



## Meeting Report

# Meeting report from the 19th meeting of the International Gynecologic Cancer Society (IGCS) 2019: Summary of selected abstracts and meeting highlights

## 1. Introduction

The 2019 18<sup>th</sup> meeting of the International Gynecologic Cancer Society (IGCS), and first annual meeting, was held in Rio De Janeiro, Brazil led by the IGCS president, Roberto Angioli, Professor and Chairman of Obstetrics and Gynecology at the University of Rome Campus Bio Medico in Rome, Italy. The 2019 program committee, chaired by Nadeem Abu-Rustum, Professor and Chair of Gynecologic Oncology at Memorial Sloan Kettering Cancer Center in New York City, included representatives from all regions of the world to assist in identifying trends, opportunities, and challenges facing their regions as well as submissions of scientific abstracts for peer review. The meeting focused on the mission of the IGCS, to enhance the care of women with gynecologic cancer worldwide through education and training and public awareness.

In his Presidential Address, Dr. Angioli highlighted the society's mission by focusing on the increasing global burden of cancer, noting that it is the leading cause of death in high income countries (HIC) and increasing in both middle (MIC) and low (LIC) income countries. He noted this result is related to increasing risk factors such as obesity, unhealthy diets, and tobacco use as well as lack of preventative measures such as screening and vaccinations. The main focus of his address was on a new initiative with the World Health Organization (WHO) to eliminate cervical cancer. The WHO and IGCS have aligned themselves to spread knowledge through education, promote easy access to health centers, create intensive vaccinations and screening programs, and optimize treatment and palliative care to women with this disease. The ultimate goal of this collaborative project is to achieve a 70% screening rate, a 90% vaccination rate and treatment of precancerous lesions, and, most importantly, the threshold of less than 4 cases/100,000 women in the next ten years. Additionally, Dr. Angioli has engaged other societies and health leaders to tackle this issue and invited speakers are listed in [Table 1](#). The hope is that this ambitious initiative will result in the eradication of cervical cancer and other HPV related diseases.

IGCS awards and recipients are listed in [Table 2](#).

This review focuses on selected abstracts presented at the meeting as well as highlighting other sessions designed to improve the delivery of care to women in limited resource settings.

## 2. Cervical cancer

The Laparoscopic Approach to Cervical Cancer (LACC) trial continues to be a focus of attention, even 18 months after its initial

presentation at the Society of Gynecologic Oncology meeting in 2018. A large retrospective study from Norway, presented by Dr. Mahmut Sert, evaluated early stage cervical cancer patients treated by minimally invasive surgery (MIS) ( $n = 230$ ) versus open approach ( $n = 357$ ). They reported a worse 5-year disease free survival (88.6% vs. 93.5%,  $p = 0.04$ ) as well as a higher rate of peritoneal relapses were noted in the MIS group. Interestingly, the IRTA trial, a retrospective evaluation of 698 women, evaluating outcomes in women who underwent open ( $n = 388$ ) versus MIS ( $n = 310$ ) radical trachelectomy for cervical cancer in tumors  $\leq 2$  cm was presented. Dr. Gloria Salvo presented the data and noted that though the tumors were larger in the open group, there was no difference in recurrence rates between the two groups; 6.4% in the minimally invasive group versus 5.7% in the open group. Of note, the open group had lower readmission rates (1.8% versus 11%) and reoperation rates (4.8% versus 1.5%); but a longer hospital stay (6 days versus 2 days). Additional interesting findings include that recurrence was more common findings in tumors that were 1–2 cm in size and those who had a prior conization had a lower rate of conization. This study somewhat contradicts the findings of the LACC trial adding to the controversy of the ideal approach.

Dr. Kathleen Schmeler presented preliminary results of the CONSERV (Conservative Surgery for Women with Low-Risk, Early Stage Cervical Cancer) trial which is a prospective trial evaluating conization and hysterectomy and lymph node assessment in early stage cervical cancer ( $\leq 2$  cm). One hundred women were included and, in addition to nodal assessment, 44% had undergone fertility sparing surgery with a conization (negative margins and endocervical curettage), 40% hysterectomy, and 16% were enrolled after undergoing a hysterectomy with final pathology revealing an occult cervical cancer. In all cases, 5% of patients had positive lymph nodes and 1 patient had residual disease in the hysterectomy specimen. To date, the recurrence rate is 4.3%. Of note, 2 of these recurrences occurred in women after an inadvertent hysterectomy for cervical cancer and resulted in modification of the protocol to exclude this group of patients from the study. Of the 44 eligible patients, the pregnancy rate is 20%. Though this study is promising, additional results, including GOG 278 and the SHAPE trial, will help clarify the true role of conservative surgery in this patient population.

Dr. Lukas Rob presented a 20 years experience on less radical fertility sparing than radical trachelectomy in early cervical cancer. They included 91 women with tumors ( $<2$  cm and  $<50\%$  stromal invasion) were assessed by ultrasound or MRI who underwent a 2 step surgical plan. First, a laparoscopic sentinel lymph node (SLN)

**Table 1**  
Invited speakers.

Ana Cristina Pinho Mendes Pereira, MD	Director General of the National Cancer Institute (INCA), Brazil
Elena Fidarova, MD	World Health Organization
Mary McCormack BSc, MSc, PhD, MBBS	University College London Hospitals
Wui Jin Koh, MD	Senior Vice President and Chief Medical Officer of the National Comprehensive Cancer Network
Ted Trimble, MD	Director of the National Cancer Institute's Center for Global Health
Angelica Nogueira-Rodrigues, MD, PhD	Brazilian Group of Gynecologic Oncology; Global Cancer Institute; Latin America Cooperative Oncology Group

**Table 2**  
IGCS awards.

Lifetime Achievement Award	Sergio Pecorelli, MD, PhD (Italy)
Excellence in Teaching Award	Groesbeck Parham, MD (USA/Zambia)
Outstanding Achievement in Gynecologic Oncology Surgery Award	Manuel Penalver, MD (USA)
Award for Community Advancement in Resource-Limited Settings	Jorge Saad Souen, MD (Brazil)
Distinguished Advocacy Award	Venus Gines (USA)
	Miho Katagi (Japan)
	Benda Kithaka (Kenya)

mapping and parametrial lymphatic channel excision was performed; if negative, a vaginal simple trachelectomy was done. The fertility procedure was successful in 76 cases; there were three (3.9%) central uterine recurrences and 1 (1.3%) patient died. Of the 62 patients who tried to conceive, 49 patients (79%) became pregnant, suggesting a high pregnancy rate when compared to other series and favorable outcomes.

In a retrospective analysis of SENTICOL I and II, Dr. Vincent Balaya evaluated the correlation between sentinel lymph node (SLN) status to the risk of parametrial invasion (PI). A total of 211 patients were included and 29 patients (13.7%) had positive SLN and 11 patients (5.2%) had PI. PI correlated with tumor size  $\geq 2$ cm and SLN status in multivariate analysis. Only 1 case (0.9%) of tumor  $< 2$ cm and negative SLN had PI. These data confirm previous series that addressed risk factors for PI in early stage cervical cancer.

Dr. Simone Marnitz-Schulze presented the results of Uterus-11 study: A randomized clinical trial on surgical staging versus CT-staging prior to primary chemoradiation in patients with FIGO 2009 stages IIB-IVA cervical cancer. A total of 255 patients with locally advanced cervical cancer were enrolled. Women with enlarged lymph nodes on CT scan underwent biopsy to determine radiation fields. Surgical staging resulted in the upstaging of 30% patients. Regardless of study group, the presence of positive lymph nodes negatively impacted survival outcomes. Cancer specific survival was better in the surgical group; and though it did not reach statistical significance, progression free and overall survival trended in favor of the surgical group.

Dr. Fabio Landoni presented the results of the randomized, prospective EORTC trial evaluating chemoradiation therapy ( $n = 312$ ) versus neoadjuvant chemotherapy followed by radical hysterectomy ( $n = 314$ ) in women with stage IB2, IIA or IIB cervical cancer. In the neoadjuvant arm, which consisted of a minimum of cisplatin 225 mg, 23% of patients had a complete response and 15% had an optimal response (defined as minimal invasion at the time of surgery); 52% of patients had a suboptimal response. However, 24% of patients did not receive surgery due to progression or toxicity from therapy. Overall survival was similar between the two groups, however, progression free survival was improved in the chemoradiation therapy (65.6% versus 56.9%).

Late and persistent symptoms (LAPERS) of radiochemotherapy in locally advanced cervical cancer was presented by Dr. Remi Nout. This study evaluated substantial and persistent symptoms at 3 months when compared to baseline/early symptoms in women enrolled in the EMBRACE prospective trial on MRI image-guided

adaptive brachytherapy. After a median of 42 months, examples of symptoms evaluated included gastrointestinal issues such as diarrhea and blood in stool; urinary frequency, neuropathy, lower back pain, leg swelling, and general symptoms such as trouble sleeping and fatigue. Leg swelling was the only significant LAPERS when compared to baseline symptoms and general symptoms (tiredness, need to rest, feeling weak) were more likely to be associated with LAPERS when compared to organ specific symptoms. This study highlights the role of LAPERS assessment to address patients' burden of toxicity.

### 3. Ovarian cancer

Dr. Rachel Grisham presented MILO/ENGOT-OV11, a phase III study of low grade ovarian cancer of binimetinib versus physician choice chemotherapy (liposomal doxorubicin, topotecan, or paclitaxel). To date, this is the largest prospective trial in this group and randomized 228 women to binimetinib, a MEK inhibitor, and 113 women to chemotherapy with cross over after progression disease. Patients may have received up to three prior chemotherapy regimens. The progression free survival was comparable; 9.1 vs 10.6 months and the objective response rate were 16% vs 13% for binimetinib and chemotherapy, respectively. Though the study was closed early due to futility, Dr. Grisham presented the results on the remaining study after closure in 2016. The progression free survival was 11.2 months for binimetinib and 14.1 months for chemotherapy (no statistical significance); there was a 24% objective response rate in both groups and overall survival was similar at ~34 months.

Further analysis revealed that 33% had a KRAS mutation. This finding was noted to have an improved progression free survival to binimetinib: KRAS mutation 17.7 months vs KRAS wildtype 10.8 months (statistically significant). A similar pattern was noted in the chemotherapy group with KRAS mutation (14.6 vs 11.5 months) though this did not reach statistical significance. Therefore, it is important to note that though binimetinib did not meet its primary endpoint, this agent did show activity in low grade serous ovarian cancer, particularly with a KRAS mutation.

Dr. Robert Coleman presented an exploratory analysis on post-progression and patient centered outcome of rucaparib maintenance from the ARIEL 3 trial. This trial which demonstrated a progression free survival with rucaparib maintenance compared to placebo in platinum sensitive relapsed ovarian cancer. In this updated analysis, the time to start of first subsequent therapy

(TSFT) was clinically significant (of note, this includes progression free survival). Interestingly, rucaparib demonstrated continued benefit in the progression free survival-2/time to start of second subsequent therapy in each cohort (BRCA mutant cohort and intention to treat population). In an evaluation of the patient centered outcomes, the quality adjusted investigator-assessed progression free survival (QA-PFS) demonstrated improvement across all cohorts in the rucaparib group. Quality-adjusted progression free time without symptoms or toxicity (Q-TWiST) was significant and demonstrated a difference of almost 7 months favoring rucaparib (13.2 months vs 6.4 months). Though overall survival is not yet mature, this abstract demonstrates the significant impact of rucaparib in this population.

Dr Richard Penson presented data from the phase III SOLO3 trial that addressed the role of olaparib versus chemotherapy for germline BRCA mutated platinum-sensitive relapsed ovarian cancer patients. Patients with 2 or more lines of previous chemotherapy were randomized to receive olaparib ( $n = 178$ ) or non-platinum chemotherapy ( $n = 88$ ). The overall response rate favored the olaparib arm (72% vs. 51%), which also had improved progression free survival (13.2 vs. 8.5 months; HR 0.49  $p < 0.001$ ). The tolerability profiles of olaparib and chemotherapy were consistent with previous data, and patients in the chemotherapy arm were more than twice likely to discontinue the study due to adverse effects. SOLO3 provides important data on the efficacy of PARP inhibitor for women with heavily pre-treated platinum sensitive recurrent germline BRCA mutated ovarian cancer.

Dr. Pauline Kramer presented a study on translating endometrial molecular risk stratification to endometrioid ovarian carcinoma. This novel application of precision medicine noted that there were lower rates of POLE mutation, MMR deficiency and P53 mutations than uterine cancers. In those with a POLE mutation, no patients recurred; whereas those with abnormal p53 had a higher rate of recurrence. It should be noted that synchronous cancers often share mutations and are clonally related, but the mutation frequencies may differ. These results demonstrated similar outcomes patterns and suggest that the Promise (Proactive Molecular Risk Classifier for Endometrial Carcinoma) subgrouping is prognostic in endometrioid ovarian cancer and these cases may be stratified like uterine cancer.

Additional presentations in ovarian cancer included the prognostic impact of immunotherapy in ovarian cancer with a focus on natural killer cells neutrophils, and PDL1 expression in ovarian cancer. MITO RT1, a large, multicenter, retrospective study evaluating the role of stereotactic body radiation therapy (SBRT) was evaluated in oligometastatic ovarian cancer. Two hundred sixty one patients were evaluated in this series and the authors noted that the 3 year toxicity free survival was 92.1% and the authors state that SBRT is an active treatment option in this setting.

#### 4. Uterine cancer

Several presentations focused on uterine cancer. Dr. Alessandro Buda presented the role of ultrastaging ( $n = 226$ ) compared to one step nucleic acid amplification (OSNA) ( $n = 183$ ) for sentinel node metastases in endometrial cancer. OSNA detected a higher rate of micrometastasis and lower rate of macrometastasis and ITC compared to traditional ultrastaging. Despite these differences, the authors noted that there were comparable findings and outcomes in regards to positive nodes and note that OSNA can be an alternative to ultrastaging.

Dr. Gabriella Ferrandina presented the prevalence of BRCA 1 and 2 mutations and alterations of homologous recombination deficient (HRD) in leiomyosarcoma. Using Next-Generation Sequencing (NGS), they were able to evaluate 81 samples. They noted that a BRCA mutations was present in 6.5% of cases and p53 mutation

was noted in 21.7% of cases. These novel findings provide insight into disease pathogenesis and elucidate the potential role of targeted therapies in this disease.

Dr. Jun Guan presented the results of a randomized trial evaluating megestrol versus megestrol plus metformin for fertility sparing management. The 16 week complete response rate were better for the megestrol plus metformin group (39.6% vs. 20.4%;  $p = 0.032$ ) among patients with atypical hyperplasia. Moreover, the 30 week complete response rates were 69.2% and 57.4% for the megestrol plus metformin and only megestrol arms, respectively ( $p = 0.16$ ). This trial presents a possible improved option for management of women with endometrial disease who desire fertility preservation.

#### 5. Miscellaneous topics

Dr. Saketh Guntupalli presented the final results of his randomized controlled trial of oral apixaban compared to subcutaneous enoxaparin for thromboprophylaxis in women undergoing surgery for suspected gynecologic malignancy. In this study, 400 women completed therapy and the authors noted no difference in bleeding incidence or non-bleeding adverse events, demonstrating that there were no significant differences in toxicity or venous thromboembolic incidence. Of note, women in the apixaban arm reported improved satisfaction, specifically less pain and ease of medication administration. This study shows that apixaban is an alternative option to enoxaparin following surgery.

Dr. Lea Moukarzel presented a series of 410 patients that underwent a rectosigmoid resection for gynecologic malignancies. Near infrared angiography (NIR) was used in 134 (32.7%) cases via proctoscopy to assess anastomotic perfusion. They found an anastomotic leak rate of 1.2% in the NIR group compared to 4.7% in non-NIR group ( $p = 0.10$ ). Diverting ostomy was less performed in NIR group (6.7% vs. 19%;  $p < 0.001$ ) and was associated with less post-operative abscesses, post-operative interventional procedures, and a lower 30-day readmissions. Therefore, this technology may be used to assess the integrity of reanastomoses.

#### 6. Conclusions

In addition to the above noted presentations, the IGCS meeting included a dedicated session, led by Dr Fernando Maluf, on developing consensus guidelines for cervical and vulvar cancer management in resource limited settings. This year was the first year that IGCS sponsored a live telesurgery session, led by Drs. Reitan Ribeiro, Audrey Tsunoda and Gustavo Guitmann, featuring complex oncologic surgeries that were transmitted from Erasto Gaertner Hospital in Curitiba, Brazil to the main meeting auditorium. IGCS also conducted an educational and hands on colposcopy course, and many other topics by multi-disciplinary experts from across the globe. By bringing this multi-disciplinary meeting of experts in gynecologic oncology to Rio De Janeiro, IGCS will undoubtedly raise the profile and standard of gynecologic cancer care for women in resource-limited settings and throughout the world.

#### Declaration of Competing interest

Ritu Salani and Glauco Baiocchi have no relevant disclosures.

#### Author contribution

Both authors contributed to the conception, design and execution of this manuscript. We would also like to acknowledge Roberto Angioli and Nadeem Abu-Rustum for their input.

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