

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Anti-androgen therapy for prostate cancer

Prostate cancer has recently received publicity as the leading cause of cancer deaths for men in Australia. An elevation of the prostate-specific antigen (PSA) is not necessarily indicative of malignancy, which is diagnosed by biopsy.

When (or whether) to treat early-stage disease is a controversial matter. For low-grade tumours “watchful waiting” may be appropriate. Tumours with a higher Gleason score need more aggressive treatment. Localised disease is usually treated by surgery (radical prostatectomy with curative intent) and/or radiotherapy.

Locally advanced disease may be treated with one or both of radiotherapy and androgen deprivation therapy. The results of a 5-year survival analysis favour the combined approach, although there is debate over the timing of androgen deprivation. Luteinising Hormone Releasing Hormone (LHRH) analogues cause androgen deprivation by blocking testosterone release, as does surgical castration. Clinically, these methods are equally effective in reducing levels of testosterone. The drugs used for “chemical castration” are administered as monthly or 3-monthly depot injections, and include goserelin and leuprorelin. Side effects include hot flushes, reduced libido and gynaecomastia.

5-alpha reductase inhibitors reduce prostate volume, and are used in benign prostatic hypertrophy (BPH) but don't impact the course of disease in prostate cancer, despite causing a reduction in PSA. They block conversion of testosterone to active metabolites, and therefore finasteride has been trialled in prophylactic prevention of prostate cancer.

Metastatic disease, although not curable, is usually controllable with hormonal therapy, which is recommended as first-line treatment. Up to 80% of these patients may respond to androgen deprivation. LHRH analogues/surgical castration may be used alone or in combination with androgen receptor blockers. The combination may provide a survival benefit; androgen receptor blockers can be given alone if LHRH analogues not tolerated.

Initial administration of LHRH analogues causes a rise in testosterone and associated disease flare; anti-androgen therapy cover should be given for the first two weeks to prevent this. Androgen receptor blockade is achieved by flutamide, nilutamide, and most commonly bicalutamide: all are equally effective, and cause less impotence but more GI side effects than LHRH analogues. Cyproterone is the only steroidal anti-androgen used widely. Oestrogens are not recommended because of thromboembolic risk.

Although disease may relapse or progress after initial response, anti-androgen therapy should not be ceased, as the subsequent rise in testosterone levels can exacerbate disease. Urinary obstruction can cause acute (often acute on chronic) renal failure, and exacerbation of disease can increase the risk of/worsen pathological fractures. Paradoxically, withdrawal of flutamide may result in reduced PSA levels.

Hormone refractory prostate cancer is unlikely to respond to cytotoxic chemotherapy, although mitoxantrone given together with prednisolone has been shown to have some palliative benefit. Docetaxel is at least as effective, and has been shown to delay progression, however there is a greater incidence of intolerable side effects. Radiotherapy to sites of pain, e.g. bone lesions, can produce symptomatic benefit.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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