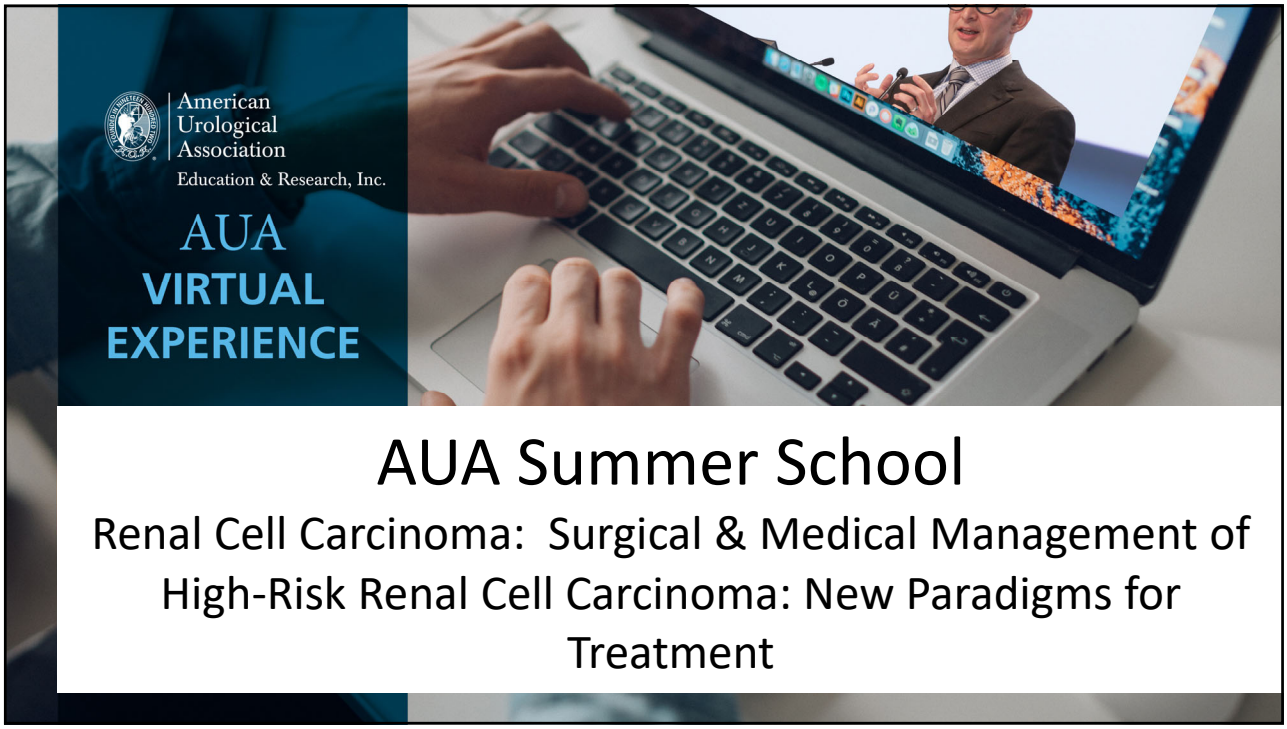

AUA Summer School

Renal Cell Carcinoma: Surgical & Medical Management of High-Risk Renal Cell Carcinoma: New Paradigms for Treatment

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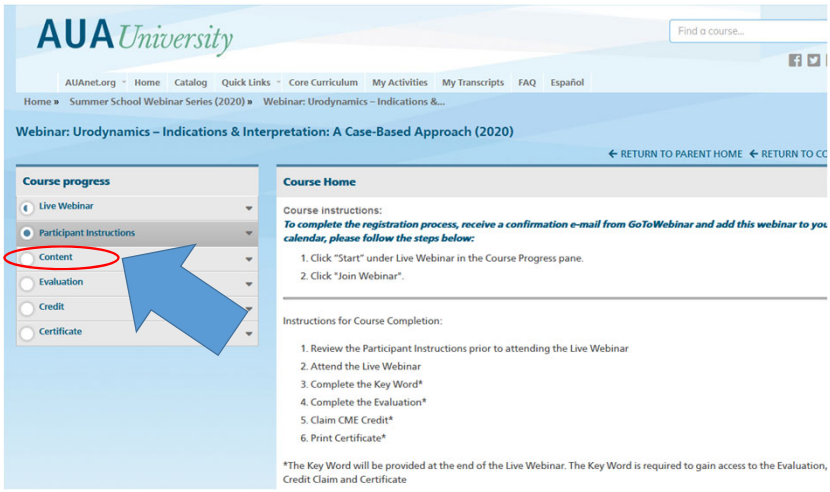
Course Handouts



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CME Credits: Upon completion of course evaluations, you will have the opportunity to claim CME credits and obtain a certificate.

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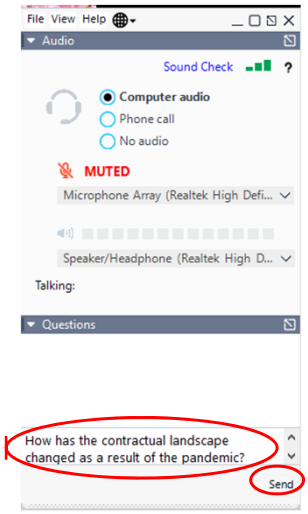

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Acknowledgements

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Knowledge Assessment

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Question 1

What mutations might be expected in type I papillary renal tumors?

A) Ret
B) Myc
C) Met
D) EGFR

Question 2

What treatment choice might you choose after complete resection for a clear cell T3N1M0 cancer.

A) Observation
B) Nivolumab
C) Sunitinib
D) Pembrolizumab

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Question 3

What imaging modality could be useful in the diagnosis of renal oncocytoma?

A) MRI with gadolinium
B) Triple phase CT
C) Sestamibi SPECT CT
D) Contrast enhanced renal ultrasound

Question 4

What is the factor that is NOT directly related to preservation of renal function after partial nephrectomy?

A) Warm Ischemia time less than 20 minutes
B) Volume of normal renal parenchyma resected
C) Preoperative renal function
D) OR time

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Question 5

Effective methods for hemostasis robotic laparoscopically for arterial bleeding include:

A) Increase pneumoperitoneum pressure to 20 mm Hg
B) Mini lap direct compression for 5 min
C) 4-0 prolene with lapraTy wrapped around tail
D) Placement of clip
E) C & D

Faculty

- Benjamin R Lee MD, Professor & Chair, The George W. Drach Endowed Chair of Urology, University of Arizona College of Medicine (Email: brlee@surgery.arizona.edu)
- Oliver Sartor MD, C.E. & Bernadine Laborde Professor for Cancer Research, Medical Director, Tulane Cancer Center, Assistant Dean for Oncology, Tulane Medical School. (Email: osartor@tulane.edu)
- Chandru Sundaram MD, Professor, University of Indiana

(Email: sundaram@iupui.edu)

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Learning Objectives

After participating in this course, attendees will be able to:

1. State how to manage bleeding complications of robotic partial nephrectomy.
2. Describe the algorithm of Immunotherapy treatment of advanced Renal Cell Carcinoma.
3. Explain how to minimize positive margin rates of robotic partial nephrectomy

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Update on Treatment of Metastatic Renal Cancers

Oliver Sartor, MD
Laborde Professor of Cancer Research
Medical Director Tulane Cancer Center
Departments of Medicine and Urology
Assistant Dean for Oncology
Tulane Medical School
New Orleans, Louisiana

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Six Areas of Focus for Today

1. **Classification/genomics**
2. **Role of surgery in metastatic disease**
3. **Optimal 1st-line therapy for metastatic clear cell**
4. **Optimal 2nd-line therapy for metastatic clear cell**
5. **Current strategies for non-clear cell disease**
6. **Adjuvant treatment**

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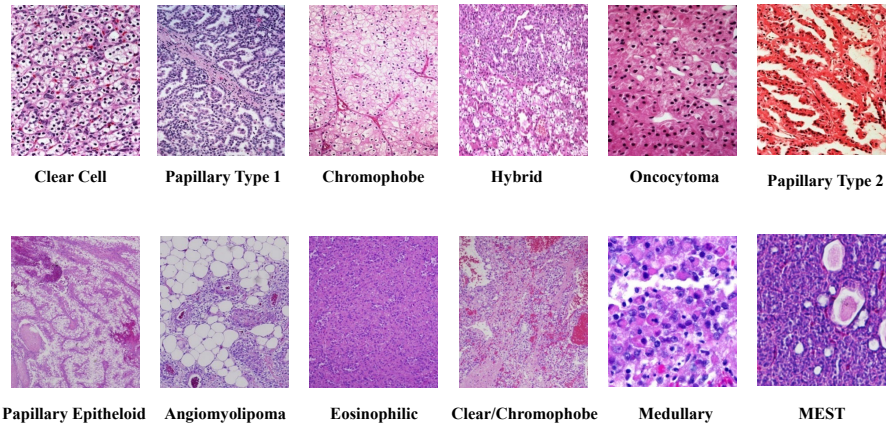
Kidney Cancer Heterogeneity



Clear Cell | Papillary Type 1 | Chromophobe | Hybrid | Oncocytoma | Papillary Type 2

Papillary Epitheloid | Angiomyolipoma | Eosinophilic | Clear/Chromophobe | Medullary | MEST

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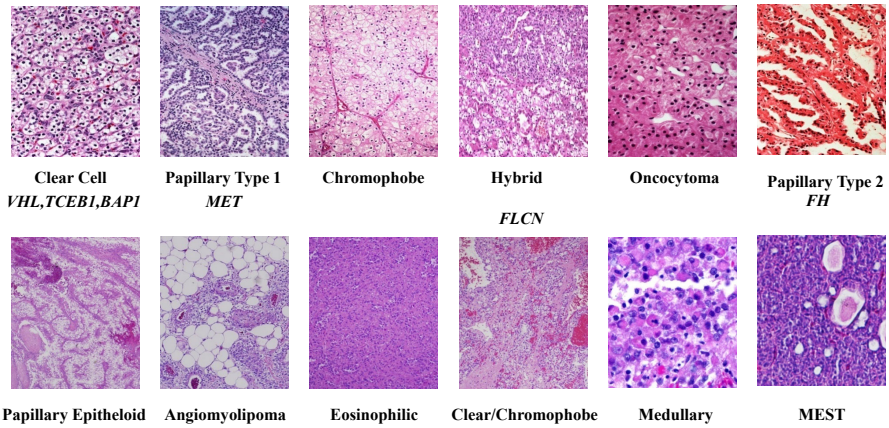
Kidney Cancer Genes



Clear Cell *VHL,TCEB1,BAP1* | Papillary Type 1 *MET* | Chromophobe | Hybrid *FLCN* | Oncocytoma | Papillary Type 2 *FH*

Papillary Epitheloid *TFE3, TFEB, MITF* | Angiomyolipoma *TSC1, TSC2* | Eosinophilic *SDHA, SDHB, SDHC, SDHD* | Clear/Chromophobe *PTEN* | Medullary *SMARCB1* | MEST *CDC73*

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Hereditary Renal Cancer Syndromes

- von Hippel-Lindau (VHL) caused by pathogenic variants in *VHL*
- Hereditary leiomyomatosis and renal cell cancer caused by pathogenic variants in fumarate hydratase (*FH*)
- Birt-Hogg-Dube caused by pathogenic variants in folliculin (*FCLN)*
- Hereditary papillary renal carcinoma caused by pathogenic variants in *MET*

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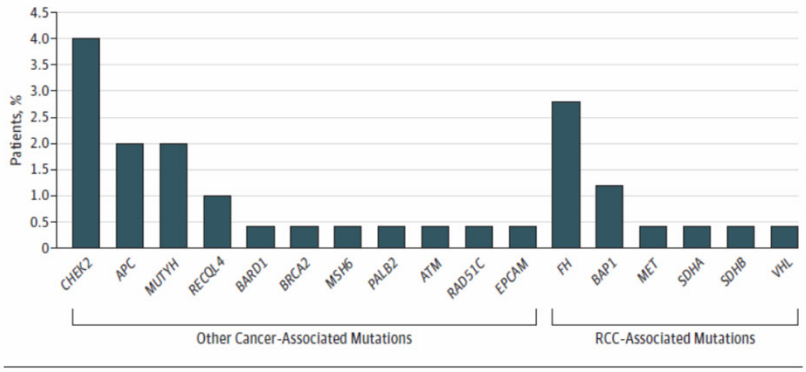
Prevalence of Germline Mutations in those with Advanced Renal Cell Cancers

Carlo et al. *JAMA Oncol*. 4:1228-1235, 2018

Figure 1. Frequency and Distribution of Pathogenic Germline Mutations

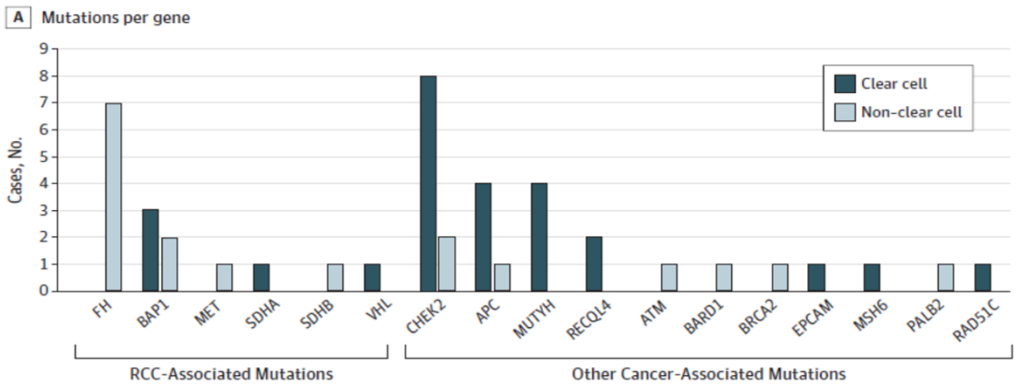


Germline mutations were found in 41 patients (16.1%): RCC-associated mutations in 14 (5.5%) and other cancer-associated mutations in 27 (10.6%). Renal cell carcinoma (RCC)–associated germline mutations include mutations in *BAP1*, *FH*, *MET*, *SDHA*, *SDHB*, and *VHL*.

Prevalence of Germline Mutations in those with Advanced Renal Cell Cancers

Carlo et al. *JAMA Oncol.* 4:1228-1235, 2018

Figure 2. Pathogenic Mutations by Histologic Subtype



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Surgical Issues in Metastatic Disease

- Resect the primary
- Resect the metastases
- Both of the above

Role of Cytoreductive Nephrectomy

- In the cytokine-era, two large studies established the role of cytoreductive nephrectomy (CN)
  - SWOG – Median OS 11 months for CN+ vs. 8 months for no surgery
  - EORTC – Median OS 17 months for CN+ vs. 7 months for no surgery
- TKI era
  - Phase III sunitinib study (CARMENA trial) had no benefit for surgery
  - Data from International Consortium Databases support the role of surgery in favorable/intermediate risk disease and good performance status (KPS > 80)
- In my opinion, no benefit in patients expected to survive <12 months but strongly "consider" nephrectomy for those with good surgical risk and favorable/intermediate prognosis

Flanigan et al, NEJM, 2001; Mickisch et al, Lancet, 2001; Choueiri et al, J Urol, 2011; Heng et al, Eur Urol, 2014; Mejean et al. NEJM, 2018

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What is the role of metastectomy in advanced renal cell?

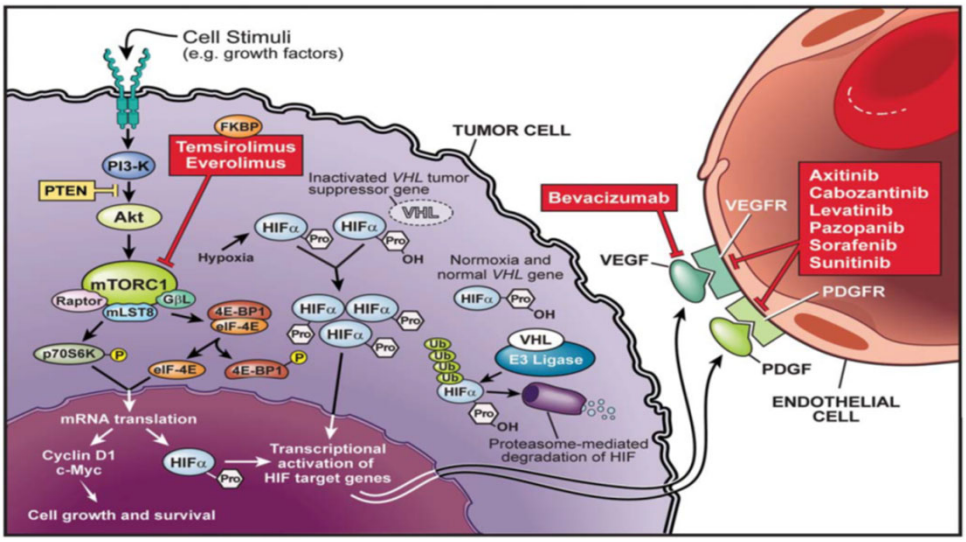
- What is the role of metastectomy?
  - Resect both the primary and metastases if there is a single metastatic site
  - Resect all metastases if they are completely resectable
  - Opinion…….if you can render the patient free of disease, or debulk 90%+ of the metastatic lesions safely, then strongly consider aggressive surgery in selected patients

Six drug treatment categories for metastatic clear cell renal cancer

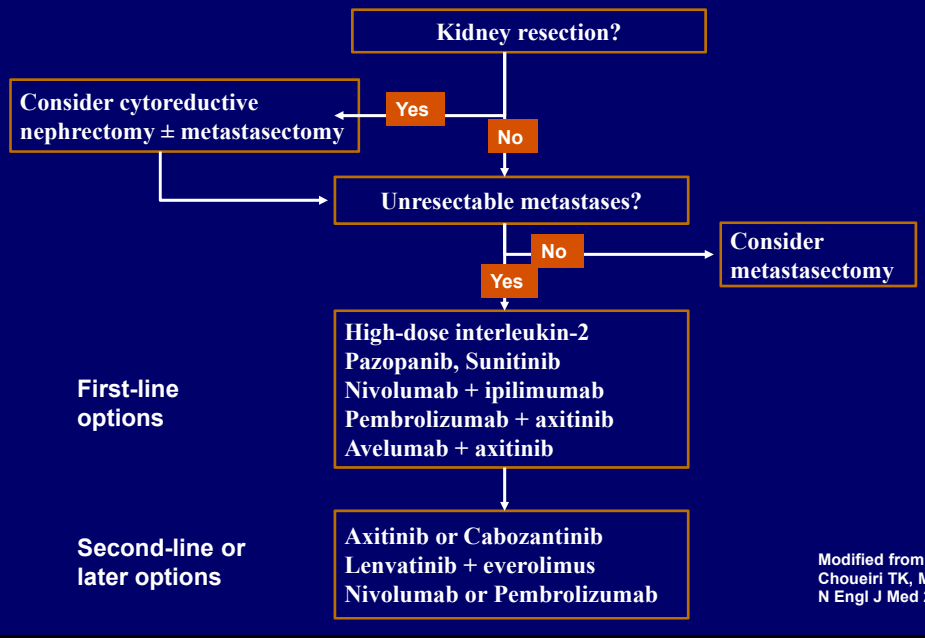
- Cytokines
  - Interferons and interleukin-2 (special case)
- Tyrosine kinase inhibitors (all hit VEGF receptor +/- more)
  - Sorafenib, sunitinib, pazopanib, axitinib, levantinib, cabozantinib
- Anti-VEGF
  - Bevacizumab
- mTOR inhibitors
  - Everolimus and temsirolimus
- PD1 inhibitors
  - Nivolumab, pembrolizumab
- CTLA4 inhibitors
  - Ipilimumab

Pathways and Current Drugs in Metastatic RCC

Barata et al, Ca J Clinicians 2017



Decision-Making Strategy for Advanced Clear-Cell RCC



Modified from Choueiri TK, Motzer RJ. N Engl J Med 2017;376:354

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Risk Stratification in Metastatic Renal Cell

Variables	Cutoff	MSKCC	Heng
Karnofsky performance status	<80%	X	X
Hemoglobin	<ULN	X	X
Calcium	>10	X	X
Time from diagnosis to treatment	<1 year	X	X
LDH	>1.5× ULN	X	
Platelet count	>ULN		X
Neutrophil count	>ULN		X

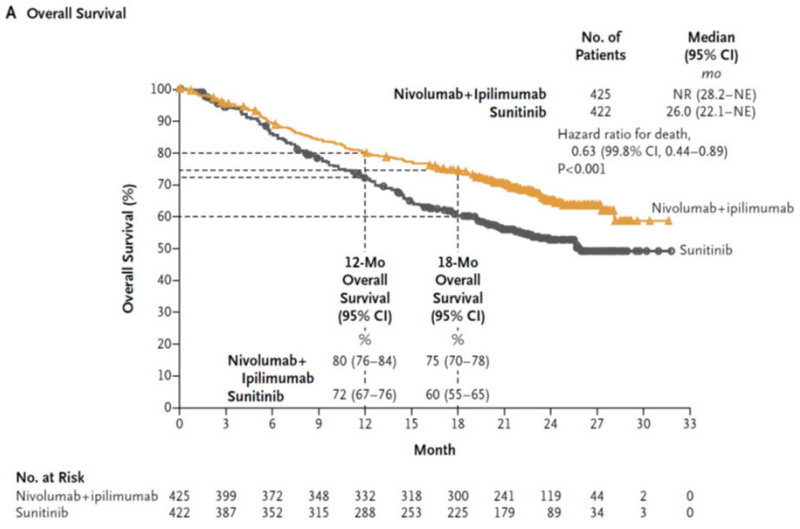
ULN: upper limit of normal.

Risk groups are defined as 0 risk factors = favorable, 1–2 risk factors = intermediate, and >2 risk factors = poor.

Some Important Comparative Studies

Nivolumab + Ipilimumab vs Sunitinib in front line metastatic renal cell (CheckMate 214)

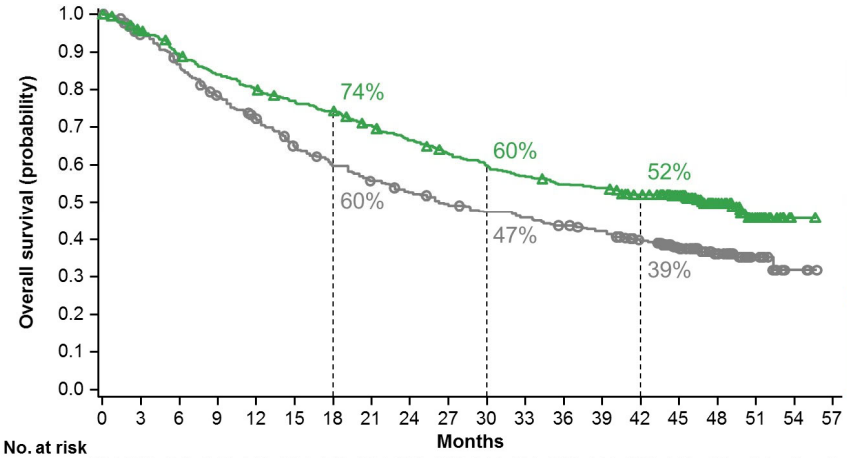
Motzer et al. NEJM April 5, 2018



CheckMate 214

Overall Survival

Primary efficacy population: Intermediate/poor-risk patients



Minimum follow-up	OS	NIVO+IPI N = 425	SUN N = 422
17.5 mo[1]	Median, mo (95% CI)	NR (28.2–NE)	26.0 (22.1–NE)
	HR (99.8% CI)	0.63 (0.44–0.89) $P < 0.001$	
30 mo[2]	Median, mo (95% CI)	NR (35.6–NE)	26.6 (22.1–33.4)
	HR (95% CI)	0.66 (0.54–0.80) $P < 0.0001$	
42 mo	Median, mo (95% CI)	47.0[a] (35.6–NE)	26.6 (22.1–33.5)
	HR (95% CI)	0.66 (0.55–0.80) $P < 0.0001$	

No. at risk

NIVO+IPI	425	399	372	348	332	317	306	287	270	254	241	230	220	216	202	162	78	27	1	0
SUN	422	388	353	318	291	258	237	220	206	193	184	178	169	161	145	118	64	25	3	0

[a]With a minimum follow-up of 42 months, the median OS of 47.0 months in the NIVO+IPI arm could be unstable due to censoring.
NE, not estimable.

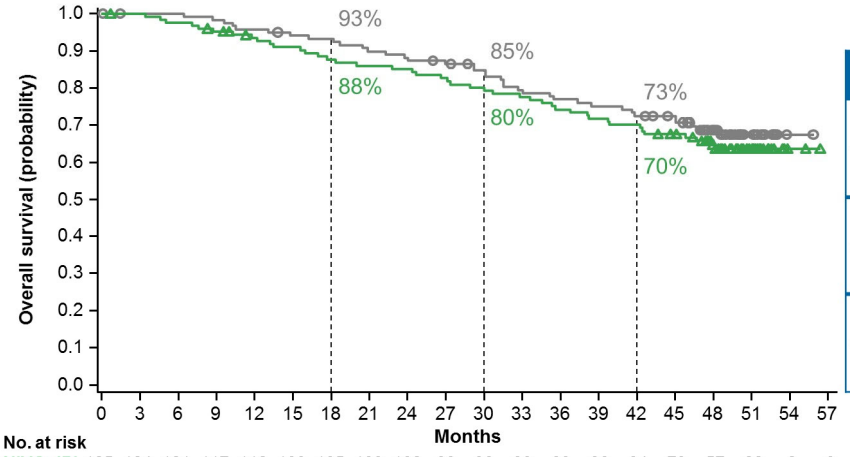
1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290. 2. Motzer RJ, et al. *Lancet Oncol* 2019;20:1370–1385.

5

CheckMate 214

Overall Survival

Exploratory efficacy population: Favorable-risk patients



Minimum follow-up	OS	NIVO+IPI N = 125	SUN N = 124
17.5 mo[1,a]	Median, mo (95% CI)	NR (NE)	NR (NE)
	HR (99.8% CI)	1.45 (0.51–4.12) $P = 0.27$	
30 mo[2]	Median, mo (95% CI)	NR (NE)	NR (NE)
	HR (95% CI)	1.22 (0.73–2.04) $P = 0.44$	
42 mo	Median, mo (95% CI)	NR (NE)	NR (NE)
	HR (95% CI)	1.19 (0.77–1.85) $P = 0.44$	

No. at risk

NIVO+IPI	125	124	121	117	112	109	105	103	102	99	96	93	89	86	84	79	57	22	2	0
SUN	124	119	119	117	114	111	110	106	104	101	97	90	88	86	83	79	61	24	1	0

[a]Only 37 deaths had occurred at the time of the database lock (21 in the NIVO+IPI arm and 16 in the SUN arm).

1. Motzer RJ, et al. *N Engl J Med* 2018;378:1277–1290. 2. Motzer RJ, et al. *Lancet Oncol* 2019;20:1370–1385.

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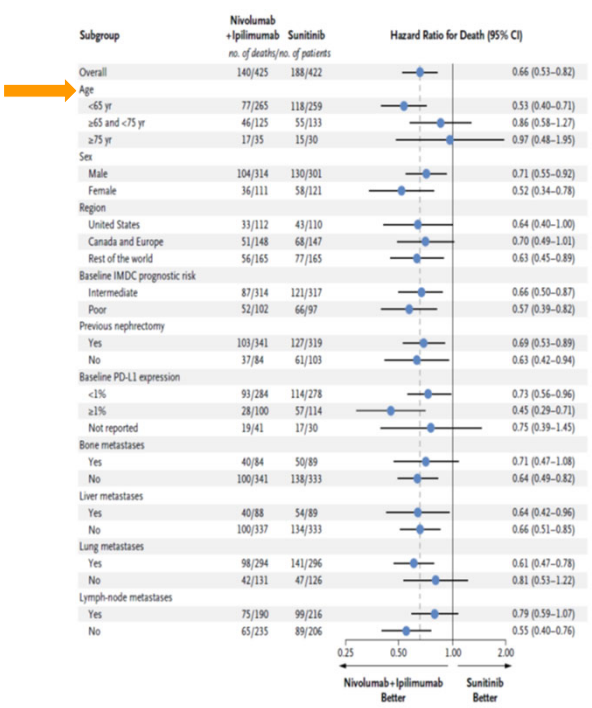

Subgroup	Nivolumab + Ipilimumab (no. of deaths/no. of patients)	Sunitinib (no. of deaths/no. of patients)	Hazard Ratio for Death (95% CI)
Overall	140/425	188/422	0.66 (0.53–0.82)
Age			
<65 yr	77/265	118/259	0.53 (0.40–0.71)
≥65 and <75 yr	46/125	55/133	0.86 (0.58–1.27)
≥75 yr	17/35	15/30	0.97 (0.48–1.95)
Sex			
Male	104/314	130/301	0.71 (0.55–0.92)
Female	36/111	58/121	0.52 (0.34–0.78)
Region			
United States	33/112	43/110	0.64 (0.40–1.00)
Canada and Europe	51/148	68/147	0.70 (0.49–1.01)
Rest of the world	56/165	77/165	0.63 (0.45–0.89)
Baseline IMDC prognostic risk			
Intermediate	87/314	121/317	0.66 (0.50–0.87)
Poor	52/102	66/97	0.57 (0.39–0.82)
Previous nephrectomy			
Yes	103/341	127/319	0.69 (0.53–0.89)
No	37/84	61/103	0.63 (0.42–0.94)
Baseline PD-L1 expression			
<1%	93/284	114/278	0.73 (0.56–0.96)
≥1%	28/100	57/114	0.45 (0.29–0.71)
Not reported	19/41	17/30	0.75 (0.39–1.45)
Bone metastases			
Yes	40/84	50/89	0.71 (0.47–1.08)
No	100/341	138/333	0.64 (0.49–0.82)
Liver metastases			
Yes	40/88	54/89	0.64 (0.42–0.96)
No	100/337	134/333	0.66 (0.51–0.85)
Lung metastases			
Yes	98/294	141/296	0.61 (0.47–0.78)
No	42/131	47/126	0.81 (0.53–1.22)
Lymph-node metastases			
Yes	75/190	99/216	0.79 (0.59–1.07)
No	65/235	89/206	0.55 (0.40–0.76)

Nivolumab + Ipilimumab vs Sunitinib in front line metastatic renal cell:

Survival Subset analysis

Motzer et al. NEJM April 5, 2018

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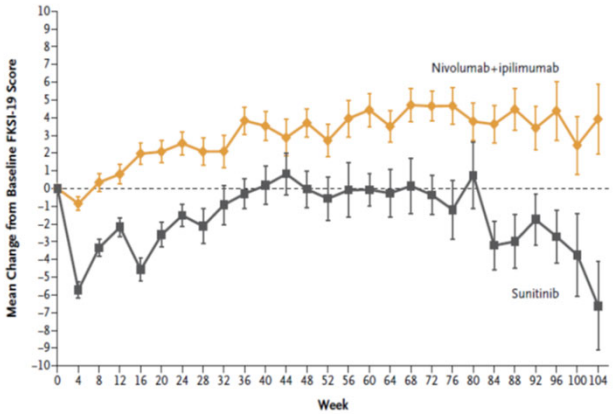


Figure 3. Health-Related Quality of Life in IMDC Intermediate- and Poor-Risk Patients.

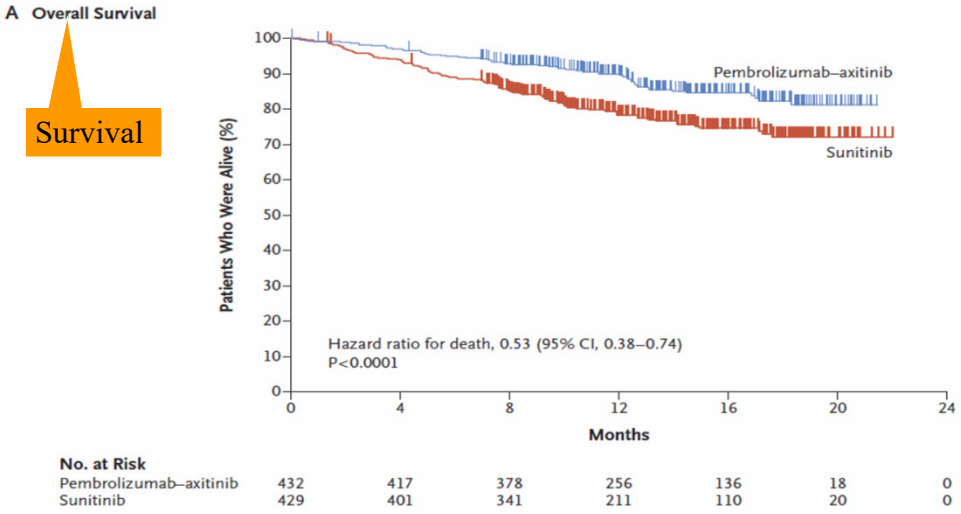
Nivolumab + Ipilimumab vs Sunitinib in front line metastatic renal cell:

Health Related QOL

Motzer et al. NEJM April 5, 2018

Pembrolizumab + Axitinib vs Sunitinib for first line Metastatic Renal Cell

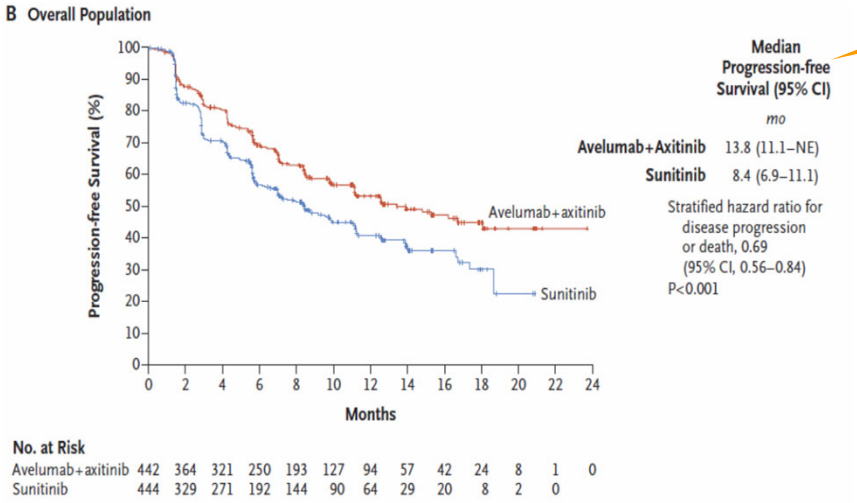
Rini et al. N Engl J Med 2019;380:1116-27.



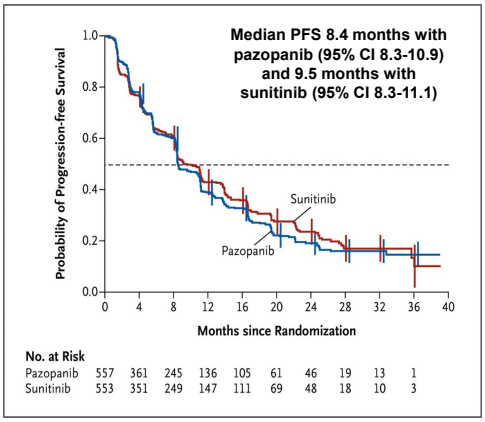
Avelumab + Axitinib vs Sunitinib for first line Metastatic Renal Cell

Motzer et al. N Engl J Med 2019;380:1103-1115.

Progression-free survival

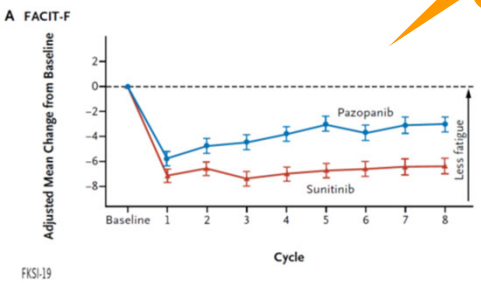


COMPARZ Trial in Clear Cell: Sunitinib vs Pazopanib



ORR 31% with pazopanib and 24% with sunitinib
and median OS 28.4 with pazopanib and 29.3 months with sunitinib

Side effects favored pazopanib



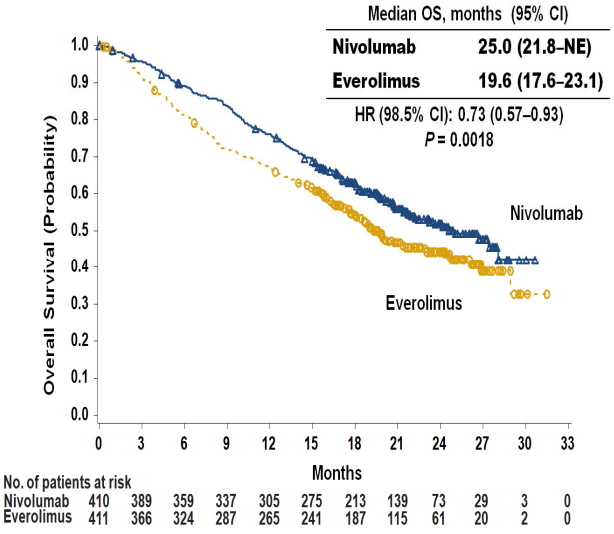
FKSI-19

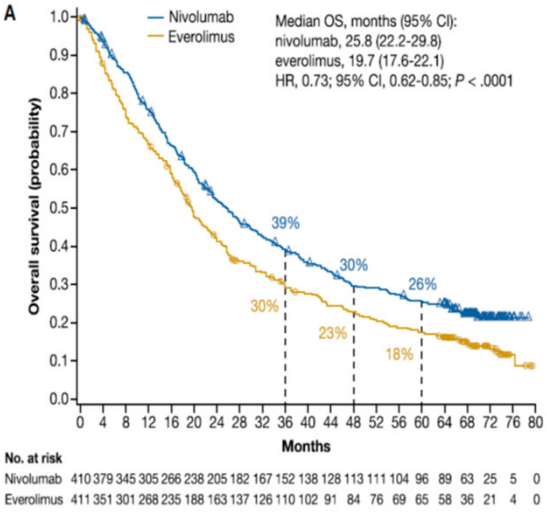
Treatment side effects**	351	382	2.28	0.31	0.03	Pazopanib
Disease-related physical symptoms	378	407	5.97	0.78	0.03	Pazopanib
Disease-related emotional symptoms	370	402	1.19	-0.05	0.41	Neither
Functional well-being	378	403	3.56	0.31	0.10	Neither
Total score	377	408	9.79	1.41	0.02	Pazopanib

Motzer et al. NEJM 369:722-31, 2013

Second-Line: Nivolumab superior to everolimus in survival for clear cell

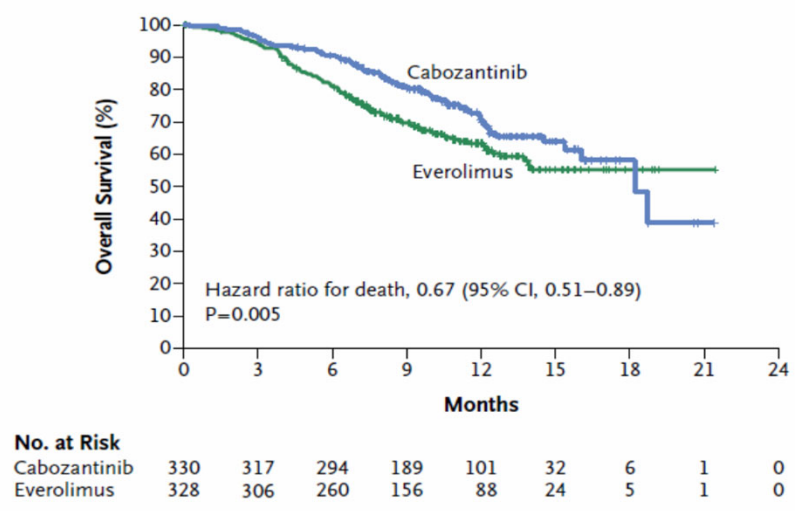
Motzer RJ et al: NEJM 373:1803-1813, 2015 and Motzer et al. Cancer 2020





Second-Line: Cabozantinib superior to everolimus in survival for clear cell

Choueiri *et al*: NEJM 373:1814-18231813, 2015



Adverse Events Vary Among Drug Classes

Agent	Hand-Foot	HTN	Cytopenias	Urinary Protein	GI	LFTs	Fatigue	Glucose Lipids
Bevacizumab	-	+	-	++	+			-
Sunitinib	+	+	+	+	+	+	+++	-
Pazopanib	-	+	-	+	+	++	++	-
Sorafenib	+	+	+	+	+	+	++	-
Axitinib	+	++	+	+	+	+	+++	-
Cabozantinib*	+	+	+	+	+	+	+++	-
Lenvatinib (+ everolimus)	-	+	+	+	+	+	+++	+
Everolimus**	-	-	+	-	+	+	+	+
Temsirolimus**	-	-	+	-	+	+	+	+
Ipilimumab***	-	-	-	-	+++	+	+	-
Nivolumab***	-	-	-	-	-	+	+	-

*Cabozantinib: also appetite suppression and dysgeusia and weight loss, **mTORs: also pneumonitis, infections, peripheral edema
***Nivolumab and Ipilimumab: Wide variety of auto-immune effects including hypothyroid, colitis, pneumonitis, nephritis, hepatitis, rare carditis, hypophysitis, adrenal dysfunction

Management of Non-Clear Cell RCC

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Management of Metastatic Renal Cell Carcinoma with Variant Histologies

Ronan Flippot, MD[a,c], Vijay Damarla, MD[b], Bradley A. McGregor, MD[a,*]

Urol Clin N Am 47 (2020) 319–327

Table 2
Results of selected prospective clinical trials in variant histology renal cell carcinoma

Clinical Trial	Treatment	Line of Treatment	Number of Patients Enrolled	Histology	ORR, %	PFS, mo	OS, mo
SUPAP[24]	Sunitinib	First line	61	pRCC	13 (type I) and 11 (type II)	6.6 (type I) and 5.5 (type II)	17.8 (type I) and 12.4 (type II)
RAPTOR[49]	Everolimus	First line	88	Metastatic pRCC	1	7.9 (type I) and 5.1 (type II)	28 (type I) and 24.2 (type II)
ESPN[20]	Sunitinib vs everolimus	First line	68	vRCC and ccRCC with >20% sarcomatoid features	9 vs 3	6.1 vs 4.1	16.2 vs 14.9
ASPEN[19]	Sunitinib vs everolimus	First line	108	vRCC	18 vs 9	8.3 vs 5.6	31.5 vs 13.2
RECORD-3[21]	Sunitinib-everolimus vs everolimus-sunitinib	First line	66/238 (vRCC/total)	vRCC and ccRCC	—	7.2 vs 5.1	16.8 vs 16.2
GLOBAL ARCC[22]	Temsirolimus vs interferon-α	First line	124/626 (vRCC/total)	vRCC and ccRCC	5 vs 8	7 vs 1.8	11.6 vs 4.3
Choueiri et al,[34] 2017	Savolitinib	Any line	109	pRCC	7	6.2 (MET driven) and 1.4 (MET independent)	—
KEYNOTE 427 (cohort B)[43]	Pembrolizumab	First line	165	vRCC	25	4.1	Not reached
McGregor et al,[44] 2019	Atezolizumab and bevacizumab	Any line	60	vRCC and ccRCC with >20% sarcomatoid features	33	8.3	Not reached

Abbreviation: ORR, objective response rate.

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Papillary Studies and TKIs

Choueiri et al. Eur Urol Oncol. 2020 Jul 8:S2588

Table 1 – Recent published trials evaluating the role of tyrosine kinase inhibitors in papillary renal cell carcinoma.

Clinical trial	Study type	Therapy	Setting	pRCC histology	Pts	ORR (%)	mPFS (mo)	mOS (mo)
SUPAP	Phase 2	Sunitinib	First line	Type 1	15	13	6.6	17.8
				Type 2	46	11	5.5	12.4
CREATE	Phase 2	Crizotinib	First or later line	Type 1	23	17	5.8	30.5
				MET-mutated type 1	4	50	NA	NA
				Non-*MET*-mutated type 1	19	11	3.0	14.5
NCT00726323	Phase 2	Foretinib	First or second line	pRCC	74	13.5	9.3	NA
SWOG S1107	Phase 2	Tivantinib	First or second line	pRCC	25	0	2.0	10.3
		Tivantinib + erlotinib	First or second line		25	0	3.9	11.3
NCT02127710	Phase 2	Savolitinib	First or later line	pRCC	109	7	NA	NA
				MET-mutated	44	18	6.2	NA
				Non-*MET*-mutated	65	0	1.4	NA
SAVOIR	Phase 2	Savolitinib	First or later line	pRCC	33	27	7.0	NR
		Sunitinib			27	7	5.6	13.2

ORR = overall response rate; mPFS = median progression-free survival; mOS = median overall survival; pRCC = papillary renal cell carcinoma; Pts = patients; NA = not available; NR = not reached.

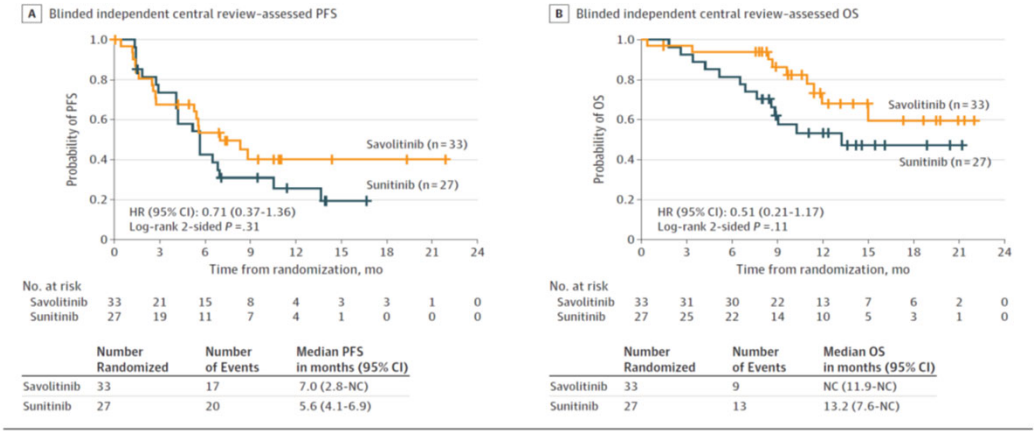
JAMA Oncology | Original Investigation

Efficacy of Savolitinib vs Sunitinib in Patients With *MET*-Driven Papillary Renal Cell Carcinoma
The SAVOIR Phase 3 Randomized Clinical Trial

Toni K. Choueiri, MD; Daniel Y. C. Heng, MD; Jae Lyun Lee, MD; Mathilde Cancel, MD; Remy B. Verheijen, PhD; Anders Mellemgaard, MD; Lone H. Ottesen, MD; Melanie M. Frigault, PhD; Anne L'Hernault, PhD; Zsolt Szijgyarto, PhD; Sabina Signoretti, MD; Laurence Albiges, MD

JAMA Oncol 2020;6(8):1247-1255

Figure 2. Kaplan-Meier Curves



	Number Randomized	Number of Events	Median PFS in months (95% CI)
Savolitinib	33	17	7.0 (2.8-NC)
Sunitinib	27	20	5.6 (4.1-6.9)

	Number Randomized	Number of Events	Median OS in months (95% CI)
Savolitinib	33	9	NC (11.9-NC)
Sunitinib	27	13	13.2 (7.6-NC)

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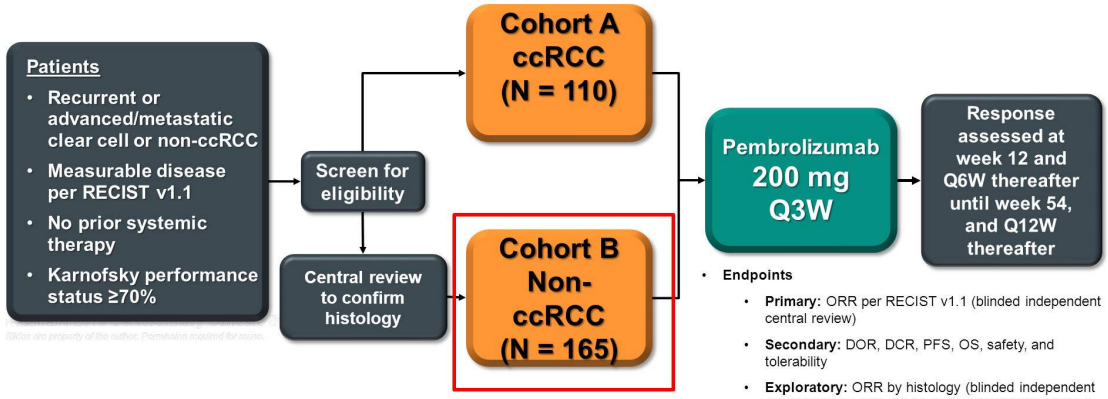
Immunotherapy in Non-Clear Cell

McKay et al. Cancer Immunol Res May 10. 2018

	Total	CR/PR	SD	PD
Papillary	14	4	4	6
Chromophobe	10		4	6
Clear cell/Sarc/Rhab	7	3	2	2
Translocation	3	1	1	1
Unclassified	9		3	6
Total	43	8	14	21

KEYNOTE-427: (NCT02853344)



[a]PD-L1 positive defined as combined positive score [CPS] ≥1.

PRESENTED AT 2019 Genitourinary Cancers Symposium | #GU19

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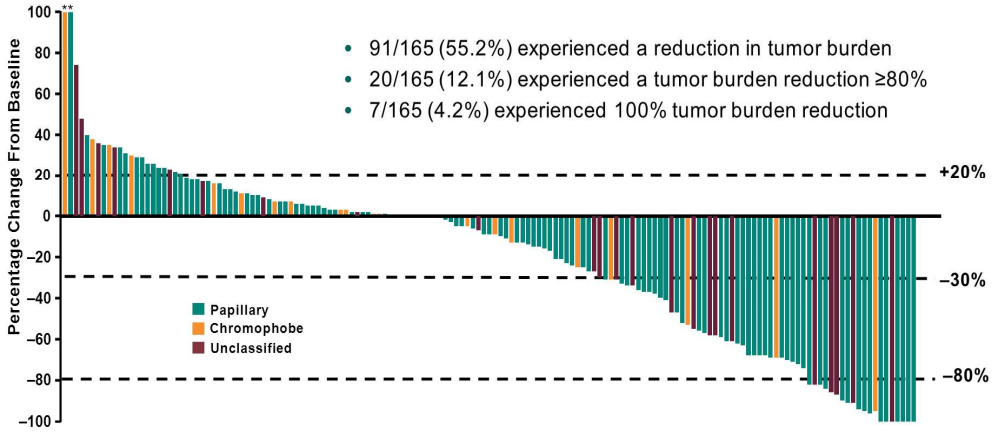
Presented by: Tracy L Rose MD MPH

Presented By Tracy Rose at 2019 Genitourinary Cancers Symposium

Maximum Change From Baseline in Target Lesions by Central Review



- 91/165 (55.2%) experienced a reduction in tumor burden
- 20/165 (12.1%) experienced a tumor burden reduction ≥80%
- 7/165 (4.2%) experienced 100% tumor burden reduction

Includes patients who received ≥1 dose of pembrolizumab, had a baseline scan with measurable disease per RECIST v1.1, and had a postbaseline assessment (n = 155).
*Patient had an increase in target lesions above 100%.
Database cutoff: September 7, 2018.

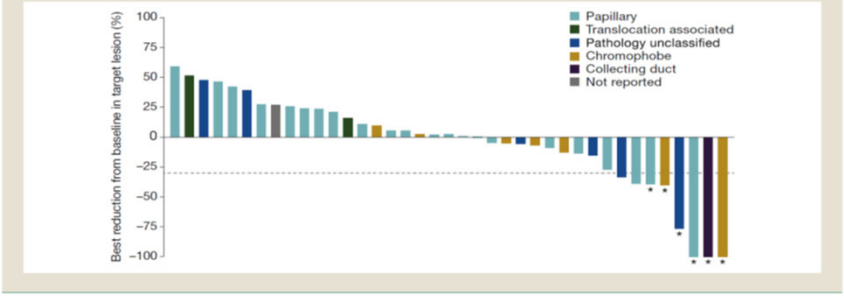
Presented By David McDermott at 2019 Genitourinary Cancers Symposium

Safety and Efficacy of Nivolumab in Patients With Advanced Non—Clear Cell Renal Cell Carcinoma: Results From the Phase IIIb/IV CheckMate 374 Study

Nicholas J. Vogelzang,[1] Mark R. Olsen,[2] Joshua J. McFarlane,[3] Edward Arrowsmith,[4] Todd M. Bauer,[5] Rohit K. Jain,[6] Bradley Somer,[7] Elaine T. Lam,[8] Mark D. Kochenderfer,[9] Ana Molina,[10] Gurjyot Doshi,[11] Brian Lingerfelt,[12] Ralph J. Hauke,[13] Vijay Gunuganti,[14] Ian Schnadig,[15] Peter Van Veldhuizen,[16] Mark Fleming,[17] Robert Galamaga,[18,a] Mukul Gupta,[19] Hugo Hool,[20] Thomas Hutson,[21] Joshua Zhang,[22] M. Brent McHenry,[22] Jennifer L. Johansen,[22] Scott S. Tykodi[23]

Clinical GU cancer: In Press 2020

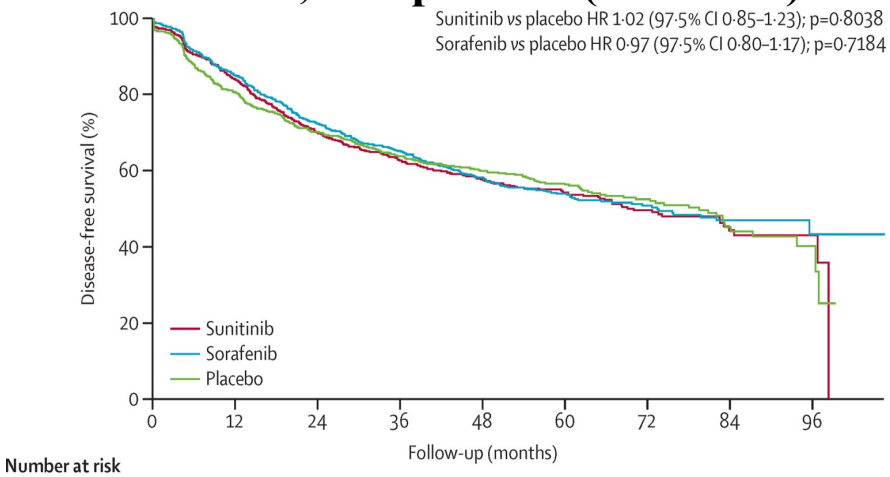
Figure 1 Best Change From Baseline in Target Lesions



*Responder per RECIST v1.1 criteria, confirmation of response required. Horizontal reference line indicates the 30% reduction consistent with a response per RECIST v1.1.
Abbreviation: RECIST = Response Evaluation Criteria in Solid Tumors.

Adjuvant Therapy

Adjuvant Therapy Disease-Free Survival: Sunitinib, sorafenib, and placebo (ASSURE)

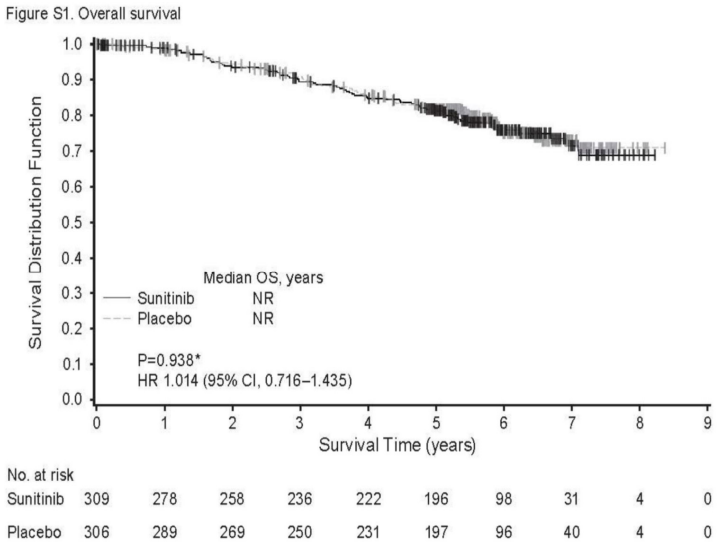


Number at risk

Sunitinib	647	500	397	338	279	194	102	42	7
Sorafenib	649	517	423	357	297	199	114	48	11
Placebo	647	499	414	360	312	200	111	48	7

Haas NB et al. Lancet 387:2008-16, 2016.

Adjuvant Therapy Survival: S-TRAC



Ravaud A et al. NEJM 375:2246-54, 2016

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Summary

- I am aggressive with surgeries and metastectomy
- Impressive ipilimumab/nivolumab data in clear cell intermediate/high risk
- Combination therapy with Axitinib and IOs are interesting
- Based on COMPARZ data, I typically use pazopanib as my first line TKI
- Based on nivolumab phase III, I typically use a PD1 inhibitor as my second line choice in those previously TKI treated
- Adjuvant therapy with TKIs provides no survival benefit

Renal Cell Carcinoma:

A comprehensive course of Surgical & Medical Management for High Risk disease

CASE PRESENTATION

- P.C. 53 Y/O WF PRESENTS RIGHT LOWER QUADRANT ABDOMINAL PAIN.

1 YEAR HISTORY OF HEMATURIA PREVIOUSLY NOT EVALUATED. NO H/O ANTICOAGULATION.

- NO H/O WEIGHT LOSS, UTI, OR KIDNEY STONES
- PMH UNREMARKABLE
- PSH NEGATIVE
- ABDOMEN SOFT, NON TENDER, NO REBOUND TENDERNESS

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- Creatinine 0.69 mg/dL
- GFR >99 mL/min/1.73 m2

- WBC 6.2
- Hct 33.9
- Platelets 214K

- **Urine culture**

Escherichia coli >100,000 CFU/mL

Proteus mirabilis <10,000 CFU/mL

Urine cytology negative

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CASE #1

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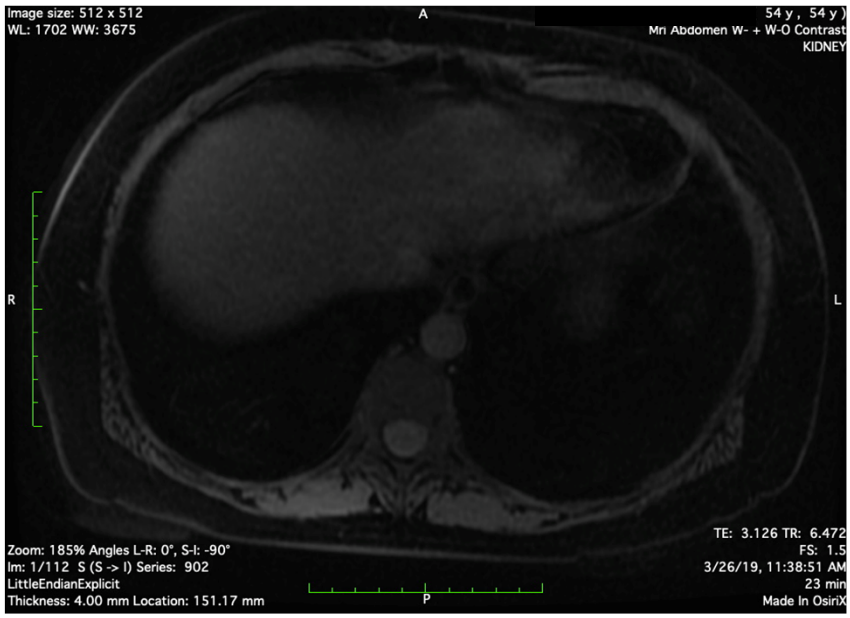

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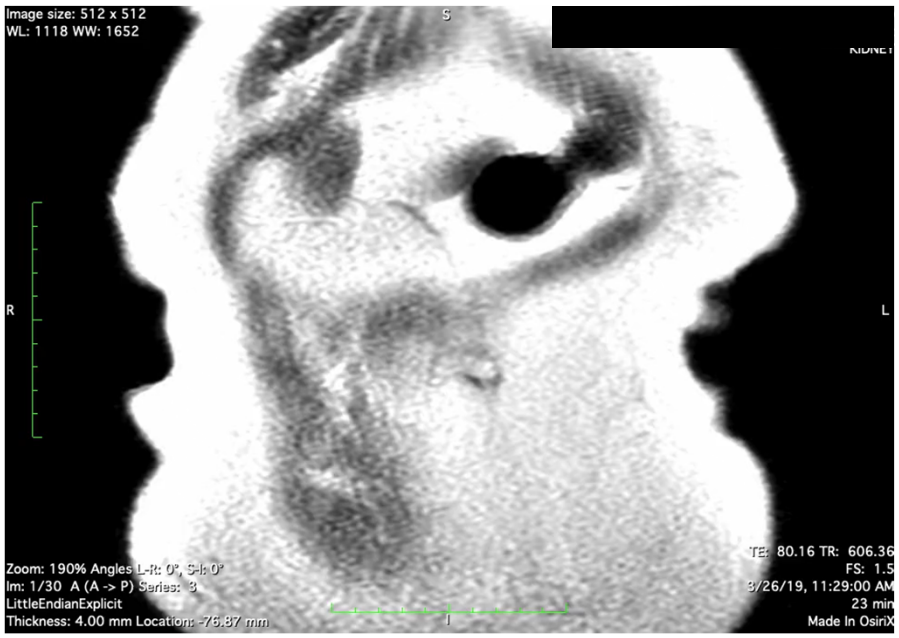

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CT SCAN: RIGHT KIDNEY **10.6 X 8.2 X 6.5 CM** SOLID MASS
NEPHROMETRY SCORE: **11A**

LEFT KIDNEY: STAGHORN CALCULUS – UPPER POLE
HYDRONEPHROSIS MID – UPPER POLE

5.1 X 4.2 X 4.3 CM LEFT MID POLE SOLID MASS
NEPHROMETRY SCORE: 10A

CHEST CT SCAN – NEGATIVE FOR METASTATIC DISEASE

- RENAL SCAN: 40% FUNCTION LEFT KIDNEY, 60% FUNCTION RIGHT KIDNEY

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OPTIONS?

1. BILATERAL NEPHRECTOMY
2. RIGHT RADICAL NEPHRECTOMY
3. LEFT PARTIAL NEPHRECTOMY
4. RIGHT PARTIAL NEPHRECTOMY
4. LEFT PERCUTANEOUS NEPHROLITHOTOMY
5. PERCUTANEOUS RENAL BIOPSY
6. NEOADJUVANT TYROSINE KINASE DOWNSIZING

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INDICATIONS FOR RENAL BIOPSY:

- AUA Guidelines 2017: suspicion of hematologic, metastatic, inflammatory, or infectious etiology.
- Not required for young, healthy patients
  - Those with higher risk of postop morbidity and mortality.
  - Prior to Active Surveillance
  - Patient counseling and clinical decision making, which may change management
- Prior to ablation
- Assessment of response for clear cell histology prior to starting tyrosine kinase therapy.

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UTI TREATED: NEGATIVE URINE CULTURE

- Underwent percutaneous Nephrolithotomy to clear left staghorn calculus 1ST.

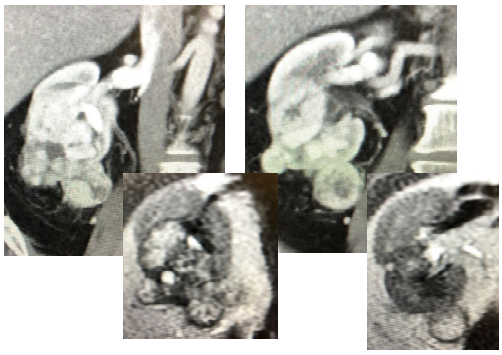
- Post Op Creatinine: 0.79 mg/dL
- GFR: 85 mL/min/1.73 m^2

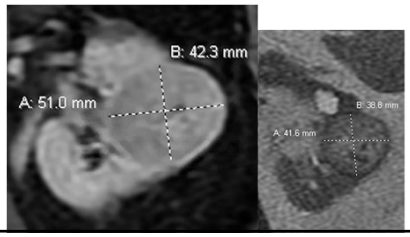
- Percutaneous renal biopsy confirms Clear Cell RCC
- Started on tyrosine kinase inhibitor therapy

- Q: How long to give TKI, when to reimage?
- Q: Which side to address first?
- Q: How counsel patient regarding any additional risks with TKI therapy?

CLINICAL COURSE

- Initiation of Tyrosine Kinase Inhibitor – Pazopanib
- Resulted in >30% reduction in size
- Right kidney, decreased from 10.6 x 8.2 cm -> 8.3 x 5.9 cm; Left kidney: Upper pole cortical thinning
  - Decreased from 5.1 cm x 4.2 cm -> 4.2 cm x 3.4 cm





LEFT ROBOTIC PARTIAL NEPHRECTOMY

- 2 months later
- **Clear cell renal cell carcinoma (5.1 cm), grade G2**
  - **Tumor confined to kidney with negative resection margins.**
  - **Background of focal segmental and focal global glomerulosclerosis, moderate tubulointerstitial fibrosis and moderate arteriosclerosis.**

Creatinine 0.7 mg/dL

GFR: 99 mL/min/1.73 m^2

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Q: HOW LONG TO WAIT BETWEEN LEFT & RIGHT SIDE?

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RIGHT ROBOTIC PARTIAL NEPHRECTOMY

3 MONTHS LATER

PREOP RENAL SCAN 30% LEFT KIDNEY, 70% RIGHT KIDNEY

- **CLEAR CELL RENAL CELL CARCINOMA, 8.5 CM**
- **TUMOR EXTENDS FOCALLY INTO PERINEPHRIC FAT (PT3A)**
- **MARGINS NEGATIVE FOR MALIGNANCY.**
- **MODERATE ARTERIOSCLEROSIS.**

FINAL RENAL FUNCTION 0.73 MG/DL

GFR 94 ML/MIN/1.73 M2

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CASE #2: CYTOREDUCTIVE NEPHRECTOMY

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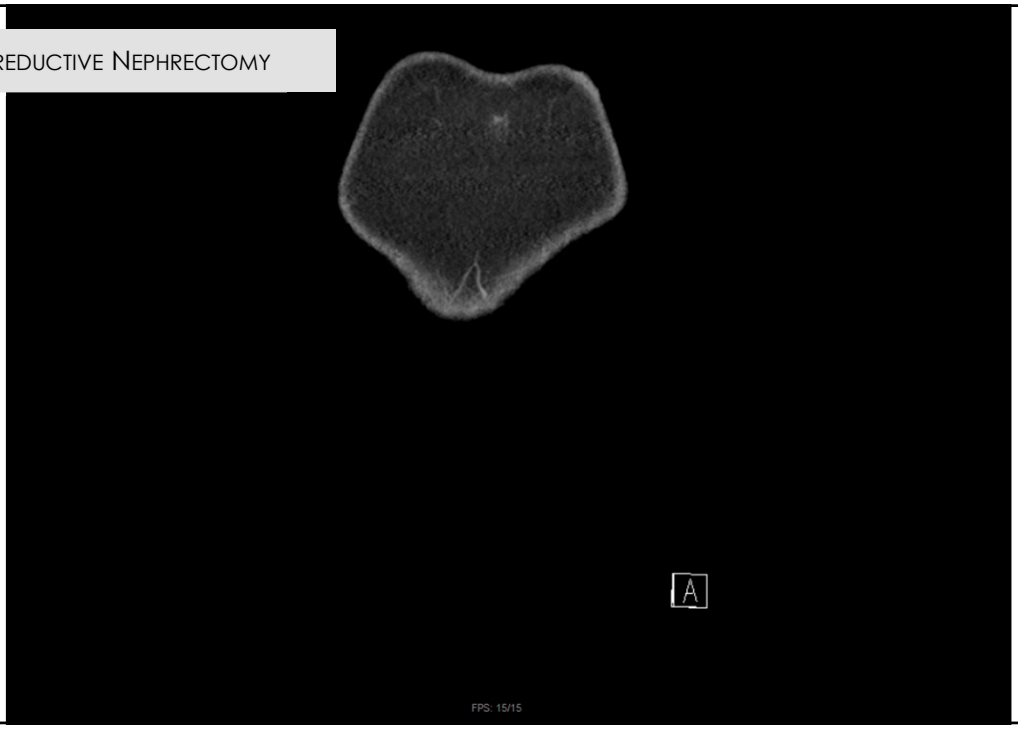
- LEFT CYTOREDUCTIVE NEPHRECTOMY



TECHNIQUE OF HEMOSTASIS – ARTERIAL BLEEDING

- Mechanical compression with non-traumatic clamp
- Exposure – Add additional trocar if bleeding controlled to allow use of suction
- Clip – Placement of clip proximal to clamp, careful not to dislodge, electrocautery
- Resist temptation to reposition clip, place correctly on initial placement
- Rescue Stitch – 4-0 prolene, 6”
- If unable to control bleeding – convert to open immediately

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HOW WOULD TREATMENT OF VENOUS BLEEDING DIFFER?

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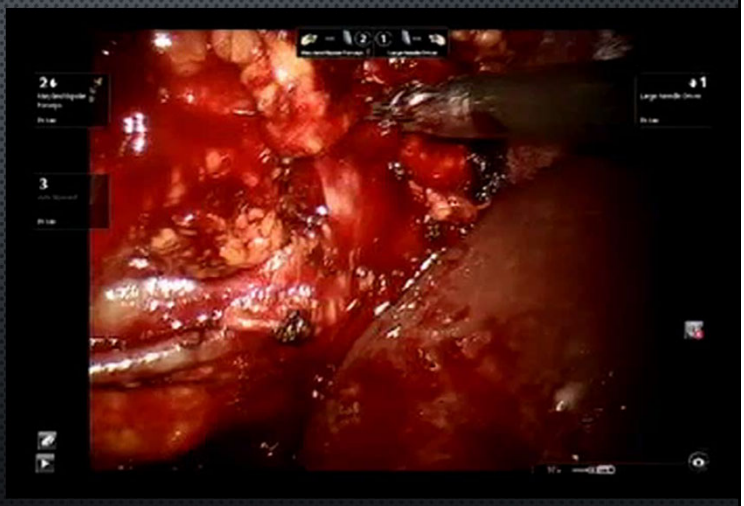
CASE #4
ROBOTIC PARTIAL NEPHRECTOMY

OPTIONS:

1. PLACE CLIP
2. CONVERT TO OPEN PROCEDURE
3. OPEN THE GIA AND DO RADICAL NEPHRECTOMY
4. SUTURE VENOTOMY
5. INCREASE PRESSURE TO 20MM HG



TECHNIQUE OF HEMOSTASIS – VENOUS BLEEDING

- MAY RAISE PNEUMOPERITONEAL PRESSURE TO 20MM HG
  - CAVEAT – IVC INJURY AND AIR EMBOLUS
- MINI-LAP SPONGE DIRECT COMPRESSION FOR 5 MINUTES
- NON-TRAUMATIC VASCULAR CLAMP
- APPLICATION OF CLIP
- EXPOSURE & PATIENCE IS KEY
- DECISION:
  1. CAUTERY VS SUTURE REPAIR?
  2. RESCUE STITCH: 4-0 PROLENE WITH LAPRATY CLIP ON END, 6CM

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CASE #3

- 80 y/o male – 2012 Presented to cardiologist c/o back pain & shortness of breath.
- Underwent CT scan - left renal mass & lytic lesion left iliac crest

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- PMH
  - Coronary artery disease
  - Diabetes mellitus
  - CHF
  - Myocardial infarction
  - HLD
- PSH
  - Cholecystectomy 1980
  - Angioplasty with stent placement 2012
- Allergies
  - Amoxicillin
  - Sulfa
- FH
  - Father – lung cancer
  - Mother – cervical cancer
- SH
  - No tobacco or drug use.
  - Previous alcohol abuse

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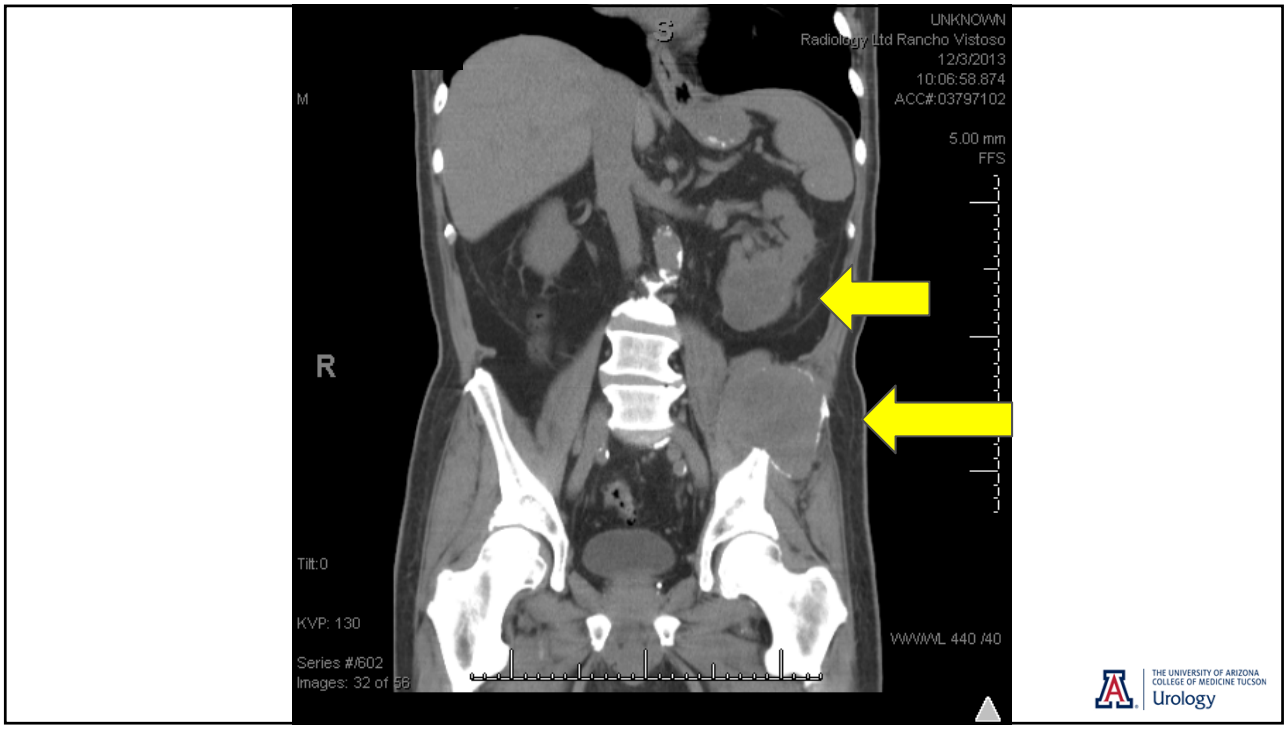

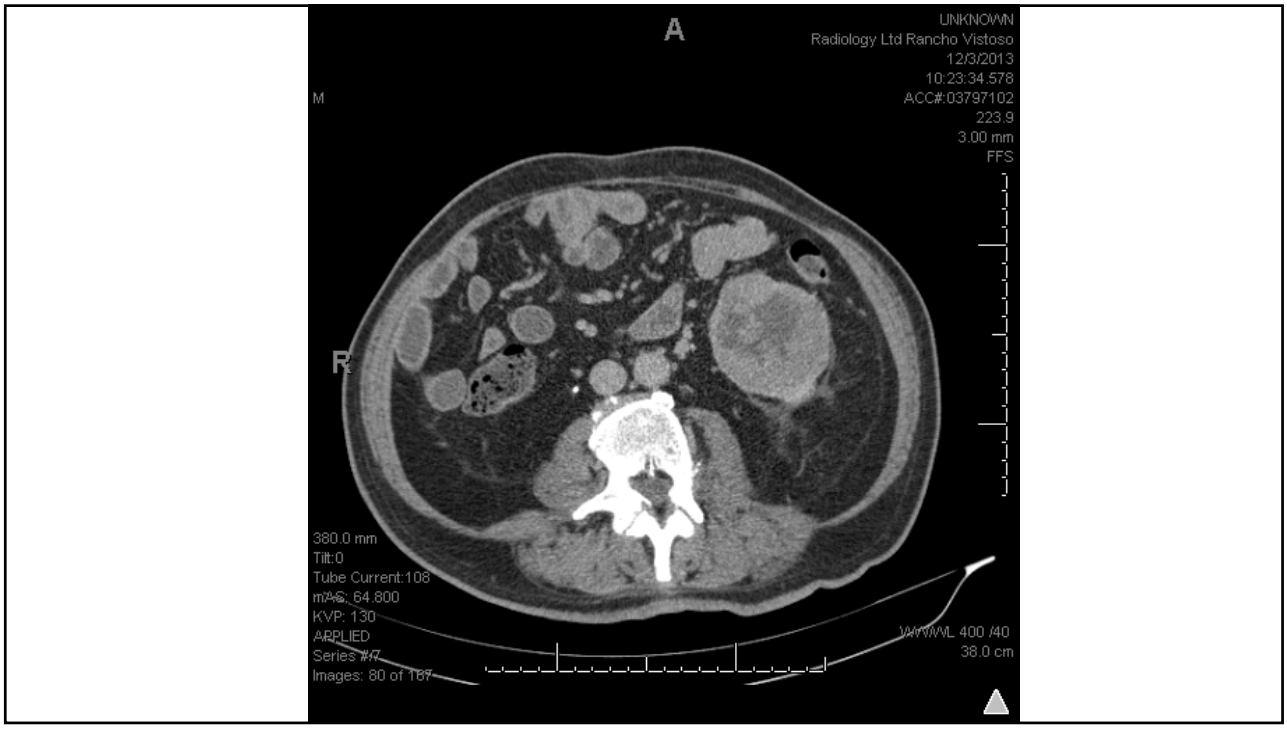

MANAGEMENT- WHAT WOULD YOU DO NOW?

1. PERCUTANEOUS BIOPSY OF KIDNEY
2. PERCUTANEOUS BIOPSY OF ILIAC MASS
3. RADIATION TO ILIAC BONE MASS
4. RESECTION OF ILIAC BONE MASS
5. NEPHRON SPARING SURGERY
6. RADICAL NEPHRECTOMY

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- Percutaneous biopsy iliac lesion confirmed metastatic renal cell carcinoma – clear cell histology
- Discussed role of nephron sparing surgery in the setting of metastatic disease.
- Had embolization of iliac met on 1/27/14

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- Underwent combination multi-disciplinary surgery on 1/28/14.
- Had Left partial nephrectomy in addition to excision of left iliac metastasis/hemipelvectomy by urology / surgery / orthopedics.

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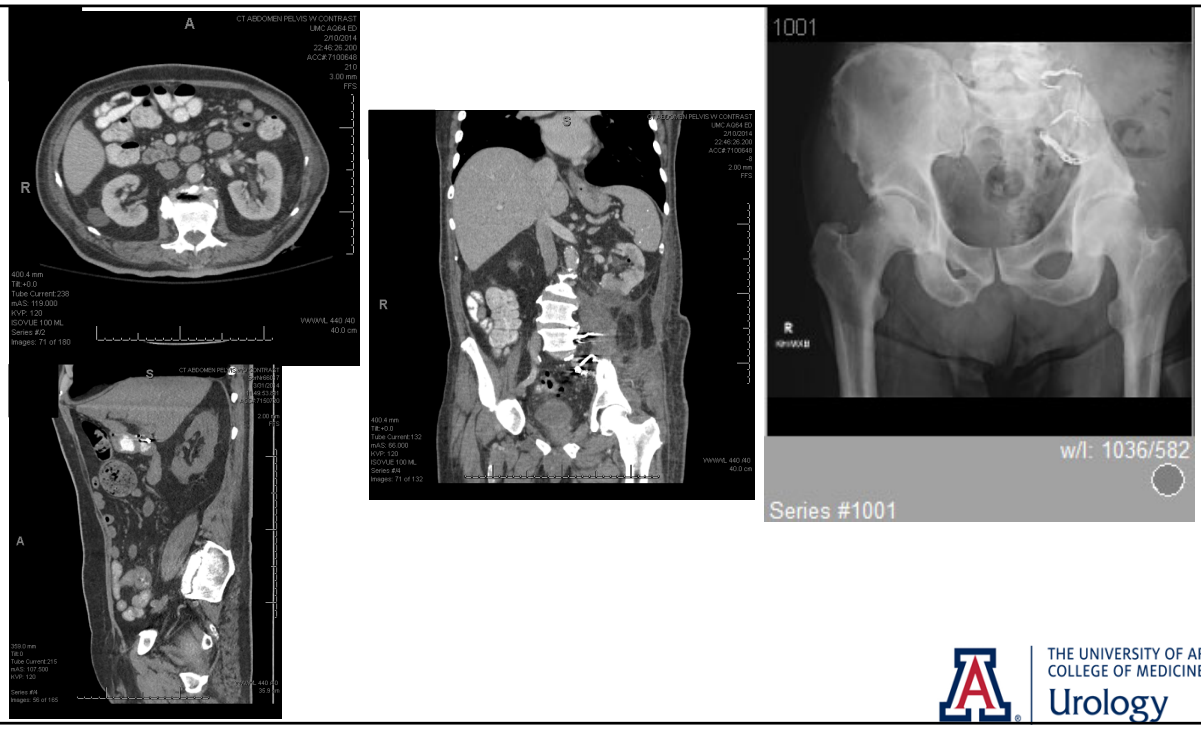

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- FINAL PATHOLOGY: RENAL CELL CARCINOMA 6.2 CM PT4: TUMOR INVADES BEYOND GEROTA'S FASCIA WITH NEGATIVE MARGINS.
- NX M1
- LEFT ILIUM SPECIMEN POSITIVE FOR METASTATIC RENAL CELL CARCINOMA.

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FOLLOW-UP IMAGING

OVERALL STABLE EXAMINATION FROM PRIOR EXAM.

SCATTERED STABLE PULMONARY NODULES (STABLE).

STATUS POST PARTIAL LEFT NEPHRECTOMY OF THE LOWER POLE.

UNCHANGED INDETERMINATE LESION WITHIN THE LEFT KIDNEY MEASURING 1 CM.

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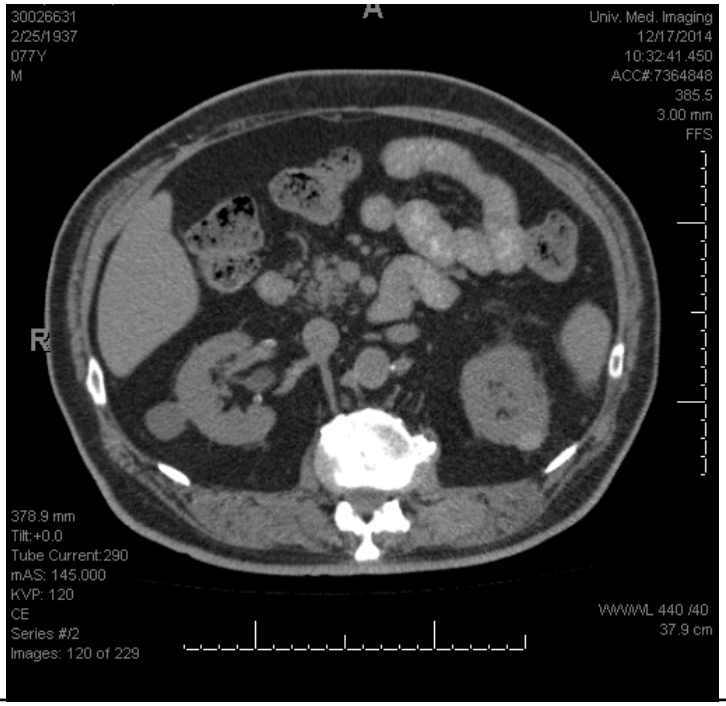

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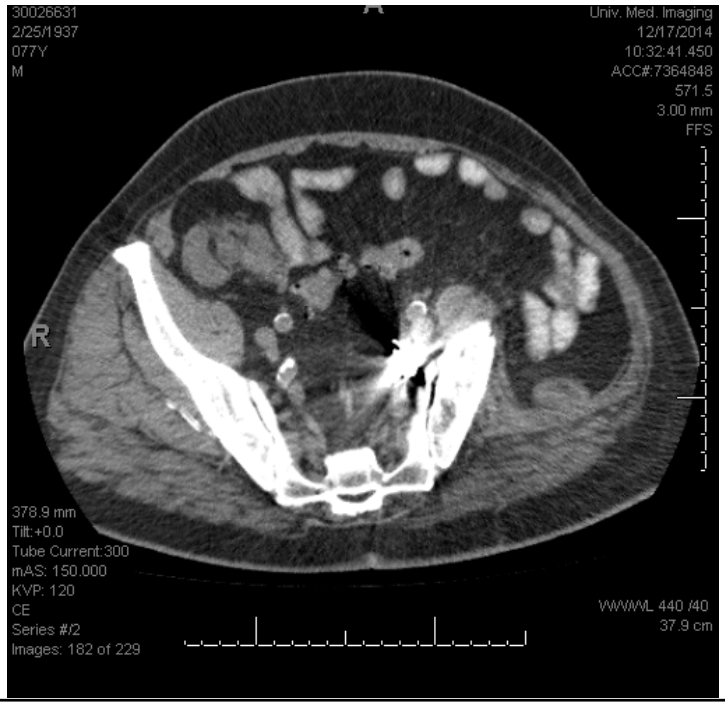

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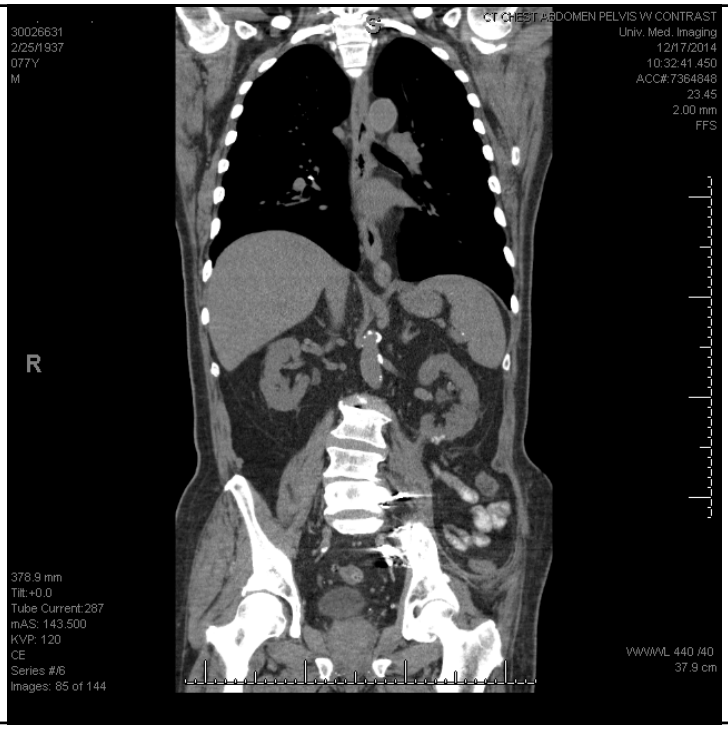

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FOLLOW-UP IMAGING

- MULTI-DISCIPLINARY FOLLOWUP: UROLOGY AND ONCOLOGY WITH SERIAL IMAGING.
- 4 YEAR FOLLOWUP IMAGING: NO EVIDENCE OF METASTASIS OR RECURRENCE.
- NEVER UNDERWENT CHEMOTHERAPY OR RADIATION.
- HOWEVER IN DECEMBER 2016, CT IMAGING INDICATED AN ENLARGING RENAL MASS SUSPICIOUS FOR RECURRENCE.

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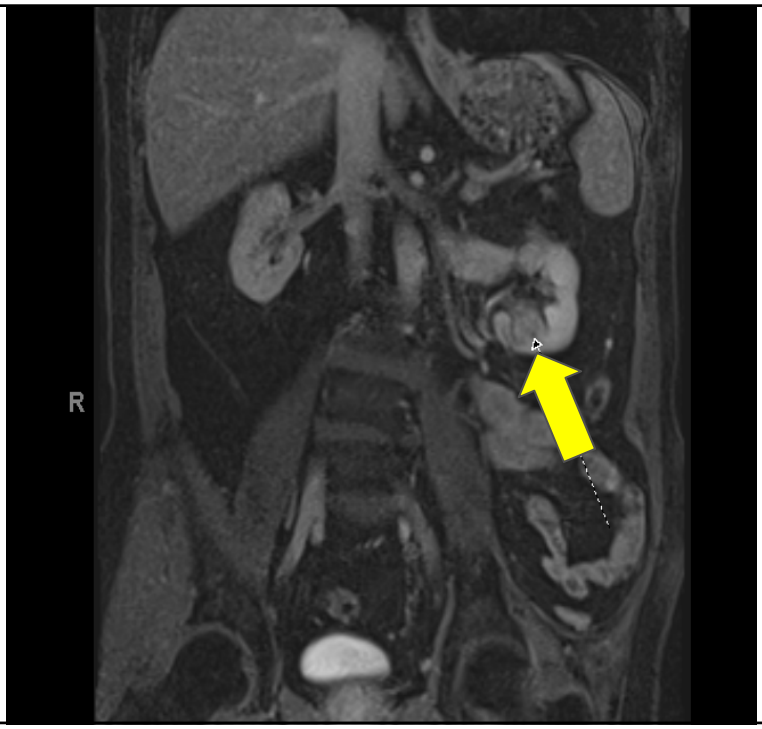

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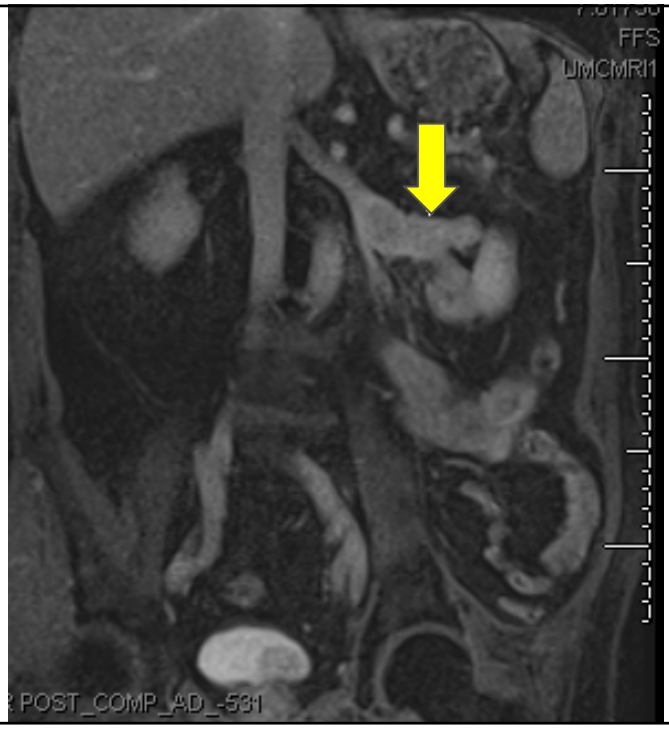

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MRI 1/2017

1. Previously questioned nodularity @ lower pole of left kidney corresponds to recurrent tumor now measuring 1.7 x 1.9 cm.
2. Contiguous tumor thrombus within the left renal vein.
3. Enlarging 1.5 cm left adrenal nodule suspicious for a slow growing metastasis.

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Urology

MANAGEMENT?

- 1. Chemotherapy – Tyrosine Kinase inhibitor vs. Immunotherapy
- 2. Left completion nephrectomy + Adrenalectomy
  - Robotic?
  - Open?
- 3. Surveillance
- 4. Adrenal hormonal function tests

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ADRENAL HORMONAL WORKUP

- Cortisol – negative
- Catecholamines – Negative
- Aldosterone – Negative

- Renal Scan Right kidney 65%, Left kidney 35%

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- On 3/27/17, patient underwent:
  - Left robotic laparoscopic completion radical nephrectomy
  - Left adrenalectomy
  - Resection of left renal vein thrombus
- Discharged on 3/28/17, POD #1
- Uneventful hospital course

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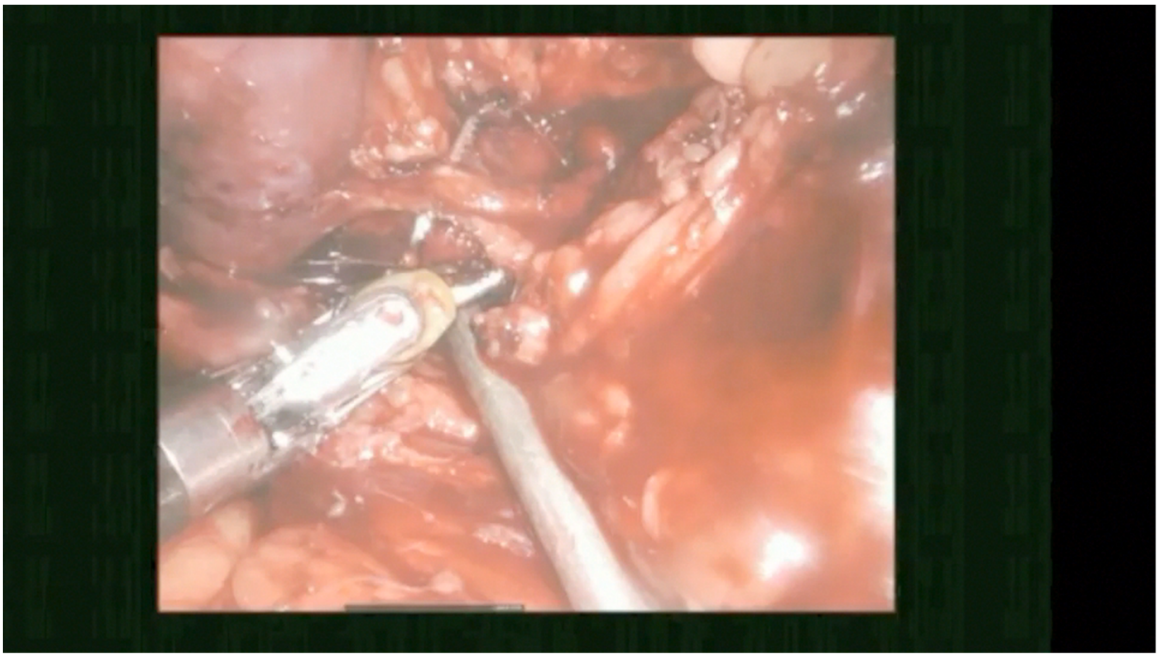
Urology



FINAL PATHOLOGY

RECURRENT CLEAR CELL RENAL CELL CARCINOMA (6.0 CM), GRADE 3 OF 4.

TUMOR INVASION INTO RENAL VEIN, INVOLVING VEIN MARGIN.

LYMPHOVASCULAR INVASION IDENTIFIED.

BENIGN ADRENAL GLAND WITH NO HISTOPATHOLOGIC ABNORMALITY.

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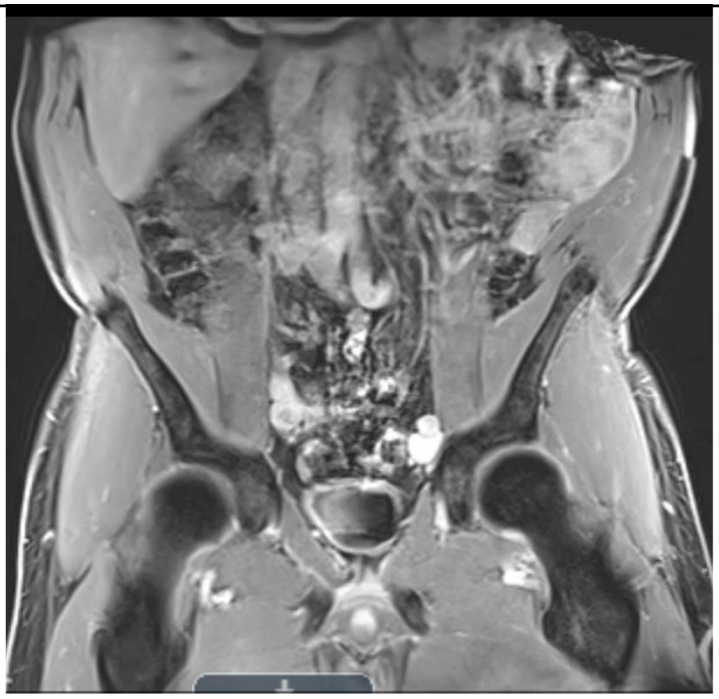
CASE PRESENTATION

- 66 Y/O WM RETIRED HOSPITAL CEO WITH RIGHT FLANK PAIN, CREATININE 1.35 MG/DL, RENAL ULTRASOUND DEMONSTRATED HYDRONEPHROSIS.
- SUBSEQUENTLY UNDERWENT MRI ABDOMEN/PELVIS

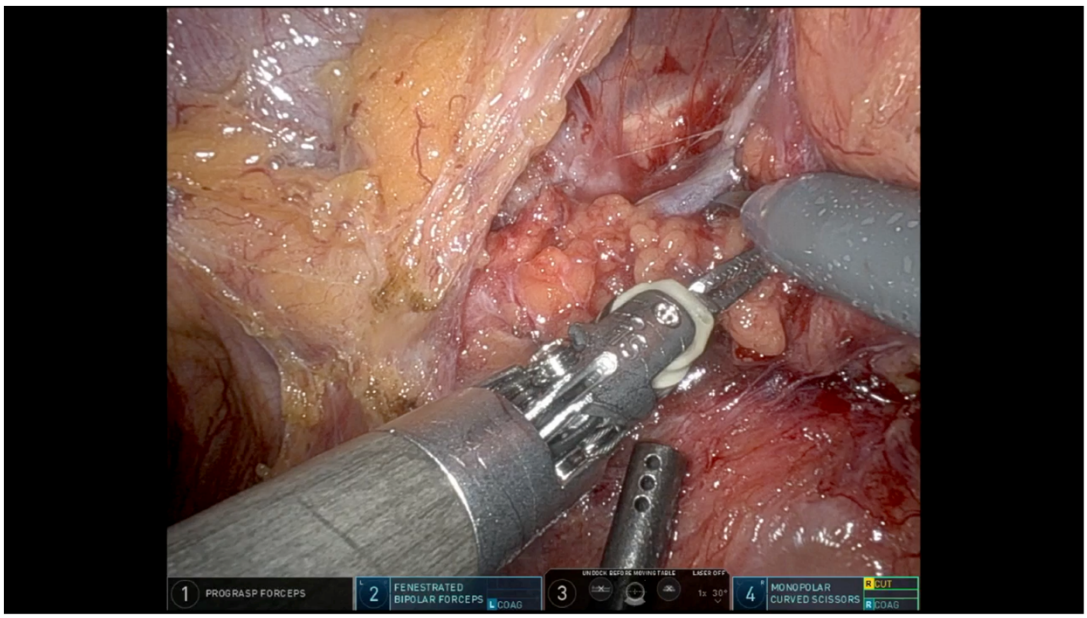
Banner University Medical Center Tucson

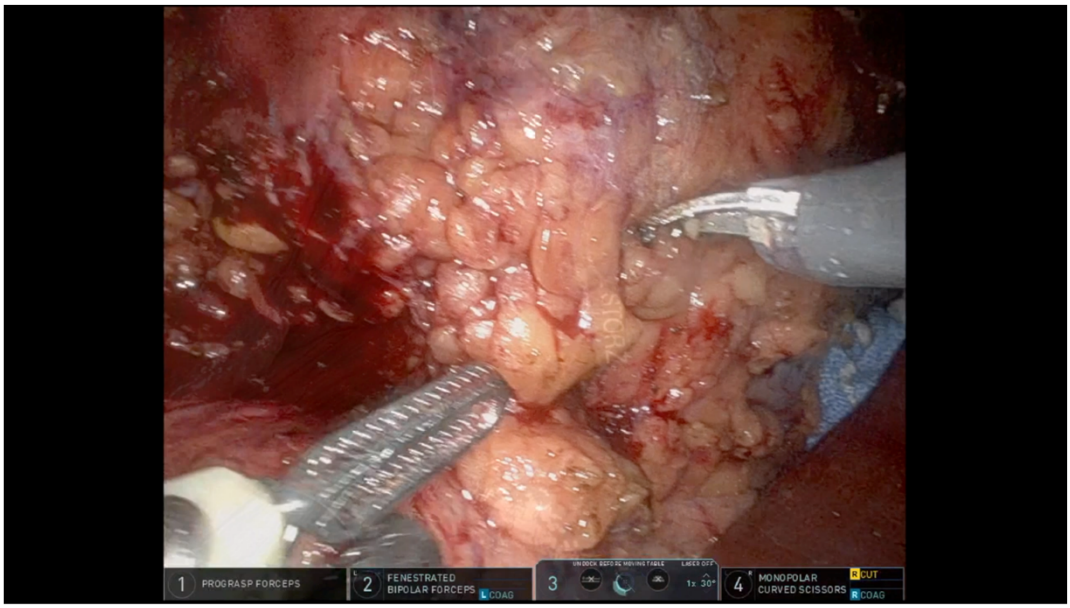


MRI – Nodular soft tissue mass within Right lower pole calyx measuring 2.2 cm, additional 10mm enhancing component at UPJ. Several <1cm paracaval lymph nodes.

- NM Renal scan: 12.2% function Right kidney
- 87.8% function Left Kidney

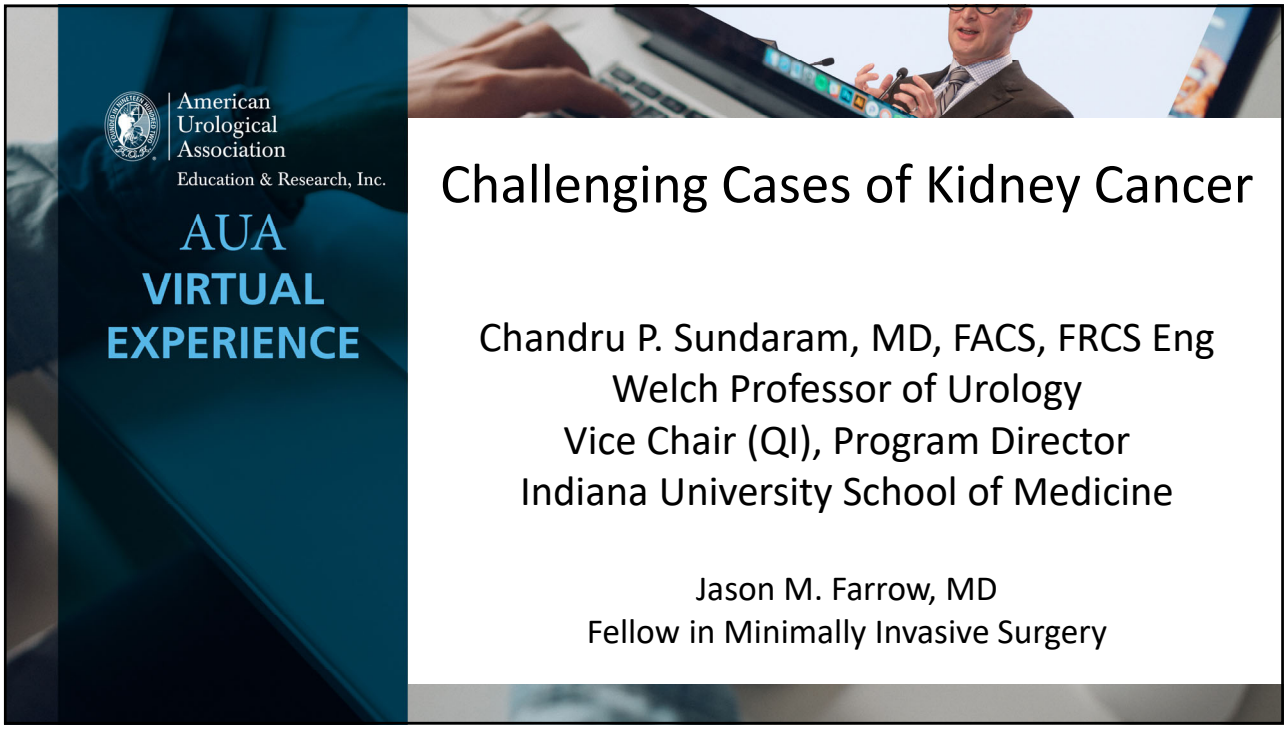
- Urine cytology positive





PATHOLOGY

- HIGH GRADE UROTHELIAL CARCINOMA (9.5CM) OF RENAL PELVIS AND URETER. INVASIVE CARCINOMA AT HILAR SOFT TISSUE MARGIN, LYMPHOVASCULAR INVASION PRESENT
- LYMPH NODE, PARACAVAL EXCISION – METASTATIC UROTHELIAL CARCINOMA, EXTRANODAL EXTENSION INTO SOFT TISSUE.
- STAGE T4N1



Challenging Cases of Kidney Cancer

Chandru P. Sundaram, MD, FACS, FRCS Eng
Welch Professor of Urology
Vice Chair (QI), Program Director
Indiana University School of Medicine

Jason M. Farrow, MD
Fellow in Minimally Invasive Surgery

Case 3

27yF w/o significant PMHx s/p mechanical fall. Reports new RIGHT flank/abdominal pain.

CT w/o reveals a large (20 cm) cystic mass. No LAD or evidence of metastatic disease. No renal vein involvement.

Pt denies hematuria or evolving constitutional symptoms such as fatigue and unintentional weight loss. No FHx of GU malignancy.

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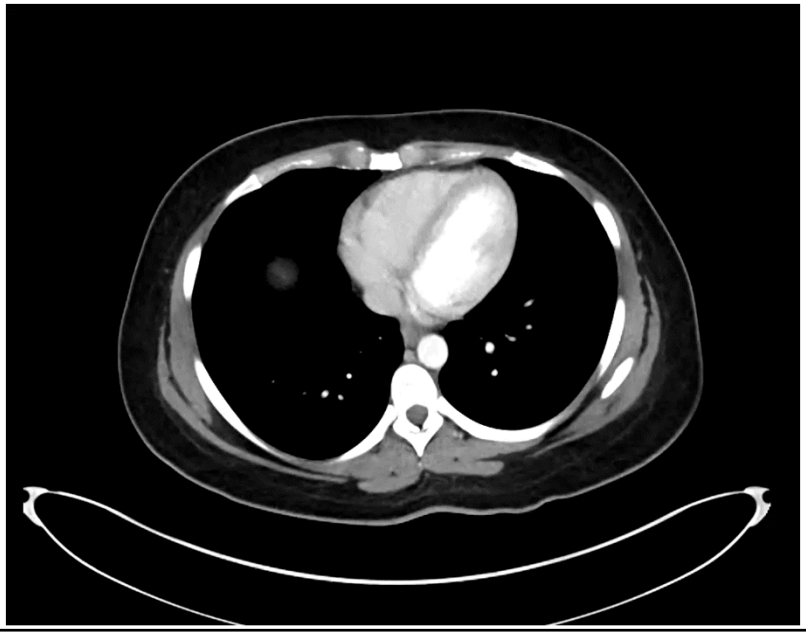

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Pt underwent **Open Radical Nephrectomy w/ Lymph Node Dissection**. The surgery was not complicated; pt discharged on POD#3.

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Final Pathologic Diagnosis:

A. Kidney, right, nephrectomy:
Histologic type:              Xp11.2 (TFE3) translocation associated renal cell
carcinoma
Sarcomatoid features (%):          Not identified
Rhabdoid features (%):          Not identified

Tumor size (greatest dimension):     16.0 cm
     Other dimensions:      9.0 x 8.5 cm
Tumor focality:              Unifocal
     Number of tumors:      1

WHO/ISUP grade:          2/4
Tumor necrosis:              Not identified
Anatomic extent of tumor:
     Confined to kidney                  Yes
     Extension into perinephric fat:          No
     Extension into renal sinus:              No
     Extension into pelvicalyceal system:          No
     Extension beyond Gerota fascia:          No
     Extension into other structures (specify):      No
Extension into renal vein or segmental branches:      No
Adrenal gland present:                    No
     Direct invasion:                    N/A
     Noncontiguous involvement:          N/A
Margin involvement:                  Not identified
     Specify location(s):                N/A
Other tumor-related findings:              Renal papillary adenoma
size

Pathologic findings in non-neoplastic kidney:     Occasional glomer
mild chronic tubulointerstitial inflammation and tubular
      atrophy

Hilar lymph nodes:               Not submitted/ Not found
     Number identified:          N/A
     Number involved:               N/A

Regional lymph nodes:
     Number of lymph nodes present:     10
     Number of lymph nodes involved:     0
     Site(s) of involved lymph nodes:     N/A
     Size of largest metastatic deposit:     N/A
     Extranodal extension:               N/A

Pathologic stage (AJCC 8th Edition):  pT2b pN0

Frozen section diagnosis is confirmed.

B. Lymph nodes, paracaval, dissection:
     Ten lymph nodes negative for tumor (0/10).
```

- Xp11.2 Translocation Associated RCC
- pT2b, pN0

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Pt scheduled for genetic testing. Will meet with hem/onc to discuss risks/benefits of systemic therapy.

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Case 4

69yM w/ Hx of 4.4 cm incidental LEFT renal mass for which he underwent a robot-assisted **Laparoscopic Partial Nephrectomy** in June 2018.

Representative imaging as follows:

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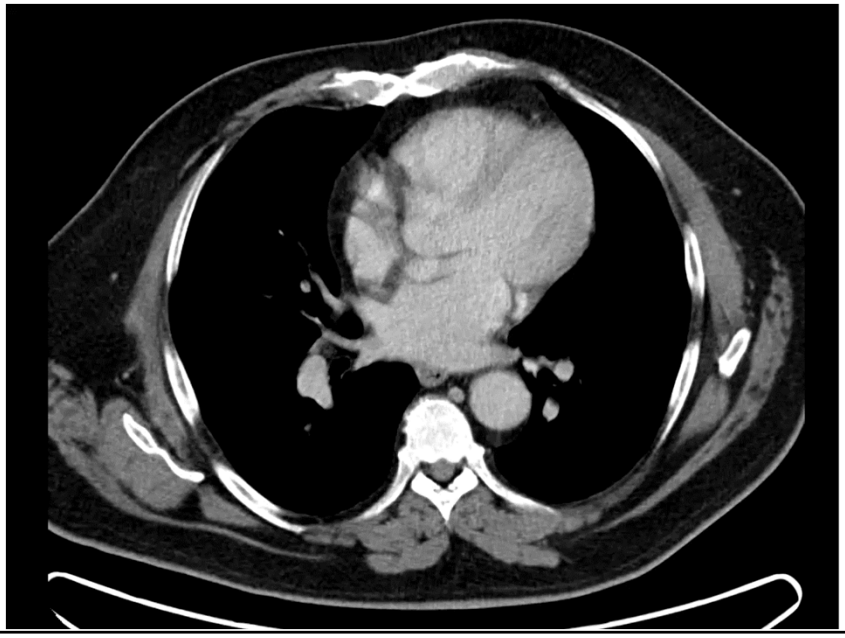

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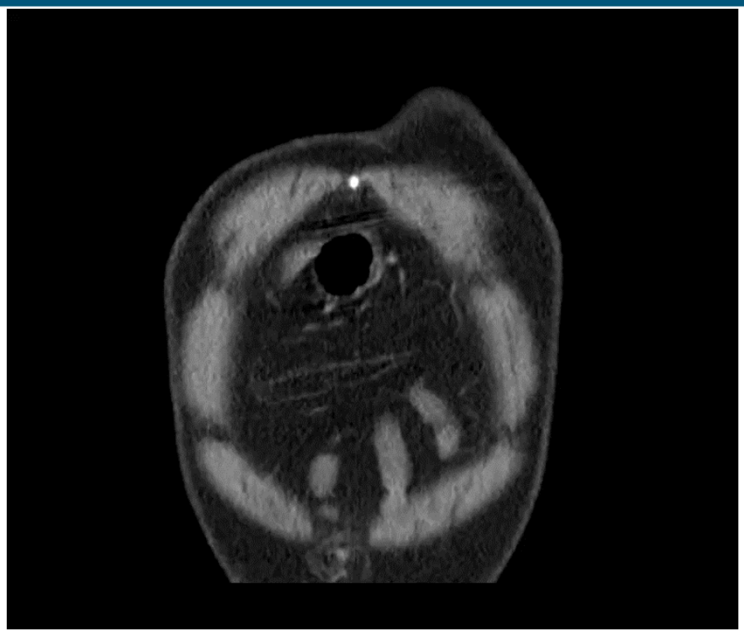

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Final Pathologic Diagnosis:

A. Kidney, left, biopsy:
     Benign renal parenchyma.
     Frozen section diagnosis confirmed.

B. Kidney, left, partial nephrectomy:
     Tumor histologic type:          Clear cell renal cell carcinoma
     Sarcomatoid features (%):       None
Tumor size:                  4.4 cm (greatest dimension)
     Other dimensions:               3.4 x 3.0 cm
Macroscopic extent of tumor:     Confined to kidney
Focality:                  Unifocal
     Number of tumors:               1
Fuhrman grade:                  2 of 4
Microscopic extent of tumor:
     Perinephric fat invasion:       No
     Renal sinus invasion:           No
     Other:                     Not applicable
Renal vein involvement:             No
Adrenal gland present:              No
     (If yes) Involved by tumor:     Not applicable
     (If yes) Direct invasion or metastasis:     Not applicable
Cancer at resection margin:         No
     Location(s):                    Not applicable
Pathologic findings in nonneoplastic kidney:     None
Hilar lymph nodes present:          No
     Number involved/number present:     Not applicable

Pathologic stage (AJCC 8th edition)     pT1b pNX pM- not applicable

Gross Description:
Part A received without fixative labeled "Bowlby, Craig" and "
kidney tumor" is a 0.9 x 0.5 x 0.2 cm aggregate of tan, irregu
submitted in toto for frozen section microscopy, now in casset

Part B received in formalin labeled "Bowlby, Craig" and "left renal mass" i
previously incised 6.3 x 5.0 x 4.7 cm partial nephrectomy specimen with a
minimal amount of attached perinephric fat. Definitive renal sinus is not
identified. Sectioning reveals a 4.4 x 3.4 x 3.0 cm tan to red, soft,
heterogeneous, focally hemorrhagic, well-delineated mass that abuts the cap
and comes to within 0.5 cm of the inked parenchymal margin. The uninvolved
parenchyma is tan and homogeneous. A gross photograph is taken. Representati
sections are submitted as follows:

     1-2     mass to inked parenchymal margin
     3-4     mass to capsule
     5     uninvolved parenchyma
```
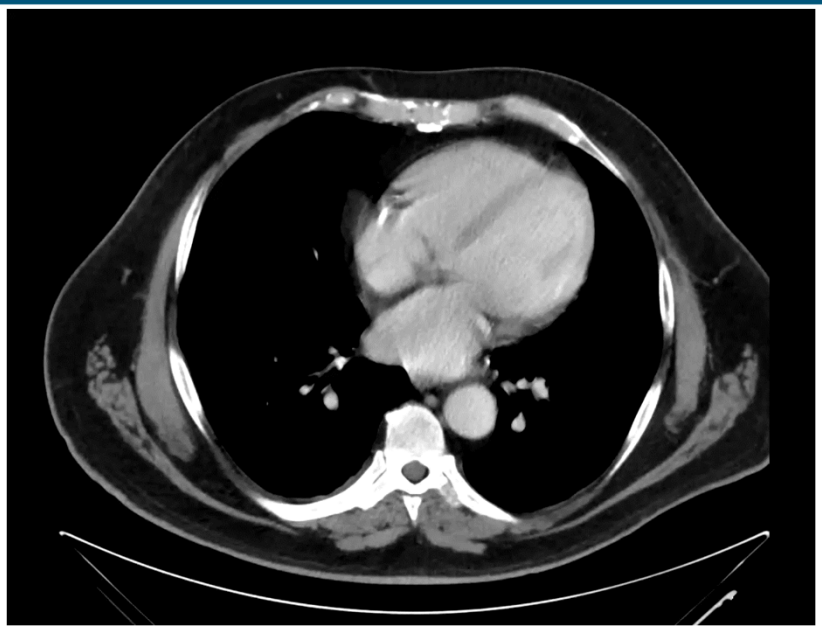

- ccRCC
- WHO/ISUP Grade II
- No perinephric fat invasion
- No renal sinus invasion
- Margins negative
- Gross description reassuring
- pT1b



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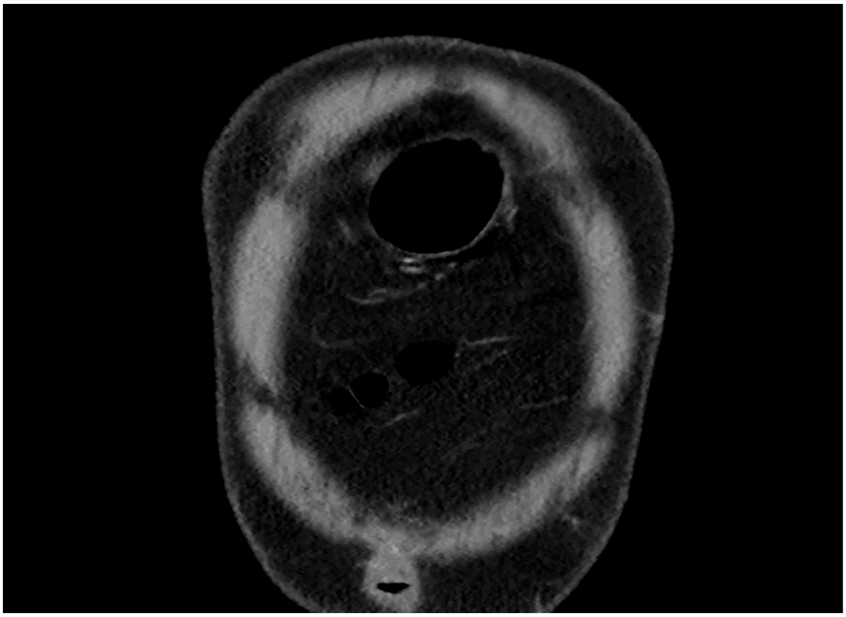

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Pt lost to follow up for 16 months and represents...

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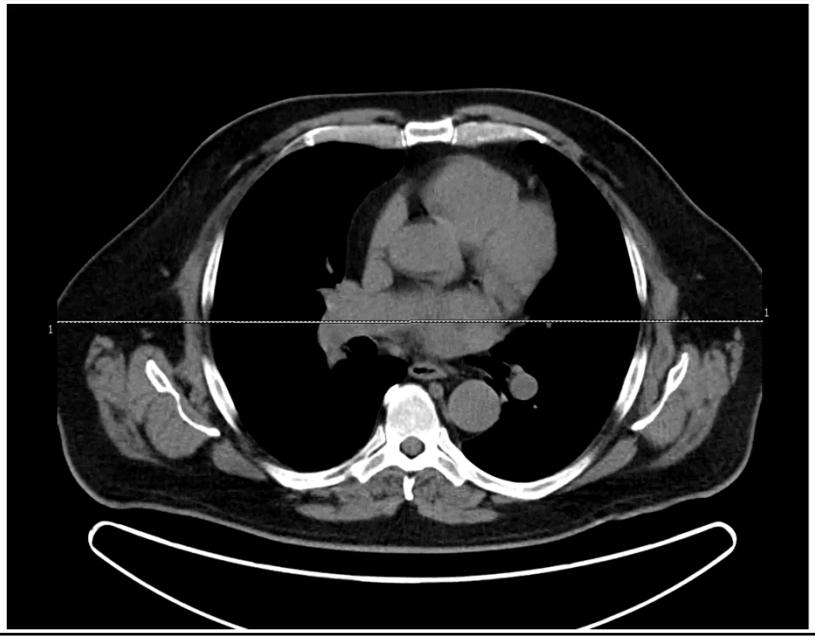

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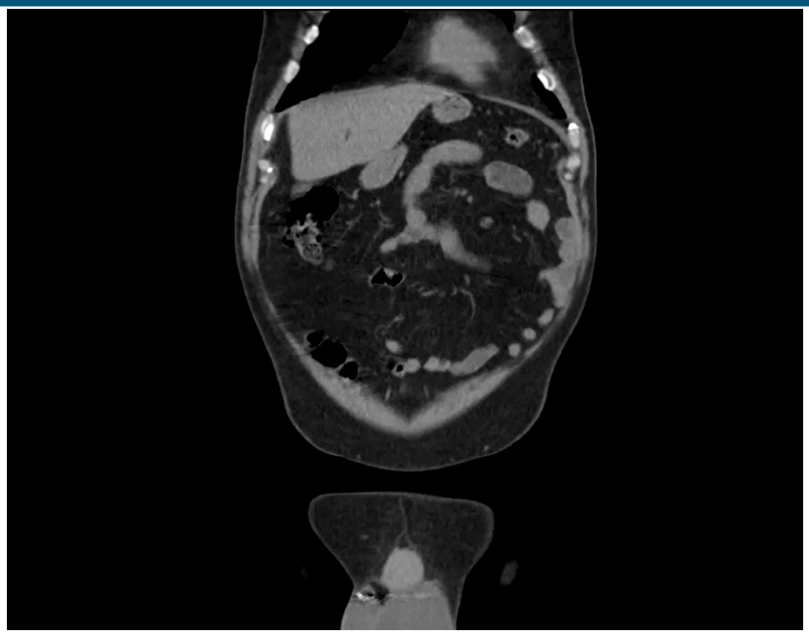

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Clinical Information:
Kidney cancer

Pre-Operative Diagnosis:
Kidney cancer

Post-Operative Diagnosis:
Kidney cancer

Specimen Received:
Tissue from mass near left kidney

Final Pathologic Diagnosis:
Kidney mass, left, biopsy:
Clear cell renal cell carcinoma (WHO/ISUP grade 2).

As the senior physician, I attest that I: (i) examined the relevant preparation(s) for the specimen(s); and (ii) rendered or confirmed the diagnosis(es).
Electronically Signed nao/2/26/2020Muhammad Idrees, M.D. (Pathologist)
David Levy, M.D. (Fellow)
Signing Location: Indiana University Health Pathology Laboratory, 350 W. 11th Street, Indianapolis, IN 46202

Gross Description:
Received is a single formalin-filled container labeled with patient name "Bowlby, Craig" and not additionally designated. The specimen consists of six fragmented and tan-white to red-tan tissue cores ranging in length from 0.3 cm to 0.8 cm. The specimen is submitted in toto in two cassettes.

kat/2/25/2020Victoria Montoya, (Pathology Asst.)
Microscopic Description:
The final diagnosis of each specimen incorporates the microscopic examination findings.

- ccRCC (WHO/ISUP Grade II)

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International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) Criteria[b]

Prognostic factors
1. Less than one year from time of diagnosis to systemic therapy
2. Performance status <80% (Karnofsky)
3. Hemoglobin < lower limit of normal (Normal: 120 g/L or 12 g/dL)
4. Calcium > upper limit of normal (Normal: 8.5–10.2 mg/dL)
5. Neutrophil > upper limit of normal (Normal: 2.0–7.0×10⁹/L)
6. Platelets > upper limit of normal (Normal: 150,000–400,000)

Prognostic risk groups
- Favorable-risk group: no prognostic factors
- Intermediate-risk group: one or two prognostic factors
- Poor-risk group: three to six prognostic factors

- Residual disease **non-resectable**
- IMDC **Favorable** Grouping
- Referred to hem/onc and started on **Pembrolizumab** plus **Axitinib**

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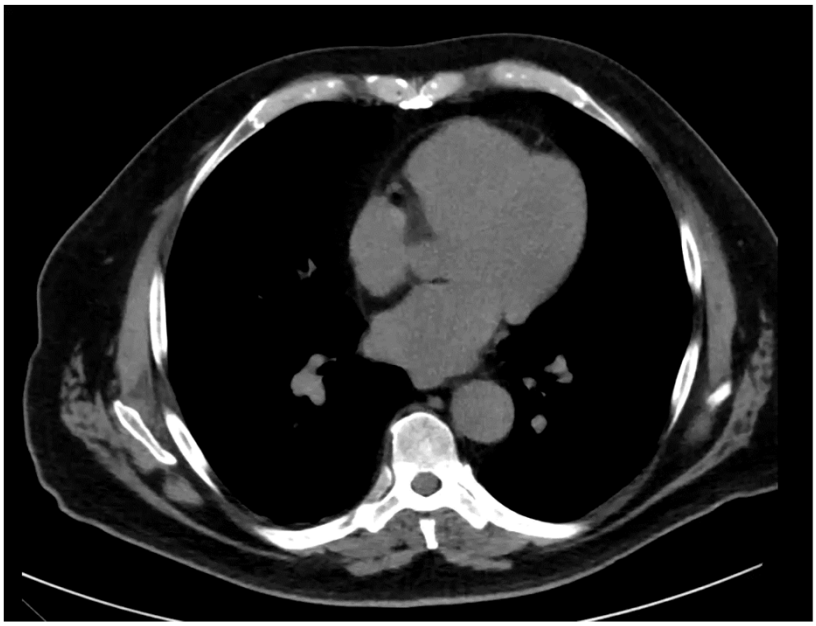

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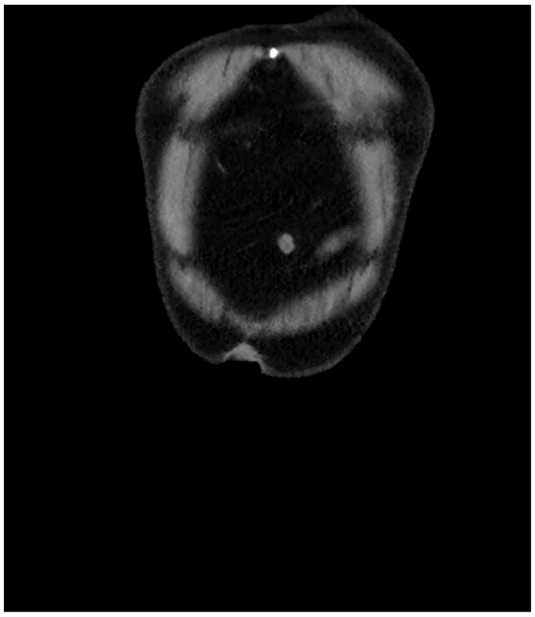

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Case 5

55yF w/ hx LEFT pT2a ccRCC s/p **Laparoscopic Radical Nephrectomy** in ’08. Interval surveillance imaging demonstrated a 2.8 cm exophytic mass in the lower pole of the RIGHT kidney.

She underwent RIGHT robot-assisted **Laparoscopic Partial Nephrectomy** in ‘17.

Representative imaging as follows:

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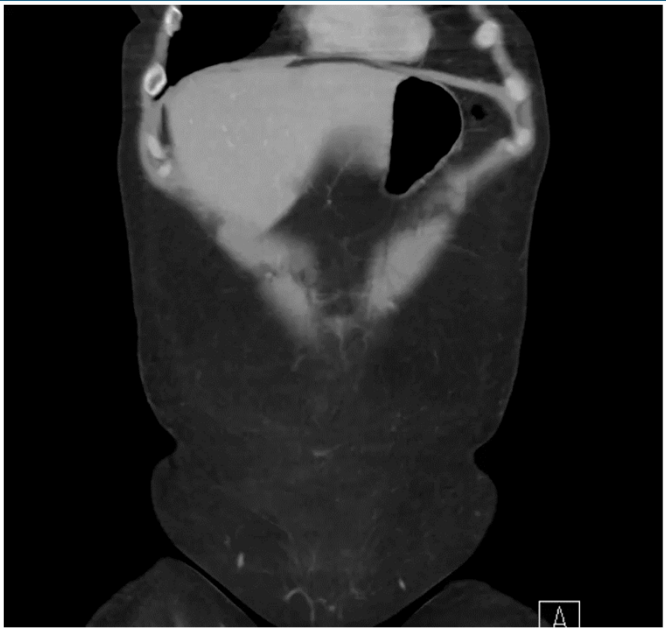

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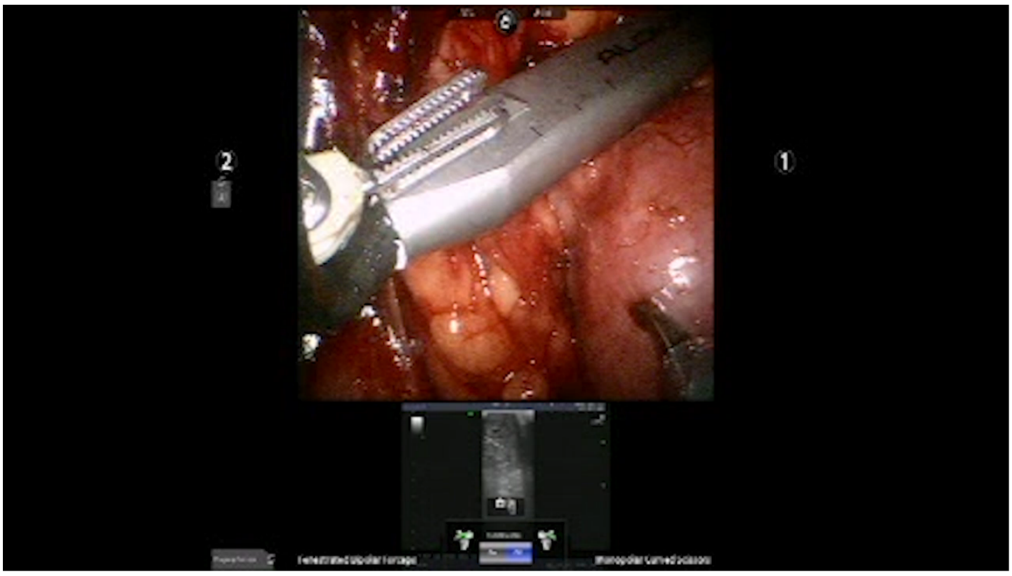

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Operative Procedure:
Da Vinci partial nephrectomy

Specimen Received:
A: Base of right kidney mass (FS)
B: Right kidney tumor



Final Pathologic Diagnosis:

A. Kidney, right, base of mass, resection:
     Renal medulla without evidence of malignancy (frozen se    n diagnosis
confirmed).

B. Kidney, right, partial nephrectomy:
     Tumor histologic type:          Clear cell r
     Sarcomatoid features (%):     No
Tumor size:                  2.5 cm (greatest dimens
     Other dimensions:           2.2 x 2 cm
Macroscopic extent of tumor:     Tumor is limited
Focality:                 Unifocal
     Number of tumors:           Not applicable
Fuhrman grade:                3 of 4
Microscopic extent of tumor:
     Perinephric fat invasion:      No
     Renal sinus invasion:           No
     Other:                 Not applicable
Renal vein involvement:           Not applicable
Adrenal gland present:            No
      Involved by tumor:           Not applicable
      Direct invasion or metastasis:      Not applicable
Cancer at resection margin:      No
     Location(s):                 Not applicable
Pathologic findings in nonneoplastic kidney:      None
Hilar lymph nodes present:       No
     Number involved/number present:      Not applicable

Pathologic stage (2010)          pT1a, pNX, pM-Not applicable
```

- ccRCC
- WHO/ISUP Grade III
- No perinephric fat invasion
- No renal sinus fat invasion
- Margins negative
- pT1a

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Interval surveillance concerning for local recurrence to include possible pancreatic metastasis.

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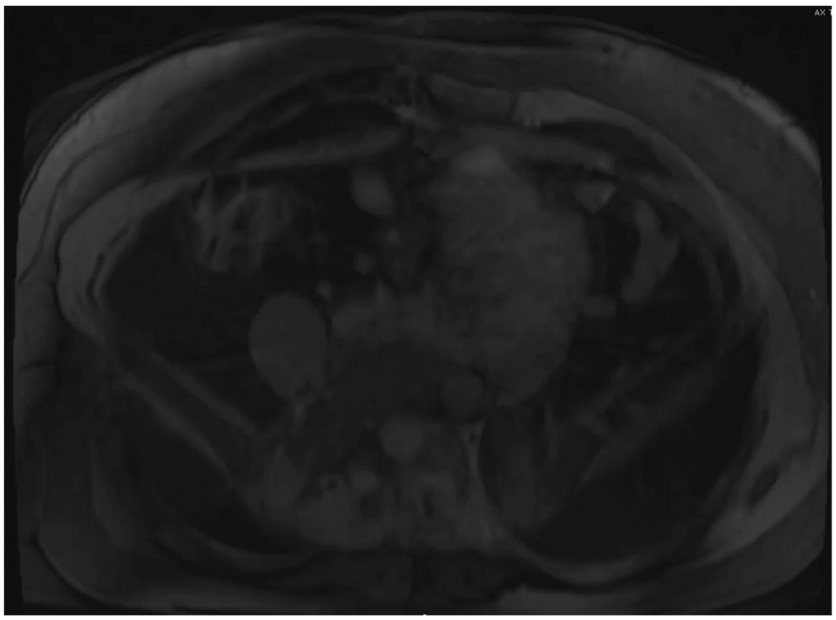

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Pt evaluated by hem/onc. Presumed diagnosis of metastatic RCC but pancreatic biopsy pending.

Treatment options reviewed:

A) TKIs (Sunitinib, Cabozantinib, Axitinib)

B) Immunotherapy (Ipilimumab + Nivolumab, IL-2)

C) Combination Therapy (Pembrolizumab + Axitinib)

D) Surgery w/wo systemic therapy

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Case 6

18yF, otherwise healthy, w/ new onset LEFT flank pain. Would undergo a MRI that revealed a LEFT large (9 cm) cystic mass w/ hydronephrosis.

Representative imaging as follows:

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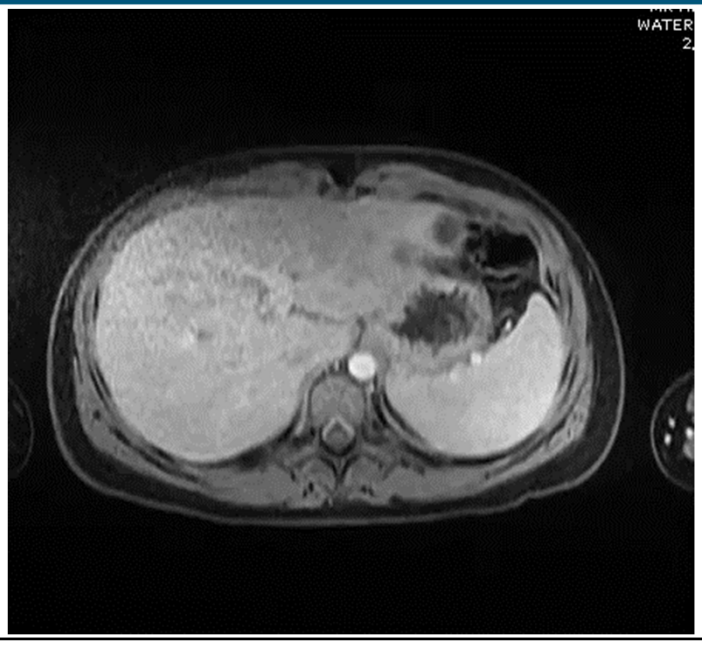

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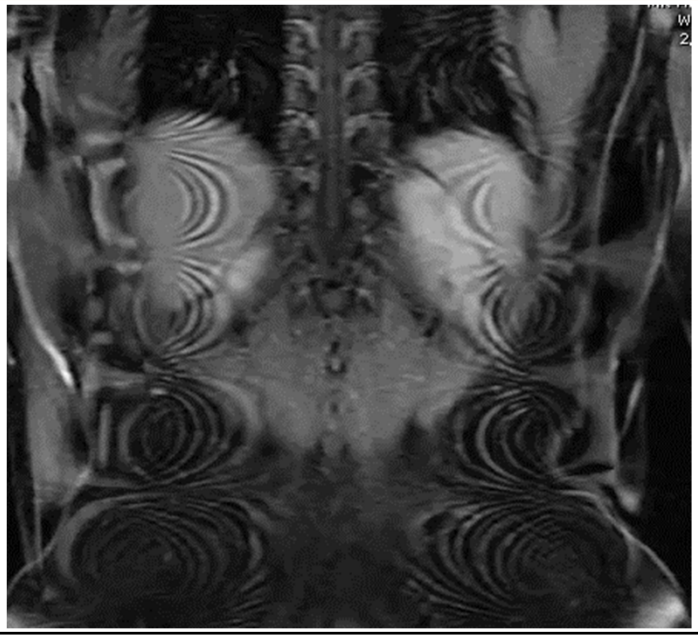

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Renal Mass Biopsy:

- Low grade cystic neoplasm
- Stroma w/ slender bland spindle cells, capillaries, and focal myoid differentiation
- Cyst lining cells:
  - Positive - cytokeratin AE1/AE3, ER, and PR
  - Negative - Melan-A and HMB45

MEST/cystic nephroma

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Specimen Received:
Left kidney and mass

Final Pathologic Diagnosis:
Kidney, left, radical nephrectomy:
Mixed epithelial and stromal tumor (MEST), 8.5 cm in greatest dimension,
see note.

As the senior physician, I attest that I: (i) examined the relevant preparation(s) for the specimen(s); and (ii) rendered or confirmed the diagnosis(es).
Electronically Signed ab5058/5/22/2020Liang Cheng, M.D. (Pathologist)
David Levy, M.D. (Fellow)
Signing Location: IUH Pathology Laboratory, 350 W. 11th Street, Indianapolis,
IN 46202
Note:

- MEST

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Case 7

66yF w/ hx of HTN, DMII, and GERD presenting w/ RIGHT flank pain and concern for UTI. Creatinine wnl.

Representative imaging as follows:

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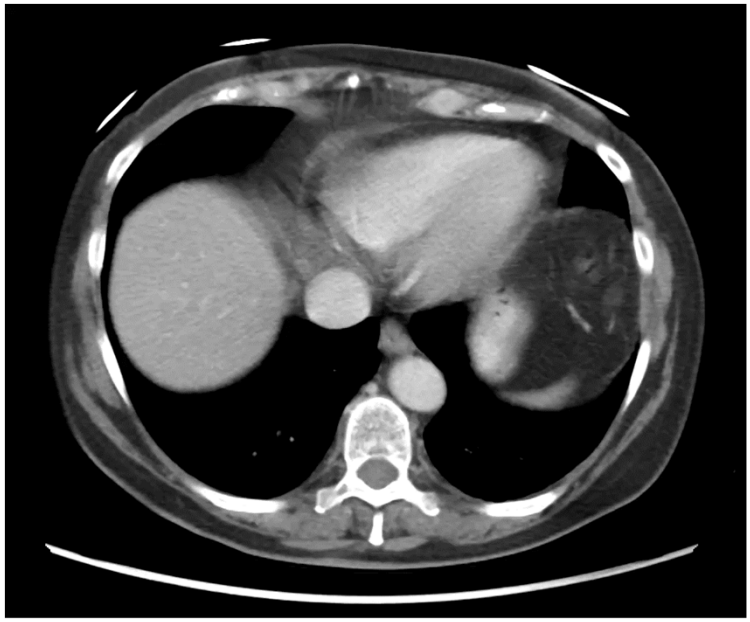

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Addendum Report

Date Ordered: 1/21/2019
Date Complete: 1/21/2019
Date Reported: 1/21/2019
Addendum Diagnosis
Addendum issued to report results of PD-L1 immunohistochemistry.

Immunohistochemical study for PD-L1 was performed on block S19-363 block A1 using DAKO 22C3 platform with the following result:

Negative: 0% of tumor cells with membranous/cytoplasmic staining.

As the senior physician, I attest that I: (i) examined the relevant preparation(s) and/or image for the specimen(s); and (ii) rendered or confirmed the interpretation(s).
***Electronically Signed *** Liang Cheng, M.D. (Pathologist)

Final Pathologic Diagnosis:

Kidney mass, right, needle biopsy:
Clear cell renal cell carcinoma
ISUP/WHO grade 2/4.

As the senior physician, I attest that I: (i) examined the relevant preparation(s) for the specimen(s); and (ii) rendered or confirmed the diagnosis(es).
Electronically Signed nao/1/7/2019 John N. Eble, M.D. (Pathologist)
Ronald Araneta, M.D. (Fellow)
Signing Location: Indiana University Health Pathology Laboratory, 350 W. Street, Indianapolis, IN 46202

Gross Description:
Received is a single formalin-filled container labeled with patient name "Kaufman, Renee" and is not additionally labeled. The specimen consists of six gray-tan to red-brown needle cores ranging from 0.3 cm to 1.3 cm in length. The specimen is submitted in toto in two cassettes.

Rapid Assessment Worksheet

Site #1, right kidney

Site #1, Episode 1, Touch Prep x 1

Fellow/Cytotechnologist R. Mickler on 1/4/2019

kat/1/4/2019 Amy Boehm
Microscopic Description:
The final diagnosis of each specimen incorporates the microscopic examination findings.

Underwent RIGHT Biopsy:

- ccRCC (ISUP/WHO Grade II)

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Pt directed to hem/onc and following options reviewed:

A) Immediate bilateral nephrectomy

B) PDL-1 staining, then systemic TKI vs Immunotherapy (Ipilimumab + Nivolumab)

C) Pending systemic treatment response, consolidative surgery

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Patient ultimately offered **Cabozatinib**, and this was followed by **Pembrolizumab**.

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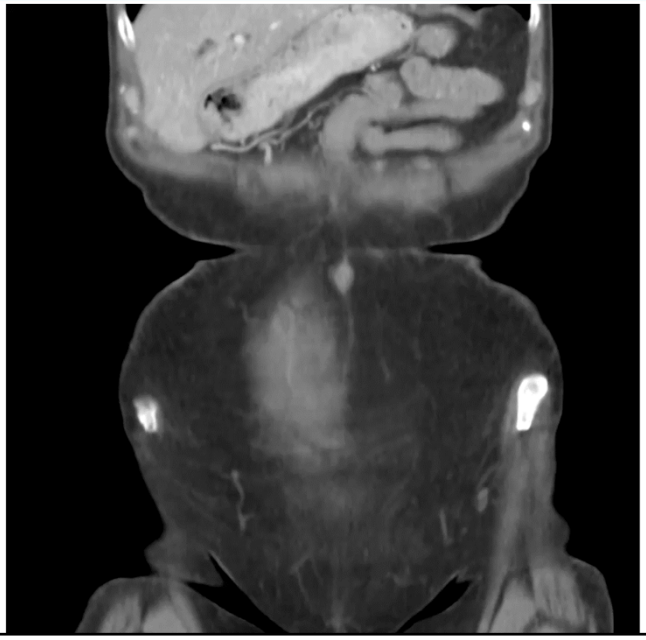

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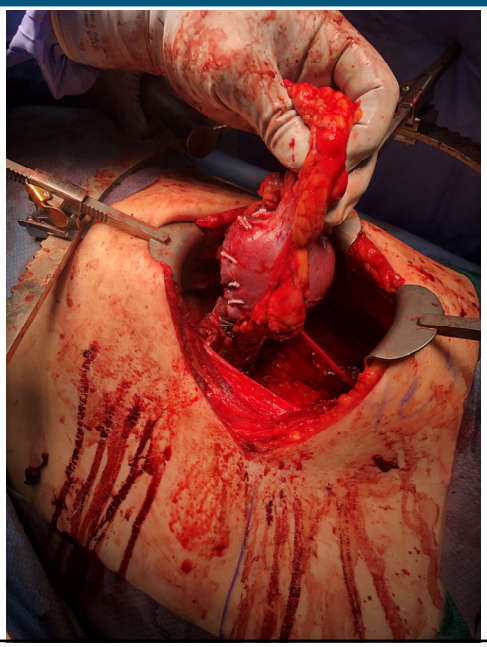
Given radiographic improvements, pt underwent a **RIGHT Open Partial Nephrectomy**.



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AUA VIRTUAL EXPERIENCE

```
Specimen Received:
 Right heminephrectomy and renal mass



Final Pathologic Diagnosis:
Kidney, right, partial nephrectomy:

Histologic type:              Clear cell renal cell carcinoma
Sarcomatoid features (%):          None
Rhabdoid features (%):          None

Tumor size (greatest dimension):     8.1 cm
     Other dimensions:     6.0 x 4.5 cm
Tumor focality:               Unifocal
     Number of tumors:     1

WHO/ISUP grade:          2/4
Tumor necrosis:               Not identified
Anatomic extent of tumor:
     Confined to kidney               No
     Extension into perinephric fat:           No
     Extension into renal sinus:               Yes
     Extension into pelvicalyceal system:          No
     Extension beyond Gerota fascia:          No
     Extension into other structures (specify):      No
Extension into renal vein or segmental branches:      No
Adrenal gland present:          Not submitted
Margin involvement:          Not involved by carcinoma
Other tumor-related findings:      N/A

Pathologic findings in non-neoplastic kidney:     Mild interstit
inflammation

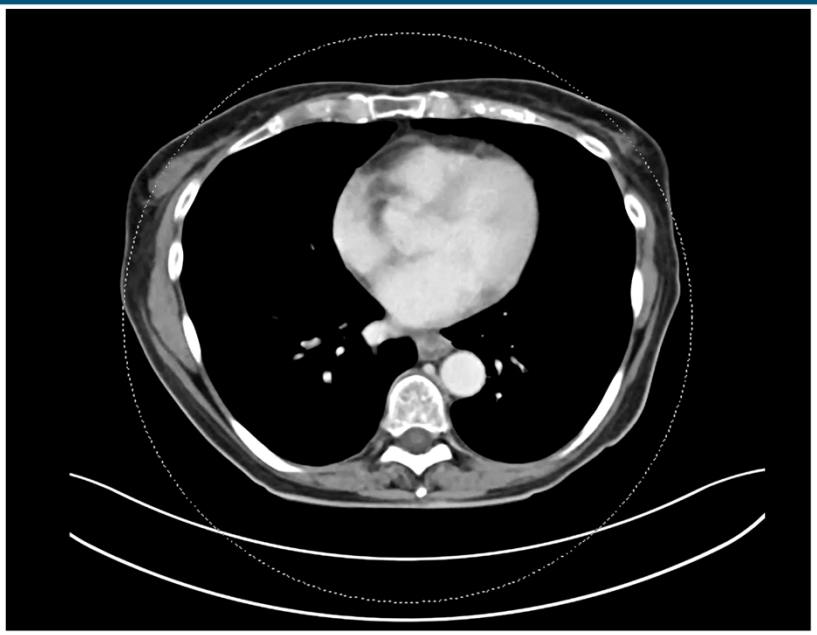
Hilar lymph nodes:          Not submitted

Regional lymph nodes:          Not submitted

Pathologic stage (AJCC 8th Edition):  pT3a pNX


As the senior physician, I attest that I: (i) examined the relevant
preparation(s) for the specimen(s); and (ii) rendered or confirmed the
diagnosis(es).
***Electronically Signed***       nao/5/28/2020Muhammad Idrees, M.D.
(Pathologist)
Mahmut Akgul (Fellow)
Signing Location:  IUH Pathology Laboratory, 350 W. 11th Street, Indianapolis,
IN 46202
```

- ccRCC
- Fuhrman Grade II
- Margins Negative
- pT3a pNX



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Case 8

63yM w/ hx of congenital solitary RIGHT kidney and prior partial nephrectomy in ‘16 for ccRCC. Surveillance imaging would identify mid-pole recurrence w/ tumor thrombus into the renal vein.

Representative imaging is as follows:

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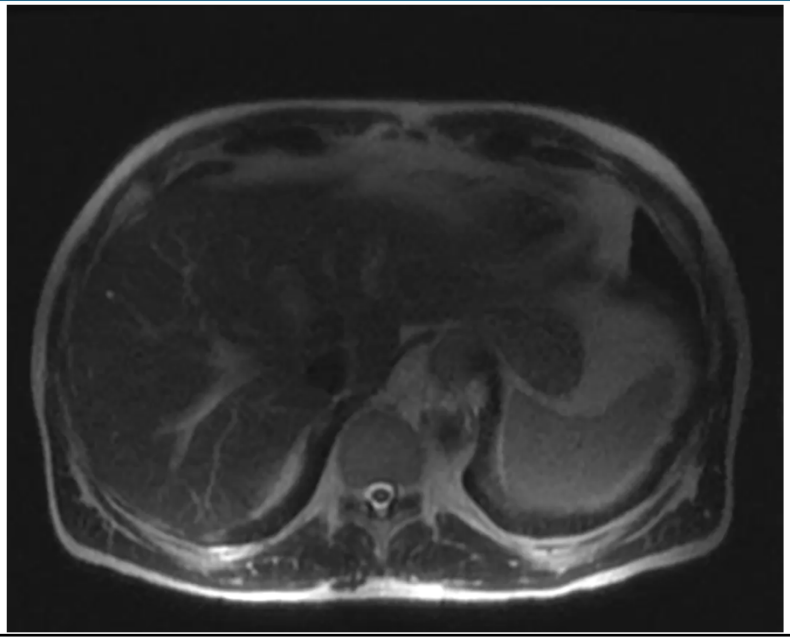

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Final Pathologic Diagnosis:
Slides for consult (S16-24264, 11/2/2016):

A. Specimen labeled as "fat over tumor", excision:
     Benign fibroadipose tissue

B. Kidney, right, deep margin, biopsy:
     Benign fibroadipose tissue

C. Kidney, right, partial nephrectomy
     Histologic type:              Clear cell renal cell carcinoma
Sarcomatoid features (%):          None
Rhabdoid features (%):             None

Tumor size (greatest dimension):     4.2 cm
     Other dimensions:      2.9 x 2.6 cm
Tumor focality:                 Unifocal
     Number of tumors:      One

WHO/ISUP grade:            2/4
Tumor necrosis:                 Not identified
Anatomic extent of tumor:            Limited to kidney
     Confined to kidney                 Yes
     Extension into perinephric fat:          No
     Extension into renal sinus:              No
     Extension into pelvicalyceal system:          Not applicable
     Extension beyond Gerota fascia:          No
     Extension into other structures (specify):       Not applicab
Extension into renal vein or segmental branches:      Not applica
Adrenal gland present:          No
     Direct invasion:           Not applicable
     Noncontiguous involvement:      Not applicable
Margin involvement:          No (see part B for final deep tumor s
     Specify location(s):       Not applicable
Other tumor-related findings:       None

Pathologic findings in non-neoplastic kidney:      None

Hilar lymph nodes:           Not submitted
     Number identified:      0
     Number involved:           Not applicable

Regional lymph nodes:           Not submitted
     Number of lymph nodes present:      Not applicable
     Number of lymph nodes involved:     Not applicable
     Site(s) of involved lymph nodes:      Not applicable
     Size of largest metastatic deposit:      Not applicable
     Extranodal extension:            Not applicable

Pathologic stage (AJCC 8th Edition):  pT1b pNX
```

Outside Pathology Reviewed:

- ccRCC
- WHO/ISUP Grade II
- No extension in perinephric fat
- Margins negative
- pT1b pNx
- Tumor proportion score 2% for PD-L1

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Options reviewed as follows:

A) Neoadjuvant therapy (TKI vs Immunotherapy)

B) Immediate radical nephrectomy w/ tumor thrombectomy (would need immediate dialysis)

C) Partial nephrectomy pending down-staging

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Started on **Cabozantinib**

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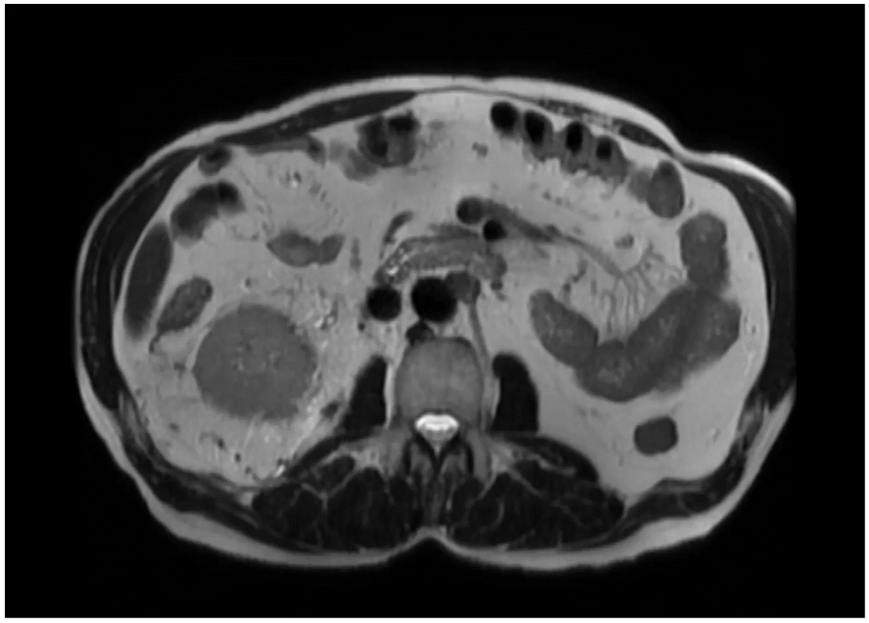

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Stable disease per repeat MRI. Pt now considering immunotherapy vs nephrectomy.

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