



**CentEast**  
Central Asia and East Europe Trial Group

***CENTEAST STUDY PROTOCOL – 003-  
(OPEC: OVARIAN PRESERVATION IN  
ENDOMETRIAL CANCERS )***

13/01/2020

[www.centeast.com](http://www.centeast.com)

## TABLE OF CONTENT

<b>I. INTRODUCTION.....</b>	<b>3</b>
a. Protocol Title:.....	3
b. Protocol Version:.....	3
c. Protocol Date:.....	3
d. Principal Investigator: .....	3
e. Research Team: .....	3
f. Financial Support: .....	3
<b>II. BACKGROUND .....</b>	<b>3</b>
<b>III. STUDY AIMS.....</b>	<b>4</b>
<b>IV. PARTICIPATING UNITS .....</b>	<b>4</b>
<b>V. STUDY DESIGN .....</b>	<b>4</b>
a. Experimental design: .....	4
b. Study population general description:.....	4
c. Sample size determination and power analyses: .....	4
d. Study endpoints: .....	4
e. Ethical Consideration: .....	4
<b>VI. STUDY PROCEDURES.....</b>	<b>4</b>
a. Subject selection procedures.....	4
<i>i. Inclusion Criteria</i> .....	4
<i>ii. Exclusion criteria</i> .....	5
<b>VII. PARAMETERS TO BE COLLECTED .....</b>	<b>5</b>
<b>VIII. ANALYSIS PLAN.....</b>	<b>5</b>
<b>IX. REFERENCES.....</b>	<b>5</b>

## I. INTRODUCTION

**a. Protocol Title:** OPEC – Ovarian Preservation in Endometrial Carcinoma

**b. Protocol Version:** CentEast003

**c. Protocol Date:** 13/01/2020

**d. Principal Investigator:**

Protocol 003 (OPEC): M. Coskun Salman, Murat Gultekin, M.D.

**e. Research Team:** Hacettepe University

**f. Financial Support:** None.

## II. BACKGROUND

Standard surgical treatment of endometrial carcinoma includes total abdominal hysterectomy, bilateral salpingo-oophorectomy with pelvic and para-aortic lymphadenectomy in selected cases. Bilateral oophorectomy is the standard treatment for all ages except for fertility saving procedures in infertile patients.

The main reason for bilateral oophorectomy in pre-menopausal patients is to decrease endogenous estrogen production and therefore prevent the cancer recurrences. At least in theory, microscopic residual disease can increase the risk of recurrence by the stimulation of endogenous estrogen hormones. Another reason for bilateral oophorectomy is an additional 5% risk of ovarian metastasis in endometrial cancers even in clinical stage I disease. Furthermore, there is also risk of concomitant endometrial-ovarian cancers in young patients that is estimated to be around around 5-15% (1,2).

On the other hand, bilateral oophorectomy causes surgical menopause in young patients that should not be underestimated. Patients will be faced with vasomotor symptoms, vaginal atrophy and related sexual problems, cardiovascular diseases together with osteoporosis and hip fractures (3,4). However, endometrial cancers in young patients usually are well differentiated and early stage tumors with long term survival (5). Accordingly, quality of life

gains more importance in these long term survivors at young ages (6). Therefore, recently; preservation of ovaries had gain importance in young patients with early stage disease. In several previous studies including some meta-analysis, this approach has also been shown to be oncologically safe (6-11). Several European and USA treatment guidelines also recommends preservation of the ovaries in selected young patients (12,13)

### **III. STUDY AIMS**

In this study, firstly we aimed to predict the clinico-pathological risk factors that determines the risk of ovarian metastasis and to define a subgroup of patients where ovaries can be safely preserved. Our second aim is to evaluate differences in survival between patients who received bilateral oophorectomy compared to patients who had ovarian preservation.

### **IV. PARTICIPATING UNITS**

CENTEAST Trial Groups who agreed:

### **V. STUDY DESIGN**

- a. Experimental design:** Retrospective study.
- b. Study population general description:** Patients with proven stage I-IV endometrial cancer treated with primary surgery, followed by any adjuvant treatment.
- c. Sample size determination and power analyses:** Not applicable.
- d. Study endpoints:** Clinico-pathologic risk factors for ovarian metastasis and survival in patients with or without bilateral oophorectomy.
- e. Ethical Consideration:** Approval of the Ethical Committee is needed.

### **VI. STUDY PROCEDURES**

#### **a. Subject selection procedures**

##### ***i. Inclusion Criteria***

\* Age 18-90

- \* All histologic types
- \* Patients who underwent primary staging surgery between 01.01.2010-01.01.2020
- \* FIGO Stage I-IV

#### ***ii. Exclusion criteria***

- Patients who received neoadjuvant radiotherapy or chemotherapy or both
- Patients who had fertility sparing surgery (oocyte cryopreservation etc)
- Disease free survival of less than 3 months after last treatment

### **VII. PARAMETERS TO BE COLLECTED**

Protocol, name, age, menopausal status, date of surgery, details of surgery, final grade, tumor size, lymphovascular space invasion, washing or ascites, myometrial invasion, pelvic nodes, paraaortic nodes, cervical involvement, stage, 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 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**

1. Gilani Modares M, Cheraghi F, Zamani N. Ovarian metastasis in endometrioid type endometrial cancer. *Int J Fertil Steril* 2011;5:148-51.

2. Soliman PT, Slomovitz BM, Broaddus RR, Sun CC, Oh JC, Eifel PJ, Gershenson DM, Lu KH. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases. *Gynecol Oncol* 2004;94:456-62.
3. Michelsen TM, Pripp AH, Tonstad S, Trope CG, Dorum A. Metabolic syndrome after risk-reducing salpingo-oophorectomy in women at high risk for hereditary breast ovarian cancer: a controlled observational study. *Eur J Cancer* 2009;45:82-9.
4. Dorum A, Tonstad S, Liavaag AH, Michelsen TM, Hildrum B, Dahl AA. Bilateral oophorectomy before 50 years of age is significantly associated with the metabolic syndrome and Framingham risk score: a controlled, population-based study (HUNT-2). *Gynecol Oncol* 2008;109:377-83.
5. Pellerin GP, Finan MA. Endometrial cancer in women 45 years of age or younger: a clinicopathological analysis. *Am J Obstet Gynecol* 2005;193:1640-4.
6. Lee TS, Lee JY, Kim JW, Oh S, Seong SJ, Lee JM, Kim TJ, Cho CH, Kim SM, Park CY. Outcomes of ovarian preservation in a cohort of premenopausal women with early-stage endometrial cancer: a Korean Gynecologic Oncology Group study. *Gynecol Oncol* 2013;131:289-93.
7. Wright JD, Buck AM, Shah M, Burke WM, Schiff PB, Herzog TJ. Safety of ovarian preservation in premenopausal women with endometrial cancer. *J Clin Oncol* 2009;27:1214-9.
8. Lee TS, Kim JW, Kim TJ, Cho CH, Ryu SY, Ryu HS, Kim BG, Lee KH, Kim YM, Kang SB; Korean Gynecologic Oncology Group. Ovarian preservation during the surgical treatment of early stage endometrial cancer: a nation-wide study conducted by the Korean Gynecologic Oncology Group. *Gynecol Oncol* 2009;115:26-31.
9. Koskas M, Bendifallah S, Luton D, Darai E, Rouzier R. Safety of uterine and/or ovarian preservation in young women with grade 1 intramucous endometrial adenocarcinoma: a comparison of survival according to the extent of surgery. *Fertil Steril* 2012;98:1229-35.
10. Gu H, Li J, Gu Y, Tu H, Zhou Y, Liu J. Survival impact of ovarian preservation on women with early-stage endometrial cancer: A systematic review and meta-analysis. *Int J Gynecol Cancer* 2017;27:77-84.
11. Sun C, Chen G, Yang Z, Jiang J, Yang X, Li N, Zhou B, Zhu T, Wei J, Weng D, Ma D, Wang C, Kong B. Safety of ovarian preservation in young patients with early-stage endometrial cancer: a retrospective study and meta-analysis. *Fertil Steril* 2013;100:782-7.
12. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR, Sessa C; ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: Diagnosis, Treatment and Follow-up. *Int J Gynecol Cancer* 2016;26:2-30.
13. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology. [https://www.nccn.org/professionals/physician\\_gls/pdf/aml.pdf](https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf).