Genitourinary Malignancies Tumor Board 2024

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24th Multidisciplinary Management of Cancers: A Case-based Approach

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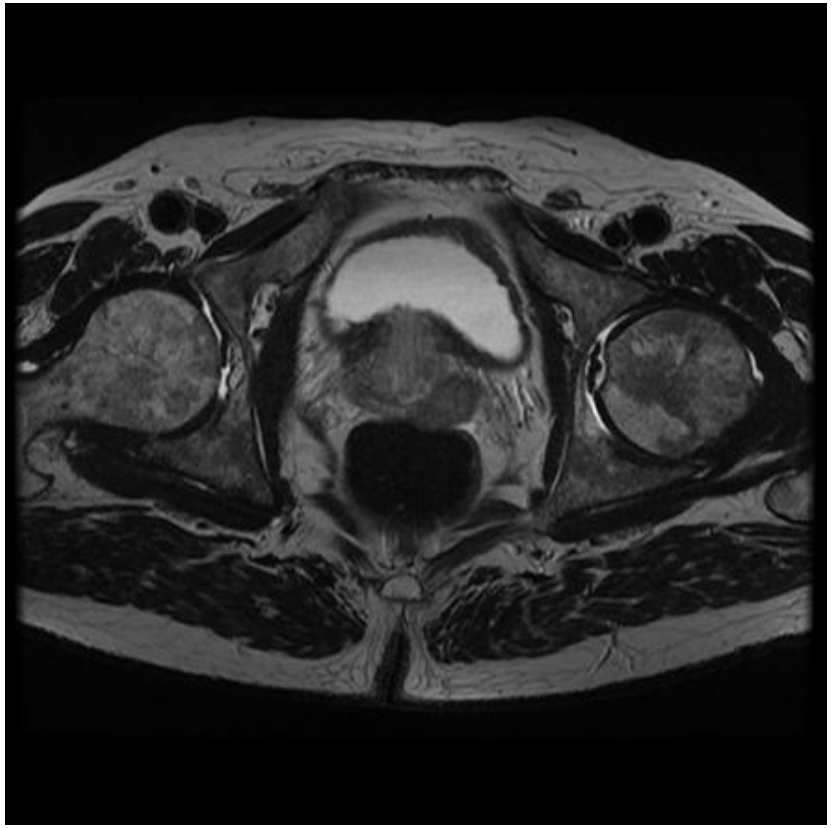
Case 1

- 60 y/o M postal worker who presents with urinary frequency
- PSA 12.3
- MRI shows a prostate tumor with macroscopic extracapsular extension and involvement of neurovascular bundle c/w T3a lesion. No lymphadenopathy
- MRI guided bx with 74% involvement with tumor, Gleason score 4 + 5= 9
- CT and bone scan negative for metastatic disease



Question 1: What would you recommend for initial management for this patient with T3a localized prostate cancer, PSA 12.3, and G4+5?

A. Androgen Deprivation Therapy (ADT) monotherapy

B. Prostatectomy

C. Radiation to the prostate and lymph nodes + ADT + ARSi (androgen receptor signaling inhibitor)

D. Radiation to the prostate + ADT + ARSi

E. Surveillance

Question 2: If he proceeds with XRT/ADT + ARSi, how long would you continue hormone therapy?

A. 6 months

B. 12 months

C. 18 months

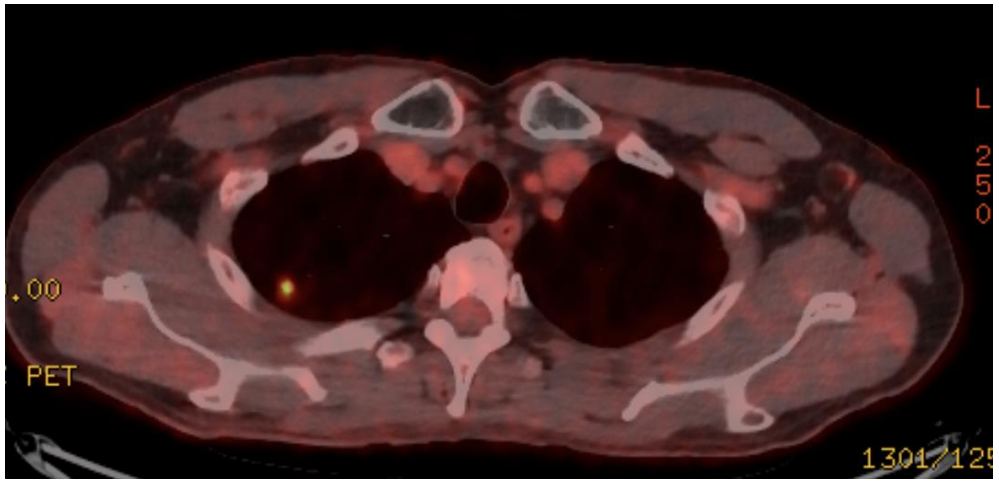
D. 24 months

E. 36 months

Case 1: 60 Y/o M with PSA 12, G4+5 prostate cancer (cont)

- Prior to receiving local therapy, a PSMA PET shows a few scattered lung nodules with bright uptake as well as a R hilar LN measuring 1.2 cm, and a 1.5cm R ext iliac node

- Biopsy of a RLL lung nodule shows prostate adenocarcinoma



Question 3: Now how would you manage this patient with metastatic hormone sensitive prostate cancer with pulmonary and nodal involvement on PSMA PET?

A. ADT+ ARSi

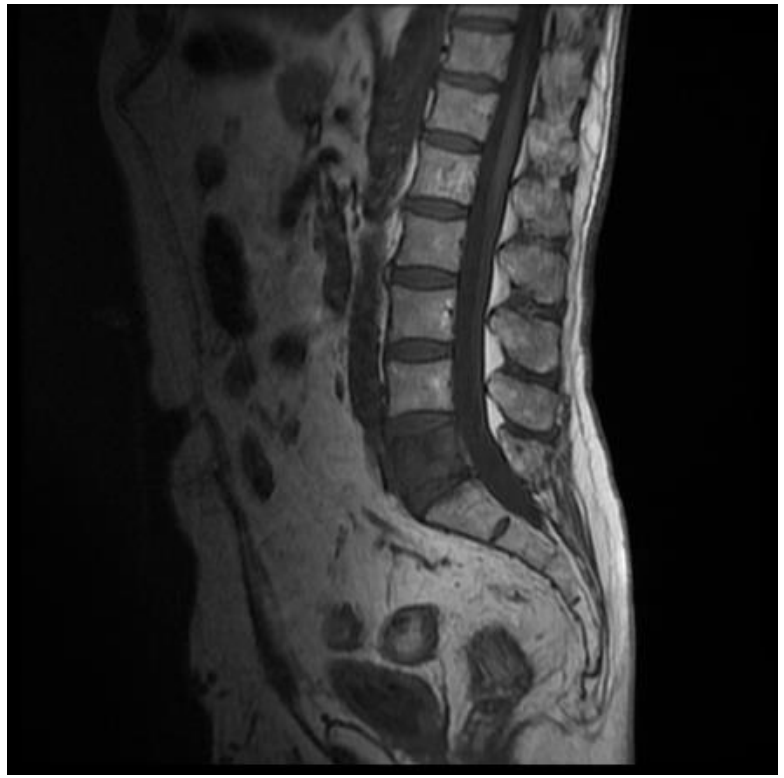
B. ADT + docetaxel

C. ADT + docetaxel + ARSi

D. XRT (prostate, pelvis and lung) + ADT + ARSi

Case 1: 60 Y/o M with mHSPC (cont)

- The patient starts on abiraterone/prednisone with leuprolide acetate and receives radiation to the prostate
- After 18 months of therapy his PSA starts to rise, PSMA PET demonstrates new solitary, painless lesion at L5, no other sites of disease. Prior sites of disease have resolved.
- Biopsy confirms metastatic prostate cancer, NGS demonstrates ATM mutation



Question 4: What do you recommend as next treatment for this patient with oligo-progressive ATM-mutated castrate resistant prostate cancer?

A. Metastasis directed radiation to L5

B. Lu-PSMA

C. Enzalutamide

D. Docetaxel

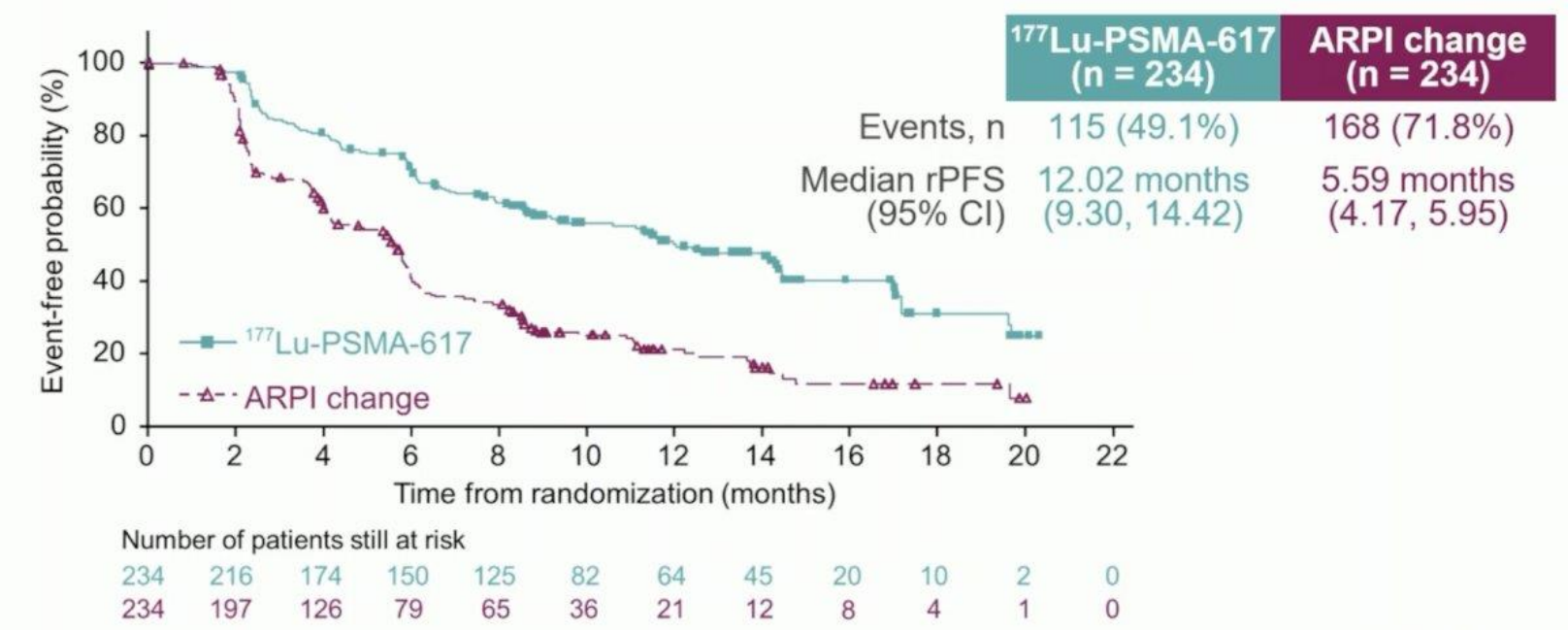
E. PARPi monotherapy

F. PARPi + ARSi

Sequencing of radioligand therapy, PSMAfore

Eligible adults

- Confirmed progressive mCRPC
- ≥ 1 PSMA-positive metastatic lesion on [^{68}Ga]Ga-PSMA-11 PET/CT and no exclusionary PSMA-negative lesions
- Progressed once on prior second-generation ARPI
  - Candidates for change in ARPI
- Taxane-naive (except [neo]adjuvant > 12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1

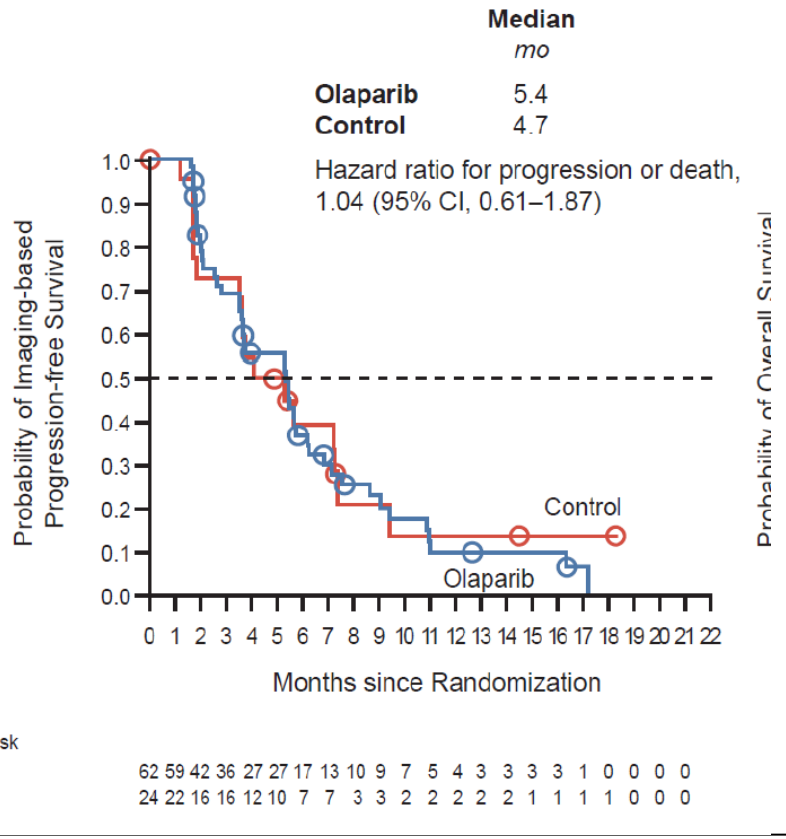


	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	115 (49.1%)	168 (71.8%)
Median rPFS (95% CI)	12.02 months (9.30, 14.42)	5.59 months (4.17, 5.95)

Sartor et al
ESMO 2023

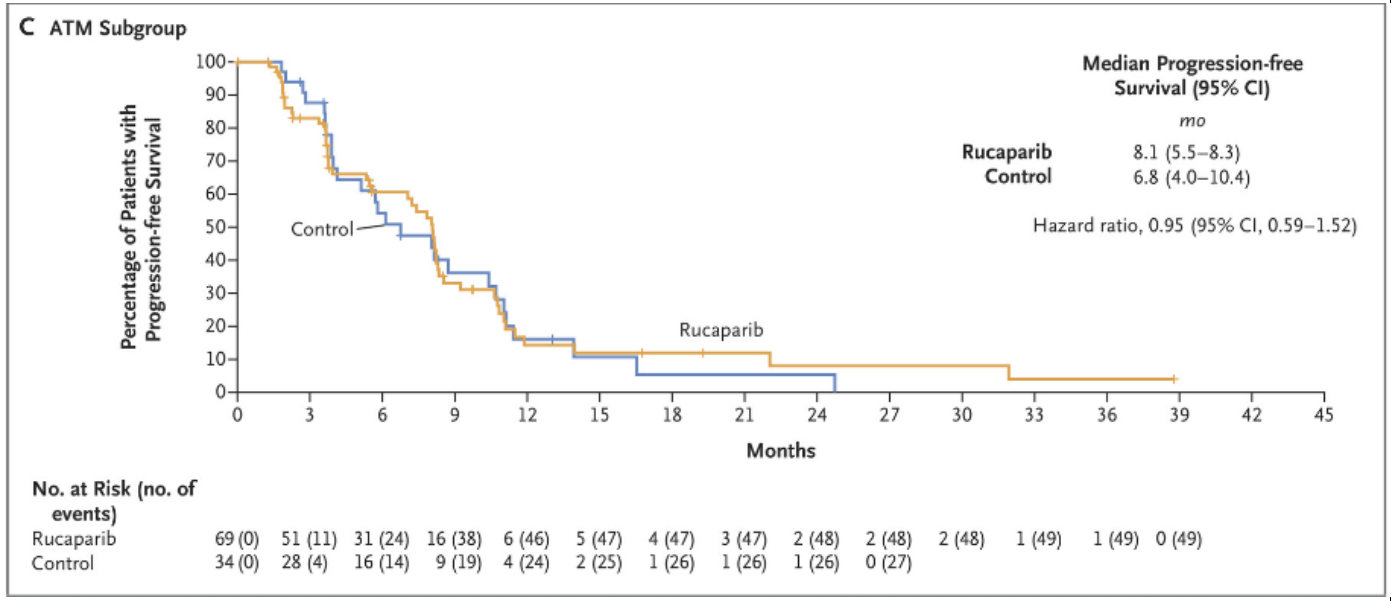
Parp-a-palooza in HRRm prostate cancer

PROfound



De bono et al 2023

TRITON-3



Fizazi et al 2023

Case 1: 60 Y/o with mCRPC ATM mut prostate cancer (cont)

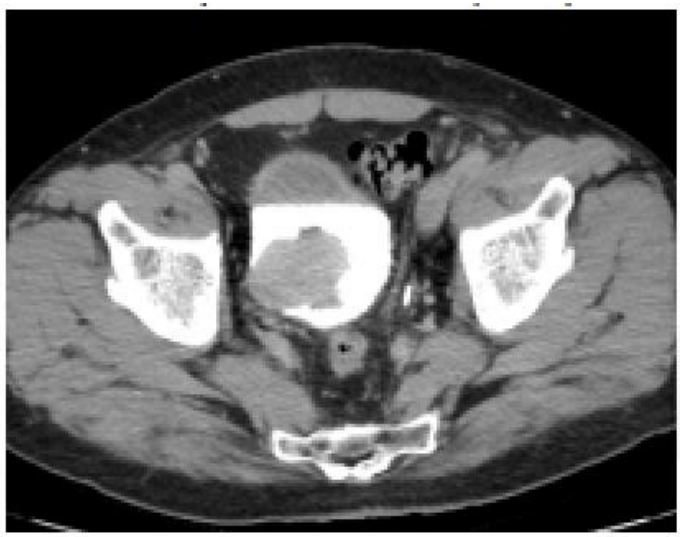
- The patient underwent metastasis directed radiation to L5 with subsequent decline of his PSA
- Continues on abi/pred + ADT for now

Take home points - Prostate

- For localized, high-risk prostate cancer, data support use of radiation together with ADT and ARSi in first line
- Metastasis directed therapy may delay need for systemic therapy and progression
- While PARP inhibitors have improved outcomes for patients with HRR mutated prostate cancer, patients with ATM mutations do not have clear benefit

Case 2

- 60-year-old male dentist presents with gross hematuria
- CT IVP shows a large bladder mass (4.5 x 3.6 x 4.8 cm) and mild R sided hydronephrosis
- TURBT shows muscle-invasive high grade urothelial cancer
- PET/CT with mass in bladder but no other metastatic disease



Hot Topic Mini Debate: Definitive therapy in localized urothelial cancer

Surgeons and Radiation Oncologists – how would you counsel this patient on cystectomy vs bladder preservation strategies?

Question 1: Prior to deciding on definitive therapy, the patient asks the medical oncologist about the role for neoadjuvant chemotherapy in bladder preservation therapy. What would you offer this patient with localized MIBC if pursuing chemo-RT?

A. ddMVAC

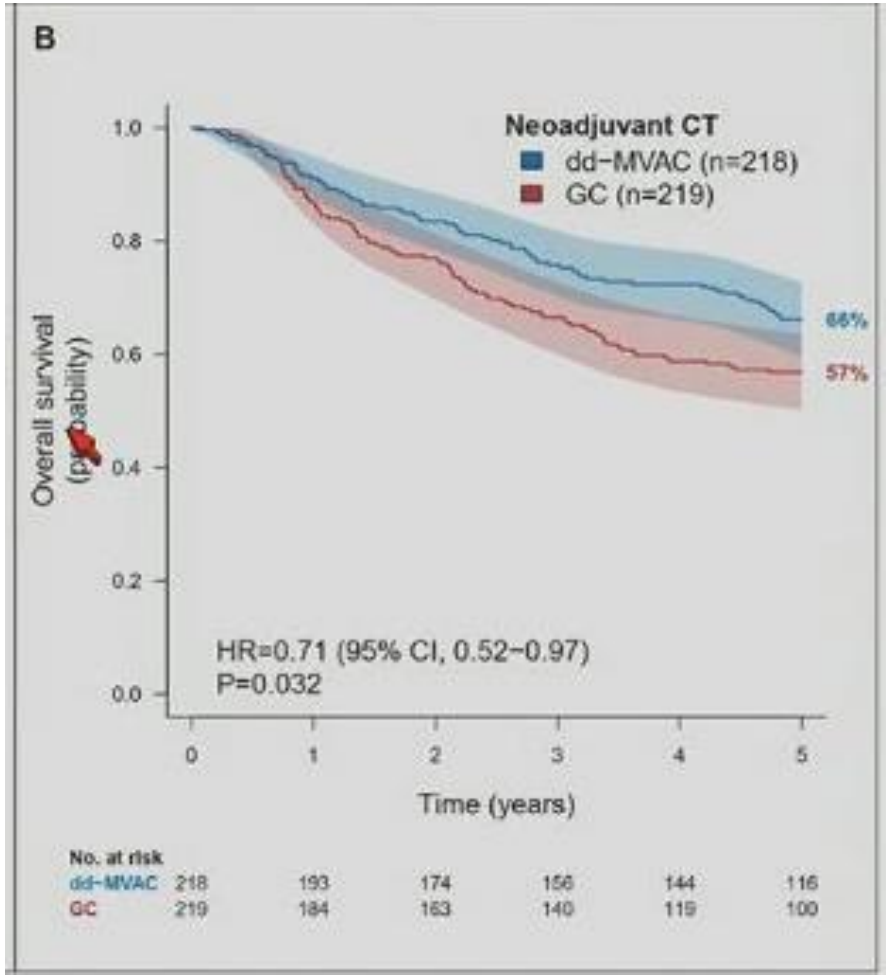
B. Gemcitabine/cisplatin

C. Enfortumab vedotin/Pembrolizumab

D. No neoadjuvant treatment

E. Pembrolizumab

VESPER trial



Pfister, ASCO 2023

Case 2: 60 y/o with MIBC (cont)

- Patient ultimately decided on pursuing cystectomy.
- Completed 4 cycles of ddMVAC followed by cystectomy.
- Cystectomy pathology showed T3 high grade urothelial cancer, no lymph node involvement.
- PD-L1 1%

Question 2: What do you offer this patient as adjuvant therapy after cystectomy with ypT3 disease?

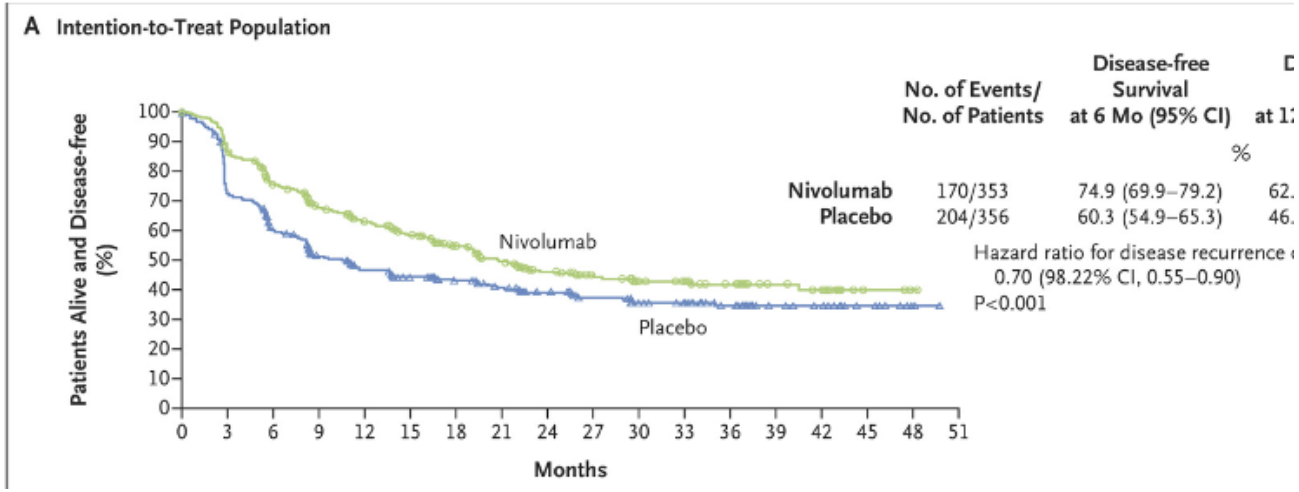
A. Immunotherapy (nivolumab or pembrolizumab)

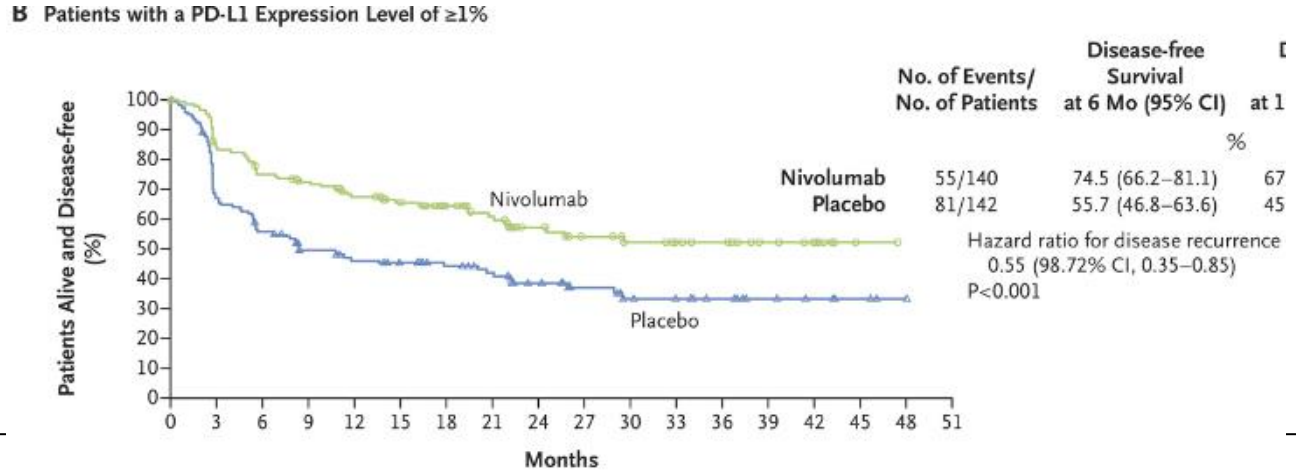
B. Immunotherapy if ctDNA positive post-cystectomy

C. Surveillance alone

Adjuvant IO in MIUC: DFS with no OS (yet)

CHECKMATE 274

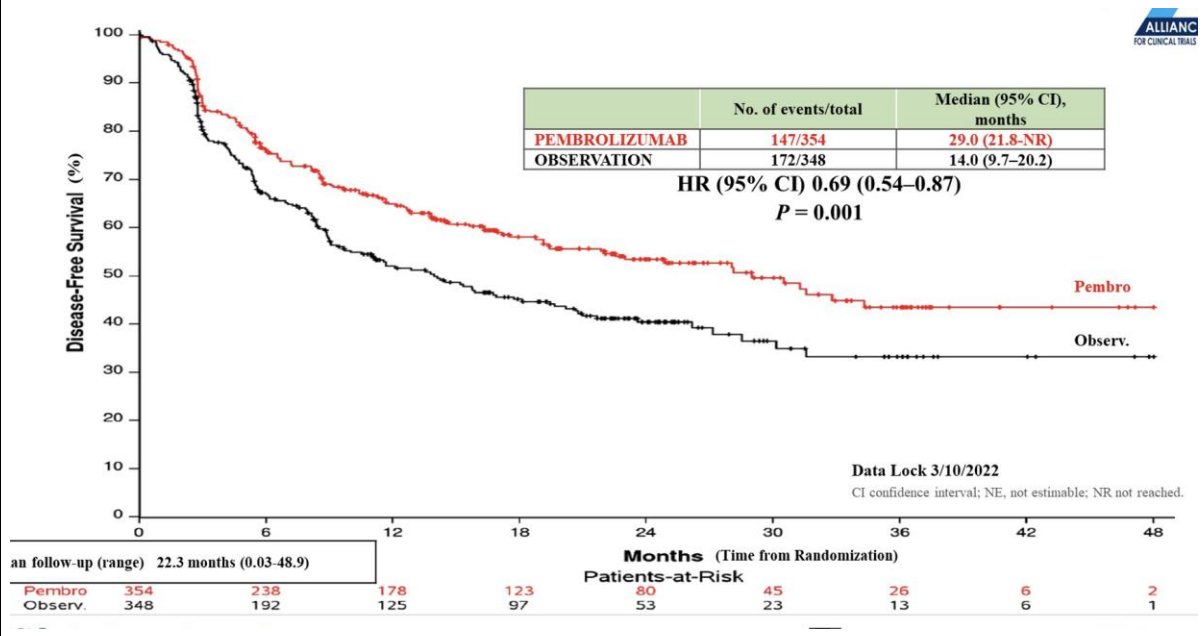


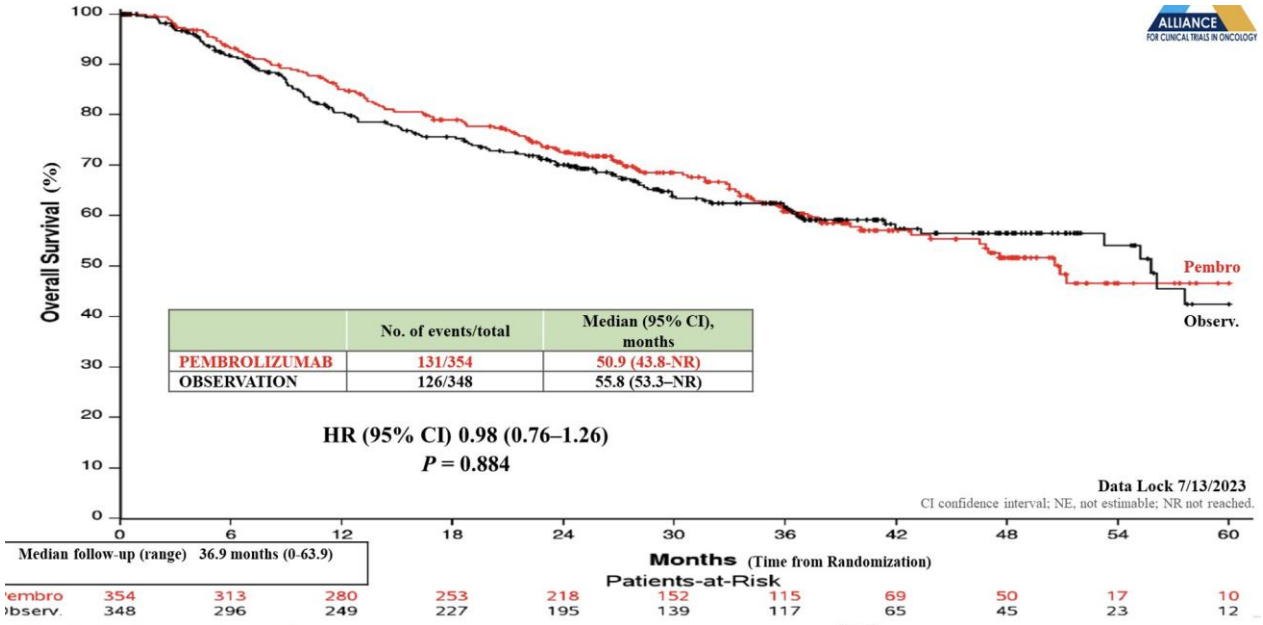


Bajorin et al
NEJM 2021

Adjuvant IO in MIUC: DFS with no OS (yet)

AMBASSADOR





Apolo et al, ASCO GU 2024

Case 2: 60 y/o with MIBC (cont)

- The patient opted to pursue surveillance alone
- 1 year later developed increasing size of lung nodules, biopsy proven metastatic recurrence
- NGS shows an FGFR3 exon 7 mutation

Question 3: What do you recommend as next line of therapy for this patient with recurrent, metastatic urothelial cancer with FGFR3mut previously treated with ddMVAC in the neoadjuvant setting?

A. Gemcitabine/cisplatin/nivolumab

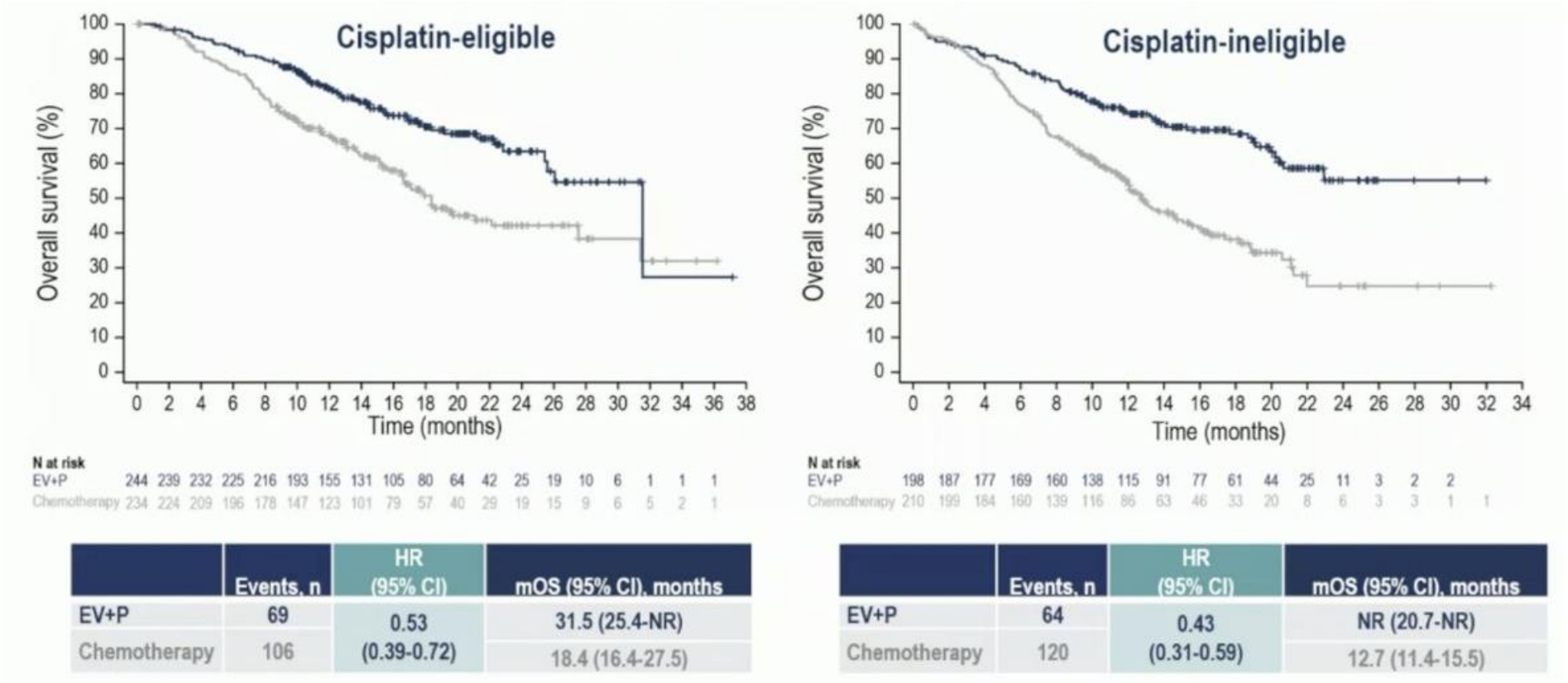
B. Enfortumab vedotin (EV)/pembrolizumab

C. Pembrolizumab

D. Erdafitinib

E. EV monotherapy

Paradigm shift in mUC--
EV 302 –KEYNOTE-A39



	Events, n	HR (95% CI)	mOS (95% CI), months
EV+P	69	0.53 (0.39-0.72)	31.5 (25.4-NR)
Chemotherapy	106		18.4 (16.4-27.5)

	Events, n	HR (95% CI)	mOS (95% CI), months
EV+P	64	0.43 (0.31-0.59)	NR (20.7-NR)
Chemotherapy	120		12.7 (11.4-15.5)

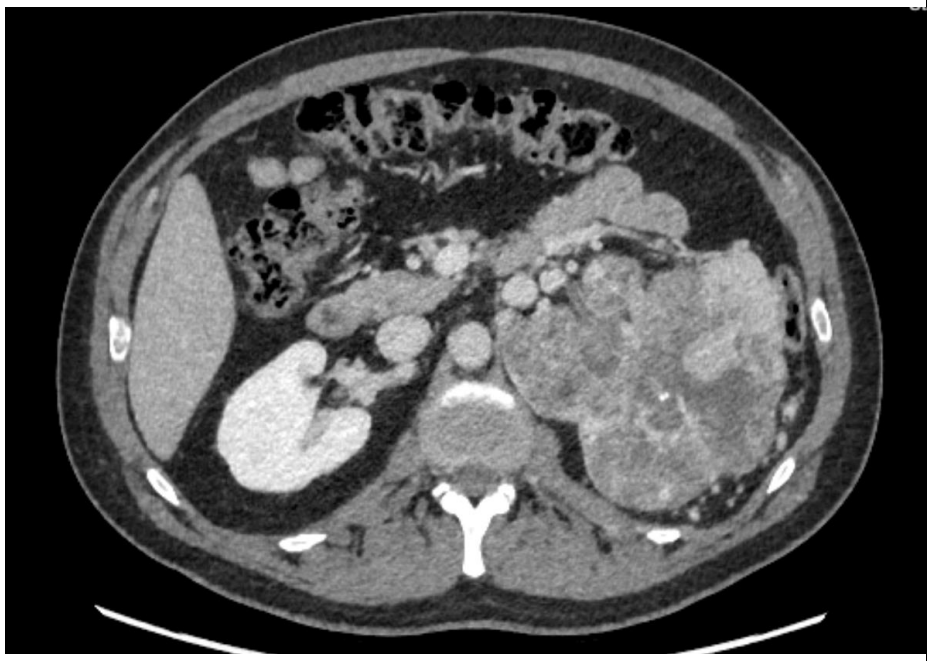
Powles et al, ESMO 2023

Take home points - Bladder

- Trimodality Treatment (TMT) is a reasonable alternative to cystectomy in select patients with MIBC
  - Choosing which modality likely depends on tumor, patient factors
- Adjuvant immunotherapy after cystectomy has shown a DFS advantage, but no + OS data to date
- EV-302 showed use of EV/Pembro as new SoC for first line treatment in locally advanced and metastatic UC

Case 3

- 51 y/o police woman who presented for mechanical back pain, found to have large (12 x 13cm) L kidney mass
- CT AP showed involvement of L renal vein
- CT Chest identified a few non-specific, pulmonary nodules <1cm



Question 1: What is your next step in evaluation/treatment for this woman with a large kidney mass with indeterminate lung nodules?

A. Biopsy of lung lesion

B. Nephrectomy

C. Systemic therapy

D. Radiation to primary tumor

Case 3 cont: 51 y/o F with large L renal mass

- Underwent L radical nephrectomy with pathology showing 12cm clear cell renal cell carcinoma, Fuhrman grade 2, with renal vein involvement (pT3)
- She is otherwise very active with ECOG 0

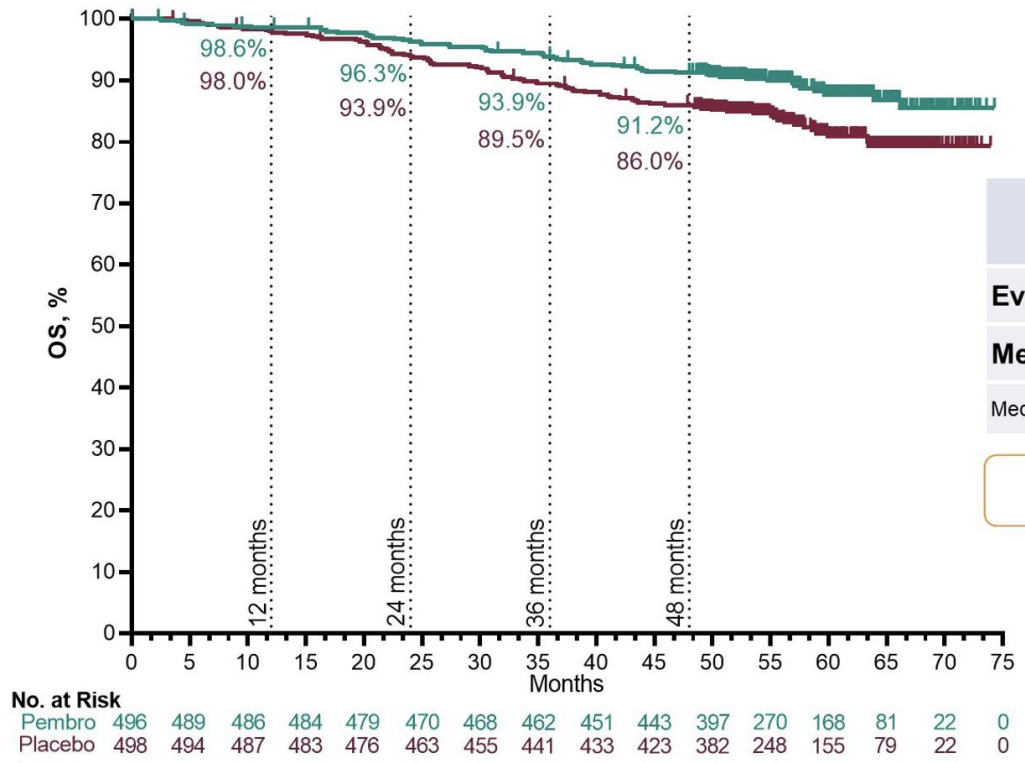
Question 2: Would you recommend adjuvant pembrolizumab for this patient with resected pT3 RCC

A. Yes

B. No

Oh me, oh my, OS: Adjuvant IO in RCC

KEYNOTE- 564



	Pembro (N = 496)	Placebo (N = 498)
Events, n	55	86
Median, mo (95% CI)	NR (NR–NR)	NR (NR–NR)

Median follow-up was 57.2 months (range, 47.9–74.5)

HR 0.62 (95% CI 0.44–0.87); *P* =.002*

* **denotes statistical significance**. P-value boundary for OS at IA3 was 0.0072 (1-sided) per Lan-DeMets O'Brien-Fleming spending approximation α-spending function. As this key secondary endpoint was formally met, any future OS analyses will be descriptive only.

Data cutoff date: September 15, 2023.

Chouieri et al
ASCO GU 2024

Case 3: 51 y/o F with pT3 RCC s/p nephrectomy (cont)

- After nephrectomy pt opted to not pursue adjuvant IO (prior to KN 564 OS data)
- 9 months later CT scan identifies several growing pulmonary nodules, now 1.4 cm
- FNA confirms metastatic ccRCC
- She is clinically well and able to do all activities
- Labs show ANC 1500, plts 250, Hgb 11, Ca 10.1

Question 3: What do you recommend for first line systemic treatment for patient with intermediate risk mRCC?

A. Ipi/nivo

B. Cabo/nivo

C. Len/pembro

D. Axi/pembro

E. Cabo/ipi/nivo

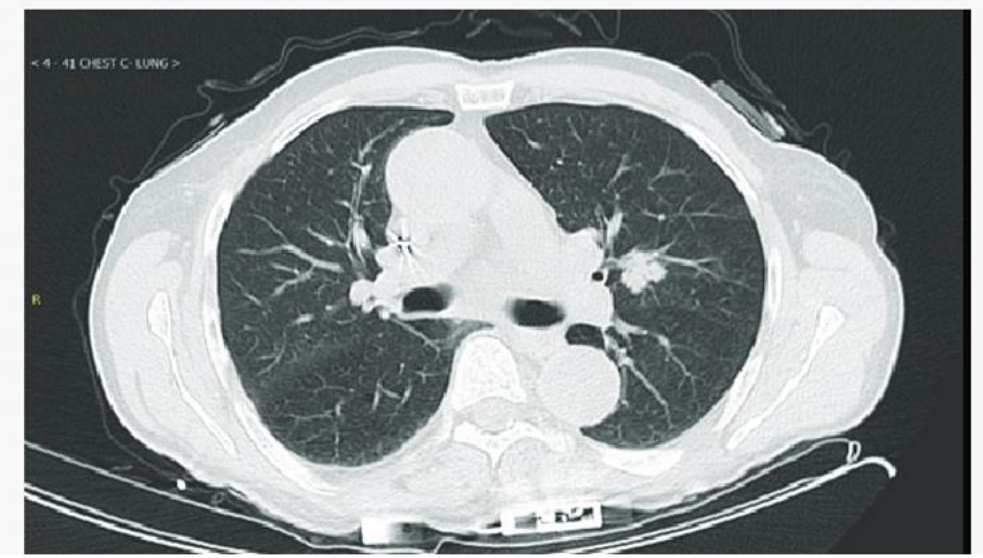
Case 3: 51 y/o F with mRCC with pulm mets (cont)

- After 3 cycles of ipi/nivo updated CT shows decrease in numerous pulmonary mets
- However, the patient developed G3 diarrhea and treatment was held

	Colitis	Diarrhea
Grade 1	Asymptomatic	Increase of < 4 stools/d over baseline
Grade 2	Abdominal pain, mucus, blood in stool	Increase of 4-6 stools/d
Grade 3	Severe pain, fever, peritoneal signs	Increase of ≥ 7 stools/d
Grade 4	Life-threatening consequences such as perforation, ischemia, necrosis, bleeding, toxic megacolon	Life-threatening consequences such as hemodynamic collapse
Grade 5	Death	Death

Case 3: 51 y/o F with mRCC with pulm mets (cont)

- Patient did well for ~ 3 years off therapy with serial scans
- Then developed increasing size of a LUL nodule, suspicious for met



Question 4: How would you approach a patient with mRCC and solitary site of progression in patient with very good response to immune therapy c/b immune related adverse event (iRAE)?

A. Retrial of immunotherapy

B. XRT to progressive nodule

C. Surgery to remove nodule

D. Switch systemic therapy (TKI)

Case 3: 51 y/o F with mRCC with pulm mets (cont)

- Underwent SBRT to the pulmonary nodule
- 6 months later a scan showed progression of several lung nodules
- Restarted on nivolumab monotherapy with stability of lung nodules
- Few months later started to have significant headaches. MRI c/w hypophysitis
- Currently off systemic therapy with stable disease

Take home points - Kidney

- There is now overall survival data supporting the use of 1 year of adjuvant pembrolizumab for high-risk resected RCC
- Between several IO and IO/TKI doublets still no clear winner for first line therapy in intermediate/poor risk disease
- Recommend early involvement of multidisciplinary teams for iRAE management

Case 4

26 yo male software engineer presents with a painless left sided testicular mass

- Ultrasound showed a large solid tumor in the left testis
- He undergoes orchiectomy showing a 9.5cm pure seminoma, pT1b
- Post orchiectomy tumor markers: AFP 3.3, HCG <0.6 LDH 134
- CT CAP shows concern for a solitary 2.4cm retroperitoneal LN

Question 1: What would you recommend for a 26 y/o with stage IIB seminoma with LN disease after orchiectomy?

A. Observation

B. Retroperitoneal Lymph Node dissection (RPLND)

C. Radiation

D. Chemotherapy

SEMS trial: RPLND as first line treatment for seminomas with low volume RP lymphadenopathy

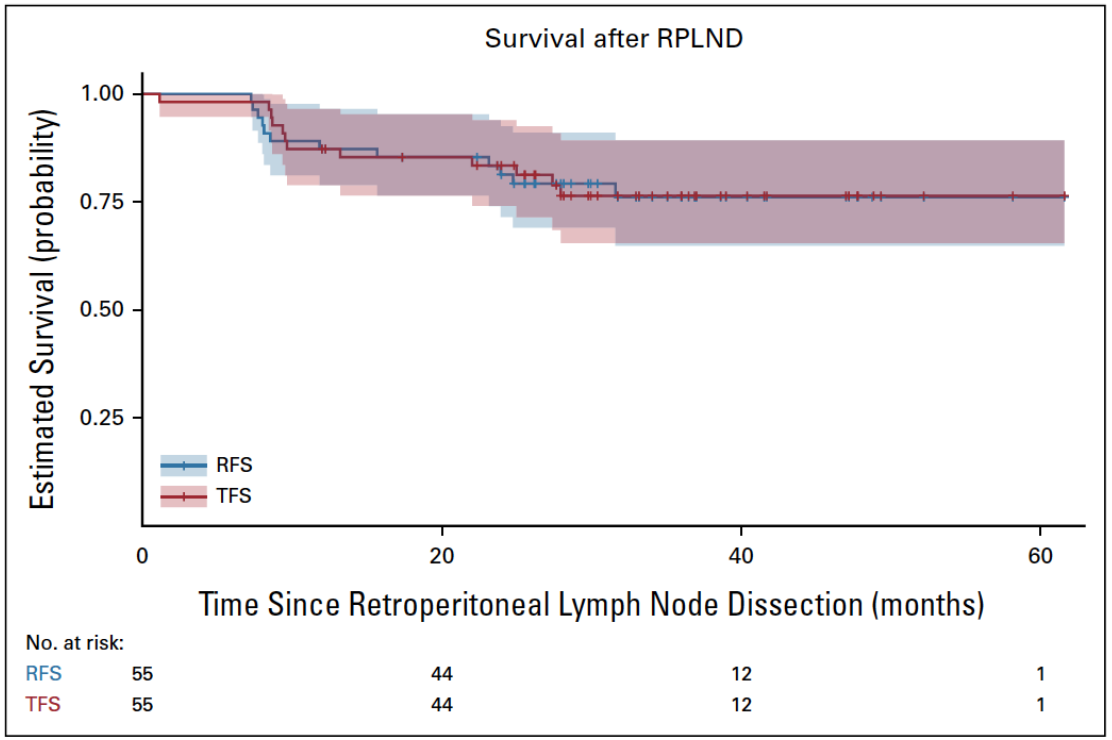
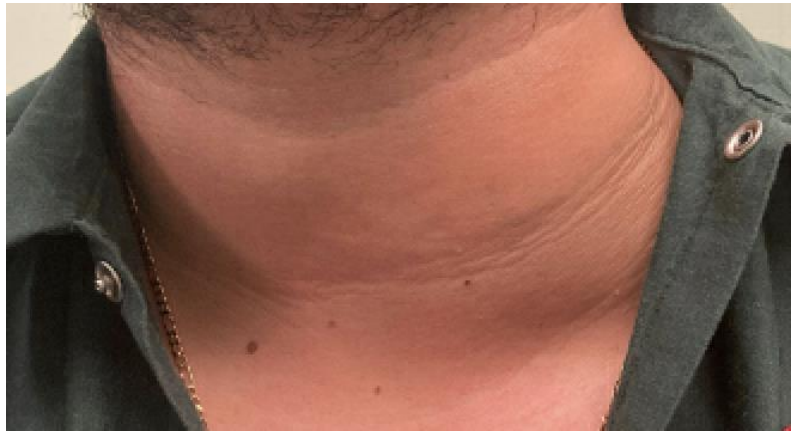


FIG 1. RFS and TFS after RPLND. RFS, recurrence-free survival; RPLND, retroperitoneal lymph node dissection; TFS, treatment-free survival.

Daneshmand et al JCO 2023

Case 4: 26 y/o with IIB seminoma

- He received radiation to ipsilateral iliac lymph nodes
- Two years later he presents with enlarging neck mass
- Repeated tumor markers show AFP 4085, HCG <0.6, LDH 175
- FNA shows metastatic yolk sac tumor
- Scrotal ultrasound was negative
- CT neck, CAP show no other areas of disease



Question 2: How would you manage this newly discovered yolk sac tumor?

A. BEP

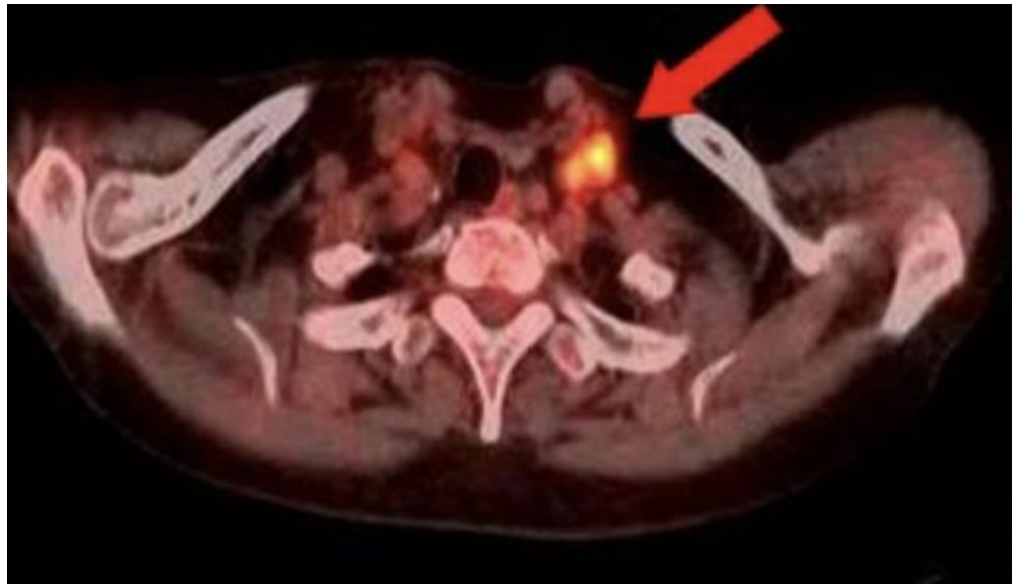
B. Radiation

C. Surgery

D. TIP

Case 4: 26 y/o with recurrent GCT (cont)

- Received 4 cycles of BEP
- AFP started to rise shortly after completing chemotherapy
- PET scan showed enlarging lymphadenopathy in the supraclavicular region



Question 3: What would be your next line of therapy for recurrent yolk sac tumor?

A. Radiation

B. High dose chemotherapy with autologous stem cell rescue

C. Convention dose chemotherapy (TIP)

Case 4: 26 y/o with recurrent GCT (cont)

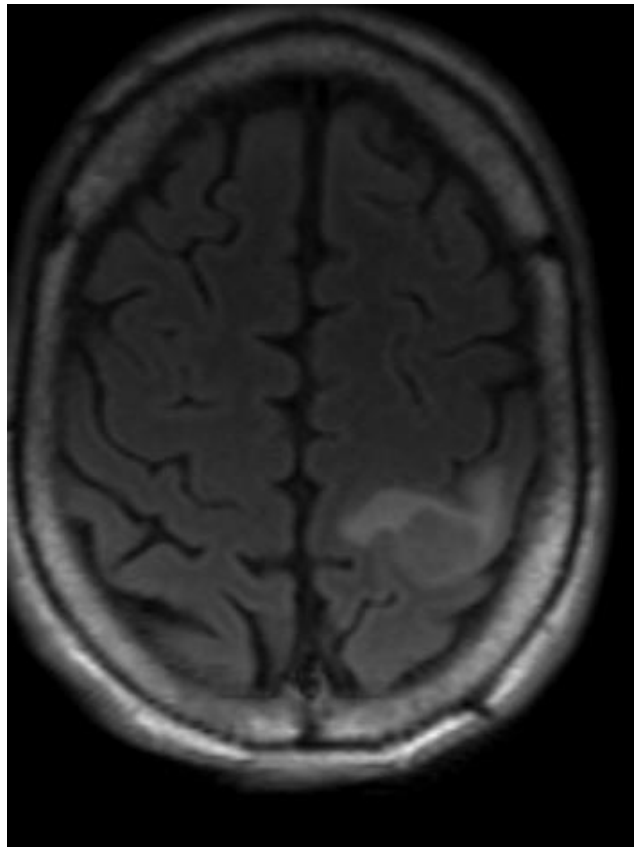
- He underwent 3 sequential carbo/etop prep with autologous stem cell rescue
- After transplant had persistent SCV nodal disease ~3cm
- Underwent neck dissection – pathology showed necrosis
- Currently in remission

Take home points - GCT

- In stage II seminoma, there is equipoise between surgery, radiation, and chemotherapy
- BEP remains standard of care as first line therapy in most patients
- We await data from TIGER trial to be able to more definitively support conventional vs high-dose chemotherapy for relapsed germ cell tumors

Case 5 (bonus)

- 68 y/o man with hx of melanoma (2018) presented with acute onset R-sided weakness and gait imbalance, ECOG 3
- Found to have multiple brain metastases of unknown primary
- CT CAP showed liver lesion and multiple mediastinal and hilar lymph nodes
- Liver biopsy had IHC staining consistent with prostatic origin
- PSA 3.1



Case 5: 68 y/o with metastatic prostate cancer with brain involvement (cont)

- MRI prostate showed a large pelvic mass centered in expected location of prostate inseparable from bladder and rectum and with invasion of pelvic sidewall. Evidence in tumor in vein of left internal iliac
- PET/CT showed large prostate mass and hypermetabolism of hilar and mediastinal LNs
- Started on degarelix
- Prostate biopsy was consistent with small cell carcinoma of the prostate

Question 1: What would you offer this patient for systemic therapy with a metastatic neuroendocrine prostate cancer

A. ADT

B. ADT + Chemotherapy (Carboplatin/docetaxel or carbo/etoposide)

C. ADT + Radiation

D. ADT + chemotherapy

E. ADT + Immunotherapy

Case 5: 68 y/o with with metastatic neuroendocrine prostate cancer

- The patient was started on carboplatin/docetaxel and ADT
- 4 weeks later, NGS from liver biopsy revealed an MSI high tumor with TMB 72
- Pembrolizumab added to chemotherapy to complete 6 cycles of chemo + IO, with marked reduction in disease burden
- Continues on pembro “maintenance”, >1 year later continues with near CR, now ECOG 1

1 year later…

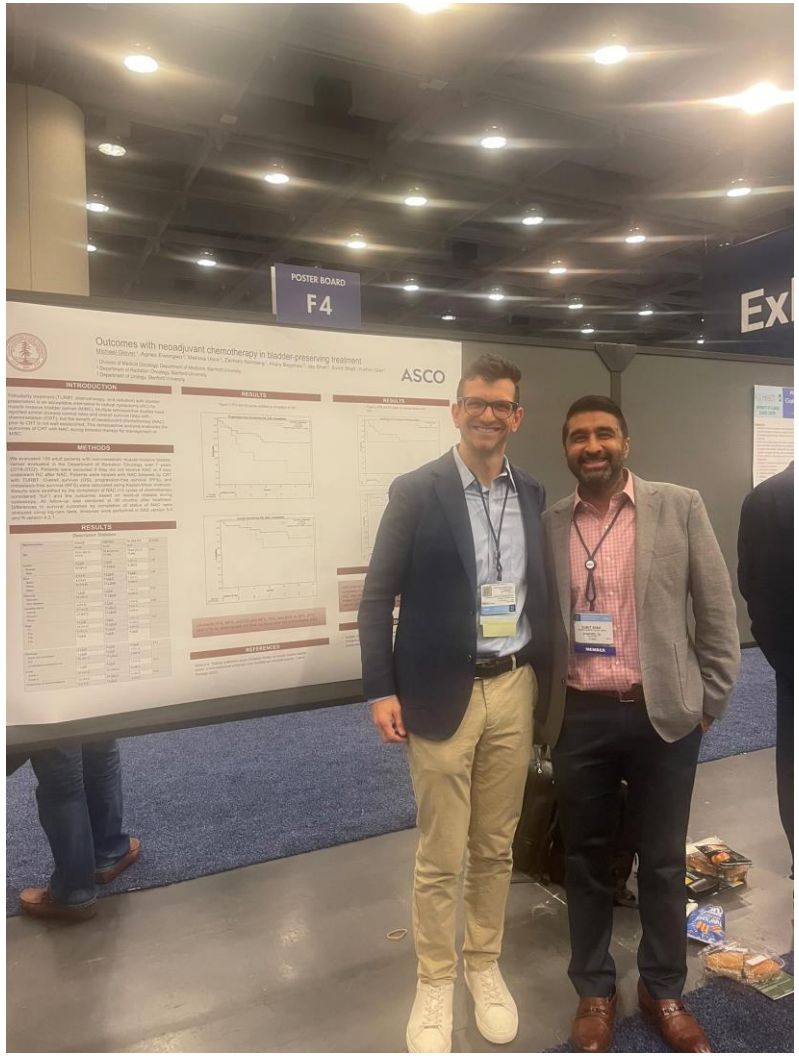
Keynote Address at Global Climate Change Summit

Photo shared with permission

Take home points – Small Cell Prostate

- Small cell prostate cancer is a rare, aggressive subtype that generally presents with advanced disease and lower PSA
- Treated similarly to SCLC with combination chemotherapy
- Both pembrolizumab and dostarlimab have tissue agnostic FDA approvals for MSI-high tumors
- Sometimes things work out better than you think!

Thank you!


POSTER BOARD
F4
Outcomes with neoadjuvant chemotherapy in bladder-preserving treatment
ASCO