key points

SELECTED BY
Dr Peter Saul
GP, Wrexham and associate GP Dean for North Wales

Prostate cancer is currently diagnosed in more than 34,000 men every year and claims more than 10,000 lives per annum in the UK. Recently, prostate specific antigen (PSA) population screening has been evaluated in two major randomised, controlled studies. Even though the more mature European study confirmed that PSA screening is capable of reducing prostate cancer mortality, anxieties still persist, particularly surrounding the issue of overdiagnosis of clinically insignificant cancer, which may never be destined to result in morbidity or mortality.

The very recent identification of 29 genetic variants that predispose towards prostate cancer offers another, more targeted, opportunity to reduce the death toll of this increasingly prevalent disease. It also raises the possibility of the identification of a sub-group of men who are especially susceptible to prostate cancer.

Once prostate cancer has been detected, usually on the basis of a transrectal ultrasound-guided biopsy of the gland, and secondary spread of the disease excluded, the patient and his family are faced with the difficult decision about which treatment option to select. In lower-risk cases a programme of active surveillance may be sufficient. In fitter men, with more clinically significant disease, eradication of the cancer by surgical removal of the gland is often involved, indeed this is the only treatment which has been proven in a randomised controlled trial to reduce both the rate of metastases and mortality compared with watchful waiting.

Metastatic prostate cancer is associated with high mortality – approximately 70% within 5 years. Androgen deprivation, which has become the mainstay of treatment, effectively reduces intraprostatic DHT concentration by more than 80%, resulting in reduced androgen receptor stimulation and increased prostate cancer apoptosis. LHRH analogues, such as goserelin acetate, buserelin and leuprolide, are highly potent LHRH agonists. After administration, there is a transient initial increase in LH secretion, and hence in testosterone secretion; this is followed by desensitisation, resulting in a fall in LH and testosterone secretion. A potential side effect is tumour flare, which 8–32% of patients experience as a result of the initial transient increase in testosterone.

In most cases, advanced prostate cancers treated with any form of androgen deprivation eventually begin to progress, a phenomenon known as hormone-refractory or androgen-independent disease. An increase in PSA level after initially successful androgen deprivation almost inevitably indicates impending clinical progression. Docetaxel, given in a 3-week schedule, is superior to mitoxantrone/prednisone in terms of decreasing disease progression, PSA response and improving pain. It also significantly improves survival.