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Case Report

IAD/Intermittent Androgen Deprivation: When is it Appropriate?

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It is common knowledge that many Prostate Cancer patients on androgen deprivation medications want to know when it is safe to stop the medications prescribed to "see what happens." This procedure is officially identified as "Intermittent Androgen Deprivation" aka IAD. However, this should not be performed haphazardly. There are prerequisites that should be met before considering.

There was a study in 2013 indicating continuous androgen deprivation provided longer survival than Intermittent Androgen Deprivation (IAD). Though that study regarded men with metastatic prostate cancer, it should not have completely ruled out intermittent androgen blockade for some of those men, as well as should have included remarks wherein IAD can be appropriate for men whose prostate cancer has not yet been found to have metastasized [1].

Interestingly, I, along with several other men must have been in the minority in this regard. At the time of that study I was nearly 17 years following beginning the ADT/IAD (androgen deprivation therapy followed by intermittent androgen deprivation on a repetitive cycle) when I put together these remarks. The medications that were prescribed to the men in the study were not explained, but in my case and in the case of others of whom I am aware, our initial journey into ADT had and has been triple hormonal/androgen blockade that included an antiandrogen, an LHRH agonist, and a 5Alpha Reductase (5AR) inhibitor, and here we were many years (well beyond the 5 and 7 years identified in the study) still looking down at the grass rather than up at the roots. Our off times permitted a return of testosterone and improvement in many quality-of-life issues. Not commented in this study of "continuous" androgen deprivation therapy vs IAD is that men on continuous shut down of testosterone production over 2 1/2 to 3 years are likely never going to recover reasonable testosterone levels, since their system goes into "andropause." There is certainly the likelihood of continuous fatigue, continued loss of libido, continued muscle loss in the absence of testosterone as part of continuous ADT.

From my experience and the experience I am aware of others, I will continue to promote not only triple hormonal/androgen blockade, but also intermittent androgen deprivation for those men whose PSA level drops to <0.05ngml and testosterone near or below 20ng/dl while on ADT medications and hold at those levels for at least 12 months. Then, when going off the antiandrogen and LHRH agonist, continue the 5AR inhibitor (dutasteride/Avodart preferred over finasteride/Proscar) to continue to inhibit returning testosterone from converting to the more powerful stimulant to PC cell growth, dihydrotestosterone/DHT. Should PSA subsequently begin elevation, my recommendation is to not wait longer than a 2.0ng/ml level before returning to the antiandrogen followed by the LHRH agonist a week or so later (or at the same time if returning to the GnRH antagonist degarelix/Firmagon). Should PSA and testosterone levels again drop to clinically castrate levels and again remain at those levels for another 12 months, again repeat the IAD cycle.

Further, by 7 months in that study their patient's PSA had fallen to only 4.0ng/ml. With appropriate ADT a patient's PSA should have dropped down into the ultrasensitive/3rd generation PSA levels below 0.1ng/ml within three to four months.

Following the protocol of internationally renowned Medical Oncologist Stephen Strum, a specialist specifically in treatment of

prostate cancer since 1983, and as I just explained above, intermittent androgen deprivation therapy (IAD) should not begin until the patient's PSA has dropped to <0.05ng/ml and testosterone to near or below 20ng/dl, and then having maintained those low, clinically castrate levels, for at least 12 months. I believe Medical Oncologist Charles "Snuffy" Myers, another specialist specifically in treatment of prostate cancer, uses these same levels as guidelines, but is comfortable with patients moving to IAD after 9 continuous months maintaining those levels. And the medications prescribed for ADT by these physicians are an antiandrogen, an LHRH agonist (or GnRH antagonist), and a 5AR inhibitor - triple hormonal blockade. I doubt that the medications prescribed during the 7-month period in this study that led to a PSA drop of only 4.0ng/ml included these three different forms of ADT medications. And I further doubt that when returning to ADT medications when PSA levels increased for those in the intermittent phase of that study, that these three different forms of medication were prescribed [2].

In other words, only reaching a down-trend of PSA to only 4.0ng/ml at 7 months would not even qualify for a move to intermittent androgen deprivation. In my opinion, using the PSA level of 4.0ng/ml as the study baseline for IAD or continuous ADT flawed the study. A drop in PSA over a 7-month period to only 4.0ng/ml is an indication that the medications prescribed as the ADT were either insufficient or only sufficient to hopefully sustain that level with continuous ADT. Under normal circumstances and using 4.0ng/ml as baseline, intermittent androgen deprivation would not even be considered.

Other articles that support IAD follow:

- Read last paragraph [3]
- Read the conclusion [4]

Please note

Medications involved in Androgen Deprivation Therapy (ADT) are known to increase cardiovascular risk. Thus, IT IS IMPORTANT that prior to prescribing any form of ADT medication the patient's other health issues, that would include already present cardiovascular issues, are determined [5].

"Androgen deprivation therapy (ADT) has been the mainstay of treatment for advanced prostate cancer for decades, and has been shown to control disease and improve symptoms. In addition, for men with high-risk localized or locally advanced prostate cancer, short-course ADT in combination with radiotherapy improves survival. There is evidence that ADT increases cardiovascular risk, particularly in men with preexisting cardiovascular disease. This increased risk may apply even with short-course ADT. In an individual patient, the benefits of ADT should be balanced against the risk, and patients who require ADT should have risk factors for cardiovascular disease optimized. There is some evidence to suggest that more contemporary methods of delivering ADT may reduce cardiovascular risk".

Dr. Matthew Roe, a Professor of Medicine at Duke University's Clinical Research Institute (DCRI), the Faculty Director of the Global Outcomes Commercial Mega Trials program, and the Director of their Fellowship Program, remarks: "If a patient who has advanced prostate cancer and known cardiovascular disease is being considered for androgen deprivation therapy, it is important that he speak with his cardiologist. (Presumably, both a cardiologist or cardiovascular specialist and a urologist or oncologist would treat him.) He needs to ensure that all the providers have a discussion about what the best and safest treatment would be before therapy begins. Obviously, this trial (the PRONOUNCE trial regarding which is safer for patients with cardiovascular issues, the GnRH agonist Lupron or antagonist Firmagon (or neither?) [6] - is not completed yet so we don't have any answers. In the meantime, it is certainly in the patient's best interest to ensure that his providers are communicating and trying to jointly determine the right approach".

Please recognize that I am not a Medical Doctor. Rather, I do consider myself a medical detective. 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 deep research and study in order to serve as an advocate for prostate cancer awareness, and, from an activist patient's viewpoint, as a mentor to voluntarily help patients, caregivers, and others interested develop an understanding of this insidious men's disease, its treatment options, and the treatment of the side effects that often accompany treatment. There is absolutely no charge for my mentoring – I provide this free service as one who has been there and hoping to make their journey one with better understanding and knowledge than was available to me when I was diagnosed so many years ago. Importantly, readers of medical information I may provide are provided this "disclaimer" to make certain they 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 their prostate cancer care.

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