ANDROGEN DEPRIVATION THERAPY – HOPEFULLY EXPLAINED IN A MANNER THAT CAN BE UNDERSTOOD BY PATIENTS AND/OR THEIR CAREGIVERS

THE FOLLOWING IS INTENDED TO EXPLAIN THE PROTOCOLS USED WHEN A PROSTATE CANCER PATIENT'S PRIMARY TREATMENT HAS MOVED TO ANDROGEN (TESTOSTERONE) DEPRIVATION WITH AN ADDED CAVEAT AT THE END REGARDING EARLY USE OF CHEMOTHERAPY

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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. I have dedicated my retirement years to continued research and study in order to serve as an advocate for prostate cancer awareness, and, from a activist patient's viewpoint, to voluntarily help patients, caregivers, and others interested develop an understanding of prostate cancer, 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 your journey one with better understanding and knowledge than was available to me when I was diagnosed so many years ago. Readers of this paper must 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 your prostate cancer care

Androgen Deprivation Therapy (ADT) known by some as Testosterone Inactivating Pharmaceuticals (TIP) or Testosterone Reducing Therapy (TRT), involve medications prescribed to shut down the Prostate Cancer patient's system from producing testosterone as well as blocking testosterone access into the nucleus of cancer cells. The reasoning is that testosterone is known to play a role in stimulating prostate cancer cell growth and proliferation (dividing/multiplying). Actually, testosterone only provides "some" stimulation – the real stimulation comes when that testosterone is able to enter the multitude of "androgen receptors" on each cancer cell wherein, if not blocked or inhibited, comes in contact with what are known as 5Alpha Reductase (5AR) isoenzymes that convert testosterone to the metabolite "dihydrotestosterone" (DHT), an up to ten times more powerful stimulant to cancer cell growth than testosterone.

Though LHRH agonists or a GnRH antagonist are expected to shut down testicular production of the main source of testosterone, they do not shut down another

source of testosterone production, the adrenal glands. So, to make sure the adrenal gland testosterone is not able to enter the nucleus of cancer cells, an anti-androgen is prescribed to block that access (bicalutamide/Casodex, flutamide/Eulexin, or nilutamide/Nilandron). Since there can be androgen receptor mutation wherein testosterone can still enter the cancer cell nucleus and come in contact with 5AR isoenzymes, a 5AR "inhibitor" to hopefully block that testosterone from coming in contact with 5AR isoenzymes and converted to DHT, is prescribed (dutasteride/Avodart – preferred – or finasteride/Proscar); further explained here: http://tinyurl.com/74bkzam

Should this protocol eventually show failure in keeping testosterone from cancer cells, and if the cancer has already metastasized away from the prostatic bed and into lymph nodes or bone, there are two recent medications still available and approved in some countries for those patients with known metastasis that have been shown as effective prior to having to move to more toxic "chemotherapy:"

These are Zytiga/abiraterone acetate that pretty much totally shuts down the three sources of testosterone production – testicular production, adrenal gland production, AND testosterone even cancer cells can produce within themselves! This medication is pretty much a "super" testosterone reducing medication. The other is Xtandi/enzalutamide that provides a much more total block of testosterone from access to the androgen receptors on cancer cells – pretty much a "super" anti-androgen. One or the other of these two drugs have been very successful for some for many months to years, and not as successful for others. For those patients wherein either medication has shown early failure, these patients may have what is known as a truncated AR-V7 splice variant in their blood stream that inhibits the effectiveness of these medications. With that possibly being the case, there are a couple drugs under study to over-ride the AR-V7 activity but as of the time of this writing still not available for prescribing – Galeterone and Neclosamide. A recent study, however, has also determined that an over-the-counter product, berberine, appears to also over-ride the activity of AR-V7, so could be tried by patients approved by their treating physician pending the results of Galeterone and/or Neclosamide trials. Another recent study made note that statins can boost the effectiveness of Zytiga.

When a patient is on either Zytiga or Xtandi successfully for quite some time, but then that protocol appears to be failing, the other of these medications could be tried (if available in the country where one lives).

The foregoing explains what is expected with being prescribed ADT/TIP/TRT to hopefully forestall having to move to the more toxic medications prescribed in "chemotherapy."

When these former protocols are evidently failing, chemotherapy then becomes the next form of treatment wherein most often docetaxel/Taxotere, usually accompanied by Prednisone or Carboplatin or other medication the physician may prefer, is administered every three weeks for a series of six such administrations. Upon completion of that series, a return to the foregoing protocols are often found to then once again having become effective in reining in one's prostate cancer enabling continued management for a hopefully long future.

An added caveat to the foregoing: Recent studies (2015) have concluded that for men with high grade high risk prostate cancer at diagnosis, or with known metastases at diagnosis, or found to have moved to metastases despite surgical removal or radiation, early intervention with chemotherapy accompanied by androgen deprivation medications provide longer subsequent survival as much as a median of 18¾ months from the time of beginning this treatment. So this, too is an alternative to consider. **But, important to keep in mind**, studies for this protocol involved mainly men with a median age of 63 years of age, thus for the most part, healthier than those older. With this in view, in a wide-ranging and comprehensive review at the ASCO Genitourinary Cancers Symposium, in San Francisco, Maha Hussain, MD, FACP, FASCO, Professor of Medical Oncology at the University of Michigan, urged caution in the selecting of patients for this protocol stating it is important they be "fit" in order to reasonably weather the side effects involved in chemotherapy treatment. See: http://tinyurl.com/jt389sl .