GOG PARTNERS CONNECTION

CERVICAL CANCER AWARENESS MONTH SPECIAL EDITION

From GOG Partners, A GOG Foundation Program

The GOG Foundation, Inc. has one mission that is dedicated to transforming the standard of care in gynecologic oncology.

IMPORTANT UPDATES IN THE TREATMENT OF LOCALLY ADVANCED AND METASTATIC/RECURRENT CERVICAL CANCER

What you need to understand about recent trials that have led to changes in the standard of care.

Despite being preventable with HPV vaccination and detected early through screening, cervical cancer continues to be a devastating disease globally that is associated with a poor prognosis and a high mortality rate. Despite advances in early screening, cervical cancer in the United States is estimated to lead to 14,100 new diagnoses of invasive disease. Cervical cancer will cause an estimated 4,280 deaths in the United States in 2022 alone. Globally, it is the 4th most deadly cancer in female patients. Women with advanced cervical cancer, meaning it has spread beyond the cervix, have an unfavorable prognosis, with the 5-year survival rate ranging from 18-58% for distant and regional disease, respectively. Despite the incorporation of immunotherapy in the treatment of recurrent disease, treatment options for all patients with locally advanced or metastatic disease continues to have a high unmet need.

Recent major medical conferences hosted in Istanbul, Madrid and Seoul shared positive data readouts on multiple important studies in locally advanced
cervical cancer and recurrent cervical cancer. Here we will provide key insights to help us better understand the newer treatment options. It is crucial to understand how to decipher the new data and how to use new information to provide the best possible cervical cancer options when treating your patients as we look to change the standard of care in cervical cancer.

In the locally advanced setting, for the first time since GOG 120 in 1999, we have two positive trials that add investigational therapy to cisplatin-based chemoradiation (CRT). The first presented at ESMO by Prof Ketta Lorusso was Keynote A18/ENGOT cx11/GOG-3047, a phase 3, randomized, placebo-controlled trial that studied the addition of pembrolizumab to standard CRT. This global trial incorporated a rigorous radiation plan evaluation process for all 1060 patients with either FIGO 2014 stage IB2-IIB with + pelvic or para-aortic nodes or FIGO 2014 stage III-IVA with any nodal status who were randomized to CRT with or without pembrolizumab given every 3 weeks for 5 cycles during radiation and then every 6 weeks as maintenance for 15 additional cycles. Co-primary endpoints were progression-free (PFS) and overall survival (OS). The average age was 50 years, 52% of the patients were non-white race or ethnicity, and 95% were PDL1+ by CPS score of at least 1. In this cohort, the addition of pembrolizumab improved PFS by 30% (HR 0.70 95% CI 0.55-0.89) and the HR for OS, not yet mature, was 0.73 (0.49-1.07). There were no new safety signals when combining pembrolizumab with RT and quality of life (EORTC Quality-of-life Core 30, QLQ-C30) was preserved. Most recently, on Friday, January 12, 2024, KN A18 was FDA approved pembrolizumab with chemoradiation for FIGO 2024 Stage III-IVA cervical cancer. KN A18 is resulted following the negative result of the CALLA trial that integrated durvalumab, a PDL1 inhibitor, into the CRT regimen with maintenance to follow. CALLA and KN A18 differed in their drug target, risk level of the population (A18 with slightly higher risk patients), and in their regions of the world with high accrual.

The second LACC trial presented was the INTERLACE trial which was led by Prof and largely accrued in the UK. This was also a GCIG trial that studied the addition of induction weekly carboplatin AUC 2 and paclitaxel 80mg/m2 x 6 weeks prior to the initiation of CRT. INTERLACE enrolled 500 patients with FIGO 2008 defined stage IB1 node + to IVA with no nodal metastases above the aortic bifurcation and was conducted over approximately 10 years. Co-primary endpoints of PFS and OS were both improved with induction therapy: PFS HR 0.65;95% CI:0.46 -0.91, p=0.013 and HR OS HR 0.61;95% CI: 0.40-0.91, p=0.04. The OS advantage reported in INTERLACE is provocative and certainly is the ultimate goal. Because the study populations were different between KN A18 and INTERLACE, cross-trial comparisons are specifically not valid. The advantage of the induction regimen is that it is mostly well-tolerated already readily available, but more detail is awaited in the study publication regarding the quality of radiation and whether that changed as expected over the 10 years that the study was conducted.

In the frontline metastatic, recurrent, or persistent setting, current standards include the KEYNOTE 826 regimen (platinum, paclitaxel, pembrolizumab with physicians-choice bevacizumab) for patients whose tumors express PDL1 (22c3 assay, CPS ≥1) (Columbo, et al) and GOG 240 for those with PDL1-tumors (Tewari et al). BEATcc (GOG-3030) trial was presented at a virtual ESMO by Prof. Ana Oaknin of the lead group, GEICO (Oaknin). BEATcc was an open-label, randomized phase III study evaluating the addition of PDL1-
inhibitor, atezolizumab to the GOG 240 regimen where bevacizumab was mandatory. The study was enriched for squamous cell histology, but PDL1 testing has not been performed to date. In this cohort, the addition of atezolizumab significantly improved both PFS and OS with HR PFS 0.62 (0.49–0.78); p<0.0001 and HR OS 0.68 (0.52–0.88); p=0.0046 and are the first evidence in cervical cancer that PDL1 inhibition is both effective and well-tolerated. Including bevacizumab might have also played a role in the improved outcomes that were seen in BEATcc.

Two trials were recently reported that will change the current landscape for the management of recurrent disease. They are:

**Tisotumab Vedotin (TV)**
TV is an investigational antibody-drug conjugate (ADC) composed of a tissue factor-directed human monoclonal antibody covalently linked to the microtubule-disrupting agent MMAE. TV received FDA accelerated approval in the United States for the treatment of adult patients with r/mCC with disease progression on or after chemotherapy, based on the phase 2 innovaTV 204/GOG-3023/ENGOT-cx6 study. TV-301 (innovaTV 301/ENGOT-cx12/GOG-3057) is a randomized, phase III evaluating TV versus investigator’s choice chemotherapy. This was the first trial in recurrent/metastatic cervical cancer that allowed for prior use of checkpoint inhibitor. The primary endpoint of the trial was overall survival. The study met its primary endpoint at the first interim analysis. There was a 30% reduction in deaths in the TV arm and a 33% reduction in recurrences or deaths in the TV arm.

**Trastuzumab Deruxican (T-DXd)**
T-DXd is an ADC with three components: a humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab; a topoisomerase I inhibitor payload, an exatecan derivative; and a tetrapeptide-based cleavable linker. T-DXd has become a standard of care in HER2-expressing unresectable/metastatic breast cancer, HER2-positive locally advanced/metastatic gastric/GEJ cancer and HER2 (ERBB2)-mutant unresectable/metastatic NSCLC. Although testing is not routine, HER2 expression (IHC 3+ or IHC 2+) is seen in a wide range of other solid tumours and is associated with a biologically aggressive phenotype. For HER2-expressing cervical cancers, there is an unmet need for effective therapies, particularly for patients with disease refractory to standard-of-care therapies. Meric-Bernstam and colleagues presented Destiny-Pan Tumor 02 results at ASCO and updated results at ESMO earlier this year. In pretreated patients with HER2 2+ or 3+ IHC cervical cancers, there was a 50% response rate to single agent T-DXd with a 14.2 month median duration of response. In patients with 3+ staining, the response rate was 75%.

The treatment landscape of advanced gynecologic malignancies continues to rapidly evolve. Results from practice changing trials have altered the landscape for how we treat our patients who suffer from this disease. Within the gynecologic oncology community, we need to educate our colleagues with up-to-date, evidence-based information. This will ultimately lead to improved patient outcomes as we increase our use of these proven treatments.

**References:**
a.) Cancer statistics, 2024.


HIGHLIGHTING SELENA RUSHTON'S JOURNEY AS A CERVICAL CANCER SURVIVOR
As we near the end of January's 2024 Cervical Cancer Awareness Month, we would like to share the patient journey of Selena Rushton, a Stage 4B Cervical Cancer Survivor.

[Click here](#) to view Dr. Abigail Zamorano's interview with Selena.

If you would like to learn more about Selena's incredible journey,[click here](#).

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**How Can We Help?**

The GOG Partners Connection Quarterly Newsletter is produced by the GOG Foundation Communications Committee.

Please contact us at [info@gog.org](mailto:info@gog.org) with any questions or suggestions regarding future content.