The evolving role of hormone therapy in the treatment of prostate cancer – part I

Dr Heather Payne is a clinical oncologist at University College Hospital in London and a Trustee of the PCRC

The management of men with all stages of prostate cancer is an increasingly complex process with a variety of available treatments and involvement of many different disciplines. There are three major stages at presentation. These are localised disease, where the cancer is confined to the prostate; locally advanced disease, where the cancer has spread to the local surrounding tissues; and advanced or metastatic cancer, where tumour cells have spread to distant organs, especially the bones.

The mainstay of prostate cancer therapy for many years has been the use of hormone therapy. This remains the first line of treatment for men with metastatic disease and in recent years has played an increasingly important role in the management of the other stages of prostate cancer, both alone and in combination with radiotherapy and surgery. Treatments for prostate cancer have advanced in the last 20 years as our understanding of the disease process has increased.

In the late 1930's prostate cancer was a very depressing disease as the only treatment was pain management. Then in the early 1940's a very important discovery was made by Canadian-born medical researcher Charles Huggins, who found that testosterone (the male sex hormone) could stimulate prostate cancer cells. This work by Huggins and his partner Hodges lead to the treatment of prostate cancer by the removal of testosterone, initially by an operation to remove the testicles (orchidectomy) which are the main source of testosterone production in the body. The first orchidectomy was performed in 1941. It rapidly became the 'gold standard' treatment for advanced prostate cancer as it not only reduced any painful symptoms associated with the cancer in the prostate or the bones but it also slowed down the progression of the disease.

Although orchidectomy was an effective treatment, surgical removal of the testicles had a profound psychological impact on many men. The next major advance was the use of drugs to remove testosterone, so called 'medical castration'. Huggins won the Nobel Prize in 1966 for his work on these drugs, called LHRH agonists, which continue to be used as the mainstay of therapy in advanced prostate cancer today. The first synthetic drug (goserelin) to be used as therapy was introduced into clinical practice in 1987. This is administered as an implant injected into the fat in the abdominal wall at 4 or 12 week intervals. These drugs were found to be as effective as the surgical approach and allowed men with prostate cancer a choice between the two treatment methods.

The use of LHRH agonists is usually recommended in men presenting with advanced prostate cancer. Response rates of over 85 per cent are expected for up to three years (sometimes longer) with these drugs alone. Studies, including one from the Medical Research Council (MRC), have shown benefits for men treated with immediate hormone therapy rather than delaying treatment until symptoms occur. Early therapy resulted in fewer cancer related complications such as fracture of bones, spinal cord compression and urinary difficulties or obstruction.

These LHRH agonists are excellent treatment for advanced prostate cancer. After a few years however some prostate cancer cells may become resistant to the therapy. In this situation it is possible to add in other hormone drugs to achieve a further remission. There

are now many other drugs that can be used in combination with the LHRH agonists. These include antiandrogens, which stop any residual testosterone in the body from stimulating the prostate cancer cells (eg bicalutamide), oestrogen therapy and steroid type hormones. Each can be used in combination one after the other to bring about further control of the disease and symptoms. When all these options have been tried, there are still other treatments available with chemotherapy drugs (eg docetaxol) or many of the newer compounds that are being studied such as tablets that alter blood supply to cancer cells, vaccines and even gene therapy. These too can be added to the LHRH agonist. The timing and exact order in which these drugs can be added and then stopped depends on a variety of factors and are individualised according to each patients' circumstances.

There are always side effects with any drugs and those of the LHRH agonists include erection problems, loss of libido and energy, hot flushes, breast swelling and sometimes a tendency to weakness of the bones (osteoporosis) and muscles which may need to be monitored and treated. Weight gain can also occur especially around the waist. It is always important to balance any side effects with the benefits of any drug.

Newer indications for treatment in locally advanced prostate cancer will be discussed in the next Horizon.