

2019 ASCO Annual Meeting Highlights for the Advanced Practitioner: Gynecologic Cancers

Laura Doherty, FNP-BC, AOCNP[®], of the Women & Infants Hospital of Rhode Island offers commentary on major gynecologic cancer abstracts featured from the ASCO Annual Meeting by *The ASCO Post*, including findings in carcinosarcoma of the uterus or ovary, effects of the Affordable Care Act on ovarian cancer diagnosis and treatment, and novel immunotherapy for cervical cancer.

Abstract 5500

Paclitaxel/Carboplatin vs Paclitaxel/Ifosfamide in Carcinosarcoma of the Uterus or Ovary

By *The ASCO Post*

Visit <https://meetinglibrary.asco.org/record/173464/abstract> to read the full abstract and view author disclosures.

Results from the phase III NRG Oncology clinical trial GOG-0261 comparing paclitaxel plus carboplatin to paclitaxel plus ifosfamide in women with stage I–IV recurrent carcinosarcoma of the uterus or ovary found that treatment with paclitaxel/carboplatin was not inferior to paclitaxel/ifosfamide based on the primary objective overall survival, and paclitaxel/carboplatin was associated with longer progression-free survival outcomes

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when compared with paclitaxel/ifosfamide. These results were presented by Powell et al at the 2019 ASCO Annual Meeting (Abstract 5500).

“While they are rare, gynecologic carcinosarcomas are extremely aggressive, and there has been a great deal of debate surrounding what the ideal or optimal treatment regimen would be for the women who have these malignancies,” stated lead study author Matthew A. Powell, MD, of the Washington University School of Medicine, St. Louis. “Previous phase II research suggested that paclitaxel combined with carboplatin may improve outcomes for this patient population in terms of safety and convenience of treatment, so we tested this against a treatment regimen that included paclitaxel and ifosfamide.”

Study Results

The trial included 449 eligible patients. In the primary uterine carcinosarcoma cohort, median overall survival was 37 months for those who received paclitaxel/carboplatin compared to 29 months for the paclitaxel/ifosfamide treatment arm (hazard ratio [HR] = 0.87; 90% confidence interval [CI] = 0.70–1.075; $P < .01$ for noninferiority, $P > .1$ for superiority). Additionally, the median progression-free survival was 16 months for women who received paclitaxel/carboplatin and 12 months for women who received paclitaxel/ifosfamide (HR = 0.73; $P = < .01$ for noninferiority, $P < .01$ for superiority).

The investigators found increased toxicity for the paclitaxel/carboplatin treatment, which was mostly hematologic, but confusion and genitouri-

nary hemorrhage were significantly worse with paclitaxel/ifosfamide (rates of toxicity grade 1, 2, 3, 4, and 5 were 1%, 8%, 40%, 48%, 2%, respectively, for paclitaxel/carboplatin; 1%, 32%, 39%, 25%, 1%, respectively, for paclitaxel/ifosfamide). During treatment, both groups experienced a similar decline in quality of life and increased neurotoxicity symptoms.

There was a similar trend in results noted for the women who participated in the smaller, secondary cohort of patients with ovarian carcinosarcoma, with a 30-month median overall survival in the paclitaxel/carboplatin arm vs 25 months in the paclitaxel/ifosfamide arm and 15-month median progression-free survival for the paclitaxel/carboplatin arm vs 10 months for the paclitaxel/ifosfamide arm.

“The hope is to continue to improve survival and quality-of-life outcomes for women who experience this rare malignancy,” concluded Dr. Powell. ●

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The results of GOG-0261 change the standard of care for women with newly diagnosed IB to IV, or recurrent chemotherapy-naive carcinosarcoma of the uterus or ovary. Previously, single-agent ifosfamide was found to be inferior to doublet therapy; therefore, this combination of paclitaxel/ifosfamide (P/I) was used as the active control in GOG-0261. Paclitaxel and carboplatin (P/C) were compared with and found noninferior to P/I in this study. In addition to the overall survival of 37 months in the P/C arm to 29 months in the P/I arm, there was a benefit in progression-free survival.

The P/C arm did show more grade 3 and 4 toxicities; however, these were hematologic toxicities that did not require management with granulocyte colony-stimulating factors (G-CSF). It should be noted that all patients on P/I received G-CSF. Benefits to the P/C arm

Key Points

- In the primary uterine carcinosarcoma cohort, median overall survival was 37 months for those who received paclitaxel/carboplatin compared to 29 months for the paclitaxel/ifosfamide treatment arm.
- Median progression-free survival was 16 months for women who received paclitaxel/carboplatin and 12 months for women who received paclitaxel/ifosfamide.
- There was a similar trend in results noted for the women who participated in the smaller, secondary cohort of patients with ovarian carcinosarcoma, with 30 months median overall survival in the paclitaxel/carboplatin arm vs 25 months in the paclitaxel/ifosfamide arm and 15 months median progression-free survival for the paclitaxel/carboplatin arm and 10 months for the paclitaxel/ifosfamide arm.


Reference

Powell, M. A., Filiaci, V. L., Hensley, M. L., Huang, H. Q., Moore, K. N., Tewari, K. S.,...Miller, D. S. (2019). A randomized phase 3 trial of paclitaxel (P) plus carboplatin (C) versus paclitaxel plus ifosfamide (I) in chemotherapy-naive patients with stage I-IV, persistent or recurrent carcinosarcoma of the uterus or ovary: An NRG Oncology trial [Abstract 5500]. *Journal of Clinical Oncology*, 37(15_suppl). https://doi.org/10.1200/JCO.2019.37.15_suppl.5500

include less confusion and genitourinary hemorrhage, and less need of G-CSF. As we know, G-CSF can present its own set of side effects for our patients, and there is a quality-of-life benefit associated with a regimen that does not require this. Providers working with the gynecologic cancer population will be familiar with managing the side effects of P/C, as this is a regimen used heavily in this patient population. The side effects we frequently manage are nausea, neuropathy, alopecia, fatigue, and bone marrow suppression.

Convenience for the patient is improved with P/C: there are 2 fewer days of chemotherapy with P/C, as that regimen is administered on day 1 of a 21-day cycle and P/I is day 1 to 3 of a 21-day cycle. Clinically, we can also attest to the significance of an additional 8 months mean overall survival for patients treated in the P/C arm.

Disclosure: Ms. Doherty has no conflicts of interest to disclose.

 Continued on the following page

Abstract LBA5563**Effect of ACA Implementation on Diagnosis and Treatment of Ovarian Cancer in Women Under 65**

By The ASCO Post

Visit <https://meetinglibrary.asco.org/record/175434/abstract> to read the full abstract and view author disclosures.

An analysis of data from the National Cancer Database found that after implementation of the 2010 Affordable Care Act (ACA), ovarian cancer was diagnosed and treated at an earlier stage among women younger than age 65. More women also received treatment within 30 days of diagnosis, thereby increasing chances of survival. The study was presented by Smith et al at the 2019 ASCO Annual Meeting (Abstract LBA5563).

“Detecting and treating ovarian cancer at an early stage saves lives and lowers health-care costs compared to treatment of cancer at a more advanced, incurable stage,” said lead study author Anna Jo Smith, MD, MPH, a resident in the Johns Hopkins Department of Gynecology and Obstetrics. “Having health insurance plays a major role in whether or not a woman has access to care providers who can monitor symptoms and act on those symptoms if necessary.”

Study Methods

The researchers examined ovarian cancer data from the National Cancer Database, which captures data on approximately 70% of all new ovarian cancer cases. Researchers collected data on women diagnosed and treated from 2004 to 2009 (pre-ACA; 35,842 patients) and 2011 to 2014 (post-ACA; 37,145 patients). They assessed data based on stage at ovarian cancer diagnosis and time to treatment for women aged 21 to 64 years.

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This research suggests that the Affordable Care Act and the accessibility to health care that it provides has possibly contributed to saving the lives of several hundred women

The investigators compared this group with a similar-sized group of women aged 65 and older. The 65 and older group was considered the control, or comparison group, as they had access to Medicare, and hence had a much lower risk of being uninsured either pre- or post-ACA.

The investigators looked at the type of insurance women had and adjusted for race, rural demographics, neighborhood household income, education level, distance traveled for care, census region, practice setting where they received care, and Charlson comorbidity score.

Results

The researchers used a “difference in differences” approach for the analysis that compares changes over time between two groups. They calculated that, compared with women 65 and older, there was a relative gain of 1.7% in early-stage diagnosis (defined as stage I or II) of ovarian cancer. There was also a relative improvement of 1.6% in women being treated within 30 days of diagnosis for those aged 21 to 64 as compared with women 65 and older.

Researchers also found that women who received public insurance post-ACA saw the greatest benefits—relative gains of 2.5% in early-stage diagnosis and timely treatment in those aged 21 to 64 compared with women aged 65 and older. All the above improvements were seen regardless of race, income, or educational level groups.

The researchers are now looking at the years beyond 2014 to glean additional insights, as well as correlation of ACA implementation with trends in other gynecologic cancers. ●

Reference

Smith, A. J., & Nickels, A. (2019). Impact of the Affordable Care Act on early-stage diagnosis and treatment for women with ovarian cancer [Abstract LBA5563]. *Journal of Clinical Oncology*, 37(18_suppl). https://doi.org/10.1200/JCO.2019.37.18_suppl.LBA5563

diagnosed with ovarian cancer in just a few short years. As we know, earlier diagnosis and treatment leads to a higher chance of survival from the disease. A woman diagnosed and treated from 1999 to 2001 had a 5-year survival rate of 89% if she had stage 1A disease, 46.7% if stage IIIA, and 18.6% if stage IV. While

we hope these numbers are becoming more favorable with the new treatments available to a woman diagnosed in 2019, there is still significant survival benefit and cost savings with earlier diagnosis.

Ovarian cancer is notoriously challenging to diagnose given its vague presenting symptoms, especially in the premenopausal population. We know that symptoms of disease often do not present until the disease is advanced, and there is no good screening test. With this in mind, these results still seem to suggest that access to care can identify some ovarian cancers earlier. We can hypothesize that patients or providers are recognizing early presenting symptoms and

are undergoing the necessary work up that leads to early diagnosis.

As advanced practice providers, we can continue to focus on education of our community providers and patients with regards to presenting symptoms of the disease, as access to care suggests early diagnosis is possible for some. Additionally, these women as well as their family members can now be genetically tested. We can more effectively screen for and prevent with risk-reducing surgery additional cancers in the 20% or so of women and their families for whom ovarian cancer is related to an inheritable mutation.

Disclosure: Ms. Doherty has no conflicts of interest to disclose.

Abstract 2358

Novel Immunotherapy for Recurrent, Metastatic, or Persistent Cervical Cancer

By *The ASCO Post*

Visit <https://meetinglibrary.asco.org/record/172802/abstract> to read the full abstract and view author disclosures.

There is a high, unmet need for effective treatments for patients with recurrent, metastatic, or persistent cervical cancer—most patients are young, and survival rates are poor. Adoptive cell transfer using tumor-infiltrating lymphocytes (TILs) has demonstrated durable responses in some patients with recurrent cervical cancer. Data from innovaTIL-04, a phase II trial investigating this treatment, were presented by Jazaeri et al at the 2019 ASCO Annual Meeting (Abstract 2358).

innoVaTIL-04 Design

The ongoing, open-label, multicenter trial is evaluating the safety and efficacy of LN-145 TIL therapy in patients with advanced cervical cancer who have undergone at least one prior line of chemotherapy. Prior checkpoint inhibitor therapy is an exclusion criterion. The primary endpoint is objective response rate per Response Evaluation Criteria in Solid Tumor version 1.1; secondary endpoints include duration of response, disease control rate, and safety. Tumors surgically har-

vested at local institutions are shipped to central Good Manufacturing Practices facilities for TIL generation in a 22-day manufacturing process. Final LN-145 TIL product is cryopreserved and shipped to sites. Patients receive 1 week of preconditioning lymphodepletion (cyclophosphamide, fludarabine), a single LN-145 infusion, followed by up to 6 doses of interleukin-2 (IL-2; 600,000 IU/kg).

As of February 2019, 27 patients have received generation 2 of LN-145, with a mean age of 47 years and 2.6 mean prior lines of therapy.

Results

According to a press release, as of May 14, 2019, 27 patients demonstrated an objective response rate of 44% (3 complete responses and 9 partial responses) and a disease control rate of 85%. At a median follow-up of 7.4 months, 10 patients maintained a response, and the median disease control rate had not been reached (range = 2.6+ to 9.2+ months).

The adverse-event profile was generally consistent with the underlying advanced disease and the profile of the lymphodepletion and IL-2 regimens.

The researchers concluded, “LN-145 results in an objective response rate of 44% in previously treated [patients with] cervical cancer, with acceptable safety and efficacy profile. LN-145 offers patients a viable therapeutic option warranting further investigation.”

Commentary

After a webcast covering these results before the ASCO Annual Meeting, Lee Schwartzberg, MD, FACP, told *The ASCO Post*, “This is an exciting new technology that holds promise in treating cervical cancer and possibly other solid tumors. TILs are present in many types of tumors and have known positive prognostic value, presumably because they denote ‘hot’ or inflamed tumors that could respond to immunotherapy. Harvesting, expanding, and reinfusing them after immunodepletive therapy, as was done here, may overcome tumor-

induced resistance to in situ TILs. Understanding host-tumor microenvironment interactions and the degree and nature of intrinsic TILs that allow successful expansion will be important to interpret these results.” ●

Reference

Jazaeri, A. A., Zsiros, E., Amaria, R. N., Artz, A. S., Edwards, R. P., Wenham, R. M.,...Monk, B. J. (2019). Safety and efficacy of adoptive cell transfer using autologous tumor infiltrating lymphocytes (LN-145) for treatment of recurrent, metastatic, or persistent cervical carcinoma [Abstract 2538]. *Journal of Clinical Oncology*, 37(15_suppl). https://doi.org/10.1200/JCO.2019.37.15_suppl.2538

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Unfortunately, we do not have any standard-of-care treatment regimens for patients with persistent or metastatic cervical cancer status post one line of chemotherapy that has been shown to increase overall survival better than the best supportive care. Overall response rates for the current second-line regimens (carboplatin, vinorelbine, paclitaxel, pemetrexed, ifosfamide, topotecan, irinotecan, pembrolizumab) range from 15% to 25%, so the need for new treatment options is great. The objective response rate of 44% and complete response of 3 patients in innovaTIL-04 is promising, and this will need to be compared to our current second-line therapy options in a phase III trial.

Tumor-infiltrating lymphocyte (TIL) therapy will be new to the advanced practitioner who works solely with gynecologic oncol-

ogy patients, as it is not standard of care for any gynecologic cancers. Side effects of TIL therapy will vary from the traditional cytotoxic and antiangiogenic therapy, and even programmed cell death ligand 1 therapy our cervical cancer patients may standardly receive. If we see this therapy in clinic in the future either as a phase III trial or if it is to become standard of care, advanced practitioners will need to educate patients on the unique side-effect profile of the associated interleukin-2 infusions, to include flu-like syndrome of fever, chills, weakness, and muscle and joint ache, among others.

Cervical cancer is preventable, and as advanced practitioners, we need to continue our community outreach, encouraging cervical cancer screening and educating about human papillomavirus vaccination.

Disclosure: Ms. Doherty has no conflicts of interest to disclose.