

Triple-hormonal blockade/Androgen Deprivation Therapy (ADT3) – a reasonable description of the importance of the medications that should be employed, and why, to manage and control prostate cancer cell development either as primary therapy for advanced disease or following earlier treatment protocols that have failed.

by Charles (Chuck) Maack – Prostate Cancer Advocate/Mentor

LHRH agonists (Lupron, for example), and antiandrogens (Casodex, for example), and 5Alpha Reductase (5AR) inhibitors (Avodart, for example), each have absolutely different, but important, individual functions in androgen deprivation therapy.

Lupron (and other LHRH agonists) shuts down a complex system of production of testosterone via luteinizing hormone (LH) leydig cell stimulation in the testicles. It DOES NOT shut down the production of androgen precursors from the adrenal glands. And the production of those androgen precursors (that convert to testosterone) is even enhanced when LH/leydig cell production via the testicles is stopped. So, here you still have adrenal gland androgen/testosterone having access to cancer cell development. Lupron has absolutely no effect on that production.

Casodex (and other antiandrogens) is an antiandrogen prescribed to hopefully block all androgen receptors in all cancer cells so that androgen/testosterone cannot access those cancer cells. But it is unlikely the multitude of androgen receptors are all blocked. And those not blocked still open access of androgen/testosterone to the cancer cell nucleus.

Then, in the cancer cell nucleus are Type I and Type II enzymes known as 5Alpha Reductase (5AR). When androgen/testosterone comes in contact with these 5AR enzymes, it converts to an up to ten times more powerful stimulant to cancer cell growth, dihydrotestosterone (DHT). (See <http://tinyurl.com/2ax4wd>) Obviously, this should be prevented. And remember, Lupron has NOT stopped adrenal gland androgen/testosterone production and it is unlikely all androgen receptors are blocked by an antiandrogen.

So, we now want to inhibit these 5AR enzymes from converting androgen/testosterone from any source to the more powerful cancer stimulant, DHT. And we do that with a 5AR “inhibitor.” And those inhibitors are primarily dutasteride/Avodart or finasteride/Proscar. And since Proscar only inhibits the

Type II enzymes, Avodart is the better inhibitor because it inhibits both Type I and Type II enzymes.

Modern thinking physicians who have followed many persons on LHRH agonists (Lupron and Zoladex) have determined how detrimental it is for patients to be on continuous Androgen/Testosterone Deprivation; they have determined that Intermittent ADT (IADT) (stopping use of the LHRH agonist and antiandrogen) can be as beneficial as continuous therapy as long as the individual has been able to obtain and maintain for 1 year a PSA level that is “undetectable” or <0.05 ng/ml and a “castrate” testosterone level <32ng/dl (but preferably <20ng/dl) before considering IADT. During any IADT interval, “maintenance” with Avodart or Proscar should be considered to continue inhibition of 5AR activity. This allows T to slowly recover but still inhibits the conversion of T to DHT so as to interfere least with the good effects of T on the rest of the body and probably to delay the onset of Androgen Insensitive PC clones.

Note these papers regarding the importance of inhibiting androgen/testosterone conversion to dihydrotestosterone:

<http://clincancerres.aacrjournals.org/cgi/content/abstract/10/21/7121>

“Conclusions: The source of dihydrotestosterone in prostatic tissue after androgen deprivation therapy involves intracrine production within the prostate, converting adrenal androgens to dihydrotestosterone. Dihydrotestosterone still remaining in prostate tissue after androgen deprivation therapy may require new therapies such as treatment with a combination of 5 α -reductase inhibitors and antiandrogens, as well as castration.”

Then there is this study that concludes that even with “low dihydrotestosterone” presence, that dihydrotestosterone can influence cancer growth: “Low dihydrotestosterone in cases of aggressive prostate cancer is probably sufficient to activate androgen receptor expression and propagate tumor growth.” (**MY NOTE: Thus all the more reason to “inhibit” this hormone by the use of a 5Alpha Reductase (5AR) inhibitor (dutasteride/Avodart or finasteride/Proscar)**)

<http://cat.inist.fr/?aModele=afficheN&cpsidt=18107663>

From renowned Medical Oncologist Charles E. “Snuffy” Myers, who specializes specifically in the treatment of advanced prostate cancer:

"Since I opened my clinic—the American Institute for Diseases of the Prostate - in 2002, I've made it a practice to measure dihydrotestosterone levels in each patient we see. And I have to tell you that medical castration, while effective at reducing testosterone from the normal range of 300-800 ng/dL to below 30 ng/dL, often leaves dihydrotestosterone levels within the normal range (30-80 ng/dL). And dihydrotestosterone is ten times more powerful than testosterone at stimulating prostate growth, so a dihydrotestosterone of 30 ng/dL is potentially as powerful as a testosterone of 300. Dihydrotestosterone formation can be blocked in most patients with either Proscar or Avodart, with Avodart being more consistently effective." In Dr. Myers November 2009 “Prostate Forum” newsletter:

“However, in our clinic, I go further. There are two forms of androgen in men: testosterone and dihydrotestosterone. There is broad agreement that dihydrotestosterone is 10 times more powerful than testosterone in stimulating the growth of prostate cells. There is now also powerful epidemiological, laboratory, and clinical trial data showing that dihydrotestosterone is important in the development and progression of prostate cancer. With this in mind, starting in 1995 I made it a standard practice to also check dihydrotestosterone levels in men on hormonal therapy. I have been surprised by the number of men who have castrate levels of serum testosterone who have serum dihydrotestosterone levels within normal ranges. If dihydrotestosterone is 10 times more powerful, then these men have enough androgen to impair response to hormonal therapy. I think this provides strong support for the use of triple hormonal blockade (addition of Proscar or Avodart) in men with elevated dihydrotestosterone levels. However, I must stress that my views on dihydrotestosterone and the use of Proscar or Avodart are not accepted by many in the prostate cancer field. Nevertheless, I am not the only one who thinks dihydrotestosterone is important. In fact, the major public advocates of this approach are (Medical Oncologists) Stephen Strum and Robert Leibowitz, who have both focused on the development of triple hormonal blockade that includes blockade of dihydrotestosterone production.”

Physicians who ignore these multiple medications that are necessary to block/inhibit androgen/testosterone production and access to the cancer cell have not done their own, personal research and study. They are following what they have been told or what they have read authored by other than Medical Oncologists who specialize specifically in research and treatment of prostate cancer. They do not have the knowledge nor developed the expertise of those Medical Oncologists

who have dedicated their lives to specializing specifically in research and treatment of prostate cancer, and more specifically, advanced prostate cancer. These are the Medical Oncologists who absolutely understand the prostate and appropriate treatment of recurring and advanced prostate cancer. Medical Oncologists Stephen B. Strum, Charles E. (Snuffy) Myers, Robert (Bob) Leibowitz, Mark Scholz, Richard Lam, Steven Tucker, Glenn Tisman, to name a few, are in this special category. Go to www.pcri.org and read the papers by these experts as well as experts in other areas of prostate cancer and its treatment. In so doing, you will know who to believe in and who to question.

For an understanding of other areas of treatment for prostate cancer, please visit <http://www.ustoowichita.org/observations.cfm> and click on any subject.