

Gynecologic Oncology *in brief*

News from the Magee-Womens Gynecologic Cancer Program of UPMC Cancer Centers

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Magee-Womens Gynecologic Cancer Program of UPMC Cancer Centers

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For more information about our services, to contact one of our gynecologic cancer specialists, or to refer a patient to the Magee High-Risk Ovarian Cancer Program, call 1-866 MY MAGEE.

Magee.UPMC.com

Magee-Womens Hospital
of UPMC

Clinical trials offer new treatment options for patients



Dr. Edwards

More than a decade ago, researchers determined that BRCA 1 and BRCA 2, when changed or mutated, increase the risk of colon, breast, and ovarian cancers.

Since this discovery, much effort has been directed toward investigating fundamental questions about hereditary cancer risk and the role of BRCA mutations. And while the answers to these and other related questions may lead to better early detection methods and treatments, our understanding of the roles these mutations play is still in its infancy.

For women with a BRCA mutation who develop ovarian cancer, determining the role of these mutations may impact the type of treatment and maintenance therapies that are offered.

In this issue of *Gynecologic Oncology in Brief*, we feature a case study that follows a patient with a family history of colon cancer and a deleterious mutation of BRCA 1 through her participation in two important clinical trials. The first trial examines the role of maintenance therapy in treating ovarian cancer, while the second trial is evaluating the role of PARP inhibitors in treatment of women with BRCA mutations.

Another focus is the use of bevacizumab for the treatment of patients with advanced-stage ovarian cancer. Results from the previous clinical trials have been promising, and have led physician-researchers to further evaluate the use of bevacizumab in two additional clinical trials, both of which are available through the Magee-Womens Gynecologic Cancer Program of UPMC Cancer Centers.

Finally, we would like to make you aware of the breadth of services available to your patients at the Magee-Womens Gynecologic Cancer Program's 16 community sites located throughout western Pennsylvania.

This is an exciting time for cancer research and care. We hope you find this information useful in your day-to-day practice, and welcome the opportunity to discuss our clinical research or patient care opportunities. Please contact us at 1-866 MY MAGEE or visit our website at Magee.UPMC.com.

Sincerely,

Robert P. Edwards, MD

Director, Research and Outreach Education,
Vice Chair, Clinical Affairs

CASE REPORT

Evaluating maintenance therapy and ABT-888 trial in treating ovarian cancer

In 2005, a 54-year-old female presented for a routine gynecologic examination. Although the patient was not experiencing any symptoms, her family history indicated a first-degree relative with a history of colon cancer. During the examination, the physician located a mass within her pelvis. She underwent a comprehensive evaluation, including a pelvic ultrasound, a CT scan of her abdomen and pelvis, which demonstrated a complex bi-lobed mass rising in the pelvis, multiple soft tissue densities in the mesentery suspicious for implants, and a small amount of ascites. During the physician's exam, the cervix appeared normal with a large mass filling out to the pelvic brims and palpable to the level of the umbilicus. There was no evidence of fluid wave. Further testing revealed that the patient's CA-125 was elevated to 1922 U/ml.

The patient underwent an exploratory laparotomy with a total abdominal hysterectomy, bilateral salpingo-oophorectomy, reduction of intra-abdominal tumor, omentectomy, and pelvic and periaortic lymphadenectomy. She was considered to have had an optimal debulking, with no gross visible residual disease.

Postoperatively, she received six cycles of intravenous carboplatin and taxol. Within three cycles of treatment, the patient's CA-125 level returned to normal. Upon completion of therapy, there was no evidence of persistent disease based on a normal CA-125 of 4 U/ml, normal radiographic imaging, and benign clinical exam.

The patient was recruited to join Gynecologic Oncology Group (GOG) protocol 212 evaluating the role of maintenance therapy in the treatment of ovarian cancer. The randomized, three-arm trial is evaluating observation versus paclitaxel 135mg/m² versus Xyotax™ 135 mg/m², with both drugs being given monthly for 12 months. Xyotax is a novel compound that is a combination of paclitaxel and a polybutumate polymer, which allows the drug to be infused rapidly over 20 minutes, compared to a normal infusion time of three hours. Initial data suggest a more favorable toxicity profile with regards to hypersensitivity reaction, neurotoxicity, and alopecia.

The patient was randomized into the paclitaxel arm, and completed treatment without any adverse side effects. During treatment, the patient's CA-125 level remained normal. The patient also was assessed for a BRCA mutation, and was found to have a deleterious mutation of BRCA 1 with an R1835X, which is a premature termination of the BRCA 1 protein at the amino acid position 1835. Patients with this mutation are considered to be at a higher risk for developing both ovarian and breast cancer in their lifetimes. Although risk estimates vary, the presence of the mutation increases the likelihood of developing these diseases prior to menopause. Their lifetime risk of developing breast cancer increases to 70 percent, and their risk of developing ovarian cancer increases to as high as 40 percent compared to the general population with a risk of 12 percent and 1.4 percent respectively.

After completing treatment, the patient remained without evidence of disease for a period of one year. She then had a slow elevation of her

CA-125 level, and was found to have evidence of mesenteric implants on CT imaging. She was started on salvage chemotherapy utilizing gemcitabine and carboplatin with the addition of bevacizumab. She received a total of six cycles, with normalization of her CA-125 level, as well as radiographic evidence of complete response. She continued to take bevacizumab for a total of 31 cycles, with each cycle given on a monthly basis. Bevacizumab is a humanized monoclonal antibody, which functions as an angiogenesis-inhibiting agent by blocking vascular endothelial growth factor A. This agent has been studied by the GOG, and has demonstrated activity as a single agent. Bevacizumab was recently reported to increase progression-free survival in patients who received this drug as maintenance therapy.



In the early part of 2010, the patient was found to again have a rising CA-125 level and radiographic evidence of recurrence based on retroperitoneal lymphadenopathy. The patient elected to participate in a new clinical trial targeted at patients with BRCA mutations. The randomized trial evaluates the use of a Poly ADP ribose polymerase (PARP), known as ABT-888, in combination with temozolomide (an alkylating agent) versus pegylated liposomal doxorubicin. The study drugs are given in an oral form. PARP is a naturally occurring protein that helps cancer cells overcome injury or damage caused by radiation and antineoplastic agents, by fostering DNA repair.

The patient started therapy in the spring of 2010. She was randomized into the PARP arm of the trial, and received a total of four cycles, with rapid normalization of her CA-125 level. A CT scan demonstrated regression of disease. The patient is now five years out from her date of diagnosis. ■

Bevacizumab as a treatment for late-stage ovarian cancer

The majority of patients diagnosed with ovarian cancer will present with advanced-stage cancer - Stages III and IV. Currently, the best treatment for advanced-stage ovarian cancer is a combination of surgery to remove the tumor, and chemotherapy. Unfortunately, many patients who respond initially to treatment will suffer from recurrent ovarian cancer.

The Gynecologic Oncology Group (GOG) performed a clinical trial that investigated the use of bevacizumab in addition to standard chemotherapy in patients with advanced-stage ovarian cancer. The goal of the trial was to evaluate the utilization of the novel agent as up-front therapy to prolong the duration of remission. The trial evaluated approximately 1,800 patients with Stages III and IV ovarian cancer. Approximately two-thirds of the patients received bevacizumab as the investigation agent. This trial compared three groups of patients: group one received standard chemotherapy with carboplatin and paclitaxol; group two received carboplatin, paclitaxol, and bevacizumab; and group three received carboplatin, paclitaxol, and prolonged doses of bevacizumab.

Results from the trial were presented at the 2010 American Society of Clinical Oncology meeting in Chicago. The majority of the patients enrolled in the trial, approximately 600 in each arm, completed therapy. The results showed that the patients who received the additional

treatment with prolonged doses of bevacizumab experienced a prolonged, progression-free survival advantage of six months.

As the first large-scale trial to evaluate bevacizumab as an initial treatment of advanced-stage ovarian cancer, this trial, in combination with the previous clinical trials, confirms bevacizumab as an active drug in the treatment of advanced or recurrent ovarian cancer. Bevacizumab was very well tolerated, with the major side effects being hypertension, headache, and in less than 3 percent of patients, spontaneous bowel perforation.

Results from the previous studies have been promising, and have led physician-researchers to further evaluate the use of bevacizumab in two additional clinical trials for the treatment of patients with advanced-stage ovarian cancer: GOG 252 and 262. The new trials will help to better define the dosing, timing, and length of treatment for bevacizumab use in the treatment of women with ovarian cancer.

The Magee-Womens Gynecologic Cancer Program of UPMC Cancer Centers is currently enrolling patients in both of these trials. For more information on eligibility criteria or for patient referrals, call 412-641-5411. ■

Patients needed for Phase III trial

Magee-Womens Hospital of UPMC is currently accruing patients for a multi-institution, Phase III trial investigating whether regimens containing cisplatin are more effective than regimens not containing cisplatin, and also examining the role of bevacizumab in the treatment of metastatic cervical cancer.

As part of Gynecologic Oncology Group (GOG) protocol 240, participants will be randomized into one of four regimens. For regimens containing bevacizumab, the National Cancer Institute is supplying the medication. Due to the logistics of providing drugs to community-based centers, this protocol will only be offered at the Magee office.

To be eligible for this trial, patients must have advanced cervical cancer and/or recurrent cervical cancer. Patients may have had prior radiation therapy to the pelvis, but may not have had prior chemotherapy. For more information on eligibility criteria or for patient referrals, call 412-641-5418. ■

Gynecologic Cancer Care in the Community

An important objective of the Magee-Womens Gynecologic Cancer Program is to provide women with gynecologic cancer convenient access to state-of-the-art care in their community through collaborations with ob-gyn, primary care, medical oncology, and radiation oncology physicians.

To support this mission, we provide:

- gynecologic oncology physician presence in 16 community sites
- regular and frequent communication with referring physicians about the status and transition of care
- referral of patients back to their community cancer center for chemotherapy and radiation therapy

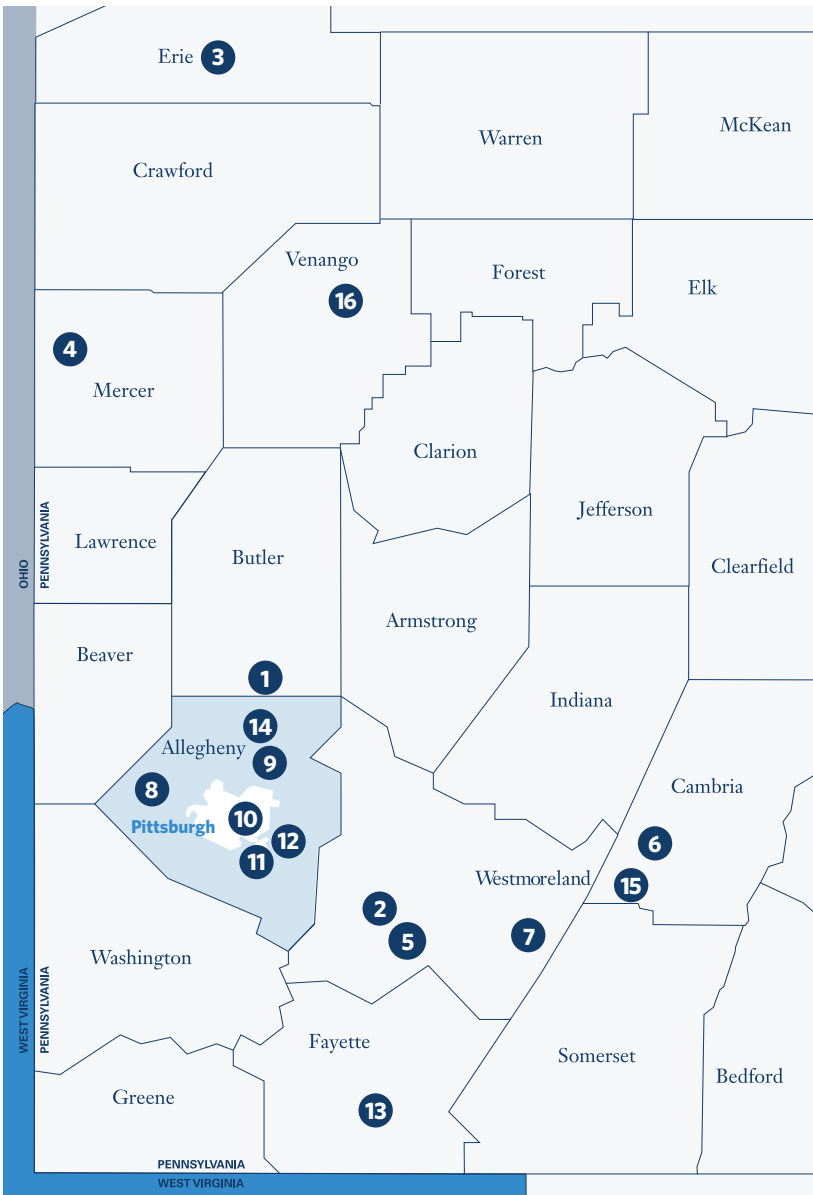
- one convenient phone number (412-641-5411) to schedule appointments at any of our community locations
- easy inpatient transfers and consultations through Medcall at 1-800-544-2500
- regular updates to physicians in the community about promising research initiatives and clinical innovations

We value your opinions about any areas where we can improve our services to you and your patients. If you have any comments or questions, call 412-641-5411. ■

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Gynecologic Oncology Service Support in Your Community

The Magee-Womens Gynecologic Cancer Program provides gynecologic oncology care at 16 locations throughout western Pennsylvania. For more information or to discuss patient referrals, call 412-641-5411.

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