HIGH GRADE, ADVANCED, METASTASIZED, AGGRESSIVE PROSTATE CANCER AT DIAGNOSIS – TREATMENT CONSIDERATIONS

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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 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. 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 prostate cancer care.

In recognizing prostate cancer has already metastasized beyond the prostate gland, surgical removal of or radiation to the prostate gland would only "debulk" the amount of cancer to have to still deal with, but would not totally eradicate the cancer. Both surgical removal and radiation are accompanied by possible side effects of impotence, erectile dysfunction, incontinence, and with radiation, side effects often are not experienced until months to years after.

There are papers that support radiation accompanied by androgen deprivation therapy, despite known metastasis, as possibly prolonging life. There are other papers that discuss going right to chemotherapy with a series of docetaxel/Taxotere, then moving to androgen deprivation medications to hopefully extend reining in continued cancer growth. There are others that, in view of known metastases, might recommend Provenge/sipuleucel-T at this point to enhance the immune system so that subsequent medications may be more effective (See: http://tinyurl.com/kd4sfkx)

Should the foregoing not be considered, the following should be considered as a reasonable and aggressive protocol:

1. ADT3 starting with the LHRH antagonist Firmagon/degarelix for the first two months to make sure testosterone is dropping down to castrate level below 32ng/dl but preferably near or below 20ng/dl – then switching to one

- of the LHRH agonists of either Lupron, Zoladex, Trelstar, or Eligard that can be administered in longer lasting doses. If known to have cardiovascular or diabetes issues, or if prone to stroke, this medication may not be appropriate and must be discussed with the prescribing physician.
- 2. At the same time, include the antiandrogen bicalutamide/Casodex at one 50mg tablet daily indefinitely for now to block testosterone still being produced by the adrenal glands from accessing androgen receptors and consequently the nucleus of cancer cells.
- 3. Also at the same time include the 5Alpha Reductase inhibitor dutasteride/Avodart at one 0.5mg capsule daily as a safeguard, should any testosterone access the nucleus of cancer cells via faulty androgen receptors, in order to inhibit conversion of that testosterone to the five times more powerful stimulant to prostate cancer cell growth and proliferation, dihydrotestosterone/DHT. If there are known liver issues, the prescribing of numbers 2 and 3 must be discussed with the prescribing physician since these medications could then cause increased liver damage.

The foregoing is triple-hormonal blockade to aggressively rein in current aggressive cancer activity as explained here http://tinyurl.com/3ulagd2 supported by http://tinyurl.com/74bkzam.

- 4. In view of known metastases, consider bone mineral imaging to determine the presence of either osteopenia or osteoporosis, and since in any event metastases will involve bone, consider prescribing either Xgeva/denosumab, a subcutaneous monthly injection, or Zometa, an IV infusion. Also consider taking a bone supplement with Strum's Bone Formula recommended since it will appropriately supplement Vitamin D3, Calcium, and other important nutrients (See: http://tinyurl.com/87n69ru then click on "Supplement Facts"). If prescribing Xgeva or Zometa is being considered, it is VERY IMPORTANT to first have all dental work completed since while on these medications there should be no tooth extractions, root canals, or any procedure that will have impact on the jawbone (See http://tinyurl.com/3m78ymg)
- 5. Have a blood draw to determine Prolactin level (want under 5.0ng/ml) and 25-hydroxy Vitamin D level (want at least 50ng/ml and for prostate cancer patients better within a range of 65 to 75ng/ml) and based on results, if Prolactin too high prescribe cabergoline one 0.25mg tablet every Monday, Wednesday, and Friday then checked again a month later; once below 5.0ng/ml no longer requires testing; if Vitamin D3 level under 50ng/ml, prescribe Vitamin D3 as a supplement with sufficient dosage to elevate to

- appropriate range; usually requires at least 6000 IU total daily intake that, if taking Strum's Bone Formula will not have to be taken separately. See http://tinyurl.com/7w5omeo regarding Prolactin and http://tinyurl.com/748cx5c regarding Vitamin D3)
- 6. Check all blood levels at least quarterly to include PSA, testosterone, DHT until certain well below 30ng/dl, 25-hydroxy Vitamin D until within appropriate range, Prolactin until below 5.0ng/ml.
- 7. If bone pain is experienced during ADT, the prescribing of Xofigo/alpharadin/Radium 223 should be discussed with the treating physician to hopefully ease the discomfort (See http://tinyurl.com/n8wqbmz)
- 8. Should ADT3 be effective in bringing PSA down to 0.05ng/ml and testosterone level down to near or below 20ng/dl and those levels remain constant for at least 12 months, intermittent androgen deprivation (IAD) could then be considered wherein the LHRH agonist/antagonist and antiandrogen could be stopped in order to permit regeneration of testosterone and improvement in quality of life, BUT the 5AR inhibitor dutasteride/Avodart must be continued in order to inhibit that returning testosterone from converting to dihydrotestosterone. With this maintenance medication the "time off" could extend for several months to years before elevating testosterone may overcome the inhibition of conversion to dihydrotestosterone at which time, with PSA rise to no more than 2.0ng/ml, a return to LHRH agonist/antagonist and antiandrogen should be added back to the continuing Avodart for a return to ADT3. The same procedure as just explained would then again be followed.
- 9. Side effects that might (not necessarily will) occur while on ADT medications and remedies to ease or eliminate those side effects are explained here http://tinyurl.com/3p9pl3p.
- 10. At such time as ADT3 shows failure because of continuing rise despite the triple hormonal blockade, the antiandrogen should be stopped since androgen receptor mutation (ARM) may be occurring wherein the antiandrogen medication then moves through androgen receptors as a fuel to cancer cell growth. If over another month or two PSA continues to elevate, or if the PSA is very aggressively elevating, it would be time to first consider the prescribing of Provenge/sipuleucel-T to enhance effectiveness of the immune system before moving to other medications important to reining in cancer cell growth prior to moving to the more toxic chemotherapy agents.
- 11. Following Provenge, or if the cancer is appearing to be too aggressive in development, either Zytiga/abiraterone acetate or Xtandi/enzalutamide

- should be considered, and should either option show subsequent failure, the other of these two medications could be considered since both have different control of cancer activity. See http://tinyurl.com/ln6elg7.
- 12. With continued failure of ADT medications it would be time to move to the chemotherapy agent docetaxel/Taxotere and possibly a combination with other chemo agents for a more synergistic effect.
- 13. With failure of usual chemotherapy agents, other medications are available or others may be approved by that time that can at least provide a palliative effect for a hopeful many years.