ORCHIECTOMY – A SURGICAL PROCEDURE IN WHICH ONE OR BOTH TESTICLES ARE REMOVED

A compilation of information by Charles (Chuck) Maack – Prostate Cancer Continuing Patient, activist, and Mentor - regarding anticipated testosterone level results following Orchiectomy, and reminding that testosterone is also produced by other sources than testicular.

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 of prostate cancer 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.

I provided information below as a response to a prostate cancer patient in Australia with a testosterone level of 1.7nmol (50ng/dl) and still rising PSA post bilateral orchiectomy.

The level 1.7 if nmol/L is equivalent to 50ng/dl, and 50ng/dl *used to be considered castrate level* but no longer so. 20ng/dl (0.68nmol/L) is the level considered castration level that has been achieved with androgen deprivation medications to reduce the testosterone level of active testicular/Leydig Cell production. With bilateral orchiectomy, testosterone, on average, falls to 15 ng/dL (0.5 nmol/L). Using the explanation as to androgen (as testosterone) produced from other sources, your orchiectomy has not sufficiently lowered testosterone to suppress PSA elevation. An antiandrogen such as bicalutamide/generic of Casodex *might* suppress adrenal gland produced androgen from accessing cancer cell androgen receptors (AR). Adding dutasteride/Avodart, a 5Alpha Reductase (5AR) inhibitor

prescribed to inhibit androgen/testosterone from conversion to the stronger stimulant to cancer cell growth, dihydrotestosterone/DHT, *might* serve to inhibit any androgen not suppressed by the antiandrogen while enroute to 5AR and bring PSA down and manageable. If these are not found effective, then either abiraterone/Zytiga to totally shut down testosterone production from all sources (testicular, adrenal glands, and that produced within cancer cells) or enzalutamide/Xtandi to block androgen access to cancer cell androgen receptors, may be alternatives – since these last two are extremely expensive medications, it would be important that they are covered under your government or private health insurance plan. Ideally, being prescribed both in combination could likely be even more effective. Unfortunately, it is unlikely health insurers would cover the prescribing of both expensive medications at the same time. Please note that I am only expressing considerations to discuss with your treating physician (Medical Oncologist?).

Testosterone from other sources than testicular:

Despite testicular shut down of testosterone production either by LHRH agonists/GnRH antagonist, the adrenal glands still secrete precursors to androgens such as testosterone and advanced androgen independent prostate cancer cells acquire complete steroidogenic ability to synthesize androgens and underline the fact that castration and inhibition of testosterone production in the testes may not achieve androgen deficiency in prostate cancer cells in advanced stages of the disease. (**MY NOTE: Though the below reference goes into detail as to how androgen can be produced from other sources (adrenal glands; and cancer cells can produce testosterone within themselves which is derived from cholesterol) to fuel androgen "independent" cancer cells, the same can occur to continue to fuel androgen "dependent" cancer cells.)**

From http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2802176/ : **(I have emphasized in bold lettering that of interest)**

Results and Discussion

The results described in this study show for the first time that androgen-independent human prostate cancer cells are able to acquire complete steroidogenic potential and are capable of synthesizing testosterone from cholesterol, indicating an intracrine regulation of AR in advanced stages of prostate cancer. **Several studies have shown the expression of key steroidogenic enzymes in prostate**

cancer cells indicating that these cells are able to synthesize androgens from adrenal precursors (El-Alfy, et. al., 1999,Nakamura, et. al., 2005,Stanbrough, et. al., 2006). The presence of functional AR in advanced stages of the disease and the presence of testosterone and DHT, sufficient to activate the AR, in cancer tissues under androgen ablation therapy, also support this notion (Gelmann, 2002,Mohler, et. al., 2004,Titus, et. al., 2005). The purpose of our studies was to **determine whether prostate cancer cells** in advanced stages of the disease **can synthesize testosterone from cholesterol hence making them completely independent of serum testosterone and/or adrenal steroid precursors**.

In conclusion, our results clearly show for the first time that advanced androgen independent prostate cancer cells acquire complete steroidogenic ability to synthesize androgens and underline the fact that castration and inhibition of testosterone production in the testes may not achieve androgen deficiency in prostate cancer cells in advanced stages of the disease. Our results also explain the essential role of AR in survival and proliferation of androgen-independent prostate cancers under androgen-ablation therapy and suggest that inhibitors of steroid biosynthesis in prostate cancer cells may be required to completely abolish the androgens in these tumors for its therapy.