ORCHIECTOMY – A SURGICAL PROCEDURE IN WHICH ONE OR BOTH TESTICLES ARE REMOVED – IS IT SUFFICIENT TO INHIBIT ANDROGEN FROM ACCESS TO PROSTATE CANCER CELLS?

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.

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 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, this patient's orchiectomy had 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 one's government or private health insurance plan. One would think that being prescribed both in combination would likely be even more effective. Well, according to this ASCO Post http://www.ascopost.com/News/59119 "Combining enzalutamide with abiraterone acetate and prednisone is not indicated after PSA progression during treatment with enzalutamide alone; hypertension and elevated liver enzymes are more frequent with combination therapy." The same can then be said that during treatment with abiraterone alone, combining with enzalutamide would not be indicated. I do have this in my files as to which might be considered first to be administered: Abiraterone to Enzalutamide slight advantage over Enzalutamide to Abiraterone sequence as far as PSA control, though no significant advantage of either as far as over-all survival. See http://tinyurl.com/mhedzjo. "This could possibly be attributable to longer prostate-specific antigen progression-free survival with second-line enzalutamide compared with abiraterone." In any event, it is unlikely health insurers would cover the prescribing of both expensive medications at the same time. Please note that I am only describing considerations to discuss with your treating physician (preferably a Medical Oncologist).

Testosterone from other sources than testicular:

Despite testicular shut down of testosterone production either by LHRH agonists or GnRH antagonist – or by orchiectomy - the adrenal glands still secrete precursors to androgens such as testosterone and prostate cancer cells acquire the ability to synthesize androgens thus castration and inhibition of testosterone production in the testes may not achieve androgen deficiency in prostate cancer cells, particularly those 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.)**
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2802176/

Of further note regarding effects of orchiectomy vs ADT, this paper https://tinyurl.com/y77762w4 concludes that a consequence of

orchiectomy is greater increases in fat accumulation and increase in insulin resistance than similar effect from ADT medications.