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Original Article

A phase II, open-labeled, single-arm study of dose-dense paclitaxel plus carboplatin in advanced or recurrent uterine endometrial cancer treatment: a KCOG-G1303, DOENCA trial

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ABSTRACT

Objective: To determine the safety and efficacy of dose-dense (dd) paclitaxel (PTX) and carboplatin (CBDCA) in treating advanced or recurrent endometrial cancer.
Methods: Women aged 20–75 years with histologically confirmed endometrial cancer, the International Federation of Gynecology and Obstetrics (FIGO) stage III disease with some residual tumor, FIGO stage IV disease, recurrence after front-line curative treatment, or recurrence after second-line chemotherapy or radiotherapy were enrolled in this study. PTX (80 mg/m^2) was administered intravenously (IV) to every participant on days 1, 8, and 15, and CBDCA (area under the curve of 5) was administered IV on day 1 once every 3 weeks until the disease progressed, unacceptable adverse events occurred, or consent was withdrawn. The primary endpoint was the response rate (RR), while the secondary endpoints were progression-free survival, overall survival, and adverse effects.
Results: Forty-eight participants were enrolled, and 46 were eligible to receive treatment. The patients' median age was 61 years (range, 43–76 years). Twenty-two participants had experienced recurrence, and the remaining patients had primary advanced endometrial cancer. There were 10 cases of serous carcinoma, 3 cases of endometrioid carcinoma G3, 2 cases of carcinosarcoma, and 2 cases of clear-cell carcinoma according to histology. Twenty-nine participants (63.0%) received ≥6 cycles of chemotherapy. The RR (complete, 13 cases; partial, 20 cases) was 71.3% (95% confidence interval: 59.0%–84.5%).
Conclusion: The dd PTX with CBDCA is feasible and available as a treatment option for advanced or recurrent endometrial cancer.

Trial Registration: UMIN Clinical Trials Registry Identifier: UMIN000017138

Keywords: Endometrial Cancer; Chemotherapy; Paclitaxel; Carboplatin

Trial Registration
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Presentation
We presented the abstract of our study at the American Society of Clinical Oncology annual meeting 2019: Journal of Clinical Oncology 37, No. 15_suppl (May 20, 2019) 5584-5584 (DOI: 10.1200/JCO.2019.37.15_suppl.5584).

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Data sharing statement
We complied with the International Committee of Medical Journal Editors recommendations for data sharing statement policy (http://icmje.org/icmje-recommendations.pdf). All the researchers who obtained an independent Institutional Review Board's (IRB's) approval to analyze our data can apply to use our anonymized data. Researchers may send their application forms along with the researcher's signature and the IRB's approval documents to hori-kensuke@kansaih.johas.go.jp within 36 months of this manuscript being published. Our trial's protocol is always open at the Kansai Clinical Oncology Group (KCOG) website (https://www.kcog.net/).

Author Contributions
Conceptualization: I.K.; Data curation: H.K.; Formal analysis: H.K.; Funding acquisition: I.K.; Investigation: N.S., U.K., K.Y., K.E., T.K.; Methodology: N.S.; Project administration: N.S.; Software: H.K.; Supervision: N.S.; Validation: N.S., I.K.; Visualization: H.K.; Writing - original draft: H.K.; Writing - review & editing: I.K.

INTRODUCTION

Recently, endometrial cancer has become the most common gynecologic malignancy in Japan. In 2014, the incidences of stages IA, IB, II, IIIA, IIIB, IIIC1, IIIC2, IVA, and IVB endometrial cancer were 54.8%, 17.1%, 6.0%, 3.7%, 0.9%, 4.5%, 4.2%, 0.3%, and 7.2%, respectively. The 5-year overall survival (OS) rates for stages I, II, III and IV endometrial cancer were 94.6%, 89.4%, 78.3%, and 25.0%, respectively. Generally, most patients with early endometrial cancer have a good prognosis. However, this is not the case in those with advanced endometrial cancer. For patients with stages IIIA, IIIB, IIIC, IVA, and IVB, the 5-year OS rates were 83.8% 60.0%, 75.5%, 16.4%, and 24.7%, respectively [1]. Endometrial cancer remains fatal despite the multidisciplinary effort.

For a long time, the combination of chemotherapies available to treat advanced and recurrent endometrial cancers have been tri-weekly doxorubicin and cisplatin (AP) or tri-weekly paclitaxel (PTX) and carboplatin (CBDCA) [2-5]. Dose-dense (dd) PTX plus CBDCA treatment for ovarian cancer results in better survival than conventional therapy, at least in Japan. A previous feasibility study of dd treatment for endometrial cancer found that 90% of patients can be treated with >3 courses of PTX 80 mg/m^2 on days 1, 8, and 15 and CBDCA (area under the curve [AUC]=5) on day 1, demonstrating the tolerability of this regimen [6]. Nevertheless, to the best of our knowledge, the efficacy of this dd treatment has not been clearly demonstrated. Therefore, our study aimed to elucidate the safety and efficacy of dd PTX combined with CBDCA in treating patients with advanced or recurrent endometrial cancer.

MATERIALS AND METHODS

Our study design (**Fig. 1**), was approved by the Institutional Review Board of each participating facility. Seventeen facilities participated in this study, and 6 facilities registered the enrolled participants in Japan. As planned, the registration started in April 2013 and ended in March 2018.

Women aged 20–75 years with histologically confirmed endometrial cancer, including endometrioid carcinoma, clear-cell carcinoma, squamous cell carcinoma, serous carcinoma, mucinous carcinoma, transitional cell carcinoma, undifferentiated carcinoma, and

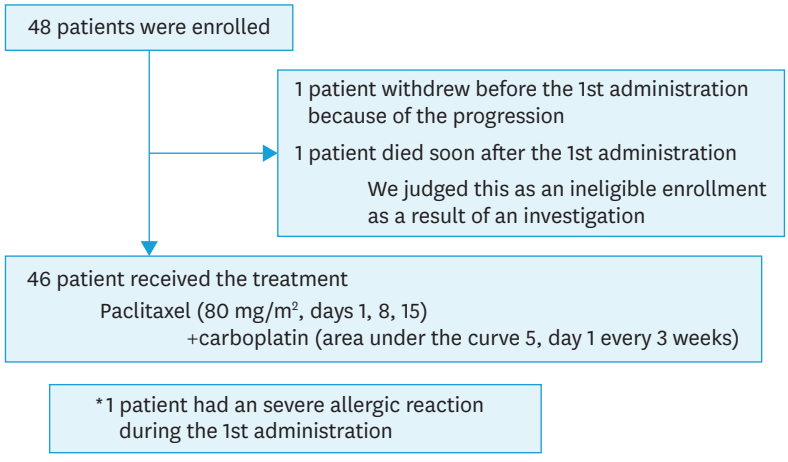

Fig. 1. A flowchart shows all eligible patients after their enrollment.

carcinosarcoma, and either the International Federation of Gynecology and Obstetrics (FIGO) stage III disease with some residual tumor, FIGO stage IV disease, recurrence after front-line curative treatment, or recurrence after second-line chemotherapy or radiotherapy were enrolled in this study. The inclusion criteria were patients: 1) without any prior therapy; 2) for whom >6 months had passed after receiving chemotherapy with platinum and taxane (only one regimen was permitted) or >3 months had passed after receiving non-platinum and non-taxane chemotherapy; 3) with a measurable lesion; 4) without bilateral hydronephrosis; 5) with an Eastern Cooperative Oncology Group performance status of 0–2; 6) with the following laboratory data available within 2 weeks of treatment: a) neutrophil count, ≥1,500/mm^3; b) platelet count, ≥100,000/mm^3; c) hemoglobin, ≥10 g/dL; d) total bilirubin, ≥1.5 mg/dL; e) serum creatinine, ≤1.5 mg/dL; f) creatinine clearance calculated by the Cockcroft's formula, ≥50 mL/min; 7) with an expected life prognosis of ≥3 months; and 8) who provided written informed consent. In contrast, the exclusion criteria were as follows: 1) motor or sensory neuropathy resulting in dysfunction; 2) extreme sensitivity to alcohol; 3) bacterial infection requiring treatment; 4) myocardial infarction occurring within 6 months; 5) unstable angina pectoris; 6) poorly controlled diabetes; 7) any multiple active malignancies; 8) interstitial pneumonia or pulmonary fibrosis; 9) PTX or CBDCA not indicated; 10) hepatitis B surface antigen positivity; 11) adynamic ileus or mechanical bowel obstruction; 12) history of any severe drug allergies; and 13) considered unfit to participate in the study as assessed by the investigators. The primary endpoint was the response rate (RR) to the study treatment, and the secondary endpoints were progression-free survival (PFS), OS, and adverse effects. The RR had been evaluated to check compliance with the response evaluation criteria in solid tumors (RECIST) guideline (version 1.1) [7].

Each patient received PTX (80 mg/m^2) on days 1, 8, and 15 intravenously (IV) and CBDCA (AUC of 5) on day 1 IV and then every 3 weeks thereafter until the disease progressed according to the RECIST guideline, unacceptable adverse events occurred, or consent was withdrawn.

The maximum cycle was not set; however, the trial treatment was continued either till the disease progressed or toxicity was intolerable. Each treatment cycle could be started if all the following conditions were met within 3 days before administration of the drugs: 1) neutrophil counts ≥1,500/mm^3; 2) platelet counts ≥75,000/mm^3; 3) performance status of 0–2; 4) serum creatinine ≤5 mg/mL; 5) axillary temperature ≤38°C; 6) liver dysfunction ≤grade 1; 7) fatigue, diarrhea, and/or nausea ≤grade 1. **Table 1** and **Supplementary Table 1** describes the dose levels and the criteria for dosage reduction.

We set the RR threshold at 40%, and the expected RR of this treatment at 60% showed that the number of patients calculated with an alpha error (type 1) of 5% and power (1-β; beta error or type 2 error) of 80% was 44. Fleming et al., reported that the RR of PTX, cisplatin,

Table 1. Setting the dose level

Drugs	Dose levels	Doses administered
Paclitaxel	0	80 mg/m^2
	–1	70 mg/m^2
	–2	60 mg/m^2
	–3	Discontinued
Carboplatin	0	AUC=5
	–1	AUC=4
	–2	AUC=3
	–3	Discontinued

AUC, area under the curve.

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and doxorubicin (TAP) regimens was 57% [8,9]. Similarly, Miller et al., [10] reported the RR of both PTX plus CBDCA (TC) and TAP to be approximately 50%. The RR of our trial treatment using one of the conventional TCs was expected to increase by 20%.

Therefore, the expected RR of this treatment was set to 60%. We set the target number of cases to 48 because we considered that some patients may withdraw for any reason.

We performed statistical analyses with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [11]. For more precision, it was designed as a modified version of R commander with statistical functions available in biostatistics.

RESULTS

Of the 48 participants that were enrolled, 46 were qualified to receive treatment. One patient withdrew before the first treatment administration because of disease progression. One patient died shortly after the first treatment. The dead patient was recognized and registered as an eligible participant by one of the co-researchers. We briefly stopped enrolling participants and afterwards, we observed the manifestations of severe adverse events. We investigated the pre-treatment status and the cause of death in detail. Finally, we determined that the patient died of the primary disease. Deviation from our eligibility criteria on performance status was observed by a co-researcher. Accordingly, we paid extra attention to all co-researchers and subsequently resumed enrollment of participants into this study. Another patient experienced a severe allergic reaction during the first cycle and we included this case for further analysis (**Fig. 1**). Finally, 46 participants received the dd treatment, and the median age was 61 years (range, 43–76 years). At the time of enrollment, 22 participants had experienced recurrence, and the remaining patients had advanced primary endometrial cancer. Regarding the histology, there were 10 patients with serous carcinoma, 3 patients with endometrioid carcinoma G3, 2 patients with carcinosarcoma, and 2 patients with clear-cell carcinoma (**Table 2**). Unfortunately, we could not diagnose the grade of endometrial carcinoma in 4 patients by endometrial biopsy because none of them underwent surgery.

Table 2. Histology and clinical stage(n=46)

Characteristics	Values
Histology	
Endometrioid carcinoma	14
G1	
G2	9
G3	3
Unidentified*	4
Serous carcinoma	10
Clear-cell carcinoma	2
Carcinosarcoma	3
Undeterminable	1
Total	46
Clinical stage	
Primary advanced	24
FIGO stage IV	22
IIIC1	1
IIIC2	1
Recurrence	22

FIGO, International Federation of Gynecology and Obstetrics.
*We could not diagnose a grading of endometrial carcinoma for 4 patients by endometrial biopsy.

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The median treatment-free interval in recurrent patients was 41.7 months (range, 6.8–76.0 months). Four of these patients had never received adjuvant therapy after cytoreductive surgery and 13 had received a taxane plus platinum regimen.

Twenty-nine participants (63.0%) underwent ≥6 cycles of chemotherapy (**Table 3**). Twenty-one participants had grade ≥3 neutropenia, and 13 participants had decreased hemoglobin levels (grade ≥3). In total, 20 participants experienced some non-hematologic events. The details of the adverse events are presented in **Table 4**. Furthermore, 29 patients experienced treatment delay. However, PTX dosage was reduced for only 7 patients, and CBDCA dosage was reduced for 2 patients. Twenty-two and 2 patients experienced grade 1 and grade 2 peripheral neuropathy, respectively.

Table 3. Clinical outcomes (n=46)

Cycles of the study treatment	Patients
Cycles	
0	1 (2.2)
1	3 (6.5)
2	2 (4.3)
3	4 (8.7)
4	4 (8.7)
5	3 (6.5)
6	24 (52.2)
7	1 (2.2)
8	0 (0.0)
9	4 (8.7)
Response rate interval*	
Complete	13 (28.3)
Partial	20 (43.5)
Stable	5 (10.9)
Progression	7 (15.2)
Undeterminable	1 (2.2)

Values are presented as number of patients (%).
*71.3% (95% confidence interval=59.0%–84.5%).

Table 4. Adverse events

Adverse events	Any grade	Grade 3/4
>G3/4 Hematologic events		
Neutropenia G3		17 (36.9)
Neutropenia G4		4 (8.7)
Anemia G3		13 (28.3)
Anemia G4		0 (0)
Severe non-hematologic events		
Alopecia	34 (73.9)	-
Anorexia	11 (23.9)	0 (0)
Nausea/vomiting	10 (21.7)	0 (0)
Constipation	10 (21.7)	0 (0)
Allergy	6 (13.0)	3 (6.5)
Infection	6 (13.0)	3 (6.5)
Diarrhea	3 (6.5)	0 (0)
Cerebral infarction	1 (2.1)	0 (0)
Wound hernia	1 (2.1)	1 (2.1)
Stomatitis	2 (4.3)	1 (2.1)
Enterocutaneous fistula	1 (2.1)	1 (2.1)
Ileus	1 (2.1)	1 (2.1)
Fatigue	1 (2.1)	1 (2.1)
Pulmonary embolism	1 (2.1)	1 (2.1)
Peripheral neuropathy	24 (52.1)	0 (0)

Values are presented as number (%).

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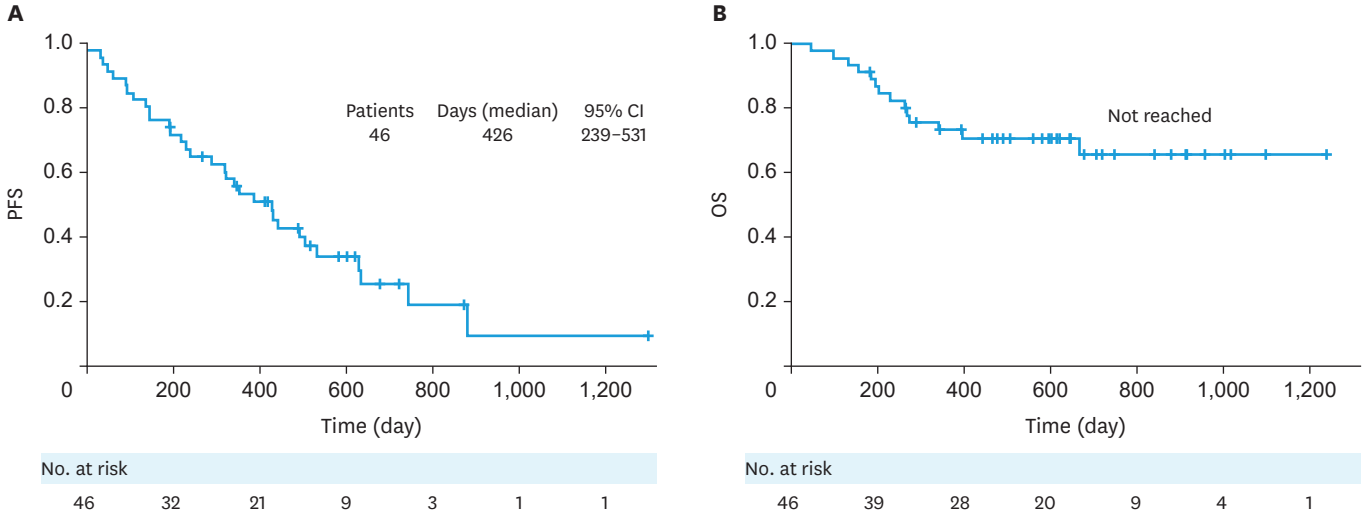

Fig. 2. PFS after the study treatment. (A) PFS, (B) OS.
PFS, progression-free survival; OS, overall survival; CI, confidence interval.

The RR (complete, 13 cases; partial, 20 cases) evaluated by RECIST was 71.3% (95% confidence interval [CI]=59.0–84.5) (**Table 4**). The median PFS was 14.2 months (95% CI=8.0–17.7), and the OS was not assessed within the planned follow-up period (**Fig. 2**).

DISCUSSION

We observed that treatment of advanced or recurrent endometrial cancer with dd PTX and CBDCA is a feasible regimen. Twenty-one patients had grade 3/4 neutropenia, 13 patients had decreased hemoglobin levels (grade 3), and 6 patients had grade 3 non-hematotoxicity. However, despite this, 29 patients (63.0%) received ≥6 cycles of chemotherapy. Therefore, we conclude that this study regimen has several acceptable side effects and is feasible.

Furthermore, severe peripheral neuropathy (grade 3 or 4), which was of concern, was not experienced. However, 3 patients did not comply with our guidelines for reduction as they requested the attending doctor for a reduction in the dosage of PTX because they could not endure grade 1 peripheral neuropathy. No participant withdrew from the study because of peripheral neuropathy. Most importantly, peripheral neuropathy is one of the most unbearable adverse events experienced by cancer patients receiving chemotherapy.

Several trials of dd PTX plus CBDCA for advanced ovarian cancer have been reported previously [12-17]. These studies observed that the toxicity of the PTX plus CBDCA regimen was stronger than that of tri-weekly PTX and CBDCA. Supposedly, the reason for these findings was that Katsumata et al., [12,13] and other researchers set the dosage of CBDCA to an AUC of 6 mg•h/L. However, the number of patients was higher in the dd regimen group than in the conventional regimen group (n=113 vs. n=69) [9,10]. The ICON8 trial was set at an AUC of 5 or 6, based on the investigators' discretion [14]. Furthermore, Jaffe's method of measuring serum creatinine, which is common in Western countries, is different from the enzymatic method used in Japan [18]. Based on these findings, we set the dosage of CBDCA to an AUC of 5 in advance to avoid this outcome.

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Second, we observed that the regimen was available for advanced or recurrent endometrial cancer. The RR of our regimen was equivalent to that of the conventional treatment. In other words, the dd treatment is not superior; rather, it is an alternative treatment for advanced or recurrent endometrial cancer.

Doxorubicin and AP had RR rates ranging between 42% to 43% in the GOG107 and EORTC55872 phase III trials. Additionally, AP with PTX (TAP) was superior to AP without PTX. The RR of TAP was 57%; however, the TAP regimen was unacceptable because of its high toxicity rate [8]. In recent times, the tri-weekly PTX plus CBDCA regimen was often used in many patients with advanced and recurrent endometrial cancer because of its high RR of 50–78%, as reported by 2 phase II clinical trials [4,5]. The RR in our study was 71.3%. Unfortunately, it remained within the previously reported RR range mentioned above. In contrast, a retro-prospective study reported that dd treatment was superior to the conventional treatment for advanced endometrial cancer [19], and we cannot deny the possibility of this phenomenon.

There are 2 limitations to our study. One of the limitations is that this was a phase II trial. Fundamentally, we should proceed to plan the phase III trial because our primary endpoint was met. However, our findings indicated that dd therapy was equivalent but not superior to previous regimens. Recent international studies have reported that the dd PTX plus CBDCA regimen is not a superior treatment option for the treatment of ovarian cancer. There are also scarce data to suggest that it is only effective in the Japanese population [12-17]. We hypothesized that these conflicting results originated not only because of racial differences but also because of the usage of bevacizumab for the treatment of patients with ovarian cancer. All the patients enrolled into the JGOG3016 trial did not receive a maintenance therapy with bevacizumab. When we had just planned our trial, there were no drugs except platinums, anthracyclines, and taxanes for the treatment of endometrial cancer. While we took more time than we had planned to collect the required number of participants, the scenario changed significantly. Particularly, new agents, including immune checkpoint inhibitors and other molecular targeted therapeutics agents for endometrial cancer patients, were introduced recently. Currently, many trials with these new agents for advanced or recurrent endometrial cancer are in progress, for example, the KEYNOTE-775 trial with pembrolizumab and lenvatinib for the treatment of patients with advanced endometrial cancer (https://clinicaltrials.gov/ct2/show/NCT03517449), and we expect favorable results from these trials. Thus, it may be unwise to continue studying the next phase of dd treatment for advanced or recurrent endometrial cancer. We have planned some trials with recent immune checkpoint inhibitors for the treatment of endometrial cancer patients. Second, most of our participants supposedly received post-treatments, including surgery, radiotherapy, additional chemotherapy, and/or hormonal therapy, after the end of each treatment. Nevertheless, post-therapies (after the completion of our study) were neither defined nor followed-up. To the best of our knowledge, 2 patients underwent surgery, and 3 received radiotherapy. Thus, we should rather institute multidisciplinary treatments for patients with advanced and recurrent endometrial cancer.

In conclusion, dd TC is feasible and available for the treatment of advanced or recurrent endometrial cancer. However, this treatment regimen is less convenient than the previously reported regimens.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1

Setting the criteria for dosage reduction

Click here to view

REFERENCES

1. Yamagami W, Nagase S, Takahashi F, Ino K, Hachisuga T, Aoki D, et al. Clinical statistics of gynecologic cancers in Japan. J Gynecol Oncol 2017;28:e32.
PUBMED | CROSSREF
2. Thigpen JT, Brady MF, Homesley HD, Malfetano J, DuBeshter B, Burger RA, et al. Phase III trial of doxorubicin with or without cisplatin in advanced endometrial carcinoma: a gynecologic oncology group study. J Clin Oncol 2004;22:3902-8.
PUBMED | CROSSREF
3. van Wijk FH, Aapro MS, Bolis G, Chevallier B, van der Burg MEL, Poveda A, et al. Doxorubicin versus doxorubicin and cisplatin in endometrial carcinoma: definitive results of a randomised study (55872) by the EORTC Gynaecological Cancer Group. Ann Oncol 2003;14:441-8.
PUBMED | CROSSREF
4. Hoskins PJ, Swenerton KD, Pike JA, Wong F, Lim P, Acquino-Parsons C, et al. Paclitaxel and carboplatin, alone or with irradiation, in advanced or recurrent endometrial cancer: a phase II study. J Clin Oncol 2001;19:4048-53.
PUBMED | CROSSREF
5. Nomura H, Aoki D, Takahashi F, Katsumata N, Watanabe Y, Konishi I, et al. Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma: a Japanese Gynecologic Oncology Group study (JGOG2041). Ann Oncol 2011;22:636-42.
PUBMED | CROSSREF
6. Ito K, Tsubamoto H, Itani Y, Kuroboshi H, Fujita H, Nobunaga T, et al. A feasibility study of carboplatin and weekly paclitaxel combination chemotherapy in endometrial cancer: a Kansai Clinical Oncology Group study (KCOG0015 trial). Gynecol Oncol 2011;120:193-7.
PUBMED | CROSSREF
7. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-47.
PUBMED | CROSSREF
8. Fleming GF, Brunetto VL, Cella D, Look KY, Reid GC, Munkarah AR, et al. Phase III trial of doxorubicin plus cisplatin with or without paclitaxel plus filgrastim in advanced endometrial carcinoma: a Gynecologic Oncology Group Study. J Clin Oncol 2004;22:2159-66.
PUBMED | CROSSREF
9. Fleming GF, Filiaci VL, Bentley RC, Herzog T, Sorosky J, Vaccarello L, et al. Phase III randomized trial of doxorubicin + cisplatin versus doxorubicin + 24-h paclitaxel + filgrastim in endometrial carcinoma: a Gynecologic Oncology Group study. Ann Oncol 2004;15:1173-8.
PUBMED | CROSSREF
10. Miller DS, Filiaci VL, Mannel RS, Cohn DE, Matsumoto T, Tewari KS, et al. Carboplatin and paclitaxel for advanced endometrial cancer: final overall survival and adverse event analysis of a phase III trial (NRG Oncology/GOG0209). J Clin Oncol 2020;38:3841-50.
PUBMED | CROSSREF

11. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452-8.
PUBMED | CROSSREF
12. Katsumata N, Yasuda M, Takahashi F, Isonishi S, Jobo T, Aoki D, et al. Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer: a phase 3, open-label, randomised controlled trial. Lancet 2009;374:1331-8.
PUBMED | CROSSREF
13. Katsumata N, Yasuda M, Isonishi S, Takahashi F, Michimae H, Kimura E, et al. Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): a randomised, controlled, open-label trial. Lancet Oncol 2013;14:1020-6.
PUBMED | CROSSREF
14. Clamp AR, James EC, McNeish IA, Dean A, Kim JW, O'Donnell DM, et al. Weekly dose-dense chemotherapy in first-line epithelial ovarian, fallopian tube, or primary peritoneal carcinoma treatment (ICON8): primary progression free survival analysis results from a GCIG phase 3 randomised controlled trial. Lancet 2019;394:2084-95.
PUBMED | CROSSREF
15. Marchetti C, De Felice F, Di Pinto A, D'Oria O, Aleksa N, Musella A, et al. Dose-dense weekly chemotherapy in advanced ovarian cancer: an updated meta-analysis of randomized controlled trials. Crit Rev Oncol Hematol 2018;125:30-4.
PUBMED | CROSSREF
16. Vrdoljak J, Boban T, Petrić Miše B, Boraska Jelavić T, Bajić Ž, Tomić S, et al. Efficacy and safety of TC dose-dense chemotherapy as first-line treatment of epithelial ovarian cancer: a single-institution retrospective cohort study. Jpn J Clin Oncol 2019;49:347-53.
PUBMED | CROSSREF
17. Chan JK, Brady MF, Penson RT, Huang H, Birrer MJ, Walker JL, et al. Weekly vs. every-3-week paclitaxel and carboplatin for ovarian cancer. N Engl J Med 2016;374:738-48.
PUBMED | CROSSREF
18. Schmidt RL, Straseski JA, Raphael KL, Adams AH, Lehman CM. A risk assessment of the Jaffe vs enzymatic method for creatinine measurement in an outpatient population. PLoS One 2015;10:e0143205.
PUBMED | CROSSREF
19. Kogan L, Laskov I, Amajoud Z, Abitbol J, Yasmeen A, Octeau D, et al. Dose dense carboplatin paclitaxel improves progression free survival in patients with endometrial cancer. Gynecol Oncol 2017;147:30-5.
PUBMED | CROSSREF