

Newsletter of the Japanese Gynecologic Oncology Group (JGOG)

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The Uterine Cancer Committee

Kazunori Ochiai, M.D., Ph.D. President, JGOG

Among JGOG disease committees is the Uterine Cancer Committee, which took a new step under the leadership of Chairperson Hatae in October of 2002 when JGOG gained NPO status. Thereafter, the Committee was chaired by Professor Nobuo Yaegashi 3 terms for 6 years, followed by Dr. Toshiaki Saito who has served as Chairperson since 2010. The most basic therapeutic method for endometrial cancer is surgery. In the U.S., radiotherapy is most commonly employed as postoperative adjuvant therapy, which is described also in medical textbooks.

Nevertheless chemotherapy has been used postoperatively in Japan. JGOG2033 compared efficacy between radiotherapy and chemotherapy, suggesting that they were identical in therapeutic efficacy. Furthermore, the subset analysis revealed that chemotherapy was more efficacious in some patients of the high recurrence risk group. These results prompted conduction of JGOG2041 which was a randomized phase II controlled trial of three arms including Docetaxel + Cisplatin (DT), Docetaxel + Carboplatin (DJ) and Paclitaxel + Carboplatin (TJ). It was shown that there was no significant difference in response rates and tolerability between the three arms. A similar phase III controlled study was launched thereafter and 788 eligible cases have already been entered. We are looking forward to its analysis results, which are expected to yield a standard therapeutic regimen that will be prescribed domestically as well as abroad.



The Past trials and research results of uterine cancer committee

Nobuo Yaegashi, M.D., Ph.D. Former Chairperson, Uterine Cancer Committee

Six studies have been conducted by the uterine cancer committee since 2002, as shown in the table. Five finished studies were reported at international meetings and in journals, and two studies are now under analysis. There is no ongoing trial right now.

JGOG2041 showed the feasibility of

taxane plus platinum combination therapy, and recommended docetaxel/cisplatin (DP) and paclitaxel/carboplatin (TC) as candidates for the phase III randomized clinical study (JGOG 2043). Unfortunately, JGOG2042 was recommended for early termination based on safety concerns by the Data Monitoring Committee. JGOG2044S and

JGOG2045S have been published in Gynecologic Oncology.

The uterine cancer committee has an important mission to improve survival in patients with uterine corpus malignancies. We hope that the JGOG members will propose new world-wide attractive concepts.

(Written by Tadao Takano)

Protocol No.	Study name	Phase	Publications
JGOG2041	Randomized phase II study comparing docetaxel plus cisplatin, docetaxel plus carboplatin, and paclitaxel plus carboplatin in patients with advanced or recurrent endometrial carcinoma.	II	Annals of Oncology 22; 636–642, 2011
JGOG2042	Phase II study of Irinotecan (CPT-11) in uterine leiomyosarcoma.	II	under analysis
JGOG2043	Randomized phase III study comparing doxorubicin plus cisplatin, docetaxel plus cisplatin, and paclitaxel plus carboplatin in patients with high-risk endometrial cancer.	III	under analysis
JGOG2044S	Practice pattern for postoperative management of endometrial cancer in Japan.	survey research	Gynecologic Oncology 115; 456–459, 2009
JGOG2045S	Status of surgical treatment procedures for endometrial cancer in Japan.	survey research	Gynecologic Oncology 105; 325–328, 2007



Completion of patient enrollment to JGOG2043, a randomized phase III trial for endometrial cancer

Daisuke Aoki, M.D., Ph.D. Studychairperson, JGOG2043 Trial

JGOG2043, entitled “A randomized phase III trial of AP (doxorubicin plus cisplatin) versus DP (docetaxel plus cisplatin) or TC (paclitaxel plus carboplatin) as post-operative chemotherapy in patients with high intermediate risk and a high-risk group of endometrial carcinoma”

(Fig.1), is the first randomized phase III trial that JGOG has conducted on patients with endometrial cancer. This trial was started on November 24, 2006 and the accrual was closed on January 7, 2011. During this period, 788 patients were enrolled and assigned to each of 3 arms. The pro-

col treatments are already finished in all of the patients and currently their outcomes are followed-up. Among the phase III trials conducted earlier by JGOG, JGOG2043 has required the greatest number of patients and the longest study period. As a matter of fact, accrual took 4

years, and the follow-up period was planned to be 5 years afterward. In addition to financial support by JGOG, this trial was partly supported by a Health and Labour Sciences Research Grant from the Ministry of Health, Labour and Welfare (Primary Investigator; Daisuke Aoki, MD).

The aim of JGOG2043 is to test superiority with regard to PFS of DP or TC compared to AP as a control arm. Roughly speaking, the progn-

osis of patients with endometrial cancer is better than that of patients with ovarian cancer. Thus a relatively larger number of patient and events are needed to detect the difference. The design of JGOG2043 was determined by taking account of the number and stage distribution of the patients treated before in more than 200 JGOG member institutes or hospitals. To avoid a statistical problem with multiple comparisons in this trial with 3 arms, the trial was statistically designed so that all possi-

ble combinations (AP vs TC vs DP) could be compared with a significance of $p < 0.05$, if the null hypothesis "AP hazard = DP hazard = TC hazard" was rejected. It is promising that the results of the trial will allow us in near future to know the post-operative role of taxane plus platinum combination therapy as standard of care in patients with endometrial cancer and maybe also improve its prognosis.

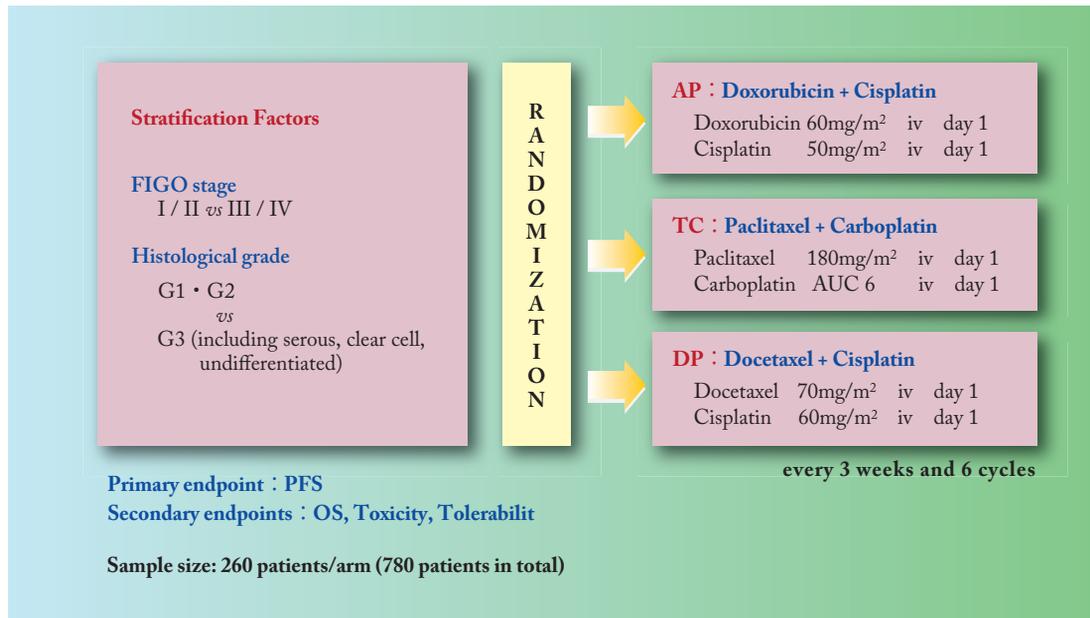


Fig. 1 JGOG2043 Study Design

Strategy against gynecologic cancer: past, present, and future.
-Uterine Cancer Committee-



Present activity and future perspective

Toshiaki Saito, M.D., Ph.D. Chairperson, Uterine Cancer Committee

The Uterine Cancer Committee is a disease committee under JGOG that is evaluating problems in the treatment of the diseases arising in the uterine corpus, such as endometrial cancer, uterine sarcoma, and gestational trophoblastic disease (GTD). Also, the committee is charged by JGOG to design, conduct, and monitor phase II to phase III trials in cancer of the endometrium, uterine sarcomas,

and GTD. Most of the results of these trials and surveillance involving uterine malignancies have been presented and/or published recently, and I believe the results have impacted the treatment of these diseases around the world. The past and present activities have already been described in detail by Prof. Yaegashi and Prof. Aoki. The description of the future activities of the Uterine Cancer Committee is my

responsibility.

The major problems in the treatment of neoplasm of the uterine corpus are connected with the management of patients with poor prognosis, such as patients with extremely advanced endometrial cancer or patients with very poor prognostic histology. The committee is now focusing on these poor prognostic subsets of the uterine

neoplasm. Two trials are presently being prepared, and we hope for future benefits. One is a feasibility study to evaluate reduction surgery following induction chemotherapy for stage IVb endometrial cancer (JGOG 2046), which is incurable with surgery alone. The study design is shown as a schema (Fig.1).

The study is planned by Dr. Nakanishi as the first step in future phase II/III randomized trials to evaluate the two treatment strategies, primary surgery plus chemotherapy versus primary induction chemotherapy followed by surgery and postoperative chemotherapy. The study will start soon, and it is anticipated that at least 50 patients will need to be enrolled.

The other study is a phase II/III prospective randomized study of conventional triweekly TC versus dose-dense TC treatment for postoperative and recurrent carcinosarcoma of the uterus (JGOG 2047). The study is being planned by Dr. Harano, using the dose dense TC (CBDCA+ Paclitaxel) that was reported by JGOG to overcome the traditional triweekly TC in the treatment of ovarian cancer. The study design is also shown as a schema (Fig.2).

This study will be started as a phase II study to evaluate if both TC and dose dense TC treatments are acceptable as standard treatments for carcinosarcoma of the uterus. After interim analysis, a decision will be made whether to go to a phase III study.

In addition to these trials, we need to prepare for the next step of the study following JGOG 2043, which will show us the best adjuvant chemotherapy following surgery of intermediate to high-risk endometrial cancer. The next step may be a combination with molecular targeting therapy or chemoradiation therapy. Several studies have already been started around the world. We will pursue the best of the bests in the postoperative adjuvant treatment of endometrial cancer.

Recent JGOG trials have achieved advances in treatment of uterine corpus neoplasm step by step, and they will continue to contribute to the development of new strategies against these diseases in future.



Fig.1

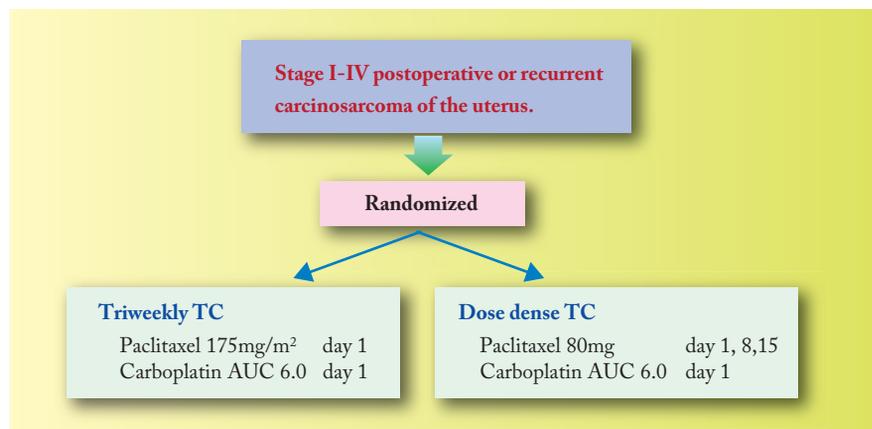


Fig.2

Editorial postscript



Matsumoto Castle

The incidence of uterine corpus cancer was only 5% to 10% of uterine cancer 50 years ago in Japan, but it has been increasing remarkably. Surgery followed by radiotherapy was a standard treatment of this disease. However, accumulating data have demonstrated the effectiveness of chemotherapy after surgery. JGOG conducted the phase II and III studies, JGOG2041, 2042, and 2043, and is planning 2046 and 2047. In Japan, many patients received chemotherapy instead of radiotherapy, but few papers discussed which regimen was better than others. In this issue, we look back on the progress of JGOG studies regarding uterine corpus cancer.

Fumitaka Kikkawa, M.D., Ph.D.
Chairperson, Public Relation Committee



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