Advanced Prostate Cancer: Lymphadenopathy

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Spectrum of Lymph Nodes

• Incidental positive lymph node in prostatectomy pathology despite negative imaging
  – Close monitoring to determine when to start hormones
  – Discuss at multidisciplinary tumor board

• Minimally enlarged / borderline lymph node on CT scan in context of high risk prostate cancer
  – Give patient benefit of doubt and start definitive therapy versus trial of hormonal therapy then reimage and if negative start radiation
  – Discuss at multidisciplinary tumor board
Spectrum of Lymph Nodes

• Real lymphadenopathy in abdomen/pelvis in context of prostate cancer
  – Treat like metastatic disease with hormones
Patient Case

- 61M T3b, Gleason 4+5=7, initial PSA 7.3 prostate adenocarcinoma
- Gland volume 42cc, perineural invasion, 10/10 cores positive
- Negative CT/Bone scans for metastases
- He was treated by radical prostatectomy August 2011 and had 1/5 lymph nodes positive with multiple positive margins and postoperative PSA October 3, 2011 of 3.55
  - YIKES!
- He was commenced on total androgen blockade at that time with Eligard and Casodex
- Casodex withdrawal Sept 21 2014 for rising PSA.
- Continues on Eligard alone and testosterone is well suppressed
- I met him at this point to discuss treatment options
Patient Case

- PSA despite well suppressed testosterone levels:
  - Sept 2014 3.6
  - Nov 2014 23.5
  - Dec 2014 25.8
- CT Scan: subcentimeter abdominal lymph nodes (not pathologic by size criteria)
- Bone scan: normal
- Consented to PROSPER clinical trial
Nonmetastatic CRPC: PROSPER
PROSPER Trial

Maintenance of androgen deprivation

Enzalutamide (160 mg/day)  
To radiographic progression

Placebo

Primary endpoint  
MFS = time to radiographic progression or death on study

M0 CRPC Patients

Randomization  
2:1

Stratification by:
- PSA doubling time < or > 6 months
- Baseline use of bone-targeting agent
I assume he got enzalutamide ...
New Lymphadenopathy

- New left supraclavicular lymphadenopathy
- CT: conglomerate of multiple 1-1.5 cm (short axis) lymph nodes seen January 2016, small (1-1.5 cm) axillary and abdominal lymph nodes
- Biopsy supraclavicular lymph node: prostate cancer confirmed
- PSA:
  - April 2016 1.8
  - June 2016 4.9
  - August 2016 7.6
  - September 2016 12.1
- Started abiraterone Sept 2016: clinical response to supraclavicular lymph node
PSA

Started PROSPER

Started Abiraterone
No response to Abiraterone

- New bone metastasis in right greater trochanter seen on CT and bone scan but asymptomatic
- Denosumab initiated to prevent skeletal related events (along with calcium and vitamin D)
- Then new rib metastases and supraclavicular nodes much larger (5 cm)
- Started Docetaxel chemotherapy Dec 2 2016
What I learned

• Combination of symptoms, PSA, imaging, physical exam guides treatment selection
• Biopsy helpful (ruling out lymphoma)
• Efficacy of abiraterone post enzalutamide failure not incredible but some responses documented in small retrospective studies
• If progresses on docetaxel will try cabazitaxel
• Ensure testosterone levels suppressed
PSA and Testosterone
Most commonly used biomarker for prostate cancer

PSA AS A BIOMARKER DURING TREATMENT
PSA during treatment

• Usually very useful but not always perfect
  – Sometimes rises before falling during chemotherapy
  – Sometimes PSA non-secretor
  – Sometimes lab error
  – Sometimes measured too soon
  – Sometimes rises as patient is still well and scans stable
Sometimes this happens

![Graph showing Docetaxel results over time with visits labeled C1 to C7. The graph shows a trend with peaks and troughs at different dates from Aug 09 2016 to Nov 22 2016.](image)
Early PSA response is an independent prognostic factor in patients with metastatic castration-resistant prostate cancer treated with next-generation androgen pathway inhibitors

Alina Fuerea, Giulia Baciarello, Anna Patrikidou, Laurence Albigès, Christophe Massard, Mario Di Palma, Bernard Escudier, Karim Fizazi, Yohann Loriot*
Early PSA Response in Abiraterone

• Early prostate-specific antigen (PSA) response defined as a decline >50% from baseline at day 28 is associated with better radiographic progression-free survival and overall survival (OS).

• Early PSA response (EPR) remained prognostic for OS in multivariate analyses that included validated pre-therapeutic prognostic factors for metastatic castration-resistant prostate cancer.

• Prognostic values of EPR for radiographic progression-free survival and OS were confirmed in an independent cohort of 95 abiraterone-treated non-trial patients.
• Used phase III TROPIC trial prospective data (Cabazitaxel vs Mitoxantrone post docetaxel)
• Decline in PSA > 30% within 3 months associated with better overall survival
• The proportion of treatment explained by drop in PSA >30% was only 0.34 indicating lack of surrogacy for OS
PSA Drop Associated with OS

>30% PSA decline

>50% PSA decline
But not enough to be surrogate endpoint

<table>
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<th>Decline in PSA (%)</th>
<th>M + P</th>
<th>C + P</th>
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<td>No. of Patients</td>
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PSA response is not a surrogate endpoint for OS

PSA RESPONSE IS ASSOCIATED WITH BUT DOES NOT EXPLAIN ALL VARIATION IN SURVIVAL
Using 1088 patients from phase III pre-docetaxel abiraterone+prednisone vs prednisone trial

rPFS to OS Spearman correlation 0.72, Kendall Tau 0.53
rPFS

• RECIST 1.1 Criteria plus
• Bone lesion progression criteria
  – First bone scan two new lesions compared with baseline was observed >12 weeks from random assignment, a second bone scan was required, taken 6 weeks later, which was required to demonstrate two additional new lesions (total of four new lesions from baseline)
  – First bone scan with two new lesions compared with baseline was observed >12 weeks from random assignment (ie, outside of flare window), a confirmatory second bone scan was required, 6 weeks later, to verify the continued presence of the new lesions, but two additional new lesions were not required
    • (total of two new lesions v baseline)
Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3

PCWG3

- Maintains PCWG2 Criteria for PSA progression
- PSA progression is the date that a 25% or greater increase and an absolute increase of 2 ng/mL or more from the nadir is documented, which is confirmed by a second value obtained 3 or more weeks later
- Also introduces endpoints such as time to skeletal related event, time to metastases (for non metastatic patients), and the concept of no longer clinically benefiting
- PSA doubling time important consideration for non-metastatic patients
- Certainly real world practice may not mirror this
In the end ...

- We use constellation of findings to determine response/progression
  - Symptoms/performance status
  - Radiographic changes
    - Bone
    - Measureable disease
  - PSA