

# 2013 State of the State of Gynecologic Cancers

*Eleventh Annual Report to the Women of America*

FOUNDATION FOR  
WOMEN'S CANCER



Gynecologic Cancer  
Awareness • Research • Education

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*The Foundation for Women's Cancer is a 501(c)3 not for profit organization whose mission, in concert with SGO, is to support research, education and public awareness of gynecologic cancer prevention, early diagnosis and optimal treatment.*

# A Letter to the Women of America

For the past 10 years, the Foundation has chronicled the impact of gynecologic cancers upon the almost 900,00 women diagnosed with these cancers during the past decade. As we publish the *2013 State of the State of Gynecologic Cancers: Eleventh Annual Report to the Women of America*, we wish to honor the caregivers who share this journey with the women they love.

The American Cancer Society Behavioral Research Center recently reported on the results of the “American Cancer Society National Quality of Life Survey for Caregivers”. This study, begun in 2002, surveyed nearly 2,000 cancer caregivers, making it the largest nationwide, long-term study looking at cancer through the eyes of caregivers.

Here are some highlights from the study:

- Caregivers spent about 8 hours a day providing care, making it a full-time job. The value of this time can equate to tens of thousands of dollars per year.
- The fear of a recurrence equally impacts both survivor and the caregiver, and affects the quality of life for each.
- Caregivers may have unrealistic expectations of themselves, feeling that they should be doing more.
- Caregivers need a strong support system, perhaps making it possible to take needed time away — maybe once a week.
- Caregiving can provide an opportunity to reflect upon life’s purpose and sometimes gain a new appreciation for it.

The Foundation for Women’s Cancer continues to seek new ways to support women diagnosed with a gynecologic cancer. Our website, [foundationforwomenscancer.org](http://foundationforwomenscancer.org), has a section on caregiving, and we welcome your suggestions about how to improve information available to caregivers.

We again thank the gynecologic oncologists who volunteered their time to provide the information contained in this year’s report. And, we respectfully dedicate the *2013 State of the State of Gynecologic Cancers: Eleventh Annual Report to the Women of America* to those who care for women diagnosed with a gynecologic cancer.

Sincerely,



David M. Gershenson, MD  
Chairman, Foundation for Women’s Cancer

# Commonly Asked Questions

## What are gynecologic cancers?

Gynecologic cancers are the uncontrolled growth and spread of abnormal cells originating in the female reproductive organs, including the cervix, ovaries, uterus, fallopian tubes, vagina and vulva.

## What causes gynecologic cancers?

There are many factors that cause gynecologic cancers. Medical research has discovered that some classes of genes, called oncogenes and tumor suppressor genes, promote the growth of cancer. The abnormal function of these genes can be acquired (e.g., through smoking, aging, environmental influences) or inherited. Almost all cervical cancers and some cancers of the vagina and vulva are caused by a virus known as HPV, or Human Papillomavirus.

## Can gynecologic cancers be prevented?

Screening and self-examinations conducted regularly can result in the detection of certain types of gynecologic cancers in their earlier stages, when treatment is more likely to be successful and a complete cure is a possibility. Diet, exercise and lifestyle choices play a significant role in the prevention of cancer. Additionally, knowledge of family history can increase the chance of prevention or early diagnosis by determining if someone may have a gene which makes them susceptible to cancer.

## Who should treat gynecologic cancers?

Gynecologic cancers should be treated by a specialist with advanced training and demonstrated competence, such as a gynecologic oncologist.

A gynecologic oncologist is a board-certified obstetrician/gynecologist who has an additional three to four years of specialized training in treating gynecologic cancers from an American Board of Obstetrics and Gynecology-approved fellowship program. This subspecialty program provides training in the biology and pathology of gynecologic cancers, as well as in all forms of treatment for these diseases, including surgery, radiation, chemotherapy and experimental treatments.

## How are gynecologic cancers treated?

Gynecologic cancers are treated by using one or more of the following: surgery, radiation therapy and/or chemotherapy. The choice of therapy(s) depends on the type and stage of the cancer.

## Who is at risk?

Every woman is at risk for developing a gynecologic cancer. It is estimated that there will be about 91,000 new cases diagnosed and approximately 28,000 deaths from gynecologic cancers in the United States during 2013.<sup>1</sup>

<sup>1</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

# Cervical Cancer

## State of Cervical Cancer

*Cervical cancer is a cancer that begins in the cervix, the part of the uterus or womb that opens to the vagina. It is the part of the uterus that dilates and opens fully to allow a baby to pass into the birth canal. The normal cervix has two main types of cells: squamous cells that are on the outside of the cervix and glandular cells which make the fluid and mucus commonly seen during ovulation that are mostly on the inside of the cervix. Cervical cancer is caused by abnormal changes in either of these cell types in the cervix, and is the only gynecologic cancer that can be prevented by regular screening and vaccination. Since nearly all cervical cancers are caused by persistent infection with the Human Papillomavirus (HPV), vaccinating women and young girls before they become sexually active and potentially exposed leads to the greatest prevention of pre-cancer and cancer. Early vaccination (currently recommended at 11 or 12 years of age) along with regular Pap tests and HPV testing when recommended is now the best way to prevent cervical cancer. Cervical cancer usually affects women between the ages of 30 and 55.*

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**Symptoms:** Bleeding after intercourse, excessive discharge and abnormal bleeding between periods. Most women will have no symptoms, and abnormal precancerous or cancer cells will be identified by screening with a Pap test and HPV testing when indicated.

**Risk Factors:** Infection with high-risk HPV has been shown to cause virtually all cervical cancers. However, HPV is very common and most women with HPV will never get any cervical disease that would require some sort of treatment. Other risk factors include smoking; weakened immunity due to HIV infection or taking medicines for chronic diseases, such as lupus, or following an organ transplant; and becoming sexually active at a young age. Failure to get regular gynecologic examinations that include Pap testing takes away the opportunity for early diagnosis through cervical cancer screening. Even in women with HIV, previously thought to be at risk for cervical cancer, appropriate screening with Pap tests may eliminate this increased risk.

**Screening/Prevention:** Over the last 50 years, routine use of the Pap test to screen for cervical cancer has reduced deaths from the disease by more than 70%. A Pap test is a standard way healthcare providers can check to see if there are any changes in the cervical cells that might cause concern. The Pap test involves looking at a sample of cells from the cervix under a microscope to see if there are any that are abnormal. It is a good test for finding not only cancer, but also finding cells that might become cancerous in the future. Healthcare providers will occasionally perform the Pap test as part of a routine pelvic exam. It is important for women to know if a Pap test was performed because it is possible to have a pelvic exam without a Pap test. Recently, guidelines for cervical cancer screening have changed. It is now recommended that for women with no history of abnormal Pap results, annual Pap tests might lead to more procedures and more treatment, but not pick up more cancers. So, the guidelines are increased intervals for screening in these women. Also, the American College of Obstetricians and Gynecologists published revised guidelines recommending cervical cancer screening before age 21 should be avoided because it could lead to unnecessary and potentially harmful overtreatment in a group of

women at very low risk for developing cervical cancer. It is also important that women know and understand their Pap test results and follow through with any recommendations made by their healthcare provider. Recently the management guidelines have also been updated. Some of the big changes include more conservative management of equivocal abnormalities in young women as well as more paths back to routine screening once the abnormality resolves or is treated. Some abnormal Pap tests will be followed by colposcopy (examination of the cervix using a magnifying device to see the cervix more clearly) and biopsy of any abnormal appearing areas on the cervix. Any pre-cancerous areas can then be seen and treated as recommended by a healthcare provider.

Current cervical cancer screening guidelines support the use of HPV testing at certain times in combination with Pap testing. HPV testing is done automatically when a Pap test is diagnosed as ASC-US (atypical squamous cells of undetermined significance). If high-risk HPV is present in these cells, then a pre-cancerous abnormality is more likely and colposcopy is recommended. In women 30 and over, HPV testing in combination with a Pap test can determine who is not at risk of having pre-cancer of the cervix. A negative HPV test with a negative Pap test can allow Pap screening to occur in five years. Active research is underway to evaluate the role of HPV testing and HPV type-specific testing in primary cervical cancer screening. In some developed countries, HPV-based screening has already begun. By this approach, if the HPV test is positive, then a second test, which might include a Pap, will be performed. This approach has been shown to improve identifying those women most at risk, while minimizing procedures, treatment, and potentially harm in those women who can continue to be screened at recommended intervals.

One of the most significant advances in the fight against cervical cancer is the development of HPV vaccines. HPV vaccines are now routinely recommended for all 11 and 12 year old girls. One of the vaccines is also routinely recommended for 11 and 12 year old boys. These vaccines can be given as young as age 9 and up to age 26. Early vaccination with regular screening, which includes a Pap test and HPV test when recommended according to standard guidelines, is now the most effective way to prevent cervical cancer.

*Incidence:* It is estimated that there will be about 12,340 new cases of invasive cervical cancer diagnosed and approximately 4,030 deaths in the United States during 2013.<sup>2</sup>

## Advances in Cervical Cancer

A continuing challenge in the treatment of cervical cancer is finding effective therapy for women whose cancer recurs after being treated initially with surgery, or the combination of radiation and chemotherapy. In 2009, the GOG reported the results of a clinical trial that showed a biologic agent called bevacizumab, that blocks new blood vessel growth in cancer, was effective in shrinking tumors in some women with recurrent cervical cancer. Based on the encouraging results of that trial, the GOG recently completed GOG protocol 240, a prospective randomized trial designed to study the effect of combining bevacizumab with paclitaxel/cisplatin vs. topotecan/paclitaxel chemotherapy on survival in women with recurrent cervical cancer. Results of this trial, presented as one of the lead presentations at ASCO in 2013, showed nearly a 30% improvement in survival when compared non-bevacizumab containing regimens. This led to an NCI alert on the results of this trial. The survival advantage identified in this trial is the largest significant survival improvement in recurrent cervical cancer patients in more than two decades.

<sup>2</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

Another active area of research and advances in cervical cancer remains in prevention, including the continued development and implementation of both the current preventative HPV vaccines as well as therapeutic targeting vaccines, and updates in screening and management. Increasing knowledge of ways to prevent HPV infection and increase access to care are key to continuing these advances. Critical to the rapid progress made in recent years in cervical cancer prevention has been the detailed understanding that HPV is the cause of nearly every cervical cancer and precancer.

More than 40 types of HPV have been identified in vaginal, vulvar and cervical diseases. Of these, approximately 13 are known to be cancer-causing types. Two types, HPV 16 and 18, are the most common HPV types associated with cervical cancer. HPV 16 causes nearly 60% of all cervical cancers and HPV 18 cause an additional 10 to 20%. HPV types 16 and 18 are the most important HPV types to include in a vaccine designed to prevent the development of cervical cancer. Both currently available HPV vaccines protect against infection with HPV types 16 and 18. There is an ongoing study of a vaccine that will protect against 9 different HPV types. Preliminary data from this study presented this year are very encouraging for a more global protection against the 9 most common types of HPV that cause about 90% of cervical cancer in women.

The results of several large clinical trials demonstrate the effectiveness of vaccines to prevent HPV infection and HPV related disease. When widespread vaccination has been achieved, cervical cancer should be reduced by more than 70%. These high vaccination rates have already been achieved in some developed countries, but the rates are still not very high in the United States. Recent reports of vaccine registries shows that while vaccine use in the United States is increasing, only a small number of young girls and boys have received all 3 doses of vaccines. The barriers remain access to care, patient and provider education, and attitudes toward the HPV vaccine. The HPV vaccine is available through almost all public health facilities and government sponsored insurance programs. Essentially all private insurers will provide coverage for the cost of HPV vaccines for those in the recommended age range. Educational efforts, including efforts by the Foundation for Women's Cancers, are ongoing. Of note, all professional stakeholder organizations recommend routine use of HPV vaccines in young women. Because HPV vaccination is so effective in preventing cervical pre-cancer and cancer, especially if given to girls before they become sexually active, several medical organizations, including the Advisory Committee on Immunization Practice, the American College of Obstetricians and Gynecologists and the Society of Gynecologic Oncologists, recommend routine vaccination of girls ages 11 and 12 years (ideally before first intercourse), and young women ages 13–26. Also, vaccination in boys is recommended as well.

Clinical trials are currently ongoing to study the role of HPV vaccines in treating women already infected with HPV and women who have cervical cancer. These vaccines work differently and are more complex than the HPV vaccines that are routinely recommended for prevention. These therapeutic vaccines in development work by boosting a woman's immune response to recognized HPV. Since cervical cancer is far from being eradicated, clinical trials of vaccines that treat as well as prevent cervical cancer are important.

Several recent clinical trials investigating HPV DNA testing for cervical cancer screening will play a role in determining future recommendations for Pap testing and cervical cancer screening programs. The FDA has approved many new HPV tests for use in cervical cancer screening. These new tests not only detect any HPV, but also specifically detect HPV 16 and 18. This gives clinicians another important tool to identify women who are at most risk for developing cervical cancer when used according to the recently updated guidelines for management and triage of Pap test results.

There have been recent changes to the terminology as to how cervical biopsies, as well as biopsies of other lower genital tract precancerous lesions such as vulva and anus, are read. This standardized terminology assists pathologists and clinicians in knowing which biopsies might be precancerous. Also, there has been an increase in the amount of sensitive testing that pathologists might use to assist them in determining which biopsies will need more treatment. The new terminology also takes these new sensitive tests into account.

Progress continues to be made in developing better treatments for women with invasive cervical cancer. Fertility-sparing surgery called trachelectomy (removing the cervix and cancer but keeping the uterus to allow a woman to carry a pregnancy) continues to be an option for select women with early-stage cervical cancer. Traditionally performed through a vaginal incision, the procedure is now being done through abdominal incisions, and by laparoscopic (minimally invasive) and robotic-assisted surgical approaches. These advances are giving more young women, when cervical cancer is often diagnosed, access to surgical management that can allow them to preserve their fertility at the most prime of their reproductive life.

For women with advanced-stage cervical cancers, treatment with a combination of radiation therapy and chemotherapy remains the standard of care. The National Cancer Institute issued a clinical alert in 1999 to emphasize the importance of combination therapy for the treatment of advanced cervical cancer. A long term follow up of women who participated in the clinical trials that tested combination therapy confirms that women treated with radiation and chemotherapy continue to have a higher survival rate than women treated with radiation alone. Further, studies suggest that continued additional chemotherapy after radiation may improve survival even further. New studies have also identified new, targeted chemotherapy drugs that improve survival with potentially fewer harmful side effects than the drugs that have been traditionally used.

## Clinical Trials

For women with early-stage cervical cancer who are treated with radical hysterectomy, the Gynecologic Oncology Group (GOG) recently opened two prospective randomized clinical trials: 1) GOG-0263 to evaluate the role of combined radiation and chemotherapy vs. radiation treatment alone for women considered at intermediate risk for recurrence; and 2) GOG-0724 to evaluate the role of continuing chemotherapy alone after combined chemoradiation treatment in women considered at high risk for recurrence. It is hoped that the results of these studies will provide further guidance to physicians and patients as to which women with early-stage cervical cancer need treatment after surgery.

Recent advances in the ability to detect cervical cancer when it has spread outside of the pelvis include new data demonstrating the accuracy of PET/CT scans to find disease that has spread beyond the cervix, especially cancer located in lymph nodes outside the pelvis. The GOG opened GOG-0233, a study that evaluates the utility of preoperative FDG-PET/CT (a specific type of PET/CT scan) and special MRI scans to detect lymph node spread of cancer in women with advanced-stage disease who will undergo surgery for accurate staging. Improved imaging of cervical cancer allows more accurate and targeted planning of the boundaries for radiation treatment, which minimizes effects of radiation on normal tissues.

# Ovarian Cancer: Epithelial

## State of Epithelial Ovarian Cancer

*Ovarian cancer is the ninth most common cancer among women in the United States, and is generally grouped with primary peritoneal and fallopian tube cancers. About 85 to 90% of ovarian cancers are classified as epithelial ovarian cancers.*

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**Symptoms:** Bleeding, pelvic or abdominal pain, difficulty eating or feeling full early after meals, and/or urinary symptoms (urgency of frequency).

Women with ovarian cancer report that symptoms are persistent and represent a change from normal for their bodies. The frequency and/or number of such symptoms are key factors in the diagnosis of ovarian cancer. Several studies show that even early-stage ovarian cancer can produce these symptoms.

Women who have these symptoms almost daily for more than a few weeks should see their doctor, preferably a gynecologist. Prompt medical evaluation may lead to diagnosis of disease at its earliest, most treatable stage. Early-stage disease is associated with an improved prognosis however, whether early stage is part of a progression of disease from Stage I to IV has yet to be determined.

Several other symptoms have been commonly reported by women with ovarian cancer. These symptoms include fatigue, indigestion, back pain, pain with intercourse, constipation and menstrual irregularities. However, these other symptoms are not as useful in identifying ovarian cancer because they are also found in equal frequency in women in the general population who do not have ovarian cancer.

**Risk Factors:** The risk of epithelial ovarian cancer increases with age, especially around the time of menopause. A family history of epithelial ovarian cancer is one of the most important risk factors. Infertility and not bearing children are also risk factors for developing ovarian cancer, while pregnancy and the use of birth control pills decrease the risk. A personal history of premenopausal breast cancer or a family history of epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer or premenopausal breast cancer are important risk factors.

**Screening/Prevention:** Currently, there is no widely accepted or effective screening test for epithelial ovarian cancer. High-risk women may be candidates for screening using transvaginal ultrasound and CA 125 blood tests on an annual or biannual schedule, though the benefits of such screening is unproven. For most women, ultrasound and CA 125 screening is not recommended because false positive results can lead to unnecessary surgery.

**Incidence:** Ovarian cancer ranks fifth in cancer deaths among women and causes more deaths than any other reproductive cancer. It is estimated there will be about 22,300 new cases diagnosed and approximately 14,100 deaths from ovarian cancer in the United States during 2013.<sup>3</sup> However, the death rates from ovarian cancer declined by 2% per year from 2005 to 2009.

<sup>3</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

## Advances in Ovarian Cancer

### *Etiology and Biology*

Remarkable advances in the understanding of the biology of ovarian cancer have been made over the last few years. Appreciation for these concepts has provided a more rational approach to prevention, screening and treatment of ovarian cancer, and continues to be the foundation for future discoveries.

Recent evidence suggests that ovarian cancer should be classified into 2 distinct categories: Type I ovarian cancers are typically low-grade cancers that include serous, endometrioid, clear cell and transitional carcinomas. They may arise from tumors of low-malignant potential ovarian tumors thus supporting a genetic continuum of tumor progression. They are usually genetically stable, slow growing in nature and thus confined to the ovary, and more likely to be diagnosed in early stage. They are less responsive to chemotherapy due to their slow growth pattern. They lack p53 and BRCA mutations, but are known to harbor KRAS, BRAF, ERBB2, PTEN and PIK3CA mutations. The clinical significance of identifying these mutations is that they can be used as therapeutic targets. For example, ongoing trials evaluating the use of MEK inhibitors in low-grade serous ovarian cancer appear promising.

Type II ovarian cancers include high-grade serous carcinomas and undifferentiated carcinomas. They are thought to arise from the fallopian tube and precursor lesions have been identified prior to the development of invasive carcinoma. The pathway to tubal ovarian cancer is thought to include secretory cell outgrowths (SCOUTS) that have low expression of PTEN, Ki67, PAX2 and typically no p53 expression. Serous tubal intraepithelial lesions (STILs) subsequently follow and are characterized by p53 overexpression (p53 signature) that lead to serous tubal intraepithelial neoplasia or STIC's prior to the development of invasive ovarian cancer. Type II ovarian cancers usually present in advanced stages and are more responsive to chemotherapy than their low-grade counterparts. However, they do account for more ovarian cancer deaths overall. P53 and BRCA mutations are common in this group of tumors.

### *Prevention*

It is with the understanding that high-grade serous ovarian cancers arise from the fallopian tubes that researchers have begun to study the impact of recommending removal of the tubes (salpingectomies) in all women undergoing tubal ligations or hysterectomies. It is thought that salpingectomy, in this context, could decrease the number of fallopian tube/ovarian cancer cases.

A large US trial is currently underway to evaluate the impact of salpingectomies in women at high risk of developing breast and/or ovarian cancer. This trial targets women who have completed child bearing, are younger than the current recommended age for risk reducing salpingo-oophorectomy (RRSO) and would like to avoid surgical menopause until RRSO is required.

A presentation at the 2013 annual meeting of the American Association for Cancer Research (AACR) showed that omega-3/6 fatty acids (found in high concentrations in fish oils and flax seeds) reduced the risk of ovarian cancer. This clinical observation is of interest as animal and laboratory studies seem to be supportive of these findings.

The possible role of the sugar lowering medication metformin in the treatment and/or prevention of cancer was also the subject of significant interest at the 2013 AACR meeting. A Phase III clinical trial comparing metformin to a placebo in combination with chemotherapy for the treatment of ovarian cancer is currently being evaluated.

## Screening

Symptom-based ovarian cancer screening using a symptom index has been shown to be feasible and acceptable at primary care visits and is undergoing further study in larger clinical trials. The idea is to screen patients and, if the symptoms index is positive, patients are referred for CA 125 and transvaginal ultrasound testing.

The Prostate, Lung, Colorectal and Ovarian Cancer screening trial (PLCO) looking at a CA 125 cutoff and transvaginal ultrasound as a screening method concluded that this did not improve ovarian cancer mortality and that, in fact, it led to unnecessary surgeries and other serious complications.

The Risk of Ovarian Cancer Algorithm (ROCA) trial evaluated a two-stage ovarian cancer screening strategy that incorporated annual CA 125 levels and referral for transvaginal ultrasound for high-risk CA 125 changes. Instead of using a CA 125 cut off for intervention (as was used in the PLCO trial), the ROCA investigators looked at the rate of change of CA 125 over time to trigger an intervention. This was a single-arm prospective trial in post-menopausal women. Based on the ROCA, women were triaged to continue follow up with an annual CA 125 (low risk), repeat CA 125 in 3 months (intermediate risk) or a referral for a transvaginal ultrasound (high risk). Ten women underwent surgery based on transvaginal ultrasound findings. Four early-stage invasive ovarian cancers, 2 borderline tumors, 1 endometrial tumor and 3 benign ovarian tumors were detected. While overall survival was not an endpoint for the study, ROCA followed by transvaginal ultrasound was shown to be more accurate in predicting ovarian cancer. This is very encouraging, but it remains to be seen if this stepwise screening strategy will offer a survival benefit to patients.

The United Kingdom Collaborative Trial of Ovarian Cancer Screening trial (UKCTOCS) using the ROCA is a prospective multi-institutional randomized trial that also employs CA 125 level changes and transvaginal ultrasound as a stepwise screening strategy. Results of this screening trial are eagerly awaited in 2014 as a smaller single-arm trial using the same approach seems promising and has shown a greater than expected ability to detect ovarian cancer. Currently, no screening method has been shown to decrease ovarian cancer mortality and screening for ovarian cancer should only be performed in well-designed clinical trials.

## Molecular Biology

The Cancer Genome Atlas (TCGA) Research Network has profiled and analyzed a large number of tumors, including ovarian, to detect molecular abnormalities that may be used as targets. With the emergence of new agents that target specific pathways, researchers can compare genetic profiles between different tumor types to detect similarities that may be used as targets using the same agent across cancer types.

## Treatment

### Surgery

The CHORUS (**chemotherapy or upfront surgery**) trial was presented at the 2013 American Society of Clinical Oncology (ASCO) meeting. It was designed to assess primary ovarian cancer surgery (cytoreductive surgery) followed by chemotherapy versus chemotherapy first (neoadjuvant) followed by interval ovarian cancer surgery. CHORUS was a multi-institutional, randomized trial that enrolled 552 Stage III and IV ovarian cancer patients. Both groups were similar in demographic and disease characteristics. Results showed that more patients (40%) in the interval cytoreductive surgery group were optimally cytoreduced in comparison to the primary surgery group (16%). Hospital stays were shorter and fewer deaths were noted in the

neoadjuvant chemotherapy group as well. More importantly, no significant difference was noted in the median progression free survival (PFS) between the two groups. Overall survival rates are still being analyzed and are eagerly awaited. These results seem to support the previous European Organization for Research and Treatment of Cancer (EORTC) 55971 trial. The EORTC trial was the first randomized controlled trial to show that neoadjuvant chemotherapy with interval cytoreductive surgery is not less effective than primary cytoreductive surgery with adjuvant chemotherapy. Both of these trials support the use of neoadjuvant chemotherapy followed by interval surgery as a potential approach to patients with poor health status, advanced age and/or increased upper abdominal tumor burden who may not be optimal surgical candidates at the time of diagnosis.

## **Chemotherapy**

### **Clinical Trials Phase III**

**Dose dense chemotherapy:** The Japanese Gynecologic Oncology Group (JGOG) recently reported on its long-term data of dose dense chemotherapy (carboplatin day 1 AUC-6 and paclitaxel 80 mg day 1, 8, 15 every 21 days). In this trial, dose dense chemotherapy provided a significant time to relapse (PFS) and overall survival (OS) benefit (dose dense: OS-100.5 months; PFS-28.2 months) compared to standard 3 week chemotherapy (OS-62.2 months; PFS-17.5 months). These results are comparable to the intraperitoneal chemotherapy trials. However, the potential impact of drug metabolism among racial groups influencing survival has been suggested as a possible cause of the improved survival in the Asian population. Dose dense chemotherapy trials in Europe and North America are currently awaiting results to confirm the Japanese data (GOG-262 and ICON 8.) The MITO 7 study has been completed and does not support dose dense chemotherapy. However, the study was not considered as dose dense as the paclitaxel dose in that it was only 60 mg/m<sup>2</sup> per weekly treatment compared to the 80 mg/m<sup>2</sup> that was used in the JGOG trial.

**Intraperitoneal (IP) chemotherapy:** Long-term results from GOG-114 and GOG-172 evaluating IP chemotherapy in women with optimally cytoreduced advanced ovarian cancer compared to standard every 3 week intravenously (IV) chemotherapy showed a survival benefit of IP over IV therapy that extended beyond 10 years (110 vs 43.2 months.) In addition, those who completed more cycles of IP therapy had a higher 5 year overall survival rate.

**Vascular targets:** The AGO-OVAR 16 trial was presented at ASCO in 2013. This is a randomized double-blinded Phase III maintenance trial of pazopanib versus placebo in women who have not progressed after standard first-line chemotherapy for advanced ovarian, fallopian tube or primary peritoneal cancer. Pazopanib is an oral multi-kinase inhibitor of VEGFR-1, -2, -3, PDGFR-alpha and beta and c-Kit. Patients with no evidence of progression after surgery and chemotherapy were randomized to oral pazopanib (800 mg daily) or placebo for up to 24 months. More than 90% of patients were Stage III or IV at diagnosis with 58% of patients having no residual disease at completion of primary cytoreductive surgery. There was a statistically significant benefit in median progression-free survival on pazopanib compared to the placebo group (median PFS: 17.9 vs 12.3 months.) However, overall survival in preliminary analysis demonstrated no difference between the two groups.

The TRINOVA-1 study has completed patient accrual to evaluate the response of trebananib (formerly AMG 386) combined with weekly paclitaxel in patients with recurrent, partially platinum sensitive or platinum-resistant epithelial ovarian cancer. This is a Phase III multi-institutional randomized controlled trial comparing trebananib and paclitaxel to a placebo group. Trebananib is an anti-angiogenesis (prevents blood vessel formation) agent that is a selective angiotensin

1/2 neutralizing antibody. It inhibits angiogenesis by preventing interaction between angiopoietins and Tie2 receptors. Preliminary results demonstrated an improved progression free survival of 7.2 month in the trebananib group compared to 5.4 months in the placebo group. The overall survival data analysis is not complete, but the interim analysis indicates a non-significant trend that favors the trebananib option (19 vs 17.3 months.)

An update of the AURELIA trial at the 2013 ASCO meeting reported on health related quality of life (HR-QOL) measures. The AURELIA trial, initially presented at the 2012 ASCO meeting, was a Phase III randomized trial evaluating the use of bevacizumab with chemotherapy compared to chemotherapy alone for platinum resistant ovarian cancer. Patients receiving bevacizumab with chemotherapy were found to have an improved progression-free survival compared to chemotherapy alone (6.7 vs 3.4 months;  $p < 0.001$ .) The updated trial demonstrated improved quality of life in platinum-resistant ovarian cancer patients who were treated with bevacizumab compared to those who were not. These quality of life measures are becoming extremely important end points for trials and are beneficial to patient care.

## Clinical Trials Phase II

Hyperthermic IP chemotherapy (HIPEC) is a new form of heated IP treatment given in the operating room immediately following optimal cytoreductive surgery. A recent study showed progression-free survival of 17.3 months and overall survival of 53 months. Further study of HIPEC is underway in a randomized Phase II trial.

The POLKA study, using volasertib, is a Phase II trial targeting Polo-kinase I, a key regulator of mitosis, in ovarian cancer patients who are resistant to platinum chemotherapy. Patients that received 300 mg Volasertib IV every 3 weeks demonstrated improved progression-free survival when compared to single agent chemotherapies.

Olaparib is an oral PARP inhibitor that demonstrated a 3.6 month improvement in progression-free survival in a Phase II randomized trial of olaparib maintenance therapy versus placebo in platinum sensitive recurrent ovarian cancer. The published study in *The New England Journal of Medicine* showed no overall survival benefit in the olaparib arm. Based on the lack of this benefit, the company considered not pursuing further trials with olaparib in ovarian cancer. However, a pre-planned subgroup analysis of the data by BRCA mutation status was presented at the 2013 ASCO meeting. A progression-free survival benefit of 6.9 months for olaparib compared to placebo was demonstrated. In addition, when including all BRCA mutations, there was a trend towards an overall survival benefit in the olaparib group (34.9 vs 31.9 months.) This data renewed interest for the use of olaparib in ovarian cancer, and the SOLO 1 and SOLO 2 studies (**Study of Olaparib in Ovarian cancer**), both randomized, double blinded, placebo controlled trials were initiated.

These are exciting times as targeted therapies have entered the clinical research arena and are becoming more available for patients. Vascular targeting agents, tyrosine kinase inhibitors and PARP inhibitors are a select few of these classes of agents being investigated in ovarian cancer with promising results.

# Uterine Cancer: Endometrial Adenocarcinoma and Uterine Sarcomas

## State of Uterine Cancer

*The endometrium is the lining layer of the uterine cavity and most uterine cancers begin because of cancerous changes in this lining. In the most common type of uterine cancer, called endometrial adenocarcinoma, cells in the endometrial lining grow out of control, may invade the muscle of the uterus and sometimes spread outside of the uterus (ovaries, lymph nodes, abdominal cavity).*

*Uterine sarcomas represent a type of uterine cancer in which malignant cells form in the muscle of the uterus (leiomyosarcoma) or in the network of support cells in the uterine lining (endometrial stromal sarcomas and carcinosarcomas). Accounting for fewer than 5% of all uterine cancers, uterine sarcomas are much less common than endometrial cancer, but have a much more aggressive clinical behavior. These cancers can spread quickly to distant sites.*

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**Symptoms:** The most common warning sign for uterine cancer is abnormal vaginal bleeding, and recognition of this symptom often affords an opportunity for early diagnosis and treatment. In older women, any bleeding after menopause may be a symptom of uterine cancer. Younger women should note irregular or heavy vaginal bleeding because they may be symptoms of uterine cancer. Sarcomas can also produce pelvic pain or pressure. In addition, a rapidly growing fibroid during the post-menopausal period should raise the suspicion of a leiomyosarcoma.

**Risk Factors:** Risk factors for endometrial cancer include: use of estrogen without progesterone; irregular menstrual cycles and infertility from polycystic ovarian disease (anovulation); obesity; diabetes; hypertension; history of breast cancer or colon cancer; tamoxifen use; and late menopause (after age 52). Women who have not been pregnant also have a higher risk for endometrial cancer. A strong family history of endometrial or colon cancer may signal an inherited risk for getting endometrial cancer. Sarcomas are twice as common in black women as in women of other racial and ethnic groups, and having pelvic radiation therapy increases the risk of developing this rare type of uterine cancer.

Risk factors for death from endometrial cancer are different than the risk factors for developing the cancer for the most curable patients. Women at the highest risk of death have a Type II cancer or grade 3 endometrioid cell types. Type II cancers include carcinosarcoma, serous and clear cell carcinomas. Women who are thin, who currently smoke, and/or have a history of breast cancer or tamoxifen use are more likely to experience Type II endometrial cancer.

**Screening/Prevention:** Women with post-menopausal bleeding or heavy, prolonged or unexpected bleeding during the menstruating years should have a biopsy of the endometrium to check for uterine cancer. For women without symptoms, there are no screening tests that are recommended on a routine basis. The Pap test is designed to find cervical cancers and its precursors, not endometrial cancer. Women can decrease their risk of endometrial cancer by exercising regularly, keeping blood sugar and blood pressure under control, and maintaining a healthy weight. Taking progesterone, either alone, or in combination with estrogen, as is found in birth control pills, lowers

the risk of endometrial cancer. Progestin can prevent cancer from developing in women who have irregular menstrual cycles and infertility. Women who are obese may benefit from a progestin containing IUD which directly distributes levonorgestyl (a progestin) into the endometrium and needs replacement only every 5 years. There are no known methods to prevent uterine sarcoma.

*Incidence:* Cancer of the uterus is the most common reproductive cancer. It is estimated that there will be about 49,560 new cases diagnosed in the United States during 2013, and more than 95% of these will be endometrial adenocarcinomas, with approximately 1,600 cases of uterine sarcoma. Approximately 8,190 women will die from uterine cancer in the United States during 2013.<sup>4</sup>

## Advances in Uterine Cancer

### Surgery

Surgical treatment has traditionally been laparotomy for a hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy. The advent of minimally invasive surgery has challenged surgeons to reduce the toxicity of surgical therapy and allow for careful evaluation of best practices with randomized controlled trials. Laparoscopic hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy have been proven superior in reducing hospital stays, complications and improving quality of life.

International clinical trials raise questions about the need to perform lymphadenectomy. Predicting which women benefit from knowing the results of pathologic evaluation of lymph nodes is complicated by the errors in the prediction models. The small size of tumor (less than 2 cm), low grade endometrioid cell type and little to no myometrial spread predicts a low risk of lymph node metastasis. Frozen sections have a 15–20% error when compared to the final diagnosis. Avoiding adjuvant radiation is the greatest benefit of having negative lymph nodes verified through histopathologic results. High-grade endometrioid as well as serous, clear cell and carcinosarcoma histologic cell types, as well as women with large tumors (>2 cm) or with deep myometrial invasion, and age over 69 years, continue to need thorough surgical staging with lymphadenectomy and peritoneal biopsies to help direct adjuvant therapy.

Alternative surgical strategies continue to be implemented, including laparoscopic, robotic and vaginal surgery, and there are studies of sentinel lymph node evaluation in the appropriate candidates. There are new studies of a molecular analysis of the Pap test and/or an endometrial biopsy to determine if a cancer is present or if metastasis is likely due to an aggressive molecular profile. This work is in an exciting preliminary stage.

### Radiation Therapy

The use of external (teletherapy) radiation continues to decline due to the results of important clinical trials including PORTEC 2 where whole pelvic radiation was compared to vaginal brachytherapy. The results of this study favored brachytherapy both for improved toxicity and survival. This finding has resulted in the use of vaginal brachytherapy alone for most intermediate-risk endometrial cancer patients. Higher-risk patients are being evaluated by GOG protocols 249 and 258 to determine if chemotherapy can replace radiation and improve survival by reducing distant recurrences while at the same time preventing local recurrences.

<sup>4</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

## Adjuvant Treatment

The outcome of GOG-209 non-inferiority randomized clinical trial was presented at the Society of Gynecologic Oncology in March 2012, and determined that the better tolerated carboplatin and paclitaxel regimen was equally effective at treating metastatic endometrial cancer, and could be substituted for TAP (taxol, adriamycin, cisplatin), which was more likely to cause neuropathy.

## Clinical Trials

The use of targeted therapy is under active investigation in uterine cancers. The targeting of angiogenesis pathways has been successful in Phase II trials with bevacizumab showing 36% of patients to be progression free at 6 months, which resulted in this agent being added to GOG-86P, a randomized Phase II trial which should be under analysis in 2014.

Another exciting pathway being studied in GOG-86P is the PI3 kinase pathway. MTOR inhibitors are being investigated to take advantage of the molecular changes in endometrial cancer with response rates of 26–44%. Temsirolimus and everolimus are FDA approved mTOR inhibitors for other indications and are the most studied.

Metformin is being studied in GOG-268B in a placebo controlled trial in combination with carboplatin and paclitaxel for women with measurable advanced endometrial cancer or recurrent disease. This study should be open for enrollment soon.

Carcinosarcomas are being studied using ifosfamide and paclitaxel versus carboplatin and paclitaxel in GOG-261. Uterine leiomyosarcoma is currently treated with gemcitabine and taxotere, and GOG-250 did not find a benefit with adding bevacizumab. The current trial GOG-277 is evaluating chemotherapy versus observation in women after hysterectomy with tumor only in the uterus.

## Survivorship after a Diagnosis of Endometrial Cancer

It is well known that more women with the diagnosis of endometrial cancer actually die of their other major health problems (36% cardiovascular deaths, 20% other cancers, 25% other causes) rather than their endometrial cancer (19% cause of death). Women are surprised to learn that obesity has caused their cancers, and need to take the cancer diagnosis as an opportunity to change their lifestyle. Gynecologic oncologists have taken an active role in referring women to weight reduction programs, including bariatric surgery, nutritionists, exercise programs and in turn are emphasizing diabetes and cardiovascular risk-reduction strategies.

The GOG is committed to a prospective trial to demonstrate a survival benefit in using this cancer diagnosis into an opportunity to encourage and incentivize women to improve their behavioral health risks with healthy diet and exercise choices. Obesity is an epidemic in our country and endometrial cancer is a downstream indicator of this problem in our society. The Foundation for Women's Cancer is exploring funding for additional programs to aid in addressing this barrier to good gynecologic health.

# Vaginal Cancer

## State of Vaginal Cancer

*Vaginal cancer originates in the vagina, usually in the squamous epithelium (lining). It is typically diagnosed in older women and radiation is the most common treatment.*

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**Symptoms:** Vaginal cancer, especially at precancerous and early stages, may not cause any symptoms. Common symptoms of more advanced stages include bleeding, pain, or problems with urination or bowel movements.

**Risk Factors:** Risk factors for vaginal cancer include HPV (Human Papillomavirus) infection, smoking, age (60 years and older), and prior treatment for cervical or vulvar cancer. The daughters of women who took DES (a hormone medication used many years ago to prevent miscarriage) while pregnant are at increased risk for both vaginal and cervical cancer.

**Screening/Prevention:** Many precancerous conditions and early vaginal cancers can be detected through routine pelvic exams and Pap tests. Because many vaginal cancers are associated with HPV types 16 and 18, vaginal cancer can be prevented by the vaccinations advocated for the prevention of cervical cancer. There is now both a quadrivalent vaccine and a bivalent vaccine approved by the FDA for the purpose preventing precancerous vaginal changes induced by HPV.

**Incidence:** Primary vaginal cancer is one of the rarest gynecologic cancers. It is estimated that there will be about 2,890 new cases diagnosed and 840 deaths from vaginal cancer in the United States during 2013.<sup>5</sup> Vaginal cancer accounts for about 3% of reproductive cancers.

## Advances and Vaginal Cancer

Because of its rarity, vaginal cancer is not amenable to comparing one form of treatment with another in a large clinical trial. Therefore, much of what is understood in vaginal cancer treatment is borrowed from clinical trials in other related cancers, such as vulvar and cervical cancer.

Although most women with vaginal carcinoma are past child-bearing years, many women with DES-associated vaginal cancers are young. Standard treatments for vaginal cancer can cause young women to lose the option of having children, but a recent report showed that fertility-sparing surgery is possible in carefully selected patients, even when the vaginal tumor extends to and requires removal of the cervix. Another advance in surgical therapy for vaginal cancer includes the adoption of a minimally invasive approach. Surgeons are demonstrating that laparoscopic techniques for surgical evaluation with lymph node biopsy may be utilized in select patients with localized disease for tumor excision, or to precisely define radiation treatment fields to permit protection of normal organs during radiation treatment.

Visualizing vaginal cancer with imaging tests can be difficult because of the other organs located near the vagina in a woman's body, including the uterus, bladder and rectum. One recent study evaluated magnetic resonance imaging (MRI) of vaginal cancer and showed that MRI correctly identified over 95% of the tumors, and correctly demonstrated disease that involved tissues beyond the vagina in 88% of patients. MRI staging correlated very well with survival. Thus, for patients with advanced disease, staging may allow a treatment plan to be enacted without need for surgery.

<sup>5</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

Positron emission tomography (PET) in combination with MRI (or CT scans) may be an even better method to image vaginal cancer. A recent study evaluated PET prior to a planned radical surgery to remove recurrent cervical or vaginal cancer. PET was found to have a sensitivity of 100% and a specificity of 73% in detecting sites of cancer beyond the pelvis. These findings are particularly important for women with vaginal cancer because PET imaging may, in a non-invasive fashion, identify otherwise non-detectable metastasis, sparing some patients unnecessary surgical procedures and allowing others to receive radiation treatment to a smaller area.

Most patients with vaginal cancer are treated with radiation therapy. Radiation therapy alone is an effective treatment for early vaginal cancer; however, results with radiation therapy for more advanced vaginal cancers are not uniformly good and better treatments are needed. For some similar cervical and vulvar cancers, chemotherapy prescribed concurrently with the radiation therapy has improved the response rates and overall survival. A recent study showed that by giving chemotherapy at the same time as radiation to women with vaginal cancer also improved the response and survival with an acceptable level of side effects. Side effects of radiation treatment for vaginal cancer include shortening and closure of the vaginal tube, and remain a significant issue for these patients.

It is hoped that the integration of PET/CT with other new imaging methods may also improve the accuracy of surgery or radiation treatment planning, resulting in improved survival and reduced treatment-related side effects for women with vaginal cancer. Intensity-Modulated Radiation Therapy (IMRT) is a newer advanced type of high-precision radiation that is the next generation of 3-Dimensional Conformal Radiotherapy. IMRT's use in vaginal cancer has improved the ability to modify the radiation and conform to tumor shapes while avoiding treatment of vulnerable structures, such as the bladder and bowel.

The addition of simultaneous chemotherapy can also improve the effectiveness of radiation therapy for this disease. Since HPV is a risk factor for many vaginal cancers, it is hoped that the widespread use of HPV vaccines will reduce the incidence of this gynecologic cancer in the future.

# Vulvar Cancer

## State of Vulvar Cancer

*Vulvar cancer is caused by the growth and spread of abnormal cells within the skin of the labia and perineum.*

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**Symptoms:** Itching, burning, bleeding, pain, or a new lump or ulcer in the genital area are common symptoms.

**Risk Factors:** Infection with Human Papillomavirus (HPV) is a common cause of vulvar cancer in young women. Vulvar cancer in older women is associated with chronic vulvar irritation from any source.

**Screening/Prevention:** Protection from infection with HPV (Human Papillomavirus), including an HPV vaccination, reduce the risk of vulvar cancer. A quadravalent HPV vaccine and a bivalent vaccine have been approved by the FDA for this purpose. Examination of the vulva for changes by a woman at home or by her gynecologist during a routine pelvic exam may lead to the detection of preinvasive disease or early vulvar cancer. Suspicious or unexplained changes on the vulva should be biopsied.

**Incidence:** Vulvar cancer is uncommon. It is estimated that there will be about 4,700 new cases diagnosed and approximately 990 deaths from vulvar cancer in the United States during 2013.<sup>6</sup> Vulvar cancer is usually diagnosed in the early stages and is most often cured with surgical treatment.

## Advances in Vulvar Cancer

Although vulvar cancer can often be cured with surgery, the side effects of the procedures traditionally used to treat this rare cancer have a major impact on quality of life. Advances in surgical techniques and strategy have improved the lives of women with vulvar cancer by preserving sexual function, reducing surgical wound complications and reducing the condition of chronic swelling of the legs, called lymphedema. These advances have been achieved by performing less radical surgeries that preserve more of the normal tissue of the genital area.

Results from a recent study showed that cure rates for women with early-stage vulvar cancer treated with less radical surgery today are as good as the survival seen in women treated with the more extensive procedures that were standard 20 years ago. In spite of these improvements in surgery for vulvar cancer, problems remain, including accurate identification of patients whose cancer has spread to the groin lymph nodes and the lymphedema that results from inguinal femoral lymphadenectomy. Lifelong lymphedema, or chronic swelling in the legs, is especially frustrating for patients and caregivers because there are few effective treatments, and it is difficult to study because it is underreported. The Gynecologic Oncology Group (GOG) recently reported a randomized control trial in 150 vulvar cancer patients investigating whether the use of a sealant sprayed on the area of lymph node dissection at the time of surgery could reduce this common complication. Although the study found that using the sealant did not prevent lymphedema, the completion of this trial does demonstrate the feasibility of studying ways to decrease the rate of this disabling complication. The study identified that women undergoing treatment for vulvar cancer

<sup>6</sup> American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta: American Cancer Society; 2013.

are at extremely high risk of developing lymphedema. The GOG is planning future trials to identify more effective methods to diagnose and prevent lymphedema in women having surgery for vulvar cancer.

One of the most significant recent advances is sentinel lymph node biopsy, which can improve detection of node metastases and can reduce the risk of lymphedema in women having surgery for vulvar cancer. The sentinel lymph node is the node that is most directly connected to the main tumor through the lymph channels, and it is the most common site to which cancer cells spread. The sentinel lymph node can be found with a technique called lymphatic mapping. This strategy has been used successfully in patients with breast cancer and melanoma to improve the detection of metastatic disease, and avoid extensive lymph node resection and the associated lymphedema in some patients.

At the 2009 American Society of Clinical Oncology (ASCO) meeting, the results from a much-anticipated GOG study designed to validate the use of sentinel lymph node biopsy in vulvar cancer were presented. Five hundred ten women with vulvar cancer were enrolled in the study. In each woman participating in the study, sentinel nodes, identified with both blue dye and radioactive dye, were removed and examined to look for tumor spread. During the same surgery, the rest of the lymph nodes in the groin area were removed and results compared with the findings in the sentinel lymph nodes. Sentinel nodes were successfully identified in more than 95% of patients, confirming that this technique is feasible and safe in women with vulvar cancer. This study confirmed the findings of a large Dutch study published in 2008 that followed 259 women with unifocal vulvar disease and negative sentinel lymph nodes for 3 years and concluded that sentinel lymph node biopsy is safe in many patients with early vulvar cancer (less than 4 cm). However, sentinel lymph node dissection alone is not advocated for larger lesions, multifocal lesions or women who have a positive sentinel node. These patients are best treated with a full lymph node dissection. Based on the encouraging results of the data to date, a woman with vulvar cancer should discuss with her gynecologic oncologist their experience with, and the risks of, a sentinel lymph node assessment given their personal clinical situation.

Further supporting the concept that less radical surgery is safe for vulvar cancer patients, GOG investigators performed a secondary analysis of a previous trial to determine whether groin recurrence was associated with the removal of fewer lymph nodes at the time of original surgery. Among 113 patients who underwent groin dissection, 9 had a recurrence in the groin, but there were no significant differences in node counts between patients who had recurrence in the groin and those who recurred outside the groin. Investigators concluded that variations within other risk factors may make node counting itself an unreliable measure of surgical quality or risk for recurrence.

In general, cancers are divided into categories or stages, with the assignment within a stage based on the risk for recurrence. For vulvar cancer, the final stage depends on the pathologic review of the surgical specimens from the vulva and the regional lymph nodes. In 2009, FIGO announced the first major revision in staging for vulvar cancer since 1988. In the revised system, Stage IA lesions do not require a regional lymph node evaluation because of the low risk of metastasis. Patients with Stage IB have tumors with deeper invasion (greater than 1 mm), however the regional lymph nodes are negative. These patients remain in the Stage I category as they have a low risk for recurrence. Stage II was reconfigured to include those patients with local extension to the urethra, anus or vagina, but still had negative lymph nodes. These patients have a lower risk of recurrence than the node positive Stage III patients with whom they were previously categorized. Stage III now includes those patients with lymph node metastases regardless of the size, location and extension of the primary vulvar tumor. The presence and extent of nodal involvement is the

single most important factor in determining the risk for recurrence in vulvar cancer patients. Stage III is now subdivided by the size of the metastatic foci, the number of nodes involved and the presence of extracapsular spread. The new staging system will hopefully identify those patients at greatest risk for recurrence who would clearly benefit from adjuvant treatment.

Another area of progress is the treatment of vulvar cancer by using a combination of therapies for more advanced-stage tumors. This strategy holds great promise for patients who have large tumors or disease that has spread to lymph nodes. Results from a recent analysis of 5 vulvar cancer trials in women with advanced-stage cancer showed that treating women with the combination of chemotherapy and radiation before surgery can shrink the size of the tumor and reduce the extent of surgical resection. This strategy helps preserve quality of life for patients who might have otherwise lost rectal, bladder or sexual function from radical surgery alone.

Another new technology being studied in the treatment of vulvar cancer is intensity modulated radiation therapy (IMRT). IMRT allows the radiation oncologist to vary the intensity of each beam of energy both in space and time, and provide a dose that more closely conforms to the contours of the tumor with less dose of radiation to normal tissues. A recent report of combining IMRT with chemotherapy for patients with locally advanced vulvar cancer before surgery showed good tumor response and lower toxic effects to normal tissues and is more commonly being utilized for these patients.

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