XTANDI/enzalutamide or ZYTIGA/abiraterone acetate Being Considered?
WAIT!

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

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.

We have become well aware that two of the newer medications, Xtandi/enzalutamide or Zytiga/abiraterone acetate, are being prescribed for men also dealing with the presence of metastases when usual androgen deprivation therapy (ADT) medications for prostate cancer appear to be losing effectiveness. But it now appears that it would be prudent to first test the patient's blood for the presence of androgen-receptor splice variant7 (AR-V7) since the presence of this variant in the blood stream may be associated with resistance to the effectiveness of either of these medications. If this is the case, treatment with Galeterone or Niclosamide should be considered or, if these medications are not yet available, other protocols of treatment must be considered. A supplement that may be considered is berberine, since this product may be what is needed for those patients who have had no success with either Zytiga/abiraterone or Xtandi/enzalutamide because they may have activity of the AR-V7 AR splice variant in their system. According to this paper berberine ***"also contributed to the reduction of the truncated AR-V7 splice variant, suggesting berberine could sensitize prostate cancer to existing treatments such as abiraterone, enzalutamide, and docetaxel."*** This should certainly be discussed with one's

treating physician and considered in one's protocol - **BUT should not be ordered/taken personally without physician approval**.

http://cdmrp.army.mil/pcrp/research_highlights/15zhang_highlight.shtml

Berberine has also been discussed in papers as an alternative to Metformin.

If considerting berberine, important to be aware of effects:
https://examine.com/supplements/berberine/

For those of you who have already been prescribed either Xtandi or Zytiga and the medication has shown failure from the onset, it would be important to check for AR-V7 splice variant, a truncated form of the AR, being present in the AR circulating in your blood stream. AR-V7 has been associated with non-response to commonly-used oral therapies for mCRPC (both Xtandi and Zytiga). If the variant is found in your bloodstream such prescribing would likely be fruitless. OR, purchasing of berberine, with the approval of your treating physician, may be a reasonable consideration to determine if Xtandi or Zytiga then show effectiveness. **PLEASE NOTE**, if already prescribed Metformin and intending to start berberine, Metformin must first be stopped since some of the activity of berberine is similar to that of Metformin and the combination could be dangerous.

Suggested doses of berberine, that seems to reduce total cholesterol, low-density lipoprotein (LDL or "bad") cholesterol, and triglyceride levels in people with high cholesterol , are explained here: http://tinyurl.com/pfd5fvh under the menu word "Uses." Your treating physician should work with you to determine the most effective dose to take daily. As suggested in this paper, 500mg two or three times daily spread out and best with meals could be considered.

Oliver Sartor, one of the top research physicians regarding prostate cancer has weighed in on this AR-V7 subject recognizing the futility of prescribing either Xtandi or Zytiga if this androgen receptor variant is found to be present in the blood stream.

See: Clinical Relevance of AR-V7 in Castrate-Resistant Prostate Cancer

http://www.practiceupdate.com/Content/18435/37/3 (if unable to open, it is free to subscribe)

A July report in the "Asco Post" provided this information: "AR-V7 Predicts Resistance to Enzalutamide and Abiraterone in Men With Castration-Resistant Prostate Cancer" http://tinyurl.com/nbsjszr

A posting on 11/19/2014 in the "Asco Post" reports: "Researchers believed that Galeterone could be effective against castration-resistant prostate cancer because it disrupts the androgen receptor signaling pathways that are involved in the cancer, and preclinical work has shown it is active against the AR-V7 variant." See:

http://www.ascopost.com/ViewNews.aspx?nid=20590

Science Daily provided a more detailed report on 11/18/2014: "Galeterone will now be tested in a phase III trial in which patients with metastatic CRPC with the AR-V7 variant will be randomised to receive either galeterone or enzalutamide. The researchers will be looking to correlate AR-V7 with response to galeterone and to see what effect the drug has on the length of time patients survive without their disease progressing. This phase III trial will be noteworthy for being the first prostate cancer trial to assess a biomarker, namely AR-V7 in circulating tumour cells, as a predictor of response at the same time as testing the efficacy of the drug,"

http://tinyurl.com/lgkwhk8

The ARMOR3-SV trial is currently accepting patients (unfortunately not in my city of Wichita, Kansas with closest either Denver or Dallas). If interested, please review https://clinicaltrials.gov/ct2/show/study/NCT02438007?show_locs=Y#locn

If the medication Galeterone is found successful as compared to enzalutamide/Xtandi, Glaleterone may be the next medication added to the prostate cancer arsenal of medications to treat metastatic castrate resistant prostate cancer (mCRPC) patients found to have the presence of AR-V7 in circulating tumor cells in their blood stream.

Clinical Cancer Research provided information regarding another possible medicine in this regard known as Niclosamide: See:
http://tinyurl.com/na97j8q

PubMed 24740322 also reports on Niclosamide. See:
http://www.ncbi.nlm.nih.gov/pubmed/24740322

In view of the foregoing, it would appear that prior to prescribing/administering either Xtandi/enzaluatide or Zytiga/abiraterone acetate, a blood draw to test one's Circulating Tumor Cells (CTC) for the androgen receptor variant AR-V7 is reasonable since with such presence, prescribing either may be ineffective and, as noted earlier, the prescribing of Galeterone or Niclosamide considered. The concern, however, is that Galeterone or Niclosamide will not be available pending results of further trials….we can only hope that availability of either mediication will be fast-tracked if trials show promise.

The form to request AR-V7 testing from Johns Hopkins laboratory can be seen below at the end of this paper.

"Galeterone acts by disrupting the androgen receptor signaling pathway, which is the primary pathway that drives prostate cancer growth. The pathway is ordinarily activated by the binding of male hormones, or androgens, such as testosterone and the more potent androgen dihydrotestosterone, or DHT, to the ligand binding domain of androgen receptors in prostate cancer cells. Galeterone disrupts the activation of the pathway through multiple mechanisms of action."

ALSO IMPORTANT TO BE AWARE IF BEING PRESCRIBED EITHER ENZALUTAMIDE/XTANDI OR ABIRATERONE ACETATE/ZYTIGA
If you are a patient also experiencing cardiovascular issues, the toxicity of the foregoing medications may be detrimental to those issues. Please read the following and discuss with your treating physician:

New Hormonal Agents for Prostate Cancer May Increase Risk of Cardiotoxicity

http://tinyurl.com/o8hmcty

FORM TO REQUEST TESTING FOR AR-V7 FROM JOHNS HOPKINS MEDICAL LABORATORIES

Johns Hopkins Genomics - MDL
1812 Ashland Ave
Room 245**Johns Hopkins Medical Laboratories**
Park SB202 600 North Wolfe Street
Baltimore, MD 21205
Baltimore, Maryland 21287
410 **410-955-955-**-14381438 **or** or 441010-614-955-1997-8363
Email: moleculardpathresults@jhmi.edu**Director: Dr.**

Molecular Diagnostics Laboratory Request

AR-V7 Prostate Cancer Assay

Kathleen Murphy

Comment:

Physician Name: _____

Address: _____

_____

Phone: _____ _____ Fax: _____

Signature: _____

UPIN# _____

History /SS#_____

Patient Name:_____

Date of Birth: _____ Sex: _____

Home Address: _____

_____

ATTACH COPY OF INSURANCE CARD (Front and Back)

Diagnosis: _____ ICD10: _____

Specimen Type:

☐ Blood: 21 cc, yellow-top ACD tubes

Time_____

Collection Date_____

Collection and Transport Instructions:

1. Specimen mus
2. Blood draws should be scheduled on Monday holidays, to allow overnight shipping and recei weekends.
3. Blood samples will be collected in three 8.5 mL BD Vacutainer ACD Solution A tubes (BD ACD Product #s for the BD ACD-A tubes in the US is 364606.
4. Ensure that at leas shipping.
5. After blood draw, invert the tubes gently 180 degrees and back 3
6. Store samples at 4-8° overnight in a refrigerator. Ship the same day
7. Activate the FEDEX cold box by pressing the actuator button wraps snugly in the shipping box, along with the sample requisition sheet.

ection. Specimens received after 24 hours will be rejected.
rsday, or, in the case of holidays, at least two days prior to the
; the next business day without interruption by holidays or

-A) (yellow top).

each tube. Avoid low volume to minimize agitation during

-4 times.
a cold box (see below) is not immediately available (maximum exposure
urs). DO NOT put the tube on ice. Do NOT leave the
ples before close of business (see below). and place the BD-
A tubes wrapped in bubble
the same day of blood draw.
ct overnight delivery, to be
tracking number on the day of shipment by an email with a

com/us/healthcare/pdf/Cold_Shipping_Info_Sheet.pdf or

8. Ship by FEDEX to the recipient address above
delivered before 10am.
subject title identifying the study.

Fedex cold boxes are available at
http://orderboxesnow.com/.

Requested Test:

☐ AR-V7 Prostate Cancer Assay

FOR LABORATORY USE ONLY

Unique Molecular Path # _____ __ Received Date/Time_____ Tech. Initials _____

CLIA License #21D0 692357 Pennsylvania License #29028A State of Maryland License #557 CAP inspected