key points

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Prostate cancer is the most common cancer in men in the UK. It accounts for nearly a quarter of all male cancer diagnoses and is the second most common cause of male cancer death in the UK. Despite a large increase in prostate cancer incidence, mortality rates have remained relatively constant through improvements in survival.

It is an extremely heterogeneous disease and although most patients present with localised disease there are still many who have metastatic disease at presentation. Metastatic disease is commonly a lethal condition and systemic treatment is the cornerstone of management for these men.

Prostate cancers are driven by androgens, such as testosterone. Androgen deprivation therapy (ADT), which is still the mainstay of systemic treatment, effectively reduces intraprostatic androgen concentrations resulting in reduced androgen receptor (AR) stimulation and increased apoptosis. Medical castration using LHRH analogues has become the gold standard in managing both locally advanced prostate cancer, in combination with radiotherapy, and metastatic disease. Response rates to ADT are around 90% and the cancer is controlled for an average of 18 to 24 months before signs of progression appear.

Eventually most men with advanced prostate cancer become resistant to ADT. This is now called castrate refractory prostate cancer (CRPC), and is associated with a poor prognosis. Signalling via the AR continues despite castrate levels of androgens and remains a critical pathway stimulating tumour growth despite castrate levels of androgens. There is now hope for patients who progress after chemotherapy with the emergence of several new agents that have been shown to benefit patients.

The first AR-targeted drug to show a definite clinical benefit is abiraterone acetate. It markedly decreases levels of androgens in CRPC and initial trials showed promising activity. Enzalutamide has a high affinity and selectivity for AR binding, blocks nuclear translocation and reduces recruitment of co-activators. Abiraterone, enzalutamide and other AR-targeted drugs are being studied in clinical trials for patients earlier in their disease history, for example in addition to ADT at first presentation of metastatic disease, where it is likely that greater benefits will be seen.

The best outcomes for prostate cancer are in dedicated centres treating large numbers of patients and where data on treatment outcomes are more readily available. For advanced prostate cancer access to the latest clinical trials and therapies is vital as evidenced by the progress seen with such drugs as abiraterone and enzalutamide. These drugs extend life and have significant palliative benefits and until recently were only available in clinical trials. GPs have a vital role in helping to direct their patients to such centres.