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Considerations Necessary Regarding Prostate Cancer with the Options of Surgical Removal of the Prostate Gland or with Androgen Deprivation (Aka Testosterone Inactivating) Therapy (ADT) as Follow-on or Primary Treatment

By Charles Maack

Introduction- Charles (Chuck) Maack (ECaP) – Prostate Cancer continuing patient since 1992, Advocate, Activist, and Mentor to Men so diagnosed and their Caregivers online Worldwide.

With surgical removal of a cancerous prostate gland, PSA nadir should drop to near total absence well into the ultrasensitive testing level below 0.5ng/ml. If this is not achieved, it is likely all cancer cell activity has not been removed, and further treatment is necessary.

A variety of tests should be performed for baseline markers among which should be free Testosterone to determine level as well as any bone issues; deoxypyridinoline (DpD) urine test to determine bone resorption; prolactin level since if high could inhibit ADT therapy as well as cause several other issues (See: https://tinyurl.com/7w5omeo); lipid or fatty acid profile since both de novo and dietary lipids seem to be important contributors to prostate cancer growth and development; inflammation markers since inflammation may drive resistance to androgen deprivation therapy (ADT); and any other markers to aid in determining the best strategy for treatment.

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Strictly as per the compliance and regulations of:

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If imaging is unable to identify the presence of metastasis, Androgen Deprivation (aka testosterone inactivating) Therapy (ADT) should be considered, or salvage radiation in company with ADT. Continuing presence of cancer activity should be met with the intent of eradication, or at least long-term control and management. Treatment with minimal ADT medications with the idea that additional medications would be added when the earlier fail, can lead to unexpected accelerated cancer activity and if not noticed early on can contribute to early mortality. All avenues that contribute to cancer cell growth and proliferation should be addressed.

Since testosterone (aka androgen) is a known stimulator to such growth, production sources of testosterone should be inhibited. Keeping in mind "do no harm," an antiandrogen, with bicalutamide (generic of Casodex) most often prescribed, (flutamide/Eulexin or nilutamide/Nilandron also available) should first be prescribed beginning a week prior to prevent a "flare" effect of sudden testosterone production if then adding the next necessary medication of LHRH agonists Lupron, Trelstar, Eligard, or Zoladex. If initially prescribing the antagonist degarelix/Firmagon, the antiandrogen can be prescribed simultaneously or following this medication since it does not cause the "flare" effect.

The antiandrogen serves to inhibit androgen precursors produced by the adrenal glands travelling to cancer cell androgen receptors. The foregoing are the two initial medications that should be prescribed, and then testosterone as well as prostate-specific antigen (PSA) levels closely monitored since both should significantly drop to indicate ADT effectiveness. If an agonist is prescribed, I would encourage initial administration be a single month dose until it is determined PSA and testosterone levels have significantly dropped indicating the lurking cancer cells are androgen dependent. A testosterone level of 20ng/dl or below indicates effective testosterone clinical castration/control. A PSA level dropping to a nadir of less than (<) 0.5ng/dl is expected and also indicates these medications are serving their role. If the PSA level does not drop below 0.5ng/ml, testosterone may still be reaching 5 Alpha Reductase (5AR) enzymes while enroute to cancer cell androgen receptors. When that is the case, these enzymes convert testosterone to dihydrotestosterone (DHT), a much more powerful stimulant to cancer cell growth and proliferation. To inhibit this conversion, the addition of the 5AR inhibitor (5ARI) dutasteride/Avodart should be considered. The prescribing of these three medications in combination is considered ADT3, also known as triple androgen/testosterone/hormonal blockade.

When ADT3 with the foregoing medications show failure by rising PSA, other medications manufactured to replace the antiandrogen and

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considered more effective (but also much more expensive) could be enzalutamide/Xtandi or apalutamide/Erleada, since these are also "next step" medications when PSA is rising for non-metastatic castration-resistant prostate cancer (nmCRPC). On the near horizon will likely be darolutamide/ODM-201, on the verge of approval by the FDA, for pre-chemotherapy nmCRPC.

The foregoing are considerations to avoid moving to chemotherapy, more toxic to the system, until necessary (again, "do no harm"). However, should even these several medications indicate failure by continuing PSA elevation, or if even early on there is evidence of high risk for metastasis, chemotherapy with docetaxel/Taxotere added to the ADT should be considered. Important to also keep in mind: if a nadir of less than (<) 0.5ng/ml is never reached with the foregoing ADT medications, then chemotherapy should be considered as an addition to the ADT at the point that determination is evident.

Recognizing that ADT has an effect on bone health as well as contributing to osteonecrosis of the jaw, imaging should be performed with Quantitative Computerized Tomography (QCT). QCT imaging can distinguish vascular calcifications and degenerative joint disease as not being bone, thus providing a more accurate bone mineral density (BMD) result. The supposed "Gold Standard" Dual-Energy X-ray Absorptiometry (DEXA) imaging falsely reads calcification and calcium in blood vessels close to bone as being bone density, giving the false impression that all is well when it is not. Whether or not the imaging identifies bone issues, treatment to prevent issues occurring should commence with ADT. Understanding these issues and recommendations for treatment can be reviewed here: https://tinyurl.com/3m78ymg.

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. As noted in: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4516188/

"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 MegaTrials 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?) https://tinyurl.com/yxnw5kb6) 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."

So much to be considered, but so important to do so.

Disclaimer: 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.