

# Feasibility of hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian cancer during COVID-19 pandemic

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## HIGHLIGHTS

- Ovarian cancer surgery should not be completely postponed during a pandemic.
- Performing cytoreductive surgery and HIPEC during a pandemic appears to be safe and feasible.
- Adherence to precautions and performing the procedure in COVID-19-free clinics will minimize potential risks.

## ABSTRACT

**Objective** This study aims to evaluate the effect of the COVID-19 pandemic and related restrictions on patients who underwent cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for ovarian cancer.

**Methods** We retrospectively evaluated ovarian cancer patients who underwent HIPEC following complete cytoreductive surgery performed during the outbreak of the COVID-19 pandemic in three different centers specializing in gynecological oncology. All patients who underwent cytoreduction plus HIPEC for a primary, interval, and recurrent surgery were evaluated. Primary outcomes was postoperative 30-day morbidity and mortality. The secondary outcome was infection of patient and/or related staff with COVID-19 during the perioperative or early postoperative period.

**Results** We performed a total of 35 HIPEC procedures during the pandemic: 15 (42.9%) patients underwent primary/interval surgery, while 20 (57.1%) patients had recurrent disease. Grade 3–4 complications occurred in one patient (2.9%) (chronic renal failure), while mortality did not occur in any patient. Neither the patients nor related staff were infected with the coronavirus during the perioperative or early postoperative period. One patient, who was diagnosed with COVID-19 pneumonia on postoperative day 80 died from the infection. Another patient died on postoperative day 85 due to progressive ovarian cancer, a disorder in vital functions, and organ failure.

**Conclusion** HIPEC during the COVID-19 pandemic seems a safe and feasible procedure, with acceptable morbidity and mortality rates. Careful selection of patients is important and precautions should be taken before the procedure.

## INTRODUCTION

The vast majority of ovarian cancer patients are diagnosed at an advanced stage, and despite all treatment options, ovarian cancer remains the most lethal cancer among gynecological neoplasms.[1] The standard treatment of ovarian cancer is cytoreductive surgery followed by intravenous chemotherapy, however, in recent years cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (HIPEC) may potentiate the therapeutic efficacy. Nonetheless, the effectiveness of HIPEC on survival in ovarian cancer patients has not been proven in prospective studies.[2 3] According to the results of a phase III study conducted in patients with recurrent ovarian cancers, although including a limited number of patients, the favorable impact of cytoreductive surgery plus HIPEC on survival compared with the application of cytoreduction alone was reported.[4] Also, van Driel et al showed that the addition of HIPEC to interval cytoreduction in ovarian cancers improves survival.[3] Recently, outcomes obtained from these studies have encouraged clinicians to use HIPEC after cytoreduction and it has become a standard practice after interval cytoreduction in many centers.[2–4]

The increasing impact of the COVID-19 pandemic has also brought regulations in gynecological oncology. With the recommendation of the European Society of Gynecological Oncology, cytoreductive surgery performed in an advanced stage or recurrent ovarian cancers has been evaluated as semi-urgent, and it has been proposed that surgery may be performed within 1–4 weeks.[5] Also, the European Society of Medical Oncology stated that considering the risk-benefit ratio for patients during the pandemic period, cytoreductive surgery in ovarian cancer may be delayed up to 6 weeks at the latest.[6] However, it was emphasized to refer patients to a COVID-19-free comprehensive cancer center specializing in the treatment of gynecological malignancies.[6] On the other hand, the FRANCOGYN group recommended that, in order to avoid postoperative complications and possible issues such as hospital bed occupancy and intensive care unit support, neoadjuvant chemotherapy, with the increased number of cycles, should be given priority in ovarian cancers, and HIPEC should not be performed unless the hospital conditions are suitable in the COVID-19 period.[7]

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In the study of Ayhan et al, as well as others, it was reported that gynecological cancer surgery may be performed during the pandemic period provided that strict measures are considered.[8 9] However, there is not sufficient information regarding the application of HIPEC following cytoreductive surgery. We aimed to examine the short-term outcomes of patients who underwent cytoreduction and HIPEC in three centers specializing in gynecological cancer treatment, during the COVID-19 pandemic.

## METHODS

### Study Population

In Turkey, the first cases and deaths from the COVID-19 pandemic were officially reported by the Turkish Republic Ministry of Health in March 2020.[10] Ovarian cancer patients who underwent HIPEC procedure following complete cytoreduction in gynecological oncology units of Baskent University Ankara Hospital, Baskent University Adana Hospital, and Vehbi Koc Foundation Healthcare Organization Departments (Koc University Hospital and Istanbul American Hospital) between March 2020 and December 2020 were included in the study. All patients who underwent cytoreduction plus HIPEC for a primary, interval, and recurrent surgery were included. Ovarian cancer patients who did not undergo HIPEC due to incomplete cytoreductive surgery were excluded. HIPEC procedures performed for non-ovarian malignancies were also excluded (appendix, pseudomyxoma peritonei, malignant mesothelioma).

### Ethical Approval and Informed Consent

In all centers, possible perioperative and postoperative complications of cytoreductive surgery plus HIPEC procedure were explained in detail and informed consent was obtained. This study was approved by the Turkish Republic Ministry of Health Scientific Research Platform (application number=2020–12–29T20-25-17) and Baskent University Institutional Review Board (project number=KA21/03) and supported by Baskent University Research Fund.

### COVID-19 Tests and Precautions

All patients were tested with oro- and nasopharyngeal swabs (COVID-19 PCR test) and thorax CT 3 to 5 days prior to surgery. The patients were asked to self-isolate during the testing process. Cases with negative COVID-19 PCR test and cases without COVID-19 pneumonia signs in chest CT were operated on. The surgical and anesthetic risks that COVID-19 confers to patients in case of falsely negative test results were also discussed with all patients preoperatively. Surgery of asymptomatic patients with positive COVID-19 test was postponed for a minimum of 1 month and was performed after the recovery period was completed. In symptomatic patients with positive COVID-19 tests, the surgical procedure was performed after recovery. In case of fever, respiratory symptoms, or suspected test results, patients were transferred to Pandemic Clinics of the center. COVID-19 treatment protocol for patients and staff was applied by the Department of Infectious Diseases in a different center.

With the onset of the pandemic, elective procedures were postponed, only gynecologic cancer surgeries and emergent cases were performed. The time of hospital stay was shortened as possible. Visitor entrances to the hospital were prohibited and the number of attendants was restricted. Telemedicine was used to avoid unnecessary hospital visits. Patients with suspected COVID-19 infection were directed to separate centers, where pandemic patients were examined and treated. Stairs and elevators used by patients and healthcare professionals were separated. During this period, healthcare personnel were employed on flexible shifts. Hygiene, distance, and isolation rules were in compliance with hospital policy, and hospital stays were arranged for personnel with high risk of contamination. The number of people in resting rooms, elevators, surgical rooms, and refectory were restricted. Personal protective equipment was used by all surgery staff. Temperatures of the staff were measured daily and COVID-19 nasopharyngeal swab samples were taken at regular intervals.

### Treatment Plan

In all centers, HIPEC application was decided in line with the joint consensus of the oncology council with multidisciplinary participation, which included gynecological oncologist, medical oncologist, radiation oncologist, experienced pathologist, and radiologist. All operations were performed by experienced gynecological oncology specialists working in the same clinics. In all three centers, HIPEC procedure is routinely recommended for interval surgeries, provided that complete cytoreduction is achieved. Individual decisions for primary/recurrent cases are made in the joint consensus of the oncology council. HIPEC is not performed in patients with extra-abdominal metastasis or unresectable liver parenchymal involvement on preoperative imaging, as well as in cases of incomplete cytoreduction. Furthermore, patient demand, additional cost, and performance status of the patient are other factors that determine the decision for HIPEC.

### Surgical Procedures

Cytoreduction was performed in all cases with complete gross resection. Immediately after the completion of surgery, HIPEC was applied using a perfusion pump and placing two inlet and two outlet drainage catheters and two heat probes, with a closed technique after closing the entire abdomen. Drains were also kept in the postoperative period. HIPEC was applied at 41.5°C–42.5°C constant temperature for 60 min with dosages of carboplatin (area under the curve 5 or 6), cisplatin as 75–80 mg/m$^2$ (at the condition of glomerular filtration rate >100 mL/min), and mitomycin as 30 mg/m$^2$.

### Postoperative Care and Follow-up

All patients were admitted to the intensive care unit for at least 24 hours after surgery in all centers. Close monitoring of vital signs, amount of input, and output as well as drainage of the catheters, daily measurement of complete blood count, urea, creatinine, and blood gases were performed regularly. Drains were kept for at least 24 hours' postoperatively and removed gradually. Patients who had grade 3–4 complications according to the Clavien Dindo classification postoperatively were recorded.[11] Intravenous chemotherapy was administered on the 21st day after surgery.

### Study Measures

Clinical characteristics of the patients including age, body mass index, co-morbidities, Eastern Cooperative Oncology Group performance status (ECOG), American Society of Anesthesiologists (ASA) Physical Status Classification System score, presence of preoperative ascites (cut-off level >500 mL), serum albumin and serum

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CA125 levels, histology, peritoneal cancer index, and grade and stage of tumor were extracted from the hospital records

Chemotherapy regimens applied before surgery, platinum sensitivity in recurrent cases, and systemic treatment characteristics including the use of bevacizumab and poly (ADP-ribose) polymerase (PARP1) inhibitors before and after surgery were determined. Data regarding details of the HIPEC procedure, type of surgery, additional surgical procedures performed (bowel resection, presence of anastomosis, stoma opening), length of stay in the intensive care unit, and duration of hospitalization were recorded. Furthermore, postoperative complications and mean follow-up months were determined. Mean follow-up time was defined as the time from surgical procedure to the last control date or death. Platinum sensitivity was defined as the development of relapse at least 6 months later after the last platinum-based chemotherapy.

Primary outcomes were determined as postoperative 30-day morbidity and mortality. The secondary outcome was infection of the patient and/or related staff with the coronavirus during the perioperative or early postoperative period.

### Data Analysis

Statistical Package for the Social Sciences (SPSS) 21.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, while continuous measurements were defined as mean and standard deviation (median and range where necessary). Descriptive statistics were performed.

## RESULTS

A total of 35 patients who underwent cytoreductive surgery plus HIPEC for ovarian cancer in gynecological oncology centers of Baskent University Ankara Hospital (n=12), Baskent University Adana Hospital (n=15), and Vehbi Koc Foundation Healthcare Organization Departments (n=8) (Istanbul Koc University (n=5), and Istanbul American Hospital (n=3)) were included in the study. Clinical features of the included patients are demonstrated in Table 1.

Fifteen (42.9%) patients had primary surgery (interval surgery, n=11), and 20 (57.1%) procedures were performed for recurrent disease. Multiple metastatic foci were observed in 33 of 35 patients. Peritoneal involvement was present in all patients who underwent cytoreduction. Also, there was intestinal involvement in 14 (70%), liver involvement in eight (22.9%), and spleen involvement in two (5.8%) patients. In patients with recurrent disease, the mean elapsed time after the last chemotherapy was 5.5 (range, 1–36) months, and platinum sensitivity was 70%. Chemotherapy and surgical treatment features of the patients are summarized in Table 2. Poly ADP-ribose polymerase inhibitors were not used before or after surgery.

HIPEC was not applied in one patient since complete cytoreduction could not be performed. The operation of one patient was postponed for 2 months due to COVID-19 infection. Neither the patients nor related staff were infected with the coronavirus during the perioperative or early postoperative period. There was no mortality in the first 30 postoperative days. One patient was infected with coronavirus on postoperative day 80 during the chemotherapy and died due to pneumonia on the postoperative day 90. Another patient died on postoperative day 85 due to progressive disease, a disorder in vital functions, and organ failure. Chronic renal failure occurred in one patient (2.85%) (recurrent ovarian cancer) who was administered cisplatin (grade 3–4 complication). Postoperative complications, hospitalization durations, and short-term survival parameters of patients who underwent cytoreductive surgery plus HIPEC are presented in Table 3.

**Table 1** Clinical characteristics of the patients

| | |
|---|---|
| Median age, years (range) | 58 (42–73) |
| <70 years | 91.4% (32/35) |
| Median BMI*, kg/m$^2$ (range) | 29.2 (20.3–40.2) |
| BMI≥30 kg/m$^2$, n (%) | 12 (34.3) |
| Median preoperative serum CA125 level, IU/ml (range) | 302.7 (8–2655) |
| Median preoperative serum albumin level, g/dl (range) | 3.7 (2.6–4.5) |
| Median peritoneal cancer index, range | 17 (11–30) |
| Ascites, n (%) | 13 (37.1) |
| Median ECOG† performance status | 1 (0–2) |
| ASA‡ score, n (%) | |
| ASA II | 19 (54.3) |
| ASA III | 15 (42.8) |
| ASA IV | 1 (2.85) |
| Co-morbidity, n (%) | 22 (62.9) |
| 2 co-morbidities | 8 (22.9) |
| ≥3 co-morbidities | 2 (5.7) |
| Tumor histology, n (%) | |
| High-grade serous | 32 (91.45) |
| Mucinous | 1 (2.85) |
| Clear cell carcinoma | 1 (2.85) |
| Carcinosarcoma | 1 (2.85) |
| Stage, n (%) | |
| IIIb | 2 (5.7) |
| IIIc | 24 (68.6) |
| IV | 9 (25.7) |

*BMI=body mass index.
†ECOG=Median Eastern Cooperative Oncology Group.
‡ASA=American Society of Anesthesiologists Physical Status Classification System.

## DISCUSSION

### Summary of Main Results

Thirty-five patients underwent cytoreduction plus HIPEC at gynecological oncology centers in three different provinces during the 10 months since the COVID-19 pandemic cases were first reported in our country. Grade 3–4 complications were observed in only one patient (2.9%) and there were no mortalities in the postoperative 30-day period. Neither patients or related staff were infected with the coronavirus during the perioperative or early postoperative period.

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**Table 2** Chemotherapy and surgical features and details of the patients

| | |
|---|---|
| Number of chemotherapy lines before surgery | |
| 1st line | 26 (74.3) |
| ≥2nd line | 9 (25.7) |
| History of bevacizumab before surgery, n (%) | 11 (55) |
| History of bevacizumab after surgery, n (%) | 12 (34.3) |
| Type of surgery, n (%) | |
| Primary | 4 (11.4) |
| Interval | 11 (31.4) |
| Secondary | 16 (45.7) |
| Tertiary | 3 (8.6) |
| Quarternary | 1 (2.85) |

| Surgery details, n (%) | Primary/interval | Recurrent | Total |
|---|---|---|---|
| Bowel resection | 4 (11.4) | 7 (20) | 11 (31.4) |
| Presence of anastomosis | 2 (5.7) | 5 (14.3) | 7 (20) |
| Presence of stoma | 1 (2.8) | 4 (11.5) | 5 (14.3) |

### Results in the Context of Published Literature

With the continuation of the pandemic, the diagnosis of gynecological cancers has been reported to decrease.[12] It has also been shown that delayed diagnosis of cancer may impact tumor stage at diagnosis and clinical prognosis.[13] Considering the risk-benefit ratio in ovarian cancers, delay in treatment negatively affects the course of disease.[8] On the other hand, hospitalization, surgery, radiotherapy, and chemotherapy treatments during the pandemic may increase the transmission risk of COVID-19 infection.[14 15] Also, the risk of serious respiratory complications associated with COVID-19 infection in cancer patients is 4–8 times higher than the general population, especially complications that increase above the age of 70.[7 16] However, in our study, similar to another multicentric study, the transmission of COVID-19 infection during the hospital stay was not seen.[8] One of the most important messages is that these surgeries were performed in COVID-19 free clinics, and the necessary precautions were taken to the maximum effort.

In a review evaluating the treatment of peritoneal tumors in the COVID-19 pandemic, it was emphasized that performing HIPEC should be in expert centers, which have adequate conditions and may provide optimal perioperative care. Neoadjuvant chemotherapy shoud be given priority in patients with increased risk of major postoperative complications (advanced age, obesity, severe cardiovascular pathology, ASA III or IV risk). However, it should be noted that neoadjuvant chemotherapy over six cycles may delay interval surgery. For each case, the decision for the use of HIPEC should be made in expert centers by multidisciplinary consensus.[9]

In a study comparing gynecological cancer surgeries performed before and during the pandemic, complications in the first 30-day postoperatively were found to be higher during the pandemic, which was especially apparent in the first 3 months.[17–19] Also, median hospital stay and rate of bowel resection with stoma requirement were similar to the findings reported in patients who underwent cytoreduction plus HIPEC before the pandemic.[20 21] Although only one morbidity was observed among the patients who underwent HIPEC in the study, morbidities due to COVID-19 infection in other gyne-oncological surgeries were also observed in our study centers.

The most important morbidity during HIPEC is renal injury. To avoid this complication, appropriate patient selection along with a proper selection of the chemotherapeutic agent, perioperative sodium thiosulphate administration, and strict monitoring in the perioperative and postoperative periods should be done.[3 22] In our study, the median age of the patients who underwent cytoreductive surgery plus HIPEC was 58 years and all had normal serum albumin levels. Median ECOG performance status was 1. Co-morbidity was ≤2 in 94.3% of the patients, and ASA score was 4 only in one patient. Adequate hydration and diuresis were provided by adhering to procedural standards. Carboplatin was used instead of cisplatin in cases with glomerular filtration rate <100 mL/min. Renal failure occurred in one patient, who was administered cisplatin alone.

**Table 3** Hospitalization, postoperative complications, and short-term survival parameters after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy procedure

| | |
|---|---|
| Intensive care unit admission, n (%) | 35 (100) |
| Median length of hospital stay, range (days) | 9 (5–85) |
| Grade 3–4 complications, n (%) | 1 (2.85) |
| Recurrence of disease, n (%) | 5 (14.3) |
| Mean follow-up months, range | 4 (1–8) |
| Death, n (%) | 2 (5.7) |

### Strengths and Weaknesses

This is the first study in which the results of the HIPEC procedure in ovarian cancer are reported during the COVID-19 pandemic. However, retrospective design, the limited number of patients, variety of surgeries (primary/interval and secondary cytoreductive surgery), non-homogeneous HIPEC protocols in different centers, the inclusion of both platinum-sensitive and resistant disease, and the short follow-up period are the limitations of the study.

### Implications for Practice and Future Research

Since cytoreductive surgery plus HIPEC combination is applied to a limited number of patients throughout the world during the COVID-19 pandemic and there are few studies on the subject, information regarding the safety and effectiveness of this procedure is lacking. Additional larger studies with a longer follow-up are needed to support the safety and efficacy of HIPEC during this pandemic.

## CONCLUSION

Cytoreductive surgery plus HIPEC may be applied with acceptable morbidity and mortality in COVID-19 free centers by strictly adhering to the precautions during the pandemic period.

**Contributors** All authors contributed to the planning, development, and approval of the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## REFERENCES

1 Colombo N, Sessa C, du Bois A, *et al*. ESMO-ESGO Consensus Conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. *Ann Oncol* 2019;30:672–705.
2 González-Moreno S, González-Bayón LA, Ortega-Pérez G. Hyperthermic intraperitoneal chemotherapy: rationale and technique. *World J Gastrointest Oncol* 2010;2:68–75.
3 van Driel WJ, Koole SN, Sikorska K, *et al*. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. *N Engl J Med* 2018;378:230–40.
4 Spiliotis J, Halkia E, Lianos E, *et al*. Cytoreductive surgery and HIPEC in recurrent epithelial ovarian cancer: a prospective randomized phase III study. *Ann Surg Oncol* 2015;22:1570–5.
5 Ramirez PT, Chiva L, Eriksson AGZ, *et al*. COVID-19 global pandemic: options for management of gynecologic cancers. *Int J Gynecol Cancer* 2020;30:561–3.
6 Colombo I, Zaccarelli E, Del Grande M, *et al*. ESMO management and treatment adapted recommendations in the COVID-19 era: gynaecological malignancies. *ESMO Open* 2020;5:e000827.
7 Akladios C, Azais H, Ballester M, *et al*. Recommendations for the surgical management of gynecological cancers during the COVID-19 pandemic - FRANCOGYN group for the CNGOF. *J Gynecol Obstet Hum Reprod* 2020;49:101729.
8 Ayhan A, Oz M, Topfedaisi Ozkan N, *et al*. Perioperative SARS-CoV-2 infection among women undergoing major gynecologic cancer surgery in the COVID-19 era: a nationwide, cohort study from Turkey. *Gynecol Oncol* 2021;160:499–505.
9 Glehen O, Kepenekian V, Bouché O, *et al*. Treatment of primary and metastatic peritoneal tumors in the Covid-19 pandemic: proposals for prioritization from the RENAPE and BIG-RENAPE groups. *J Visc Surg* 2020;157:S25–31.
10 Demirbilek Y, Pehlivantürk G, Özgüler Zeynep Özge, *et al*. COVID-19 outbreak control, example of Ministry of health of turkey. *Turk J Med Sci* 2020;50:489–94.
11 Dindo D, Demartines N, Clavien P-A. Classification of surgical complications. *Ann Surg* 2004;240:205–13.
12 Tsibulak I, Reiser E, Bogner G, *et al*. Decrease in gynecological cancer diagnoses during the COVID-19 pandemic: an Austrian perspective. *Int J Gynecol Cancer* 2020;30:1667–71.
13 Neal RD, Tharmanathan P, France B, *et al*. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? systematic review. *Br J Cancer* 2015;112(Suppl 1):S92–107.
14 Yu J, Ouyang W, Chua MLK, *et al*. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol* 2020;6:1108–10.
15 Zhang L, Zhu F, Xie L, *et al*. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020;31:894–901.
16 COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet* 2020;396:27–38.
17 Leung E, Pervaiz Z, Lowe-Zinola J, *et al*. Maintaining surgical care delivery during the COVID-19 pandemic: a comparative cohort study at a tertiary gynecological cancer centre. *Gynecol Oncol* 2021;160:649–54.
18 Perrone AM, De Palma A, De Iaco P. COVID-19 global pandemic: options for management of gynecologic cancers. The experience in surgical management of ovarian cancer in the second highest affected Italian region. *Int J Gynecol Cancer* 2020;30.
19 Perrone AM, Dondi G, Giunchi S, *et al*. COVID-19 free oncologic surgical hub: the experience of reallocation of a gynecologic oncology unit during pandemic outbreak. *Gynecol Oncol* 2021;161:89–96.
20 Cascales-Campos P, Gil J, Gil E, *et al*. Cytoreduction and HIPEC after neoadjuvant chemotherapy in stage IIIC–IV ovarian cancer. critical analysis in elderly patients. *Eur J Obstet Gynecol Reprod Biol* 2014;179:88–93.
21 Gonzalez Bayon L, Steiner MA, Vasquez Jimenez W, *et al*. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for the treatment of advanced epithelial ovarian carcinoma: upfront therapy, at first recurrence, or later? *Eur J Surg Oncol* 2013;39:1109–15.
22 Angeles MA, Quenet F, Vieille P, *et al*. Predictive risk factors of acute kidney injury after cytoreductive surgery and cisplatin-based hyperthermic intra-peritoneal chemotherapy for ovarian peritoneal carcinomatosis. *Int J Gynecol Cancer* 2019;29:382–91.

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