



CentEast

Central Asia and East Europe Trial Group

Study Protocol 001-002

SATEN-3, ECATS

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I. INTRODUCTION

- a. **Protocol Title:** SATEN – Splitting of Adjuvant Treatment of Endometrial Cancers in Stage III, Ecats-Endometrial cancer adjuvant therapy sequencing
- b. **Protocol Version:** CentEast001-002
- c. **Protocol Date:** 01/03/2018
- d. **Principal Investigator:**
 - Protocol 001 (SATEN-3): İlker Kahramanoğlu, M.D.
 - Protocol 002 (Ecats): Mustafa Erkan Sarı, M.D.
- e. **Research Team:**
- f. **Financial Support:** None.

II. BACKGROUND

Despite the development in adjuvant treatment modalities, survival of patients with stage III endometrial cancer patients remains the same for more than 30 years (1-5). We have 2 recent randomized clinical trials targeting this group: PORTEC-III and GOG 258.

The analysis of patients with stage 3 patients in PORTEC-III trial demonstrated 69% and 58% 5-year DFS after treatment with CTRT and RT alone, respectively ($p=0.03$) (6). However, OS did not differ between groups.

Results of the GOG 258 study was presented in ASCO Annual Meeting 2017 (5). This trial included patients with stage III to IVA disease and with clear cell or serous histologic type having stage I-II disease. Patients with residual disease of less than 2 cm were also included. Randomisation was as CTRT to CT. Results showed that RT does not add overall benefit to chemotherapy in stage III endometrial cancer, even though it significantly improves local-regional control (HR= 0.43 (CI: 0.28-0.66) for pelvic and paraaortic recurrence).

Previous retrospective studies showed that patients treated with chemotherapy alone were seven and two times more likely to develop vaginal and pelvic recurrences, respectively compared to those treated with chemotherapy and radiotherapy (7). Broad eligibility for stage, histology and residual disease on GOG 258 study may be a possible explanation for the discordance between GOG 258 and PORTEC-III along with retrospective studies.

Unfortunately, all available RCTs have handled all stage III patients in a cluster. However, stage III endometrial cancer includes whether a patient with an isolated pelvic and/or paraaortic lymph node metastasis or a patient with an ovarian metastasis. Combining both groups and giving the same adjuvant treatment may cause an unnecessary or incomplete treatment for many patients.

Additionally, another issue, the optimal sequencing of adjuvant radiotherapy and chemotherapy delivery is still controversial. Combined-modality adjuvant therapy is routinely administered using various schedules at many centers. Evaluation of differences in survival and toxicity between patients who received sequential therapy (chemotherapy followed by radiation) and “sandwich” (radiation therapy is applied between split intervals of chemotherapy) approaches is currently a hot topic (8).

With the completion of this study, we will have the data shows whether adjuvant treatment of stage III should differ according to the subgroups. Therewithal another data will be shown

whether survival and toxicity differs according to sequencing of adjuvant radiotherapy and chemotherapy delivery.

By this way, next randomized trials will use our data as a guide for dividing stage III patients to different adjuvant treatment groups.

III. STUDY AIMS

In this study, firstly we aimed to predict the patterns of relapse and to evaluate the adjuvant treatment modalities in patients with stage III endometrioid type endometrial cancer (Protocol 001, SATEN-3). Our second aim is to evaluate differences in survival and toxicity between patients who received sandwich and sequential therapy (Protocol 002, Ecats).

IV. PARTICIPATING UNITS

CENTEAST Trial Groups who agreed are below:

V. STUDY DESIGN

- a. Experimental design: Retrospective study.
- b. Study population general description: Patients with proven stage III endometrioid type endometrial cancer treated with primary surgery, followed by any adjuvant treatment.
- c. Sample size determination and power analyses: Not applicable.
- d. Study endpoints: Recurrence locations and rate, disease-free survival, overall survival, toxicity
- e. Ethical Consideration: Approval of the Ethical Committee is needed.

VI. STUDY PROCEDURES

- a. Subject selection procedures
 - i. Inclusion Criteria
 - * Age 18-90
 - * Endometrioid histologic type
 - * Patients who underwent primary staging surgery
 - * FIGO Stage III
 - ii. Exclusion criteria
 - Patients who received neoadjuvant radiotherapy or chemotherapy or both
 - Non-endometrioid histologic types
 - Disease free survival of less than 3 months after last treatment

VII. PARAMETERS TO BE COLLECTED

Protocol, name, age, menopausal status, preoperative histology, preoperative grade, serum CA 125 level, date of surgery, details of surgery, residual tumor, final grade, tumor size, lymphovascular space invasion, washing or ascites, myometrial invasion, pelvic nodes, paraaortic nodes, cervical involvement, stage, adjuvant treatment, chemotherapy regimen, number of cycles of chemotherapy, sequencing modality of adjuvant treatment, acute

toxicities of chemotherapy and radiation treatment (if possible, scored according to the Common Terminology Criteria for Adverse Events version 4), recurrence, time of recurrence, location of recurrence, treatment after recurrence, survival status, time of death,

VIII. ANALYSIS PLAN

Patients' characteristics and clinical features will be summarized using standard descriptive statistics. Patients' characteristics and clinical features will be compared using chi-square test, Fischer exact test, and Mann-Whitney U test, where appropriate. Kaplan-Meier estimates will be used to generate survival curves. Survival curves will be compared by using log rank test. Risk factors which will be found to be associated with disease-free survival (DFS) and overall survival (OS) will be evaluated using Cox proportional hazard models. Hazard ratios and corresponding 95% confidence intervals will be calculated to summarize any associations. All p-values were two sided and $p < 0.05$ will be considered as statistically significant. Statistical analyses will be performed using SPSS version 21.

IX. REFERENCES

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