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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).

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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.

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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.

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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.

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