Figure 2)**.

The hazard ratio of simple hysterectomy to radical hysterectomy with one-sided 95% confidence interval will be computed based on a Cox regression model with a single treated covariate and stratified by the following factors at randomization **(Table 26)**:

- Intended use of SN mapping: yes, no
- Histological stage: IA2, IB1
- Histological type: squamous, adenocarcinoma/adenosquamous
- Tumour grade: 1-2, 3, not assessable

Non-inferiority of simple hysterectomy to radical hysterectomy in PRFS will be claimed when the upper limit of the one-sided 95% confidence interval for the hazard ratio of simple hysterectomy to radical hysterectomy is lower than or equal to 2.04, which is corresponding to a margin of 4% for the 3-year pelvic recurrence rate between simple hysterectomy and radical hysterectomy when the 3-year pelvic recurrence rate in radical hysterectomy arm was estimated at 4%. For each level of the baseline factors listed in Section 7.5.2, the 3 year PRFS and the hazard ratio (unstratified) of simple hysterectomy over radical hysterectomy with upper limit of the one-sided 95% C.I. will be presented. A "per-protocol" sensitivity analysis will also be performed **(Table 26)**.

7.5.4 Extra-pelvic Relapse Free Survival (EPRFS)

Extra-pelvic relapse free survival (EPRFS) is defined as the date from randomization (as recorded in Centralized Randomization File) to the documented reappearance of disease provided that this recurrence is outside of pelvic (as recorded in Extra-pelvic Recurrence Section in Recurrence Report). Patients found to have more advanced stages of cervical cancer on intraoperative findings consistent with extra-pelvic disease will be considered to have extra-pelvic disease relapse as of the date of the surgical procedure. Patients who relapse in pelvic field will be censored at the time of first documented pelvic relapse (as recorded in Pelvic Recurrence Section in Recurrence Report). Patients who die before any relapse or alive without recurrence will be censored at the date of death (as recorded in Death Report) or last disease assessment date (as defined in Section 7.5.1).

A summary of all intention to treat patients who have extra-pelvic recurrence and sites of recurrences will be displayed (**Table 24**). The Kaplan-Meier plot of EPRFS will be presented in each of the treatment arms **(Figure 3)**.

The Kaplan-Meier estimate for the 3 year EPRFS will be provided for each treatment arm and the difference between the two treatment arms in EPRFS will be tested using a two-sided log-rank test stratified by the stratification factors at randomization as listed in Section 7.5.3. Hazard ratio with two-sided 95% C.I. of simple hysterectomy over radical hysterectomy will also be computed based on the Cox model adjusting for the same stratification factors at randomization. Subset analyses by each level of the baseline factors listed in Section 5.1.2 and sensitivity analysis based on per-protocol patients will also be performed **(Table 27**).

7.5.5 Relapse Free Survival (RFS)

Relapse free survival (RFS) is defined as the date from randomization (as recorded in Centralized Randomization File) to the first time when either a pelvic or extra-pelvic recurrence is documented Patients who die before any recurrence or alive without recurrence will be censored at the date of death (as recorded in Death Report) or last disease assessment date (as defined in Section 7.5.1).

The analysis of RFS will be done using a similar methodology for EPRFS **(Table 24, Figure 4, and Table 28).**

7.5.6 Overall Survival

Overall survival (OS) is defined as the time from randomization (date of complete of Randomization File) until death from any cause (as recorded in Death Report). The

living patients will be censored as the date of last disease assessment (as defined in Section 7.5.1).

The number of patients who died and cause of death will be summarized **(Table 29)** and the Kaplan-Meier curve for the OS in each treatment arm will be displayed **(Figure 5).** The analysis of overall survival will be done using a similar methodology for EPRFS and RFS **(Table 30)**.

7.5.7 Rates of Sentinel Node Detection, Parametrial Involvement, Margins Involvement, and Pelvic Nodes Involvement

Rate of sentinel node detection, parametrial involvement, involvement of surgical margins and pelvic node involvement is defined as the proportion of all intention-to-treat patients with respectively metastatic nodes detected in any of the node sites by sentinel or non- sentinel lymph nodes assessment (from Sentinel Lymph Nodes Assessment and Non-Sentinel Lymph Nodes Assessment sections of Surgery Report), tumour present in the parametrium (from Tumor Description section of Surgery Report), resection margins involved (from Tumor Description section of Surgery Report), metastatic nodes detected in node sites of pelvic NOS left and pelvic NOS right by sentinel or non- sentinel lymph nodes assessment (from Sentinel Lymph Nodes Assessment and Non-Sentinel Lymph Nodes Assessment sections of Surgery Report). Two-sided exact confidence intervals will be calculated and a two-sided Fisher's exact test will be used compare these rates between two treatment groups **(Table 31)**.

7.6 Safety

The safety analyses will be based on the all treated population defined in Section 6. Adverse events are graded and categorized using the NCI CTCAE.

7.6.1 Adverse Events and Serious Adverse Events

Adverse Events (AEs) sections of CRF Surgery REPORT, CRF FOLLOW UP REPORT and CRF SHORT FOLLOW UP REPORT record ongoing or new AEs related (possibly, probably, or definitely) to surgery observed respectively within 4 weeks of surgery, during follow-up but before the first pelvic relapse, and after the first pelvic relapse. AEs reported on CRF SURGERY REPORT are defined as acute AEs and those reported on CRF FOLLOW UP REPORT and CRF SHORT FOLLOW UP REPORT as late AEs. Severe adverse events are those events reported with a CTCAE Grade of 3 or higher.

The following variables are summarized:

- Acute adverse events: worst CTCAE grade per patient **(Table 32)**
- Severe acute adverse events: worst CTCAE grade per patient (**Table 33)**
- Late adverse events: worst CTCAE grade per patient **(Table 34)**
- Severe late adverse events: worst CTCAE grade per patient (**Table 35**)

7.6.2 Other Safety

- Any pelvic exam after 4 weeks of surgical treatment but before the first pelevic recurrence (reported on CRF Follow-up Report): yes, no (**Table 36**)
- Results of pelvic exams after 4 weeks of surgical treatment but before the first pelvic recurrence (reported on CRF Follow-up Report): all normal, at least one abnormal but all non-malignant, all abnormal and malignant (**Table 36**)

- Any pelvic exam after the first pelvic recurrence (reported on CRF Follow-up Report): yes, no (**Table 36**)
- Results of pelvic exams after the first pelvic recurrence (reported on CRF Short Follow-up Report): all normal, at least one abnormal but all non-malignant, all abnormal and malignant (**Table 36**)
- Any other radiologic investigations within 4 weeks of surgical treatment (reported on CRF Surgery Report): yes, no (**Table 37**)
- Results of other radiologic investigations within 4 weeks of surgical treatment by site and method of investigations: all normal, at least one abnormal but all non-malignant, all abnormal and malignant (**Table 37**)
- Any other radiologic investigations after 4 weeks of surgical treatment but before the first pelvic recurrence (reported on CRF Follow-up Report): yes, no (**Table 37**)
- Results of other radiologic investigations after 4 weeks of surgical treatment but before the first pelvic recurrence (reported on CRF Follow-up Report): all normal, at least one abnormal but all non-malignant, all abnormal and malignant (**Table 37**)
- Any other radiologic investigations after the first pelvic recurrence (reported on CRF Follow-up Report): yes, no (**Table 37**)
- Results of other radiologic investigations after the first pelvic recurrence (reported on CRF Short Follow-up Report): all normal, at least one abnormal but all non-malignant, all abnormal and malignant (**Table 37**)
- Any hospitalization after 4 weeks of surgical treatment but before the first pelvic recurrence (reported on CRF Follow-up Report): yes, no **(Table 38)**
- Any hospitalization after the first pelvic recurrence (reported on CRF Follow-up Report): yes, no **(Table 38)**

7.7 Other Anti-Cancer Treatments and Tobacco Smoking History During Follow-up

Patients may receive surgical, systemic or radiation treatments for cervical cancer other than the protocol surgery and adjuvant treatments given 4 weeks within the protocol surgery treatment or smoke tobacco during the follow-up.

- Any surgery/procedure given 4 weeks after the surgery but before the first pelvic recurrence (reported on Follow Up Report) **:** yes, no **(Table 39)**
- Type and reason for surgery/procedure given 4 weeks after the surgery but before the first pelvic recurrence (reported on Follow Up Report) **(Table 39)**
- Any surgery/procedure given after the first pelvic recurrence (reported on Short Follow Up Report)**:** yes, no **(Table 39)**
- Type and reason for surgery/procedure given after the first pelvic recurrence (reported on Short Follow Up Report) **(Table 39)**
- Any other anti-cancer treatment given 4 weeks after the surgery but before the first pelvic recurrence (reported on Follow Up Report)**:** yes, no **(Table 40)**
- Type and treatment name or site for other anti-cancer treatment given 4 weeks after the surgery but before the first pelvic recurrence (reported on Follow Up Report) **(Table 40)**
- Any other anti-cancer treatment given after the first pelvic recurrence (reported on Short Follow Up Report)**:** yes, no **(Table 40)**

- Type and treatment name or site for other anti-cancer treatment given after the first pelvic recurrence (reported on Short Follow Up Report) **(Table 40)**
- Smoked tobacco 4 weeks after the surgery but before the first pelvic recurrence (reported on Follow Up Report)**:** yes, no **(Table 41)**
- Smoked tobacco after the first pelvic recurrence (reported on Short Follow Up Report)**:** yes, no **(Table 41)**

7.8 Patient Reported Outcomes

The patient report outcomes (PROs) of patients in this study include the quality of life assessed by using EORTC QLQ-C30 (version 3.0) with module QLQ-CX24 and sextual health by the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS-R) before randomization (baseline), at 3 months, 6 months, 12 months, 24 months, 36 months after the surgery but before the first pelvic recurrence, and at the time of the first recurrence. The following are the scoring algorithms for EORTC QLQ-C30, EORTC QLQ-CX24, FSFI and FSDS-R with Qi denoting the i-th question in the PRO questionnaire.

7.8.1 Scoring Algorithms

7.8.1.1 EORTC QLQ-C30

The EORTC core questionnaire, QLQ-C30 (version 3.0), consists of five Functional Scales, one Global Health Status, and nine Symptoms Scales. Each scale in the questionnaire will be scored (0 to 100) according to the EORTC recommendations in the EORTC QLQ-C30 Scoring Manual. The scoring method for EORTC QLQ-C30 is summarized below.

Functional scales:

- Physical functioning: (1 - ((Q1+Q2+Q3+Q4+Q5)/5 -1)/3) * 100
- Role functioning: (1 - ((Q6+Q7)/2-1)/3) * 100
- Emotional functioning: (1 - ((Q21+Q22+Q23+Q24)/4-1)/3) * 100
- Cognitive functioning: (1 - ((Q20+Q25)/2-1)/3) * 100
- Social functioning: (1 - ((Q26+Q27)/2-1)/3) * 100

Global health status:

- Global health status: ((Q29+Q30)/2-1)/6 * 100

Symptom scales:

- Fatigue ((Q10+Q12+Q18)/3-1)/3 * 100
- Nausea and vomiting ((Q14+Q15)/2-1)/3 * 100
- Pain ((Q9+Q19)/2-1)/3 * 100
- Dyspnea ((Q8-1)/3 * 100
- Insomnia (Q11-1)/3 * 100
- Appetite loss (Q13-1)/3 * 100
- Constipation (Q16-1)/3 * 100
- Diarrhea (Q17-1)/3 * 100
- Financial difficulties (Q28-1)/3 * 100

7.8.1.2 EORTC QLQ-CX24

The EORTC Cervical Cancer Module, QLQ-CX24, consists of three multi-items scales: symptom experience, body image, and sexual/vaginal functioning and five single items pertaining to menopausal symptoms, lymphedema, lower back pain, tingling and numbness and sexual enjoyment. The following are the scoring algorithms for these scales and items of EORTC QLQ-CX24:

- Symptom Experience ((Q31+…+Q37+Q39+Q41+…+Q43)/11-1)/3 * 100
- Body Image ((Q45+…+Q47)/3-1)/3 * 100
- Sexual/Vaginal Functioning ((Q50+…+Q53)/4-1)/3 * 100
- Lymphoedema (Q38-1)/3 * 100
- Peripheral Neuropathy (Q40-1)/3 * 100
- Menopausal Symptoms (Q44-1)/3 * 100
- Sexual Worry (Q48-1)/3 * 100
- Sexual Activity (1 - (Q49-1)/3) * 100
- Sexual Enjoyment (1 - (Q54)-1)/3) * 100

7.8.1.3 FSFI

The FSFI is a 19-item self-report measure of female sexual function that provides scores on six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction and pain) as well as a total score:

- Desire (Q1+Q2) * 0.6
- Arousal (Q3+…+Q6) * 0.3
- Lubrication (Q7+…+Q10) *0.3
- Orgasm (Q11+…+Q13) * 0.4
- Satisfaction (Q14+…+Q16) * 0.4
- Pain (Q17+…+Q19) * 0.4
- Total Score (Q1+…+Q19) / 19 * 1.2

7.8.1.4 FSDS-R

The FSDS-R is a 13-item unidimensional measure of sexual-related distress.

- Total Score Q1+…+Q13

For all the above PRO questionnaire, missing items in a multiitem scale will be handled by the following methods: Values will be imputed for missing items by "assuming that the missing items have values equal to the average of those items which are present" for the total score in which at least half the items are completed. The total score will be treated as missing if less than half of the items are completed.

7.8.2 Data Sets

The analyses of PRO data will be restricted to treated patients who have completed at least one PRO questionnaire.

7.8.3 Compliance

Compliance with each PRO questionnaire will be described for each treatment arm, at each time of evaluation, by the number and percentage of expected subjects who filled

out a questionnaire (per subject, at least one question answered) in time of evaluation. The expected number used in calculating the percentage will be all alive subjects who are required to complete the assessment in each treatment arm at each assessment time point except at the first pelvic recurrence time point, which will be the number of alive patients who have the first pelvic recurrence **(Table 42).**

7.8.4 Analyses of PRO

7.8.4.1 Baseline and Change Score Analysis

Descriptive statistics for EORTC QOL-C30, CX24, FSDI and FSDS-R scores (mean, standard deviation) will be presented for each scale and summary scale at baseline for each treatment group **(Table 43)**. The change scores from baseline will be generated at each time of post-baseline evaluation and compared between two arms by Wilcoxon test **(Table 44)**.

7.8.4.2 Profile Analysis

The profile of change scores over time between two treatment arms will be compared using linear mixed models with the treatment effect, time of assessment from randomization (in months), and their interaction as fixed effects and the intercept and time as two random effects. The estimates for the terms of fixed effect with standard errors and p-values will be presented **(Table 45).**

8. Appendices

Appendix 1: Tables and Figures

Table 1: Patient Disposition

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy	Radical Hysterectomy	Total
Randomized	N=***	N=***	N=***
Treated with surgery	*** (**)	*** (**)	*** (**)
Not Treated with surgery	*** (**)	*** (**)	*** (**)
Reason for not treated with surgery			
Intercurrent illness	*** (**)	*** (**)	*** (**)
More advanced disease	*** (**)	*** (**)	*** (**)
Patient refusal	*** (**)	*** (**)	*** (**)
Death	*** (**)	*** (**)	*** (**)
Others	*** (**)	*** (**)	*** (**)

Table 2: Follow-up of Patients

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy	Radical Hysterectomy	Total
Number of patients alive	*** (*)	*** (*)	*** (*)
Follow-up (months)			
Median	**	**	**
Minimum-maximum	**-**	**-**	**-**

Table 3: Accrual by Group and Center

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N = ***
CCTG	*** (**)	*** (**)	*** (**)
Center #1	*** (**)	*** (**)	*** (**)
Center #2	*** (**)	*** (**)	*** (**)
Center #3	*** (**)	*** (**)	*** (**)
...	*** (**)	*** (**)	*** (**)
BGOG	*** (**)	*** (**)	*** (**)
Center #1	*** (**)	*** (**)	*** (**)
Center #2	*** (**)	*** (**)	*** (**)
Center #3	*** (**)	*** (**)	*** (**)
...	*** (**)	*** (**)	*** (**)
…	*** (**)	*** (**)	*** (**)

Figure 1: Accrual by Calendar Time

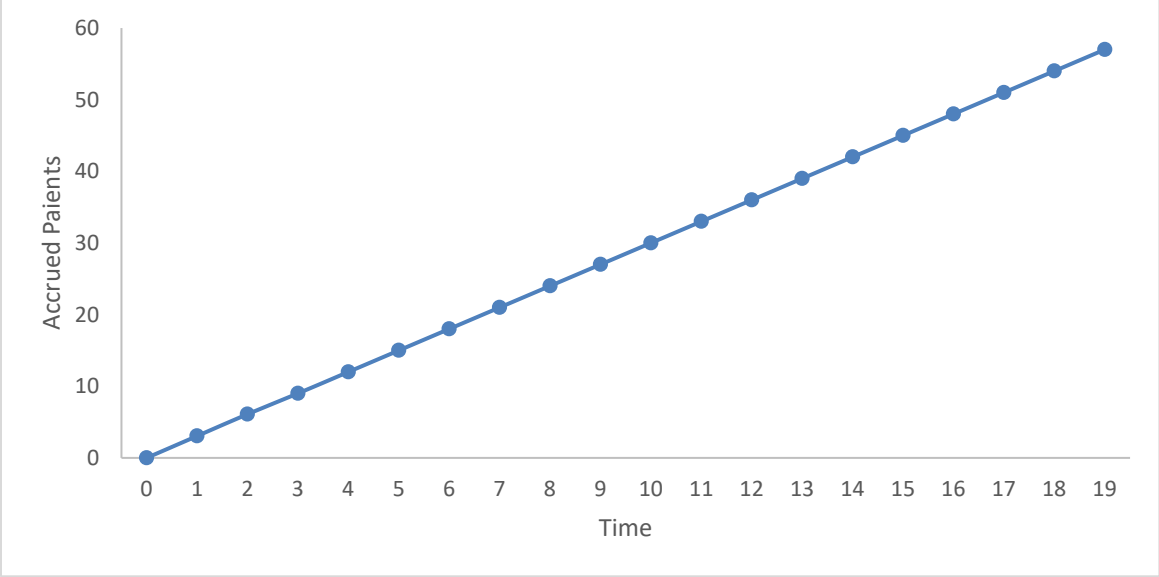

Table 4: Accrual by Stratification Factor at Randomization

Dataset: All Intention-To-Treat Patients

	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N = ***
Cooperative group			
CCTG	** (**)	** (**)	** (**)
KGOG	** (**)	** (**)	** (**)
AGO-AUSTRIA	** (**)	** (**)	** (**)
UK NCRI	** (**)	** (**)	** (**)
ICORG	** (**)	** (**)	** (**)
BGOG	** (**)	** (**)	** (**)
DGOG	** (**)	** (**)	** (**)
Fudan University Shanghai Cancer Center	** (**)	** (**)	** (**)
GINECO	** (**)	** (**)	** (**)
Intended use of SN mapping			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Stage			
IA2	** (**)	** (**)	** (**)
IB1	** (**)	** (**)	** (**)
Histological type			
Squamous	** (**)	** (**)	** (**)
Adenocarcinoma/adenosquamous	** (**)	** (**)	** (**)
Tumour grade			
1-2	** (**)	** (**)	** (**)
3	** (**)	** (**)	** (**)
Not assessable	** (**)	** (**)	** (**)

Source: Centralized Randomization File

Table 5: Eligibility and Reasons for Ineligibility and Major Protocol Violations

Dataset: All Intention-To-Treat Patients			
	Number of Patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Eligible	*** (**)	*** (**)	*** (**)
Not Eligible	*** (**)	*** (**)	*** (**)
Reason for ineligibility			
<Reason 1>	**	**	**
<Reason 2>	**	**	**
...	**	**	**
Major protocol violation			
<violation type 1>	**	**	**
<violation type 2>	**	**	**
...			

Table 6: Treatment as Randomized Versus as Treated

Dataset: All Intention-To-Treat Patients			
	Number of Patients (%) Randomized Arm		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Treatment received			
Simple Hysterectomy	*** (**)	*** (**)	*** (**)
Radical Hysterectomy	*** (**)	*** (**)	*** (**)
Not treated	*** (**)	*** (**)	*** (**)

Table 7: Pre-treatment Characteristics at Baseline

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Race			
White	** (**)	** (**)	** (**)
Black or African American	** (**)	** (**)	** (**)
....	** (**)	** (**)	** (**)
Age (years)			
N	**	**	**
Median (Min – Max)	** (** - **)	** (** - **)	** (** - **)
< 65	** (**)	** (**)	** (**)
≥ 65	** (**)	** (**)	** (**)
ECOG Performance Status			
0	** (**)	** (**)	** (**)
1	** (**)	** (**)	** (**)
Body mass index (BMI)			
N	**	**	**
Median (Min – Max)	** (** - **)	** (** - **)	** (** - **)

Table 8: Pathological Diagnosis of Tumor

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Months from initial pathological diagnosis of cervical cancer to randomization			
N	**	**	**
Median (Min – Max)	** (** - **)	** (** - **)	** (** - **)
Diagnostic procedure			
LEEP	** (**)	** (**)	** (**)
Cone	** (**)	** (**)	** (**)
Cervical biopsy	** (**)	** (**)	** (**)
Histological type			
Squamous	** (**)	** (**)	** (**)
Adenocarcinoma	** (**)	** (**)	** (**)
Adenosquamous	** (**)	** (**)	** (**)
FIGO stage			
IA2	** (**)	** (**)	** (**)
IB1 (low risk)	** (**)	** (**)	** (**)
Histologic Grade			
1	** (**)	** (**)	** (**)
2	** (**)	** (**)	** (**)
3	** (**)	** (**)	** (**)
Not assessable	** (**)	** (**)	** (**)

Table 9: Tumour Description at Baseline

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Diagnostic Procedure			
Cervical biopsy	** (**)	** (**)	** (**)
LEEP/Cone	** (**)	** (**)	** (**)
Clinical visibility of lesion			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Tumour thickness			
N	**		
Median	**	**	**
Min-Max	** -**	**	**
		** **	** **
Depth of stromal invasion			
N	**	**	**
Median	**	**	**
Min-Max	** -**	** -**	** -**
Lateral extension			
≤7.0mm	** (**)	** (**)	** (**)
>7.0mm	** (**)	** (**)	** (**)
Not stated	** (**)	** (**)	** (**)
Lymphovascular invasion			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Not stated	** (**)	** (**)	** (**)
Resected Margin involvement			
Yes	** (**)	** (**)	** (**)
Margin(s) involved			
Exocervical	** (**)	** (**)	** (**)
Endocervical	** (**)	** (**)	** (**)
Deep	** (**)	** (**)	** (**)
Unknown	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Not stated	** (**)	** (**)	** (**)
Intra-epithelial lesion			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Not stated	** (**)	** (**)	** (**)

Table 10: Pelvic Exam and Imaging at Baseline

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Pelvic exam result			
Normal	** (**)	** (**)	** (**)
Abnormal – not malignant	** (**)	** (**)	** (**)
Abnormal - malignant	** (**)	** (**)	** (**)
Maximum dimension			
N	**	**	**
Median	**	**	**
Min-Max	** -**	** -**	** -**
Detection of disease on pelvic imaging			
Yes	** (**)	** (**)	** (**)
No	** (**)	** (**)	** (**)
Not applicable/not required	** (**)	** (**)	** (**)
Location of tumour			
Cervix	** (**)	** (**)	** (**)
Lymph node	** (**)	** (**)	** (**)
Other	** (**)	** (**)	** (**)
Percentage of stroma involved			
≤ 50%	** (**)	** (**)	** (**)
>50%	** (**)	** (**)	** (**)
Maximum tumour dimension			
≤20.0mm	** (**)	** (**)	** (**)
>20.0mm	** (**)	** (**)	** (**)

Table 11: Baseline Symptom Status

Dataset: All Intention-To-Treat Patients on Simple Hysterectomy arm						
	Number of patients (%) N=***					
	Grade					Any grade
	1	2	3	4	5	
Patients with any symptom at baseline	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with particular symptom, within body system:						
Body System 1(1)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Body System 2(1)						
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a body system

Note: Same table to be made for Radical Hysterectomy arm.

Table 12: Major Medical Problems at Baseline

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Patients with at least one past or current major medical problem	** (**)	** (**)	** (**)
Medical Problem(1)			
Problem 1	** (**)	** (**)	** (**)
...			

(1) patients may report more than one medical problem reported

Table 13: Tobacco Smoking History at Baseline

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Ever smoked any tobacco product			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Current smoker			
No	** (**)	** (**)	** (**)
Yes	** (**)	** (**)	** (**)
Current average cigarettes per day			
N	**	**	**
Median (Min-max)	** (** - **)	** (** - **)	** (** - **)
Years from quitting smoking to randomization			
N	**	**	**
Median (Min-max)	** (** - **)	** (** - **)	** (** - **)
Smoking history			
Pipe or cigar smoker only	** (**)	** (**)	** (**)
100 or fewer cigarettes during lifetime	** (**)	** (**)	** (**)
Greater than 100 cigarettes during lifetime	** (**)	** (**)	** (**)
Number of years smoked cigarettes			
N	**	**	**
Median (Min-max)	** (** - **)	** (** - **)	** (** - **)
Average number of cigarettes per day			
N	**	**	**
Median (Min-max)	** (** - **)	** (** - **)	** (** - **)
Pack Years			
N	**	**	**
Median (Min-max)	** (** - **)	** (** - **)	** (** - **)

Table 14: Hysterectomy Procedure

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Procedure performed		
Hysterectomy with parametrium	**(**)	**(**)
Hysterectomy with no parametrium	**(**)	**(**)
Unilateral/Bilateral salpingectomy	**(**)	**(**)
Unilateral/Bilateral oophorectomy	**(**)	**(**)
Vaginal cuff	**(**)	**(**)
Length of vaginal cuff		
N	**	**
Median	**	**
Min-Max	**-**	**-**
Type of surgical approach		
Abdominal	**(**)	**(**)
Laparoscopic	**(**)	**(**)
Vaginal	**(**)	**(**)
Robotic	**(**)	**(**)
Total time of hysterectomy		
N	***	***
Median (Min-Max)	** (**_**)	** (**_**)

Table 15: Prophylactic Medications

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Prophylactic antibiotics used pre-operatively		
Yes	**(**)	**(**)
No	**(**)	**(**)
Prophylactic antibiotics used post-operatively		
Yes	**(**)	**(**)
No	**(**)	**(**)
Prophylactic anticoagulation used pre-operatively		
Yes	**(**)	**(**)
No	**(**)	**(**)
Prophylactic anticoagulation used post-operatively		
Yes	**(**)	**(**)
No	**(**)	**(**)

Table 16: Transfusion or Blood Products

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Estimated amount of blood loss during surgery		
<500cc	**(**)	**(**)
500-1000cc	**(**)	**(**)
>1000cc	**(**)	**(**)
Transfusions or blood products during surgery and/or in the 4 weeks following surgery		
No	**(**)	**(**)
Yes	** (**)	** (**)
Prophylactic hemoglobin used pre-operatively		
Yes	**(**)	**(**)
No	** (**)	** (**)
Prophylactic hemoglobin used post-operatively		
Yes	**(**)	**(**)
No	** (**)	** (**)
Type of transfusion		
Red Cell Concentrates Transfusion	**(**)	**(**)
Platelets	**(**)	**(**)
Others	**(**)	**(**)
Total number of units of red cell concentrates		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Total number of units of platelets		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Total number of units of other transfusions		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)

Table 17: Surgical Complications

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Intraoperative Injury		
No	**(**)	**(**)
Yes	**(**)	**(**)
Location of intraoperative injury		
Bladder	**(**)	**(**)
Ureter	**(**)	**(**)
…	**(**)	**(**)
Admission to hospital for hysterectomy		
No	**(**)	**(**)
Yes	**(**)	**(**)
Days from admission to hospital to discharge		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Discharge Destination		
Home	**(**)	**(**)
Assisted living	**(**)	**(**)
……	**(**)	**(**)
Admission to intensive care for hysterectomy		
No	**(**)	**(**)
Yes	**(**)	**(**)
Days in intensive care for hysterectomy		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)

Table 18: Results of Tumor Assessment After Hysterectomy

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Cervical cancer detected in hysterectomy specimen		
No	**(**)	**(**)
Yes	** (**)	** (**)
Histologic tumour type		
Squamous	**(**)	**(**)
Adenocarcinoma	**(**)	**(**)
Adenosquamous	**(**)	**(**)
Histologic grade		
1	**(**)	**(**)
2	**(**)	**(**)
3	**(**)	**(**)
Not assessable	**(**)	**(**)
Depth of stromal invasion		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Location of stromal invasion		
Inner half cervical wall	**(**)	**(**)
Outer half cervical wall	**(**)	**(**)
Horizontal spread/greatest diameter		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Lymphovasular invasion		
Yes	**(**)	**(**)
No	**(**)	**(**)
Undetermined	**(**)	**(**)
Resection margins involved		
Yes	**(**)	**(**)
No	**(**)	**(**)
Presence of associated intra-epithelial Lesion		
Yes	**(**)	**(**)
No	**(**)	**(**)
Presence of tumour in parametrium		
No	**(**)	**(**)
Yes	**(**)	**(**)
Location of tumour in parametrium		
Continuity with tumour	**(**)	**(**)
Lymphovascular space	**(**)	**(**)
Parametrial lymph node	**(**)	**(**)

Table 19: Sentinel Node Mapping and Lymph Node Dissection

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Success of protocol-defined sentinel node mapping		
Yes	**(**)	**(**)
No	**(**)	**(**)
Not Applicable	**(**)	**(**)
Technique for sentinel node mapping		
Laparoscopic	**(**)	**(**)
Open	**(**)	**(**)
Reason for unsuccessful protocol-defined sentinel node mapping		
Technical reasons	**(**)	**(**)
Patient refusal	**(**)	**(**)
Allergy to blue dye	**(**)	**(**)
Other reason	**(**)	**(**)
Not Applicable	**(**)	**(**)
Pelvic node dissection done		
No	**(**)	**(**)
Yes	**(**)	**(**)
Technique of node discection		
Laparoscopic	**(**)	**(**)
Open	**(**)	**(**)
Para aortic lymph dissection done		
No	**(**)	**(**)
Yes	**(**)	**(**)
Technique for para aortic lymph node dissection		
Laparoscopic	**(**)	**(**)
Open	**(**)	**(**)

Table 20: Results of Sentinel Lymph Node and Non-Sentinel Node Assessments

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N=***	Radical Hysterectomy N=***
Sentinel lymph node assessment		
Bifurcation left		
Nodes Removed		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Metastatic Nodes Detected		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Size of Largest Metastasis		
<0.2mm	**(**)	**(**)
0.2-2.0mm	**(**)	**(**)
>2.0mm	**(**)	**(**)
Extracapsular Invasion		
Yes	**(**)	**(**)
No	**(**)	**(**)
…		
Non-Sentinel lymph node assessment		
Bifurcation left		
Nodes Removed		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Metastatic Nodes Detected		
N	**	**
Median (Min-Max)	** (**-**)	** (**-**)
Size of Largest Metastasis		
<0.2mm	**(**)	**(**)
0.2-2.0mm	**(**)	**(**)
>2.0mm	**(**)	**(**)
Extracapsular Invasion		
Yes	**(**)	**(**)
No	**(**)	**(**)
…		

Note: Size of largest metastasis and extracapsular invasion are not applicable for sentinel lymph node assessment of pelvic NOS left and pelvic NOS right sites.

Table 21: Results of Assessment of Extrauterine Tissue Other Than Lymph Node and Extra-Pelvic Tissue

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Disease in extrauterine tissue other than lymph node		
No	**(**)	**(**)
Yes	**(**)	**(**)
Location of disease in other extrauterine tissue		
Fallopian Tube	**(**)	**(**)
Parametrium	**(**)	**(**)
…	**(**)	**(**)
Disease in extra-pelvic tissue		
No	**(**)	**(**)
Yes	**(**)	**(**)
Location		
Omentum	**(**)	**(**)
Abdominal Organs	**(**)	**(**)
Peritoneal Disease	**(**)	**(**)
Lung	**(**)	**(**)
…	**(**)	**(**))

Table 22: Adjuvant Treatment Within 4 Weeks After the Hysterectomy

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Planned to receive adjuvant radiation and/or chemotherapy		
Yes	**(**)	**(**)
Treatment Planned		
Radiation alone	**(**)	**(**)
Chemotherapy alone	**(**)	**(**)
Radiation and Chemotherapy	**(**)	**(**)
No		
Reason for not to receive adjuvant treatment	**(**)	**(**)
Lesion size > 2cm	**(**)	**(**)
Extra pelvic spread	**(**)	**(**)
…	** (**)	** (**)
Received Adjuvant Chemotherapy		
No	**(**)	**(**)
Yes	**(**)	**(**)
Chemotherapy treatment		
Drug name 1		
Dose (unit)		
N	**	**
Mean (SD)	** (**)	** (**)
Median (Min-Max)	** (**-**)	** (**-**)
…		
Received adjuvant radiotherapy		
No	**(**)	**(**)
Yes	**(**)	**(**)
Type of radiotherapy		
External radiotherapy	**(**)	**(**)
Boost radiotherapy	**(**)	**(**)
Brachytherapy	**(**)	**(**)
Total dose of external radiotherapy (cGy)		
N	**	**
Mean (STD)	** (**)	** (**)
Median (Min-Max)	** (**-**)	** (**-**)
Total dose of boost radiotherapy (cGy)		
N	**	**
Mean (STD)	** (**)	** (**)
Median (Min-Max)	** (**-**)	** (**-**)
Total dose of Brachytherapy (cGy)		
N	**	**
Mean (STD)	** (**)	** (**)
Median (Min-Max)	** (**-**)	** (**-**)

Table 23: Other Surgeries/Procedures Within 4 Weeks After Hysterectomy

Dataset: All Treated Patients		
	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Patients received other surgeries/procedures within 4 weeks after hysterectomy		
No	**(**)	**(**)
Yes	**(**)	**(**)
Surgery/Procedure 1		
Reason 1	**(**)	**(**)
Reason 2	**(**)	**(**)
…	**(**)	**(**)
……		

Table 24: Summary of Events for Analyses of Recurrence

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***	Total N=***
Patients who had pelvic recurrence			
No	**(**)	**(**)	**(**)
Yes	** (**)	** (**)	** (**)
Site of pelvic recurrence			
Vaginal Vault	**(**)	**(**)	**(**)
Parametrium	**(**)	**(**)	**(**)
Pelvic Lymph Nodes	**(**)	**(**)	**(**)
Other	**(**)	**(**)	**(**)
Patients who had extra-pelvic recurrence			
No	**(**)	**(**)	**(**)
Yes	** (**)	** (**)	** (**)
Site of extra-pelvic recurrence			
Para-aortic lymph node	**(**)	**(**)	**(**)
Bone	**(**)	**(**)	**(**)
Brain	**(**)	**(**)	**(**)
…	**(**)	**(**)	**(**)
Patients who had both pelvic and extra-pelvic recurrences	**(**)	**(**)	**(**)
Patients who had either pelvic or extra-pelvic recurrences	**(**)	**(**)	**(**)
Patients who had more advanced stages of cervical cancer on sentinel node mapping, pelvic node dissection or other intraoperative findings	**(**)	**(**)	**(**)
Patients who died			
No	**(**)	**(**)	**(**)
Yes	** (**)	** (**)	** (**)
Cause of death			
Cervix cancer only	**(**)	**(**)	**(**)
Other primary malignancy	**(**)	**(**)	**(**)
…	**(**)	**(**)	**(**)
Patients who had an event for PRFS	**(**)	**(**)	**(**)
Patients who were censored for PRFS	** (**)	** (**)	** (**)
Patients who had extra-pelvic recurrence as the first recurrence	**(**)	**(**)	**(**)
Patients who died without recurrence	** (**)	** (**)	** (**)
Patients who were alive without recurrence	** (**)	** (**)	** (**)
Patients who had an event for EPRFS	**(**)	**(**)	**(**)
Patients who were censored for EPRFS	** (**)	** (**)	** (**)
Patients who had pelvic recurrence as the first recurrence	**(**)	**(**)	**(**)
Patients who died without recurrence	** (**)	** (**)	** (**)
Patients who were alive without recurrence	** (**)	** (**)	** (**)
Patients who had an event for RFS	**(**)	**(**)	**(**)
Patients who were censored for RFS	** (**)	** (**)	** (**)
Patients who died without recurrence	**(**)	**(**)	**(**)
Patients who were alive without recurrence	** (**)	** (**)	** (**)

Table 25: Analysis for Pelvic Recurrence Rate at 3 Years

Factors	Value	Simple Hysterectomy		Radical Hysterectomy		Difference** (%) (Upper limit of one-sided 95% C.I.)
		N	Rate*	N	Rate*	
Intention-to-treat patients	All	**	**.**	**	**.**	**.** (**.**)
Age	≤65	**	**.**	**	**.**	**.** (**.**)
	>65	**	**.**	**	**.**	**.** (**.**)
Race	White	**	**.**	**	**.**	**.** (**.**)
	Asian	**	**.**	**	**.**	**.** (**.**)
	Others	**	**.**	**	**.**	**.** (**.**)
Intended use of sentinel node mapping	Yes	**	**.**	**	**.**	**.** (**.**)
	No	**	**.**	**	**.**	**.** (**.**)
Histologic Stage	IA2	**	**.**	**	**.**	**.** (**.**)
	IB1	**	**.**	**	**.**	**.** (**.**)
Histologic type	Squamous	**	**.**	**	**.**	**.** (**.**)
	Adenocarcinoma/ adenosquamous	**	**.**	**	**.**	**.** (**.**)
Tumor grade	1-2	**	**.**	**	**.**	**.** (**.**)
	3	**	**.**	**	**.**	**.** (**.**)
	Not assessable	**	**.**	**	**.**	**.** (**.**)
Per-protocol patients	All	**	**.**	**	**.**	**.** (**.**)

*Pelvic recurrence rate at 3 years
**Between simple hysterotomy and radical hysterectomy

Figure 2: Kaplan-Meier Curves for Pelvic Relapse Free Survival

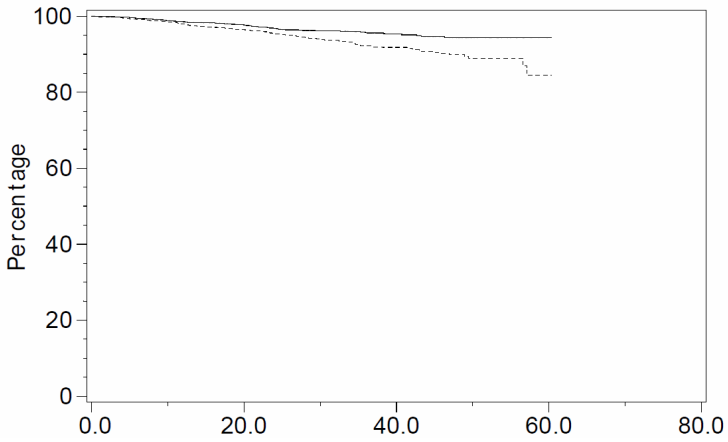

Table 26: Analysis for Pelvic Relapse Free Survival (PRFS)

Factors	Value	Simple Hysterectomy		Radical Hysterectomy		Hazard Ratio* (Upper limit of one-sided 95% C.I.)
		N	3-year PRFS	N	3-year PRFS	
Intention-to-treat patients	All	**	**.**	**	**.**	**.** (**.**)
Age	≤65	**	**.**	**	**.**	**.** (**.**)
	>65	**	**.**	**	**.**	**.** (**.**)
Race	White	**	**.**	**	**.**	**.** (**.**)
	Asian	**	**.**	**	**.**	**.** (**.**)
	Others	**	**.**	**	**.**	**.** (**.**)
Intended use of sentinel node mapping	Yes	**	**.**	**	**.**	**.** (**.**)
	No	**	**.**	**	**.**	**.** (**.**)
Histologic Stage	IA2	**	**.**	**	**.**	**.** (**.**)
	IB1	**	**.**	**	**.**	**.** (**.**)
Histologic type	Squamous	**	**.**	**	**.**	**.** (**.**)
	Adenocarcinoma/ adenosquamous	**	**.**	**	**.**	**.** (**.**)
Tumor grade	1-2	**	**.**	**	**.**	**.** (**.**)
	3	**	**.**	**	**.**	**.** (**.**)
	Not assessable	**	**.**	**	**.**	**.** (**.**)
Per-protocol patients	All	**	**.**	**	**.**	**.** (**.**)

*Between simple hysterotomy and radical hysterectomy

Figure 3: Kaplan-Meier Curves for Extra-Pelvic Relapse Free Survival

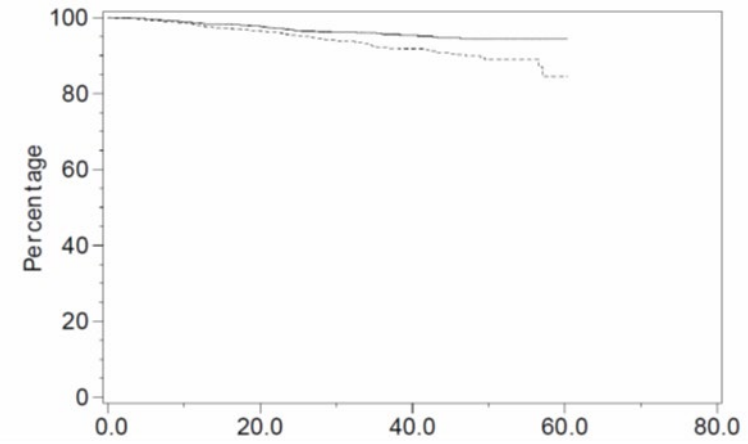

Table 27: Analysis for Extra-Pelvic Relapse Free Survival (EPRFS)

Factors	Value	Simple Hysterectomy		Radical Hysterectomy		Hazard Ratio[1] (Two-sided 95% C.I.)	P-value[2]
		N	3-year EPRFS	N	3-year EPRFS		
Intention-to-treat patients	All	**	**.**	**	**.**	*.** (*.**-*.**)	0.**
Age	≤65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	>65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Race	White	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Asian	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Others	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Intended use of sentinel node mapping	Yes	**	**.**	**	**.**	**.* (**.*-**.*)	0.**
	No	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic stage	IA2	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	IB1	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic type	Squamous	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	Adenocarcinoma/ adenosquamous	**	**.**	**	**.**	**.* (**.*-*.**)	0.**
Race	1-2	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	3	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Not assessable	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Per-protocol patients	All	**	**.**	**	**.**	*.** (*.**_*.**)	0.**

(1)Between simple hysterotomy and radical hysterectomy;
(2) From two-side log-rank test stratified by stratification factors except corporative group at randomization.

Figure 4: Kaplan-Meier Curves for Relapse Free Survival

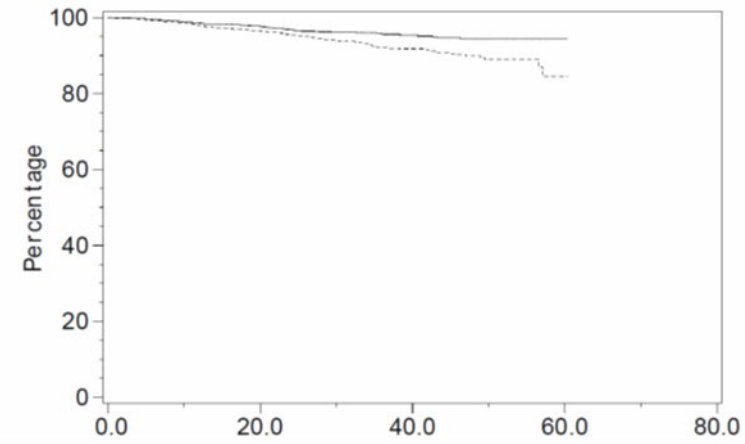

Table 28: Analysis for Relapse Free Survival (RFS)

Factors	Value	Simple Hysterectomy		Radical Hysterectomy		Hazard Ratio[1] (Two-sided 95% C.I.)	P-value[2]
		N	3-year RFS	N	3-year RFS		
Intention-to-treat patients	All	**	**.**	**	**.**	*.** (*.**-*.**)	0.**
Age	≤65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	>65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Race	White	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Asian	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Others	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Intended use of sentinel node mapping	Yes	**	**.**	**	**.**	**.* (**.*-**.*)	0.**
	No	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic stage	IA2	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	IB1	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic type	Squamous	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	Adenocarcinoma/ adenosquamous	**	**.**	**	**.**	**.* (**.*-*.**)	0.**
Race	1-2	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	3	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Not assessable	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Per-protocol patients	All	**	**.**	**	**.**	*.** (*.**_*.**)	0.**

(1)Between simple hysterotomy and radical hysterectomy;
(2) From two-side log-rank test stratified by stratification factors except corporative group at randomization.

Table 29: Summary of Events for Analyses of Survival

Dataset: All Intention-To-Treat Patients			
	Number of patients (%)		
	Simple Hysterectomy N=***	Radical Hysterectomy N=***	Total N=***
Patients who died			
No	**(**)	**(**)	**(**)
Yes	** (**)	** (**)	** (**)
Cause of death			
Cervix cancer only	**(**)	**(**)	**(**)
Other primary malignancy	**(**)	**(**)	**(**)
…	**(**)	**(**)	**(**)
Patients who had an event for OS	**(**)	**(**)	**(**)
Patients who were censored for OS	** (**)	** (**)	** (**)
Patients who were alive	**(**)	**(**)	**(**)

Figure 5: Kaplan-Meier Curves for Overall Survival

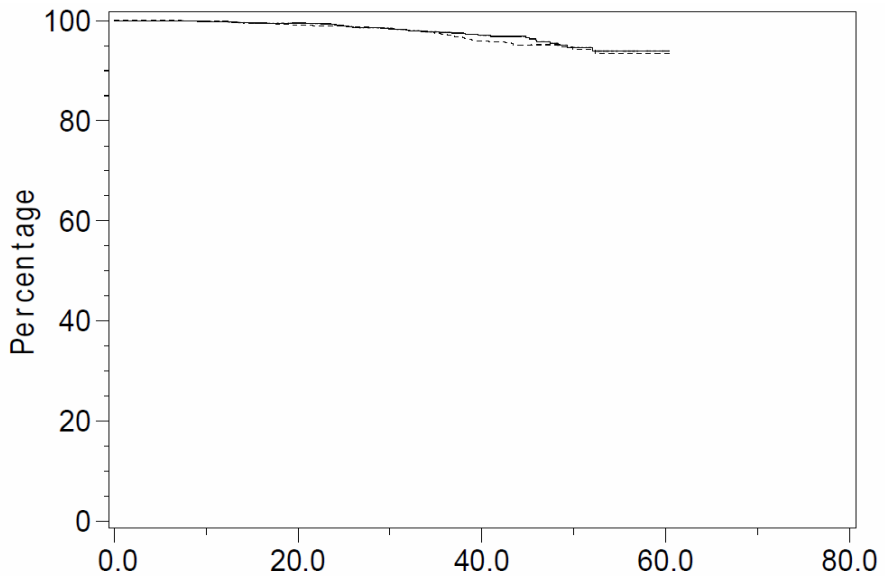

Table 30: Analysis for Overall Survival (OS)

Factors	Value	Simple Hysterectomy N	Simple Hysterectomy 3-year OS	Radical Hysterectomy N	Radical Hysterectomy 3-year OS	Hazard Ratio[1] (Two-sided 95% C.I.)	P-value[2]
Intention-to-treat patients	All	**	**.**	**	**.**	*.** (*.**-*.**)	0.**
Age	≤65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	>65	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Race	White	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Asian	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Others	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Intended use of sentinel node mapping	Yes	**	**.**	**	**.**	**.* (**.*-**.*)	0.**
	No	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic stage	IA2	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	IB1	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
Histologic type	Squamous	**	**.**	**	**.**	**.* (*.**-*.**)	0.**
	Adenocarcinoma/ adenosquamous	**	**.**	**	**.**	**.* (**.*-*.**)	0.**
Race	1-2	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	3	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
	Not assessable	**	**.**	**	**.**	*.** (*.**_*.**)	0.**
Per-protocol patients	All	**	**.**	**	**.**	*.** (*.**_*.**)	0.**

(1)Between simple hysterotomy and radical hysterectomy;
(2) From two-side log-rank test stratified by stratification factors except corporative group at randomization.

Table 31: Rates of Sentinel Node Detection, Parametrial Involvement, Margins Involvement, and Pelvic Nodes Involvement

	Number of patients with event/number of patients (%)		
	Simple Hysterectomy	Radical Hysterectomy	P-value*
All intention-to-treat patients			
Rate of Sentinel Nodes Detection	**/**(**)	**/**(**)	.**
Rate of Parametrial Involvement	**/**(**)	**/**(**)	.**
Rate of Margin Involvement	**/**(**)	**/**(**)	.**
Rate of Pelvic Node Involvement	**/**(**)	**/**(**)	.**
All per-protocol patients			
Rate of Sentinel Nodes Detection	**/**(**)	**/**(**)	.**
Rate of Parametrial Involvement	**/**(**)	**/**(**)	.**
Rate of Margin Involvement	**/**(**)	**/**(**)	.**
Rate of Pelvic Node Involvement	**/**(**)	**/**(**)	.**

*From two-sided Fisher's exact test.

Table 32: Acute Surgery-Related Adverse Event

Data set: All Treated Patients on Simple Hysterectomy arm							
	Number of patients (%) N=***						
	Worst grade						Any grade
	NR	1	2	3	4	5	
Patients with any AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE within category							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...							

(1) Patients may have more than one event within a category.

Note: Same table will be made for patients on Radical Hysterectomy Arm.

Table 33: Severe Acute Surgery-Related Adverse Events

Data set: All Treated Patients on Simple Hysterectomy Arm				
	Number of patients (%) N=***			
	Worst grade			Any grade 3 or higher AE
	3	4	5	
Patients with any AE	** (**)	** (**)	** (**)	** (**)
Patients with AE within category				
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a category.

Note: Same table will be made for patients on Radical Hysterectomy Arm.

Table 34: Late Surgery-Related Adverse Event

Data set: All Treated Patients on Simple Hysterectomy arm							
	Number of patients (%) N=***						
	Worst grade						Any grade
	NR	1	2	3	4	5	
Patients with any AE	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)	** (**)
Patients with AE within category	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...							
	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)	**(**)
...							

(1) Patients may have more than one event within a category.

Note: Same table will be made for patients on Radical Hysterectomy Arm.

Table 35: Severe Late Surgery-Related Adverse Events

Data set: All Treated Patients on Simple Hysterectomy Arm				
	Number of patients (%) N=***			
	Worst grade			Any grade 3 or higher AE
	3	4	5	
Patients with any AE	** (**)	** (**)	** (**)	** (**)
Patients with AE within category				
Category 1[(1)]	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)
Event 2	**(**)	**(**)	**(**)	**(**)
Event 3	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)
Category 2[(1)]	**(**)	**(**)	**(**)	**(**)
Event 1	**(**)	**(**)	**(**)	**(**)
...	**(**)	**(**)	**(**)	**(**)

(1) Patients may have more than one event within a category.

Note: Same table will be made for patients on Radical Hysterectomy Arm.

Table 36: Pelvic Exams During Follow-up

Data set: All Treated Patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Any pelvic exam after 4 weeks of surgical treatment but before the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
At least one abnormal and clinically significant	** (**)	** (**)
At least one abnormal but none clinically significant	** (**)	** (**)
All normal	** (**)	** (**)
Any pelvic exam after the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
At least one abnormal and clinically significant	** (**)	** (**)
At least one abnormal but none clinically significant	** (**)	** (**)
All normal	** (**)	** (**)

Table 37: Other Radiology Investigations

Data set: All Treated Patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Any radiology investigation within 4 weeks of surgical treatment		
No	** (**)	** (**)
Yes	** (**)	** (**)
At least one abnormal and clinically significant	** (**)	** (**)
At least one abnormal but none clinically significant	** (**)	** (**)
All normal	** (**)	** (**)
Any radiology investigation after 4 weeks of surgical treatment but before the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
At least one abnormal and clinically significant	** (**)	** (**)
At least one abnormal but none clinically significant	** (**)	** (**)
All normal	** (**)	** (**)
Any radiology investigation after the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
At least one abnormal and clinically significant	** (**)	** (**)
At least one abnormal but none clinically significant	** (**)	** (**)
All normal	** (**)	** (**)

Table 38: Hospitalization During Follow-up

Data set: All Treated Patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Any hospitalization after 4 weeks of surgical treatment but before the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
Any hospitalization after the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)

Table 39: Surgeries/Procedures During Follow-up

Data set: All Treated patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Number of patients with any surgery/procedure after 4 weeks of surgical treatment but before first pelvic recurrence	*** (**)	*** (**)
Surgery/procedure 1 (1)	*** (**)	*** (**)
…	*** (**)	*** (**)
Reason 1 (1)	*** (**)	*** (**)
…	*** (**)	*** (**)
Number of patients with any surgery/procedure after first pelvic recurrence	*** (**)	*** (**)
Surgery/procedure 1 (1)	*** (**)	*** (**)
…	*** (**)	*** (**)
Reason 1 (1)	*** (**)	*** (**)
…	*** (**)	*** (**)

(1) Patients could have more than one type of surgery/procedure and reason.

Table 40: Systemic and Radiation Treatments During Follow-up

Data set: All Treated patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Number of patients with any systemic or radiation treatment after 4 weeks of surgical treatment but before first pelvic recurrence	*** (**)	*** (**)
Systemic therapy (1)	*** (**)	*** (**)
Treatment 1 …	*** (**)	*** (**)
Radiotherapy (1)	*** (**)	*** (**)
Site 1 …	*** (**)	*** (**)
Other (1)	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)
Number of patients with any systemic or radiation treatment after first pelvic recurrence	*** (**)	*** (**)
Systemic therapy (1)	*** (**)	*** (**)
Treatment 1 …	*** (**)	*** (**)
Radiotherapy (1)	*** (**)	*** (**)
Site 1 …	*** (**)	*** (**)
Other (1)	*** (**)	*** (**)
Drug 1 …	*** (**)	*** (**)

(1) Patients could have more than one type of systemic and radiation treatment.

Table 41: Tobacco Smoking During Follow-up

Data set: All Treated Patients

	Number of patients (%)	
	Simple Hysterectomy N = ***	Radical Hysterectomy N = ***
Smoked tobacco after 4 weeks of surgical treatment but before the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)
Smoked tobacco after the first pelvic recurrence		
No	** (**)	** (**)
Yes	** (**)	** (**)

Table 42: Compliance Rate of PRO Assessments by Treatment Arms

	Simple Hysterectomy		Radical Hysterectomy	
	Expected	Received (%)	Expected	Received (%)
EORTC QoL Questionnaire				
Prior to randomization	***	** (**)	***	** (**)
After surgery prior to recurrence				
3 months	***	** (**)	***	** (**)
6 months	***	** (**)	***	** (**)
12 months	***	** (**)	***	** (**)
24 months	***	** (**)	***	** (**)
36 months	***	** (**)	***	** (**)
At Recurrence	***	** (**)	***	** (**)
Sexual Health Questionnaire				
Prior to randomization	***	** (**)	***	** (**)
After surgery prior to recurrence				
3 months	***	** (**)	***	** (**)
6 months	***	** (**)	***	** (**)
12 months	***	** (**)	***	** (**)
24 months	***	** (**)	***	** (**)
36 months	***	** (**)	***	** (**)
At Recurrence	***	** (**)	***	** (**)

Table 43: Summary of Baseline PRO Scale Scores

	Simple Hysterectomy	Radical Hysterectomy	P value*
EORTC QLQ-C30			
Physical Functioning			0.***
N	***	***	
Mean (STD)	**.* (**.*)	**.* (**.*)	
…	...	...	
EORTC QLQ-CX.24			
Symptom Experience			0.***
N	***	***	
Mean (STD)	**.* (**.*)	**.* (**.*)	
…			
FSFI			
Desire			
N	**	**	0.***
Mean (STD)	**.* (**.*)	**.* (**.*)	
….	…	…	
FSDS-R			
Total Score			0.***
N	***	***	
Mean (STD)	***	***	

* From Wilcoxon test.

Table 44: Summary of Change Scores from Baseline for PRO Scale/Domain/Item at Each Time of Assessment

	Simple Hysterectomy	Radical Hysterectomy	P Value**
Scale/Domain/Item*			
After surgery prior to recurrence			.**
Month 3			
N	***	***	
Mean (STD)	** (**)	** (**)	
Month 6			.**
N	***	***	
Mean (STD)	** (**)	** (**)	
Month 12			.**
N	***	***	
Mean (STD)	** (**)	** (**)	
Month 24			.**
N	***	***	
Mean (STD)	** (**)	** (**)	
Month 36			.**
N	***	***	
Mean (STD)	** (**)	** (**)	
At Recurrence			.**
N	***	***	
Mean (STD)	** (**)	** (**)	

* Table will be provided for each scale/domain/item. ** From Wilcoxon rank sum test

Table 45: Summary of Analysis From Linear Mixed Models for Change Scores

	Estimate	Standard Error	P value
EORTC QLQ-C30			
Physical functioning			
Treatment	**.*	**.*	0.**
Month	**.*	**.*	0.**
Treatment*Month	**.*	**.*	0.**
…			
EORTC QLQ-CX24			
Symptom Experience			
Treatment	**.*	**.*	0.**
Month	**.*	**.*	0.**
Treatment*Month	**.*	**.*	0.**
…			
FSFI			
Desire			
Treatment	**.*	**.*	0.**
Month	**.*	**.*	0.**
Treatment*Month	**.*	**.*	0.**
…			
FSDS-R			
Total Score			
Treatment	**.*	**.*	0.**
Week	**.*	**.*	0.**
Treatment*Month	**.*	**.*	0.**