The Diagnosis and Treatment of Ovarian Cancer

Overview
This presentation takes a look at the diagnosis and treatment of ovarian cancer with an emphasis on the significant advances made in the last 20 years. It also examines some of the latest information associated with the risk factors for ovarian cancer, including ovulation induction, ERT, HRT, oral contraceptives and genetics.

Ovarian Cancer Epidemiology
Ovarian cancer continues to pose a major clinical challenge, with up to 75 percent of cases diagnosed at Stage III or IV, indicating spread beyond the pelvis. It is the second most common gynecologic malignancy, but has the highest mortality rate. Diagnosing ovarian cancer at an early stage, when the disease is confined to the ovaries or tumor volume burden is low, is pivotal in effecting an optimal outcome. Patients diagnosed with stage I of the disease have a survival rate of well over 90 percent.

The majority of ovarian tumors derive from epithelial cells on the ovary surface. Other types include sex-cord stromal tumors or germ cell tumors. The pathogenesis of ovarian cancer is poorly understood. Some hypothesis include: Repeated ovulation / trauma / repair to ovarian epithelium that allows genetic mutation and neoplasia; and, excess gonadotropin secretion leads to increased estrogen, which leads to epithelial proliferation and potential for malignant transformation. A new theory proposes the fallopian tubes as the site of origin.

Assessing Family History
A significant family history includes having two first degree relatives with breast or ovarian cancer with one diagnosed at under age 50; one unilateral breast cancer at under age 30; one bilateral breast cancer diagnosed at less than 40 or one male breast cancer. The SGO recommends that a cancer predisposition testing should be offered only when the individual has personal or family history features suggestive of a genetic cancer susceptibility condition in order for the test to be adequately interpreted and the results useful in influencing medical management.

Risk Reduction Strategies
Women who should consider risk reducing strategies include those with the BRCA 1 or BRCA 2 mutations, high-risk of personal or family histories who have had inconclusive genetic testing or women with high-risk personal or family history who have not had genetic testing, although genetic counseling and or testing is the preferred first approach.
Once a high-risk patient has been identified, screening approaches such as the CA-125 biomarker, ultrasound, proteomics and pelvic exams may be appropriate. The presentation details the discovery and use of CA-125 and other biomarkers.

**Early Stage Disease Considerations and Treatment**
Accurate surgical staging, the patient’s child bearing potential and pathology results should be considered when outlining a treatment plan for early stage ovarian cancer. The presentation details what has been learned as a result of the ACTION and ICON-1 trials that compared platinum-containing adjuvant chemotherapy to observation following surgery. A subgroup of the ACTION trial also looked at the role surgical staging played in the patient’s outcome. Additional data comparing the use of three versus six cycles of chemotherapy is also featured in the presentation. In a recent post-hoc analysis, patients with serous ovarian tumors appear to benefit from six versus three additional cycles of chemotherapy.

**Advanced Stage Disease Treatment**
Results from trials with primary cytoreduction, randomized interval debulking and neoadjuvant chemotherapy are examined. The increased use of intraperitoneal therapy in the treatment of advanced stage ovarian cancer is discussed, including a review of key trials comparing survival rates using IP to IV therapy. Incorporation of novel biologics, the role of maintenance therapy, and methods to reduce toxicity from IP therapy are currently being explored. The recent trials illustrate the improvement of survival for ovarian cancer in recent years.

**Recurrent Ovarian Cancer**
Treating recurrent ovarian cancer involves the patient and physician working together to control the disease and extend survival while maintaining quality of life. Numerous treatments are available, but rarely curative. Secondary cytoreduction and secondary debulking may be a beneficial option, particularly with solitary tumors.

**New Agents**
Several new agents are in late-phase trials and pending registration in the U.S. including ET-743 (Yondelis™), TLK286 (Telcyta™), Taxanes (CTI-2103), Epothilones, Abagovomab, Phenoxodiol, Karenitican and anti-anigogenesics (bevacizumab, cedarinib).

**Metronomic and Palliative Chemotherapy**
Metronomic chemotherapy, or the steady, low dose use of chemotherapy drugs has shown promise for advanced cases of ovarian cancer. Results from a phase II metronomic chemotherapy trial using cyclophosphamide and bevacizumab showed 56 percent of participants disease-free at 6 months. Finally, the presentation takes a look at a study that evaluated the expectations and quality of life of patients undergoing palliative chemotherapy.

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