tumor-infiltrated aperistaltic bowel are common. Limited surgery to relieve intestinal obstruction, localized radiation therapy to relieve pressure or pain from masses, or palliative chemotherapy may be helpful. Agents with >15% response rates include gemcitabine, topotecan, liposomal doxorubicin, pemetrexed, and bevacizumab. Approximately 10% of ovarian cancers are HER2/neu positive, and trastuzumab may induce responses in this subset.

Five-year survival correlates with the stage of disease: stage I, 85–90%; stage II, 70–80%; stage III, 20–50%; and stage IV, 1–5% (Table 117-1). Low-grade serous tumors are molecularly distinct from high-grade serous tumors and are, in general, poorly responsive to chemotherapy. Targeted therapies focused on inhibiting kinases downstream of *RAS* and *BRAF* are being tested. Patients with tumors of low malignant potential are managed by surgery; chemotherapy and radiation therapy do not improve survival.

OVARIAN SEX CORD AND STROMAL TUMORS

Epidemiology, Presentation, and Predisposing Syndromes Approximately 7% of ovarian neoplasms are stromal or sex cord tumors, with approximately 1800 cases expected each year in the United States. Ovarian stromal tumors or sex cord tumors are most common in women in their fifties or sixties, but tumors can present in the extremes of age, including the pediatric population. These tumors arise from the mesenchymal components of the ovary, including steroid-producing cells as well as fibroblasts. Essentially all of these tumors are of low malignant potential and present as unilateral solid masses. Three clinical presentations are common: the detection of an abdominal mass; abdominal pain due to ovarian torsion, intratumoral hemorrhage, or rupture; or signs and symptoms due to hormonal production by these tumors.

The most common hormone-producing tumors include thecomas, granulosa cell tumor, or juvenile granulosa tumors in children. These estrogen-producing tumors often present with breast tenderness as well as isosexual precocious pseudopuberty in children, menometrorrhagia, oligomenorrhea, or amenorrhea in premenopausal women, or alternatively as postmenopausal bleeding in older women. In some women, estrogen-associated secondary malignancies, such as endometrial or breast cancer, may present as synchronous malignancies. Alternatively, endometrial cancer may serve as the presenting malignancy with evaluation subsequently identifying a unilateral solid ovarian neoplasm that proves to be an occult granulosa cell tumor. Sertoli-Leydig tumors often present with hirsutism, virilization, and occasionally Cushing's syndrome due to increased production of testosterone, androstenedione, or other 17-ketosteroids. Hormonally inert tumors include fibroma that presents as a solitary mass often in association with ascites and occasionally hydrothorax also known as Meigs' syndrome. A subset of these tumors present in individuals with a variety of inherited disorders that predispose them to mesenchymal neoplasia. Associations include juvenile granulosa cell tumors and perhaps Sertoli-Leydig tumors with Ollier's disease (multiple enchondromatosis) or Maffucci's syndrome, ovarian sex cord tumors with annular tubules with Peutz-Jeghers syndrome, and fibromas with Gorlin's disease. Essentially all granulosa tumors and a minority of juvenile granulosa cell tumors and thecomas have a defined somatic point mutation in the *FOXL2* gene at C134W generated by replacement of cysteine with a guanine at position 402. About 30% of Sertoli-Leydig tumors harbor a mutation in the RNA-processing gene *DICER* in the RNAIIIb domain.

TREATMENT SEX CORD TUMORS

The mainstay of treatment for sex cord tumors is surgical resection. Most women present with tumors confined to the ovary. For the small subset of women who present with metastatic disease or develop evidence of tumor recurrence after primary resection, survival is still typically long, often in excess of a decade. Because these tumors are slow growing and relatively refractory to chemotherapy, women with metastatic disease are often debulked because disease is usually peritoneal-based (as with epithelial ovarian cancer). Definitive data that surgical debulking of metastatic or recurrent disease prolongs survival are lacking, but ample data document women who have survived years or, in some cases, decades after resection of recurrent disease. In addition, large peritoneal-based metastases also have a proclivity for hemorrhage, sometimes with catastrophic complications. Chemotherapy is occasionally effective, and women tend to receive regimens designed to treat epithelial or germ cell tumors. Bevacizumab has some activity in clinical trials but is not approved for this specific indication. These tumors often produce high levels of müllerian inhibiting substance (MIS), inhibin, and, in the case of Sertoli-Leydig tumors, α fetoprotein (AFP). These proteins are detectable in serum and can be used as tumor markers to monitor women for recurrent disease because the increase or decrease of these proteins in the serum tends to reflect the changing bulk of systemic tumor.

GERM CELL TUMORS OF THE OVARY

Germ cell tumors, like their counterparts in the testis, are cancers of germ cells. These totipotent cells contain the programming for differentiation to essentially all tissue types, and hence the germ cell tumors include a histologic menagerie of bizarre tumors, including benign teratomas and a variety of malignant tumors, such as immature teratomas, dysgerminomas, yolk sac malignancies, and choriocarcinomas. Benign teratoma (or dermoid cyst) is the most common germ cell neoplasm of the ovary and often presents in young woman. These tumors include a complex mixture of differentiated tissue including tissues from all three germ layers. In older women, these differentiated tumors can develop malignant transformation, most commonly squamous cell carcinomas. Malignant germ cell tumors include dysgerminomas, yolk sac tumors, immature teratomas, and embryonal carcinoma and choriocarcinomas. There are no known genetic abnormalities that unify these tumors. A subset of dysgerminomas harbor mutations in c-*Kit* oncogenes (as seen in gastrointestinal stromal tumors [GIST]), whereas a subset of germ cell tumors have isochromosome 12 abnormalities, as seen in testicular malignancies. In addition, a subset of dysgerminomas is associated with dysgenetic ovaries. Identification of a dysgerminoma arising in genotypic XY gonads is important in that it highlights the need to identify and remove the contralateral gonad due to risk of gonadoblastoma.

Presentation Germ cell tumors can present at all ages, but the peak age of presentation tends to be in females in their late teens or early twenties. Typically these tumors will become large ovarian masses, which eventually present as palpable low abdominal or pelvic masses. Like sex cord tumors, torsion or hemorrhage may present urgently or emergently as acute abdominal pain. Some of these tumors produce elevated levels of human chorionic gonadotropin (hCG), which can lead to isosexual precocious puberty when tumors present in younger girls. Unlike epithelial ovarian cancer, these tumors have a higher proclivity for nodal or hematogenous metastases. As with testicular tumors, some of these tumors tend to produce AFP (yolk sac tumors) or hCG (embryonal carcinoma, choriocarcinomas, and some dysgerminomas) that are reliable tumor markers.

TREATMENT GERM CELL TUMORS

Germ cell tumors typically present in women who are still of childbearing age, and because bilateral tumors are uncommon (except in dysgerminoma, 10–15%), the typical treatment is unilateral oophorectomy or salpingo-oophorectomy. Because nodal metastases to pelvic and para-aortic nodes are common and may affect treatment choices, these nodes should be carefully inspected and, if enlarged, should be resected if possible. Women with malignant germ cell tumors typically receive bleomycin, etoposide, and cisplatin (BEP) chemotherapy. In the majority of women, even those with