

Newsletter of the Japanese Gynecologic Oncology Group (JGOG)

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We deepen international collaboration to accelerate new drug development

Toru Sugiyama, M.D., Ph.D. President, JGOG

Japanese Gynecologic Oncology Group (JGOG) is a clinical research group that works with 188 major universities and cancer centers throughout Japan in an effort to establish the optimal and latest diagnostic and therapeutic methods for patients with gynecologic malignancies. JGOG is practicing clinical researches always aiming toward establishment of medical care that will be needed by patients with gynecologic malignancies. Our Disease Committee discusses the concept of each clinical research proposed by our members and judges its feasibility. Acquisition of research funds from private entities is becoming increasingly difficult due to various regulations imposed by the government of Japan. A research that gains concept approval may require acquisition of governmental external funds, such as from Japan Agency for Medical Research and Development (AMED), as a collateral condition for its implementation. Our academic partners include data centers such as Translational Research Informatics Center (TRI), Kitasato University, and the Clinical Research, Innovation and Education Center of Tohoku University Hospital (CRIETO). Tissue and blood specimens are stocked in Tohoku University Tohoku Medical Megabank Organization, which is a global-scale biobank, as translational study (TR) specimens.

We, including President, Vice Presidents and Future Planning Committee, have started investigating conference with pharmaceutical companies related to drug development and research as well as clinical trial initiated by a medical investigator with an aim of rapid and certain development of new drug, which is increasing

in speed, for gynecologic malignancies. At present, JGOG's patient introduction system has effectively worked in pharmaceutical company trials, leading to increased accumulation of cases.

JGOG is strengthening international collaboration by gaining diverse knowledge from Gynecologic Oncology Group in the US and using accumulated experiences. Today, we are also promoting collaboration with Asian regions, mainly Korea, Taiwan and Shanghai, using the network of Translational Research Informatics Center (TRI). Joint researches are already ongoing with Korean Gynecologic Oncology Group (KGOG) and Shanghai Gynecology Oncology Group (SGOG), such as on JGOG3020 study and SUNNY Trial (TDS vs IDS) in ovarian cancer. We are quite confident that we will show high-level evidence, dispatched from Asia, in the near future. Obviously, we will also continue active efforts in international joint research as a member of Gynecologic Cancer InterGroup (GCIG).

JGOG's activities



Report of the 15th JGOG Annual Meeting 2016

Takayuki Enomoto, M.D., Ph.D. Vice President, JGOG

The 15th Japanese Gynecologic Oncology Group (JGOG) Annual Meeting was held on December 2, 2016 at Kokuyo Hall in Shinagawa, Tokyo. After the opening address by Professor Toru Sugiyama, President of JGOG, reports from the Audit and Membership Committee, Education Committee, and Supportive and Palliative Care Committee were presented. Next, the current status of international collaborations with the GCIG, KGOG and AGOG was presented. The highlights of the morning session were special lectures given by Dr. Yong Man Kim, President of the Korean Gynecologic Oncology Group, and by Dr. Masanori Fukushima, President of the Translational Research Informatics Center. At the General Assembly the accounts for 2016 were ratified and budget statements for 2017 were approved. Business reports for 2016 and plans for 2017 were also approved.

In the afternoon session, ongoing clinical trials were introduced and their progress was reported. Concepts for new clinical trials were also presented and discussed.

Since the JGOG Educational Seminar was started in

2007, a slideshow in which pictures of all previous attendees were shown, was presented as a special event for the 10th anniversary of this seminar.

At the end of the annual meeting, Dr. Akiko Shibata, Head of the Analysis Section, Center for Cancer Registries, National Cancer Center, gave an ethics seminar entitled "Medical records and amendment act of the protection of personal information". The meeting was adjourned with remarks by Prof. Daisuke Aoki.





History of 10 years in JGOG Education Seminar

Takeshi Hirasawa, M.D., Ph.D. JGOG Education Seminar Vice chairman
Tokai University School of Medicine, Obstetrics and Gynecology

Overview of JGOG Education Seminar

At the 3rd meeting of JGOG's Education Committee held in July 2016, the Committee decided to start Education Seminar as a new project of JGOG. The program aims to "cultivate young gynecologic oncologists capable of acting globally toward construction of standardized chemotherapeutic method for gynecologic cancer", or in other words, cultivate young gynecologic oncologists who are deeply versed in chemotherapy and clinical study for gynecologic cancers and can act globally. Participants to the program are required to be a young member (a physician who is or aims to become a certified gynecologic oncologist or who is or aims to become a certified medical oncologist) of JGOG and recommended by a responsible person of the institute. The program is a participatory workshop with a heavy schedule of 3 days and 2 nights, where about 20 participants extract clinical questions (CQ) and present and discuss planned clinical study in three groups of cervical, endometrial and ovarian cancers.

The workshop is supported by JGOG Office, Kitazato Clinical Research Center (KCRC, data center), Education Committee of JGOG, and advisory specialists.

Protocol concepts created by young doctors during 10 years

This trial is on going as JGOG 3020

Seminar	Ovarian ca.	Cervical ca.	Endometrial ca.
1st	Phase III	Phase III	Phase II
2nd	Phase II	Phase II/III	Phase III
3rd	Phase III	Phase III	Randomised Phase II
4th	Phase II	Phase III	Phase III
5th	Prospective Cohort	Phase III	Phase III
6th	Phase III	Phase III	Phase III
7th	Phase III	Phase III	Phase III
8th	Phase II (→Retrospective study)	Phase II	Prospective Cohort (→Retrospective study)
9th	Phase II/III	Phase III	Phase III
10th	Phase II	Phase III	Phase III



Application conditions and number of participants to JGOG Education Seminar

The Education Committee decided and improved the application conditions for participating in the seminar on a trial and error basis. As of 2016, participants are invited from May to August each year by giving priority to full-fledged member physicians of JGOG having interest in medical gynecologic oncology and clinical study and setting different requirements between a gynecologist and a physician of another field (such as medical oncology). In principle, 21 to 24 participants (three groups of either 7 or 8) to be accepted are decided by the Education Committee based on points obtained by each applicant at JGOG institute plus his or her contribution. The program started with two advisors per group. Since the 7th workshop, one candidate advisor was added to each



Final presentation and discussion

group; thus each group actually has three advisors today.

Up to present (from the 1st to 10th workshops), 215 received the program, including 141 male and 74 female physicians. Participants in their 30s accounted the largest percentage with 83.3% (participants in the age of 29 or below: 6, 30-34: 107, 35-39: 72, 40-44: 24, 45-49: 3, and 50-: 3). Of the 215, 206 were gynecologists, accounting for 96%; and 138 were from a university hospital, 47 were from a cancer hospital, and 30 were from a general hospital. The ratio of acquiring the Certification was 214/ 215

or 99.5%.

Products from 10 years of JGOG Education Seminar

In these 10 years, 32 clinical studies were prepared (phase III studies: 21, phase II studies: 9, and prospective cohort studies: 2). Of the studies, only one study (JGOG3020) has been enforced by JGOG. It is a big future topic to increase the number of Education Seminar's products that are implemented as a clinical study of JGOG.

JGOG's topics

JGOG2043: A randomized phase III trial of docetaxel plus cisplatin or paclitaxel plus carboplatin compared with doxorubicin plus cisplatin as adjuvant chemotherapy for endometrial cancer at a high risk of recurrence

Hiroyuki Nomura, MD., Ph.D.
 Secretary and sub-investigator of JGOG2043 trial
 Department of Obstetrics and Gynecology, Keio University School of Medicine



Surgical treatment is initially provided for endometrial cancer patients, and adjuvant therapy is indicated for patients at a high risk of recurrence. Although radiotherapy has been mainly used as adjuvant therapy, the efficacy of chemotherapy in advanced cases has been demonstrated in the GOG122 trial. Doxorubicin has been the key drug and doxorubicin plus cisplatin (AP) has been the standard regimen in endometrial cancer. Recently, the superiority of a paclitaxel plus platinum regimen was demonstrated in the GOG177 and GOG209 trials. On the other hand, JGOG conducted a randomized phase II trial on advanced or recurrent endometrial cancer (JGOG2041 trial) that showed adequate efficacy of the taxane plus platinum regimens (response rate: 48.3-60.0%) [Ann Oncol. 2011;22:636-42].

The aim of the JGOG2043 trial (Principal investigator: Daisuke Aoki, M.D., Ph.D.) is to evaluate the clinical benefit of the taxane plus platinum regimens, including docetaxel plus cisplatin (DP) or paclitaxel plus carboplatin (TC), as compared with AP therapy in adjuvant chemotherapy for endometrial cancer patients at a high risk of recurrence after surgery. In this trial, the postoperative highrisk group for recurrence was defined as follows: stage I, II with G2/G3 and a myometrial invasion >1/2, stage III, and stage IV with no metastatic lesions beyond the abdominal cavity. As a result, the lowrisk group, which could be cured by surgical treatment alone, was excluded, and the veryhighrisk group, which would not achieve clinical remission by the initial treatment, was also excluded. The primary endpoint is progression-free survival (PFS), and the secondary endpoints are overall sur-

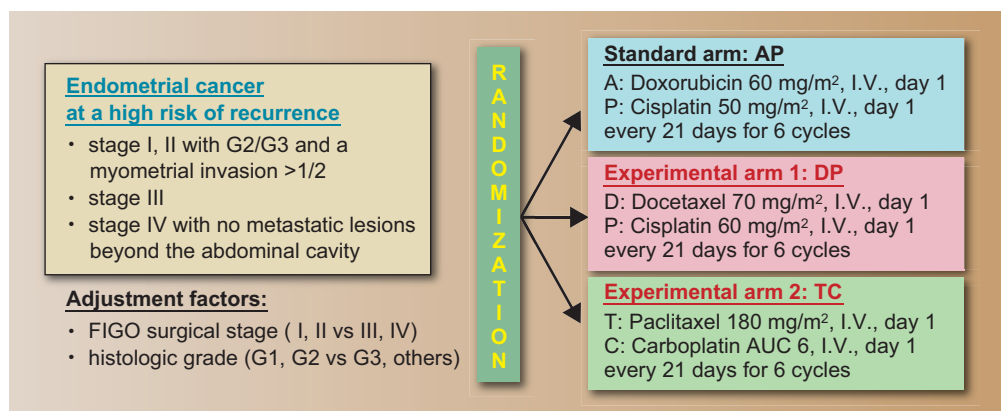


Figure 1 JGOG2043 trial design

vival (OS), adverse events, and tolerability of treatment. From November 2006 to January 2011, 788 patients were enrolled from 118 institutions in Japan. Enrollment into this trial was almost done as planned, and the final analysis was carried out after the data cut-off on January 2016.

There was no significant difference in PFS and OS among patients receiving AP, DP or TC. However, the taxane plus

platinum regimens were well tolerated, indicating that they can be used as alternative adjuvant chemotherapy regimens in endometrial cancer. Especially, because of its good tolerability, DP is suggested as being worth considering as a future treatment arm. These results were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2017 [Abstract Number: 5503].

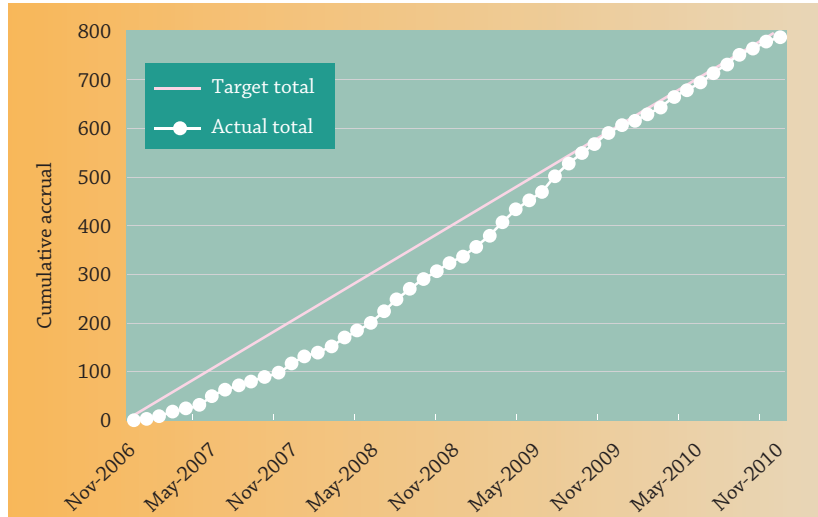


Figure 2 Trial Recruitment

JGOG's topics

JGOG3020: A Phase III randomized clinical trial to investigate the necessity of adjuvant chemotherapy for surgical stage I epithelial ovarian cancer



Hiroshi Tanabe, M.D., Ph.D.
Study chairperson, JGOG3020 Trial

JGOG3020 (Figure 1) is a randomized control trial (RCT) for stage I epithelial ovarian cancer after surgical staging.

Registration was started from July 2012, and it is in the fifth year of trial this year. Standard treatments for stage I ovarian

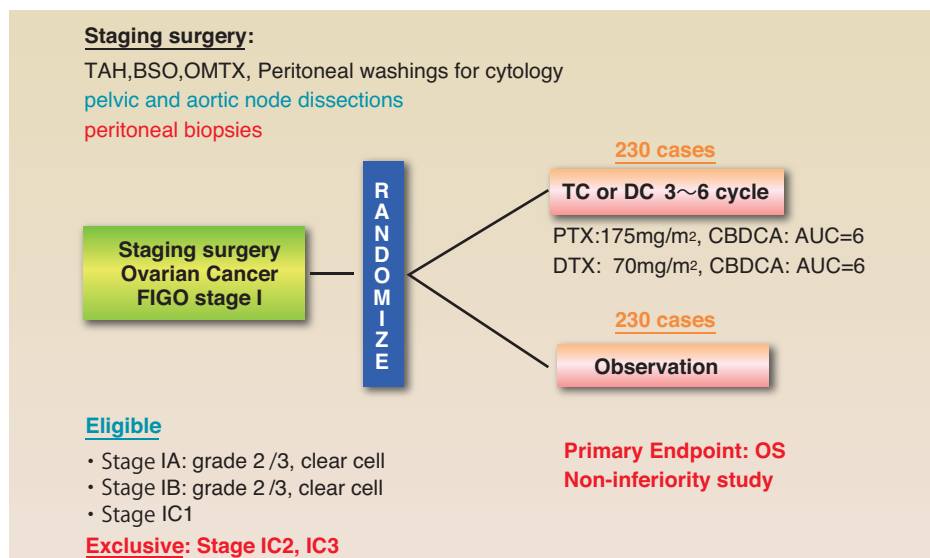


Figure 1 JGOG3020

cancer are surgery and adjuvant chemotherapy based on the results of two RCTs, namely EORTC-ACTION and ICON1. A clinical question has arisen doubting the need of adjuvant chemotherapy for ovarian cancer in stage I that has been treated by surgical staging (Figure 2). JGOG3020 was launched by JGOG to deal with this clinical question and is attracting attention. If the trial ends in a success, the majority of stage I ovarian cancer patients will not need to receive adjuvant chemotherapy, not only improving their quality of life (QOL) but also bringing huge economic benefits.

Last year, the protocol was revised, reducing the target num-

ber of cases from 620 to 460 by elongating the duration of registration. Today, the number of registered cases exceeded 100. To further promote registration, JGOG asked the Korean counterpart for cooperation; and Korean Gynecologic Oncology Group (KGOG) decided to officially participate in the trial starting this year. We will also ask the Taiwanese Gynecologic Oncology Group (TGOG) and the Gynecologic Cancer Intergroup (GCIG) for their participation aiming toward early completion of registration by making it a new international randomized control trial and examine the clinical question.

[Hysterectomy]
Simple or extended total hysterectomy, and modified radical hysterectomy

[Omentectomy] Partial omentectomy is acceptable.

[Peritoneal cytology] Ascites or peritoneal washings.

[Peritoneum biopsy]
Douglas' pouch
bladder peritoneum
left and right-sided ilium
left and right-sided colon
right diaphragm peritoneum (acceptable scraping cytology)

In addition, biopsy of any peritoneum sites macroscopically determined with possible dissemination must be performed.

[Retroperitoneal lymph node dissection]
Para-aortic lymph nodes and pelvic lymph nodes

The upper border of lymph node dissection should be up to the lower border of the left and right renal veins.

The dissection number of retroperitoneal lymph nodes is defined that dissection is performed with more than 15 pelvic lymph nodes and more than 10 para-aortic lymph nodes.

Figure 2 Staging surgery

Editorial postscript



Himeji Castle

This newsletter features a message from President Toru Sugiyama of JGOG entitled, "We deepen international collaboration to accelerate new drug development", which focuses on future directions and goals of JGOG.

For further development of JGOG, cultivation of young gynecologic oncologist, who will bear the next generation, is indispensable. Thus, JGOG is holding JGOG Education Seminar every year since 2007 aiming to cultivate young gynecologic oncologists who are deeply versed in chemotherapy and clinical study for gynecologic cancers and can act globally. Celebrating the 10th anniversary of the program, an overview of Education Seminar and its 10 years of history were summarized by Vice-chairman of JGOG Education Seminar, Takeshi Hirasawa, who have played active parts as a participant as well as a member of Education Committee.

As recent topics, two studies conducted by JGOG are featured: JGOG3043 by Hiroyuki Nomura and JGOG3020 by Hiroshi Tanabe. The latter, or JGOG3020: A Phase III randomized clinical trial to investigate the necessity of adjuvant chemotherapy for surgical stage I epithelial ovarian cancer, was a product of the aforementioned Education Seminar and was adopted as a clinical trial as well as an international joint trial now.

JGOG was launched in 2002 as a non-profit organization. This year, it will celebrate its 15th anniversary. International collaboration, quick new drug development and cultivation of young human resource will surely be the key for further development of JGOG.

Kiyoshi Ito, M.D., Ph.D.

Chairman, JGOG Public Relations Committee



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