EAU Lecture

Management of the Spectrum of Hormone Refractory Prostate Cancer

Urological Oncology, Manchester University, Christie Hospital and Salford Royal Hospitals NHS Trusts, Manchester, UK
Noel W. Clarke

Most men with Hormone Refractory Prostate Cancer (HRPC) will die of their disease in the absence of an intercurrent illness. In the interval following development of castrate resistance to the point of death, a spectrum of problems may arise which are a direct consequence of local and/or distal cancer progression. These problems require treatment by a team of professionals with specific expertise in the therapeutic and palliative aspects of urological cancer.

Docetaxel based chemotherapy has shown small but significant improvements in survival and associated improvement in quality of life (QoL) in men with castrate resistant disease receiving treatment. Docetaxel can be given to all age groups although some complications occur at a higher rate in the elderly, particularly haematological toxicity. This therapeutic modality has a treatment related morbidity, with a small but finite mortality rate and for this and other reasons, it may not be a suitable option for all patients. There are also uncertainties about how long therapy should be given for and whether further treatment can be administered following treatment relapse in patients who have responded previously.

New agents used alone or in combination with Docetaxel are currently under trial in an attempt to provide much needed improvements in outcome. These include systemic anticancer therapies and bone targeted treatments. Numerous novel approaches to anticancer therapy are currently under trial using drugs targeting cellular pathways for proliferation, angiogenesis, apoptosis and metastatic propagation. None of these has proven to be of definitive benefit in large scale randomised phase three trials but there is a gathering body of promising data from phase 2 studies using novel agents which suggest that some of these will be important in the future. Further multi-centre testing in well constructed studies is required to establish their true utility. Bone targeted therapy is included in this area. Traditionally, this has involved use of external beam radiotherapy. This is still a valuable treatment modality but there are additional agents, including bone seeking radionuclides, late generation Bisphosphonates and RANK Ligand Inhibitors, used alone or in combination, which have added to the range of options, reducing the incidence of skeletal complications in some men. New data relating to RANK Ligand inhibitors, powerful inhibitors of osteoclast mediated bone destruction and the anti Endothelin-1 agent ZD4054 are particularly promising. Further work to target bone related therapies more effectively is also needed; such treatment stratification may be facilitated by measurement of bone breakdown markers and the use of novel MRI techniques.

Complications arising as a consequence of upper and lower tract dysfunction, haematological, neurological and psychological disorders also occur in a significant proportion of men in their final year of life. These represent a considerable work burden for Urology Departments. Patients presenting in this way often have problems which are amenable to effective palliative interventions decisions on whether or not to treat actively may produce difficult clinical and ethical dilemmas. A holistic and supportive approach to patient care, taking due consideration of the Quality of Remaining Life is vital in this situation. This holistic patient approach is best provided by a coordinated, multi-disciplinary team including Urologists, Oncologists and Specialist Urological Cancer Nurses.