



Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

A Focus on Genitourinary Cancers Case Studies

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Case 1



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- 78 year old presents with gross hematuria and flank pain
- Imaging revealed a bladder mass and retroperitoneal lymphadenopathy causing hydronephrosis as well as liver metastasis.
- PMHx : Diabetes, Hypertension and Hyperlipidemia
- Soc Hx: 50 pack / year history, active smoker. Social alcohol use.
- Liver Biopsy revealed urothelial cancer with squamous differentiation.
- GATA 3 positive, PDL1 > 50%
- Labs normal except Hb of 9 and Creat of 1.9



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- How would you treat the patient?
 1. Carboplatin/gemcitabine
 2. Pembrolizumab
 3. Carboplatin/gemcitabine followed by Avelumab
 4. Supportive care
- How would you treat upon progression?

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Mr. AS (Case 2)



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68 year-old male with metastatic renal cell carcinoma with metastases to lung who started 2 weeks ago a combination IO-TKI regimen consisting of **Nivolumab plus Cabozantinib**. He was previously treated with **Nivolumab plus Ipilimumab** 2 months prior but discontinued before his 4th dose due to worsening neuropathy.

PMH significant for:

- Neuropathy with Autonomic dysfunction
- Type II diabetes poorly controlled
- Hypertension controlled



Mr. AS

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He presents to clinic today for routine follow up. He has been losing weight ~ 7lbs in 1 week. He also complains of macular popular rash mostly to face as well as frequent bowel movements up to 8 in a day. He feels BMs are more diet related as he has been eating lots of greasy and high sugar content foods.

What other information do we want to know from him?



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Mr. AS

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- Symptoms ongoing for about 1 month. Unchanged in frequency or intensity with his new cancer treatment
- His stools are watery and certain foods make it worse like red meat.
- He has no sick contacts. Uses 4-6 Imodium pills to manage. Sometimes Lomotil.

PE: VSS in clinic are stable

Labs: Unremarkable for active infection or significant dehydration.

What are your next steps?

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Mr. AS

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- Check medication list
- Stool sample r/o infection Ova/parasites, cdiff
- Defer abdominal imaging since no pain and had recent staging scans with no colitis seen.
- Discussed eating healthier more clean diet
- Recommend IV hydration
- Refer to GI for colonoscopy given immunotherapy history
- Communicate with Endocrinology team to inform them patient may need to start steroids soon given history of diabetes



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Mr. AS

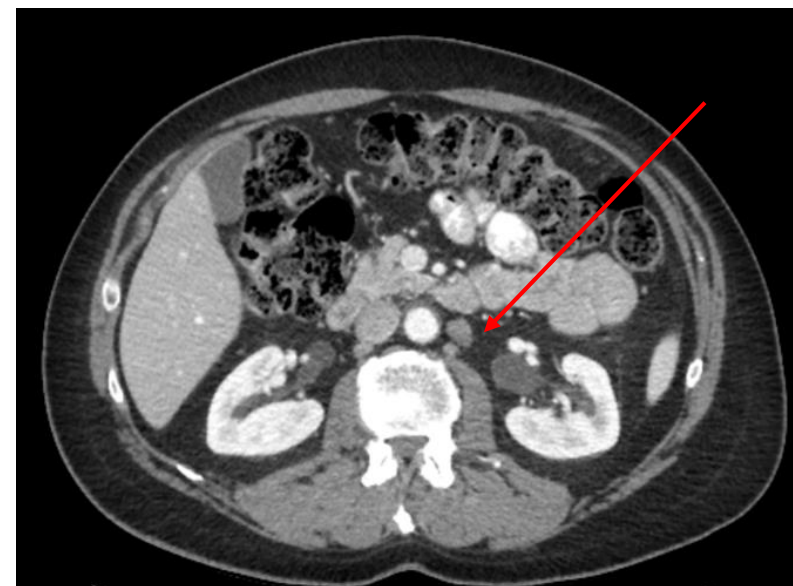
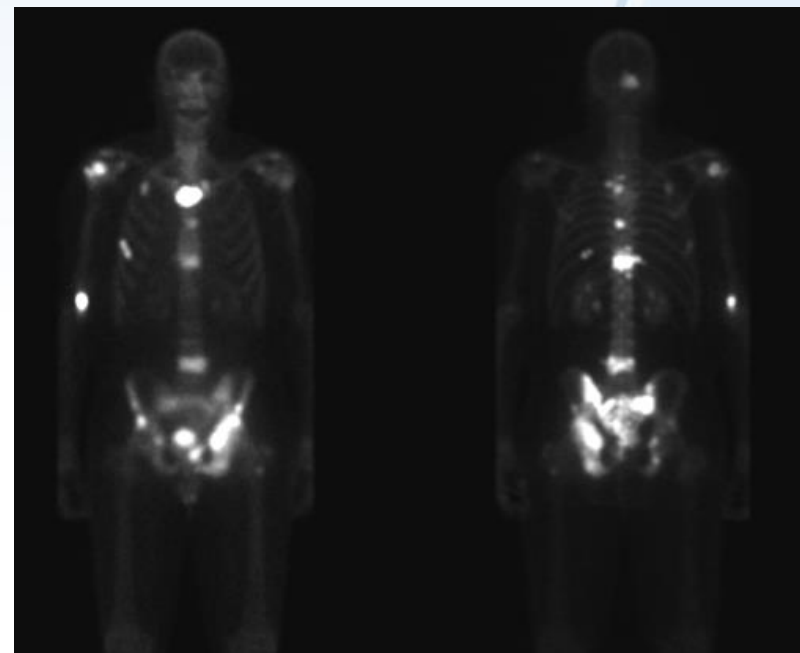
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- Colonoscopy is positive for microscopic healing colitis.
- IO indefinitely on hold.
- Refer back to GI for management
- Hold immunotherapy and resume TKI once colitis is controlled or resolved.
- Rash could be related to immunotherapy but no steroids for this for now just supportive measures gentle soap and water, moisturizer etc

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Case 3

- 58 year old man presents with worsening low back pain.
 - Imaging + osseous mets
 - PSA 109
- Treated with ADT + docetaxel x 6 doses
 - PSA nadir 0.12 at 7 months
 - PSA began to rise at 12 months, reached 4.5 at 18 months
- Imaging shows new enlarging LN in pelvis & RP, new bone metastatic focus

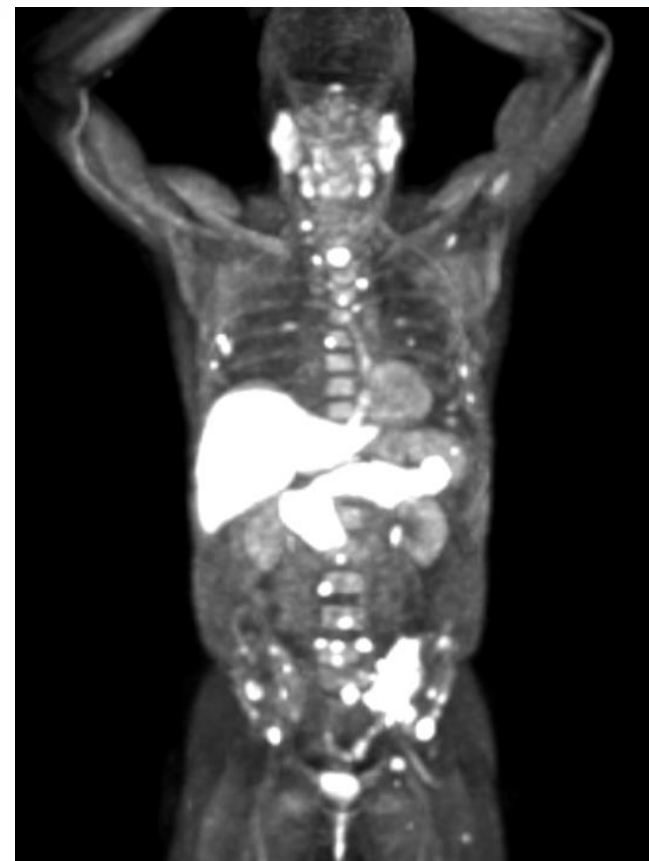


Case 3 (cont.)

- Abiraterone + prednisone initiated
 - PSA drops to 0.4 after 6 months, then starts to rise
 - After 9 months PSA is 0.8 and at 1 year PSA is 1.5
- Genomic sequencing reveals MSI high
- Treated with pembrolizumab
 - Disease stable radiographically, but PSA continues to rise
 - After 6 months he develops symptomatic progression
- Treated with cabazitaxel

Case 4

- 72 yo physician treated with radical prostatectomy in 2005. Received salvage radiation in 2009.
 - Treated with intermittent ADT 2012-2017.
- Oct 2017 found to have metastatic disease, treated with abiraterone
 - May 2019 switched to enzalutamide without response
- Nov 2019 began docetaxel. Upon progression received cabazitaxel
- Feb 2021 received radium223, completed 6 courses



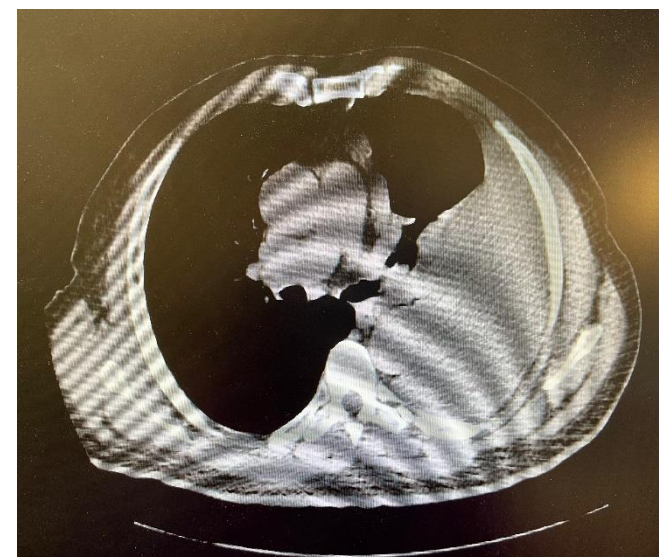
Case 4

- Presents with fatigue, weight loss, and rapidly rising PSA
- Starts AMG160 with bPSA 907
- Grade 2 CRS with first 2 infusions
- PSA drops to 33.4 after 1 month
- Regained weight, began exercising again

RCC Case 5

67 yoM with history of HTN presented to his PCP for dyspnea on exertion. Chest xray showed a large left pleural effusion, and CT CAP showed a large left renal mass, a 2cm hepatic mass, and the known pleural effusion.

Labs notable for Ca 11.6, Hb 11.5, normal WBC and platelets. He has excellent performance status. Brain MRI was negative.



RCC Case 5

Biopsy of the liver mass confirmed clear cell RCC. Thoracentesis was performed with 1100mL removed.

Would you consider cytoreductive nephrectomy in this patient?

What is your recommended first-line treatment?

Case Study 6

56 year old man presents with 3 months of left flank pain, cough, progressive dyspnea and intermittent hematuria.

Vital Signs:

- T 97.2°F HR 102 RR 16 BP 111/69 O2 Sat 98%

Labs:

- Hemoglobin 7.2
- Corrected Calcium 11.9
- ANC 14.6
- Platelets 959

Case Study 6

CT Chest/Abdomen/Pelvis

- Right lower lobe pulmonary embolism
- Numerous bilateral pulmonary nodules, largest 2.9 cm in left lower lobe
- 7.1 x 8.3 x 9.7 cm mass of the left kidney
- Adjacent metastatic seeding with lesions measuring 2.1 cm, 1.7 cm, 1.1 cm
- Bulky retroperitoneal lymph nodes, largest 4.5 x 4.0 cm
- No lytic bone metastases

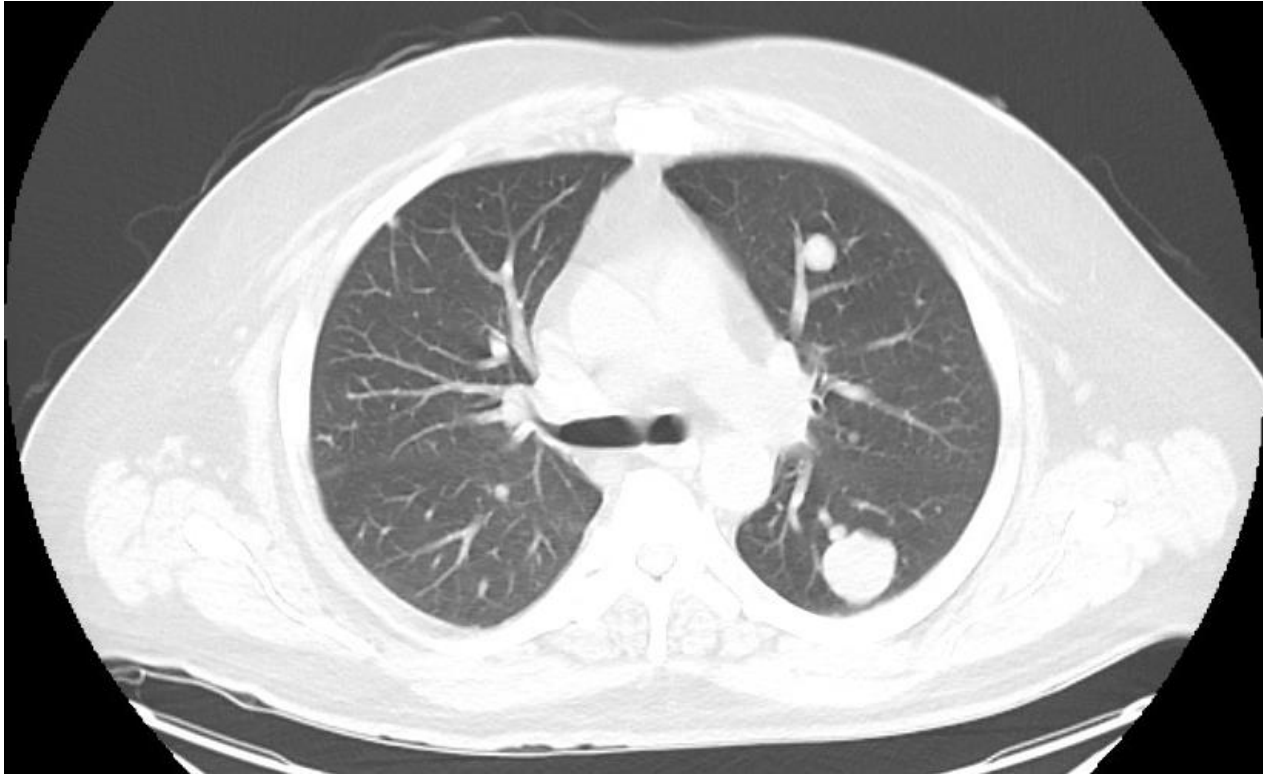
Bone Scan:

- No metastases

Kidney Biopsy:

- Clear cell renal cell carcinoma

CT Chest/Abd/Pelvis w/ contrast



Question 1

Which of the following is the most appropriate first line therapy for this patient (intermediate risk IMDC)?

- A) High-dose IL-2
- B) Combination CTLA-4/PD-1 Blockade
- C) Single Agent VEGF Blockade
- D) Combination VEGF/PD-1 Blockade

Question 2

If you chose Combination VEGF/PD-1 Blockade, which of the following is the most appropriate first line therapy for this patient and why?

- A) axitinib/pembrolizumab
- B) cabozantinib/nivolumab
- C) axitinib/avelumab
- D) lenvatinib/pembrolizumab

Case Study 7: mUC

A 68 year old man is referred to you by a urologist, after TURBT identified muscle invasive urothelial cancer. His Medical History is notable for CAD, for which he had 2 stents placed last year, no active angina. Last stress test reported as normal.

He has hypertension and hyperlipidemia which are well controlled.
Labs reveal creatinine of 1.1 which calculates to GFR of 60 mL/min

You perform staging and CT identifies enlarged RPLN, up to 2.5 cm in short axis, as well as 4 pulmonary nodules, largest 1.5 cm

What treatment would you recommend to this patient?

- A) Pembrolizumab
- B) Atezolizumab
- C) Gemcitabine + Cisplatin
- D) Gemcitabine + Carboplatin

Case Study 7 (mUC) continued

Because his GFR is good and he has no contraindication to cisplatin, you treat him with 6 cycles of Gem/Cis. He achieves a partial response. No major toxicities, just grade 1 nausea, fatigue, and thrombocytopenia.

You send his tissue for PD-L1 staining and identify that he has low PD-L1 staining.

He asks about additional treatment. What would be your recommendation?

- A) Radical cystectomy
- B) Avelumab maintenance
- C) Observation
- D) 2 additional cycles of gemcitabine + cisplatin

Case Study 7 (mUC) continued

Avelumab maintenance is offered due to the survival advantage seen in the JAVELIN Bladder 100 trial, which was present for the study population as a whole and not restricted to those with high PD-L1 expression. He receives 10 mg/k² every 2 weeks, with acetaminophen and diphenhydramine pre-medication before the first 4 doses.

He develops new liver metastasis after 6 months. Performance status remains good. Genomic profiling is ordered to help determine whether he is a candidate for erdafitinib, with a plan for Enfortumab Vedotin while waiting for the results.

Case Study 8: mRCC

A 56 year old woman presents to the emergency room with cough and shortness of breath. She reports a history of nephrectomy 2 years earlier for renal cell carcinoma, but hasn't been following with her physician for surveillance because she lost her insurance during the pandemic. CT scan of the chest, abdomen and pelvis identifies multiple bilateral pulmonary nodules.

She has no significant medical history. Her mother had breast cancer in her 70's. Her grandmother had rheumatoid arthritis. Labs reveal normal CBC, Calcium and LDH.

Biopsy of a lung nodule confirms clear cell renal carcinoma.
You perform staging MRI brain which is negative for metastases.
What treatment would you recommend to this patient?

- A) High-dose IL-2
- B) Combination CTLA-4/PD-1 Blockade
- C) Single Agent VEGF Blockade
- D) Combination VEGF/PD-1 Blockade

Case Study 8 (mRCC) continued

Because she has good risk disease and is symptomatic, you recommend cabozantinib + nivolumab. She develops diarrhea and hand-foot syndrome. These are improved after holding cabozantinib for a week and reducing the dose upon resumption. Imaging shows a very good partial response.

6 months later she reports a new left sided headache. Mri brain reveals a 9 mm hemorrhagic focus in the left parietal lobe with mild surrounding vasogenic edema. She is started on dexamethasone, evaluated by neurosurgery, and the decision is made to treat with stereotactic radiation.

She returns to your office 2 weeks after the radiation. She has been tapered off dexamethasone and her headache has resolved. Her CT chest, abdomen and pelvis shows stability of the lung nodules. What do you advise her regarding treatment next:

- A) Start second-line therapy with Lenvatinib + everolimus
- B) Resume cabozantinib + nivolumab
- C) Surgical resection of the brain metastasis
- D) Observation

Case Study 8 (mRCC) continued

CNS metastases do not necessarily reflect systemic failure. Thus it would not be optimal to start second-line therapy.

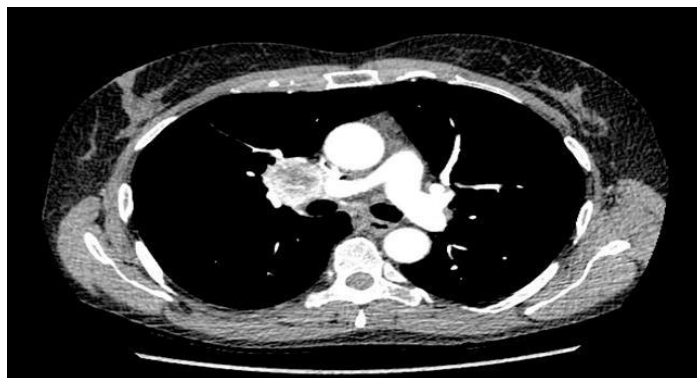
Since she has residual active systemic disease and did not have major toxicity nor irAE, Cabozantinib + nivolumab may safely be resumed and would potentially be important for ongoing cancer control.

Surgical resection has not been shown to improve outcomes in mRCC after SRS to solitary brain metastases and would delay resumption of systemic therapy.

Observation is not favored, given active metastatic disease which was symptomatic at presentation.

Patient Case 9 – RCC (Good Risk IMDC)

- 62 F with renal cell carcinoma
 - Initially T3aN0M0 14 cm clear cell RCC margin negative 0/3 nodes, no sarcomatoid post radical nephrectomy Oct 2012
 - November 2015: relapsed with hilar/neck lymphadenopathy 3.5 cm and small pulmonary nodules
 - KPS 100%
 - All labs in normal range
 - Well-controlled hypertension, otherwise healthy



Question

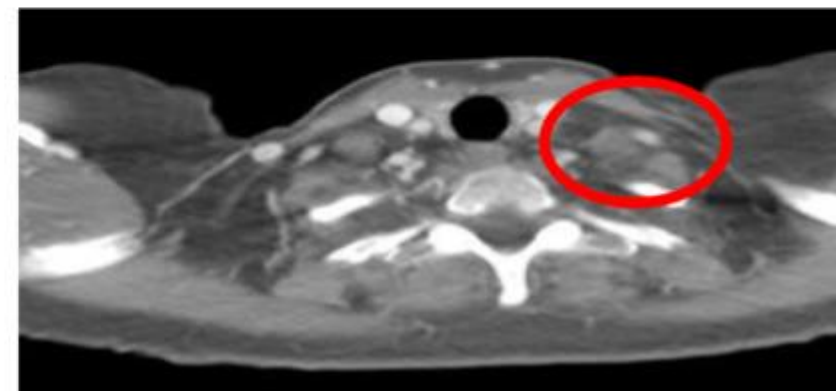
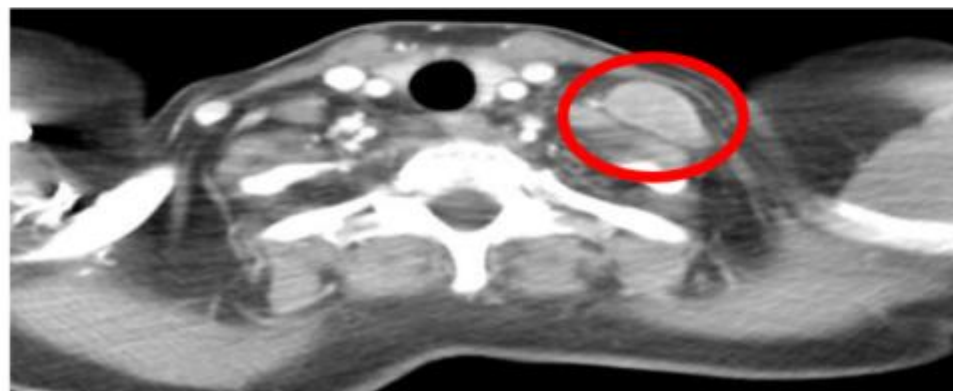
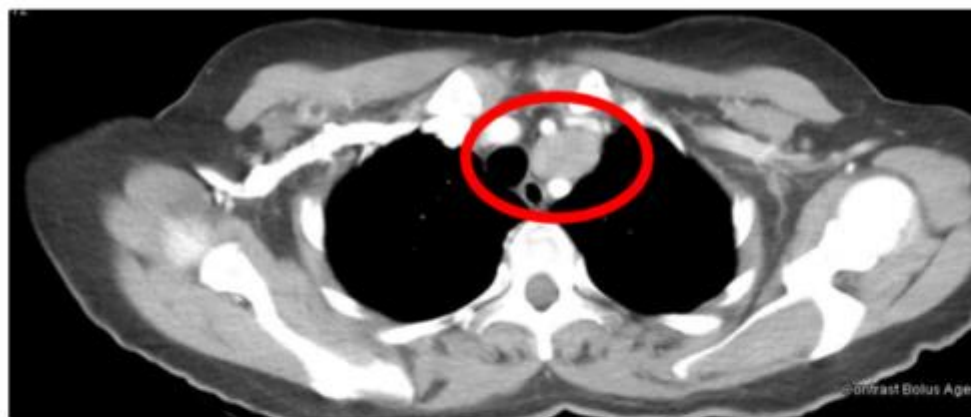
Which of the following is the most appropriate first line therapy for this patient (good risk IMDC)?

- A) High-dose IL-2
- B) Combination CTLA-4/PD-1 Blockade
- C) Single Agent VEGF Blockade
- D) Combination VEGF/PD-1 Blockade

62 yo Female with Treatment-Naïve aRCC: Good Risk IMDC - Rx Ipi/Nivo

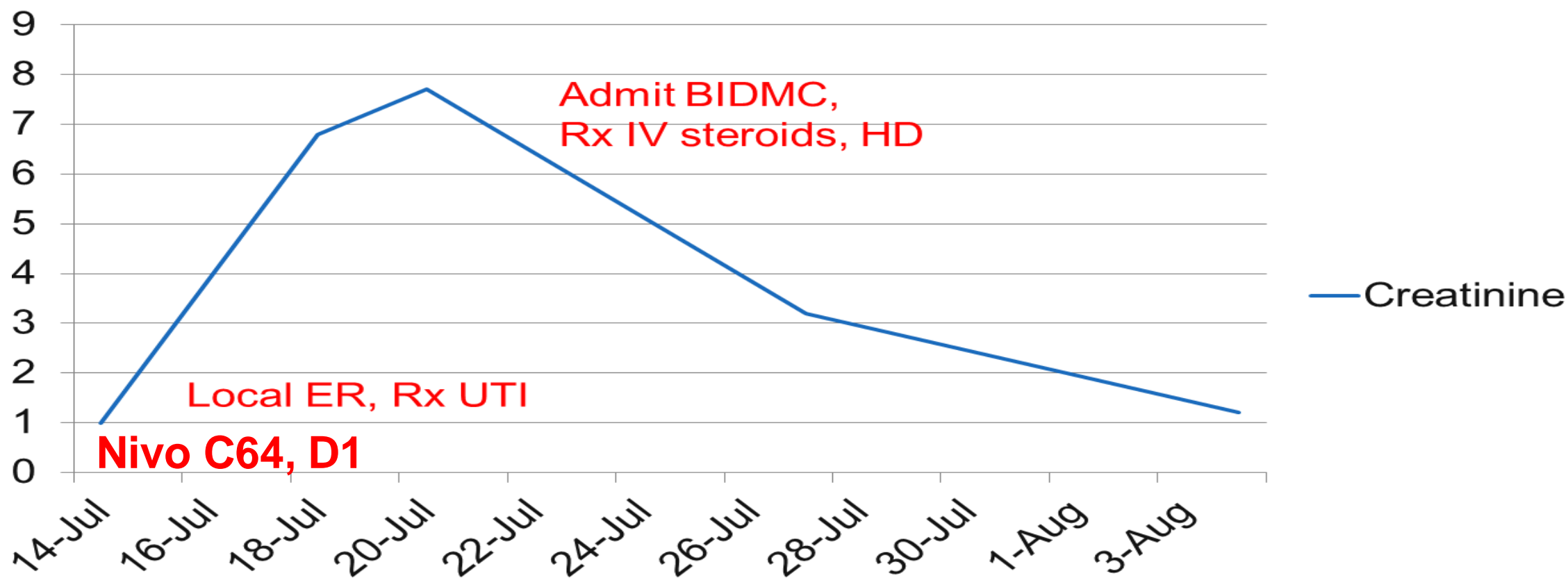
December 2015 C1D1

June 2016



Late PD-1 Toxicity?: Acute Renal Failure

Creatinine



#LearnACI 62 yo female, mRCC, Ipi/Nivo then Nivo

Case 9: Second-line Therapy

- Patient receives axitinib/pembrolizumab
- Tolerates therapy well
- Develops left hip pain after 15 months
- CT shows definitive progression
- Multiple new lung metastases



Panel Discussion

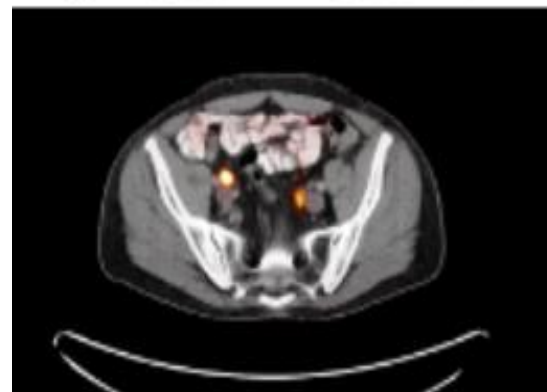
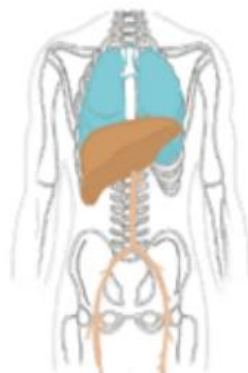
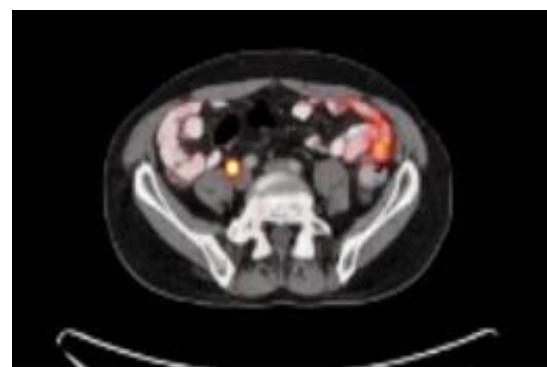
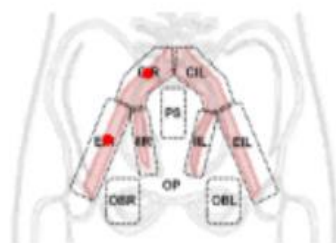
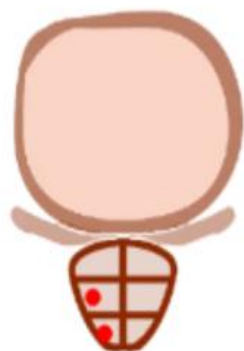
- **For a patient with progression on axitinib/pembrolizumab, what would you choose as your next treatment?**
- A. Cabozantinib
- B. Axitinib
- C. Lenvatinib/pembrolizumab
- D. Lenvatinib/everolimus
- E. Sunitinib
- F. Nivolumab/ipilimumab

Case 10

- 60 year old male with rising PSA
PSA 13 , increased from PSA 10 (pre-COVID)
- Prostate MRI: possible extracapsular extension
- MRI guided fusion biopsy: prostate adenocarcinoma 4+3 and 3+4
- PMHx: Hypertension, hyperlipidemia
- Soc Hx: social alcohol use, prior smoking history

- Patient is interested in treatment with curative intent!
- Undergoing Staging with PSMA imaging.

Staging Prior to Surgery with PSMA



IMPRESSION:

- New diagnosis of prostate cancer with possible extracapsular extension
- Prominent Right Common Iliac and Right External Iliac lymph nodes suspicious for nodal metastasis

How would you treat this patient ?