

WHY THE USE OF EITHER 5ALPHA REDUCTASE (5AR) INHIBITORS DUTASTERIDE/AVODART (MY CHOICE) OR FINASTERIDE/PROSCAR IN ANDROGEN DEPRIVATION THERAPY?

by Charles (Chuck) Maack, Prostate Cancer Advocate

Let me begin by bringing to the attention of readers that dutasteride/Avodart at 0.5mg or finasteride/Proscar at 5mg takes up to three months of daily use to eventually successfully suppress dihydrotestosterone (DHT) well below 30ng/dl and more preferably closer to 5ng/dl or less. Dutasteride/Avodart has a several day effectiveness, so for those considering taking this medication every-other day, or at least no more than every third day, this should not be considered for at least three months. Thereafter, if inclined to take dutasteride/Avodart every other day or every third day, it would be appropriate to have one's DHT level checked monthly to make sure that suppression continues. If it does so, future checking of the DHT level could accompany scheduled PSA and testosterone checks.

Personally, I prefer dutasteride/Avodart to finasteride/Proscar. My personal reasoning: 5Alpha Reductase (5AR) consists of two enzymes, type 1 (SRD5A1 - Steroid-5-alpha-reductase, alpha polypeptide 1) and type 2 (SRD5A2 - Steroid-5-alpha-reductase, alpha polypeptide 2), that are present on prostate cancer (PC) cells. Both are involved in the conversion of Testosterone (T) to Dihydrotestosterone (DHT). T has more difficulty accessing androgen receptors on prostate cancer cells, and it is when T comes in contact with the 5AR enzymes that it is converted to DHT, with DHT having a better propensity to access the androgen receptors and stimulate PC cell growth. Antiandrogens are administered to block the androgen receptors from T, and DHT access, yet it is difficult to entirely block all androgen receptors. Though LHRH agonists down-regulate the pituitary hormone LH, and consequently LH no longer stimulates Leydig cell testosterone synthesis secretion, they do not diminish T (androgen) 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 enzymes, while dutasteride/Avodart is known to inhibit both types 1 and 2 enzymes, 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. It has been established that type 2 expression is more pronounced in low grade prostate cancer (LGPC) wherein type 1 expression is more pronounced in high grade prostate cancer (HGPC). With the use of 5AR inhibitors, there will be some loss of libido, but not to the extent when administered an LHRH agonist.

Supporting the foregoing is this study from URO Today:

Activity of dutasteride plus ketoconazole in castration-refractory prostate cancer after progression on ketoconazole alone – Abstract

Thursday, 05 November 2009

Dana-Farber Cancer Institute, Boston, MA Tulane Cancer Center, New Orleans, LA.

Ketoconazole is a commonly used secondary hormonal therapy in castration-refractory prostate cancer (CRPC), but disease progression inevitably occurs. Both prostatic and metastatic lesions in patients with CRPC overexpress 5-alpha reductase (SRDA5) type I. We hypothesized that SRDA5 inhibition in combination with ketoconazole would mitigate progression after treatment with ketoconazole alone.

A total of 10 patients with CRPC with progression after ketoconazole treatment were treated with a combination of ketoconazole plus dutasteride 0.5 mg/day, a dual SRDA5 inhibitor.

After dutasteride addition, 8 (80%) of the 10 patients had varying degrees of prostate-specific antigen (PSA) decline relative to baseline. Median progression-free survival after dutasteride addition was 4.9 months (range, 2.7+ to 9.8 months); no patient had a \geq 50% PSA decline.

We conclude that dutasteride added to ketoconazole at the time progression might prolong time to PSA progression in patients with CRPC.

Written by:

Sartor O, Nakabayashi M, Taplin ME, Ross RW, Kantoff PW, Balk SP, Oh WK.

Reference:
Clin Genitourin Cancer. 2009 Oct 1;7(3):E90-E92.

[PubMed Abstract](#)
PMID:19815488

Here is another paper in this same regard:

Phase II trial of ketoconazole, hydrocortisone, and dutasteride (KHAD) for castration resistant prostate cancer (CRPC).

<http://tinyurl.com/y2grqgn>

Reduction by Dutasteride of [Prostate Cancer](#) Events (REDUCE) Trial results:

“The mechanism of dutasteride is not primarily prevention **but the inhibition of growth of small, well differentiated cancers as a result of the intracellular reduction of 5a-dihydrotestosterone (DHT)**. This mechanism which results in the prevention of disease progression is called 'tertiary prevention' and in this setting can be seen as treatment of minimal disease. This effect is seen in spite of the simultaneous, up to 40 times increase in [testosterone](#) (T). It remains unclear why the rise in T does not prevent the effect of the reduction in DHT.”

<http://tinyurl.com/2f7cgz2>

How often do we hear that a physician has told one of our prostate cancer patients that "the jury is still out" on the use of dutasteride/Avodart or finasteride/Proscar?

Here is substantial rebuttal from renowned Medical Oncologist Stephen B. Strum, MD, FACP, who has SPECIALIZED specifically in prostate cancer research and treatment since 1983, and below that are my supportive articles I have compiled:

“The jury. What about this peer-reviewed paper (PRP) published in 2006 in the Journal of Urology.

Scholz MC, Jennrich RI, Strum SB, et al: Intermittent use of testosterone inactivating pharmaceuticals using finasteride prolongs the time off period. J Urol 175:1673-1678, 2006.

Men with prostate cancer treated intermittently with TIP benefit from improved quality of life when TOP with recovered testosterone is prolonged. We examined factors influencing the duration of TOP.

Materials and Methods: We retrospectively reviewed the charts of 101 men treated with intermittent TIP in a 9-year period. Men with positive bone scan, men in whom a PSA nadir of less than 0.1 ng/ml on TIP failed to be achieved and maintained and men in whom testosterone failed to recover to greater than 150 ng/dl during the first 12 months of TOP were excluded. Potential factors predicting prolonged TOP or accelerated time to AIPC were studied with Cox regression analysis.

Results: Patient characteristics were clinical stage T1c-T2a in 51 and T2b-T3b in 11, PSA relapse in 29, and T3c, D0 or D1 in 10. Median PSA was 7.6 ng/ml, Gleason score was 3 + 4 = 7 and TIP duration was 15.8 months. The 60 group 1 patients received finasteride and the 41 in group 2 received no finasteride. Median TOP in groups 1 and 2 was 31 and 15 months, respectively, using Kaplan-Meier analysis. Cox regression analysis indicated that longer TIP, finasteride and increased age predicted longer TOP. A slow PSA decrease while on TIP, higher baseline PSA and increased Gleason score predicted shorter TOP. Cox regression analysis indicated that only higher clinical stage but not finasteride predicted the earlier onset of AIPC.

Conclusions: Finasteride doubles the duration of TOP. AIPC was not increased by finasteride after almost 9 years of observation.

How about this PRP from the Prostate going to the basics of biology.

Eggener SE, Stern JA, Jain PM, et al: Enhancement of intermittent androgen ablation by "off-cycle" maintenance with finasteride in LNCaP prostate cancer xenograft model. Prostate. 2005. PMID 16372330

BACKGROUND: Intermittent androgen ablation (IAA) was developed with the intention of delaying progression of prostate cancer to androgen-independence and improving quality of life. Our previous studies suggest that relative to dihydrotestosterone (DHT), testosterone (T) is a weak inducer of proliferation and a more potent inducer of differentiation. We hypothesize that administration of finasteride (F), a type-II 5-alpha-reductase inhibitor that increases T and decreases DHT, during the IAA "off-cycle" would enhance the efficacy. **METHODS:** After LNCaP tumor establishment, nude mice were castrated and randomized to continuous androgen ablation (CAA), continuous androgen ablation plus finasteride (CAA + F), intermittent androgen ablation (IAA), or intermittent androgen ablation plus finasteride (IAA + F). **RESULTS:** After one cycle of therapy, mice treated with IAA + F had significantly less tumor growth than the other treatment groups ($P = 0.002$). Mice treated with IAA + F had the best survival ($P = 0.048$) and were 3-5 times more likely to be alive 70 days following treatment initiation. **CONCLUSIONS:** IAA with finasteride provides the most favorable tumor growth kinetics and survival compared to both CAA and standard IAA.

How about this "old" paper

Bologna M, Muzi P, Biordi L, et al: Finasteride dose-dependently reduces the proliferation rate of the LnCap human prostatic cancer cell line in vitro. *Urology* 45:282-90, 1995.

OBJECTIVES. To assess the effects of finasteride, a 5-alpha-reductase inhibitor, and of classic antiandrogens on the growth rate of the LnCap human prostate carcinoma cell line, derived from a primary and well-differentiated neoplasm. **METHODS.** Cell proliferation experiments in vitro with and without the antiandrogens cyproterone acetate, hydroxyflutamide, and finasteride in the 0.0001 to 10.0 microM range. **RESULTS.** The growth rate of the LnCap cell line can be dose-dependently inhibited by 5-alpha-reductase inhibition (finasteride) and by antiandrogens (cyproterone acetate and hydroxyflutamide) in vitro, in defined conditions. **CONCLUSIONS.** Besides other human prostate cell lines derived from metastatic sites (PC3, DU145), also in the LnCap cell line an autonomous androgen-dependent mechanism of growth stimulation can be hypothesized, since testosterone and dihydrotestosterone are unable to stimulate the cell proliferation rate at the same molar concentrations. The clinical implications of these results in prostate cancer therapy and the possible

future use of these molecules in the prevention of cancer incidence are discussed.

We are dealing with human lives. What's the big friggin deal about the use of a drug currently given to men for BPH or for hair loss. What is the fuss about using an agent that has been shown to reduce PC incidence by 25% (Proscar) or by 50% (Avodart). How backwards can we be. This is not a drastic measure. The use of Faslodex is far more aggressive than the use of an agent like finasteride (Proscar) or dutasteride (Avodart). If I were one of the leaders of a major support group like Us Too I would be pretty damned angry about the crappy medicine being practiced throughout the world as it relates to many illnesses, one of which is PC, the most common malignancy of men.”

MORE?

<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>

Here is a more recent study.....click on this subject line, then read not only the paper but also the conclusions of The “New” Prostate Cancer InfoLink sitemaster,

but also the comments made by me and others who support a 5AR inhibitor as part of androgen deprivation therapy:

Finasteride, PSA doubling time, and intermittent hormone therapy

AND BELOW ARE MY OWN SUPPORTIVE PAPERS FOR THE USE OF DUTASTERIDE/AVODART:

I have always been a proponent of the addition of a 5Alpha Reductase (5AR) inhibitor when androgen deprivation therapy is prescribed. This is additional information that recognizes the role of 5AR in prostate cancer development and that dutasteride/Avodart plays an important role in inhibiting both Type 1 and Type 2 5AR isoenzyme expression in that development.

Type 1 and Type 2 5alpha-Reductase Expression in the Development and Progression of Prostate Cancer – Abstract

DHT suppression data for the 5alphaR2-specific inhibitor, finasteride, and the dual 5alphaR1/2 inhibitor, dutasteride, show that both isoenzymes are active in benign prostate. Furthermore, immunostaining studies have shown that 5alphaR1 expression increases and 5alphaR2 expression decreases in prostatic intraepithelial neoplasia (PIN) and prostate cancer, compared with nonmalignant prostate tissue. Both isoenzymes appear increased in high-grade compared with low-grade localized cancer. Dual inhibition of both isoenzymes with dutasteride may, therefore, be effective in preventing or delaying the growth of prostate cancer.

<http://tinyurl.com/2ax4wd>

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

<http://www.prostateforum.com/article-03-26-07.html>

"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. I've found this can aid in inducing remission in patients who've failed Lupron. Luckily, Proscar and Avodart don't cause any additional side effects in men on hormonal therapy. But again, we have to measure dihydrotestosterone levels to see if Proscar or Avodart are in fact suppressing dihydrotestosterone. "

And more from Medical Oncologist Myers:

Question posed to Dr. Myers:

The recently published results of a large clinical trial (REDUCE), aimed at evaluating Avodart's effectiveness in reducing the incidence of prostate cancer, found a 23% risk reduction over a four-year period, a result consistent with those from earlier studies (NEJM 4/1/2010). The new study also found, however, that those taking Avodart had a higher incidence of cardiac failure than those in the placebo group (0.7% vs 0.3%), a result that I believe is a new finding. Do you consider the negative cardiac results significant and do they alter your views about Avodart's use as a preventive medication or as a treatment for prostate cancer?

Dr. Myers reply:

"I think this is a very important study on many levels. Proscar and Avodart both work by blocking the conversion of

testosterone to dihydrotestosterone. As water backs up behind a dam, serum testosterone levels will typically increase as the serum dihydrotestosterone levels fall. In prostate cancer cells, dihydrotestosterone is much more powerful at stimulating growth than testosterone. Additionally, dihydrotestosterone specifically stimulates blood flow to both normal prostate tissues and prostate cancer, while testosterone is not very effective at this. We have long had population studies that have shown the risk of prostate cancer is related to the serum dihydrotestosterone and not to the serum testosterone. This led to the hypothesis that dihydrotestosterone was a major factor fueling the appearance and then progression of prostate cancer. An earlier large randomized controlled trial showed that Proscar reduced the risk of prostate cancer, confirming the role of dihydrotestosterone in the development of prostate cancer. Now, Avodart has also been shown to significantly reduce the risk of prostate cancer. Taken together, these two large randomized controlled trials prove beyond all reasonable doubt that dihydrotestosterone is one of the causes of prostate cancer. Further, because both drugs increase serum testosterone by 20-50%, these studies show that testosterone itself is not a major factor in the progression of prostate cancer. I cannot stress how fundamentally important this is. I do not think most physicians caring for men with prostate cancer have fully thought through the implications of these findings. One implication is that as long as the testosterone receptor is present and linked to cancer growth, the presence of dihydrotestosterone has the potential to continue to fuel the progression of the cancer. The obvious question now is whether it might not be better to always suppress dihydrotestosterone.

As indicated in your question, the REDUCE trial did find an increased risk of heart failure in men in the Avodart arm compared with placebo. There were 6,729 patients randomized between

the two arms. In the placebo arm, 0.4% developed congestive heart failure compared with 0.7% in the Avodart arm. This calculates out to 13 cases in the placebo group and 23 cases in the Avodart arm. So, the additional risk of heart failure in the Avodart arm is still quite low.

Dr. Andriole, the author of the paper, has speculated that this was linked to coadministration of drugs like Flomax. Flomax and related drugs, like Hytrin and Cardura, work by blocking epinephrine at what are called alpha 1-adrenergic receptors. This class of drugs has already been reported to exacerbate heart failure and so Dr. Andriole's suggestion is very reasonable. From his comments, I gather they do not specifically know if the patients who developed heart failure on Avodart were also taking an alpha 1 blocker. So, at present, this remains a speculation.

How should we respond to this? Well, first I think that until this is clarified, Avodart should be given to men in congestive heart failure only if the patient is carefully monitored and only if the clinical benefit warrants the use of Avodart. The combined administration of Flomax and related drugs with Avodart should similarly be done with caution in general and not at all in patients in heart failure.”

More:

In a presentation at the February 2007 Symposium of the American Society of Clinical Oncology (ASCO) (the organization for physicians treating cancer), it was reported that dutasteride/Avodart upregulates gene IGEBP3 and down regulates genes TMPRSS2 and TFF3, thus causing PC cell apoptosis and inhibiting cell proliferation (not to mention that this 5Alpha Reductase inhibitor also inhibits the conversion of testosterone (T) to the ten times more powerful stimulant to PC cell growth, dihydrotestosterone (DHT), as well as, for those still having a prostate gland, reducing the size of the gland to provide more efficient surgery or radiation effectiveness). (MY NOTE: The report mentioned “IGEBP3,” but I believe it was a miss-print for “IGFBP3:”

Insulin-like Growth Factor Binding Protein-3, a tumor suppressing gene that showed increased activity with high dose dutasteride).

"Twenty-six men were randomized to 0.5 mg of dutasteride and 24 to 3.5 mg of dutasteride daily for four months before surgery. Twenty-five men had surgery alone. Gene expression profiling was performed, finding 32 unique genes that were upregulated by treatment with dutasteride and 98 genes that were down regulated.

From that group of genes, the researchers said they found at least three specific genes that may play a major role in cancer development: IGEBP3, TMPRSS2, and TFF3.

She said that IGEBP3, which appears to be upregulated by dutasteride, PROMOTES APOPTOSIS AND INHIBITS CELL PROLIFERATION (my emphasis). Previous studies have reported that the expression of this gene is decreased in patients with prostate cancer.

The other two genes-TMPRSS2 and TFF3-both appeared to be downregulated. (by dutasteride/Avodart)

Dr. Mostaghel said TMPRSS2, which is regulated by androgen, PROMOTES THE GROWTH OF PROSTATE CANCER, (my emphasis) while TFF3 BLOCKS APOPTOSIS AND PROMOTES INVASIVE ACTIVITY (again, my emphasis). In addition to its role in prostate cancer, TFF3 is overexpressed in breast cancer and gastrointestinal cancers."

See: <http://www.medpagetoday.com/MeetingCoverage/ASCOProstate/tb/5119>

Or <http://tinyurl.com/3u3jpk>

Here is other information by different researchers making note that TMPRSS2 is a primary factor in promoting the growth of prostate cancer, and in this case estrogen-receptor-beta can also play an important role in suppressing TMPRSS2 and cancer cell growth: "An estrogen-receptor-beta agonist, diarylpropionitrile, limited growth and suppressed expression of *TMPRSS2-ERG* (0.57-fold increase compared with one-fold increase with ethanol; difference 0.43, 95% CI 0.29 to 0.57).

The estrogen-receptor antagonist fulvestrant (Faslodex) also reduced *TMPRSS2-ERG* expression (0.58-fold increase compared with one-fold increase with control; difference 0.42, 95% CI 0.16 to 0.68).

"Taken together," the researchers said, "these results indicate that *TMPRSS2-ERG* fusion can be regulated by [estrogen-receptor] action and that [estrogen-receptor-beta] agonism leads to reduced *TMPRSS2-ERG* transcript expression, resulting in growth suspension."

Full article at:

<http://www.medpagetoday.com/Urology/ProstateCancer/tb/9636>

Also of interest is that it appears the presence of *TMPRSS2-ERG* is less common in prostatic intraepithelial neoplasia (PIN), considered a possible precursor to prostate cancer development, and may not be involved in the *initiation* of prostate cancer cell development. However, once prostate cancer cell development has occurred, the presence of *TMPRSS2-ERG* becomes more prevalent. See:

<http://tinyurl.com/qv3p96>

Here is other information regarding preventing TFF-3 expression:

Treating and preventing cancer characterized by differential expression of trefoil factor 3 (TFF3) include administering to a patient an agent that modulates TFF3 activity or expression and to reducing the physiological effects of TFF3 expression in cells, including inhibiting cell motility and resistance to apoptosis.

Full article at:

<http://www.medpagetoday.com:80/MeetingCoverage/ASCOProstate/tb/5119>

AND HERE IS SOME MORE recent news from a London study regarding the importance to stem the aggressiveness of *TMPRSS2*:

"Researchers knew that prostate cancers commonly contain a fusion of the *TMPRSS2* and *ERG* genes, but the new study found that in 6.6 percent of cases this fusion was doubled up, creating a deadly alteration known as 2+Edel.

Patients with 2+Edel have only a 25 percent survival rate after eight years, compared with 90 percent for those with no alterations in this region of DNA.

"If you get two copies it's really bad news," Cooper said.

Exactly how the duplication makes tumours more aggressive is not clear, though Cooper speculates it could result in higher expression of proteins needed to drive tumour growth or be a more general indicator of genome instability.

Whatever the mechanism, 2+Edel is a clear-cut marker for risk that Cooper hopes will soon be used alongside existing techniques at the time of diagnosis to decide whether men require treatment."

MY POINT IS THAT WITH IT OBVIOUS THAT TMPRSS2 HAS BEEN PROVEN IN RESEARCH TO PLAY A ROLE IN PROSTATE CANCER DEVELOPMENT, ANY MEDICATION FOUND TO SUPPRESS THIS GENE SHOULD BE A REASONABLE ASSET FOR PRESCRIBING – IN THIS CASE, DUTASTERIDE/AVODART!

AND HERE IS ANOTHER:

Read this article from Medical News Today:

They made these comments:

Important reasoning why dustasteride/Avodart should be a component of androgen deprivation therapy

Dutasteride Induces Apoptosis In Androgen Sensitive Prostate Cancer Cell Lines

UroToday...

To read the full article, please go to:

<http://www.medicalnewstoday.com/medicalnews.php?newsid=45741>

AND YET MORE:

<http://www.news-medical.net/?id=30352>

The authors reviewed the published literature to evaluate the progress towards developing an evidence-based prostate cancer prevention strategy. Current studies using existing drugs to prevent cancer have found that androgen suppressing 5-alpha reductase inhibitors (5ARI), such as finasteride and dutasteride, and the selective estrogen receptor modifier, toremifene, have showed promise in reducing the number of cancers at biopsy in men. For example, dutasteride, has reduced by 50 percent the number of cancerous biopsies among men with benign prostatic hypertrophy. A large clinical trial is underway to evaluate whether this drug prevents malignant biopsies in men with elevated prostate specific antigen levels but previously negative biopsies.

AND EVEN MORE: Our results show that **dutasteride reduces cell viability and cell proliferation in both cell lines tested.** AndroChip 2 gene signature identified in LNCaP a total of 11 genes differentially expressed (FC \geq +/-1.5). Eight of these genes, were overexpressed and three were underexpressed. Overexpressed genes included genes encoding for proteins involved in biosynthesis and metabolism of androgen (HSD17B1;HSD17B3;CYP11B2), androgen receptor and androgen receptor co-regulators (AR;CCND1), and signal transduction(ERBB2; V-CAM; SOS1) whereas, underexpressed genes (KLK3; KLK2; DHCR24) were androgen-regulated genes (ARGs).

<http://tinyurl.com/35opvh>

AND THE LIST GOES ON AND ON comparing dutasteride as having attributes somewhat improved over finasteride:

<http://tinyurl.com/2otnbo>

A QUESTION OFTEN COMES UP REGARDING THE PSA LEVEL WHILE ON DUTASTERIDE/AVODART OR FINASTERIDE/PROSCAR:

Per Medical Oncologist Stephen Strum, specializing specifically in research and treatment of prostate cancer since 1983:

<Stephen Strum, MD>

The only time I reset the PSA in the context of the use of Proscar or Avodart is in a man without a diagnosis of PC who is started on one of these agents for BPH. I then use his nadir PSA after 6 months on Avodart or Proscar as the starting point for any PSA kinetic determinations or evaluation of subsequent rise in PSA. Of course, if any man shows a serial rise in PSA at any time, I do not wait for months to evaluate this patient as a likely PC patient.

The use of any 5-alpha reductase inhibitor does not change my nadir requirements for an undetectable PSA in a man with established PC on ADT (androgen deprivation therapy). Insofar as restarting ADT in a man who has been on an IAD (intermittent androgen deprivation) approach, I take into account whether or not the prostate has been removed by RP or treated with RT or Cryo. If there is no discernible prostate tissue, then any rise in PSA during IAD must be assumed to be PC until proven otherwise. I then use the kinetic determinations of PSAV and PSADT + the patient's overall health to decide when to resume another cycle of ADT.

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. **The comments or recommendations I make are not intended to be the procedure for you to now follow; rather, they are to be reviewed along with the comments or recommendations of others for your own further research, study, and discussion with the physician providing your prostate cancer care to come to your own, personal conclusion.**