

THE UROLOGY GROUP

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HORMONAL THERAPY – ANDROGEN DEPRIVATION

Prostate cancer is the most common type of cancer in men. Treatment of prostate cancer depends on a variety of factors which include stage, grade, and the volume of disease. One part of the overall treatment of prostate cancer may include a type of therapy known as "hormonal therapy", which is also known as "androgen deprivation".

Prostate cancer cells depend on testosterone – the male hormone – to grow and flourish. Most of the testosterone in the body, approximately 90%, is made in the testicles. The remaining 10% of testosterone is made in the adrenal glands, which are structures that sit on top of the kidney. There are a variety of ways to remove testosterone. Androgen deprivation are the words used to describe the removal of testosterone. The original technique developed to remove testosterone was orchiectomy, which means surgical removal of the testicles. From the first recognition in the 1940's that prostate cancer depends on testosterone to grow and flourish, orchiectomy was used frequently in the management of men with prostate cancer. Orchiectomy was a permanent procedure. Once the testicles were removed, the body was depleted of testosterone on an ongoing basis. Orchiectomy had the advantage of being a one-time event. However it had the disadvantage of the need for a surgical procedure and the negative impact on self-image that developed in men who suffered the loss of the testicles. In the 1990's, several medications were developed that produced the same effect as orchiectomy. These medications, called GNRH analogs, and more commonly known as Lupron or Zoladex, are given by intramuscular injection and cause the testis to stop making testosterone. Lupron, one of the most commonly used GNRH analogs, comes in depot formulations that can cause one, three, or four months of no testosterone production. There are other products available which can prevent testosterone production for six-month or 12-month periods (e.g., Viadur).

GNRH analogs such as Lupron may be used in a variety of circumstances. For men undergoing treatment with external beam radiotherapy, six to eight months of androgen deprivation (i.e., Lupron treatment) combined with the external beam radiotherapy provides a better response to treatment. For those men undergoing seed implant, Lupron may be used prior to the procedure to reduce the size of the prostate, making the implantation of the seeds an easier procedure. Lupron may also be used at times in those men who are scheduled for treatment for localized prostate cancer (i.e., prostate cancer confined within the prostate and not spread to some other site) who must postpone their treatment for some reason. Lupron may be used in this setting to keep the prostate cancer cells quiet until treatment can be initiated.

Some of the most common uses of Lupron are for men who have disease outside the prostate or for those men who have a rising PSA after having been treated for localized prostate cancer with external beam radiotherapy, seed implant, or radical prostatectomy. In a subset of men who undergo treatment for localized prostate cancer with one of the above treatments, PSA may recur and gradually rise, indicating some residual activity by prostate cancer cells. In these circumstances, androgen deprivation therapy can cause these prostate cancer cells to become quiet as manifest by a lowered PSA level. Androgen deprivation therapy does not eliminate prostate cancer, but rather it places the cancer cells into a state of inactivity which often persists for an extended period of years.

As a result of androgen deprivation therapy, a man essentially has diminished or no testosterone present in his body. Without testosterone, men may notice the following changes. There can be weight gain, mood fluctuations, perhaps a decrease in mental concentrating ability, and potential weakening of the bones which may lead to an increased risk of fracture. All men who are on androgen deprivation notice a decrease or loss of libido and loss of erection. About one-third of men on androgen deprivation develop hot flashes.

When GNRH analogs first became available, they were used on an ongoing basis, referred to as continuous androgen deprivation, to mimic the experience of men treated with orchiectomy. In recent years, there has been a trend to using androgen deprivation on a stop/start basis known as intermittent androgen deprivation therapy. In these circumstances, Lupron is given for a four- or eight-month period to quiet the prostate cancer cells and allow the PSA to decline. Lupron is then stopped which allows the body to resume testosterone production to offset some of the unwanted effects of absent testosterone. As the PSA gradually rises once the treatment has been stopped, Lupron treatment is then resumed. Controversy exists regarding the merits of continuous androgen deprivation versus intermittent androgen deprivation, and there is no clear cut consensus on the level of PSA which should prompt initiation of either form of treatment.

In addition to the GNRH analogs, there are other types of medications which fall under the heading of hormonal therapy known as antiandrogens. These medications, typically in pill form, act by blocking the uptake of testosterone in some cells. These antiandrogens, some of the common forms of which are known as Eulexin (flutamide) and Casodex (bicalutamide), may be used in combination with a GNRH analog (Lupron) to produce a form of treatment known as total androgen blockade. Although there was initial enthusiasm for total androgen blockage in years past, current consensus does not favor its routine use.

In summary, androgen deprivation is frequently used in the management of prostate cancer and offers another useful treatment option to help men with prostate cancer.