Oncology Notes 2

• Surgical resection is the primary treatment modility for almost all malignancies.

• For nearly all solid tumors, the potential for cure is usually related to whether or not the tumor and its local extensions can be completely removed at surgery.

• If cure of a tumor is unlikely,. a palliative approach is indicated to prolong life With a focus on quality of life.

• Most solid tumors are staged accord.i.fig to the TNM classification

• Treatment of patients with similar tumors and stages is beginning to be individualized rather than standardized for all of these patients.

• New targeted agents for treatment of cancer include vascular endotheliail growth factor pathway inhibitors, epidermal growth factor receptor pathway inhibitors, and aromatase inhibitors.

**Breast· Cancer**:

Excluding skin cancer, breast cancer is the most common malignancy among women in the United States.

Risk factors for breast CA include nulliparity, first childbirth after age 30 years, early menarche, late menopause, older age, postmenopausal obesity, lack of physical activity, alcohol, and a maternal and paternal

family history of breast CA.

Testing for *BRCA1/BRCA2* gene mutations should be performed in patients with a history suggestive of a breast and ovarian cancer.

Both tamoxifen and· raloxifene reduce the incidence Of hormone receptor-positive invasive breast cancer by approximately 50%, but railoXifene is less effective than tamoxifen in reducing the incidence of noninvasive breast cancer, and these treatments do not translate into a survival advantage.

Treatment of ductal carcinoma in situ involves local breast-conserving therapy or mastectomy with consideration of tamoxifen in estrogen receptor-positive cases.

The standard of care for patients with invasive breast cancer is mastectomy followed by whole-breast radiation therapy.

Adjuvant endocrine therapy can reduce the relative risk of breast cancer recurrence by approximately 50% and is indicated for almost all patients with ER-positive or progesterone receptor-positivetumors.

Tamoxifen is the standard endocrine therapy for premenopausal women with early-stage breast cancer, whereas postmenopausal women with hormone receptor-positive breast cancer are treated with aromatase inhibitors.

Adjuvant trastuzumab, given for 1 year sequentially or concurrently with chemotherapy, can significantly reduce breast cancer recurrence and improve overall survival in patients with tumors that over express

*HER2/neu*

Follow-up for survivors of early-stage breast cancer includes a detailed history and physical examination every 6 months for at least 5 years, monthly breast self-examination, and annual mammography.

Antidepressants that are potent inhibitors of the CYP2D6 enzyme, such as bupropion, fluoxetine, and paroxetine, are contraindicated in women taking tamoxifen.

Metastatic breast cancer is generally an incurable disease with a median survival of 2 years

Lung, liver, and bone are the most common metastatic sites for breast cancer.

Systemic therapy is the cornerstone of treatment for patients with metastatic breast cancer, and local therapy such as surgery or radiation therapy is used for symptom palliation and treatment of spinal cord compression.

For patients with metastatic bone disease, monthly administration of l intravenous bisphosphonate reduces new bone metastases and fractures.

**Ovarian Cancer**:

is the fifth most common cause of cancer-related death in women.

90% of primary ovarian tumors are derived from epithelial cells.

Ovarian cancer is predominantly a disease of postmenopausal women. It is rarely diagnosed in women younger than 40 years of age unless they have a genetic predisposition for the disease.

The incidence of ovarian cancer is higher in white ' women than in black.

The most significant risk factor for developing ovarian cancer is the presence of *BRCA1/BRCA2* gene mutations.

Use of oral contraceptive agents decreases the risk of ovarian cancer by as much as 50% with the protective effect lasting up to 20 years after oral contraception cessation.

screening for ovarian cancer is not recommended for average-risk women.

In women at high risk. for developing ovarian cancer, prophylactic bilateral salpingo-oophorectomy before age 40 years reduces the risk of developing cancer by 95%.

The symptoms of early-stage ovarian cancer are vague and nonspecific. However, ·this diagnosis should be considered in any woman with the recent onset of abdominal or pelvic symptoms.

Most patients with ovarian cancer have advanced disease at initial

evaluation and present with signs and symptoms of abdominal distention, pain, nausea, bloating, and anorexia, all of which are due to ascites and .bulk tumor effects.

Findings on ultrasonography suggestive of ovarian canter include a solid mass, a cyst with thick septations and ascites.

the diagnosis of advanced ovarian cancer is usually made by CT or ultrasound guided biopsy of a suspicious mass or cytologic examination of ascitic fluid.

Optimal tumor debulking (no residual tumor mass > 1 cm ) is associated with increased survival in patients with ovarian cancer.

Adjuvant chemotherapy is indicated for patients with high risk, early stage ovarian cancer and those with advanced disease.

Patient who have completed initial treatment for ovarian ·cancer require routine follow-up·clinical evaluations, -including history, physical examination, and serum CA-125· measurement.

Use of hematopoietic growth fac:tors to maintain adequate blood. counts has helped improve the quality of life-and decrease complication rates ·in patients With ovarian cancer who are receiving chemotherapy.

**Colorectal Cancer**

Colorectal cancer is the fourth most common cause of cancer in the United States and the second leading cause of cancer related deaths.

No specific signs or symptoms indicate whether a patient has colorectal cancer or a benign process, and many cancers remain asymptomatic until reaching an advanced stage.

Bleeding per rectum, melena, cramping, bloating, change in the frequency of bowel movements, and other nonspecific signs and symptoms may indicate the presence of a benign polyp, another nonmalignant process, or cancer.

Current recommendations indicate colorectal cancer screening (stool based test, flexible sigmoidoscopy, or optical colonoscopy) for all men and women at average risk, beginning no later than age 50.

Patients with local or locoregional colon cancer should undergo surgical resection of the primary tumor.

Adjuvant chemotherapy is used to eradicate any residual micrometastatic

disease that may still be present after surgery.

All patients with stage III colon cancer, regardless of age, should receive adjuvant chemotherapy unless contraindicated.

Randomized controlled trials have demonstrated that adjuvant chemotherapy regimens incorporating the cytotoxic agent 5-fluorouracil (5-FU) can reduce the risk. of death in these patients.

FOLFOX chemotherapy for approximately 6 months is the current standard adjuvant treatment of patients with stage III disease.

High-risk patients with stage II colon cancer are also treated with FOLFOX adjuvant chemotherapy.

Onresectable metastatic colorectal cancer is almost always incurable, and the goal of treatment is to extend survival and palliate symptoms.

5-FU is usually given intravenously with leucovorin, which has no intrinsic

antitumor activity of its own but causes 5-FU to bind more tightly to its target enzyme in preclinical models. The oral prodrug capecitabine is an acceptable alternative to 5-FU in reliable, motivated patient who is able to comply with the complex oral medication schedule required. Irinotecan and oxaliplatin also have modest activity against colorectal cancer.

Bevacizumab, a monoclonal antibody against vascular endothelia! growth factor (VEGF), modestly improves outcome when added to chemotherapy regimens. Cetuximab and panitumumab are monoclonal antibodies that block theligand binding site of the epidermal growth factor receptor (EGFR). Recent studies indicate that the antitumor activity of these agents is limited to those tumors that do not have mutations in the *K-ras* gene. Therefore, *K-ras* genotyping is now a routine part of the management of patients with stage IV colorectal cancer.

**Pancreatic Cancer**:

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States

Patients With metastatic pancreatic cancer has Median survival ranges from 4 to 6 months

Patients with locally unresectable disease have a slightly better prognosis, with a median survival of about l year.

Few risk factors have been clearly identified, Chronic pancreatitis predisposes to the development of pancreatic cancer, and tobacco use appears to increase risk. Obesity, diabetes mellitus, a diet high in red meat, and heavy alcohol use are implicated as risk factors in some studies but not in others.

approximately 5% to l 0% of patients have a strong family history of this cancer or an identifiable gene mutation that confers increased risk. Patients with a *BR CA2* gene mutation are at increased risk for development of pancreatic cancer.

Signs and symptoms are nonspecific. Patients may present with unexplained weight loss, painless jaundice, abdominal pain, fever of unexplained origin, or evidence of gastric outlet obstruction.

CT of the chest and abdomen is the preferred imaging study for the initial evaluation of possible pancreatic malignancy. MRI is an acceptable alternative but is not superior to CT. PET scanning is not part of standard evaluation.

Surgery is the only potentially curative intervention for patients with a technically resectable pancreatic rumor with- out evidence of metastases

Single-agent gemcitabine is standard therapy for most patients with metastatic pancreatic cancer. Combining gemcitabine with cisplatin or oxaliplatin increases the response rate.

Combining gemcitabine with cisplatin or oxaliplatin increases the response rate. However, toxic effects are also increased, and a survival benefit has not been demonstrated.

a randomized trial comparing 5-FU, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) with single-agent gemcitabine showed a survival benefit

(10.5 months versus 6.9 months) for patients in the FOLFIRINOX arm, although these patients experienced substantially greater toxicity.

**Multiple Myeloma and Related Disorders**

Multiple myeloma is a malignancy of plasma cells involving bone and bone marrow.

The median age at diagnosis is 70 years, and blacks are more commonly affected than whites.

Most myelomas produce a monoclonal (M) protein consisting of an intact immunoglobulin composed of a heavy chain (IgG, IgA, or IgD) and a K or A light chain, but they may secrete free light chains alone (16% of cases), or, rarely, no immunoglobulin.

Fifty- eight percent of patients with newly diagnosed symptomatic myeloma have bone pain due to lytic bone lesions.

Anemia occurs in 73% of patients. Leukopenia and thrombocytopenia are present in 20% and 5% of patients, respectively.

Hypercalcemia occurs in 28% of patients, and the serum creatinine level is elevated in 48% of patients.

The most common cause of kidney dysfunction is cast nephropathy in

which filtered monoclonal free light chains cause obstruction from intratubular precipitation.

Protein electrophoresis and immunofixation of serum and a 24-hour

urine collection will identify an M protein in 97% of patients, and these studies can be used to monitor treatment response.

Symptomatic myeloma is diagnosed by the presence of lO% or more clonal plasma cells on bone marrow biopsy, presence of an M protein, and evidence of myeloma-related end-organ damage.

The ***CRAB*** criteria for myeloma-related organ dysfunction are defined as (l) hypercalcemia (serum calcium > 10.5 mg/dl [2.6 mmol/L (2) Renal failure (serum crea1inine *>2* mgldl. (3) anemia (Hg < 10g/dl.) or 2 gldl below the lower limit of normal; (4) bone disease (lytic bone lesions osteoporosis)

The core therapeutics include the immunomodulatory drugs thalidomide and lenalidomide, the proteasome inhibitor bortezomib and the alkylating agent melphalan.

Thalidomide and lenalidomide are teratogenic agents and are associated with an increased risk for venous thrombosis. The risk of venous thrombosis is further increased by concomitant use of anthracyclines or high-dose corticosteroids or the presence of other risk factors, including

immobilization and hyperviscosity.

Somnolence, constipation, and peripheral neuropathy are common with thalidomide, whereas myelosuppression occurs more often with lenalidomide.

Bortezomib may cause thrombocytopenia and peripheral neuropathy.

Melphalan is well tolerated at low doses but can cause myelosuppression and stem cell toxicity, precluding its use as induction therapy in autologous hematopoietic stem cell transplantation (HSCT) candidates.

The choice of initial chemotherapy is dictated by the patient's candidacy for autologous HSCT.

For older patients and those with comorbidities precluding HSCT, treatment may consist of low-dose melphalan and prednisone with the

addition of thalidomide or bortezomib.

For all others, autologous HSCT remains an important component of treatment. Transplant candidates are treated initially with bortezomib

and dexamethasone with or without thalidomide or lenalidomide.

Autologous HSCT with high-dose melphalan is used as consolidation after initial induction therapy and improves disease- free and overall survival compared with continued chemotherapy.

Maintenance thalidomide, used with or with-out corticosteroids, improves disease-free survival after HSCT but causes cumulative toxicities and has inconsistent effects on overall survival.

Relapsed disease is typicaly treated with a lenalidomide- or bortezomib-based regimen

Lytic bone disease is a major cause of morbidity inmyeloma. The bisphosphonates amidronate and zoledronic acid help prevent pathologic

Fractures, Nephrotoxicity is uncommon, but focal segmental glomerulo-sclerosis and acute tubular necrosis can occur with pamidronate and zoledronic acid, respectively.

Bisphosphonate-associated osteonecrosis of the jaw can occur and is commonly characterized by pain.

On physical examination, exposed bone can be seen in the maxilla

or mandible. Risk factors include recent dental extraction, poor dentition, and periodontal disease

Management of myeloma-related kidney failure consists of treatment of hypercalcemia, if present, including intravenous fluids to achieve euvolemia, and bisphosphonate therapy.

Kidney failure can be precipitated by intravenous CT contrast dye, Aminoglycosides , and NSAIDs, and exposure to these and other nephrotoxic agents should be avoided.

plasmapheresis should be considered in those with probable or biopsy-proven cast nephropathy to reduce the concentration of serum free light chains by at least 50%.

Transfusions are used to treat anemia, and erythropoiesis- stimulating agents may be used for symptomatic, chemotherapy-related anemia.

Vaccinations for pneumococcus and influenza virus should be provided.