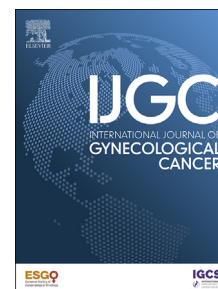


MEETING SUMMARY

Highlights from the third Colombian conference on women's cancers

María Clara Santía^{a,*}, Vanessa Alvarenga-Bezerra^b, William Andrés Piñeros Castillo^c, Carolina Morante-Caicedo^c, Heng-Cheng Hsu^{a,d}, Florencia Noll^e

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This report covers the “Third Colombian Conference on Women’s Cancers” held in Medellín, Colombia on 31 January and 1 February 2025. The meeting gathered over 345 participants from 18 countries. The event featured 32 speakers, including 21 national and 11 international experts. The conference provided an educational experience focused on the latest advances in gynecologic oncology and breast cancer. The program featured both local and international speakers and addressed key topics in our field.

OVARIAN CANCER

Fertility Preservation in Borderline Ovarian Tumors

Uterine preservation with unilateral or bilateral cystectomy or unilateral salpingo-oophorectomy is acceptable for all stages. This also includes comprehensive surgical staging with peritoneal washings, biopsies, omentectomy, and cavity inspection for complete resection.^{1,2} For stage IB, an ultra-conservative fertility-sparing strategy (bilateral cystectomy) improves pregnancy rates without impacting survival, though recurrence time is shorter. The incidence of recurrence as carcinoma is 2.3% and represents the primary risk factor impacting overall survival. Mucinous tumors have a higher risk (13%) of invasive progression, favoring adnexectomy over cystectomy. The endometrioid subtype is managed like serous tumors but requires endometrial assessment due to a 52% risk of related pathology.³ The management of recurrence remains a topic of debate; however, conservative treatment may be considered when histology indicates low malignant potential and complete resection is achievable. Before treatment, fertility assessment and reproductive counseling are crucial, with options such as ovarian stimulation and oocyte retrieval available. Completion surgery following childbearing is generally not recommended.¹⁻³

Lymphadenectomy in Early-Stage Ovarian Cancer

Because only 14.2% of patients with early-stage ovarian cancer exhibit lymph node involvement, this raises an important question: Are we over-treating the remaining 86% by routinely performing systematic lymphadenectomy? The risk of lymphatic involvement depends on tumor grade and histologic subtype. Lymph node metastases are present in approximately 20% of grade 3 tumors, with rates varying by histotype: 28% in undifferentiated carcinoma, 23% in serous carcinoma, 14% in clear cell carcinoma, 17% to

30% in infiltrative mucinous tumors, 2% in expansive mucinous tumors, and 0% to 1.4% in endometrioid tumors.⁴ Imaging alone is insufficient, as 30% of radiologically normal lymph nodes still have metastases.⁵

A recent systematic review and meta-analysis reinforced the survival benefit in the lymphadenectomy group, reporting improved overall survival (HR 0.75, 95% CI 0.68 to 0.82, $p = .00001$) and progression-free survival (HR 0.62, 95% CI 0.50 to 0.78; $p = 0.0001$).⁶ However, complications arise in 3.5% of cases, with severe complications in 13.8%.⁷ To address this issue, the ongoing LOVE trial⁸ is designed to evaluate the efficacy and safety of staging surgery with or without lymphadenectomy in these patients. Lastly, while sentinel lymph node biopsy shows promise in ovarian cancer, further evidence is needed to establish its clinical utility.

Primary Cytoreduction in Low-Grade Serous Ovarian Cancer

In patients with low-grade serous carcinoma, primary cytoreduction surgery is preferred when complete or optimal cytoreduction can be achieved. Neoadjuvant chemotherapy is a less favorable option with lower rates of complete cytoreduction compared to those treated with neoadjuvant chemotherapy/interval cytoreductive surgery.⁹

One of the questions that arises is: What should be done for patients with a high disease burden? Does primary suboptimal cytoreduction have any role? Retrospective analyses have shown that the best overall survival and progression-free survival outcomes occur in patients who achieve complete cytoreduction (R0).¹⁰ Multivariate analyses from other retrospective studies have indicated no differences in overall survival (HR 1.66, 95% CI 0.45 to 6.1, $p = .45$) or progression-free survival (HR 1.09, 95% CI 0.56 to 2.13, $p = .79$) between patients with no residual disease and those with residual disease <1 cm.⁹ Additionally, patients with complete resection or minimal residual disease (<2.5 mm) have similar prognoses and better progression-free survival compared to those with >2.5 mm (HR 3.68, 95% CI 1.44 to 9.39).¹¹ More recently, Matsuo and colleagues¹² reported that the extent of cytoreduction and overall survival were not statistically significant. Five-year overall survival rates were 80.8% for complete, 75.3% for optimal (R1) (R1 vs R0, HR 1.04, 95% CI 0.75 to 1.45), and 63.0% for suboptimal cytoreduction (R2) (R2 vs R0, HR 1.19, 95% CI 0.66 to 2.12). Therefore, suboptimal primary cytoreduction in low-grade

* Correspondence to Dr María Clara Santía, Department of Obstetrics and Gynecology, Houston Methodist Hospital, Houston, TX, USA; claritasantia@gmail.com (M.C. Santía), msantia@houstonmethodist.org (M.C. Santía)

serous carcinoma may still render a benefit, but complete cytoreduction should remain the goal.

Stage IV Ovarian Cancer: Primary Cytoreduction Versus Neoadjuvant Chemotherapy

Stage IV ovarian cancer consists of stage IVA—pleural effusion with positive cytology, and stage IVB—metastases to the liver, spleen, or lymph nodes in the groin or chest. A longstanding debate persists regarding whether aggressive surgical resection can overcome the influence of tumor biology. While some surgeons advocate for maximal surgical effort in all cases, others emphasize that prognosis is primarily driven by the biological behavior of the tumor. Since the 1990s, Hoskins and colleagues¹³ have demonstrated that the amount of residual disease following primary cytoreductive surgery directly impacts survival; patients with less residual disease experience better outcomes. In 2013, a meta-analysis confirmed that the proportion of patients remaining with no visible residual disease was an essential independent predictor of survival. For every 10% increase in the rate of complete cytoreduction, there was a corresponding increase of 2.3 months in median survival.¹⁴ In a retrospective analysis of the GOG 182 clinical trial, Horowitz and colleagues¹⁵ reviewed data from 2655 patients with stage III or stage IV ovarian cancer. The investigators assessed progression-free and overall survival based on 3 parameters: pre-operative disease score, surgical complexity score, and post-operative residual disease. A high disease score was defined by extensive upper abdominal involvement, including disease affecting the diaphragm, spleen, liver, or pancreas. Their findings indicated that patients with high disease scores had the poorest survival outcomes. Even among those who achieved no visible residual disease, a high disease score was still linked to significantly worse progression-free and overall survival compared to patients with low or moderate disease scores. After adjusting for residual disease and disease score, the surgical complexity score did not remain an independent predictor of survival. These results suggest that, while complete cytoreduction is crucial, the initial tumor burden is a powerful determinant of prognosis, and aggressive surgery alone may not suffice to improve outcomes in patients with biologically unfavorable diseases.¹⁵ This concept is underscored by the 2025 American Society of Clinical Oncology (ASCO) guideline,¹⁶ which recommends primary cytoreductive surgery for stage III and IV patients with good performance status and a high likelihood of achieving complete resection. In contrast, neoadjuvant chemotherapy is recommended for patients who are unlikely to benefit from immediate surgery due to extensive disease or elevated peri-operative risk. The potential benefit of primary debulking in patients with stage IV disease exists, but clinical context is essential. For instance, not all liver or splenic findings indicate metastases, as some may correspond to benign lesions such as cysts, hemangiomas, or focal nodular hyperplasia. Other findings, such as scalloping of the liver, must be interpreted carefully. Distinguishing isolated metastatic lesions from widespread disseminated disease is also crucial.

Accurate pre-operative imaging is a key component in surgical decision-making. A non-randomized phase II trial compared gated fluorodeoxyglucose positron emission tomography combined with computed tomography (CT) to standard intravenous contrast-

enhanced CT in the evaluation of thoracic involvement in patients with advanced ovarian cancer before treatment. Of 84 patients enrolled based on conventional CT, 67 underwent gated positron emission tomography-CT. The diagnostic accuracy of the gated scan was greater than 80% for lesions located in the lungs, liver, pleura, and other extra-abdominal sites, but less than 50% for extra-abdominal lymph nodes. Compared to standard CT, 46% of patients were upstaged from stage III to stage IV, and 8% were downstaged. However, these changes in disease staging resulted in a change in clinical management in only 5% of patients.¹⁷

In conclusion, the management of stage IV ovarian cancer must be individualized. Treatment decisions should consider tumor burden, functional status, and the patient's ability to tolerate systemic therapy. Ultimately, surgery in this setting should be considered a complement to systemic treatment rather than a curative strategy on its own.

HIPEC in Advanced Ovarian Cancer

The OVHIPEC-1 trial¹⁸ showed improvement in recurrence-free (HR 0.66, 95% CI 0.50 to 0.87, $p = .003$) and overall survival (HR 0.67, 95% CI 0.48 to 0.94, $p = .02$) in stage III epithelial ovarian cancer undergoing interval cytoreduction. However, its role in recurrent disease remains unclear. The CHIPOR trial,¹⁹ a phase III study in platinum-sensitive recurrent, randomized patients who responded to 6 cycles of chemotherapy to surgery \pm HIPEC, reporting an overall survival benefit (54.3 vs 45.8 months, HR 0.73, $p = .024$) but no significant difference in progression-free survival (10.2 vs 9.5 months, HR 0.79). Methodological concerns include limited data on disease burden at relapse diagnosis, percentage of patients with oligo-metastatic disease, percentage of patients with massive carcinomatosis, ascites, and laparoscopy timing. While HIPEC may benefit selected patients, its impact at the time of recurrence remains inconsistent, warranting further trials to refine patient selection.^{20,21}

Secondary Cytoreduction in the Era of Targeted Therapy

The results of the phase III trials GOG-213,²² SOC-1,²³ and DESKTOP III²⁴ were discussed in the context of the evolving role of surgery alongside systemic treatments. Results were mixed: GOG-213²² found no overall survival benefit with surgery (50.6 vs 64.7 months, HR 0.29, 95% CI 0.97 to 1.72, $p = .08$). SOC-1²³ showed improved progression-free survival (HR 0.58, 95% CI 0.45 to 0.74, $p < .0001$) but no significant overall survival difference (HR 0.80, 95% CI 0.61 to 1.05, $p = .11$). DESKTOP-III²⁴ reported a survival benefit when complete resection was achieved (HR 0.75, 95% CI 0.59 to 0.96, $p = .02$). Overall, the debate emphasized that while secondary cytoreduction can enhance specific outcomes under certain conditions (complete resection), its effectiveness depends on the clinical context and appropriate patient selection.

Moreover, access to appropriate maintenance therapy is essential for improving the prognosis of patients with ovarian cancer. The incorporation of PARP inhibitors into treatment protocols further enhances patient outcomes by delaying disease progression.²⁵ Ongoing research into biomarkers such as BRCA and HRD status holds promise for more personalized treatment strategies. When integrated with advanced therapeutic approaches—such as PARP inhibitor maintenance therapy following surgery

or during recurrence management—these biomarkers could contribute to improved overall survival outcomes.²⁶

First-Line Treatment in Newly Diagnosed Advanced Epithelial Ovarian Cancer: 10 Years of Progress/PARP for Everyone or Only for Those who Benefit the Most

In 2011, 2 landmark trials demonstrated that the addition of bevacizumab resulted in a benefit in progression-free survival.^{27,28} However, overall survival was only observed in *post hoc* analyses of high-risk/stage IV patients. Beginning in 2018, multiple phase III randomized controlled trials indicated that maintenance PARP inhibitors were not only beneficial for patients with BRCA-mut patients but also for HRD patients. Furthermore, substantial overall survival was finally noted in a molecular subgroup of ovarian cancer, specifically in BRCA mutation patients.^{25,26,29-31} A *post hoc* analysis of the PAOLA-1 trial suggests that the location and type of BRCA mutation may influence response to PARP inhibitors. Specifically, patients with mutations in the DNA-binding domain of BRCA1—and similarly those with BRCA2 mutations in the same region—appear to derive greater benefit.³² Patients with HRD status are recommended to receive PARP inhibitors. For patients with HRP status, options include bevacizumab or PARP inhibitors, such as niraparib or rucaparib.^{26,30}

However, certain challenges exist in Latin America. What percentage of patients in these trials were from Latin America? Is genetic testing widely available in Colombia and other Latin American regions? Are PARP inhibitor treatments reimbursed for HRD or even BRCA-mutated cases in Latin America? Would niraparib be a more cost-effective option than olaparib and bevacizumab for HRD patients? Given economic disparities worldwide, a one-size-fits-all approach to PARP inhibitor treatment may not be feasible. As de-escalation strategies become more prominent in the next wave of gynecologic oncology treatments, could they lower costs to extend patient survival or even save more lives?

ENDOMETRIAL CANCER

Recurrent Metastatic Endometrial Cancer: Changing Paradigms and Looking to the Future

Historically, progress in treating advanced and recurrent endometrial cancer has been slow. However, recent clinical trials have brought about meaningful advancements in the field. The Keynote-775³³ trial showed that pembrolizumab and lenvatinib provided superior survival compared to single-agent chemotherapy chosen by the physician, marking the first trial to demonstrate a survival benefit in second-line treatment for endometrial cancer. In 2023, 2 landmark trials confirmed that adding immunotherapy to carboplatin-paclitaxel significantly improved survival compared to chemotherapy alone. GY018³⁴ was a phase III randomized trial that stratified patients into mismatch repair-deficient (dMMR) and mismatch repair-proficient (pMMR) cohorts in advanced and recurrent endometrial cancer. The 12-month analysis showed that both the dMMR and pMMR cohorts exhibited superior progression-free survival with the addition of pembrolizumab (74% vs 38%, HR 0.30, 95% CI 0.19 to 0.48, $p < .001$; 13.1 vs 8.7 m, HR 0.54, 95% CI 0.41 to 0.71, $p < .001$). RUBY³⁵ was a phase III, prospective, randomized trial in advanced and recurrent endometrial cancer, comparing dostarlimab with chemotherapy versus placebo with

chemotherapy. RUBY met both of its primary endpoint for improvement of progression-free survival at 24 months in the dMMR cohort and in the overall population (61.4% vs 15.7%, HR 0.28, 95% CI 7.2 to 27.0; 36.1% vs 18.1%, HR 0.64, 95% CI 0.51 to 0.80, $p < .001$). Additional trials, including AtTend³⁶ and DUO-E,³⁷ reinforced these findings, demonstrating that immunotherapy combined with chemotherapy improves survival across all patient groups.

It remains uncertain whether the limited treatment effect seen with the addition of PARP inhibitors can be further enhanced. Currently, the DUO-E³⁷ and RUBY part 2³⁸ trials have demonstrated only modest improvements with PARP inhibitors. Given the highly immunogenic nature of dMMR/MSI-H tumors, the necessity for chemotherapy in this subgroup remains unclear. The C93³⁹ and DOMENICA⁴⁰ trials are exploring this issue.

CERVICAL CANCER

Minimally Invasive Surgery: Still an Option?

Details were presented on the final analysis of overall survival in the LACC trial.⁴¹ The overall survival rate at 4.5 years was 90.6% for the minimally invasive group compared to 96.2% for the open surgery group (HR 2.71, 95% CI 1.32 to 5.59, $p = .007$). The locoregional recurrence rate at 4.5 years was also higher in the minimally invasive group (49% vs 1.8%, HR 4.70, 95% CI 1.95 to 11.37, $p = .001$). Finally, the incidence of recurrence as carcinomatosis was greater with the minimally invasive approach, indicating that the open approach should be considered the standard of care.

Concerns have arisen regarding the utility of minimally invasive surgery for low-risk patients. The ConCerv⁴² study evaluates the feasibility of conservative surgery for low-risk early-stage cervical cancer, reporting a 0% recurrence rate when conization is followed by a simple hysterectomy. Subsequently, the SHAPE⁴³ trial compared simple vs radical hysterectomy in low-risk cervical cancer, finding no difference in pelvic recurrence rates over 3 years. The question of whether minimally invasive surgery can be safely performed in this low-risk population remains a topic of debate. These 2 trials were not designed to address the safety of minimally invasive surgery in low-risk cervical cancer patients. The ongoing LASH trial⁴⁴ compares simple hysterectomy performed via open surgery to minimally invasive surgery with lymph node evaluation and will provide data on oncological outcomes.

Ovarian Transposition in Cervical Cancer

Following whole pelvic radiation (20-30 Gy), ovarian failure rates can reach as high as 97%.⁴⁵ Symptoms of premature ovarian failure can significantly impact a patient's quality of life. A systematic review that included 1377 patients who underwent ovarian transposition before radiotherapy indicated an ovarian function preservation rate of 61.7%, a complication rate of 8.5%, and ovarian metastasis reported at 0.36%.⁴⁵ A meta-analysis that included 1160 patients who underwent ovarian transposition revealed that in the group that had surgery alone, 91% of the women preserved ovarian function, and 99% (95% CI 1 to 5) of women did not suffer metastases to the transposed ovaries. In the external beam pelvic radiotherapy ± brachytherapy ± surgery group, the proportion of women with preserved ovarian function

was 61% (95% CI 55 to 69), with no metastases to the transposed ovaries in that group.⁴⁶ In conclusion, ovarian transposition provides a safe and effective approach to protect ovarian tissue from radiation damage, potentially preserving fertility options and preventing premature menopause.

Surgery for Cervical Cancer Recurrence in the Era of Immunotherapy

In the past, pelvic exenteration was considered the only treatment option that significantly improved overall survival in recurrent cervical cancer, despite its high intra- and post-surgical mortality. Ideal candidates should be young women with isolated central recurrence in the pelvis, excellent performance status, no comorbidities, a disease-free interval of more than 6-12 months, no evidence of lower extremity edema, no hydronephrosis, and anticipated tumor-free margins. The surgical team must possess the skills to perform complex pelvic surgeries, reconstructive urostomies, colostomies, and pelvic reconstruction. In 2024, Levin and colleagues⁴⁷ compared outcomes of patients undergoing pelvic exenteration across 2 time periods, before and after 2017. No differences were reported, with an overall complication rate of 78%, of which 32% were classified as major. The only noted change was a reduction in hospital stays. Colombo and colleagues⁴⁸ reported benefits from adding pembrolizumab to chemotherapy (with or without bevacizumab) in terms of progression-free survival (10.4 months vs 8.1 months) and overall survival at 24 months (53% vs 41.7%) in patients with persistent, recurrent, or metastatic cervical cancer. Coleman and colleagues⁴⁹ evaluated the efficacy of a tissue factor-directed antibody–drug conjugate (tisotumab-vedotin) in second-line recurrent or metastatic cervical cancer, achieving an objective response rate of 24% (with 7% complete responses and 17% partial responses), representing excellent options even for patients with progression during chemotherapy.

Locally Advanced Cervical Cancer: INTERLACE, KEYNOTE-A18

A discussion was held on the treatment of locally advanced cervical cancer focusing on the recent INTERLACE, KEYNOTE-A18 trials. The INTERLACE⁵⁰ compared induction chemotherapy followed by concomitant chemoradiotherapy to standard treatment. After 5 years, progression-free survival increased from 64% to 73%, and overall survival improved from 72% to 80%. The study population included 74% stage II patients and only 14% stage III to IV, suggesting a lower risk profile for locally advanced disease. Concerns were raised regarding hematologic toxicity, and that only 30% of patients received the standard radiotherapy treatment.

The KEYNOTE-A18 trial⁵¹ evaluates the combination of chemoradiotherapy with pembrolizumab, followed by pembrolizumab maintenance for 15 cycles, compared to standard chemoradiotherapy plus placebo. This trial included patients with stage IB2–IIB disease who had positive lymph nodes and stage III to IVA disease, representing a high-risk population. Notably, 95% of patients had PD-L1 positive tumors, 65% were stage III to IV, 85% had positive lymph nodes, 22% had para-aortic lymph node involvement, and 90% received modern radiotherapy. The results indicate that progression-free survival improved by 12% at 3 years, with ongoing data analysis. At 3 years, overall survival

demonstrated a 33% reduction in the risk of death (HR 0.67, 95% CI 0.5 to 0.9, $p = .004$) with pembrolizumab. Despite the impressive data, there are still several questions to answer in the future: Is there a role for induction immunotherapy in locally advanced cervical cancer? Is there a rationale for using an anti-PD1 agent after anti-PD1?

RESEARCH AND ONGOING CLINICAL TRIALS

This section covers the presentation and discussion of 3 ongoing prospective trials in gynecologic cancers. The ENDO-3 trial⁵² (phase III, multicenter, randomized) evaluates sentinel node biopsy versus no retroperitoneal lymph node dissection in early-stage endometrial cancer (stage I, grade 1-3 endometrioid, clear cell, serous, or carcinosarcoma). The ANVU trial⁵³ (phase IIb, multicenter, randomized) compares high-resolution groin ultrasound with standard lymph node dissection in stage 1b2 vulvar cancer. The LANCE trial⁵⁴ (phase III, multicenter, international, non-inferiority) investigates whether minimally invasive surgery is non-inferior to laparotomy regarding disease-free survival in advanced-stage epithelial ovarian cancer after 3 or 4 cycles of neoadjuvant chemotherapy.

Author Affiliations

^aHouston Methodist Hospital, Department of Obstetrics and Gynecology, Houston, TX, USA

^bHospital Israelita Albert Einstein, Gynecologic Oncology, Sao Paulo, Brazil

^cInstituto Nacional de Cancerología, Gynecologic Oncology, Bogota, Colombia

^dNational Taiwan University Hospital, Department of Obstetrics and Gynecology, Taipei, Taiwan

^eSanatorio Allende Cerro de Córdoba, Department of Gynecologic Oncology, Córdoba, Argentina

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