

Important Steps in the Conquest of Ovarian Cancer

Peg Ford

Writing about ovarian cancer this month provided me with the chance to reflect on how things have changed not only in treatment, but also in research over the past several years since I entered the world of medicine as an advocate. In addition, I recently was invited to participate in a National Cancer Institute (NCI) site visit at Scripps Research Institute, where I was privileged to learn firsthand about the studies conducted at a cancer research lab, and to appreciate the challenges.

As a layperson, my idea of the scientific world was of a distant sphere of higher learning where only the very few who were capable and trained could comprehend even the most basic science. Yet because of the emerging paradigm shift to include the patient stakeholder's presence and voice in medicine, opportunities and support are available for individuals who wish to learn and become informed and involved advocates. I am grateful to have discovered these in my journey, and I am confident that more people will be able to participate and represent the patient community in the scientific arena, to the benefit of both communities.

Strides have been made in ovarian cancer treatment options and there has been an increase in research since my entry into the world of advocacy in 2008 as an ovarian cancer survivor. However, mortality rates have not changed much, as most women when diagnosed with ovarian cancer have late-stage disease and, sadly, most will face recurrences. We still do not have a screening test for early detection of ovarian cancer, but researchers are endeavoring to change this. The one aspect that is certain—one the patient community is working hard to increase—is awareness, through education of medical students and outreach programs for the general public emphasizing that if detected in the early stage, the overall 5-year survival rate for the few women diagnosed at this point greatly increases from 45% to over 90%.

The American Cancer Society estimates that about 22,400 women will be diagnosed with ovarian cancer in 2013 and that 14,230 women will die from the disease, which is the fifth leading cause of cancer deaths among women in this country. Approximately 1 in 72 women will develop ovarian cancer, and their risk of dying is 1 in 100.

Generally, ovarian cancer is considered an older woman's disease and although women have a higher risk as they age,



Peg Ford with Luis Alberto Diaz, MD, of Johns Hopkins Kimmel Cancer Center and a researcher of the new "PapGene" test, a 3-in-1 screening test for gynecologic cancers. Photo taken on October 30, 2013, after a presentation by Diaz at Illumina, Inc.

more young women are facing this deadly disease. One such brave 25-year-old, Kristina Anderson, is attempting something quite extraordinary and certainly out of the ordinary as she is competing in the upcoming Miss Arizona pageant. She was diagnosed with a rare form of ovarian cancer last July and is determined to go forward on her own terms despite having to deal with this disease.

Because ovarian cancer is very heterogeneous molecularly, the need for personalized precision treatment is advancing the interest and focus of the scientific

world. Owing to its relative connections to the BRCA gene mutations in breast and other types of cancer (Lynch syndrome), ovarian cancer research efforts have increased. PARP inhibitors, vaccines, angiogenesis inhibitors, and targeted chemotherapy are all examples addressing this urgency, and a grateful patient community knows, without question, how important it is to support and fund research now more than ever.

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There is an experimental study at Columbia University Medical Center that uses hyperthermic intraoperative chemotherapy (HIPEC), also known as heated chemotherapy. After removing the tumor, the area is treated with

heated (to about 108 degrees) chemotherapy delivered directly into the patient's abdomen for approximately 60 to 90 minutes. The new "PapGene" test, a 3-in-1 screening for gynecologic cancers, combines a traditional Pap smear for cervical cancer with a DNA test for gene mutations linked to endometrial and ovarian cancers. According to lead researcher and MD-PhD candidate Isaac Kinde and Luis Alberto Diaz, MD, of Johns Hopkins Kimmel Cancer Center, the screening is not

yet ready for clinical practice...but could this prove to be another important step toward a screening test? The PapGene screening uses advanced DNA sequencing technology to look for mutations in 12 genes associated with endometrial or ovarian cancers in cells collected for Pap smears. The PapGene test often found one or more of the mutations from the samples. In contrast, the samples from women without cancer showed no mutations. The screening proved highly sensitive for endometrial cancer: every woman known to have the disease tested positive for mutations. However, it captured only 40% of patients known to have ovarian cancer.

Interesting studies have been funded, including the prospect that man's best friend could sense cancers. One anecdote supporting this possibility is a female patient whose dog was poking at her breast for months before she was diagnosed with stage III breast cancer. A study is currently under way regarding dogs and the detection of ovarian cancer.

One extremely promising update from a study from the University of Texas MD Anderson Cancer Center is that gauging CA-125 (the protein recognized and used for predicting ovarian cancer recurrence, discovered by Robert Bast, MD, who is the study's senior author) over time may be a screening tool for early stage in postmenopausal women at average risk for the disease. Karen Lu, MD, professor and chair of the Department of Gynecologic Oncology and the study's corresponding author, indicated that research is ongoing and that she and her team plan to study other markers along with CA-125 to determine the screening impact of their combined change over time.

This finding is certainly encouraging, but thus far is neither conclusive nor ready to change current practice, as a large, randomized prospective screening trial still needs to be conducted. However, such research is currently under way in the United Kingdom, where results from more than 200,000 women should be known by 2015.

Of note are the diverse as well as private contributors funding the CA-125 study: it was supported by the NCI and was a research project of MD Anderson's ovarian cancer Specialized Program of Research Excellence (SPORE; NCI P50 CA83639), the Bioinformatics Shared Resources of MD Anderson (CCSG NCI P30 CA16672), and the National Foundation for Cancer Research. Philanthropic support was also received from Golfers Against Cancer, the Tracy Jo Wilson Ovarian Cancer Foundation, the Mossy Foundation, the Norton family, and Stuart and Gaye Lynn Zarrow.

In my work with newly diagnosed patients and those who are dealing with recurrences as they prepare to participate in the Ovarian Cancer Alliance of San Diego's Outreach Programs (my organization), I am inspired to find that although heavy of heart, these women are struggling to fight this lethal disease and are thankful for the dedicated physicians and researchers who are working diligently to combat it. ●

Resources for Patients, Survivors, Providers, Researchers, and Supporters

Peg Ford

Ovarian Cancer Alliance of San Diego

www.ocaofsd.org

Peg Ford, Cancer Research Advocate, Founder/Chair

The Alliance strives to affect change in the way medical doctors consider the diagnosis and treatment of ovarian cancer; educate the medical community, patient organizations, and the community at large about early diagnosis; further research on evidence-based treatment options; and, ultimately, eradicate the disease.

The Clarity Foundation

www.clarityfoundation.org

The Foundation helps patients with ovarian cancer and their physicians in making better-informed treatment decisions based on the molecular profile of the tumor (the “tumor blueprint”), thus enabling a more individualized approach to therapy selection. Patient support services include lab test coordination, tumor blueprint interpretation, and clinical trial identification free of charge.

FORCE (Facing Our Risk of Cancer Empowered)

www.facingourrisk.org

FORCE is a national nonprofit agency dedicated to improving the lives of individuals and families affected by hereditary breast and ovarian cancer. Information on cancer management and treatment, clinical trials and research, support, advocacy, and events is offered on the website. A toll-free helpline can be reached at 1-866-288-RISK.

Foundation for Women's Cancer

www.foundationforwomenscancer.org

The Foundation offers many awareness, educational, and fundraising programs as well as comprehensive information about gynecologic cancer risk prevention, early detection, and optimal treatments provided by gynecologic oncologists and other healthcare experts.

Guidelines International Network (G-I-N)

www.g-i-n.net

G-I-N offers partnership opportunities for guideline organizations, assists in improving the efficiency and effectiveness of healthcare guideline development, and promotes best practices through opportunities for learning and the establishment of standards. G-I-N/North America provides a community for North American guideline users, developers, and other stakeholders to form partnerships and discuss regional guideline issues.

National Ovarian Cancer Coalition (NOCC)

www.ovarian.org

The Coalition is committed to improving the survival rate and quality of life for women with ovarian cancer. Through national programs and local chapter initiatives, NOCC's goal is to make more people aware of the early symptoms of the disease. In addition, NOCC provides information to assist the newly diagnosed patient as well as hope and support to survivors and caregivers.

Ovarian Cancer National Alliance

www.ovariancancer.org

The Alliance advocates at a national level for increases in research funding for the development of an early detection test, improved healthcare practices, and life-saving treatment protocols. The Ovarian Cancer Symptom Diary App (www.ovariancancer.org/app) helps individuals learn about the risks, signs, and

symptoms of the disease. This first-of-its-kind application allows a woman to track symptoms that could indicate ovarian cancer, and alerts her if she should make an appointment with her doctor for further testing.

Ovarian Cancer Research Fund

www.ocrf.org

The Ovarian Cancer Research Fund is the oldest and largest philanthropic organization in the United States funding ovarian cancer research. Through its auspices, more than \$50 million has been granted to the most innovative and promising ovarian cancer research.

Patient Advocate Foundation (PAF)

www.patientadvocate.org/myresources

PAF advocates and mediates on behalf of patients to provide access to evolving therapies, therapeutic agents, and devices. Professional patient assis-

tance is offered by telephone, email, or live web chat. PAF's free My Resource Search app is an easy-to-use tool for healthcare, financial, and insurance help that allows both insured and uninsured patients to identify the community and national programs that can assist in their healthcare needs.

Society of Gynecologic Oncology (SGO)

www.sgo.org

With more than 1700 domestic and international members, SGO is the premier medical specialty society for healthcare professionals trained in the comprehensive management of gynecologic cancers. SGO contributes to the advancement of women's cancer care by promoting research, providing education, raising standards of practice, advocating for patients and members, and collaborating with other national and global organizations. ●

Pazopanib: First Positive Maintenance Trial

Phoebe Starr

Previous trials of maintenance therapy for patients with ovarian cancer have failed to show improved survival. A study presented at the 2013 American Society of Clinical Oncology Annual Meeting is the first successful phase 3 trial in this setting—targeted therapy pazopanib extended progression-free survival (PFS) in women with ovarian cancer by a median of 5.6 months. Women enrolled in the trial were disease free after initial treatment with surgery and chemotherapy.

“Pazopanib maintenance therapy prolongs the time the patient has control over the disease versus the time the disease controls the patient's life. Pazopanib might be a valuable option for treatment of stage II to IV ovarian cancer,” stated lead author Andreas Du Bois, MD, PhD, professor of gynecologic oncology at the Kliniken Essen-Mitte in Germany.

Although patients with ovarian cancer typically respond to initial therapy with surgery and chemotherapy, the relapse rate is about 75%. The rationale for maintenance therapy is to keep patients in remission, but studies to date have been disappointing. Given the cost and the added toxicity of maintenance therapy, demonstrating improved survival is important.

Pazopanib is an oral multikinase inhibitor approved by the US Food and Drug Administration for the treatment of renal cell carcinoma and soft tissue sarcoma. Medication toxicities reported in the current trial were class specific to angiogenesis inhibitors: hypertension, elevated liver enzymes, neutropenia, and diarrhea.

Most Patients Had Advanced Disease

The phase 3 multicenter trial enrolled 940 patients with advanced epithelial ovarian, fallopian tube, or primary peri-

toneal cancer. Eligibility criteria included patients with stage II to IV disease, but most patients had stage III or IV ovarian cancer. Participants were randomized in a 1:1 ratio to receive 800 mg of pazopanib orally versus placebo for 2 years after standard surgery and chemotherapy.

The median time to disease progression was 17.9 months for the pazopanib group versus 12.3 months for the placebo group, representing a 5.6-month advantage for those on the targeted therapy.

At 24 months, however, no significant difference in overall survival was observed. Longer follow-up is needed to see if there is an overall survival benefit.

“There is currently no standard of care for maintenance therapy. Evidence continues to mount that targeting angiogenesis is important in ovarian cancer. The bottom line from several studies is that targeting angiogenesis is effective in ovarian cancer. These results show that pazopanib extends PFS as maintenance therapy, similar to the results of previous trials of bevacizumab,” said Carol Aghajanian, MD, chief of Gynecologic Medical Oncology Service at Memorial Sloan-Kettering Cancer Center, New York City.

“This large trial shows us that targeting multiple molecular cancer drivers can have a substantial impact on this cancer's ability to grow,” Aghajanian said. “This study offers a real-world example of how the precision medicine era of cancer research is paying off in areas where no alternate approved drugs exist.” ●

Reference

Du Bois A, Floquet A, Weon Kim J, et al. Randomized, double-blind, phase III trial of pazopanib versus placebo in women who have not progressed after first-line chemotherapy for advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (AEOC): results of an international Intergroup trial (AGO-OVAR16). *J Clin Oncol*. 2013;31(suppl):Abstract LBA5503. Presented at: 2013 American Society of Clinical Oncology Annual Meeting; May 31-June 4, 2013; Chicago, IL.