The evolving role of hormone therapy in the treatment of prostate cancer part2

We discussed in the last issue of Horizon the development of hormone therapy for advanced or metastatic disease. Hormone therapy has also recently evolved to play a critical role in the management of locally advanced prostate cancer *(where the cancer has spread to the local surrounding tissues but not to distant sites such as the bones)* when given in combination with radical radiotherapy with curative intent. Locally advanced prostate cancer is a common presentation in the UK accounting for one third of all new diagnoses. Treatment has traditionally included external beam radiotherapy but more than one-third of patients experienced disease progression within 5 years with radiotherapy alone. There is evidence that increased radiotherapy dose is associated with increased cancer cell kill for men with prostate cancer. The advent of new radiotherapy techniques (such as 3D Conformal, Intensity Modulated Radiotherapy (IMRT), High Dose Rate Brachytherapy Boost) have allowed the delivery of increased doses of radiation without unacceptable additional side effects to the surrounding normal structures such as the bladder and the bowel. The benefits of higher doses of radiotherapy have been clearly shown in a number of clinical studies or trials which have shown better control of the prostate cancer.

A further challenge in the treatment of locally advanced prostate cancer is that some of these tumours (not all) have a risk of spreading to distant sites in the body (such as the bones). These can be tiny microscopic metastases that are too small to be seen on any X Rays or scans at the initial presentation of prostate cancer. This means that despite better local treatment with radiotherapy, some men will ultimately progress to metastatic or advanced disease and the prostate cancer could come back in other places in the body. There is now strong evidence that the addition of hormone therapy to radiotherapy is better than radiotherapy alone for some patients with locally advanced disease and that they can help stop the cancer coming back.

Hormone therapy such as LHRH agonists (which stop testosterone production and treats prostate cancer cells) can be given before (called neoadjuvant) during and after (called adjuvant) radiotherapy treatment.

Neoadjuvant hormone therapy can have several advantages when given before radiotherapy treatment. It is an immediate treatment and will start to treat the prostate cancer straight away which is obviously very reassuring for many men and their families. The

hormones also can reduce the size and shrink the prostate gland by about 25-30%. This means that smaller beams of radiotherapy can be used to treat the prostate and this could reduce the dose of radiation to the surrounding normal structures such as the bladder and the bowel and help prevent side effects. There have also been reports that hormone therapy may make the prostate cancer cells more sensitive to the effects of the radiotherapy treatment.

There is a lot of evidence that continuing with hormone therapy after radiation treatment can be beneficial for men with locally advanced or high risk prostate cancer. Several large international studies have shown that a combination of hormones and radiotherapy as opposed to radiotherapy alone can prevent the disease progressing and make men with high risk locally advanced prostate cancers live longer. This has been a very exciting discovery. The exact length of time that the hormones need to be continued for is still not certain and we wait for the results from other ongoing clinical trials. It is usually somewhere between 6 months to 3 years depending on the individual risk factors of the prostate cancer. It may also vary with the any side effects experienced. In this situation hormone therapy is being used in the preventative setting to try and stop the prostate cancer returning after radiotherapy treatment.

The results from these studies were with the LHRH agonist drug, goserelin, which is given as an injection into the fatty tissue in the abdominal wall at monthly or 3 monthly intervals. There are side effects to all hormone therapies which must be balanced with the benefits for each man on an individual basis. There is an alternative hormone that has also been shown to increase survival when given after radiotherapy for locally advanced prostate cancer. This is a daily tablet which is an antiandrogen called bicalutamide. Antiandrogens do not stop the testicles from producing testosterone in the way that the LHRH agonists do. Instead they attach themselves to receptors on the surface of the cancer cells preventing androgens from stimulating growth. A very large international study has showed that bicalutamide can also increase survival in men with locally advanced prostate cancer after radiotherapy. This has now allowed some men a choice in which type of hormone therapy best fits in with their individual lifestyle and needs. Both are effective hormone therapies but have different side-effects. Bicalutamide may not have such a big effect on sexual functioning and energy as the LHRH agonists. It also does not cause any tendency to weak bones but it can cause more swelling and tenderness of the breast tissue.

Hormone therapy has remained a gold standard in the management of prostate cancer for more than 60 years. This has evolved from surgical to medical castration with the introduction of the LHRH agonists and more recently effective antiandrogens for the management of locally advanced disease. The treatment intent has also evolved from palliation in advanced prostate cancer to treatment with curative intent when hormones are used in combination with radiotherapy for locally advanced disease.