

# Gynecological cancer update

Every year millions of new diseases being reported worldwide and cancer seems to be tightening its grip globally. According to published report by World Health Organization in the year 2012 global burden rises to 14.1 million new cases and 8.2 million cancer deaths globally. Experts suggest that the incidence of the killer disease (cancer) is expected to rise 5-fold by 2025.<sup>[1]</sup> More than one-fourth of new cases of cancer are in females related to gynecological cancer which starts in a woman's reproductive organs such as; "cervical cancer (fourth most common cancer affecting women worldwide)," "ovary cancer (eight most common cancer in worldwide)," and "endometrial cancer (fifth most common malignancy among females worldwide)." Cancer registries have also reported that more than 80% of cancers in females occur in the age group of 35–64.

Each specific type of gynecologic cancer has a unique set of risk factors such as human papillomavirus (HPV) infections that increase the risk of getting several types of gynecologic cancers and other risk factors are smoking and using birth control pills for a long time.

Gynecological cancers treatment is frequently multimodal including coordination of surgical care with chemotherapy, radiotherapy, targeted therapy, immunotherapy, or hormonal therapy.

Cervical cancer begins in the cervix, the lower part of the uterus (or womb). Previously, surgery or radiation was treatment alone is employed for the initial stages but today new ways to prevent and treat cancer of the cervix are being researched. "Sentinel lymph node biopsy" can be used to target just the few lymph nodes most likely to contain cancer as compared to removing of many lymph nodes in surgery. Currently available "HPV vaccine" is intended to produce immunity to HPV types 16 and 18 and being developed to prevent infection with some of the other HPV types that also cause cancer. "Targeted therapy" like pazopanib is drugs that block the effect of certain growth factors on cancer cells and work differently from standard chemotherapy and showed lesser side effects. A published meta-analysis of six randomized clinical trial (1078 women) in Cochrane database of systematic reviews suggest that both overall survival (hazard ratio 0.77, confidence interval 0.62–0.96,  $P = 0.02$ ) and progression-free survival (hazard ratio 0.75,

confidence interval 0.61–0.93,  $P = 0.008$ ) were improved with neoadjuvant chemotherapy.<sup>[2]</sup>

Ovary cancer found in women aged over forty, and other risk factor is women tested positive for a genetic abnormality called a BRCA1 or BRCA2. Early detection or screening with CA-125 blood tests and transvaginal ultrasound are recommended to reduce mortality by ovarian cancer. Treatment research includes testing the value of currently available methods as well as developing new approaches to treatment. New chemotherapy (chemo) drugs and drug combinations are being tested. The drugs "trabectedin and belotecan" have shown a significant effect in some studies.<sup>[3]</sup> Today, "carboplatin" drug is preferred over cisplatin or platinum resistant patients in treating ovarian cancer. New approach is to give intraperitoneal (IP) chemo during surgery using heated drugs or heated IP chemotherapy are effective but is very toxic.<sup>[4]</sup> Few newer targeted therapies have been developed, i.e., bevacizumab, pazopanib, poly (ADP-ribose) polymerases (PARPs) inhibitor - olaparib drugs and vintafolide (EC145). PARP inhibitors inhibit PARP-1 help fight cancers caused by mutations in *BRCA1* and *BRCA2*. Vintafolide (EC145) is a newer drug that targets the folic acid receptor. This receptor is found on some ovarian cancers. Another newer approach is "immunotherapy" or tumor vaccines and monoclonal antibodies like "farletuzumab" and "catumaxomab" act direct against the folic acid receptor, which is on the surface of some ovarian cancer cells and binds to a protein that is in some cancer cells/immune system cells, respectively. Cediranib is an oral antiangiogenic vascular endothelial growth factor receptor 1–3 inhibitor that has shown antitumor activity in recurrent ovarian cancer.<sup>[5]</sup>

Endometrial cancer is predominantly a disease of postmenopausal women and most common in women over 50 years of age. Over 70% of women with endometrial cancer present with International Federation of Gynecology and Obstetrics Stage I disease, which is associated with a 5-year survival rate of >90%. Only a small proportion of women (13%) present with advanced disease, with 5-year survival rates of around 60% and 30% for Stage III and IV, respectively, which decrease with advancing age.<sup>[6]</sup> The standard surgical treatment of women with endometrial cancer includes the removal of the uterus, both fallopian tubes and ovaries (total hysterectomy

and bilateral salpingo-oophorectomy), with or without lymphadenectomy. After surgery, a woman may be offered radiation therapy, or platinum-based chemotherapy, or both. Treatment of advanced disease (Stage III and IV) is individualized and usually involves a combination of cytoreductive surgery, radiotherapy, or chemotherapy. According to a recent Cochrane review of neoadjuvant chemotherapy for advanced, recurrent or metastatic disease, the use of “more chemotherapy” compared with “less chemotherapy” is associated with longer survival.<sup>[2,7]</sup> Molecular pathology of endometrial cancer suggests that tumor suppressor gene, i.e., retinoblastoma gene, TP53 gene, and PTEN, is often abnormal in endometrial cancers. Newer approach to treat endometrial cancer is targeted therapies such as “temsirolimus, bevacizumab, brivanib, and gefitinib.”<sup>[8,9]</sup> Experts suggest that hormone therapy of endometrial cancer has often involved progestins, but drugs that affect estrogen may also be helpful, and a study on “fulvestrant” drug shows that it blocks estrogen receptors and effective in endometrial cancer.

**RUPINDER SEKHON, NEERJA BHATLA<sup>1</sup>**

Rajiv Gandhi Cancer Institute and Research Centre,

<sup>1</sup>Department of Obstetrics and Gynaecology, AIIMS, New Delhi, India

**Address for correspondence:** Dr. Rupinder Sekhon,  
Rajiv Gandhi Cancer Institute and Research Centre, Sector 5,  
Rohini, New Delhi - 110 085, India.  
E-mail: rupindersekhon2017@gmail.com

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