Gyn Oncology Clinical Trials and Research

Disease Type	Protocol
Cervical Genmab GCT1015-04	A Single arm, Multicenter, International Trial of Tisotumab Vedotin (HuMax¢ç-TF-ADC) in Previously Treated, Recurrent or Metastatic Cervical Cancer
Cervical KEYNOTE-826	A Phase 3 Randomized, Double-Blind, Placebo-Controlled Trial of Pembrolizumab (MK-3475) Plus Chemotherapy Versus Chemotherapy Plus Placebo for the First-Line Treatment of Persistent, Recurrent, or Metastatic Cervical Cancer
Endometrial MK3475-KN775/ E7080-G000-309	A Multicenter, Open-label, Randomized, Phase 3 Trial to Compare the Efficacy and Safety of Lenvatinib in Combination with Pembrolizumab Versus Treatment of Physician's Choice in Participants with Advanced Endometrial Cancer
Ovarian ATHENA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Nivolumab and Rucaparib Combination Switch Maintenance following Front-Line Platinum-based Chemotherapy in Ovarian Cancer Patients
Ovarian JAVELIN OVARIAN PARP 100	A RANDOMIZED, OPEN-LABEL, MULTICENTER, PHASE 3 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF AVELUMAB IN COMBINATION WITH CHEMOTHERAPY FOLLOWED BY MAINTENANCE THERAPY OF AVELUMAB IN COMBINATION WITH THE POLY (ADENOSINE DIPHOSPHATE [ADP]-RIBOSE) POLYMERASE (PARP) INHIBITOR TALAZOPARIB IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED OVARIAN CANCER (B9991030)
Ovarian VB-111-701 / GOG-3018	The OVAL Study: A Randomized, Controlled, Double-Arm, Double-Blind, Multi-Center Study of Ofranergene Obadenovec (VB-111) Combined with Paclitaxel vs. Paclitaxel Combined with Placebo for the Treatment of Recurrent Platinum-Resistant Ovarian Cancer

Please note: If you are unable to find a clinical trial that works for you, contact 888.972.CURE and ask for the Research Department.
Disclaimer: Studies may close promptly when target enrollment is met.

To refer a patient visit AoAppt.com

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Arizona Oncology ■ 888.972.CURE ■ April 2019

GynOncology UPDATE

Updates in HPV vaccination – Gardasil 9 approved to age 45

by | SNEHAL BHOOLA, MD

Cervical cancer is unique in the field of oncology; unlike other cancers, cervical cancer has a known and preventable cause. This lends itself to an incredible public health opportunity to significantly reduce the incidence (and subsequent morbidity and mortality associated with) cervical cancer. High risk HPV infection causes the vast majority of cervical, vaginal, and vulvar cancers in women as well as penile cancers in men. HPV infections are also responsible for oropharyngeal and anal cancers. Low risk HPV infections cause genital warts. The Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination at age 11 or 12 since 2006 for females and since 2011 for males. The first vaccine to be approved was the Quadrivalent (Gardasil) vaccine covering HPV types 6,11,16,18. A bivalent (Cervarix) and most recently, a 9 valent (Gardasil 9) vaccine were subsequently approved. None of the vaccines are live, and hence all are noninfectious. Each of these vaccines have been approved in a 3-dose series at intervals of 0, 1-2, and 6 months. In October 2016, as a result of new clinical trial results, the FDA and ACIP recommended a 2-dose schedule for boys and girls aged 9 through 14. Below, I have highlighted data supporting these and other updated recommendations regarding these vaccines.

2-Dose Vaccination Schedule and Immunogenicity

In October 2016, the ACIP Vaccines Work Group recommended a 2-dose schedule of the 9vHPV Vaccine. This came after a systematic review of published data. The most compelling data was published after an open-label, noninferiority, immunogenicity trial conducted at 52 ambulatory care sites in 15 countries. These studies compared the 2 and 3 dose schedules in girls and boys aged 9 to 14. Among 1377 participants, >97.9% seroconverted to all nine vaccine-preventable HPV types by 4 weeks after the last dose. Geometric mean antibody titers were significantly higher for all 9vHPV types among persons aged 9 through14 years who received 2 doses compared with females aged 16-26 years who received 3 doses. Similar results were found in six additional studies. Based on this evidence, the recommended 2-dose schedule is at 0 and 6-12 months for patients age 9-14 years at time of initial vaccination. The minimum interval between dose one and two is 5 months. Those 15 years and older are still recommended the 3-dose schedule at 0, 1-2, and 6 months.

Continued on page 2

WELCOME

Welcome to Arizona Oncology's The Gyn Oncology Update newsletter. We are dedicated to educate and serve patients in our community. We hope you enjoy the educational content presented within. If you have any questions or feedback, please do not hesitate to contact us.

In This **ISSUE**

ARIZONA ONCOLOGY
The US Oncology Network

(cont'd) Updates in HPV vaccination

The minimum time interval between dose one and two is 4 weeks, and between dose one and three there must be 5 months. In all age groups, if a subsequent dose is delivered sooner than the minimum interval, a repeat dose should be given. If a valid 4v HPV or 2v HPV vaccine series has been completed by a patient, there are no ACIP recommendations to retreat with the 9vHPV vaccine.

Gardasil 9 approved to age 45 (ages 9 through 45)
On Oct 7, 2018, the FDA approved the expanded use the Gardasil 9 vaccine in males and females ages 9 through 45. This was based off a large trial in women aged 27 to 45. Gardasil demonstrated an efficacy of 88% in preventing persistent infection, genital warts, and dysplasia. This was also supported by immunogenicity data in 160 men aged 27 to 45. Gardasil 9 protects against HPV types 6, 11, 16,18,31,33,45, 52, 58.

Recommendations
ACIP recommends routine vaccination at age 11 to 12 years (can start at age 9 years) with one of the three available vaccines. For those not previously vaccinated, vaccines may be given to female up to age 26 and males up to age 21.

Ages 9-14 years at initiation: 2-dose series at 0 and 6-12 months. Minimum interval: 5 months (repeat a dose given too soon at least 12 weeks after the invalid dose and at least 5 months after the 1st dose).

Ages 15 years or older at initiation: 3-dose series at 0, 1-2, and 6 months. Minimal intervals: 4 weeks between 1st and 2nd dose: 12 weeks between 2nd and 3rd dose; 5 months between 1st and 3rd dose (repeat dose(s) given too soon at or after the minimum interval since the most recent dose).

New Hope for Ovarian Cancer

by | LYNDSAY WILLMOTT, MD

Ovarian cancer is a rare malignancy but important source of cancer related cost and mortality. In 2018, there were 22,240 estimated new cases and 14,070 deaths related to disease (1). An aggregate estimate of five-year survival based on analysis from 2008 to 2014 was 47.4%. This translates to a significant number of women who are currently alive with disease and who could benefit from treatment innovations.

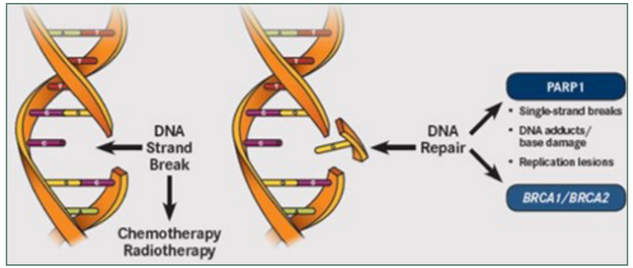
An important consideration in regard to ovarian cancer is the lack of screening and subtle presenting symptoms, which in aggregate contribute to the fact that the majority of these cancers are diagnosed in advanced stages. This also means that, unfortunately, the likelihood of cure is low. The majority of women with advanced stage disease will have a recurrence, which translates to multiple cycles of various types of chemotherapy and potentially adverse impact on quality of life. Thus, an important target of treatment should be to improve progression free survival and subsequently time off of chemotherapy.

Another advance in ovarian cancer management is the recognition of the frequency of genetic mutations in this disease. Specifically, up to 18 percent of ovarian cancer patients actually carry germline BRCA 1 or 2 mutations, with perhaps an additional 8 percent of patients with somatic BRCA mutations. Because of the frequency of these mutations and other genetic errors that can contribute to disease development, the current recommendation is that all patients diagnosed with ovarian cancer should undergo germline high-risk gene testing (2,3,4).

BRCA proteins are responsible for double stranded DNA repair via homologous recombination, the most perfect form of repair. If there is a deficiency in this repair mechanism, the cells rely on other types of DNA repair to fix errors. Luckily, we can use these genetic errors to our advantage via a concept called synthetic lethality. This entails knocking out the compensatory mechanism that allows an otherwise defective cell to survive, hence causing cell death. PARP-inhibitors are a class of drugs that capitalize upon this phenomenon. Poly-ADP ribose polymerase is a protein responsible for single-stranded DNA repair. When this protein is inhibited, double stranded breaks will occur. In cells that are unable to effectively correct these double stranded breaks because of deficiencies in the homologous recombination repair pathway, cell death will occur.

There are currently three PARP-inhibitors commercially available for use in ovarian cancer: olaparib, rucaparib, and niraparib.

Cancer Biology: PARP Inhibitors



PARP inhibitors have shown a 34% ORR in patients on 4th line chemotherapy for Ovarian Cancer

PARP Inhibitors are now being studied in first line chemotherapy for Ovarian Cancer

The drugs are FDA approved for multiple indications, including treatment for women with recurrent cancer (olaparib and rucaparib) and maintenance for women after completion of treatment (olaparib, rucaparib and niraparib). Maintenance therapy is a drug administered after completion of chemotherapy if a patient has had at least partial response to said therapy. The aforementioned PARP-inhibitors are all indicated in platinum sensitive recurrent disease with three separate trials demonstrating statistically and clinically meaningful improvement in progression free survival.

Most recently, olaparib achieved the FDA indication for upfront maintenance in women with BRCA mutations who had at least a partial response to their upfront platinum based chemotherapy. The SOLO-1 trial demonstrated a hazard ratio of 0.3 favoring treatment with olaparib, and this translated to an estimated 3-year progression free survival of 60% at 3 years. This was in contrast to PFS of 27% in women who were treated with placebo (5).

Current clinical trials are evaluating the use of PARP-inhibitors in combination with other categories of medications to try to improve upon already impressive advances in progression free survival. The goal of clinical research will always be to find treatments that improve survival while allowing patients to maintain quality of life. Certainly, we have many miles to go before we sleep, but the improvements in survival outcomes that have been observed in recent trials assure us that we are making progress.

References

NCI, Surveillance, Epidemiology, and End Results Program.
NCCN Guidelines. Genetic/familial high-risk assessment: Breast and Ovarian. Version 2.2019.
Norquist BM, et al. *JAMA Oncol.* 2016.
Alsop K, et al. *J Clin Oncol.* 2012.
Moore K, et al. *N Engl J Med.* 2018.

Annual Gynecological Oncology Update for Referring Providers

FREE CME/CEU program 4.5 Credits

OCTOBER 12, 2019 • 7:30am – 2:30pm

HonorHealth Shea, Brady Conference Center
9003 E. Shea Blvd., Scottsdale, AZ 85260

Breakfast and lunch will be served

Ovarian Cancer Update
Parp/Immunotherapy
Anti-angiogenic's, new treatments Prevention Gyn Cancers Update
Cancer Genetics
Breast Cancer Update
Physician resilience and burnout
Navigating ACO's and Managed Care
Appropriate work up for adnexal mass
Update on Surgery
Minimal Invasive Surgery "Pros and Cons"
Techniques (Endrimotosis SX – how to identify important structures)

Gynecological Cancer Support Group *(First Saturday of Every Month)*

When: First Saturday of Every Month
Time: 11:00 am to 1:00 pm
Hosted by: Arizona Oncology and National Ovarian Cancer Coalition
Where: Arizona Oncology East Valley Cancer Center 7695 South Research Drive, Tempe 85284

Who: Members of the Ovarian Cancer Community (survivors, family and friends) are welcome
Cost: FREE, light lunch is served
RSVP INFO: sbaker@ovarian.org or (480) 566-0031