A discussion on PCa Metastasis RVA Us Too Meeting March 15, 2018

1 Location, Location, Location as related to QOL and Survival???

A. Prostate bed mass – May Effect Urination in time??

B. Lymph nodes in prostate bed -Few better than many- Slowest progression

C. Published in Urology · March 13, 2018

Local Treatment for Men with Prostate Cancer and Clinically Pelvic Lymph Node-Positive Disease (12% at diagnosis) European Association of Urology

Hazard Ratio of Mortality=0.31 ADT + Rad or Surgery vs. ADT only.

http://www.practiceupdate.com/C/64703/56?elsca1=emc_enews_topic-alert

D. Lymph nodes outside prostate bed harder to find – need to look for them.

E. Bone Mets- 80+% mets, Femur 30%, backbone, ribs, upper arm, pelvis, skull

F. Soft Tissue – **Liver**, Kidney, Brain, Lung-(2 mets Lung & Bone better Survival).

G. Focus of treatment changes as mets progress: Nodes➔Bone➔ soft tissue

Table: Key Recommendations from the RADAR Group for the Early Identification of Metastatic Disease in M0 Patients & M0 Castrate-Resistant patients

• First scan when PSA level ≥2 ng/mL (scans work to a lower degree at lower PSA)

• Imaging frequency if negative – Second scanning when PSA equals 5

- **Repeat scan at every doubling of PSA level thereafter (based on PSA testing every 3 months)**
- **Table 1. Available Imaging - Imaging Test Sensitivity (%) Specificity (% decrease at lower PSA)**
- 99mTc 78 % 48 %
- 18F–NaF PET/CT 100 97
- Pelvis MRI

95 90 (no detection of my nodes)

- Need wide field MRI for bones outside of pelvis
- CT 74 56 Only Hi PSA
- 18 F Axumin 90% 80% best short doubling time-my 5mo.
- PSMA 66 96
- PSMA= prostate-specific membrane antigen

American Urology Association Behind the times???

http://auanet.org/guidelines/castration-resistant-prostate-cancer-(2013 amended-2015)

Table of median times to metastasis with CRPC:

PSADT	Time to Mets formation
< 3mo.	9 months
3 to 8 mo.	19 months
9 to 14.9 mo.	40 months
15 + mo.	50 months

Calculate PSADT : need two PSAs and their draw dates.

http://nomograms.mskcc.org/Prostate/PsaDoublingTime.asp

2. Hormone naïve (no Lupron) VS Castration Refractory (CRPC)? with Lupron & time

A. Variable CRPC as PSA rises in ~ 3 year and others PSA no rise in 11 years on Lupron. CRPC is evident if PSA rises on Lupron and testosterone is measured <20.

Many Bone mets after being on Lupron usually assign as CRPC

B. Lupron was the standard systemic treatment is the ADT=Androgen deprivation treatment for advanced PCa until about 2016. It can be improved by adding Casodex and Avodart to the Lupron treatment. New treatments with Ztiga(w/prednisone?) or Xtandi alone or with Lupron or replaced by Firmagon (less side effects but 1 monthly Injection). Now Aplutamide has been added by FDA added to the mix 2018

C. New Treatments for CRPC or - Chemotherapy docetaxel (Taxane) or Cabazitaxel Early

· March 14, 2018

Adding Abiraterone or Docetaxel to Long-Term Hormone Therapy for Prostate Cancer

Annals of Oncology

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- Randomized data from the STAMPEDE trial were analyzed to evaluate differences in outcomes among men with locally advanced or metastatic prostate cancer treated with ADT plus either abiraterone or docetaxel. The primary endpoint was death from any cause. Among the 566 men randomized, 149 deaths were reported over a median follow-up of 4 years.
- There were no differences in terms of overall or prostate cancer–specific survival between the two groups. Similarly, there were no differences in other clinically relevant outcomes, such as symptomatic skeletal events.

– Neil Majithia, MD

D. Treatment confusing w. multiple combinations/timing. Side effects &response?

http://www.practiceupdate.com/content/advanced-prostate-cancer-in-2018-a-look-aheadpart-1-hormone-sensitive-metastatic-disease/63925/61/11/3

Few Bone Mets <5 = Oligo metastasis- Dr. Myer believes this is treatable by multiple treatment hits to keep lowering PSA to undetectable. Few Bone Mets <5 = Oligo metastasis Cancer

***SBRT USE**: http://www.aboutcancer.com/oligomets_milano_0108.htm

SBRT = Stereotactic Body Radiation Therapy = 1 to 5 blasts each ~8 grey < week.

X-rays can be pinpointed to margins~ 2mm at individual mets.

With many more Mets than >5, it is likely that the cancer is CRPC which triggers many bone treatments when bone pain present (with Many side effects of concern): Xofigo- 39 Listed SEs dry mouth; Bisphosphonates (Zometa etc.)- necrosis of the Jaw and non-healing spiral fractures of bone etc.; Xgeva- necrosis of the Jaw and non-healing spiral fractures of thigh bone etc. Necrosis of the Jaw is related to bacterial infections in perio pockets or extractions need complete dental treatment and healing before mets treatment. **Opioids for pain Grow cancer!**

3**. Estrogen a factor in PCa progression** especially of Bone Mets that should be block to reduce met formation??? Prostate cancer is called osteoblastic because the cancer builds up bone by activating the Osteoblast bone cells. If you have testosterone active (Not on ADT) the testosterone can break down to estrogen by means of aromatase enzymes this is most likely to happen if you are on antiandrogen like Casodex, Enzalutamide or Aplutamide which raise the testosterone greatly if you are not on ADT which also raises the estrogen greatly. This most evident as breast enlargement and painful breasts especially the nipples.

There are aromatase inhibitors which may prevent the estrogen formation and thus keep the testosterone high. These are some of the aromatase inhibitors:

Femara, Dostinex, Zinc, Vitamin B6, Fisetin, Calcium Gluterate, Red Clover extract, Grape Seed Extract

Expert Review of Endocrinology and Metabolism

Estrogen Action and Prostate Cancer

Jason L Nelles; Wen-Yang Hu; Gail S Prins
Expert Rev Endocrinol Metab. 2011;6(3):437-451.

Website: https://www.medscape.com/viewarticle/742985_1

Bone supplements- Boron, Vitamin D3, Vitamin K2, Melatonin, Vitamin C