

APPROPRIATE ANDROGEN DEPRIVATION THERAPY FOR ADVANCED AND RECURRING PROSTATE CANCER

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

http://www.urotoday.com/index.php?option=com_content&task=view_ua&id=2221381 supports a belief I have always maintained that despite androgen deprivation with, for example, LHRH agonists or GnRH antagonists as monotherapy or in company with antiandrogens, or with antiandrogens as monotherapy, that androgen receptors (AR) are not entirely blocked from testosterone/androgen that might still be produced, albeit minimal, via testicular leydig cell production, or certainly still being produced via the adrenal glands. And with this recognition, the importance of 5Alpha Reductase (5AR) inhibition by dutasteride/Avodart (more effective) or finasteride/Proscar to prevent conversion of testosterone/androgen to the more powerful stimulant to prostate cancer cell growth, dihydrotestosterone (DHT) is evident. And when we realize that with LHRH or GnRH monotherapy androgen receptors are not restricted from the activity of 5AR by antiandrogen blockade, the importance of 5AR inhibition is even more evident. Thus, the importance of triple androgen/hormonal blockade when treating advanced or recurring prostate cancer.

Should the LHRH agonist/antiandrogen/5AR inhibitor treatment fail, I would expect that the antiandrogen would be withdrawn and HDK/HC would be the next line of defense. And should the LHRH agonist/5AR inhibitor/HDK-HC treatment fail, Medical Oncologist Charles E. “Snuffy” Myers, recognized for expertise in the treatment of advanced and recurring prostate cancer, considers the mTOR pathway as a promising new next target to curtail androgen independent prostate cancer. The mTOR (mammalian target of rapamycin) pathway is activated in many cancers and has become an exciting new target for inhibition with agents, known as mTOR inhibitors, now showing promise in clinical trials in different tumors.

The following by Dr. Robert A. Figlin, Arthur and Rosalie Kaplan Professor of Medical Oncology and Chairman of Medical Oncology and Therapeutics Research at the City of Hope National Medical Center, Duarte, California, [describes evidence of the importance of inhibition of the mTOR pathway:](#)

Prostate cancer

Inhibition of the mTOR pathway may also be highly relevant in prostate cancer. Loss of the tumor suppressor gene *PTEN* occurs in 30%–60% of prostate cancers and leads to activation of the PI3K/Akt pathway and mTOR. Loss of *PTEN* correlates with a high Gleason score, advanced stage, and androgen independence. This pathway provides a target in androgen-resistant patients.

There are a number of ongoing mTOR-based trials in prostate cancer evaluating temsirolimus, everolimus, rapamycin, and deforolimus in a variety of combinations. “My bias is that we have to recognize that most patients will not benefit from mTOR inhibition monotherapy, but will need combinations with other agents, although some tumors may be exceptions to this,” he said. “It’s rare that mTOR inhibition by itself is sufficient to turn off cancer cell growth.”

More at:

<http://www.nccn.org/professionals/meetings/13thannual/highlights/1316.html>

or if doesn’t open, try <http://tinyurl.com/cbwmou>