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Meeting Report

The 34th Annual Meeting of the Korean Society of Gynecologic Oncology 2019: meeting report

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ABSTRACT

The 34th Annual Meeting of Korean Society of Gynecologic Oncology (KSGO) was held in Busan, Korea from 26 to 27 April. Around 460 Korean and international clinicians gathered in Busan to share and discuss their latest work and key issues of gynecologic oncologic research and treatment. The scope of this meeting included recent clinical trials and updates in gynecologic oncology, advances in ovarian cancer treatment, targeted therapy and immunotherapy in gynecologic cancer, management of hereditary gynecologic cancer, and newly revised staging of cervical cancer. As expected, the ongoing debate regarding the recent clinical trial on minimally invasive surgery for early-stage cervical cancer was addressed throughout the congress and the initial outline of the KSGO position statement was open for discussion. The meeting was an opportunity for all participants to come together and explore scientific insights of gynecologic cancer.

Keywords: Uterine Cervical Neoplasms; Ovarian Neoplasms; Endometrial Neoplasms; Molecular Targeted Therapy; Immunotherapy

INTRODUCTION AND OVERVIEW

The 34th Annual Meeting of Korean Society of Gynecologic Oncology (KSGO) was held in Busan, Korea from 26 to 27 April. Around 460 Korean attendees from all parts of the country as well as international participants gathered in the heart of Busan to share and discuss the latest findings and key issues of gynecologic oncologic research and treatment (**Figs. 1** and **2**). The congress was commenced with a warm welcome address by Professor Seung Cheol Kim, the president of KSGO and was moderated by Professor Dong Hoon Suh, the secretary general of KSGO. This year, two renowned international researchers, Professor Warner Huh (president of the Society of Gynecologic Oncology [SGO] and division director of gynecologic oncology, Alabama University, USA) and Professor Nobuo Yaegashi (chairman of the Department of Obstetrics and Gynecology, Tohoku University, Japan) were appointed as honorary KSGO members for their dedication and contribution to the work of the society and in the field of gynecologic oncology (**Fig. 3**).

Author Contributions

Conceptualization: G.W.Y., D.H.S., J.W.K., S.C.K., Y.T.K.; Investigation: G.W.Y., D.H.S.; Supervision: G.W.Y., D.H.S., J.W.K., S.C.K., Y.T.K.; Writing - original draft: G.W.Y., D.H.S., Y.T.K.; Writing - review & editing: G.W.Y., D.H.S., J.W.K., S.C.K., Y.T.K.

Fig. 1. The main venue for the Annual Meeting of Korean Society of Gynecologic Oncology.

Fig. 2. Chair, invited speakers, and honorary members of the 34th Annual Meeting of Korean Society of Gynecologic Oncology.

Minimally invasive surgery (MIS) in early-stage cervical cancer was a big issue and an ongoing debate in this year's meeting based on the recent findings of the Laparoscopic Approach to Cervical Cancer (LACC) trial [1]. The pre-congress session was dedicated to this topic along with the suggestion to frame the formal KGSO position statement on MIS in patients with early cervical cancer. The first plenary session of the congress consisted of selected presentations given by the young doctors of the KSGO and Asia-Oceania Research Organization in Genital Infection and Neoplasia (AOGIN) Young Doctor Program. In session 2, invited international speakers shared their work and updates in gynecologic oncology. The luncheon symposium covered the topic of human papillomavirus (HPV) test for primary screening for cervical cancer presented by Professor Tay Sun Kuie from Singapore General Hospital.

In this year's meeting, over 115 abstracts were submitted and 20 selected topics were chosen for oral presentation during the Free Communications session. In addition, a total of 93 abstracts were presented through electronic posters. Four main topics were discussed in

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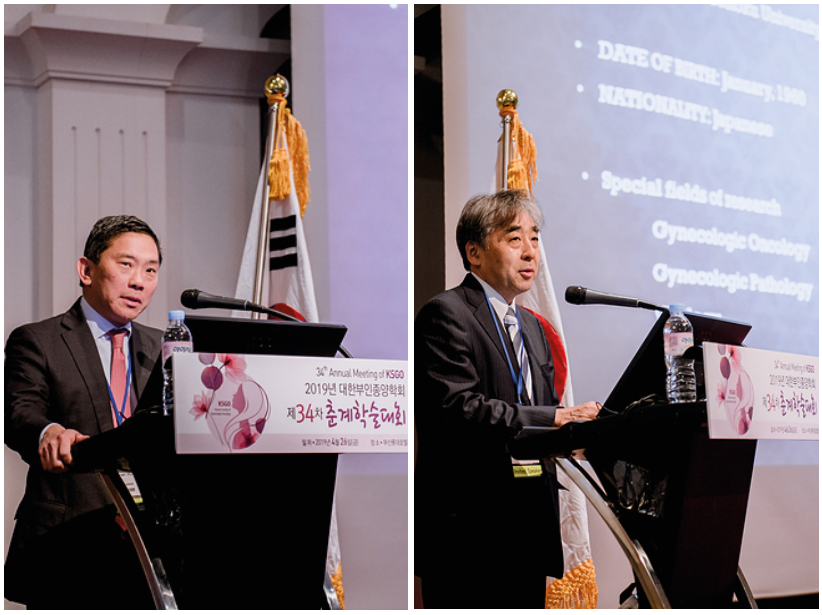

Fig. 3. Appointed international honorary members of Korean Society of Gynecologic Oncology. Professor Warner Huh (USA, president of the Society of Gynecologic Oncology, left) and Professor Nobuo Yaegashi (Japan, chairman of Tohoku University, right).

parallel sessions, including recent advances in ovarian cancer treatment, targeted therapy in gynecologic cancer, management of hereditary gynecologic cancer, and newly revised 2018 International Federation of Gynecology and Obstetrics (FIGO) staging of cervical cancer. KSGO has been successfully hosting parallel academic sessions on nursing division since 2017. Therefore, in this year's nursing division session, active discussions were made on recent updates on gynecologic oncology and symptom management.

The last event of the day was the KSGO banquet including awards presentation, appreciation ceremony, and featured acoustic band performance (**Fig. 4**). As always, the delightful social event was an opportunity for members and invited guests to come together and network, hoping to spur future collaborations and maintain long-lasting friendship.

In the morning of 27th April, the *Journal of Gynecologic Oncology* (*JGO*) Workshop for Good authors & Reviewers was held to help clinicians understand and practice the process of paper writing and obtain insights on the design and methodology of biomarker and big-data research. In parallel with the *JGO* workshop, an expert meeting on the paradigm shift in cervical cancer screening test was held in an effort to gather scientific evidence and expert opinions on the role of HPV test as primary cervical cancer screening tool.

This report summarizes the main topics and highlights of each session in chronological order.

PRECONGRESS SESSION: MINIMALLY INVASIVE SURGERY (MIS) IN EARLY-STAGE CERVICAL CANCER

1. Post LACC trial status in other countries

One of the major clinical research that had drawn much attention in 2018 was undoubtedly the randomized trial of MIS in patients with early-stage cervical cancer published in *The New*

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Fig. 4. Scenes from the banquet and social program. (From upper left to right) Congratulatory address by Professor Seung Cheol Kim, president of KSGO; participants enjoying the Gala Dinner; Professor Hee-Sug Ryu (president of ASGO) announcing the upcoming ASGO meeting; Professor Young Tae Kim (vice president of KSGO) drawing the lucky lot; the winner of the grand prize lottery, taking a commemorative photo with the MC of the social program, Dr. Yoo-Young Lee; Korean acoustic band performance.
KSGO, Korean Society of Gynecologic Oncology; ASGO, Asian Society of Gynecologic Oncology.

England Journal of Medicine by Ramirez et al. [1]. There is still substantial amount of debate on the inferior survival outcomes of laparoscopic and robotic surgery to open surgery and the efforts to build further scientific reasoning are ongoing. Several possibilities for the inferior results of MIS are proposed, including risk of tumor spillage with use of uterine manipulator, tumor cell dissemination by carbon dioxide gas insufflation, and variation in surgical techniques and skills among surgeons. Despite the ongoing debates and limitations of the trial, the LACC trial is the first prospective study to compare minimally invasive to open surgical approaches and evaluate survival outcomes. In this session, Yoo-Young Lee reviewed different opinions and position statements published from experts and various societies after the introduction of LACC trial. Expert opinions generally agreed on the need for careful assessment and scrutiny of the trial results in regard to some of the study limitations including early study termination, incomplete data, uneven distribution of laparoscopy (84%) and robotic surgery (16%), and lack of quality assessment of participating surgeons' skills [2-5]. At the same time, they stressed the importance of level 1 evidence in that clinicians should accept the data results and offer open radical hysterectomy (RH) as standard treatment for IA1–IB1 cervical cancer and that MIS should be carefully tailored [5,6]. Recently announced position statements including those from Canadian and German gynecologic societies generally accept and recommend incorporating the trial evidence into clinical practice [7,8]. Other societies such as the British Gynaecological Cancer Society and the Society of European Robotic Gynaecological Surgeons state that there is not enough evidence to suggest current change in practice [9,10]. Similarly, the Japan Society of Obstetrics and Gynecology suggested that MIS can still be an acceptable option in properly selected cases with qualified surgeons. Position

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statements by the Taiwanese Association for Minimally Invasive Gynecology have expressed opposing views towards the conclusion of the recent trials and questioned the surgeon factor as a major limitation [11]. Groups that stated reserved opinions on switching from MIS to open surgery expressed similar opinions in that each institution or country should put an effort to investigate further survival outcomes with their own data for tailored treatment approach and should provide additional evidence before changing the entire practice [7,10,11]. A recent survey performed by the European Society of Gynaecological Oncology showed results of 400 responses from members related to their practice after the LACC trial. Fifty-seven percent of members stated that they have changed their practice to open RH for cervical cancer and MIS reserved for selected small tumors [12]. Most members (90%) responded that they would inform and discuss the results of the recent trial with the patients and thought it would be unethical (75%) if they do not. Despite different opinions and statements from experts and societies, all statements stressed the importance of informed consent and thorough discussion with the patients on choosing the appropriate surgical approach for early cervical cancer.

2. KSGO position statement on MIS in patients with early cervical cancer

There was an opportunity during the pre-congress session for public hearing and discussions among members on the need for the KSGO position statement on MIS for cervical cancer. Yong Bum Kim gave an overview of the previous activities and forthcoming plans of the position statement task force team. KSGO has performed a member survey on this issue in March 2019 and the results were shared with the audience. One-hundred six out of 268 (40%) board certified members in gynecologic oncology responded to the survey and 51% of them had 10 to 19 years of clinical experience. Ninety-five percent of them were practicing RH and were aware of the recent LACC trial results. Responders' opinion on the major three reasons of poor survival outcome in the MIS group were the use of uterine manipulator, inappropriate tumor traction and manipulation, and the lack of radicality in the MIS group. Nearly 60% of the responders stated that they would change the mode of surgical approach after the trial, despite the fact that more than 80% of them had been routinely performing MIS for early cervical cancer. The members chose FIGO stage 1A1 to 1B1 as appropriate candidates of MIS. In order to improve the survival outcomes in MIS, members suggested minimal manipulation of tumor, colpotomy immediately before the end of surgery to avoid tumor-peritoneal contact, and retrieving resected lymph nodes using a closed bag. Most respondents (66%) answered that they would discuss the recent study results with the patient before surgery, and that it would be unethical (65%) if they do not. Sixty-eight percent agreed on the need for another prospective randomized study to verify the results of the LACC trial and 70% had intention to participate in the relevant trial. Based on the opinions of the KSGO members, the society is preparing a position statement in collaboration with the Korean Society of Obstetrics and Gynecology and the Korean Society of Gynecologic Endoscopy and Minimally Invasive Surgery. The initial abstract of the position statement was open for discussion and the need to define 'optimal candidates' of MIS in detail was suggested. In addition, further analysis of institutional data on the survival of patients with various tumor size was suggested since the data from some of the high-volume institutions in Korea showed similar survival outcomes between open and MIS even in tumors greater than 2 cm. The importance of surgical skills was stressed and there were concerns on performing multi-institutional study since the lack of surgical standardization itself can become a bias in studies. Comments were added on the need for an accreditation system for laparoscopic surgeons similar to Japan. Also, due to the ethical difficulties in performing another randomized prospective trial (RCT), the launching of a prospective

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observational study as well as interpretation of national data prior to designing another RCT were recommended. Lastly, there were suggestions to include future study plans in the KSGO position statement. The task force team is planning to write a position statement in collaboration with other relevant Korean gynecologic societies and will finalize its contents for publication in the following months.

SESSION I. PLENARY SESSION

1. Comparison of survival outcomes between MIS and conventional open surgery for RH as primary treatment in patients with stage IB1–IIA2 cervical cancer

Three out of six plenary topics discussed the issue of minimally invasive RH in early cervical cancer. Se Ik Kim and colleagues shared the results of their recent retrospective study on the survival outcomes of MIS and conventional open surgery for RH in stage IB1–IIA2 cervical cancer [13]. After a median follow up of 114.8 months, the MIS group showed poorer progression-free survival (PFS) compared with the open group (5-year rate, 78.5% vs. 89.7%; p<0.001). Consistent results were observed among 349 patients with stage IB1, where MIS showed higher recurrence rates (adjusted hazard ratio [HR]=2.276; 95% confidence interval [CI]=1.039–4.986). However, an interesting finding was that MIS was not a poor prognostic factor in stage IB1 disease with cervical mass size ≤2 cm. Therefore, the group insisted that the advantage of MIS should not be given up in small sized IB1 disease, through careful patient selection and appropriate surgical techniques.

2. Selection criteria and colpotomic approach for safe minimally invasive RH in early cervical cancer

Tae Wook Kong and colleagues suggested two possible reasons for poor oncological outcomes in the MIS group of the LACC trial, which are related to selection of candidates without parametrial invasion and difference in surgical technique with colpotomic approach. Using a previously established nomogram to predict microscopic parametrial infiltration (PMI) by identifying the disruption of the cervical stromal ring on magnetic resonance imaging (MRI) [14], the authors evaluated the oncologic outcomes of MIS in FIGO stage IB–IIA cancer using this prediction criterion and vaginal colpotomy. Prospective group of patients who had PMI on MRI received vaginal colpotomy only (PMI-VC group) and were compared with a retrospective group of patients in which PMI criterion on MRI was not applied and received intracorporal or vaginal colpotomy (PMI-IVC group). The PMI-IVC group showed significantly higher rate of positive cuff margin than that in the PMI-VC group (10.8% vs. 1.2%, p=0.008) and significantly lower 5-year disease-free survival (83.6% vs. 97.5%, p=0.013). Disruption of the cervical stromal ring on MRI and intracorporeal colpotomy were significant factors of disease recurrence and therefore Kong suggested optimal selection of surgical candidates based on these factors.

3. Comparison of laparoscopic vs. open RH in early cervical cancer after completing learning curve and reducing intraperitoneal tumor exposure

Jeong-Yeol Park and colleagues explained poor surgeon proficiency and increased intraperitoneal tumor exposure as possible factors of poor survival outcomes in LACC and Surveillance, Epidemiology, and End Results (SEER) data [15]. Therefore, Park shared their study outcomes of patients that underwent laparoscopic or open RH by surgeons who have already completed the learning curve for laparoscopic RH. A noticeable difference in

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surgical practice in their institution was that all broken tumor tissues were washed out before colpotomy and then the colpotomy and stump repair were entirely performed transvaginally. By analyzing surgical cases that were only performed by proficient laparoscopic surgeons, the 5-year disease-free survival and overall survival (OS) in 854 open and 1,368 laparoscopic cases did not show significant difference, regardless of tumor size stratified into greater or less than 4 cm. Therefore, these results provided evidence in that laparoscopic approach may be comparable to open method after controlling surgeon learning curve and reducing intraperitoneal tumor exposure during surgery. Also, Park suggested that at least 50 cases are required to achieve proficiency in laparoscopic RH for comparable oncologic outcomes.

4. Real-world experience of olaparib maintenance in high grade serous recurrent ovarian cancer with BRCA1/2 mutation

The role of maintenance therapy with a poly (ADP-ribose) polymerase (PARP) inhibitor olaparib, has shown efficacy with manageable tolerability in phase 3 trial in patients with platinum-sensitive, high-grade serous recurrent ovarian cancer with BRCA mutation [16]. In Korea, the Korea Food & Drug Administration permitted the use of olaparib since August 2015. E Sun Paik and colleagues presented the results of real-world data of olaparib use from 4 institutions. Complete response was shown in 46 out of 100 patients (46%) and partial response in 53 (53%). During the median follow up of 10.2 months, 37 recurrences and 5 deaths were observed. Grade 3 or more hematologic adverse events (AEs) occurred in 23 (23%) patients with anemia, neutropenia, and thrombocytopenia, and two patients developed oral mucositis and soft tissue infection. Therefore, the safety and effectiveness of olaparib maintenance treatment in their study were consistent with the results of previous clinical trials.

5. Efficacy of therapeutic HPV vaccine in patients with cervical intraepithelial neoplasia (CIN) 3: phase 2 clinical trial

Youn Jin Choi and colleagues presented their work on the development of therapeutic HPV vaccine GX-188E and showed results of prospective, randomized, multicenter, open-label, phase 2 clinical trial to determine the efficacy of the vaccine for inducing regression of HPV type 16/18-associated CIN 3. Of 72 patients that were enrolled, 52% (33/64) at visit 7 (V7; 20 weeks after the first GX-188E injection) and 67% (35/52) of patients at visit 8 (V8; 36 weeks post vaccination) presented histopathological regression. More than 70% in both groups showed HPV clearance as well. Compared to baseline levels of IFN-γ ELISPOT responses in patients without HPV clearance, patients at V8 with HPV clearances showed significantly higher fold-changes. GX-188E is the first therapeutic vaccine to show greater than 50% efficacy in CIN 3 patients and further promising results are expected in treating pre-malignant cervical lesions in the future.

6. Sentinel lymph node biopsy (SLNB) in early endometrial cancer: Does it reduce the incidence of lower limb lymphedema? An interim report from a single center in Singapore

Selected presentations were given by the young doctors of the KSGO and AOGIN Young Doctor Program in this year's plenary session. Among five international young doctor members, Hui Xian Chin from KK Women's and Children's Hospital (Singapore) presented their work on SLNB. Their hypothesis was that SLNB will reduce the risk of lower limb lymphedema in early endometrial cancer patients and their interim analysis supported this finding. Further analysis on the efficacy of SLNB and the number of retrieved lymph nodes to the risk of developing lymphedema are underway.

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SESSION II. UPDATES IN GYNECOLOGIC ONCOLOGY

In session II, updates in gynecologic oncology were presented by four invited international speakers.

1. LACC trial: impact in the USA

Warner Huh from Alabama University (USA) discussed the huge impact and changes of practice in the US after the LACC trial. Some of the criticisms and limitations of the study regarding data completion, patients per site, recurrences per site, tumor size, unequal balance between laparoscopy vs. robotics, lack of surgical details such as colpotomy and use of uterine manipulator, and early termination of study were addressed as points of discussion. Despite the limitations, the trial has already changed clinical practice in the USA and SGO has not announced a position statement due to the lack of necessity after such a high-powered trial. Therefore, Huh emphasized the importance of discussing the next steps for both clinical practice and further research.

2. Reappraisal of cervical adenocarcinoma treatments.

The incidence of non-squamous cell carcinoma (SCC) has gradually increased over the three decades and the same applies to the situation in Japan [17]. Cervical adenocarcinoma is increasing in incidence with poorer prognosis in Japan, and therefore Nobuo Yaegasi from Tohoku University (Japan) and colleagues conducted a nation-wide retrospective study (Japanese Gynecologic Oncology Group [JGOG] 1072s) of women who underwent open RH for stage I–II cervical cancer with pelvic and/or para-aortic lymph node metastasis between 2004 and 2008 (n=6,003). In this study, one of the reasons of poor prognosis of cervical adenocarcinoma was the resistance to radiotherapy [18], especially in the mucinous subtypes of adenocarcinoma. Since the finding of gastric type mucinous carcinoma (GAS) by Kojima et al. [19] in 2007, active investigations on the distinct prognostic outcomes of GAS have been performed [20]. In a recent JGOG study of 95 cases of GAS, GAS was more significantly associated with bulky mass, deep stromal invasion, lymphovascular space invasion, parametrial invasion, ovarian metastasis, pelvic lymph node metastasis, and pathological T stage compared to the usual type endocervical adenocarcinoma, but was not related to the degree of histological differentiation [21]. The response rate to radiation was reported to be 50% in GAS compared to 82% in the usual type. Chemoresistance of GAS has also been found in several studies [20,22] and the possibility of human epidermal growth factor receptor 2 (HER2) overexpression as molecular target is under investigation [23].

3. Taiwan Association of Gynecologic Oncologists (TAGO) clinical practice guidelines

Hung-Hsueh Chou from Chang Gung University (Taiwan) shared their experience in making of the Clinical Practice Guidelines of Gynecologic Oncology in Taiwan, which is written and updated by the TAGO and Taiwan Gynecologic Oncology Group. Around 6,000 new gynecological cancers arise in Taiwan every year and uterine corpus cancer has the highest incidence (2,440 cases per year) among all gynecological cancers. The need for a practical guideline was agreed upon, and the society are getting together to update version 2 which was published in 2011. Although the guideline booklet is written by gynecologic oncologists, it is made to be understandable by the general population as well and is easily available online and in bookstores. Chou stressed the importance of multidisciplinary team meetings and holds weekly meetings to discuss the most appropriate treatment modality of patients.

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4. Identification of genomic linkage from uterine endometrium to endometriosis and clear cell carcinoma of the ovary

Takayuki Enomoto from Niigata University (Japan) shared his work on the clonal expansion and diversification of cancer-associated mutations in endometriosis and normal endometrium. The linkages from endometriosis to ovarian clear cell carcinoma has been epidemiologically and pathologically proven [24,25]. Whole exome sequencing and target-gene sequencing were performed to identify somatic mutations in normal uterine and endometriotic epithelium. Mutant allele frequency and mutation frequency in cancer-associated genes showed variation from endometrium to endometriosis and cancer. Consequently, the process of PIK3CA and NRAS mutation in uterine endometrium, ARID1A splicing in endometriosis, ARID1A frameshift in atypical endometriosis to cancer were proposed. His work on genomic analyses showed that epithelial cells with cancer-associated gene mutations in uterine endometrium and endometriosis are the origin of endometriosis-associated ovarian cancer.

SESSION III. RECENT ADVANCES IN OVARIAN CANCER TREATMENT

1. Prediction of optimal cytoreductive surgery in advanced ovarian cancer

Since the CHORUS trial in 2015, it is known that patients treated with neoadjuvant chemotherapy (NAC) and interval cytoreductive surgery show higher complete cytoreduction rates and lower surgical morbidity without compromising the survival outcomes [26]. If there is a high likelihood of achieving a cytoreduction to less than 1 cm, primary cytoreductive surgery (PCS) is recommended over NAC due to the risk of inducing chemotherapy resistance during NAC [27]. Dae Hyung Lee introduced several methods on the selection of patients for PCS, including organization of care by specialized surgical teams, clinical and laboratory markers, histologic and genomic factors, radiographic and nuclear imaging and finally diagnostic laparoscopy. The recent work by Bregar et al. [28] showed that computed tomography (CT) findings could predict surgical outcome in patients undergoing NAC. Several studies propose a combined predictive score incorporating clinical, laboratory, and imaging factors to predict optimal cytoreductive surgery rather than using only one significant factor [29,30]. Therefore, Lee suggested that combined variables and/or laparoscopic findings may help improve the ability of patient selection for complete cytoreduction.

2. Role of PARP inhibitors as front-line maintenance therapy in advanced ovarian cancer: SOLO-1

Heon Jong Yoo reviewed the SOLO-1 trial introduced in October 2018 [31]. It was the first phase III trial to show substantial improvement in PFS in patients with newly diagnosed, advanced ovarian cancer with BRCA mutations. Approximately 391 patients were randomized in 2:1 ratio to receive either olaparib 30 mg twice daily or placebo for 24 months. A 70% reduction in risk of disease progression or death was observed in olaparib group compared to placebo (HR=0.3; $p<0.001$). The safety profile was tolerable with no decrease in quality of life from baseline for olaparib-treated patients over the 24-month treatment period.

3. Combination treatment of PARP inhibitor with other therapies in ovarian cancer: benefit and risk

NOVA, SOLO2, and ARIEL3 trials demonstrated significant improvements in PFS with PARP inhibitors as maintenance treatment in platinum-sensitive ovarian cancer patients who had

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complete or partial response after platinum-based chemotherapy [16,32,33]. To improve efficacy and expand treatment indication, Lee suggested several options of PARP inhibitor use, such as PARP inhibitor as front-line treatment, use in patients with mutations other than BRCA, and as combination therapy with other drugs rather than monotherapy. Multiple combination studies are ongoing which combined PARP inhibitor, immune checkpoint inhibitor and anti-angiogenic agents. DUO-O (olaparib+bevacizumab+durvalumab, NCT03737643), ENGOT-ov42 (olaparib+pembrolizumab, NCT03740165), ATHENA (rucaparib+nivolumab, NCT03522246) are some of the current ongoing phase 3 trials as front-line setting. One of the combination treatment method is combining PARP inhibitor and conventional chemotherapy although there could be overlapping toxicity such as myelosuppression. Another option is PARP inhibitor with anti-angiogenic agent and olaparib with cediranib combination is thought to induce HR deficiency in HR compliant tumors [34]. Results of NRG GY-004 and NRG GY-005 trial will soon clarify its efficacy in recurrent ovarian cancer. The last combination of choice could be PARP inhibitor plus immune checkpoint inhibitor since efficacy and safety have been shown in several trials [35,36]. Lee introduced an ongoing trial from his institution, which is AMBITION trial combining PARP inhibitor and immune checkpoint inhibitor or antiangiogenic agent.

SESSION IV. TARGETED THERAPY, IMMUNOTHERAPY IN GYNECOLOGIC CANCER

1. How to select targeted therapy in platinum sensitive or resistant ovarian cancer

In targeted therapy, the potential targets are the signaling pathway, homologous recombination deficiency, hormone receptors, angiogenesis, and immunologic factors. The current status of anti-angiogenetic agents (bevacizumab), PARP inhibitor (olaparib, niraparib, rucaparib), and immunotherapy (pembrolizumab) were reviewed by Won Moo Lee. Abiding by the National Comprehensive Cancer Network guidelines and the Korean National Health Insurance policies, the following algorithms could be considered in selecting targeted therapy for recurrent ovarian cancer. In platinum sensitive and non-BRCA mutated patients, platinum-based combination chemotherapy for previous bevacizumab-treated patients and gemcitabine/carboplatin with bevacizumab could be considered for bevacizumab-naïve patients. For platinum sensitive and BRCA mutated patients, same algorithm applies except the addition of maintenance therapy with PARP inhibitor in case of complete or partial response after platinum-based combination chemotherapy. In platinum resistant patients, conventional chemotherapy including gemcitabine, pegylated liposomal doxorubicin (PLD), paclitaxel or topotecan are used in previous bevacizumab-treated patients, and in bevacizumab-naïve patients bevacizumab could be added to paclitaxel, PLD, or topotecan. In all situations, the status of programmed death-ligand 1 (PD-L1) positivity could be assessed for the possibility of pembrolizumab therapy.

2. Targeted agents and chemotherapy in endometrial cancer

The mainstay of adjuvant chemotherapeutic regimen for endometrial cancer is paclitaxel plus carboplatin (PC) with an additional option of doxorubicin. Jae Yun Song gave an overview on the role of target therapy and immunotherapy agents evidenced by recent clinical trials. Bevacizumab has been the leading anti-angiogenic target agent in the treatment of endometrial cancer as shown in the END-2 trial, where increased response rate with PC plus bevacizumab (54% vs. 73%) and improved PFS (8.7 vs. 13 months, HR=0.57; CI=0.34–0.96)

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were shown [37]. In the recurrent setting, a recent phase 2 trial by Aghajanian et al. [38] evaluated the efficacy of frontline PC plus bevacizumab, PC plus temsirolimus (mTOR inhibitor) or ixabepilone (microtubule stabilizing agent) and carboplatin plus bevacizumab were compared to conventional PC. The overall response rates were 59%, 55%, 53%, and although the PFS was not significantly increased in any arm, the OS duration was statistically significantly ($p<0.039$) increased in PC plus bevacizumab arm relative to reference PC arm. Other anti-angiogenic therapies including sunitinib and cediranib are under investigation. The PI3K/ALT/mTOR signaling pathway alteration are described in 92% and 60% of type 1 and 2 tumors of endometrium. Therefore, the efficacy of mTOR inhibitors such as everolimus and temsirolimus have been evaluated in several clinical trials with encouraging results, however the response rate and toxicity seem to be related according to prior therapy which necessitated further research [39,40]. Targeted therapy for uterine serous carcinoma (USC) is another area of attention since USC show poorer outcomes compared with endometrioid type. A randomized phase 2 trial in 2018 evaluated the efficacy of trastuzumab, a human monoclonal antibody against HER2/neu to PC regimen. In this study, the trastuzumab group showed increased PFS in advance stage or recurrent HER2/neu positive USCs. The objective response rates were 75% in the experimental arm and 44% in the control PC arm with similar drug toxicity. Immune checkpoint inhibitor is another option of targeted therapy since endometrioid types have relatively higher incidences of mismatch repair defects. KEYNOTE-028 study in 2017 demonstrated partial response in 13% and stable disease in another 13% of 24 patients in PD-L1 positive advanced endometrial cancer. The median duration of stable disease was 24.6 weeks and showed favorable safety profiles in heavily pretreated patients [41].

3. Immunotherapy combination for HPV related cancer

Several phase 1 and 2 clinical trials related to HPV therapeutic vaccines are ongoing and phase 1 trials are in place for checkpoint inhibitors including pembrolizumab and ipilimumab. The results of HPV positive head and neck SCC could be adopted in planning cervical SCC trials since HPV is a common pathogen. Seung Soo Han introduced the most recent phase 2 basket study (KEYNOTE-158) on the antitumor activity and safety of pembrolizumab in previously treated cervical cancer [42]. Among 98 patients with recurrent cervical cancer, 83.7% had PD-L1 positive tumors. During the median follow up of 10.3 months, the objective response rate was 12.2% with three complete response and nine partial response. Grade 3 AEs occurred in 12.2% of patients and treatment-related AE occurred in 65.3%, the most common being hypothyroidism. Based on these results the U.S. Food and Drug Administration granted accelerated approval of pembrolizumab in 2018 for patients with PD-L1 positive recurrent cervical cancer. Promising outcomes of single or combination immunotherapy in cervical cancer are expected, however further research on optimal timing, dosage, and appropriate combination with conventional therapy is still needed.

SESSION V. MANAGEMENT OF HEREDITARY GYNECOLOGIC CANCER

1. Treatment of ovarian cancer with PARP inhibitors: the importance of BRCA status

PARP inhibitors have changed the course of treatment in ovarian cancer with the release of SOLO-1 and 2 trial results. The clinical hallmark of BRCA mutation lies in its prognostic and predictive properties. The BRCA status became more essential than ever since patients

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with BRCA mutation exhibited an 80% reduction in the risk of progressive disease after olaparib treatment. Both maintenance and single agent therapy with PARP inhibitors showed promising results in BRCA mutated tumors. Therefore, ancillary tests to select patient that may benefit beyond BRCA may be considered unnecessary, however recent research proposed several strategies to identify the appropriate candidates for PARP inhibitor therapy in preparation of potential resistance. Recent research from Kondrashova and colleagues [43] showed that methylation zygosity of BRCA1 copies are related to the responsiveness to rucaparib. Also, in the ARIEL 2 trial, BRCA1 methylation zygosity was evaluated in human tumor cells from BRCA1-methylated platinum-sensitive high-grade serous ovarian cancer patients before PARP inhibitor therapy [44]. The PFS was longer in homozygous BRCA1-methylated patients compared to BRCA1/2 wild type non-BRCA1 methylated patients (14.5 vs. 5.5 months, p=0.062) although not statistically significant. Therefore, the quantitative analysis for BRCA1 methylation before PARP inhibitor therapy may provide predictive information on treatment response. In conclusion, the importance of BRCA status in ovarian cancer patients surpasses the role of hereditary cancer risk assessment.

2. Real-world management of genetic counseling clinic in real practice

Mi-Kyung Kim discussed clinical practice guidelines on genetic risk assessment and shared potential barriers to ideal genetic testing and counseling for gynecologic cancer patients in the real practice [45]. Advances in genetic testing technologies and wider acceptance of targeted therapy in cancer treatments mandate appropriate genetic counseling. However, long-term psychosocial outcomes on patients and their family members and adherence to post-test surveillance programs are issues to be resolved. The major subject of genetic counseling in hereditary gynecologic cancer are hereditary breast-ovarian cancer syndrome and Lynch syndrome. The key components of genetic counseling are 1) cancer risk assessment and pre-test counseling, 2) genetic testing, 3) post-test counseling, 4) post-test surveillance, 5) planning or risk-reducing strategies. Important considerations of genetic testing are that an affected individual most likely to carry the mutation should be tested first, and comprehensive genetic testing should include full sequencing and testing for large genomic rearrangements. Also, the pros and cons of multi-gene testing should be taken into consideration since one of the disadvantages of multi-gene testing is the increased likelihood of genetic variants of unknown significance (VUS) detection up to 33%–40%. A study showed about 2.7% of BRCA VUS were reclassified as 'likely pathogenic' during follow up and therefore, regular updates of VUS reclassification are needed and should be addressed during the post-test counseling [46]. In real world, there is low uptake of genetic testing. A study by Childers et al. [47] reported the low rate of discussion on genetic testing and even lower rates (15.3% of breast cancer and 10.5% of ovarian cancer patients) of actual testing according to the National Health Interview Survey data. In order to improve the acceptance of genetic testing, Kim suggested a multidisciplinary team approach for genetic counseling, increasing the number of well-trained genetic counselors, and the need for proper reimbursement fee by the Korean government.

3. Updated KSGO position statement for genetic testing and management

Miseon Kim informed on the updated version of the KSGO position statement on genetic testing for peritoneal, ovarian, and fallopian tubal cancers and management that will soon be released in 2019 [48]. A great demand for the updated guidelines that meet the Korean standards was expected, considering the recent approval of National Health Insurance coverage on part of somatic genetic testing along with germline genetic testing through next-generation sequencing.

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SESSION VI. NEWLY REVISED FIGO STAGING OF CERVICAL CANCER 2018

1. Key points of revised FIGO staging of cervical cancer 2018

Dae Woo Lee gave an overview on the key changes of the new FIGO staging system. First, although the FIGO staging system is still considered clinical staging, the revised version allowed advanced radiologic imaging and conformational pathology if used to develop treatment plans. Second, major change has been made on tumor size and lymph nodes involvement since they are known to be important prognostic factors in cervical cancer. In detail, stage IB1 has been divided into three stages stratifying tumor size into 5 mm to 2 cm (IB1), 2 to 3.9 cm (IB2), and equal to or larger than 4 cm (IB3). Stage 3 has been stratified into stage IIIC1 and IIIC2, which are pelvic and para-aortic lymph node metastasis, respectively. The presence of nodal metastases can be determined by advanced imaging or pathology and notations 'r' and 'p' which indicate the method used to derive the stage should be recorded. Third, the size of horizontal spread in stage IA has been deleted from the stage definition. Two retrospective cohort study was performed by Matsuo et al. [49] using the SEER program to validate the revised staging system with a particular focus on stage IB and III disease. Stage IB2 disease was independently associated with a nearly 2-fold increased risk of cervical cancer mortality compared to stage IB1 disease. However, in the stage III cohort, stage IIIC1 was independently associated with improved cause-specific survival compared to stage IIIB disease and the survival significantly differed based on T stage (5-year rates: 74.8% for T1, 58.7% for T2, and 39.3% for T3). Further research is expected for stage IIIC disease for its heterogeneous entity and the effect of local tumor factors on survival outcomes warrants future investigation.

2. Impacts of revised FIGO staging 2018 on daily practice and research: gynecologic oncology

Dong-Hyu Cho addressed the impact of the revised FIGO system to the gynecologic oncologist. The new category of stage IB1 is expected to improve decision making between surgery and radiotherapy according to risk stratification. In addition, since the value of lymph node metastasis is incorporated in the new staging system, the role of sentinel lymph node mapping in cervical cancer may need more evidence. Since stage IIIC1 cervical cancer is not a single disease entity, clinicians should be aware of the wide range of local tumor variance and its effect on survival outcome. Also, the new staging system may bring changes in fertility-sparing approaches; the reasonable indication for trachelectomy for patients with stage IB1 had been lesions less than or equal to 2 cm in diameter. In the new FIGO system it would be both stages IB1 and IB2 and this change will aid further risk stratification in stage IB.

3. Impacts of revised FIGO staging 2018 on daily practice and research: radiation oncology

Jun Won Kim stated that the revised FIGO stage IB2 disease (2–4 cm) are more likely to undergo RH with pelvic lymphadenectomy, while women with stage IB1 disease (<2 cm) are less likely to have received postoperative radiotherapy. Moreover, the new system incorporates lymph node metastasis which is an important prognostic factor in treatment planning. Advanced imaging system such as ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-CT will allow noninvasive nodal assessment and pelvic MRIs will accurately depict the primary tumor. These pretreatment imaging will triage women with locoregional advanced disease to other curative treatment options with less morbidity such as primary radiation, instead of unnecessary dual-modality treatment that combines surgery followed by chemoradiation [50]. Kim pointed out that further studies are warranted to investigate the role of definitive radiotherapy especially for stage IB2 (2 cm to <4 cm) and para-aortic diseases.

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4. Impacts of revised FIGO staging 2018 on daily practice and research: cancer epidemiology

Young-Joo Won presented the global epidemiology data and trends of cervical cancer in Korea. Won noted that the additional factors in the modified staging system will greatly increase the imaging data during diagnosis, treatment, and follow-up. Therefore, it is important to accurately analyze these new variables for epidemiological study. As shown in the Korea Central Cancer Registry data example, information regarding specific sub-stages and paraaortic lymph node metastasis were lacking for complete survival analysis. Therefore, a prospective epidemiological study that could comprehensively sort and analyze the national datasets and incorporate changes of the revised staging system is needed.

NURSING DIVISION SESSION

This year's session for the nursing division dealt with updates on gynecologic oncology and symptom management. In session I, fertility preservation in gynecologic oncology, sentinel lymph node mapping in endometrial cancer, and update on clinical trials in gynecologic oncology were reviewed. In the second part of the session, evidence-based symptom management including intravenous access management on gynecologic cancer patients, chemotherapy-induced hypersensitivity, and decisions on life-sustaining treatment in gynecologic oncology were discussed. Also, practical information needed to become an Oncology Certified Nurse was introduced.

2019 *JGO* WORKSHOP FOR GOOD AUTHORS & REVIEWERS

JGO workshop was held on April 27th, 2019. The aim of this year's workshop was to help clinicians understand and practice the process of paper writing and reviewing and obtain insights on the design and methodology of biomarker and big-data research. Session I was a practice session for paper writing and reviewing. Three original manuscripts were presented for discussion. For each manuscript draft presented, two reviewers commented on the originality, general structure and potential factors for improvement. For the third manuscript that has already been accepted to the *JGO*, detailed reviewer comments and steps of editing process were shown. The second part of the workshop was on research planning and manuscript writing. The topics covered in this session were, design and analysis of biomarker research, data structure and utilization of the National Health Insurance big data, and clinician's experience with big data research. It was a valuable time for the audience to gain insights and learn practical tips of scientific writing and research planning.

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