Report from the European Society of Gynaecological Oncology (ESGO) 2020 State-of-the-Art Virtual Meeting

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ABSTRACT

This is a report from the European Society of Gynaecological Oncology State-of-the-Art Virtual Meeting held December 14–16, 2020. The unique 3-day conference offered comprehensive state-of-the-art summaries on the major advances in the treatment of different types of gynecological cancers. Sessions opened with a case presentation followed by a keynote lecture and interactive debates with opinion leaders in the field. The speakers also presented scientific reviews on the clinical trial landscape in collaboration with the European Network of Gynecological Oncological Trial (ENGOT) groups. In addition, the new ESGO-ESRTO-ESP endometrial cancer guidelines were officially presented in public. This paper describes the key information and latest studies that were presented for the first time at the conference.

INTRODUCTION

General Information

The scientific gynecological cancers calendar includes a congress organized by the European Society of Gynecological Oncology (ESGO) every second year. The event attracts large numbers of participants from around the world.[1 2] Between biannual meetings, the society also organizes a State-of-the-Art Conference (ESGO SoA). In 2020, the fourth ESGO conference was held in a virtual format due to the COVID-19 pandemic. Between December 14 and 16, more than 800 participants from 74 countries joined the meeting. A total of 29 speakers addressed 16 scientific sessions, and 21 abstracts were presented. Eight satellite symposia were held online.

The conference was chaired by Professor Philippe Morice (ESGO president 2019–2021), Professor Mansoor Raza Mirza (ESGO scientific committee chair), and Professor Christina Fotopoulou (ESGO SoA Conference 2020 chair).

ENGOT: IMPROVING PATIENTS' OUTCOME THROUGH CLINICAL TRIALS

The European Network of Gynecological Oncological Trial (ENGOT) group was founded in 2007. It is a research network under the umbrella of ESGO that develops cooperation between national and regional groups performing clinical trials. Multicenter and multinational studies include translational research, research on rare gynecological malignancies, early drug development, academic clinical trials, and industry-sponsored clinical trials.

ENGOT Collaboration Explained by Dr Antonio González-Martín

ENGOT currently consists of 21 groups from 25 countries. ENGOT's mission and vision focus on enabling access to participation in clinical trials for both patients and clinicians. Clinical trials within the ENGOT group are patient-oriented and aim to address unmet clinical needs. Due to unified standards, all collaborators work according to a unique protocol, an agreed statistical analysis plan, and use one specific database. The engagement of academic groups in the clinical trials, specially those sponsored by pharmaceutical companies, improves the credibility and the quality of the research. The network is continuously developing and increasing its cooperation with other international groups. As evidence of this principle, it has recently published details of the cooperation between ENGOT and Gynecologic Oncology Group Foundation with industry in the *International Journal of Gynecological Cancer* and *Gynecologic Oncology*.[3–7] As a result, ENGOT is continuously providing clinicians and society with evidence that changes clinical practice.[8–15]

A Decade of Achievements Reviewed by Professor Mansoor Mirza

Even though ENGOT is a relatively young organization, it has already managed to provide data that improve patients' care.

The role of surgery in ovarian cancer management was examined in a study by du Bois et al, proving that residual tumor has a significant impact on patients' outcome.[16] A few maintenance therapy protocols have been investigated to prevent ovarian cancer relapse. Studies focusing on PARP inhibitors as first-line maintenance therapy include the SOLO1, PAOLA-1, and PRIMA trials.[10 11 13 17] It is worth emphasizing that both the PAOLA-1 trial and PRIMA trial are trials led by ENGOT. New data about the the role of cytoreductive surgery for relapse in ovarian cancer have been recently provided by another ENGOT trial—AGO-OVAR OP.4/DESKTOP III.[15] Medical treatment with PARP inhibitor in platinum-sensitive relapse was investigated in the NOVA and SOLO2 ENGOT trials.[10 12] The introduction of bevacizumab in platinum-resistant recurrent ovarian cancer was established due to the AURELIA ENGOT trial.[9 18]

Ongoing ENGOT trials focusing on endometrial cancer treatment include a phase III trial of post-operative chemotherapy or no further treatment for patients with node-negative stage I–II intermediate or high-risk endometrial cancer (ENGOT-EN2-DGCG, NCT01244789). Endometrioid cancer treatment with endocrine therapy and palbociclib or placebo is the topic of the ENGOT-EN3/NSGO-PALEO trial.[19] The role of immunotherapy in the treatment of advanced/metastatic endometrial cancer is also addressed in ongoing trials: EN6-RUBY (ENGOT), EN7-ATTEND (ENGOT), EN9-LEAP-1 (ENGOT), and DUO-E.

The ENGOT CX11 trial is a randomized phase III double-blind study of chemoradiotherapy with or without pembrolizumab to treat high-risk locally advanced cervical cancer and is currently actively recruiting

patients. Metastatic cervical cancer management is examined in the BEATcc trial: ENGOT-Cx10/GEICO 68 C/GOG#3030/JGOG1084.

Apart from the new data achieved due to numerous trials, ENGOT has inspired multiple national and regional groups to form cooperative research groups and contribute to attaining new practice-changing results.

Importance of Translational Research and Biobanking for Personalized Treatment by Professor Elena Ioana Braicu

The word 'biobank' was used for the first time in 1996 by Loft and Poulsen. Since then, the idea of biobanking has been continually developing. Currently, the total number of patients with ovarian cancer included in the ENGOT retrospective biobank exceeds 6000. Due to international cooperation, it is possible to obtain higher numbers of paired samples and samples from patients with rare diseases. What is more, biobanking helps in the development of organoid models for further cancer research. Planning appropriate sample collection for future translational research is one of the critical elements during trial preparation. A few prospective biobanks were developed or are currently under development as part of ongoing trials: ENGOT Ov48/BGOG/EUDARIO, ENGOT Ov59/NOGGO Ov42-MAMOC, ENGOT Ov47-TR/NOGGO-HELP-ER, ENGOT Ov56/NSGO-CTU-DOVACC.

THREE-MINUTE THESIS SESSION

During the ESGO State-of-the-Art 2020 Virtual Meeting, the scientific program included a "Three-minute thesis" session with a selection of 12 top abstracts from the accepted posters.[20–31] Authors presented their results in a 3 min summary and participated in a discussion at the end of the session.

Cervical Cancer Screening

Assessing Trends in Stage and Outcomes of Uterine Cervix Cancer in an Opportunistic Screening Setting (abstract No 595)

The first presentation by Professor Francisco Jose Candido dos Reis demonstrated the results of a retrospective cohort study that analyzed the outcome of an opportunistic cervical cancer screening program in Brazil.[20] The analyzed aspects included 5-year cervical mortality, stage distribution, and screening coverage. The authors evaluated the outcome of 18 206 patients diagnosed with cervical cancer between 2000 and 2014. The estimated screening coverage was between 81% in 2003 and 85% in 2013. The proportion of patients diagnosed with advanced-stage cancer was between 71% (2006) and 77% (2000). During the 5-year follow-up 6479 patients (35.6%) died due to cervical cancer. The mortality rate during the analyzed period remained at the same level. The authors concluded that opportunistic cervical cancer screening is not as effective as organized screening programs for the number of patients diagnosed with early-stage disease and the mortality rate.

Sentinel Lymph Node Biopsy in Breast Cancer and Upper Limb Function

Effect of Sentinel Lymph Node Biopsy on Upper Limb Function in Women with Early Breast Cancer: A Systematic Review of Clinical Trials (abstract No 611)

In the second presentation, Professor Francisco Jose Candido dos Reis presented a systematic review of randomized control trials examining the incidence of complications following sentinel lymph node biopsy in patients with early breast cancer—that is, lymphedema and pain, sensory, and motor disorders.[23] Sentinel lymph node biopsy is a less invasive method than axillary dissection. However, it is also associated with post-operative complications. The search was performed using PubMed, EMBASE, CINAHL, and Web of Science databases. The risk of bias was evaluated with the Cochrane RoB 2.0 tool. The review included nine articles with a total of 4110 patients. Lymphedema occurred in up to 11% of included patients 6 months after the surgery and up to 14% of patients during the follow-up 24 months after the surgery. Upper limb pain was reported by 11–16% of patients 6 months after sentinel lymph node biopsy and 8–16% of patients 24 months after the procedure. Sensory and motor disorders were diagnosed in 2–22% and 0–9% of patients 6 months after the surgery. They persisted in 1–10% of patients (sensory disorders rate) and 0–2% of patients (motor disorders rate) 2 years after the procedure. The authors concluded that complications following sentinel lymph node biopsy can be heterogeneous, long-term, and should be taken into consideration.

Niraparib: Patient-Reported Outcomes

Patient-Reported Outcomes in Patients Receiving Niraparib in the PRIMA/ENGOT-OV26/GOG-3012 Trial (abstract No 294)

Professor Johanna U Mäenpää et al analyzed patient-reported outcomes in patients receiving niraparib and placebo in the PRIMA/ENGOT-OV26/GOG-3012 trial.[24] Patient-reported outcomes were a secondary endpoint of the trial and were collected every 8 weeks for 56 weeks and every 12 weeks after that. When treatment was discontinued, patient-reported outcomes were collected at 0, 4, 8, 12, and 24 weeks. The validated questionnaires used included: FOSI, EQ-5D-5L, EORTC-QLQ-C30, and EORTC-QLQ-OV28. No differences were obtained in the analysis of the EORTC-QLQ-C30 and EORTC-QLQ-OV28. Quality of life scores related to the health of patients receiving niraparib and placebo were similar at each time point. A slight improvement in the health utility index was seen for patients in the niraparib arm compared with those in the placebo arm. Results are consistent with the NOVA study, concluding that niraparib intake is not associated with a decreased patient-reported quality of life.

Niraparib: Older Patients with Advanced Ovarian Cancer

Efficacy and Safety of Niraparib in Older Patients with Advanced Ovarian Cancer: Results from the PRIMA/ENGOT-OV26/GOG-3012 Trial (abstract No 347)

In a study by Professor Hanna Dahlstrand et al, the authors focused on niraparib's efficacy and safety in the group of older patients with advanced ovarian cancer, based on the results from the PRIMA/ENGOT-OV26/GOG-3012 trial.[25] The analysis included 733 patients with newly diagnosed, advanced, high-grade serous or endometrioid ovarian, primary peritoneal, or fallopian tube cancer. Two hundred and eighty-nine patients were aged 65 years old or older, and their outcome was compared with a younger group of 444 patients aged under 65 years. The efficacy of niraparib was similar in the analyzed age groups. Any-grade and grade 3 or higher adverse event rates were comparable in the age groups examined. Cases of grade 3 or higher thrombocytopenia events in patients under 65 years old depended on the dosing. They were reported in 43% of patients receiving a fixed starting dose of 300 mg a day and in 18% of patients receiving individualized starting doses according

to basal body weight or platelets count. In older patients, the values were 57% and 26%, respectively. No differences between the age groups were observed in the patient-reported outcomes and quality of life assessed by FOSI and EQ-5D-5L instruments. The authors concluded that most of the analyzed factors—that is, niraparib efficacy, safety, and quality of life during therapy, were similar in the compared age groups. An individualized starting dose was shown to be beneficial for older patients due to the improved rates of three or more thrombocytopenia events.

Maintenance Olaparib: Newly Diagnosed Advanced Ovarian Cancer and BRCA Mutation

Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer and a BRCA Mutation: Subgroup Analysis by Risk in the Phase III SOLO1 Study (abstract No 392)

Professor Nicoletta Colombo presented the results of an exploratory analysis from higher-risk and lower-risk subgroups from the phase III SOLO1 study (NCT01844986) of patients with newly diagnosed advanced ovarian cancer and a BRCA mutation, in whom maintenance olaparib significantly improved progression-free survival compared with placebo.[26] The high-risk group included patients with stage IV disease, stage III disease and residual disease after primary debulking surgery, inoperable stage III disease, or stage III disease treated with neoadjuvant chemotherapy followed by interval surgery. Lower-risk patients were diagnosed with stage III disease and no residual disease after primary debulking surgery. Two hundred and nineteen patients were included in the high-risk group, and 172 patients in the lower-risk group. The median follow-up was 41 months. The risk of disease progression/death per investigator was significantly reduced in the olaparib arm compared with the placebo arm, both in the higher-risk group (HR 0.34, 95% CI 0.24 to 0.48; 66% reduction) and the lower-risk group (HR 0.33, 95% CI 0.20 to 0.52; 67% reduction). The investigator-assessed median progression-free survival was 39.0 versus 11.1 months for olaparib versus placebo in the high-risk group, and not reached versus 21.9 months in the lower-risk group. Similar results were obtained per blinded independent central review. So far, SOLO1 is the first trial investigating maintenance monotherapy with PARP inhibitor. proving a substantial reduction in the risk of progression/death for both higher-risk and lower-risk patients with newly diagnosed advanced ovarian cancer.

Fertility-Sparing Treatment: Advanced Borderline Ovarian Tumors

Fertility-Sparing Treatment in Advanced Borderline Ovarian Tumors: An Analysis from the MITO14 Study Database (abstract No 227)

In a study by Dr Francesca Falcone et al, the authors presented the results of a multicenter retrospective study of patients with advanced borderline ovarian tumors registered in the MITO14 database between 1995 and 2019.[27] The analyzed factors included recurrence rate, predictors of recurrence, disease-free survival, disease-specific survival, pregnancy, and live birth rates. One hundred and one conservatively treated patients were included in the study. The median follow-up was 124 months. The recurrence rate was 54.5%, with a median time to first relapse of 21 months. Identified independent factors of the recurrence were the size of the extra-ovarian lesions and the presence of invasive implants. Median disease-free survival was 96 months, and the median disease-specific survival was 290.4 months. At the end of the observation period, 96 (95%) patients had no signs of the disease. Thirty-one (30.7%) patients attempted to conceive. Twenty-three patients conceived at least once. Twenty patients gave birth to a healthy child. The authors concluded that, despite the high recurrence rate, there is a place for fertility-sparing surgery in patients with borderline ovarian tumors due to longer survival and promising pregnancy outcomes.

Resistance Mechanism to PARP Inhibitors

Elucidating Resistance Mechanism to PARP Inhibitors for the Development of Novel Therapeutic Approaches in High-Grade Serous Ovarian Cancer (abstract No 416)

The presentation by Professor Hagen Kulbe aimed to describe the key signaling pathways of resistance to PARP inhibitor treatment in a group of 52 patients with high-grade serous ovarian cancer.[28] Gene expression data were collected before PARP inhibitor therapy initiation. Molecular and regulatory mechanisms in the subgroup of 25% extreme respondents (n=26, 13 in each group) were examined with comprehensive bioinformatics analysis of differentially expressed genes. The results showed that non-responders were characterized by higher levels of MYC activity and deregulation of the Wnt/ß-catenin signaling pathway. Specific pathways were also associated with PARP inhibitor resistance, particularly: PDGFR, FGFR, PI3K/mTOR, and MAPK. The authors identified key kinases, which could mediate PARP inhibitor resistance: JAK1/1, SRC. The proposed biomarker of PARP inhibitor treatment efficacy is folate receptor 1; the authors observed that it had a significantly higher expression in the non-responders.

Advanced Ovarian Cancer: Primary and Interval Cytoreductive Surgery

Post-operative Outcomes of Primary and Interval Debulking Surgery for Advanced Ovarian Cancer Registered in the Dutch Gynecological Oncology Audit (abstract No 565)

In a multicenter retrospective study by Dr Nishita Baldewpersad Tewarie et al, the authors examined the outcome of cytoreductive surgery in patients with advanced ovarian cancer, together with the short-term post-operative morbidity and mortality.[29] The analysis included 2382 patients with FIGO IIB–V ovarian cancer managed with primary or interval cytoreductive surgery between 2015 and 2018 in eight regions in the Netherlands. Higher complication rates with re-intervention (5.7% vs 3.6%, respectively, p=0.048) and more frequent complete cytoreduction (69.7% vs 62.1%, respectively, p<0.001) were observed in the primary cytoreductive surgery group (n=1027). The authors emphasize the importance of adequate aggressive surgery in order to obtain complete cytoreduction and assess the risk of complications, and the possibility of following re-intervention and delayed chemotherapy.

Sex Cord Stroma Cell Tumors: Treatment Strategies and Survival

Treatment Strategies and Survival of Women with Sex Cord Stroma Cell Tumors: Analysis of the AGO-CORSETT Database (abstract No 284)

Professor Maximilian Klar presented the results from the Current Ovarian geRm cell and SEx cord stromal Tumor Treatment

strategies (CORSETT) database, including registered patients from 20 German centers.[30] The reference pathology panel results of included patients were as follows: granulosa cell tumor in 143 patients, Sertoli-Leydig cell tumor in 14 patients, and other tumors in five patients. Laparoscopic treatment was introduced in 81 patients with granulosa cell tumor and in eight patients with Sertoli-Leydig cell tumor. Fertility-sparing surgery was performed in 57 patients with granulosa cell tumor and in eight patients with Sertoli-Leydig cell tumor. Adjuvant chemotherapy was introduced in 19 patients with granulosa cell tumor and two patients with Sertoli-Leydig cell tumor. Relapse was observed in 59 patients from the granulosa cell tumor group and two patients with a Sertoli-Leydig cell tumor. The median progression-free survival for all enrolled patients with sex cord cell stroma tumors was 80.4 months. An advanced FIGO stage was associated with decreased progression-free survival . No statistically significant association between adjuvant chemotherapy and progression-free survival was observed.

High-Grade Serous Ovarian Cancer: Response to Platinum Therapy

Novel 3D Model Systems to Assess Heterogeneity in Response to Platinum Therapy in High-Grade Serous Ovarian Cancer (abstract No 550)

Dr Jennifer Ploski et al investigated the influence of the local microenvironment on the response of disseminated tumor cells to cisplatin treatment, and the possibility of developing a screening tool to predict drug response.[31] Three ex vivo models were developed for this study: organotypic, organoid, and tumor slice model. Tumor specimens were obtained during radical debulking surgery in patients with advanced stage high-grade serous ovarian cancer. Organotypic models were developed from tumor cells extracted from disseminated tumors, added to normal omental fibroblasts and mesothelial cells embedded in collagen-1. Organoid models used similarly obtained tumor cells embedded in basement membrane extract. Tumor slice models were established from tumors sliced into 350 µm sections using a vibratome. All models were treated with cisplatin. Data from organotypic models showed a trend towards reduced response to treatment in 3D models compared with 2D tumor cultures. The response to cisplatin observed in 3D models was heterogeneous. Long-term growth of over 15 passages was successfully obtained for organoid models. Authors determined that organoid models must be generated within 24 hours of tumor cell extraction. Viability of tumor slices was achieved for up to 5 days. Both organotypic and organoid models can be generated from fresh and viably frozen tumors. Owing to development of the presented models and investigation of the tumor microenvironment, improved management with personalized treatment could lead to more effective therapeutics strategies.

PRESIDENTIAL SESSION

The presidential session was chaired by Professor Philippe Morice (ESGO president 2019–2021) and Professor Mansoor Raza Mirza (ESGO SoA Conference 2020 chair). The scientific program included nine presentations on ovarian and cervical cancer.[32–40]

Triple Kinase Inhibitor in Recurrent Ovarian Clear-Cell Carcinoma

A Randomized Phase II Study of Nintedanib (BIBF1120) Compared with Chemotherapy in Patients with Recurrent Clear-Cell Carcinoma of the Ovary or Endometrium (NICCC/ENGOT-OV36) (abstract No 596)

Clear-cell carcinoma is a rare subtype of ovarian cancer. It carries a poor prognosis, and response to chemotherapy in recurrent disease is low.[41] As angiogenesis pathways are activated in clear-cell carcinoma, Dr Rosalind Glasspool presented the results from an international, multicenter, randomized, open-label phase II trial comparing nintedanib (BIBF1120), an orally available, triple kinase inhibitor targeting vascular endothelial growth factor receptors VEGFR), platelet-derived growth factor receptors (PDGFR), and fibroblast growth factor receptors (FGFR), with physician's choice of chemotherapy in patients with recurrent ovarian clear-cell carcinoma who relapsed within 6 months of the last platinum chemotherapy.[32] Patients were randomized to nintedanib 200 mg orally twice daily or chemotherapy [paclitaxel (80 mg/m^2 IV days 1, 8, 15), pegylated liposomal doxorubicin (40 mg/m^2 IV) or topotecan (4 mg/m^2 IV days 1, 8, 15) every 28 days). Treatment was given until disease progression or unacceptable toxicity. The primary endpoint was progression-free survival. Secondary objectives included overall survival, response rate, disease control rate, and patient-reported outcomes. Ninety-one patients with ovarian cancer were included in the analysis. The median age was 54 years. The median number of previous lines was two. After a median follow-up of 20.7 months, the median progression-free survival was 2.3 months with nintedanib and 1.9 months with chemotherapy (HR=0.79, 80% CI 0.58 to 1.06, p (one-sided)=0.152). The median overall survival was 9.0 and 4.9 months, respectively. The differences in overall survival estimates at six and 12 months were 19.7% and 8.9%, respectively, demonstrating non-proportional hazards. The response rate was 2.1% and 0%, and disease control rate at 16 weeks was 23.4% and 9.1% (OR=5.81, 80% CI 1.79 to 18.89, p (one-sided)=0.027) with nintedanib and chemotherapy, respectively.

The study failed to demonstrate sufficient activity of nintedanib as a monotherapy to support a phase III trial. However, the benefit in progression-free survival, disease control rate, and overall survival suggests it may be interesting to combine nintedanib with other agents in ovarian clear-cell carcinoma. Chemotherapy is ineffective, and the outcomes for patients with ovarian clear-cell carcinoma are extremely poor, confirming the need for continued research into novel targets and therapies.

Stage II–IV Ovarian Cancer Treatment Strategies and Survival in England

Significant variation in Treatment and Survival Outcomes in Stage II–IV Ovarian Cancer in England: Results from the National Ovarian Cancer Feasibility Audit Pilot (abstract No 604)

Complete cytoreductive surgery and platinum-based chemotherapy is the standard of care in ovarian cancer management.[42] Recent work from the Netherlands shows variations in treatment for ovarian cancer across regions; however, contribution to survival was unclear.[43] Care that is not compliant with guidelines may affect survival from ovarian cancer.[44] With this background, Professor Sudha Sundar, as part of the ovarian cancer audit feasibility pilot,

aimed to investigate geographic variation in treatment of all patients diagnosed with ovarian cancer in England.[33]

Patients diagnosed with invasive ovarian cancer FIGO stage II–IV between January 2016 and December 2018 were audited using data extracted from the national UK Cancer Registry. Treatment variations across the 19 cancer alliances (units of geography) were evaluated. Survival analyses were extracted from a previous cohort diagnosed in 2013–2017. In all, 13 889 patients with ovarian cancer were analyzed. The weighted average probability (range) for cancer alliances of a patient with stage II–IV ovarian cancer receiving any treatment, any surgery, and any chemotherapy across England was 73.8% (70.4%–79.3%), 51% (37.2%–58.9%), and 66.5% (61.8%–73.6%), respectively. One-year net survival for the 19 cancer alliances in England varied between 62.9% and 75.2%; 5-year net survival varied between 28.6% and 49.6%. Cancer alliances that were statistically less likely to undertake surgery generally had lower than average survival. Therefore, with their study, Professor Sundar and collaborators demonstrated a significant variation in treatment and survival across England. Efforts to understand and reduce variation in treatment decision-making and reducing the proportion of patients not receiving treatment are critical to improving survival in ovarian cancer.

Cervical Conization and Risk of Recurrence in Cervical Cancer

SUCCOR Cone: Is Cervical Conization a Protective Maneuver? (abstract No 235)

In 2018, a randomized trial (Laparoscopic Approach to Cervical Cancer trial LACC)) demonstrated better survival outcomes when patients with early-stage cervical cancer underwent open versus minimally invasive radical hysterectomy.[45] Subsequent studies focused on looking for the reasons that led to such results. A few recent studies assessed the potential role of pre-operative conization in reducing risk of recurrence in patients with cervical cancer undergoing primary radical surgery.[46–49]

Dr Enrique Chacón compared the survival of patients with stage IB1 cervical cancer who underwent radical hysterectomy (2013–2014) after cervical conization with patients who underwent no cervical conization.[34] The analysis was performed on 1272 patients from the European database belonging to the SUCCOR study; 1156 patients met inclusion criteria.[50] Of these, after propensity-match analysis, 374 patients were included (187 patients with cervical conization and 187 patients with no cervical conization). Survival analysis showed a 65% reduction in the risk of relapse (HR=0.35, 95% CI 0.16 to 0.75, p=0.007) and 75% reduction in the risk of death (HR=0.25, 95% CI 0.07 to 0.90, p=0.033) for patients who underwent cervical conization.

The authors also developed a predictive score to estimate the risk of recurrence, assigning four points in cases of no pre-operative conization, three points in cases of minimally invasive niraparib (a poly(ADP-ribose) polymerase inhibitor), and two points if the pre-operative imaging tumor size was >2 cm. A point score of 0–3 (low), 4–6 (medium), and 7–9 (high) identified a risk of recurrence of 3.4%, 9.8%, and 21.3%, respectively.

Subgroup analyses showed that cervical conization seemed to have a protective effect in tumors of between 2 and 4 cm (HR=0.33, 95% CI 0.11 to 0.99, p=0.049) and in patients receiving minimally invasive surgery (HR=0.35, 95% CI 0.14 to 0.89, p=0.028). Additionally, the patients receiving minimally invasive surgery who underwent conization had similar survival to those operated on by the open approach regardless of conization or not. The study concludes that patients undergoing cervical conization have a significantly lower risk of relapse and death; this effect is more evident in those patients with 2–4 cm tumors and in those who are operated by minimally invasive methods.

COVID-19 and Gynecological Cancer Surgery

Impact of the COVID-19 Pandemic on Gynecological Cancer Surgery: Results from the CovidSurg Gynecological Cancer International Study (abstract No 594)

COVID-19 has resulted in a significant number of elective surgeries being delayed or canceled worldwide, with an estimated 86 million patients being affected (update on January 6, 2021).[51 52] Studies show that peri-operative COVID-19 infection has a high mortality of 23.8%.[53] Complications increase with any additional treatment, such as cytotoxic chemotherapy, radiotherapy, or immunotherapy.[54] In an effort to reduce treatment-related morbidity and mortality during the COVID-19 pandemic, many elective anticancer treatments have been postponed or modified.[55 56]

Professor Sudha Sundar presented the data from a multicenter, international, observational cohort study, to assess the 30-day COVID-19 infection rate in patients with gynecological cancer following elective cancer surgery; secondary endpoints were 30-day mortality, impact of resource constraints due to the pandemic, impact of the pandemic on patient selection and treatment and consequent potential surgery postponement (in this case, patients were followed up for 3 months).[35]

In all, 4722 patients were recruited across 55 countries. Distribution of tumor sites was: 42.86% (n=2024) uterine, 39.64% (n=1872) ovarian, 11.39% (n=538) cervical, and 5.93% (n=280) vulval-vaginal cancer. Eight patients have missing data on tumor type. The patients entered were from 73.38% (n=3465) high-income, 17.37% (n=820) upper middle-income, 9.21% (n=435) lower middle-income, and 0.04% (n=2) low-income countries.

Surgery was received by 4490/4472 (95%) patients; of these, 17% (n=758) experienced change or adaptation of surgery. The main impact was on surgical timing: 11% (n=483) experienced delay in surgery, 3% (n=119) a change in choice of operation, and 10% (n=452) received surgery in an alternative hospital. In particular, 21.4% of patients with uterine cancer, 21.7% with ovarian cancer, 15.8% with cervical cancer, and 22.9% with vulvo-vaginal cancer experienced a change in first-line treatment during the pandemic.

Patients in this study had confirmed resolved COVID-19 prior to surgery in 0.95% (n=45) patients with an additional 0.34% (n=16) with probable resolved COVID-19 infection. A post-operative COVID-19 rate of 2.27% (n=25) and pulmonary complication rate of 1.8% (n=20) was found in the initial analysis of the CovidSurg cancer data, analyzing outcomes for 1102 patients with gynecological cancers. The overall 30-day mortality rate in that cohort was 1.18% (n=13).

The large multicenter analysis of gynecological cancer surgery during the COVID-19 pandemic has demonstrated significant adjustments of timing, indications, and radicality of surgery in an effort to reduce COVID-19-related complications and has exposed constraints, even in high-income countries. Nevertheless, peri-operative pulmonary complications and death rates of COVID-19

affecting operated patients were overall low compared with data reported for other cancers. Fail-safe systems are urgently needed to ensure continuity of high-standard oncologic care to preserve cancer survival.

Niraparib and BRCA Status in Advanced Ovarian Cancer

Efficacy of Niraparib Therapy in Patients with Newly Diagnosed Advanced Ovarian Cancer by BRCA Wild-type Status: PRIMA/ENGOT-OV26/GOG-3012 study (abstract No 364)

Niraparib is a poly(ADP-ribose) polymerase inhibitor that has recently been approved for maintenance treatment of patients with primary advanced or platinum-sensitive, recurrent ovarian cancer.[11] In addition, niraparib is approved in the United States for the treatment of patients with BRCA-mutated or homologous recombination deficient platinum-sensitive ovarian cancer who received three or more lines of therapy. The PRIMA/ENGOT-OV26/GOG-3012 trial showed that niraparib significantly improves progression-free survival in patients with newly diagnosed advanced ovarian cancer that responded to first-line platinum-based chemotherapy (HR=0.62; 95% CI 0.50 to 0.76).[11]

With this background, Dr Elena Ioana Braicu reported results on niraparib's efficacy in patients with BRCA wild-type status within the PRIMA/ENGOT-OV26/GOG-3012 study.[36] This double-blind, placebo-controlled, phase III trial explored the role of niraparib in patients with first diagnosis of advanced, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer with a complete or partial response to first-line platinum-based chemotherapy. Patients were stratified according to the best response to the first-line chemotherapy (complete/partial response), receipt of neoadjuvant chemotherapy (yes/no), and homologous recombination status (deficient/proficient and not determined). Patients were randomized 2:1 to receive either niraparib or placebo once daily. BRCA and homologous recombination deficient status were determined by tumor samples at screening via the myChoice test (Myriad, Salt Lake City, Utah, USA). BRCA wild-type subgroups included the intention-to-treat/BRCA wild-type (all patients who were homologous recombination not determined/BRCA wild-type, homologous recombination deficient/BRCA wild-type, and homologous recombination proficient/BRCA wild-type); subgroup analyses on the homologous recombination deficient/BRCA wild-type and homologous recombination proficient/BRCA wild-type were performed. Of 733 randomized patients, 473 (64.5%) had BRCA wild-type tumors (74 patients had unknown BRCA status). Of these 473, 150 (31.7%) had homologous recombination deficient/BRCA wild-type tumors, 249 (52.6%) had homologous recombination proficient/BRCA wild-type tumors, and 74 (15.6%) had homologous recombination not determined/BRCA wild-type tumors. Niraparib-treated patients with BRCA wild-type tumors had a significant progression-free survival benefit irrespective of homologous recombination status. HR=0.69 (95% CI 0.54 to 0.88, p=0.0029) in overall BRCA wild-type, HR=0.51 (95% CI 0.31 to 0.85, p=0.0085) in homologous recombination deficient/BRCA wild-type, and HR=0.64 (95% CI 0.46 to 0.89, p=0.0079) in homologous recombination proficient/BRCA wild-type patients. No new safety issues were identified. Implementation of the individual starting dose improved the overall safety profile and reduced grade ≥3 hematological adverse events (compared with patients who received a fixed starting dose). No quality-of-life difference was detected between niraparib and placebo. The study concluded that niraparib improved progression-free survival when used as maintenance therapy after first-line treatment of ovarian cancer in patients with BRCA wild-type tumors, including homologous recombination proficient/BRCA wild-type tumors.

Niraparib and Advanced Ovarian BRCA Mutation Cancer

Niraparaib in Patients with newly Diagnosed Advanced Ovarian BRCA Mutation Cancer: A Post Hoc Analysis of the PRIMA/ENGOT-OV26/GOG-3012 Trial (abstract No 571)

Dr Jacob Korach presented a post hoc analysis from the PRIMA/ENGOT-OV26/GOG-3012 trial.[37] Data were collected from 733 randomized patients in the trial with the emphasis on efficacy and safety of fixed (niraparib/placebo 300 mg orally once daily) versus individualized starting doses (niraparib/placebo 200 mg orally for patients with body weight <77 kg or platelet count <1 50 000/μL, and 300 mg in patients with body weight ≥77 kg and platelet count ≥1 50 000/μL), (fixed starting dose vs individualized starting dose). The intention-to-treat population comprised 733 randomized patients, of which 223 (30%) had BRCA mutated tumours. Of those, 144 (65%) received a fixed starting dose, and 79 (35%) received individualized starting dose. The conclusions indicated that progression-free survival was comparable between fixed starting dose and individualized starting dose cohorts, while the individualized starting dose group showed an improved safety profile. The individualized starting dose of niraparib should be considered a standard clinical practice for the maintenance treatment of patients with ovarian cancer with low body weight or decreased platelet count.

Ovarian Cancer Prevention

Attitudes Towards Risk-Reducing Early Salpingectomy with Delayed Oophorectomy for Ovarian Cancer Prevention: A Cohort Study (abstract No 505)

To prevent premature menopause, risk-reducing early salpingectomy and delayed oophorectomy is considered to be an alternative option to risk-reducing salpingo-oophorectomy. Dr Faiza Gaba presented data from the UK Multicentre cohort survey study aiming to determine the acceptability of risk-reducing early salpingectomy and delayed oophorectomy and the effect of surgical prevention on menopausal sequelae/satisfaction/regret in patients with increased ovarian cancer risk.[39] Patients aged ≥18 years, carrying ovarian cancer predisposing genes (BRCA1, BRCA2, RAD51C, RAD51D, BRIP1 mutations) were eligible to complete the 39-item customized questionnaire survey. In all, 683 patients participated in the study, and 346 of these underwent risk-reducing salpingo-oophorectomy while 337 did not. In total, 69.1% of premenopausal patients (181/262) who had not undergone risk-reducing salpingo-oophorectomy found it acceptable to participate in a research study offering risk-reducing early salpingectomy and delayed-oophorectomy. Sexual dysfunction was the primary concern for premenopausal patients, and they were three times more likely (OR=2.9, 95% CI: 1.2 to 7.7, p=0.025) to find risk-reducing early salpingectomy and delayed-oophorectomy acceptable. Some 38% (61/159) patients who underwent premenopausal risk-reducing salpingo-oophorectomy would have chosen risk-reducing early salpingectomy and delayed-oophorectomy retrospectively, had it been an option. Patients with sexual dysfunction after risk-reducing salpingo-oophorectomy were five times more likely to

find risk-reducing early salpingectomy and delayed-oophorectomy acceptable in retrospect (OR=5.3, 95% CI 1.2 to 27.5, p<0.031). Meanwhile, 88.8% premenopausal and 95.2% postmenopausal patients who underwent risk-reducing salpingo-oophorectomy, respectively, were satisfied with their decision. Use of hormone replacement therapy did not significantly affect satisfaction/regret levels but reduced symptoms of vaginal dryness (OR=0.4, 95% CI 0.2 to 0.9, p=0.025). In premenopausal patients, risk-reducing salpingo-oophorectomy satisfaction remains high and regret rates are much higher for premenopausal patients than postmenopausal patients. Data show high risk-reducing early salpingectomy and delayed-oophorectomy acceptability, particularly in patients concerned about sexual dysfunction .

Robot-Assisted Radical Hysterectomy for Early-Stage Cervical Cancer: A Nationwide Study

Increased Institutional Surgical Experience in Robot-Assisted Radical Hysterectomy for Early-Stage Cervical Cancer Reduces Recurrence Rate: Results from a Nationwide Study (abstract No 601)

In the last few years, several studies have raised concerns about the oncologic safety of robotic radical hysterectomy.[45 50 57] The authors have shown that the survival rate for open radical hysterectomy is higher than with minimally invasive radical hysterectomy. However, the low number of robotic radical hysterectomy per center is a subject for discussion.

Dr Linnea Ekdahl presented data on the impact of institutional surgical experience on recurrence rate after robotic radical hysterectomy in early-stage cervical cancer.[40] The nationwide study included all Swedish patients with stage IA2–IB1 cervical cancer who underwent a robotic radical hysterectomy at tertiary referral centers between December 2005 and June 2017. Recurrence rate and its patterns were compared between institutional series with <50 and >50 procedures. Six hundred and thirty-five patients were included in the final analysis. Among the 489 patients who did not receive adjuvant radiochemotherapy, recurrence rate was 3.6% in the experienced cohort (>50 procedures), compared with 9.3% in the introductory cohort (p<0.05). Additionally, it was also seen in tumors <2 cm regardless of radiochemotherapy (p<0.05). No difference in recurrence rate was seen when analyzing all patients receiving radiochemotherapy. In summary, the recurrence rate after robotic radical hysterectomy in early-stage cervical cancer decreased with increased institutional surgical experience in tumors <2 cm and in patients who did not receive adjuvant radiochemotherapy.

ESGO-ESTRO-ESP GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH ENDOMETRIAL CARCINOMA

A European consensus conference on endometrial cancer was held in 2014. As a result, multidisciplinary evidence-based guidelines were created.[58] Growing evidence on endometrial cancer treatment strategies since 2014 indicated the need for new guidelines. Professor Nicole Concin presented for the first time the collaboratively created guidelines of the European Society of Gynaecological Oncology (ESGO), the European SocieTy for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP).[59] The work updates the previously published guidelines and covers new topics. The international group was chaired by Professor Nicole Concin (ESGO), Professor Carien L Creutzberg (ESTRO), and Professor Xavier Matias-Guiu (ESP).

The guidelines are supported by a significant level of evidence and/or a large consensus among experts. An adapted version of the 'Infectious Diseases Society of America-United States Public Health Service Grading System' was used to indicate the level of evidence and grade for each of the recommendations.[60] A conclusion was based on the professional experience and the development group's consensus when no clear scientific evidence was available.

General recommendations include a multidisciplinary approach and treatment based on the prognostic and predictive factors for outcome, morbidity, and quality of life. In addition, specialists should counsel patients about the diagnostic and treatment options, including their risks and benefits. Patients should be treated at a specialized center.

The guidelines were published in the *International Journal of Gynecological Cancer* shortly after the conference.[59]

MAJOR ADVANCES IN GYNECOLOGICAL CANCERS 2020—PART II

An extremely interesting session on the gynecological cancers' latest advances was chaired by Professor Mansoor Raza Mirza and Professor Luis Chiva.

The first talk was delivered by Professor David Cibula, who presented the ABRAX trial results on the role of abandoning radical surgery when a positive lymph node is found intra-operatively.[61] This is a multicenter, international retrospective analysis of 515 patients with cervical cancer (51 institutions, 19 countries). The patients were treated with primary curative surgery between 2005 and 2015 (stage IA–IIB, common tumor types), and lymph node involvement was detected intra-operatively. Patients were divided into a completed surgery group (n=361) or abandoned group (n=154). With a median follow-up of 58 months, the risk of recurrence (HR=1.15, 95% CI 0.799 to 1.666, p=0.45), pelvic recurrence (HR=0.84, 95% CI 0.458 to 1.523, p=0.56), or death (HR=1.06, 95% CI 0.690 to 1.641, p=0.78) were not significantly different between the groups. No difference in progression-freel survival and overall survival was seen. The morbidity profile was different: post-operative complications grade ≥2 until day 30 were higher in the completion group (p=0.040), while late adverse events grade ≥2 after day 30 were higher in the abandoned group (p=0.030). The authors concluded that in patients with intra-operative diagnosis of lymph node involvement, abandoning radical uterine procedure should be considered, and the patient should be referred for definitive chemoradiation.

Professor Andreas du Bois presented the final results of the AGO DESKTOP III/ENGOT-OV20 study.[15] Patients with recurrent ovarian cancer and the first relapse after a 6-month platinum-free interval were eligible if they had a positive AGO-score (ECOG 0, ascites ≤500 mL, complete resection at initial surgery) and were prospectively randomized to second-line chemotherapy alone versus cytoreductive surgery followed by the same chemotherapy. Four hundred and seven patients were randomized between 2010 and 2014. Complete resection was achieved in 75%; almost 90% in both arms received platinum-containing, second-line chemotherapy.

Primary endpoint analysis showed a median overall survival of 53.7 months with, and 46.2 months, without surgery (HR=0.76, 95% CI 0.59 to 0.97, p=0.03). Median progression-free survival was 18.4 and 14 months (HR=0.66, 95% CI 0.54 to 0.82, p<0.001), the median time to start of first subsequent therapy was 17.9 vs 13.7 months in favor of the surgery arm (HR=0.65, 95% CI 0.52 to 0.81, p<0.001). An analysis according to treatment showed an overall survival benefit exceeding 12 months for patients with complete resection compared with patients without surgery (median 60.7 vs 46.2 months); patients with surgery and incomplete resection did even worse (median 28.8 months). Grade 3/4 adverse events did not differ significantly between arms. In conclusion, the surgery in patients with first relapse and platinum free-interval of more than 6 months and selected by a positive AGO score resulted in a significant increase in progression-free survival and overall survival and time to start of first subsequent therapy, with acceptable morbidity. This trial was compared with other studies analyzing the survival outcomes of cytoreductive surgery compared with chemotherapy in recurrent ovarian cancer: GOG-213 and SOC1.[62 63]

Professor Antonio González-Martín presented the latest update on immunotherapy in gynecological malignancies. Starting with the results from the phase II innovaTV 204/GOG-3023/ENGOT-cx6 study: 'Tisotumab vedotin in previously treated recurrent or metastatic cervical cancer'.[64] The study concluded that tisotumab vedotin demonstrated durable, clinically meaningful activity in a broad patient population, with a manageable and tolerable safety profile. Therefore, tisotumab vedotin might be a potential new therapy for patients with recurrent or metastatic cervical cancer. Moreover, results obtained with phase II trials using immune checkpoint inhibitors allowed the design of several currently ongoing phase III trials. The use of immune checkpoint inhibitors was also presented in endometrial cancer. In particular, following a phase II trial combining lenvatinib with pembrolizumab in patients with advanced non-microsatellite instable endometrial cancer showing a 36% response rate at 6 months, the Food and Drug Agency approved this combination in advanced endometrial cancer without microsatellite instability.[65] However, immune checkpoint inhibitors alone have limited activity in patients with recurrent ovarian cancer.[66] The presenter highlighted the potential lack of reliable biomarkers for checkpoint inhibitors for ovarian cancer. For this reason, checkpoint inhibitors have been combined with anti-angiogenic agents or with PARP inhibitors.

Profesor Jonathan Ledermann presented advances in targeted therapy in gynecological cancers. In the ovarian cancer setting, SOLO1 5 year follow-up results have been presented concluding that for patients with BRCA mutations and newly diagnosed advanced ovarian cancer, the benefit derived from 2 years of maintenance olaparib was sustained beyond the end of treatment, and after 5 years, almost half of the patients were progression-free compared with 20% receiving placebo.[17] A final analysis of the second progression-free survival in the phase III PAOLA-1/ENGOT-ov25 trial demonstrated that adding maintenance olaparib to bevacizumab provided a benefit beyond the first progression, with a substantial second progression-free survival benefit in BRCA-mutated and homologous recombination deficient positive patients. The statistically significant improvement in second progression-free survival seen with olaparib + bevacizumab versus placebo + bevacizumab was supported by a similar time to second subsequent therapy benefit.[67] In the recurrent ovarian cancer setting, the ARIEL 3 trial looked at post-progression outcomes of the BRCA1 and BRCA2 population. All post-progression efficacy endpoints were longer with rucaparib maintenance than with placebo in both BRCA-mutant subgroups. Safety data for the two subgroups were similar and were consistent with the overall safety population.[68] SOLO2 trial and TAPAZ trial results were also presented.[69 70] For endometrial cancer, results from the ENGOT-EN3 trial were presented, showing that letrozole plus palbociclib combination demonstrated an increased progression-free survival with manageable toxicity, meriting phase III investigation.[19] Lastly, the phase II study of PARP inhibitor talazoparib and PD-L1 inhibitor avelumab in patients with microsatellite stable recurrent/persistent endometrial cancer demonstrated that avelumab and talazoparib should be considered worthy of further evaluation in patients with microsatellite stable endometrial cancer.[71]

Overall, 2020 was an important year for research in gynecological cancers: significant progress in bringing targeted therapies to the clinic, benefiting patients with gynecological malignancies, and changing clinicians' treatment approach.

CONTROVERSIES SESSION

Professor Christina Fotopoulou and Professor David Cibula chaired the most challenging session with the rapid panel discussion.

Establishing Sentinel Lymph Node as Standard of Care in Endometrial and Cervical Cancer?

In the first talk, Professor Denis Querleu presented the current state of the sentinel lymph node concept, the reasons it became popular, and its role in management of endometrial and cervical cancer. The sentinel lymph node concept has changed surgical approaches due to finding 'unexpected' lymph nodes outside traditional templates, drawing attention to the presacral pathway, and omitting unnecessary removal of lymph nodes.[72–74] Surgical complications, potential pitfalls, and the importance of using surgical algorithms with the proper dye were highlighted; not using indocyanine green means accepting failures.[75 76] The significance of the ultra-staging protocol, which is a powerful tool to identify low-volume metastasis, and dedicated pathologists are crucial for the whole sentinel lymph node concept, bringing new challenges like uncertainties about the management of micrometastasis in patients with cervical cancer.[77] Current evidence for sentinel lymph node in early cervical cancer based on SENTICOL 1, 2 and SENTIX studies suggested that bilateral negative sentinel lymph node accurately predicts the absence of lymph node metastasis and reduction of post-operative complications, but, for oncological safety, a long-term follow-up is required.[78] The ESGO guidelines consider sentinel lymph node staging only in acceptable patients with cervical cancer with IA1 lymphovascular space invasion and IA2 without lymphovascular space invasion stages; for the IA2 lymphovascular space invasion + cervical cancer, sentinel lymph node is still acceptable and should be performed. For the IB1–IIA1 cervical cancer stages, lymph node assessment should be performed as the first step of surgical management. Still, the standard lymph node staging procedure is systematic pelvic lymphadenectomy with intra-operative assessment of lymph node status (sentinel lymph node from both sides

of the pelvis/or suspicious lymph node), and sentinel lymph node is strongly recommended.

The rationale for using the sentinel lymph node concept in endometrial cancer is low, but identification of the incidence of lymph node involvement demonstrated a benefit of full lymph node dissection.[79] The sensitivity of sentinel lymph node mapping reached 96% with a pooled negative predictive value of 99.7%. Bilateral negative sentinel lymph node accurately predicts the absence of lymph node metastasis, which is true for patients with high-risk endometrial cancer.[80–83] The recently published ESGO-ESTRO-ESP guidelines for endometrial cancer considered sentinel lymph node for staging purpose at low-/intermediate-risk disease (systematic lymph node dissection is not recommended in this group of patients) as an alternative to systemic lymphadenectomy in high-intermediate/high risk. If pelvic lymph node involvement is found intra-operatively, further systematic lymph node dissection should be omitted, but debulking of enlarged nodes and para-aortic staging can still be considered. In conclusion, sentinel lymph node has become an emblematic technique with the potential to reduce the long-term effects of full lymph node dissection. It improves the precision of staging and can already be used in cases of unresolved controversy about lymphadenectomy. Surgical management of early cervical cancer will be preceded by a minimally invasive surgery sentinel lymph node procedure with permanent pathology, and the mainstay of surgical management of endometrial cancer will be hysterectomy and sentinel lymph node.

Decision-Making Processes, Patient Selection, and Allocation of Healthcare Resources in Times of Crisis

Professor Nadeem Abu-Rustum from Memorial Sloan Kettering Center in New York shared his center's experience in the decision-making process, patient selection, and allocation of healthcare resources in times of COVID-19 crisis. Cancer surgery during the COVID-19 crisis can be performed depending on institutional capacity. Many patients are cured with the surgery alone, and minimally invasive surgery has a role. There are no compromises in surgical oncology; care should be done and adjuvant therapy allowed to be started 6 to 8 weeks after a COVID-19 surge finishes.

Open versus Minimally Invasive Surgery Approach for Radical Hysterectomy: Limits and Challenges

Professor Pedro Ramirez gave a brief overview of the initial results of the LACC trial. It showed that disease-free survival was worse with the minimally invasive surgery approach, and the recurrence rate was significantly higher in the laparoscopic or robotic groups.[15] In October 2019, 4.5 years follow-up data on disease-free survival was subsequently updated to 84.2%. Minimally invasive surgery was associated with a four times higher recurrence rate than open surgery. He also presented an overview of recently published articles with multiple studies aiming to evaluate different surgical modalities in the surgical treatment of patients with cervical cancer.

In a large multicenter retrospective study from China with 10 314 patients randomized to evaluate comparisons in robot-assisted radical hysterectomy and open radical hysterectomy for cervical cancer (9266 open and 1048 robotic), results of overall survival and disease-free survival were worse than with the open approach.[84] An Italian study also confirmed similar results to those of the LACC trial.[85] A publication from an experienced robotic surgical group at the Mayo Clinic revealed that, although surgical radicality according to pathology measurements was similar between the two approaches, patients who underwent robotic radical hysterectomy had inferior disease-free survival and overall survival compared with the open approach.[86] Interestingly, the later time and results in survival rates remained worse in the group of robotic surgery, even when the surgeon had become proficient in surgery. Similar results were published in a retrospective series from high-volume centers in the USA and Canada, where patients who underwent minimally invasive radical hysterectomy, including those with tumors ≤2 cm on final pathology, had decreased disease-free survival but not overall survival in the entire cohort.[46]

A further controversial concept is the use of minimally invasive surgery in patients with cervical cancer <2 cm. In a Chinese study, minimally invasive surgery was associated with worse progression-free survival for patients with stage IB1 cervical cancer. The laparoscopic approach was an independent poor prognostic factor for progression-free survival with an adjusted HR of 4.64.[84] In the SUCCOR study, which aimed to evaluate progression-free survival in patients with stage IB1 cervical cancer undergoing open versus minimally invasive surgery, the secondary objective was investigating the association with the protective surgical maneuvers and the risk of relapses in patients with cervical cancer. Among all patients who underwent a radical hysterectomy, 387 (50.1%) underwent open surgery, 91 (11.8%) robotic surgery, and 294 (38.1%) laparoscopic surgery. The main conclusions of the study were that minimally invasive surgery in European patients with FIGO 2009 IB1 cervical cancer stage had an increased rate of relapse and death, patients using a uterine manipulator had a 2.76 times higher hazard of relapse, and avoiding a uterine manipulator and implementing a protective vaginal closure was associated with progression-free survival similar to that of open surgery.[50] The speaker highlighted that these conclusions are a misconception because this study was not designed to statistically explore protective maneuvers and uterine manipulator use as a cause of the minimally invasive surgery worse outcomes; thus results could be considered as hypothesis only.

Since the LACC publication, NCCN, ESGO, ESMO, and FIGO guidelines consider an open surgical approach to be safe and serve as the 'gold standard' in the surgical management of patients with cervical cancer. The study characterized the USA's changes in rates of minimally invasive surgery radical hysterectomy after the LACC trial data presentation. It revealed a significant decline in minimally invasive surgery procedures and rise in open radical hysterectomy procedures.[87] For the adverse event rate and quality of life of patients with cervical cancer who underwent surgical treatment, it was revealed that minimally invasive surgery compared with open radical hysterectomy resulted in a similar overall incidence of post-operative adverse events, and the quality of life, which was evaluated by numerous methods, was similar between the groups of minimally invasive surgery and open surgery.[88 89]

In systematic review and meta-analysis of survival rate of minimally invasive surgery versus open radical hysterectomy for patients with early-stage cervical cancer, using the Newcastle classification with properly designed retrospective studies, the open surgery approach should again be favored due to the lower risk of recurrence and death.[90] There are two ongoing trials—Robot-assisted Approach to Cervical Cancer (RACC) and comparison of

open versus minimally invasive surgery approaches, but time is needed to analyze the data.[91 92] In conclusion, only one prospective trial, which was supported by the numerous retrospective trials, considered open approach as a standard approach in the surgical treatment of patients with cervical cancer.

CONCLUSION

ESGO State of the Art 2020 was the first fully virtual meeting organized by the European Society of Gynecological Oncology. We encourage the readers to explore the conference program on the ESGO eAcademy website and in the *International Journal of Gynecological Cancer* (supplement 4, volume 30).[93 94]

In 2021, the 22nd ESGO biannual conference will take place in Prague, Czech Republic, October 23–25.

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