Tumors that are sensitive to steroid hormones may be either 1-hormone responsive, in which the tumor regresses following treatment with a specific hormone; or 2-hormone dependent, in which removal of a hormonal stimulus causes tumor Tumors that are sensitive to steroid hormones may be either 1-hormone responsive, in which the tumor regresses following treatment with a specific hormone; or 2-hormone dependent, in which removal of a hormonal stimulus causes tumor regression; or 3-Both.Etoposide finds its major clinical use in the treatment of lung cancer and in combination with bleomycin and cisplatin for testicular carcinoma.Etoposide finds its major clinical use in the treatment of lung cancer and in combination with bleomycin and cisplatin for testicular carcinoma.D. Leuprolide, goserelin, and triptorelin Gonadotropin-releasing hormone (GnRH) is normally secreted by the hypothalamus and stimulates the anterior pituitary to secrete the gonadotropic hormones: 1-Luteinizing hormone (LH), the primary stimulus for the secretion of testosterone by the testes, and 2-Follicle-stimulating hormone (FSH), which stimulates the secretion of estrogen.D. Leuprolide, goserelin, and triptorelin Gonadotropin-releasing hormone (GnRH) is normally secreted by the hypothalamus and stimulates the anterior pituitary to secrete the gonadotropic hormones: 1-Luteinizing hormone (LH), the primary stimulus for the secretion of testosterone by the testes, and 2-Follicle-stimulating hormone (FSH), which stimulates the secretion of estrogen.Removal of hormonal stimuli from hormone-dependent tumors can be accomplished by surgery (for example, in the case of orchiectomy--surgical removal of one or both testes--for patients with advanced prostate cancer) or by drugs (for example, in breast cancer treatment with the antiestrogen tamoxifen prevents estrogen stimulation of breast cancer cells).As GnRH analogs, they occupy the GnRH receptor in the pituitary, which leads to its desensitization and, consequently, inhibition of release of FSH and LH. Thus, both androgen and estrogen synthesis are reduced.Removal of hormonal stimuli from hormone-dependent tumors can be accomplished by surgery (for example, in the case of orchiectomy--surgical removal of one or both testes--for patients with advanced prostate cancer) or by drugs (for example, in breast cancer treatment with the antiestrogen tamoxifen prevents estrogen stimulation of breast cancer cells).As GnRH analogs, they occupy the GnRH receptor in the pituitary, which leads to its desensitization and, consequently, inhibition of release of FSH and LH. Thus, both androgen and estrogen synthesis are reduced.SN-38 (the active metabolite of irinotecan) is approximately 1000 times as potent as irinotecan as an inhibitor of topoisomerase I. The topoisomerases relieve torsional strain in DNA by causing reversible, singlestrand breaks.SN-38 (the active metabolite of irinotecan) is approximately 1000 times as potent as irinotecan as an inhibitor of topoisomerase I. The topoisomerases relieve torsional strain in DNA by causing reversible, singlestrand breaks.Adverse effects Adverse effects caused by tamoxifen include : Hot flashes, nausea, vomiting, skin rash, and vaginal bleeding and discharge (due to estrogenic activity of the drug and some of its metabolites in the endometrial tissue).Tamoxifen has the potential to cause endometrial cancer, thromboembolism and effects on vision.This agent blocks cells in the late S to G2 phase of the cell cycle, and the major target is topoisomerase II. Binding of the drug to the enzyme-DNA complex results in persistence of the transient, cleavable form of the complex and, thus, renders it susceptible to irreversible double-strand breaks.Adverse effects Adverse effects caused by tamoxifen include : Hot flashes, nausea, vomiting, skin rash, and vaginal bleeding and discharge (due to estrogenic

activity of the drug and some of its metabolites in the endometrial tissue).Tamoxifen has the potential to cause endometrial cancer, thromboembolism and effects on vision.This agent blocks cells in the late S to G2 phase of the cell cycle, and the major target is topoisomerase II. Binding of the drug to the enzyme–DNA complex results in persistence of the transient, cleavable form of the complex and, thus, renders it susceptible to irreversible double–strand breaks.They compete with the natural hormone for binding to the androgen receptor and prevent its action in the prostate Adverse effects include : gynecomastia, constipation, nausea, and abdominal pain.They compete with the natural hormone for binding to the androgen receptor and prevent its action in the prostate Adverse effects include : gynecomastia, constipation, nausea, and abdominal pain.B. Fulvestrant and raloxifene Fulvestrant is an estrogen receptor antagonist that is given via IM injection to patients with hormone receptor–positive metastatic breast cancer.Exemestane A steroidal, irreversible inhibitor of aromatase, Exemestane, is well absorbed after oral administration and widely distributed.The major limiting toxicity is dose–related nephrotoxicity, involving the distal convoluted tubule and collecting ducts.B. Fulvestrant and raloxifene Fulvestrant is an estrogen receptor antagonist that is given via IM injection to patients with hormone receptor–positive metastatic breast cancer.Exemestane A steroidal, irreversible inhibitor of aromatase, Exemestane, is well absorbed after oral administration and widely distributed.The major limiting toxicity is dose–related nephrotoxicity, involving the distal convoluted tubule and collecting ducts.Mechanism of action Tamoxifen competes with estrogen for binding to estrogen receptors in the breast tissue, and inhibits estrogen induced growth of breast cancer.Raloxifene is an oral SERM that blocks estrogen effects in the uterine and breast tissues, while promoting effects in the bone to inhibit resorption.Platinum Coordination Complexes A. Cisplatin, carboplatin, and oxaliplatin Cisplatin was the first member of the platinum coordination complex class of anticancer drugs, but because of severe toxicity, carboplatin was developed.It has found wide application in the treatment of solid tumors, such as metastatic testicular carcinoma in combination with VBL and bleomycin, ovarian carcinoma in combination with cyclophosphamide, or alone for bladder carcinoma.Unlike cisplatin, carboplatin causes only mild nausea and vomiting, and it is rarely nephro–, neuro–, or ototoxic.Topoisomerase Inhibitors These agents exert their mechanism of action via inhibition of topoisomerase enzymes, a class of enzymes that reduce supercoiling of DNA.Acute and delayed diarrhea with irinotecan may be severe and require treatment with atropine during the infusion or high doses of loperamide in the days following the infusion.Mechanism of action Tamoxifen competes with estrogen for binding to estrogen receptors in the breast tissue, and inhibits estrogen induced growth of breast cancer.Raloxifene is an oral SERM that blocks estrogen effects in the uterine and breast tissues, while promoting effects in the bone to inhibit resorption.Platinum Coordination Complexes A. Cisplatin, carboplatin, and oxaliplatin Cisplatin was the first member of the platinum coordination complex class of anticancer drugs, but because of severe toxicity, carboplatin was developed.It has found wide application in the treatment of solid tumors, such as metastatic testicular carcinoma in combination with VBL and bleomycin, ovarian carcinoma in combination with cyclophosphamide, or alone for bladder carcinoma.Unlike cisplatin, carboplatin causes only mild nausea and vomiting, and it is rarely nephro–, neuro–, or ototoxic.Topoisomerase Inhibitors These agents exert their mechanism of action via inhibition of topoisomerase enzymes, a class of

enzymes that reduce supercoiling of DNA.Acute and delayed diarrhea with irinotecan may be severe and require treatment with atropine during the infusion or high doses of loperamide in the days following the infusion.It is an estrogen antagonist in breast tissue and an agonist in other tissues, such as bone and the endometrium.Tamoxifen is used for first-line therapy in the treatment of estrogen receptor-positive breast cancer.The result is o depletion (down-regulation) of estrogen receptors, and the o growth-promoting effects of the natural hormone and other growth factors are suppressed.C. Aromatase inhibitors The aromatase reaction is responsible for extra-adrenal synthesis of estrogen from androstenedione, which takes place in liver, fat, muscle, skin, and breast tissues, including breast malignancies. Leuprolide is available as: 1) A subcutaneous daily injection, 2) A subcutaneous depot injection, or 3) An intramuscular depot injection to treat metastatic carcinoma of the prostate.Goserelin acetate is a subcutaneous implant, and triptorelin pamoate is injected intramuscularly.In the high-chloride milieu of the plasma, cisplatin persists as the neutral species, which enters the cell and loses .chloride in the low-chloride milieu.1.2.1.2