THREE OPINIONS IN ONE REGARDING TESTOSTERONE REPLACEMENT THERAPY (TRT) AND TREATMENT OF BENIGN PROSTATIC HYPERPLASIA (BPH) AND ANDROGEN DEPRIVATION THERAPY (ADT)

By Charles (Chuck) Maack – Prostate Cancer Activist/Mentor

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.

Though you may find these subjects addressed separately on my website "Observations" webpage http://www.theprostateadvocate.com/observations.html they are addressed again here since too often these three subjects come up as one in online prostate cancer discussions.

Testosterone Replacement Therapy (TRT)

1) No, testosterone replacement therapy (TRT) should not be prescribed to men with known active prostate cancer.
2) Yes, TRT could be prescribed to men who have been treated for prostate cancer, BUT, only after a couple years of no elevation of PSA after reaching a nadir following that treatment.
3) TRT might be prescribed to men diagnosed with very low grade (one or two biopsy tissue samples with very low percentage development) BUT, I would only recommend patients go to Medical Oncologist Bob Leibowitz in Los Angeles who has administered TRT to such patients at high doses to escalate testosterone level rapidly to levels between 1800ng/dl to as much as 3000ng/dl and has data to support his manner of treatment. See: http://www.compassionateoncology.org/pdfs/TRTHANDOUT.0206.pdf. In my opinion, low dose administration of TRT to patients with any level of cancer development will rather stimulate cancer cell development. (Hope I am

eventually proven wrong).

Benign Prostatic Hyperplasia (BPH)

1) Dihydrotestosterone/DHT is as much as five times more powerful a stimulant to cancer cell growth and proliferation than testosterone. 5Alpha Reductase (5AR) enzymes Types I and II are present on prostate cells, both healthy and cancerous, and serve to convert testosterone that comes in contact with those enzymes to DHT. Since BPH is found to include an increase in the presence of DHT, the appropriate medication to both reduce the volume/size of BPH as well as presence of DHT is a 5AR "inhibitor." Finasteride/Proscar was the first 5AR inhibitor produced for this purpose, but only inhibits the activity of Type II enzymes. Dutasteride/Avodart was then produced and inhibits both Types I and II enzyme activity. Thus, the more appropriate 5AR inhibitor is dutasteride/Avodart. Since BPH is often accompanied with difficulty urinating from the compression of BPH on the urethra, the medication tamsulosin/Flomax is often prescribed. A newer medication is now available that is a combination of both dutasteride and tamsulosin known as "Jalyn" and can be considered for prescribing in lieu of being prescribed these medications separately, particularly if the cost is less.

Androgen Deprivation Therapy (ADT)

1) As explained above and reiterated here with some editing: Dihydrotestosterone/DHT is as much as five times more powerful a stimulant to cancer cell growth and proliferation than testosterone. 5Alpha Reductase (5AR) enzymes Types I and II are present on prostate cancer cells and serve to convert testosterone that comes in contact with those enzymes to DHT. DHT is an up to five times more powerful stimulant to cancer cell growth and proliferation than testosterone. With this recognition, finasteride/Proscar was an earlier medication know to inhibit the 5AR activity of converting testosterone to DHT, however, finasteride/Proscar only inhibits the activity of 5AR Type II enzymes. Dutasteride/Avodart was then produced and inhibits both Types I and II enzyme activity, and often with more advanced prostate cancer, Type I is more prevalent. Thus, the more appropriate 5AR inhibitor is dutasteride/Avodart.

2) When prostate cancer is not eradicated by surgical removal of, or radiation to, the prostate gland, androgen deprivation therapy (ADT) then becomes the next treatment option. ADT medications include LHRH agonists (Lupron, Zoladex, Eligard, Trelstar, Vantas) or antagonist (Firmagon) to shut down "testicular" production of testosterone; these medications have no effect on testosterone metabolized from androgen precursors produced by the adrenal glands. Any source of testosterone still present must be stopped from activating the multitude of androgen receptors on each cancer cell since

when activated, that testosterone now has access into the cancer cell nucleus. For this purpose an antiandrogen should be prescribed to block androgen receptors from testosterone access (bicalutamide/Casodex, flutamide/Eulexin, nilutamide/Nilandron). HOWEVER, with the multitude of androgen receptors the likelihood of faulty androgen receptors exists, so as yet another safeguard to prevent testosterone from accessing the cancer cell nucleus via faulty receptors and coming in contact with 5AR enzymes (as explained in #1) is the prescribing of one of the 5AR inhibitors (dutasteride/Avodart or finasteride/Proscar) since we do not want that testosterone to be converted to the more powerful DHT. Thus, when androgen deprivation therapy (aka Testosterone Inactivating Pharmaceuticals/TIP) becomes necessary to rein in cancer cell growth, it is more appropriate as well as more effective to prescribe triple-androgen/hormonal blockade with an LHRH agonist or antagonist, an antiandrogen, and a 5AR inhibitor (aka ADT3 – using three initial medications). FYI: When we use numbers following the letters ADT, we are noting the number of medications being included in the ADT, and that number can be higher if other medications are added to the ADT.
3) And I'll add that when moving to intermittent ADT (IAD) by stopping the LHRH agonist/antagonist and antiandrogen in order to permit a return of testosterone to enhance energy and general improvement of quality-of-life, it is still important to prevent that returning testosterone that in the absence of an antiandrogen will now have free access into the cancer cell nucleus from coming in contact with 5AR enzymes and converting to the more powerful dihydrotestosterone by continuing the 5AR inhibitor (dutasteride/Avodart or finasteride/Proscar - whichever having been prescribed while on ADT) during IAD.