PALLIATIVE CARE

by Charles (Chuck) Maack – Prostate Cancer Activist/Mentor

Palliative care regarding prostate cancer begins with diagnosis to help the patient understand his disease and its treatment as well as ease side effects that may accompany treatment. Palliative care becomes even more important when cure is unlikely because prostate cancer has returned following earlier treatment options (surgical removal of or radiation to the prostate gland) or when a man is initially diagnosed with advanced, high grade, and aggressive prostate cancer wherein metastases – the migration of cancer to other locations in the body - may have already occurred.

Following prostate cancer recurrence or for advanced, high grade, aggressive prostate cancer, palliative care at this time usually involves the prescribing of androgen deprivation medications to shut down testosterone production and starve cancer cells since testosterone, also known as androgen, is considered the primary stimulant to prostate cancer growth and proliferation. Luteinizing hormone releasing hormones are prescribed to shut down testicular production of testosterone, the main source of testosterone. Injectible medications prescribed for this purpose are known as either the agonists Lupron, Zoladex, Eligard, or Trelstar, or a more recent "antagonist" known as Firmagon, generic name degarelix. Since these agonists or the antagonist have no effect on testosterone also produced by the adrenal glands, though in a very much smaller amount than testicular production, it is important to recognize this other source of testosterone. Anti-androgens are prescribed to block testosterone from activating a multitude of androgen receptors on cancer cells and permitting that testosterone to enter the cancer cell nucleus. Primary anti-androgen oral medications are bicalutamide, flutamide, or nilutamide. There are Medical Oncologist specialists in specifically prostate cancer who consider the possibility of faulty androgen receptors - wherein testosterone could still access the cancer cell nucleus - who prescribe yet another medication known as a 5Alpha Reductase inhibitor; either the medication dutasteride brand name Avodart, or finasteride brand name Proscar are prescribed. The reasoning is that should testosterone enter the cancer cell nucleus and come in contact with 5Alpha Reductase isoenzymes, that testosterone will be converted to dihydrotestosterone, a five to ten times more powerful stimulant to prostate cancer cell growth and proliferation. The 5Alpha Reductase inhibitors block testosterone from making this contact, and thus aid in prolonging the period in which androgen deprivation therapy can be effective in reining in and managing one's prostate cancer. For many men, this three-medication approach depriving cancer cells of testosterone - also known as triple-hormonal blockade - can cause at least some

cancer cell apoptosis (death) as well as control cancer development and permit managing prostate cancer as somewhat a chronic disease for many years before eventually losing effectiveness and the cancer becoming what is known as hormone refractory prostate cancer. When this occurs, there are still several medications that can be employed to keep the cancer reined in from further development. The medication Provenge, also known as sipuleucel-T, can be prescribed to boost the immune system for medications to become more effective. For patients who already show metastases of the cancer elsewhere in the system, recently new medications Zytiga, also known as abiraterone acetate, or Xtandi, also known as enzalutamide, can be prescribed. Our hope is that these medications will soon become available to men who are failing the usual androgen deprivation therapy but not yet showing signs of metastasis.

Zytiga is an irreversible inhibitor of CYP17. CYP17 is an enzyme that plays a central role in allowing the body to produce testosterone and cholesterol. When Zytiga binds to this enzyme, it is permanently disabled and the production of testosterone is blocked in the testicles, in the adrenal glands, and within cancer cells. In the absence of this "fuel," apoptosis/cell death can occur.

Xtandi has a mode of action that is intended to block the binding of testosterone/androgen to the androgen receptor and thus interfere with the process of testosterone access to the cancer cell nucleus via androgen receptors that otherwise drives tumor cell growth. As with Zytiga, in the absence of this "fuel," apoptosis/cell death can occur.

In the absence of availability of either of these medications, ketoconazole accompanied by hydrocortisone or triamcinolone can be prescribed to provide a similar but weaker effectiveness than these newer drugs.

If and when the former medications lose their effectiveness, men are then moved to the prescribing of chemotherapy agents, with docetaxel, also known as Taxotere, the more commonly prescribed initial chemotherapy medication. There are then several other chemotherapy agents that can be presribed to hopefully extend the patient's survival for several years.

With research around the world constantly identifying the many pathways that are involved in the development and growth of prostate cancer, and several medications available to control or ease the side effects of chemotherapy medications, as well as many new medications in trials, our hope is that sometime

in the not too distant future scientists will discover that elusive “something” that will prevent prostate cancer, and hopefully all cancers, from developing in our bodies.