



## Current Treatment Approaches in Prostate Cancer

### Watchful waiting

- Watchful waiting, also known as active surveillance, where physicians monitor the tumour's behaviour and only initiate treatment when it is judged of benefit for the patient. This is standard treatment for some patient groups.<sup>1</sup>
- Watchful waiting is most commonly used in early localized and in locally advanced prostate cancer.<sup>1</sup>
- Patients for whom watchful waiting is appropriate are:
  - Patients with more than 10 years of life expectancy whose tumours are well- and moderately-differentiated, small and judged to be growing relatively slowly; more commonly referred to as active surveillance, waiting for adequate timing of curative intent therapy.<sup>1</sup>
  - Patients whose life expectancy is less than 10 years, who have no symptoms and whose tumours are well- and moderately-differentiated slow-growing tumours.<sup>1</sup>
  - Men whose life expectancy is between 10 to 15 years, who are well informed about their treatment options and whose tumours are well-differentiated and with slow growth.<sup>1</sup>
  - Men in whom cure is unlikely, who have high PSA levels but have no symptoms.<sup>1</sup>
  - Patients not willing to accept side-effects of active treatment.<sup>1</sup>
- Some men may find the uncertainty associated with watchful waiting unacceptable.<sup>2</sup>

### Radical prostatectomy

- Radical prostatectomy is a surgical procedure in which the prostate, seminal vesicles and often nearby lymph nodes are removed. It is a major operation and carries certain risks.
- It is a common way of treating early prostate cancer where the goal is to cure.
- Radical prostatectomy is recommended for men with early prostate cancer and a life expectancy greater than 10 years, but can be considered in cases of locally advanced prostate cancer.<sup>1</sup>
- There is a survival advantage with surgery compared to not operating but it has serious consequences, especially in terms of erectile dysfunction and incontinence. This has a major significance for the increasing number of young men recommended radical prostate surgery.<sup>3</sup>
- In locally advanced prostate cancer half of all men who have radical prostatectomy will experience a recurrence of prostate cancer necessitating other treatments.<sup>4</sup>

### Radiotherapy

- Radiotherapy for prostate cancer is often given from an external machine (external beam radiotherapy), but it can be given by inserting small radioactive seeds into the tumour (brachytherapy).
- Radiotherapy has a role in all stages of prostate cancer.

- As an active treatment with curative intent, radiotherapy is appropriate for patients with a life expectancy greater than 10 years, in whom surgery is considered too risky, those who are unfit with 5 to 10 years of life expectancy, and patients who have poorly differentiated tumours.<sup>1</sup>
- In locally advanced prostate cancer radical radiotherapy should be combined with GnRH agonists, before, during and after radiotherapy for a period of time that may last up to three years.<sup>1</sup>
- Radiotherapy as a palliative therapy can help patients with painful bone metastases in hormone-refractory disease; intravenous administration of a radionuclide offers pain relief.<sup>1</sup>
- Studies suggest that brachytherapy with permanent implants delivers similar long-term survival to radical prostatectomy with fewer sexual function problems.<sup>5</sup> Brachytherapy is most appropriate for patients with early disease.<sup>1</sup>
- Radiotherapy can cause bleeding from the rectum, changes in bowel habits, and many men develop erectile dysfunction. Problems with leakage of urine or urinary incontinence occur rarely.<sup>4</sup>
- Palliative radiotherapy for bone pain may take up to six weeks to work and the pain may worsen before it improves.<sup>4</sup>
- Brachytherapy can cause problems such as cystitis, which may be more severe than bladder problems seen with conventional radiotherapy. However, bowel problems and erectile dysfunction are less.<sup>6</sup>
- Sexual dysfunction as a result of radiotherapy or surgery can continue for years after treatment.<sup>4</sup>

## **Hormonal therapy**

- Prostate cancer is dependant on the male hormone testosterone for its growth. Reducing testosterone levels means the cancer cells either grow more slowly, or stop growing. This effect can last for years. In some men, the cancer will start to grow again and this is called hormone refractory prostate cancer (HRPC).<sup>1</sup>
- Therapies that reduce testosterone are known as androgen deprivation therapy (ADT).<sup>1</sup>
- Hormonal therapies are often used in conjunction with radiotherapy in local advanced prostate cancer and as the basis of treatment in advanced prostate cancer.<sup>1</sup>
- In advanced prostate cancer hormonal therapies delay progression, prevent complications and palliate symptoms.<sup>1</sup>

## **Orchidectomy**

- Bilateral orchidectomy, surgical removal of both testicles. It is an immediate but irreversible solution. Surgical castration is considered the 'gold standard' for androgen deprivation therapy against which all other treatments are rated.<sup>1</sup>
- Orchidectomy is irreversible and associated with adverse psychological outcomes,<sup>7</sup> which has led to the development of medical forms of castration.

## **GnRH agonists**

- Gonadotropin-releasing hormone (GnRH) agonists reduce the production of testosterone and are widely used in advanced prostate cancer, in patients with localised disease who have poor prognosis, and in association with radiotherapy and surgery.<sup>1</sup>
- GnRH agonists bind with the GnRH receptors in the pituitary gland, which eventually suppresses the production of luteinising hormone (LH). LH is responsible for triggering the production of testosterone in the testes' Leydig cells.
- Testosterone suppression using GnRH agonists is delayed. Before suppressing testosterone, the agonists stimulate the GnRH receptors causing a testosterone surge.<sup>1</sup> It can take up to a month to achieve castration levels of testosterone and up to 10 % of men will not maintain castration levels on GnRH agonists.<sup>1</sup>
- The testosterone surge may trigger a flare in the prostate cancer, which is the reason why guidelines recommend the use of anti-androgens when GnRH agonists are first prescribed.<sup>1</sup>

## **GnRH antagonists / blockers**

- GnRH receptor blockers directly prevent the release of LH and testosterone, without an initial surge in testosterone with associated risks. When using a GnRH blocker there is no need to administer other medications to protect against a testosterone surge.

## **Antiandrogens**

- Antiandrogens block testosterone and may be steroidal or non-steroidal. The two groups act in different ways; the non-steroidals compete with androgens at the receptor level while steroidal antiandrogens also have central inhibition of the pituitary gland inhibiting the production of gonadotrophins.<sup>1</sup>

## **Complete androgen blockade**

- Because GnRH agonists do not suppress all testosterone it is possible to combine them with androgen blockers; this is known as complete androgen blockade (CAB).

## ***The side effects of hormonal therapy***

- Loss of libido
- Erectile dysfunction
- Hot flushes
- Gynaecomastia and breast pain
- Weight gain
- Muscle wasting
- Anaemia
- Osteoporosis
- Cognitive decline

- Oestrogens and steroidal antiandrogens may cause cardiovascular toxicity<sup>1</sup>
- Hormonal therapy can affect men's quality of life because of the side effects, and men who are on combination therapy have lower quality of life compared to men on one type of hormonal therapy.<sup>1</sup>

## Chemotherapy

- Chemotherapy is reserved for patients with hormone refractory prostate cancer (HRPC) once other therapies have been exhausted.<sup>1</sup>
- Docetaxel, a drug derived from a compound found in the European yew tree has shown a significant survival benefit.<sup>1</sup>

## Other options

- Intravenous bisphosphonates, drugs used to strengthen bone, can help patients whose bone pain is resistant to palliative radiotherapy and conventional analgesics.<sup>1</sup>

## Future trends

- Intensity modulated radiotherapy (IMRT) is under development and will deliver higher, more effective doses of radiation to the tumour while minimising damage to the healthy surrounding tissue.
- Keyhole surgery and robot surgery for radical prostatectomy is commonly performed. Studies show less blood loss than in open surgery and possibly reduced urinary incontinence and erectile dysfunction.<sup>1</sup>
- A number of centres are evaluating cryotherapy (also called cryosurgery and cryoablation) in which the cancer is frozen by inserting a metal probe through an incision between the rectum and the scrotum. The therapy may be useful for early-stage cancer or for men who cannot have a radical prostatectomy.<sup>8</sup>

## References

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