



Conference Report

The European Society of Gynecologic Oncology (ESGO) 19th biannual meeting: Overview and summary of selected topics

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1. Overview

The 19th international meeting of the European Society of Gynecologic Oncology (ESGO) was held from October 24th–October 27th in Nice, France. Ninety-four countries were represented as more than 2744 delegates and speakers met in Nice, France to participate in this biannual meeting. There were 1458 abstracts presented describing original research, 211 as oral, 439 as poster board, and the remainder as electronic poster presentations.

There were more than 50 educational sessions included as part of the ESGO 2015 program. Original research was presented in a series of “Plenary Sessions”, “Best Oral Presentations”, “Young Investigator Sessions” and “Late Breaking News”. There were myriad intimate learning sessions such as, “Glass with the Experts”, “Tumour Board Sessions”, “State of the Art” and “Parallel Sessions”. “National Society Sessions” allowed individual countries and affiliates to design a track dedicated to specific research and topics of interest.

2. Best oral presentations

2.1. Prospective evaluation of lymphocele incidence in patients after pelvic and paraaortic lymphadenectomy and analysis of risk factors for their development (abstract ESGO-1249)

Dr. Michal Zikan of Charles University, Prague, presented the prospective evaluation of 921 women (800 available for long term follow up) scheduled for pelvic and/or paraaortic lymphadenectomy and, if performed, were followed with ultrasound every 3 months. Pelvic nodes only were performed in 59% and combined pelvic and aortic nodes in 41%. The mean nodal counts for these procedures were 31 and 52, respectively. Dissections were done via laparoscopy in 17.5% and postoperative RT was given to 26%. The incidence of screen-detected lymphocele was 20% with a median time to diagnosis of 4.8 months and 5.8% symptomatic. The median diameter for symptoms vs. no symptoms was 6.7 cm vs. 4.7 cm, respectively, and lymphoceles were usually located on the external iliac vessels. Risk factors for any lymphocele on multivariate analysis included combined pelvic and para-aortic node

dissection, number of nodes obtained and BMI OR 1.777 ($p = 0.007$), total number of nodes, OR 3.137 for 45 nodes vs. 35 nodes, ($p < 0.001$). Risk factors for symptomatic lymphocele included surgery for ovarian cancer OR 2.3 ($p = 0.029$), radical hysterectomy OR 2.2 ($p = 0.035$), and number of nodes >27 OR 1.858 ($p = 0.046$). This study is the only one able to calculate a true incidence rate of lymphocele, though most lymphoceles were asymptomatic and of questionable clinical significance, and the risk factors identified, especially for symptomatic lymphocele, can aid in patient monitoring and counseling postoperatively. Longer-term follow up would be required to calculate the rate of spontaneous resolution of asymptomatic lymphocele.

2.2. The impact of lymph node resection and adjuvant chemotherapy on survival in early-stage ovarian cancer (abstract ESGO-0442)

Dr. Kleppe, et al. reported retrospective data from the Netherlands Cancer Registry on the outcome of 3658 women with stage I–IIA and IIIA1 epithelial ovarian cancer who underwent surgery with or without staging from 2000 to 2012. Of the 3658 patients, 1855 (51%) had nodal staging (LND+) and 1816 did not (LND–), and 7% of patients had nodal metastases. Overall survival (OS) was improved with staging among those with negative nodes, and the number of nodes was directly proportional to survival, which the authors concluded was due to stage migration. To determine if chemotherapy further improves survival after adequate LND, the authors compared OS in patients with >10 lymph nodes removed treated with chemotherapy ($n = 134$) or without ($n = 527$) and found no difference in OS, even in high risk patients (FIGO IC, grade 3, or clear cell), provided there were no lymph node metastases. No post hoc power analysis for these small groups was provided. Finally, to determine if chemotherapy compensates for lack of nodal staging, they compared OS in unstaged patients who had chemotherapy ($n = 825$) vs. those who did not ($n = 1020$) and found significantly better OS in unstaged patients receiving chemotherapy [HR = 0.60 (95% CI 0.44–0.80)], consistent with EORTC-ACTION [1] and ICON 1 trials [2]. However, when the LND–/chemotherapy + group was compared with the LND+/chemotherapy – group, OS was better in the LND+/chemotherapy – group [HR = 0.60 (95% CI 0.41–0.87)].

2.3. Outcome of 129 children after antenatal exposure to cancer treatment: results of a case-control study from The International Network on Cancer, Infertility, and Pregnancy registry (abstract ESGO-0758)

Prof. Amant presented results of this 10-year, multi-center study designed to determine the growth, cognitive function, and cardiac

development of children of mothers with cancer, 100 of whom received chemotherapy and/or radiation during pregnancy. The most common maternal primaries were breast cancer (55%) and hematologic malignancies (16%), followed by cervical (8%) and ovarian (7.2%) cancers. There was no difference in median gestational age or birth weight between cases and controls, but median maternal age was greater in cases than in controls (33 vs. 31 years, $p = 0.001$). Preterm delivery was equally prevalent at 61.2% between the groups. There was no detectable difference in general health, growth, cognitive outcome, or cardiac function. Prematurity was negatively associated with cognitive function, but this was independent of cancer treatment. The full publication of this study is now available [3].

3. Late breaking news

3.1. *ENGOT-OV-6/TRINOVA-2: Randomized, double-blind, phase 3 study of pegylated liposomal doxorubicin (PLD) plus trebananib or placebo in women with recurrent partially platinum-sensitive or resistant ovarian cancer (abstract ESGO-1482)*

Prof. Marth presented results of this trial designed to evaluate the efficacy and safety of trebananib, a biologic peptibody that blocks neovascular quantity and quality through a VEGF-independent, angiopoietin (Ang1 and Ang 2) mechanism, in combination with PLD. The study planned to randomize 380 subjects, but enrollment was stopped for one year during the PLD shortage. In the end, 223 subjects were enrolled, providing an 80% power to detect a 52% relative increase in median PFS in the experimental group, but this difference was not detected [HR 0.92 (95% CI 0.68–1.24) ($p = 0.59$)]. No subgroup of patients by prior anti-angiogenic therapy, number of prior lines of therapy, platinum free interval, or bulky disease showed a favorable PFS with experimental treatment, but those with baseline ascites treated with trebananib showed a trend toward improved PFS [HR 0.60 (95% CI 0.35–1.04)]. Trebananib use was associated with an improved response rate and duration of response, but no improvement in overall survival. Adverse events associated with trebananib included localized edema and ascites which were a common reason for treatment discontinuation.

3.2. *Systematic evaluation of BRCA1/2 mutations in unselected women with ovarian cancer—the genetics in epithelial ovarian cancer (GTEOC) study (abstract ESGO-1522)*

Dr. Crawford presented results from a multicenter, prospective study of 232 women with ovarian cancer who underwent BRCA1 and BRCA2 testing by next generation sequencing (NGS) regardless of age or family history and were referred to genetic counseling only if diagnosed with a deleterious mutation or a variant of undetermined significance (VUS). The overall mutation yield was 7.3% and 18 VUS were detected. The mutation yield was highest in women under age 70 (10.9% vs. 2.1% in women 70+). The 70-year threshold also reduces the deleterious to VUS ratio from 1:1 to 2:1. The GTEOC model of reserving counseling for mutation detected women was estimated to deliver a cost savings of £2104 or \$3197 US dollars per mutation. There was no psychological distress associated with testing, and subjects were satisfied with the testing process. The authors concluded that all women under 70 with epithelial ovarian cancer should be tested by this genetic coordinated model of oncology-led testing with genetic follow up for those positive or with VUS.

3.3. *Tissue and imaging biomarkers for hypoxia predicts poor outcome in endometrial cancer*

A translational evaluation of 837 specimens of complex atypical hyperplasia, endometrioid type of all grades, and non-endometrioid cancers was presented by Dr. Berg, et al. Increased expression of hypoxia

marker, HIF-1 α , correlated with worse prognosis and with negative prognostic markers (high-risk histology, deep myometrial invasion, nodal metastases, and ER –/PR – status). High HIF-1 α expression also correlated with functional MRI markers for increased cellular density and less tumor blood flow. Relevant to the tumor microenvironment, stromal HIF-1 α activated cells correlated with hypoxia, inflammation, and glycolysis especially via the PI3Kinase pathway, with cancer grade, and with SUV max on PET scan. These markers might aid in the molecular staging of endometrial cancer and possibly guide adjuvant therapy, but these findings require validation prior to clinical application.

3.4. *Activation of TGF- β pathway through mir-181 α and pSMAD2 overexpression drives resistance to neoadjuvant chemotherapy (NACT) in epithelial ovarian cancer (abstract ESGO-1467)*

Prof. Petrillo presented a translational evaluation using tumor samples at diagnosis from 82 patients treated with NACT. More than 1000 microRNAs were interrogated using cDNA microarray analysis and were validated by RT-PCR. Only 4 miRNAs showed changes with NACT, and only one, mir-181 α , was elevated at diagnosis prior to NACT administration. mir-181 α was associated with survival outcome (PFS and OS) and tumor resectability at interval debulking. Given the association of mir-181 α to TGF- β expression, a protein shown to predict suboptimal debulking [4], its effector, pSMAD was evaluated and found to also correlate negatively with survival and platinum-free interval. The patients with the worst survival and most platinum resistant disease were those with high mir181 α and high pSMAD expression. These markers also require validation but are good candidates to be pretreatment markers of chemo-resistance and suboptimal surgical outcome, even at interval as opposed to primary debulking surgery. Moreover, improved treatment options for chemorefractory patients are needed for these markers to bear clinical utility.

3.5. *Laparoscopy to predict the result of primary cytoreductive surgery in advanced ovarian cancer (LAPOVCA): A multicenter randomized controlled trial (abstract ESGO-1522)*

Buist and colleagues presented results from the first randomized control trial to evaluate the role of screening laparoscopy to determine ability to perform an optimal (<1 cm) cytoreductive surgery in advanced ovarian cancer. Two-hundred and one patients eligible for primary debulking based on imaging and performance status were randomized to immediate laparotomy (LAP) versus laparoscopy (LSC). Decision for surgery versus neoadjuvant chemotherapy in the LSC group was determined based on a validated scoring system [5]. Primary surgery was performed in 94% and 61% of the LAP and LSC groups, respectively. This led to lower level of suboptimal cytoreduction/futile laparotomy in the LSC (10%) compared to the LAP group (10% vs. 42%; RR 0.25, 95%CI 0.13–0.48, $p < 0.001$). Certainly, these results provide support to the use of laparoscopy as a screening tool for presumed advanced ovarian cancer.

4. Highlights of disease-specific plenary sessions

4.1. Endometrial cancer

Translational research and prognosis were the predominant topics of the endometrial cancer oral session. PORTEC investigators evaluated the success of the four molecular endometrial cancer subtypes identified by The Cancer Genome Atlas (TCGA) to provide risk assessment among women with intermediate risk endometrial cancer (Abstract ESGO-0585). They found that molecular testing was feasible and a large proportion (~70%) of the 854 endometrial cancers studied had potentially actionable mutations. Interestingly, they looked at recurrence free survival (RFS) in the context of

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