

5-ALPHA REDUCTASE (5AR) INHIBITOR ROLE IN ANDROGEN DEPRIVATION THERAPY

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Disclaimer: Please recognize that I am not a Medical Doctor. I have been an avid student researching and studying prostate cancer as a survivor and continuing patient since 1992. I have dedicated my retirement years to continued research and study in order to serve as an advocate for prostate cancer awareness, and, from a activist patient's viewpoint, to help patients, caregivers, and others interested develop an understanding of prostate cancer, its treatment options, and the treatment of the side effects that often accompany treatment. Readers of this paper must understand that the comments or recommendations I make are not intended to be the procedure to blindly follow; rather, they are to be reviewed as my opinion, then used for further personal research, study, and subsequent discussion with the medical professional/physician providing prostate cancer care.

With removal of the prostate that includes all cancer cells, production of T increases while at the same time conversion to DHT decreases, and without any presence of CaP, patients should expect full recovery.

From my personal research, I came to the following conclusions of the importance of 5-Alpha Reductase (5AR) inhibitors if all prostate cancer cells were not removed or eradicated and androgen deprivation therapy (ADT) is to be prescribed:

Androgen-sensitive human prostate cancer cells (LNCaP) have increased 5Alpha Reductase (5AR) activity. This increased activity, along with involvement of cancer cell lines DU145 and HPC-36M, stimulates the metabolic conversion of testosterone (T) to dihydrotestosterone (DHT).

It appears it is the presence of CaP, when not having been totally removed or eradicated, that influences increased conversion of T to DHT.

With any CaP being left behind in the prostatic bed or having migrated, but so insignificant as to not being visible in imaging, the remaining CaP and increased T production will stimulate increased 5AR activity. Increased 5AR activity will stimulate T conversion to DHT and consequent CaP development.

DHT is known to be a much more powerful stimulant to CaP development than T.

With an increase in 5AR activity causing an increase of T conversion to DHT it stands to reason that this conversion must be inhibited.

5Alpha Reductase (5AR) consists of two enzymes, type 1 and type 2, that are present on prostate cancer (PC) cells. Both are involved in the conversion of T to DHT. T has more difficulty accessing androgen receptors (AR) on prostate cancer cells, and it is when T comes upon the 5AR enzyme that it is converted to dihydrotestosterone (DHT) that has a better propensity to access the AR and then stimulate PC cell growth. Antiandrogens are administered to block the AR from T access and the consequent conversion to DHT, yet it is difficult to entirely block all AR. Though LHRH agonists are administered to diminish T production by wearing out leydig cells in the testicles, they do not diminish T production from the adrenal glands. Thus, to provide yet another safeguard to PC cell growth, a 5AR inhibitor (dutasteride/Avodart or finasteride/Proscar) is administered to inhibit the conversion of T to DHT. With finasteride/Proscar only known to inhibit type 2, while dutasteride/Avodart is known to inhibit both types 1 and 2, many physicians, as well as advocates with experience with ADT3, opt for dutasteride/Avodart as the third medication in triple hormonal blockade. And with other trials/studies having determined that dutasteride fills a role in PC cell apoptosis as well as inhibiting cell proliferation, dutasteride/Avodart has gained more acceptance.

There have been studies that have determined that 5AR type 1 is even increased and type 2 somewhat decreased during development of prostate cancer. And both type 1 and type 2 expression is increased in recurrent and metastatic cancers, suggesting that both enzymes may be important in the development and progression of prostate cancer.

This leads to the argument I totally support, as do those Medical Oncologists we know who specialize specifically in prostate cancer research and treatment, that a

5AR inhibitor such as dutasteride/Avodart (my preference) or finasteride/Proscar should be an integral part of androgen deprivation therapy (ADT).

PLEASE TAKE SPECIAL NOTE: Since there can be cardiac risk associated with the administration of ADT medications, it is important the prescribing physician first perform necessary testing to rule out this possibility.