Panel Discussion: Genitourinary Cancers

March 17th, 2018

18th Multidisciplinary Management of Cancers: A Case-based Approach

Chair:

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Clinical Vignette 1

- 60 yr. healthy male without significant comorbidities and sporadic PSA follow up
- PSA at age 50 was 3.0, age 53 was 4.0, age 55 6.0, age 58 was 10.0, PSA now at age 60 found to be 20.5
- Outside urologist performed standard TRUS biopsy 6 months prior, with prostate volume calculated at 30 grams
- Biopsy done, 12 cores showed 2/12 involved with Gleason 3+3 cancer in 5% and 15% of core, respectively
- Pt advised to have brachytherapy, sees you for a second opinion

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Question 1.1

Next steps in management?

1. Brachytherapy
2. Radical prostatectomy
3. MRI pelvis
4. Bone scan
5. Option 3 and 4
6. Oncotype Dx or Prolaris genetic test

Clinical Vignette 1 (Cont)

- Had discussion of options, including active surveillance, surgery, and radiation
  - **Bone scan** done showing no evidence of disease
  - **Oncotype Dx** score consistent with low risk cancer
  - **MRI** with PI-RADS 5 lesion transition zone 2 cm in size, no lesions in area of positive biopsy in peripheral zone

Question 1.2

Next step?

1. Continue with active surveillance protocol, PSA in 3 months
2. MRI fusion biopsy targeting lesion with concomitant 12 core template biopsy
3. MRI fusion biopsy targeting only transitional zone lesion
4. Radiation Consult for options
5. Radical prostatectomy

Clinical Vignette 1 (Cont)

- MRI fusion biopsy
  - Gleason 4+4 in transitional zone targets in 3 cores
  - Gleason 3+3 in peripheral zone small foci

Question 1.3

Next step?

1. Open radical prostatectomy
2. Robotic radical prostatectomy
3. Brachytherapy +EBRT/ADT
4. External beam radiation /ADT
5. Watchful waiting

Clinical Vignette 1 (Cont)

- Pt elects for RALP
- Extended LND performed
- Final pathology pT3aN0 neg margins
- Post op recovery routine

Question 1.4

Next step in management?

1. Adjuvant radiation
2. Routine PSA follow up with early salvage radiation in event of biochemical failure

Clinical Vignette 1 (Cont)

- Discussion of adjuvant XRT initiated, patient refuses
- PSA follow up initiated
- First PSA 0.12 at week 6 post operative
- Pt referred to Rad Oncology for discussion of salvage XRT

Question 1.5

- You recommend which of the following

1. Radiation to the prostate bed
2. Radiation to prostate bed/pelvis
3. RT to prostate bed +ADT
4. RT to prostate bed/pelvis+ADT

Clinical Vignette 2

- 63 year-old male undergoing annual PSA screening
  - 2014- 2.3 ng/mL
  - 2015- 5.1 ng/mL
  - 2016- 15.6 ng/mL
- Abnormal DRE; PNBx- 7/12 cores w/ G 4+4 and 3/12 cores w/ G 4+5
- Bone scan- multiple sites of metastases
- CT A/P shows no visceral disease/abnormal LAD

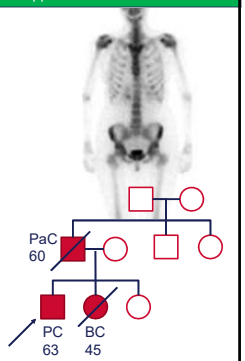
Question 2.1

What front line treatment will you recommend?

1. Combined ADT +bicalutamide
2. Brief bicalutamide followed by Androgen-deprivation therapy (ADT)
3. ADT + docetaxel
4. ADT + abiraterone + prednisone

Clinical Vignette 2 (Cont)

- Patient is started on ADT + docetaxel and achieves excellent response with normalization of PSA and decrease in bone lesions
- During follow up visit, patient asks you about need for **genetic screening.**
- He has a family history of a sister with breast cancer diagnosed at age 45 and father with pancreatic cancer diagnosed at age 60.



Question 2.2

Your recommendation regarding **genetic testing** is to proceed with:

1. Somatic screening for BRCA1 and BRCA2
2. Germline screening for BRCA1 and BRCA2
3. Germline screening for MLH1, MSH2, MSH6, PMS2, and EPCAM
4. Genetic testing not recommended based on current NCCN guidelines

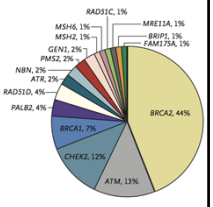
Clinical Vignette 2 (Cont)

- NCCN recommends screening for patients with:

  Personal history of prostate cancer (Gleason ≥7) at any age and:

  - family history of one or more close blood relatives with ovarian (any age) or breast cancer (≤ 50 yrs)
  - or two relatives with breast, pancreatic or prostate cancer (Gleason ≥7) at any age

- 23% of metastatic castration-resistant prostate cancers harbor DNA repair alterations



Pritchard CC, et al. *N Engl J Med.* 2016;375:443-453. Copyright © 2017

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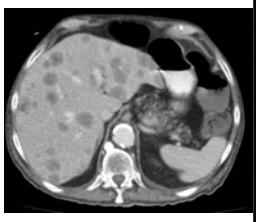
Clinical Vignette 2 (Cont)

- Germline testing for BRCA1 and BRCA2 mutations is negative
- Patient continues on CAB
- Two years later PSA trending up to 5 despite bicalutamide withdrawal, new LFT elevation noted on routine labs, CT CAP with new liver lesions



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Question 2.3

At this time what would be your next step in management?

1. Perform a biopsy of a liver lesion
2. Start cabazitaxel
3. Start abiraterone
4. Start enzalutamide
5. Start docetaxel

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Clinical Vignette 2 (Cont)

- You perform a liver biopsy confirming recurrent prostate cancer
- Patient is started on enzalutamide given elevated LFTs with normalization of PSA and decrease in size and number of liver lesions
- 6 months later, PSA begins to trend up to 3.5 and progression of visceral and bone metastases noted on subsequent scans

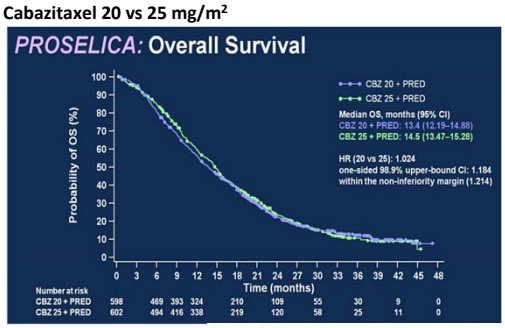
Question 2.4

At this time what would be your next step in management?

1. Start cabazitaxel 20mg/m2
2. Start cabazitaxel 25mg/m2
3. Start cabazitaxel/carboplatin
4. Switch patient to abiraterone
5. Start radium 223

The PROSELICA Study–

Cabazitaxel 20 vs 25 mg/m²



De Bono JS, et al. J Clin Oncol. 2016;34(Suppl):abstract 5008.

The PROSELICA Study–

Cabazitaxel 20 vs 25 mg/m²

PROSELICA: Treatment-Emergent Adverse Events

	CBZ 20 + PRED N = 580	CBZ 25 + PRED N = 595
Patients, n (%)		
Any Grade TEAE	529 (91.2)	559 (93.9)
Grade 3–4 TEAE	230 (39.7)	324 (54.5)
Serious TEAE	177 (30.5)	257 (43.2)
TEAE leading to permanent treatment discontinuation	95 (16.4)	116 (19.5)
Most frequent Grade 3–4 TEAEs reported in ≥ 5% pts, n (%)		
Febrile neutropenia	12 (2.1)	55 (9.2)
Hematuria	11 (1.9)	25 (4.2)
Diarrhea	8 (1.4)	24 (4.0)
Fatigue	15 (2.6)	22 (3.7)
Urinary tract infection	10 (1.7)	13 (2.2)
Bone pain	10 (1.7)	13 (2.2)
Asthenia	11 (1.9)	12 (2.0)
Vomiting	7 (1.2)	8 (1.3)
Nausea	4 (0.7)	7 (1.2)

De Bono JS, et al. J Clin Oncol. 2016;34(Suppl):abstract 5008.

Clinical Vignette 2 (Cont)

- Patient tolerates cabazitaxel 20mg/m2 well for 4 cycles, however after 4 months of therapy additional biochemical and radiological progression noted
- Patient continues to have robust performance status and asks if any further therapy is available for him at this time?

Question 2.5

Which of the following statements are true?

1. Even if germline testing is negative, HRD alterations can still be present as somatic mutations and are associated with PARP activity
2. PARP inhibitors are active only in setting of germline homologous recombination deficiency (HRD) mutations
3. Response to PARP inhibitors is around 6% in patients with a HRD mutation
4. BRCA1 and BRCA2 are the only HRD mutations associated with response to PARP inhibitors

Clinical Vignette 3

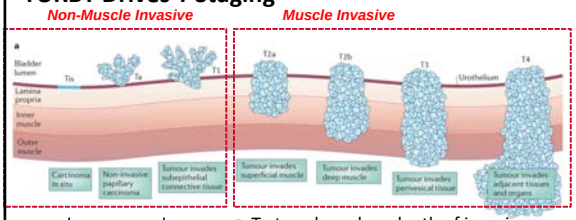
- 66 year old former smoker diagnosed with high grade Ta bladder cancer after a work up of hematuria and dysuria in 2010. He received 6 weeks of intravesical BCG with subsequent surveillance cystoscopy. In 2016 cystoscopy showed an erythematous patch and a TURBT revealed high grade Ta disease. A CT IVP is negative

Question 3.1

His options at this time include

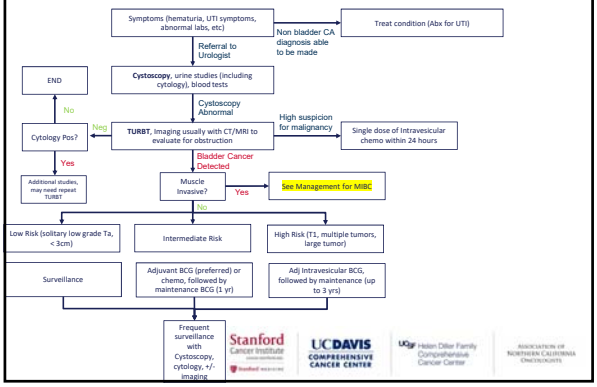
1. Induction BCG
2. intravesical chemotherapy
3. Intravesical BCG plus IFN
4. Cystectomy

TURBT Drives T Staging



- T-stage based on depth of invasion
- Grade of tumor based on how abnormal cells appear
  - Most important for non-muscle invasive

Non-Muscle Invasive Disease (Summary)



Clinical Vignette 3 (Cont.)

- Patient undergoes another 6 week induction BCG with similar tolerance but on first follow-up cystoscopy in clinic he has patchy erythema and cytology that shows malignant cells.
- IPSS-15/35; Bother-6/6; SHIM-7/25.

Question 3.2

What other workup should he have now?

1. CT IVP
2. Blue light cystoscopy with upper tract washing and TUR biopsy prostatic urethra
3. PET scan
4. UroVysion© FISH test (Abbott labs)

Clinical Vignette 3 (Cont.)

- CT IVP is normal. Rigid white light cystoscopy revealed a normal appearing urethra. There was an erythematous patch along the right postero-lateral wall next to a prior resection site scar. This area fluoresces on blue light cystoscopy with no other lesions seen. Pathology reveals persistent CIS.

Question 3.3

At this time what would you recommend?

1. More BCG
2. Cystectomy
3. Salvage intravesical chemotherapy

Clinical Vignette 3 (Cont.)

- Patient underwent a cystectomy which did reveal pT1 disease with extensive CIS. He had surveillance scans and at 6 months scan had large pelvic sidewall metastases. Biopsy confirmed urothelial cancer. His serum creatinine was 1.0. Additional staging studies revealed bilateral lung metastases >2 cm.

Question 3.4

At this time you would recommend

1. Gemcitabine and cisplatin chemotherapy
2. Dose-Dense (DD)-MVAC
3. Gemcitabine and carboplatin chemotherapy
4. Pembrolizumab
5. Atezolizumab

Clinical Vignette 3 (Cont.)

- Patient started cis/gemcitabine and after 3 cycles had progressive disease

Question 3.5

At this time you would recommend

1. Atezolizumab
2. Pembrolizumab
3. Durvalumab
4. Nivolumab
5. Avelumab

Clinical Vignette 3 (Cont.)

- Patient received pembrolizumab and after 4 doses achieved a complete response

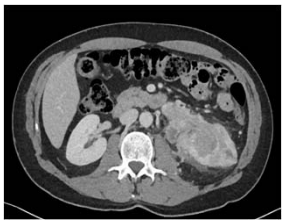
Question 3.6

At this time you would recommend

1. Continue Pembrolizumab
2. Stop PD-1 therapy after 6 months
3. Stop PD-1 therapy after 12 months

Clinical Vignette 4

- 56 year old venture capitalist male with h/o HTN, hyperlipidemia, who presents with gross hematuria CT CAP done reveals a large 9.1 X 9 X 11.4 cm Left renal mass with thrombus in Left renal vein and possible IVC, scattered lung lesions none larger than 2 mm.



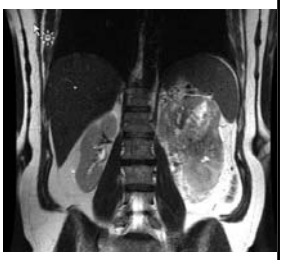
Question 4.1

What additional imaging is indicated?

1. MRI of the abdomen
2. Brain scan
3. PET scan
4. All of the above

Clinical Vignette 4 (Cont)

- Patient undergoes an MRI- Left renal mass with thrombus in Left renal vein and 8 mm in to the IVC
- Patient undergoes a nephrectomy; 10 cm: ccRCC- grade3; tumor necrosis- 30%; perinephric fat invasion, renal sinus fat invasion, RV invasion, LVI, adrenal gland- continuous invasion



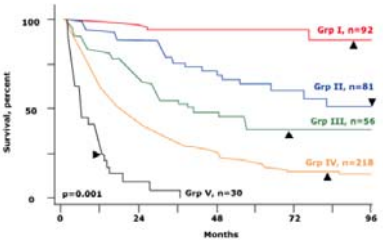
Question 4.2

Patient wants to know his risk of relapse; You use which of the following to determine risk?

1. UCLA Integrated Staging System (UISS)
2. Score for Clear Cell Renal Cell Carcinoma (SSIGN)
3. Kattan Nomogram
4. Oncotype Dx
5. None of the above

Clinical Vignette 4 (Cont)

- Based on the above risk assessment he is estimated to have a 38-55% 5 yr DSS



Zisman, et al. J Clin Oncol 2001; 19:1654

Question 4.3

You recommend

1. Adjuvant sunitinib x 1 year
2. Adjuvant nivolumab x 1 year
3. Surveillance

Clinical Vignette 4 (Cont)

- Patient opted for surveillance. Repeat CT in 8 weeks reveal multiple small lung nodules, largest is 1.6 cm; His CBC with diff is normal and calcium is 9.2. His ECOG is 1

Question 4.4

His risk assessment

1. Good risk
2. Intermediate risk
3. Poor risk

Question 4.5

Your treatment recommendations:

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Ipilumimab/Nivolumab
5. Atezolizumab/Bevacizumab

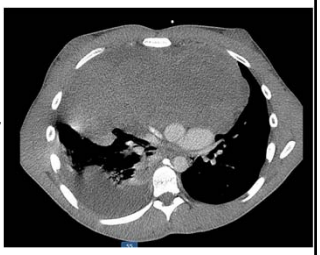
Clinical Vignette 5

22 year old male presents with severe SOB, weight loss, night sweats of 3 weeks duration.

CT CAP shows mediastinal mass 11x22 cm, multiple liver lesions, large RP mass;

AFP-11993; **HCG**- 144; **LDH**-1665

Testicular US reveals extensive microcalcifications on the left side and a normal right testes



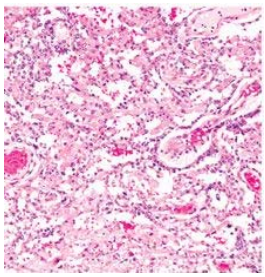
Question 5.1

You recommend:

1. Left Orchiectomy
2. Biopsy of the RP mass/Mediastinal mass
3. Start systemic therapy

Clinical Vignette 5 (Cont)

- Patient underwent a CT guided biopsy of the mediastinal mass – malignant germ cell tumor with yolk sac features.
- Started BEP chemotherapy at UCLA and transferred care to Stanford where his parents live.
- On exam had a cough which was new since start of chemotherapy.
- PFT's revealed a DLCO of 62%



Question 5.2

You do the following

1. Continue BEP
2. Switch to VIP
3. Start steroids and continue BEP

Clinical Vignette 5 (Cont)

- Patient was switched to VIP and completed a total of 4 cycles
- His AFP came down to 41 after the last cycle; HCG & LDH: completely normalized
- CT scan- significant decrease in mediastinal mass, improvement of liver and lung lesions as well.

Question 5.3

At this time you recommend the following

1. Surgical evaluation of the mediastinal mass
2. Referral to BMT for HDCT
3. Switch to TIP
4. PET scan

Clinical Vignette 5 (Cont)

- **PET scan** showed intensely FDG avid anterior mediastinal mass with central necrosis, FDG avid lesions in the liver and bilateral lung metastases.
- **AFP** rose the following week to 439 and patient was referred to BMT