Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

Tuesday, May 4, 2021
5:00 PM – 6:00 PM ET

Faculty

Chung-Han Lee, MD, PhD
Mamta Choksi, MD

Moderator

Neil Love, MD

Faculty

Chung-Han Lee, MD, PhD
Assistant Attending Physician
Genitourinary Oncology Service
Memorial Sloan Kettering Cancer Center
New York, New York

Mamta Choksi, MD
Florida Cancer Specialists and Research Institute
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Walter Stadler, MD
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Dean for Clinical Research
Deputy Director, Comprehensive Cancer Center
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Commercial Support

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Dr Love — Disclosures

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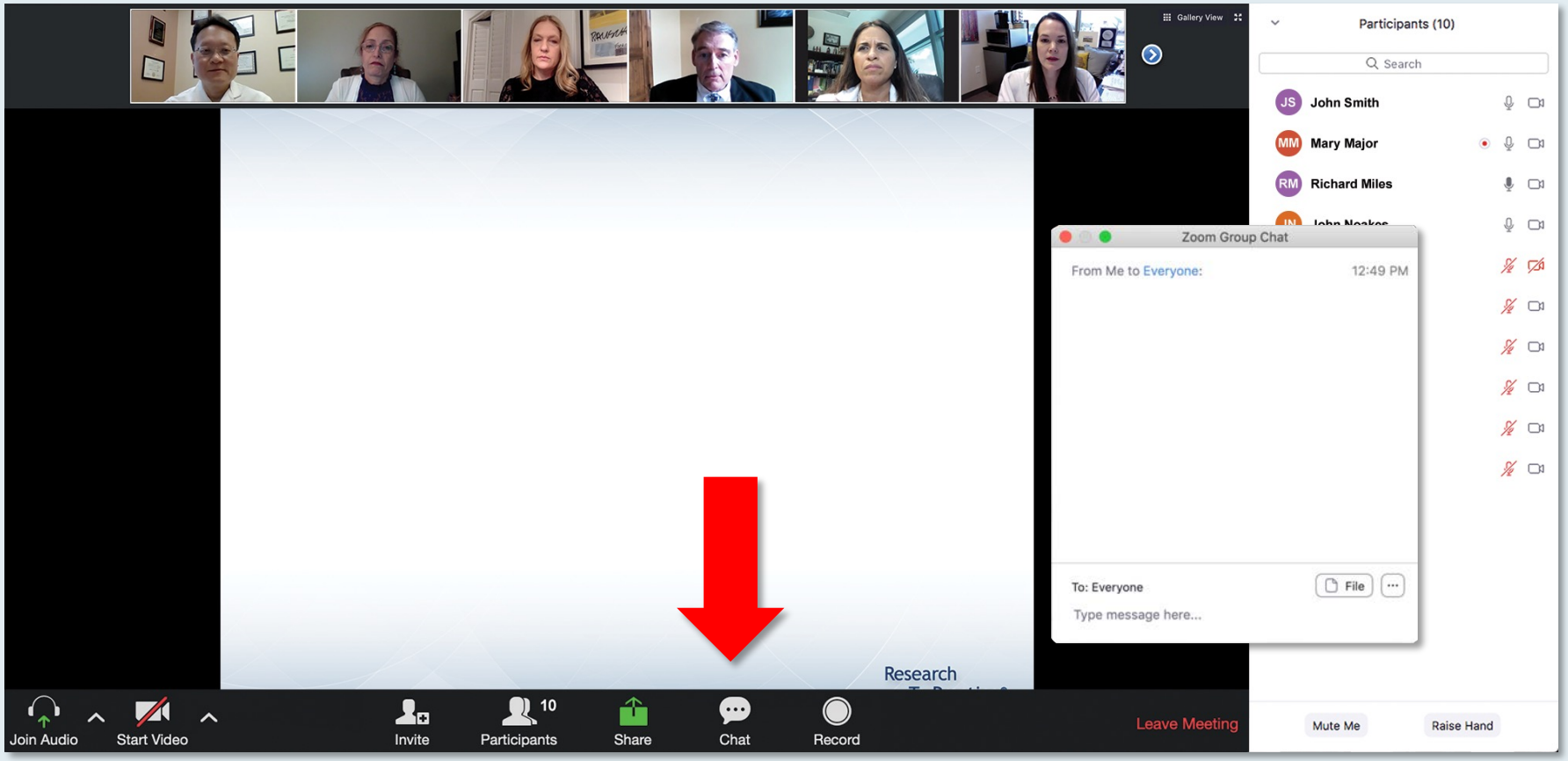
Dr Lee — Disclosures

Consulting Agreements	Bristol-Myers Squibb Company, Eisai Inc, EMD Serono Inc, Exelixis Inc, Merck, Pfizer Inc
Contracted Research	Bristol-Myers Squibb Company, Calithera Biosciences, Eisai Inc, Exelixis Inc, Lilly, Merck, Pfizer Inc

Dr Choksi — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



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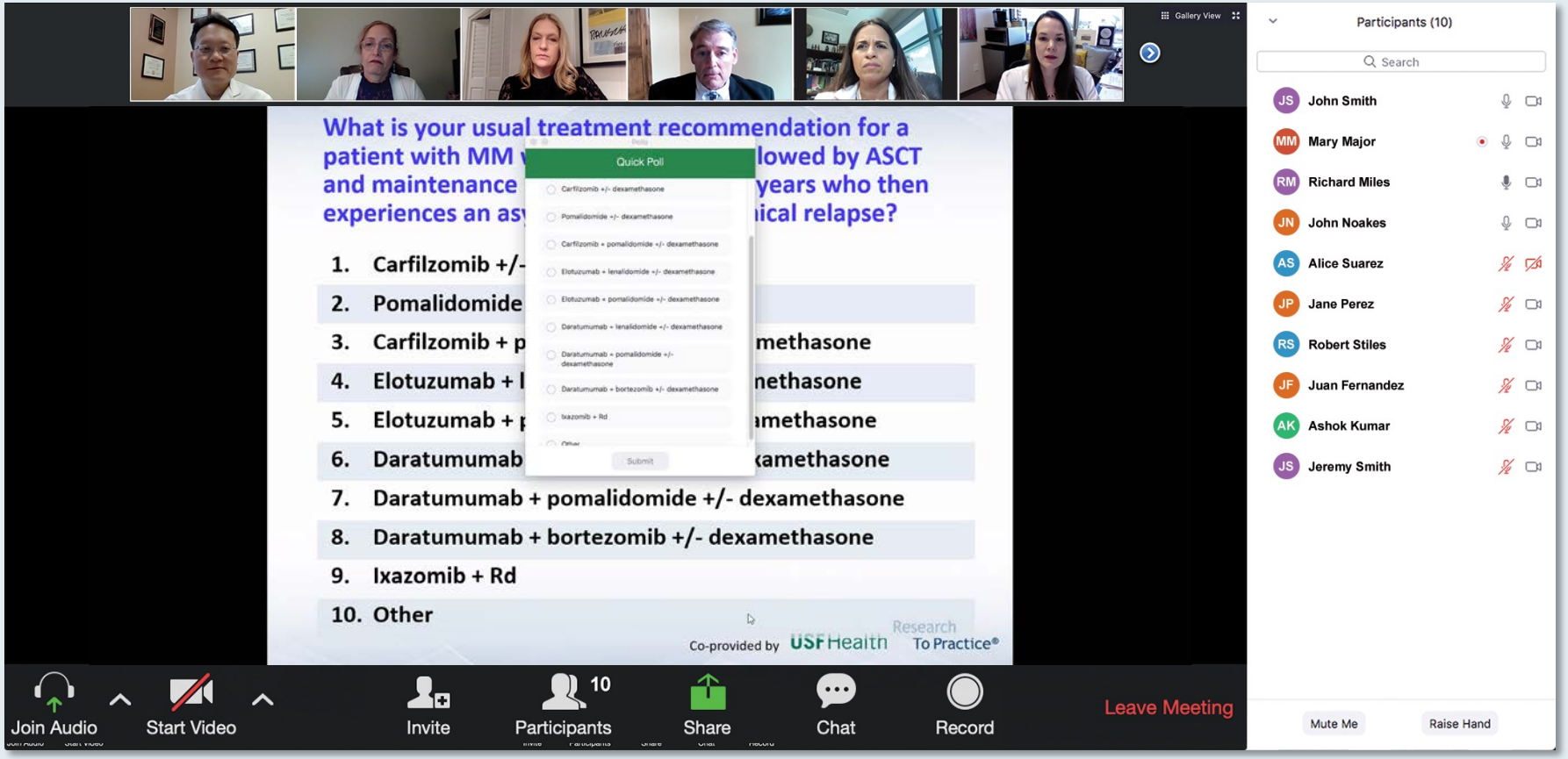
How to answer poll questions



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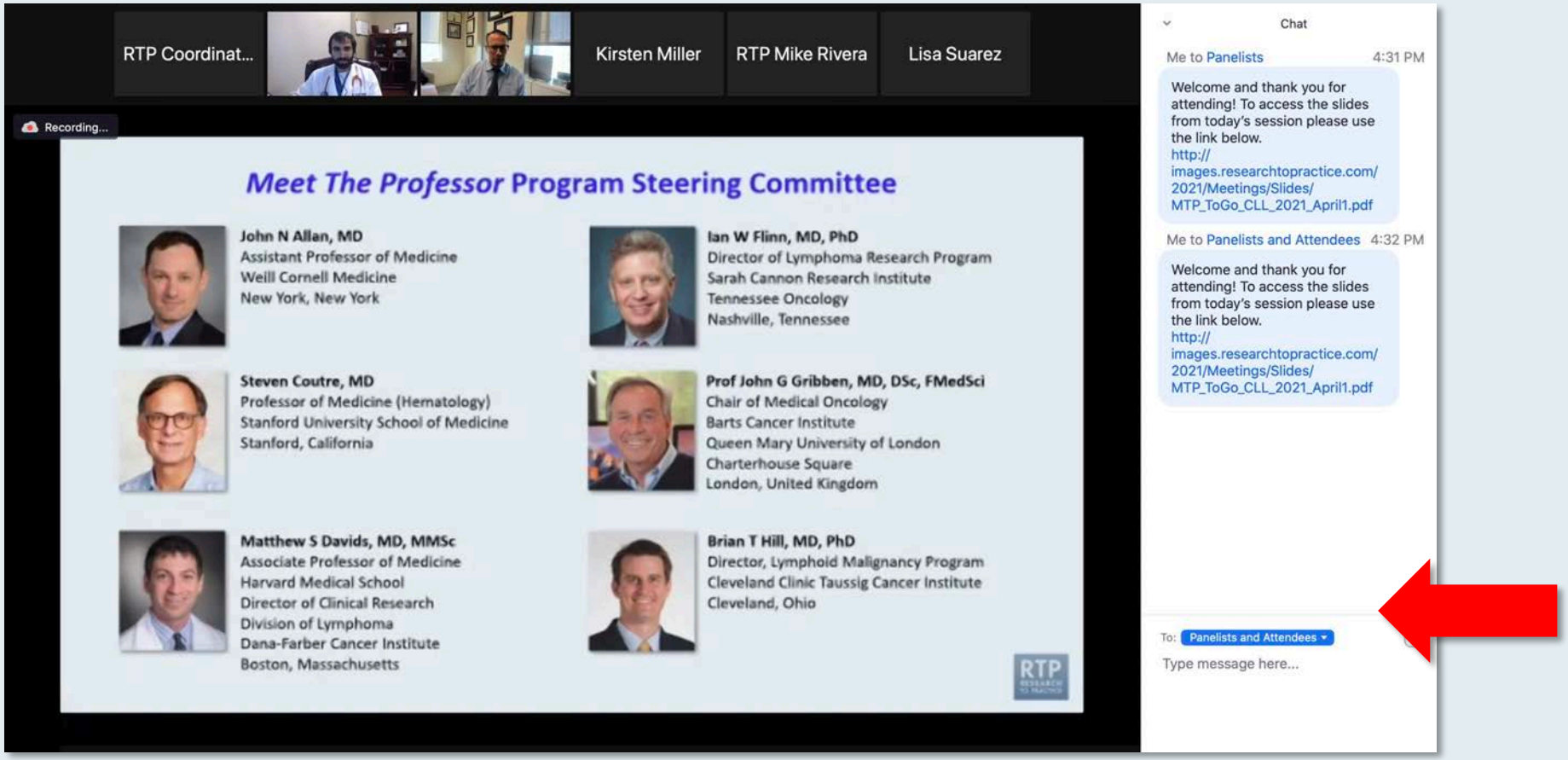

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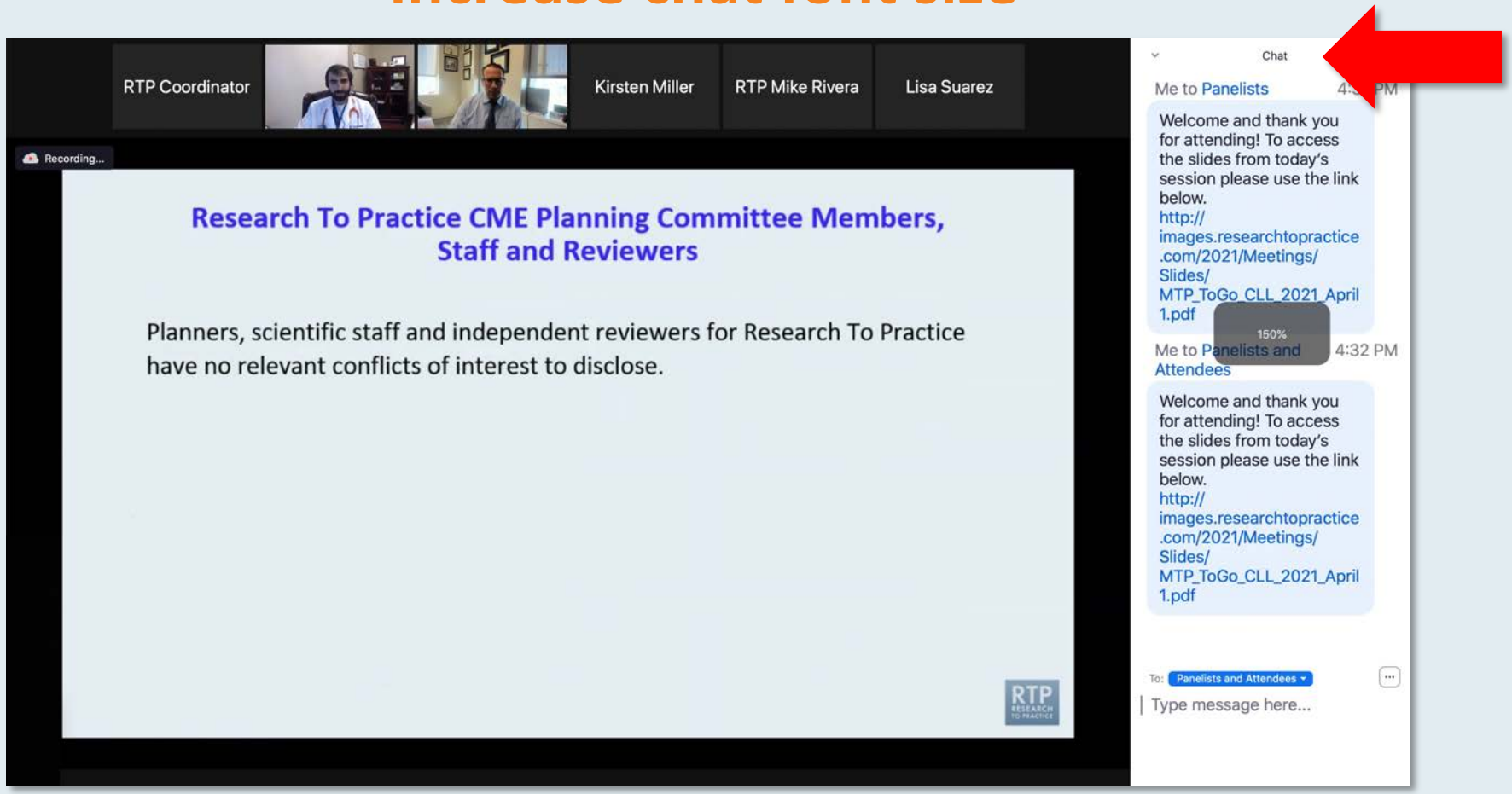

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma

DR CHUNG-HAN LEE

MEMORIAL SLOAN KETTERING CANCER CENTER

NEW YORK, NEW YORK

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Wednesday, May 5, 2021
5:00 PM – 6:00 PM ET

Faculty

Jeremy Abramson, MD

Moderator

Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Wednesday, May 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Michael J Birrer, MD, PhD

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

Current Concepts and Recent Advances in Oncology

A Daylong Clinical Summit Hosted in Partnership with Medical Oncology Association of Southern California (MOASC)

Saturday, May 15, 2021
10:30 AM – 6:30 PM ET

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Saturday, May 15, 2021

10:30 AM — Breast Cancer
Ruth O'Regan, Tiffany A Traina

11:30 AM — Multiple Myeloma
Kenneth Anderson, Noopur Raje

12:50 PM — Chronic Lymphocytic Leukemia and Lymphomas
Craig Moskowitz, Jeff Sharman

1:50 PM — Genitourinary Cancers
Joaquim Bellmunt, Sumanta Kumar Pal

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Saturday, May 15, 2021

3:15 PM — Gastrointestinal Cancers
Wells A Messersmith, Eileen M O'Reilly

4:15 PM — Acute Myeloid Leukemia and Myelodysplastic Syndromes
Harry Paul Erba, Rami Komrokji

5:35 PM — Lung Cancer
D Ross Camidge, Benjamin Levy

Meet The Professor
Management of Renal Cell Carcinoma

Tuesday, May 18, 2021
5:00 PM – 6:00 PM ET

Faculty
Brian I Rini, MD

Moderator
Neil Love, MD

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TO PRACTICE

Up for Debate: Oncology Investigators Provide Their Take on Current Controversies in Patient Care

A Daylong Multitumor Educational Webinar
in Partnership with Florida Cancer Specialists

Saturday, May 22, 2021
10:15 AM – 4:15 PM ET

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Saturday, May 22, 2021

10:15 AM — Lung Cancer
John V Heymach, Stephen V Liu

11:30 AM — Genitourinary Cancers
Maha Hussain, Elizabeth R Plimack

12:45 PM — Chronic Lymphocytic Leukemia and Lymphomas
Jonathan W Friedberg, Laurie H Sehn

2:00 PM — Multiple Myeloma
Irene M Ghobrial, Sagar Lonial

3:15 PM — Breast Cancer
Virginia Kaklamani, Nancy U Lin

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Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

Webinar 1 – Tuesday, April 6, 2021

Faculty
Sumanta K Pal, MD

Webinar 2 – Tuesday, May 4, 2021

Faculty
Chung-Han Lee, MD, PhD

Webinar 3 – Tuesday, June 1, 2021

Faculty
Walter Stadler, MD

Webinar 4 – Tuesday, July 6, 2021

Faculty
David I Quinn, MBBS, PhD

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Thank you for joining us!

CME and ABIM MOC credit information will be emailed to each participant within 5 business days.

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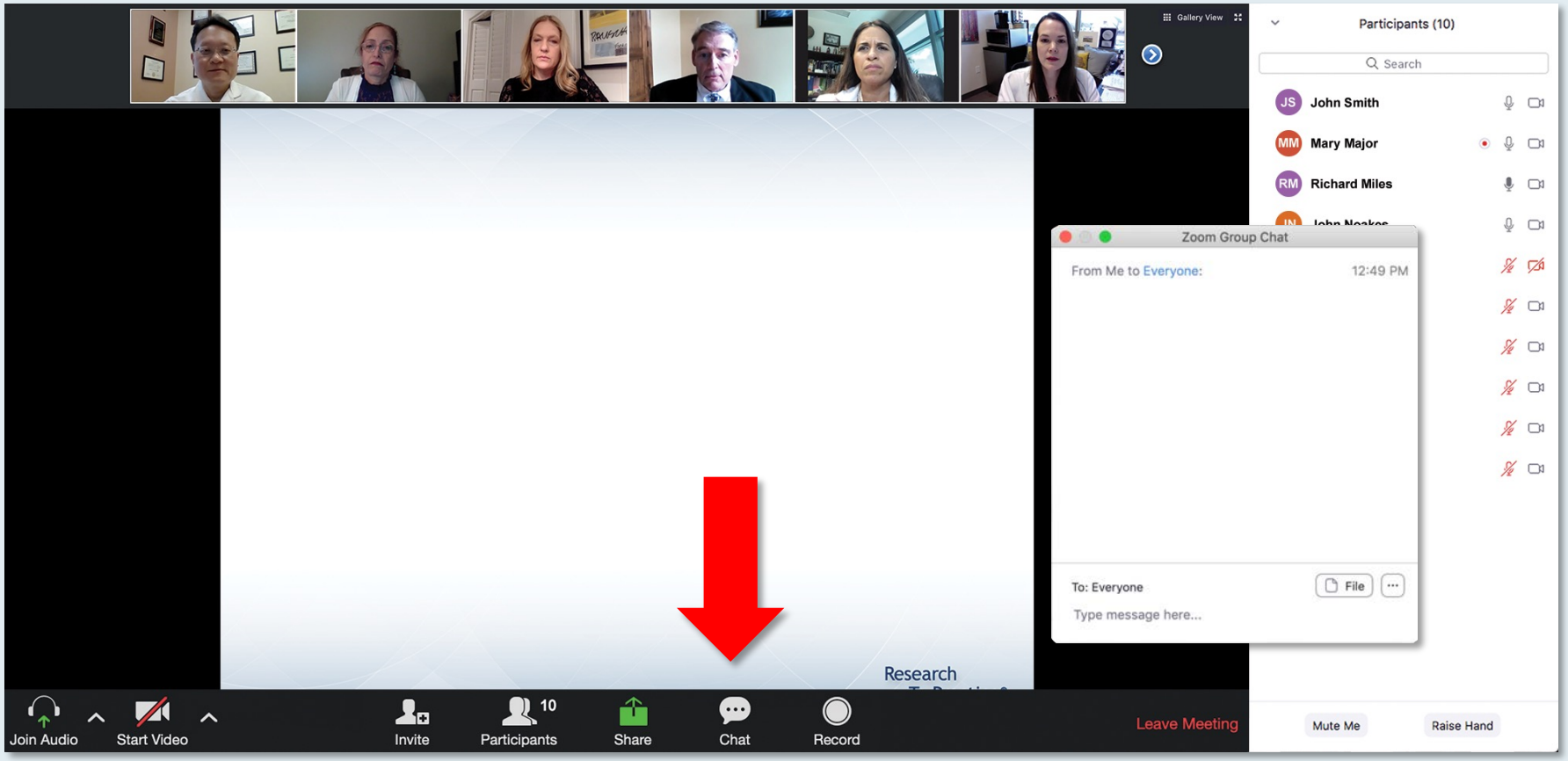

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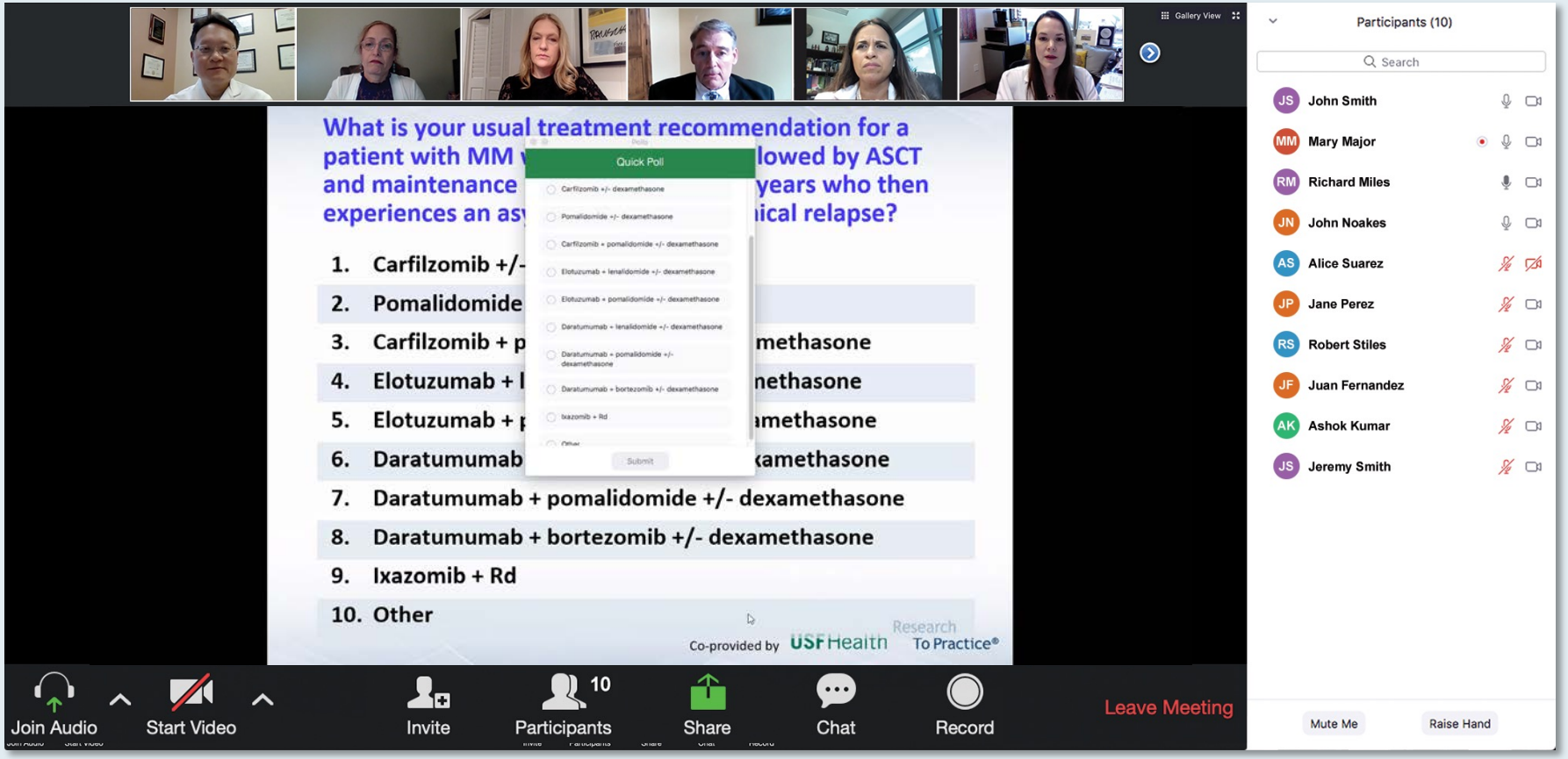

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Agenda

MODULE 1: Cases from the Practice of Dr Choksi

- A 63-year-old man with metastatic renal cell carcinoma (RCC) treated with ipilimumab/nivolumab
- A 67-year-old man with metastatic RCC and high-risk oncocytic features who responded to ipilimumab/nivolumab
- A 65-year-old man with Stage III RCC

MODULE 2: Consensus or Controversy – Clinical Investigator Approaches to Clinical Scenarios

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Lee

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

Case Presentation: Dr Choksi – A 63-year-old man with metastatic RCC treated with ipilimumab/nivolumab

- Patient developed pathologic fracture of RIGHT HUMERUS after falling out of bed in March 2020. MRI of right humerus showed fracture of right humerus with surrounding soft tissue mass.
- He lives at ALF, has underlying history of chronic liver disease and thrombocytopenia from ALCOHOL ABUSE, he quit drinking at the time of the diagnosis of the liver damage in 2013. He is a chronic smoker, lately has tried to cut down.
- PET scan done on 3/8/2020 showed multiple scattered subcentimeter pulmonary nodules up to 9 mm in size, large hypermetabolic mass of the left kidney about 4.8 x 4.4 x 4.1 cm in size with SUV of 4.7, multiple lytic lesions throughout the axial skeleton, with the largest in right superior pubic ramus and right humerus.
  - Also showed hepatosplenomegaly with cirrhotic liver morphology. His transaminases were within normal range. Alkaline phosphatase was slightly elevated 146.

Case Presentation: Dr Choksi – A 63-year-old man with metastatic RCC treated with ipilimumab/nivolumab (continued)

- He underwent CT-guided renal biopsy on 5/18/2020. It showed renal cell carcinoma. He also underwent CT-guided bone biopsy on 5/21/2020, which showed metastatic renal cell carcinoma.
- Surgery could not be considered due to his comorbidities, lockdown effect in ALF DUE TO COVID, etc.
- He was initiated on nivolumab 3mg/kg IV; ipilimumab 1mg/kg q21d X 4 cycles. He completed 4 cycles on 8/13/2020. He tolerated it quite well. Restaging PET/CT scan showed interval decrease in left kidney mass, overall improvement of bony metastasis and intraoperative ultrasound version of subcentimeter bilateral pulmonary nodules.
- He underwent surgery by orthopedic oncologic surgeon for further stabilization of pathologic fracture of the right humerus. He underwent adjuvant radiation therapy by radiation oncologist for palliative radiation therapy. He has been initiated on maintenance single-agent immunotherapy with nivolumab.

Case Presentation: Dr Choksi – A 67-year-old man with metastatic RCC and high-risk oncocytic features who responded to ipilimumab/nivolumab

- He is a a pleasant 67 y/o male who presented on 1/20/19 to local hospital ER for the symptoms of left-sided flank pain and hematuria that started the day before. He did not have any history of hematuria in the past. CT of the abdomen and pelvis showed 8.1 x 7.8 x 7.60 cm large exophytic mass arising from the lower part of the left kidney concerning for renal cell carcinoma, adjacent 11 mm exophytic hyperdense nodule, mild left perirenal stranding, enlarged retroperitoneal lymph node at the left renal hilum about 18 mm in size. Findings were highly concerning for primary renal cell carcinoma. PET/CT was ordered and obtained on 1/30/19 which showed previously noted left renal mass is hypermetabolic as is the adjacent adenopathy.

- He was evaluated by urologist and was recommended nephrectomy. He underwent a radical left nephrectomy on 2/21/19, tolerated the procedure well. Pathology of left kidney showed clear cell renal cell carcinoma, grade 3, tumor measuring 6 x 6 x 5 cm at the inferior pole with extensive tumor necrosis. Margins were uninvolved by invasive carcinoma. 6 of 14 lymph nodes positive, largest metastatic deposit 2.6 cm. Primary tumor T3a, regional lymph nodes pN1. He had stage III renal clear cell carcinoma and was high risk due to his large tumor size and 6/14 lymph-node involvement. NCCN guidelines recommended treatment options of trial, surveillance, or sunitinib x 1 year.

Case Presentation: Dr Choksi – A 67-year-old man with metastatic RCC and high-risk oncocytic features who responded to ipilimumab/nivolumab (cont)

- Sunitinib 50 mg 4 wks on, 2 wks off was initiated on 3/12/19. CT of the abdomen and pelvis performed on 5/28/19 showed subcentimeter lymph nodes in the retroperitoneum similar to the prior study. PET scan performed on 7/3/19 was essentially negative. He reported significant fatigue and weakness with activity intolerance.
- Regimen was changed to sunitinib 50 mg 2 weeks on, 1 week off and he reported this had improved his fatigue. He took it for total 1 year until 3/12/2020.
- A follow-up CT C/A/P was obtained in April of 2020 which showed worsening retroperitoneal adenopathy suggesting possible metastatic carcinoma with no other significant findings. A PET/CT was then obtained and it does show +SUV activity to these lymph nodes with SUV 10.9.
- He underwent CT-guided biopsy of the retroperitoneal lymph node. Biopsy showed renal cell carcinoma with oncocytic features, high grade.
- He was initiated on ipilimumab with nivolumab once every 3 weeks for 4 cycles on 4/16/2020.

Case Presentation: Dr Choksi – A 67-year-old man with metastatic RCC and high-risk oncocytic features who responded to ipilimumab/nivolumab (cont)

- 4 cycles was given with nivolumab only as he had developed skin rashes grade 2-3 for which steroid use had been required for 6 days, it was thought to be due to ipilimumab. After completion of 4 cycles he was initiated on single-agent nivolumab every 2 weeks as of 7/9/2020.
- Repeat PET/CT imaging showed a great response to treatment with resolution of the hypermetabolic lymph nodes in the peritoneal and pelvic areas. He was then switched to once a month dosing of nivolumab on 8/6/20. Overall he is tolerating it well with grade 1 skin rashes especially over his forearms. So far he is doing well. He is scheduled for restaging workup soon.

Case Presentation: Dr Choksi – A 65-year-old man with Stage III RCC

- On 7/29/19, he presented to the PCP with complaint of hematuria with clots. He was referred to urologist for further evaluation and was first seen on 8/5/19. CT urogram performed on 8/14/19 showed 9.5 x 10.3 cm mass arising from the mid to lower pole medially of the left kidney. Also noted was tiny subcentimeter low-density lesion in the left hepatic lobe, thought to probably be small cysts, and mild chronic interstitial changes of the lung bases without focal parenchymal nodule mass or infiltrate.
- MRI of the abdomen performed on 9/19/19 showed large centrally necrotic left renal mass. Severe secondary compression of the left renal vein without evidence of thrombosis was seen at this time. No renal vein invasion was noted. CT of the chest was performed on 9/23/19 which did not show any significant thoracic abnormalities. Cystoscopy was performed by urologist on 9/26/19 which was negative.
- He was admitted to local hospital on 10/15/19 for open left radical nephrectomy with adrenalectomy. Tumor size was 11 cm at its greatest dimension and was unifocal.

Case Presentation: Dr Choksi – A 65-year-old man with Stage III RCC (continued)

- Histopathologic grade was G3 and stage was pT3a. Tumor necrosis was present. Tumor extended into renal vein. Margins were uninvolved by invasive carcinoma. No lymph nodes were submitted. Adrenal gland was benign. According to NCCN guidelines, his diagnosis was considered Stage III and treatment with adjuvant sunitinib was to be initiated.
- Baseline PET scan was obtained on 11/21/19 and showed no evidence of FDG avid malignancy. It did show a large collection within the left nephrectomy bed extending into the left retroperitoneal region and abutting the left psoas muscle containing fluid, multiple foci of air with mildly thickened wall. He was evaluated by urologist and referred for drainage.
- On 12/6/19, 600 mL of fluid was drained at local hospital by IR and drain was placed. Fluid was milky-colored, likely representing lymphatic duct fluid. Drain was removed on 12/19/19 and repeat ultrasound was performed on 1/3/20.

Case Presentation: Dr Choksi – A 65-year-old man with Stage III RCC (continued)

- He had follow-up appointment with urologist on 1/6/20 and was cleared to start sunitinib, which he did on 1/7/20, 50mg for 4 weeks on, 1 week off. ECHO performed on 10/19/20 showed EF of 55-60%.
- Given issues with continued neutropenia and HTN, sunitinib was changed to 50mg for 2 weeks on, 1 week off on 11/25/20. CT scan of chest abdomen and pelvis performed on 12/3/20 showed no evidence of malignancy.
- He completed his final dose of sunitinib on 2/7/21. Clinically he shows no evidence of disease, we will continue to monitor him closely.

Agenda

MODULE 1: Cases from the Practice of Dr Choksi

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MODULE 3: Renal Cell Carcinoma Journal Club with Dr Lee

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with a history of nephrectomy for clear cell renal cell carcinoma (RCC) who on routine follow-up 3 years later is found to have asymptomatic bone metastases (PS 0)?

1. Nivolumab/ipilimumab
2. Avelumab/axitinib
3. Pembrolizumab/axitinib
4. Pembrolizumab/lenvatinib
5. Nivolumab/cabozantinib
6. Tyrosine kinase inhibitor (TKI) monotherapy
7. Anti-PD-1/PD-L1 monotherapy
8. Other

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with a history of nephrectomy for clear cell renal cell carcinoma (RCC) who on routine follow-up 3 years later is found to have asymptomatic bone metastases (PS 0)?

 Dr Lee	Pembrolizumab/lenvatinib
 Dr Pal	Nivolumab/cabozantinib
 Dr Quinn	Nivolumab/cabozantinib
 Dr Stadler	Cabozantinib

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient who presents with clear cell RCC with multiple painful bone metastases and hemoglobin (Hb) of 11.4 g/dL (PS 1)?

1. Nivolumab/ipilimumab
2. Avelumab/axitinib
3. Pembrolizumab/axitinib
4. Pembrolizumab/lenvatinib
5. Nivolumab/cabozantinib
6. TKI monotherapy
7. Anti-PD-1/PD-L1 monotherapy
8. Other

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient who presents with clear cell RCC with multiple painful bone metastases and a hemoglobin (Hb) of 11.4 g/dL (PS = 1)?

 Dr Lee	Nivolumab/cabozantinib
 Dr Pal	Nivolumab/cabozantinib
 Dr Quinn	Cabozantinib
 Dr Stadler	Nivolumab/ipilimumab

In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear cell RCC who receives first-line ipilimumab/nivolumab and experiences disease progression after 12 months?

1. TKI monotherapy
2. Everolimus
3. Lenvatinib + everolimus
4. Avelumab/axitinib
5. Pembrolizumab/axitinib
6. Nivolumab/cabozantinib
7. Anti-PD-1/PD-L1 monotherapy
8. Other

In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear cell RCC who receives first-line ipilimumab/nivolumab and experiences disease progression after 12 months?

 Dr Lee	Cabozantinib
 Dr Pal	Cabozantinib
 Dr Quinn	Cabozantinib or axitinib
 Dr Stadler	Cabozantinib

In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear cell RCC who receives first-line nivolumab/cabozantinib and experiences disease progression after 12 months?

 Dr Lee	Lenvatinib + everolimus
 Dr Pal	Lenvatinib + everolimus
 Dr Quinn	Axitinib
 Dr Stadler	Axitinib

What would be your most likely third-line systemic therapy recommendation for a 65-year-old patient with metastatic RCC who experienced disease progression on first-line pembrolizumab/axitinib and second-line cabozantinib (PS 0)?

 Dr Lee	Lenvatinib + everolimus
 Dr Pal	Lenvatinib + everolimus
 Dr Quinn	Tivozanib
 Dr Stadler	Lenvatinib + everolimus

In general, how would you compare the efficacy of tivozanib to that of other commercially available tyrosine kinase inhibitors (TKIs) (eg, axitinib, cabozantinib, lenvatinib) in patients with relapsed metastatic RCC?

 Dr Lee	Other commercially available TKIs are more efficacious
 Dr Pal	Efficacy is about the same
 Dr Quinn	Efficacy is about the same
 Dr Stadler	Efficacy is about the same

In general, how would you compare the tolerability of tivozanib to that of other commercially available TKIs (eg, axitinib, cabozantinib, lenvatinib) in patients with relapsed metastatic RCC?

 Dr Lee	Tivozanib is more tolerable
 Dr Pal	Tivozanib is more tolerable
 Dr Quinn	Tivozanib is more tolerable
 Dr Stadler	Tolerability is about the same

Agenda

MODULE 1: Cases from the Practice of Dr Choksi

MODULE 2: Consensus or Controversy – Clinical Investigator Approaches to Clinical Scenarios

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Lee

- Prevalence and landscape of actionable genomic alterations in renal cell carcinoma (RCC)
- FRACTION-RCC trial: Innovative, high-throughput assessment of nivolumab + ipilimumab for treatment-refractory metastatic RCC
- DNA damage repair pathway alterations in metastatic clear cell RCC and implications for systemic therapy
- Current role for adjuvant and neoadjuvant therapy in RCC
- Genomic biomarkers of response to lenvatinib/pembrolizumab (Len/Pembro) in patients with advanced RCC (aRCC)
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- Clinicogenomic predictors of extreme responses to anti-PD-1/PD-L1 checkpoint inhibitors in metastatic urothelial cancer

MODULE 4: Key Data Sets

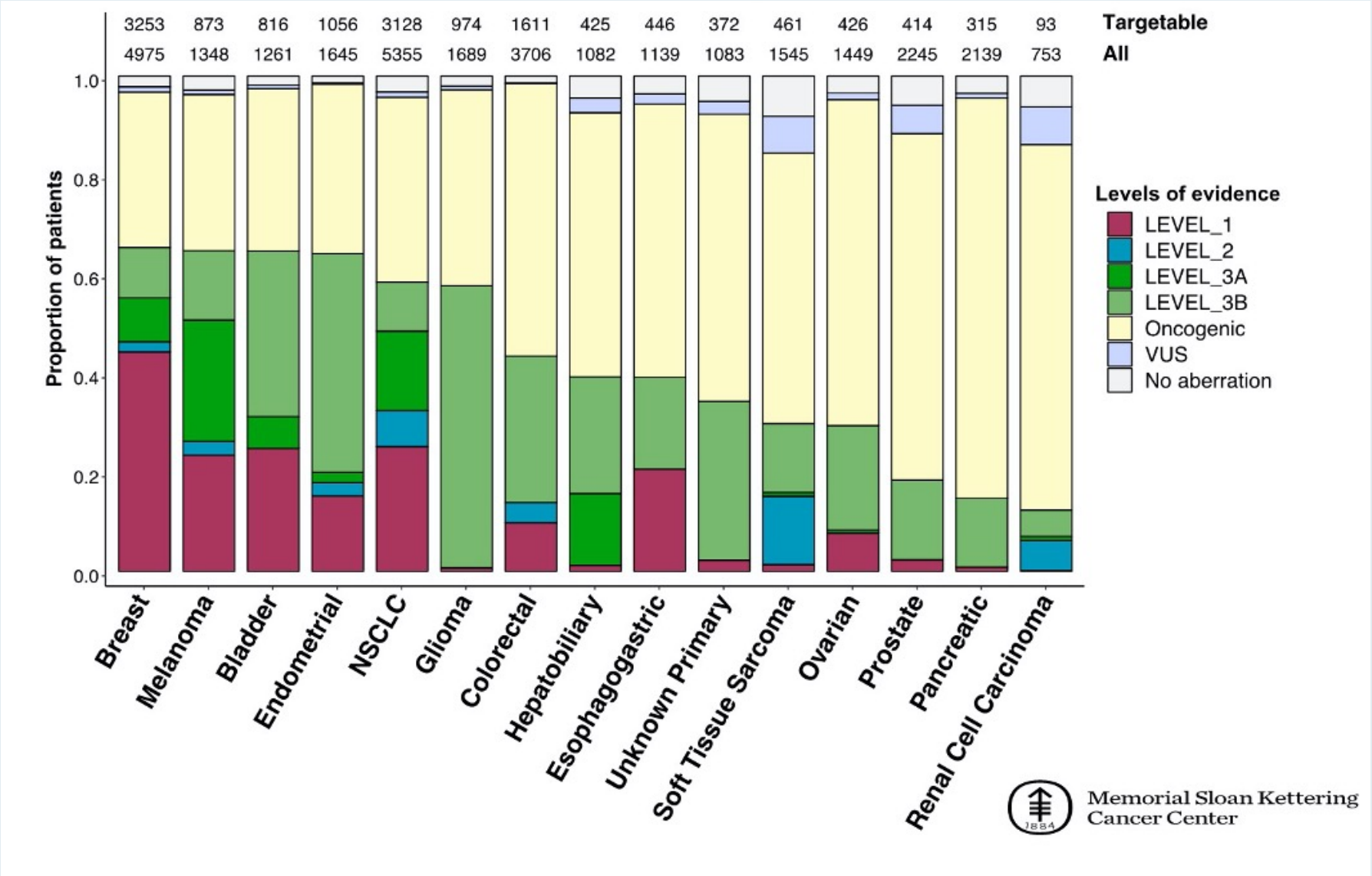
MODULE 5: Other Recent Data Sets

Prevalence and Landscape of Actionable Genomic Alterations in Renal Cell Carcinoma

Attala K et al.

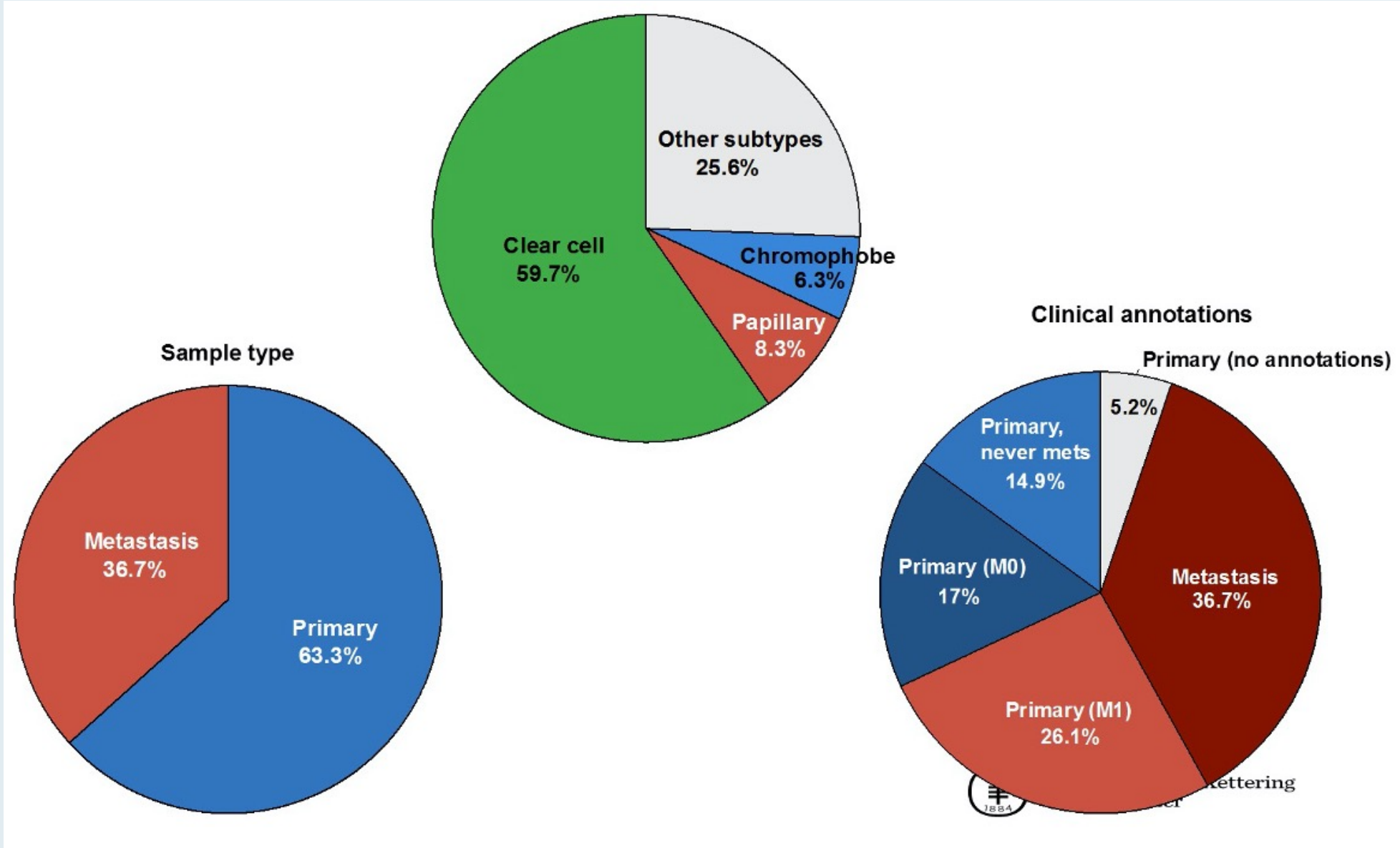
Genitourinary Cancers Symposium 2020;Abstract 616.

Pan-Cancer MSK-IMPACT Cohort
Targetable Alterations by Cancer Type (15 Most Common)



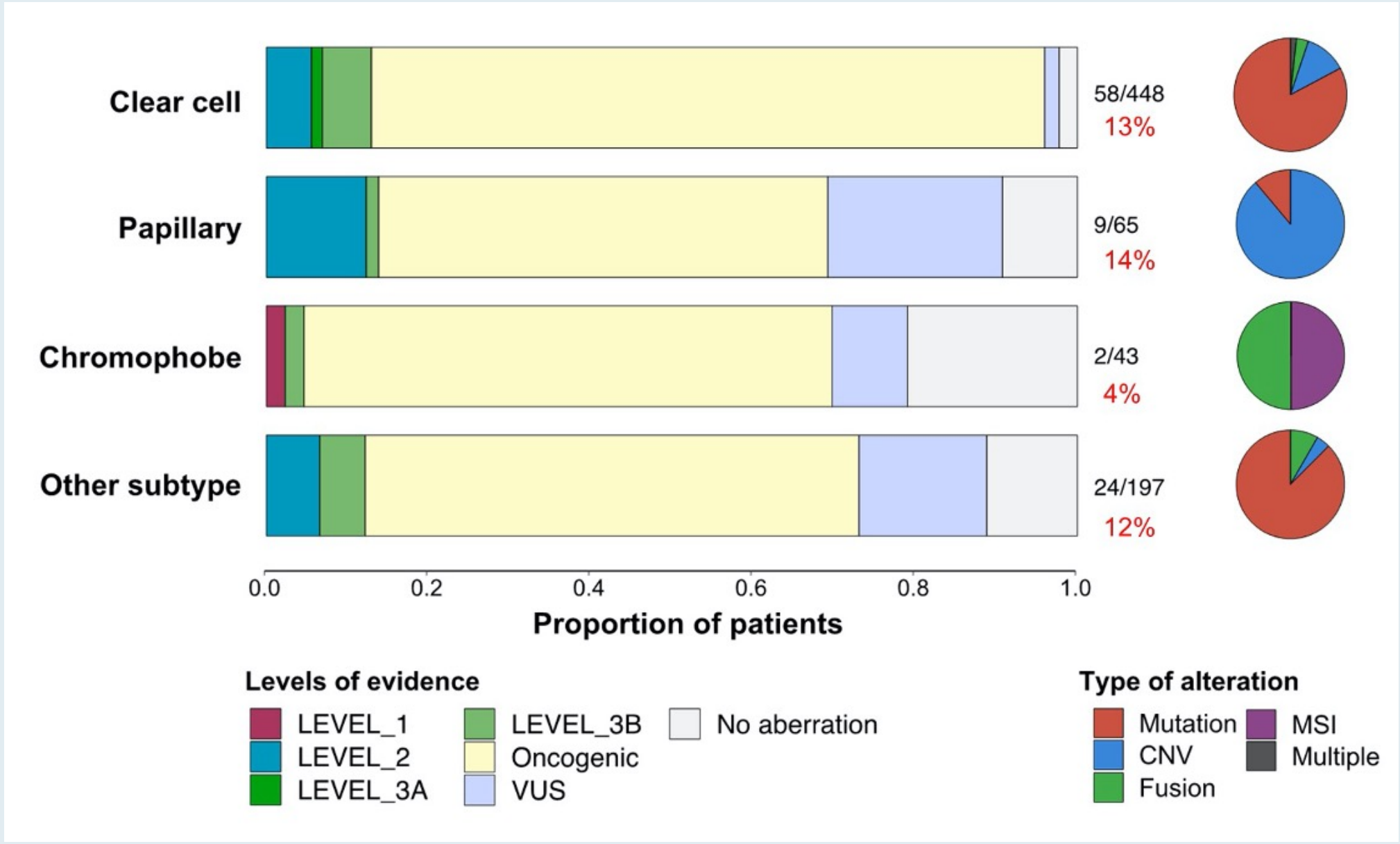
Attala K et al. Genitourinary Cancers Symposium 2020;Abstract 616.

RCC Histologic Subtypes



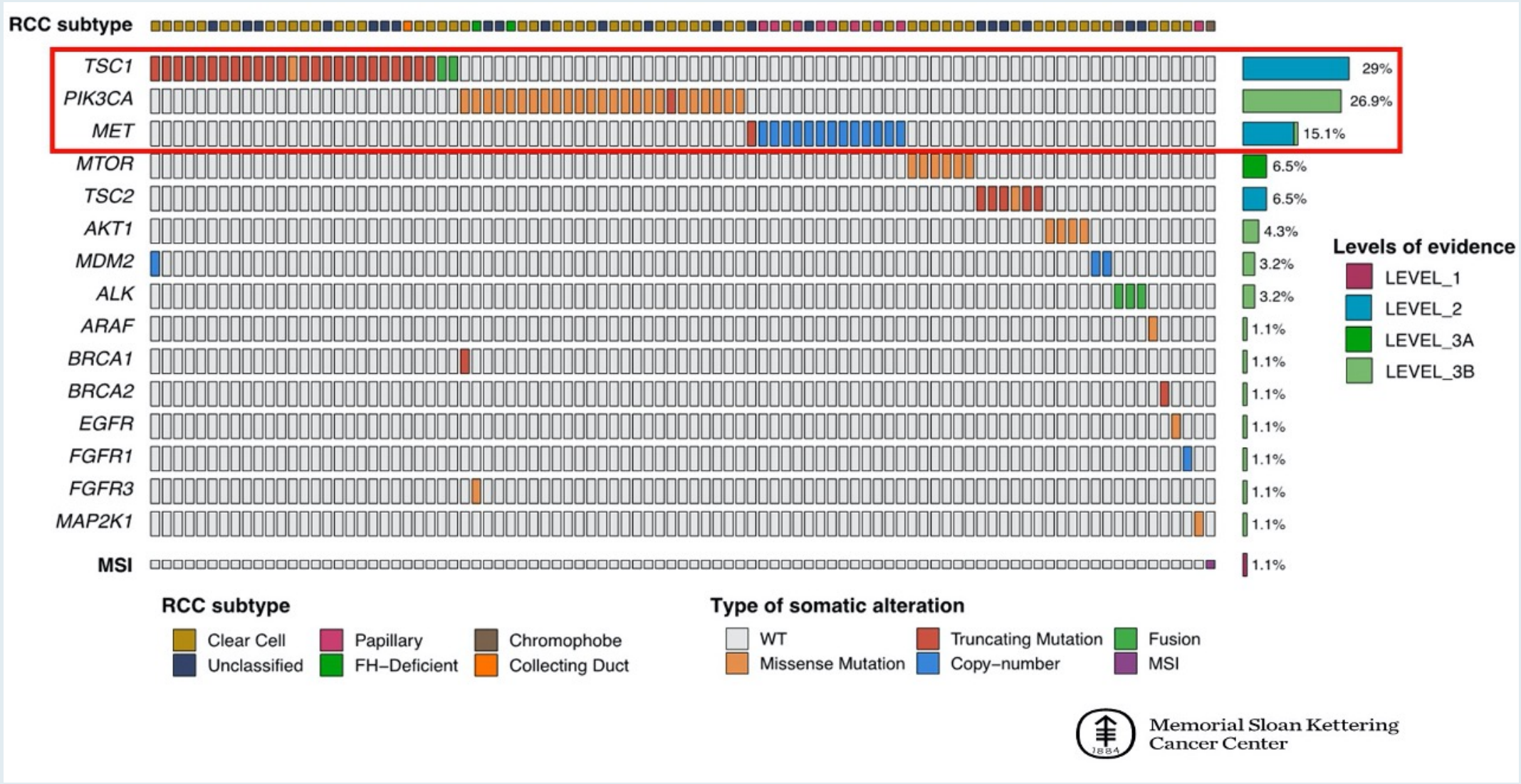
Attala K et al. Genitourinary Cancers Symposium 2020;Abstract 616.

Targetable Alterations in RCC (n = 753)



Attala K et al. Genitourinary Cancers Symposium 2020;Abstract 616.

Targetable Alterations in RCC



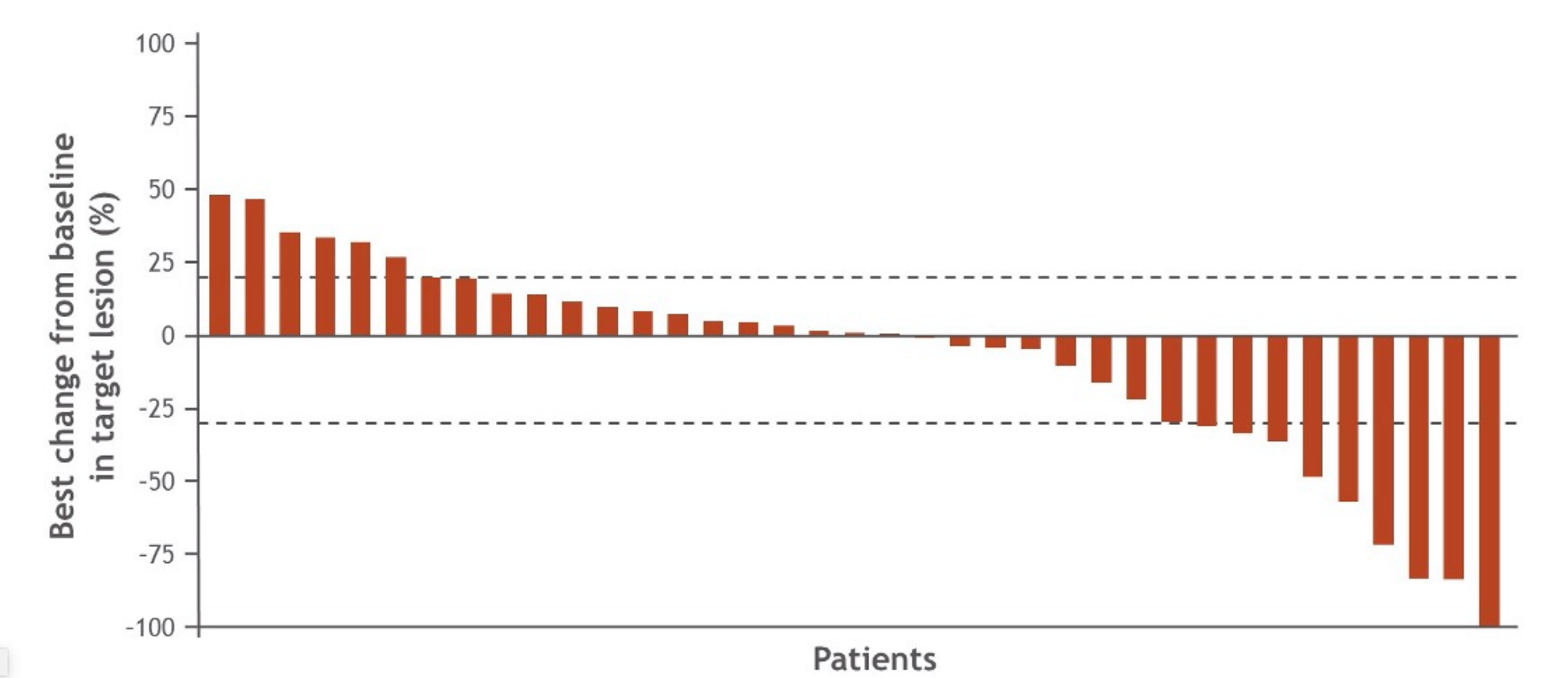
Attala K et al. Genitourinary Cancers Symposium 2020;Abstract 616.

FRACTION-RCC: Innovative, High-Throughput Assessment of Nivolumab + Ipilimumab for Treatment-Refractory Advanced Renal Cell Carcinoma (aRCC)

Choueiri TK et al.

ASCO 2020;Abstract 5007.

FRACTION-RCC: Best Change from Baseline in Target Lesion Tumor Burden



Patients with baseline and at least 1 postbaseline assessment of target lesion are presented. Positive change in tumor burden indicates tumor growth, negative change in tumor burden indicated tumor reduction. Horizontal lines denote 30% decrease and 20% increase.

Choueiri TK et al. ASCO 2020;Abstract 5007.

DNA damage repair pathway alterations in metastatic clear cell renal cell carcinoma and implications on systemic therapy

Yasser Ged,[1] Joshua L Chaim,[2] Renzo G DiNatale,[3] Andrea Knezevic,[4] Ritesh R Kotecha ,[1] Maria I Carlo,[1] Chung-Han Lee,[1] Ashley Foster,[1] Darren R Feldman,[1] Min Yuen Teo,[1] Gopakumar Iyer,[1] Timothy Chan,[5] Sujata Patil,[4] Robert J Motzer ,[1] A Ari Hakimi,[3] Martin H Voss [1]

J Immunother Cancer 2020;8:e000230.

REVIEW

Curr Opin Urol 2019;29(6):636-42.

CURRENT OPINION

The current role for adjuvant and neoadjuvant therapy in renal cell cancer

Jack P. Gleeson, Robert J. Motzer, and Chung-Han Lee

RTP RESEARCH TO PRACTICE

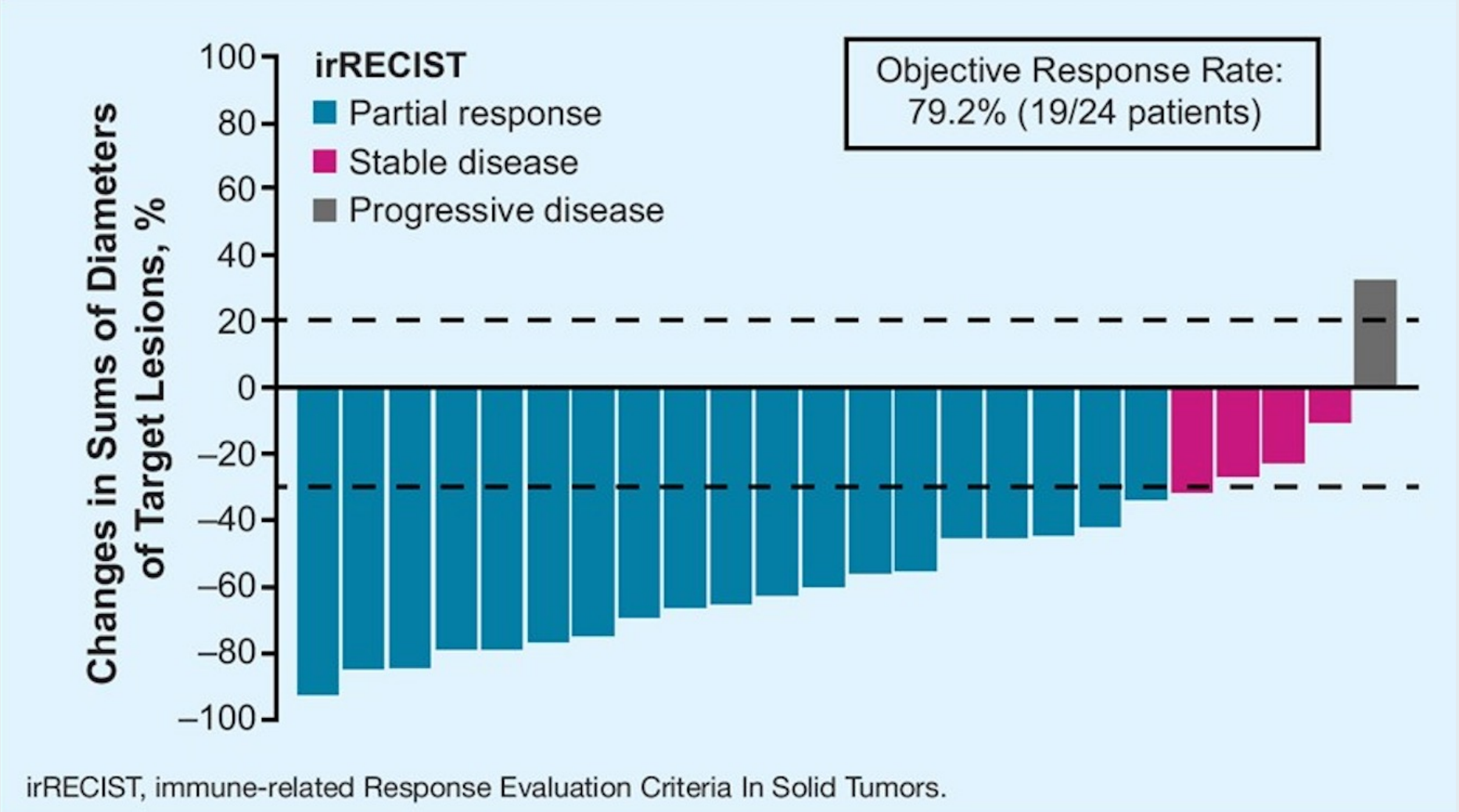
Project ECHO

Genomic Biomarkers of Response to Lenvatinib/Pembrolizumab (Len/Pembro) in Patients with Advanced Renal Cell Carcinoma

Lee C-H et al.

Genitourinary Cancers Symposium 2020;Abstract 733.

KEYNOTE-146/Study 111 RCC Cohort: Percent Change in the Sum of Diameters of Target Lesions at Postbaseline Nadir



irRECIST, immune-related Response Evaluation Criteria In Solid Tumors.

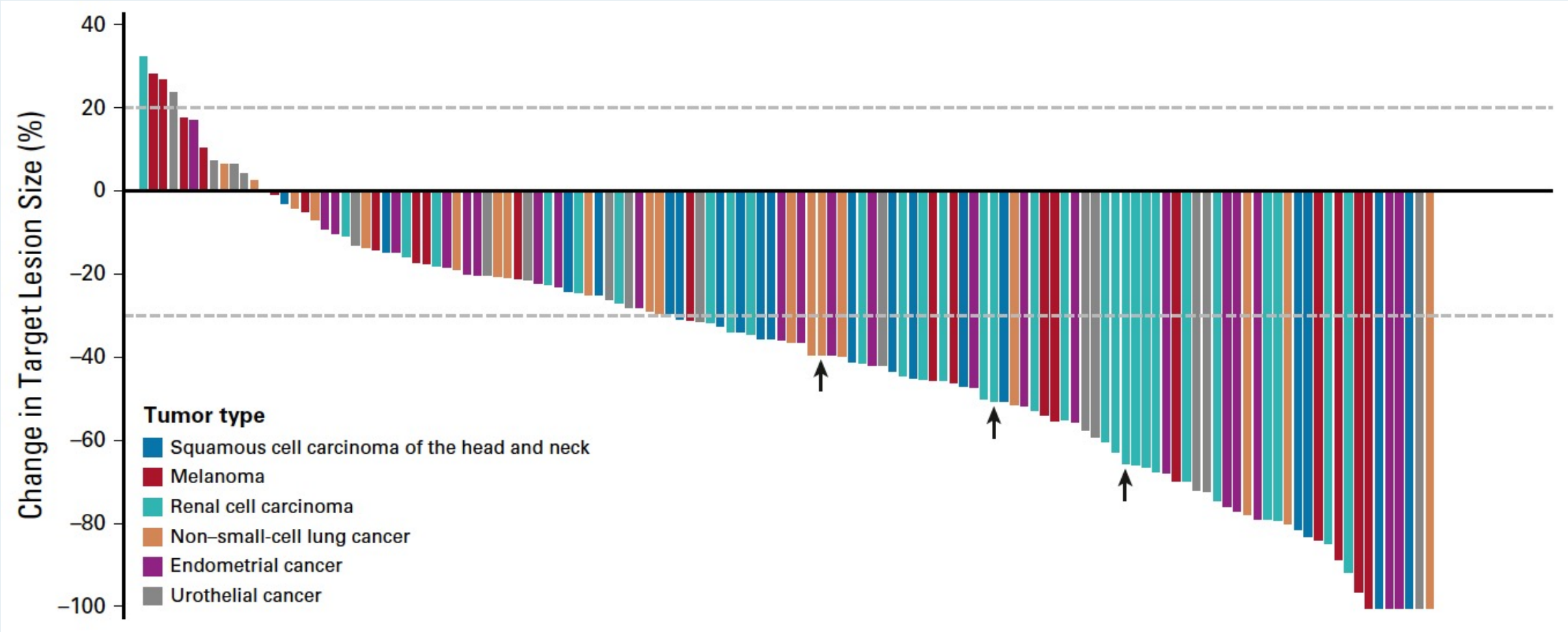
Lee C-H et al. Genitourinary Cancers Symposium 2020;Abstract 733.

J Clin Oncol 2020;38(11):1154-63.

Phase IB/II Trial of Lenvatinib Plus Pembrolizumab in Patients With Advanced Renal Cell Carcinoma, Endometrial Cancer, and Other Selected Advanced Solid Tumors

Matthew H. Taylor, MD[1]; Chung-Han Lee, MD, PhD[2]; Vicky Makker, MD[2]; Drew Rasco, MD[3]; Corina E. Dutcus, MD[4]; Jane Wu, PhD[4]; Daniel E. Stepan, MD[5]; Robert C. Shumaker, PhD[4]; and Robert J. Motzer, MD[2]

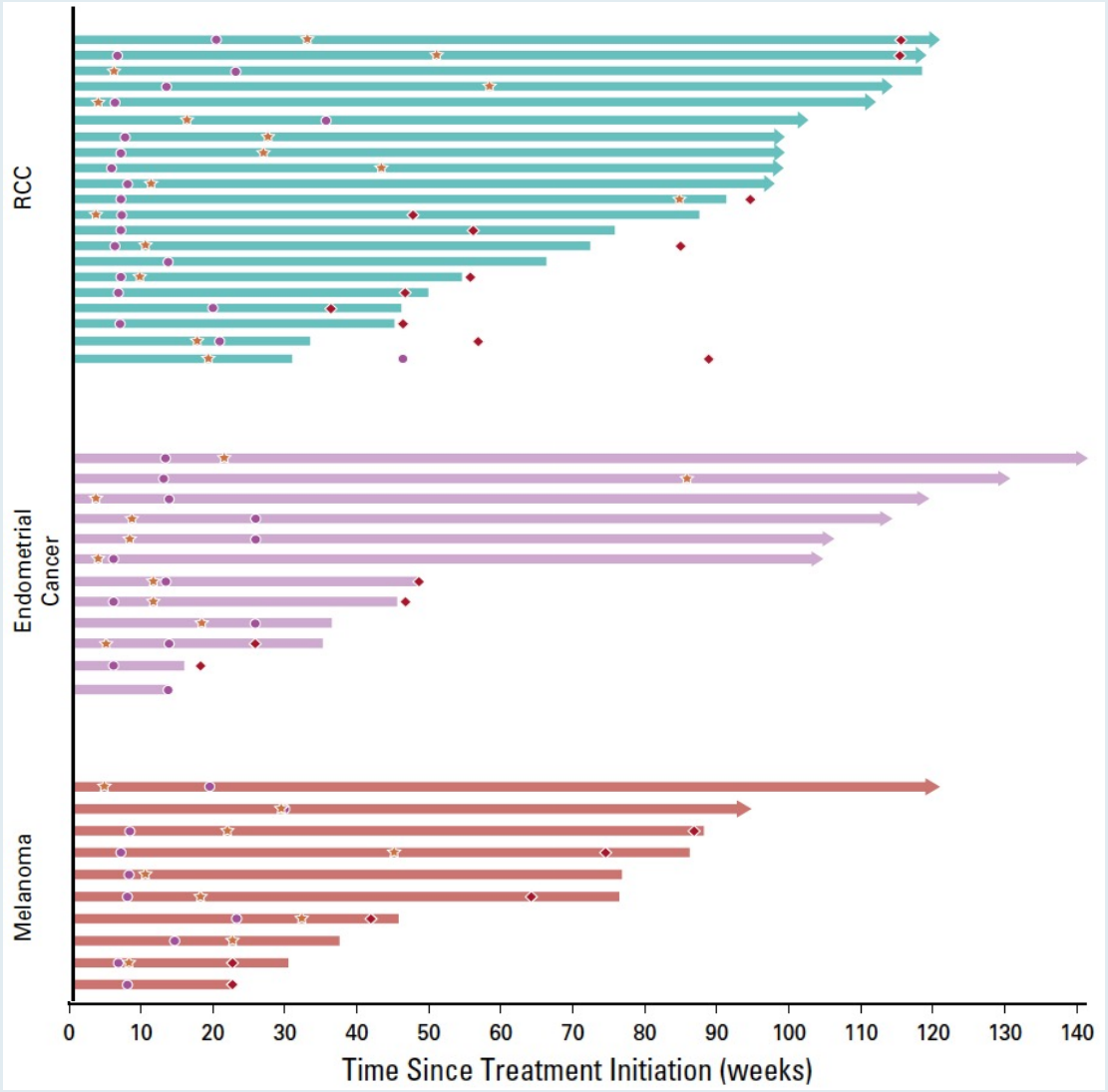
Maximum Change in Target Lesion Size by Tumor Type

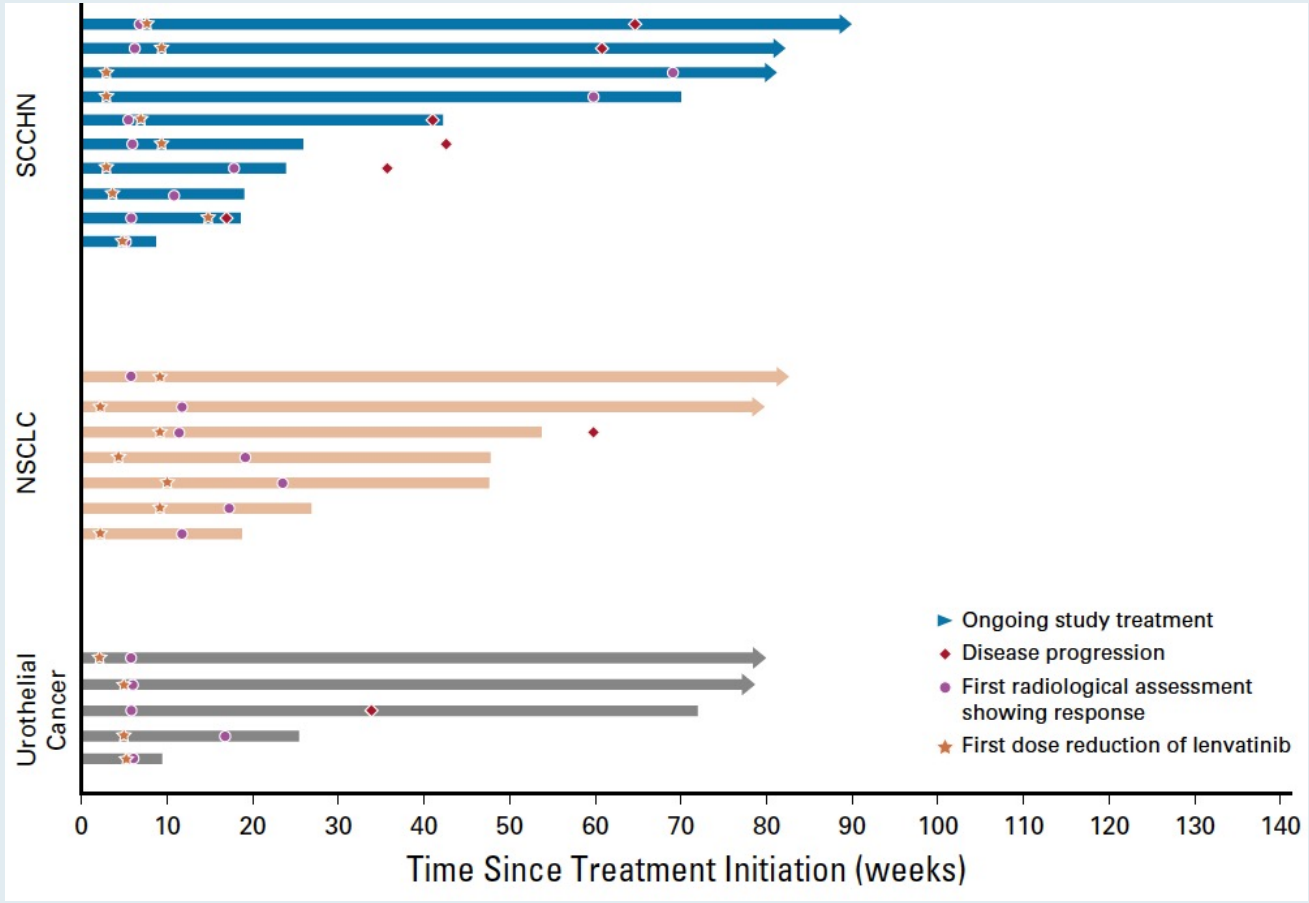


Arrows indicate patients from Phase Ib treated with lenvatinib 24 mg/day

Taylor MH et al. *J Clin Oncol* 2020;38(11):1154-63.

Treatment Response and Duration for Patients Achieving a Partial Response or Complete Response





Taylor MH et al. *J Clin Oncol* 2020;38(11):1154-63.

Clinicogenomic Predictors of Extreme Responses to Anti-PD1/PDL1 Checkpoint Inhibitors (CPI) in Metastatic Urothelial Cancer (mUC)

Teo MY et al.

ASCO 2020;Abstract 5050.

Agenda

MODULE 1: Cases from the Practice of Dr Choksi

MODULE 2: Consensus or Controversy – Clinical Investigator Approaches to Clinical Scenarios

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Lee

- Prevalence and landscape of actionable genomic alterations in renal cell carcinoma (RCC)
- FRACTION-RCC trial: Innovative, high-throughput assessment of nivolumab + ipilimumab for treatment-refractory metastatic RCC
- DNA damage repair pathway alterations in metastatic clear cell RCC and implications for systemic therapy
- Current role for adjuvant and neoadjuvant therapy in RCC
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MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

RTP RESEARCH TO PRACTICE

Project ECHO

Pembrolizumab Demonstrated Superior Disease-Free Survival Compared with Placebo as Adjuvant Therapy for Patients with RCC Following Surgery

Press Release: April 8, 2021

"The pivotal Phase 3 KEYNOTE-564 trial evaluating pembrolizumab met its primary endpoint of disease-free survival (DFS) for the potential adjuvant treatment of patients with RCC following nephrectomy or following nephrectomy and resection of metastatic lesions.

Based on an interim analysis conducted by an independent Data Monitoring Committee, pembrolizumab monotherapy demonstrated a statistically significant and clinically meaningfully improvement in DFS compared with placebo. The trial will continue to evaluate overall survival (OS), a key secondary endpoint.

The safety profile of pembrolizumab in this trial was consistent with that observed in previously reported studies. Results will be presented at an upcoming medical meeting and will be submitted to regulatory authorities."

https://www.merck.com/news/mercks-keytruda-pembrolizumab-demonstrated-superior-disease-free-survival-dfs-compared-with-placebo-as-adjuvant-therapy-in-patients-with-renal-cell-carcinoma-rcc-following-surgery/

Indirect comparison of the 4 regimens available.

	CheckMate 214 (Ipi/Nivo) [1] (n=550 vs n=546)	KEYNOTE-426 (Axi/Pembro)[2] (n=432 vs n=429)	CheckMate 9ER (Cabo/Nivo)[3] (n=323 vs n=328)	CLEAR (Len/Pembro)[4] (N=355 vs n=357)
mOS, months HR (CI);	NR vs 38.4 **0.69** (0.59–0.81);	NR vs 35.7 **0.68** (0.55-0.85);	NR vs NR **0.60** (0.40–0.89);	NR vs NR **0.66** (0.49-0.88)
Landmark OS 12 mo Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%	**90%** vs. 79% **74%** vs. 66%	**87%** vs. 78% (est) **74%** vs 60% (est)	**90%** vs 79% (est.) **79%** vs. 70%
mPFS, months HR (CI)	**12.2** vs 12.3 0.89 (0.76–1.05)	**15.4** vs 11.1 0.71 (0.60–0.84)	**16.6** vs 8.3 0.51 (0.41–0.64)	**23.9** vs 9.2 0.39 (0.32-0.49)
ORR, %	**39** vs 32	**60** vs 40	**56** vs 27	**71** vs 36
CR, %	**11** vs 3	**9** vs 3	**8** vs 5	**16** vs 4
Med f/u, months	**55**	**30.6**	**18.1**	**27**
Prognostic risk, % Favorable Intermediate Poor	 23 61 17	 32 55 13	 23 58 19	 31 59 9
Prior nephrectomy	82%	83%	69%	74%
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)	Overall (69%) IO (48%)	Overall (40%) IO (29%)	NR

Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

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Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

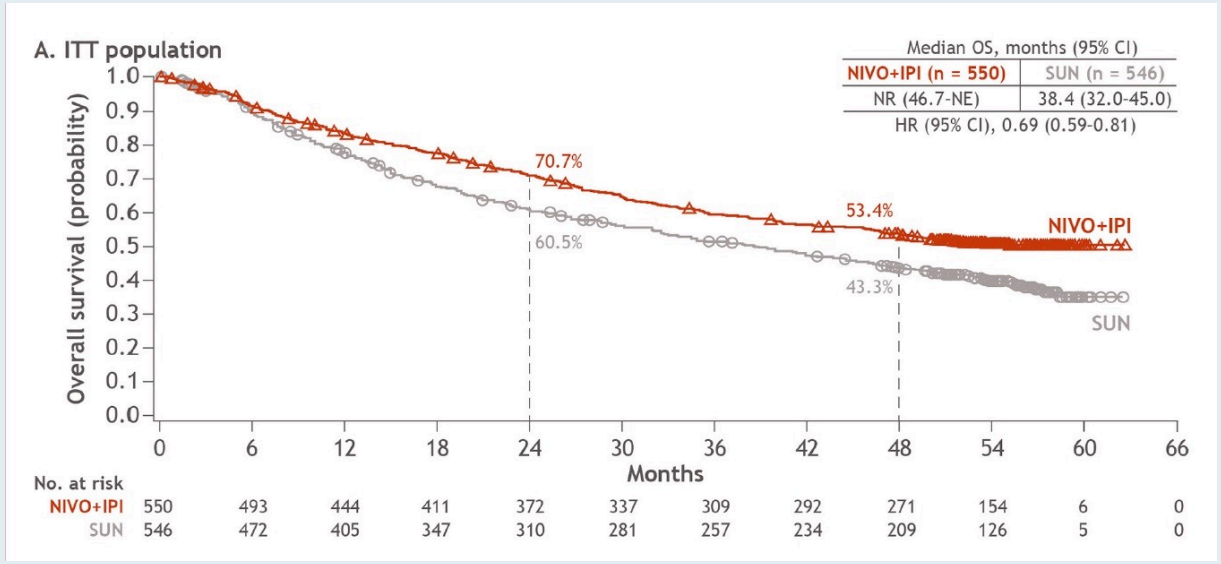
Open access Original research

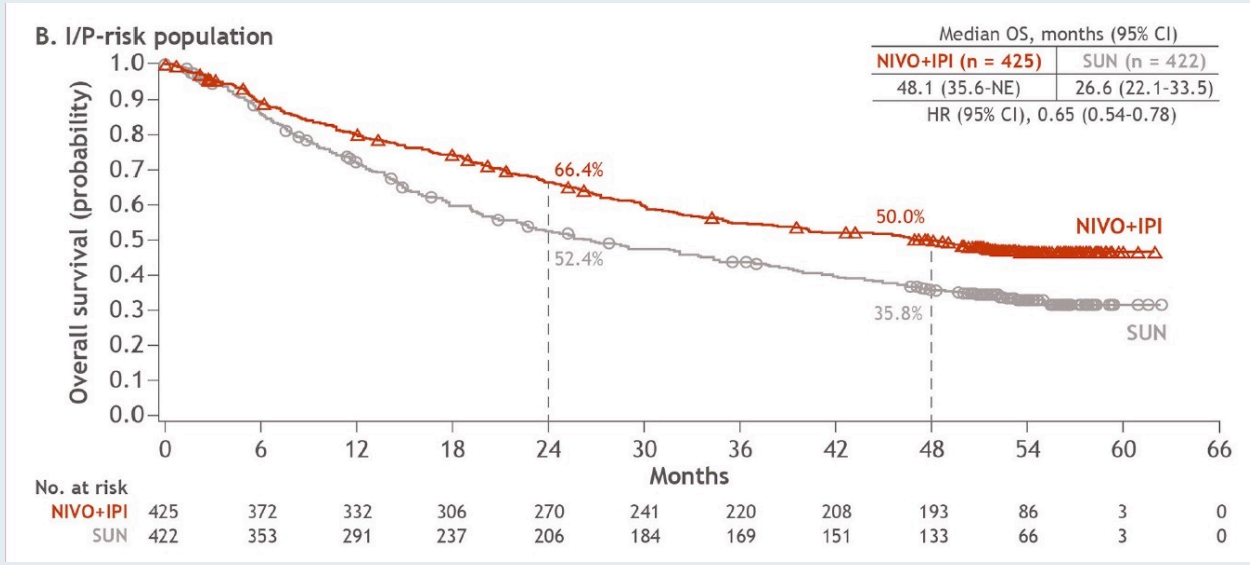
Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial

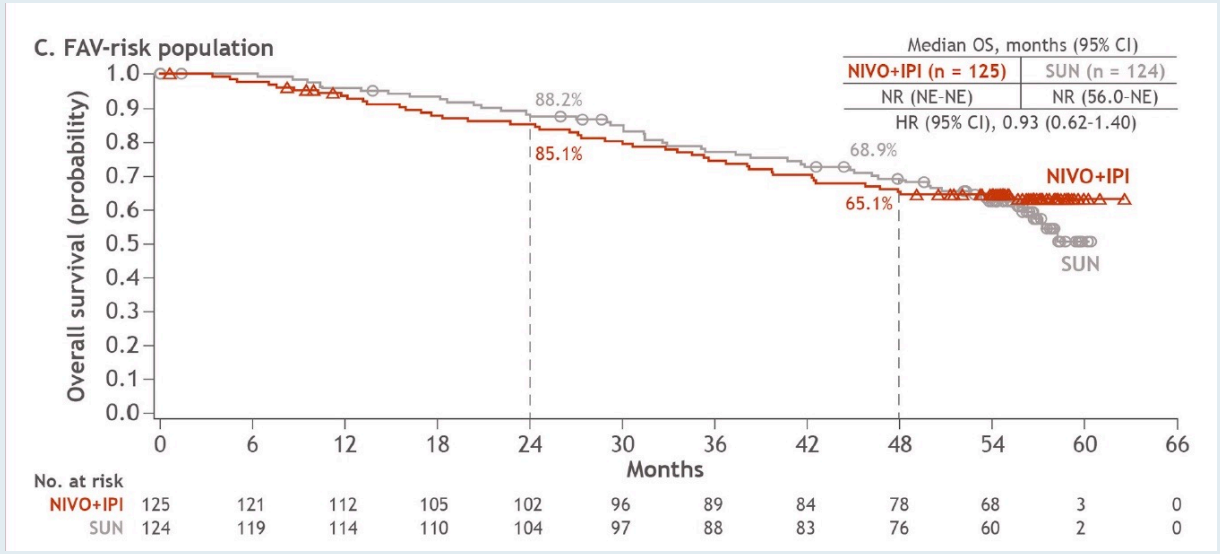
Laurence Albiges ,[1] Nizar M Tannir,[2] Mauricio Burotto,[3] David McDermott,[4,5] Elizabeth R Plimack,[6] Philippe Barthélémy,[7,8] Camillo Porta ,[9] Thomas Powles,[10,11] Frede Donskov,[12] Saby George,[13] Christian K Kollmannsberger,[14] Howard Gurney,[15,16] Marc-Oliver Grimm,[17] Yoshihiko Tomita,[18] Daniel Castellano,[19] Brian I Rini,[20] Toni K Choueiri,[21] Shruti Shally Saggi,[22] M Brent McHenry,[23] Robert J Motzer[24]

ESMO Open 2020;5(6):e001079

CheckMate 214: OS in ITT, Intermediate/Poor-Risk and Favorable-Risk Populations

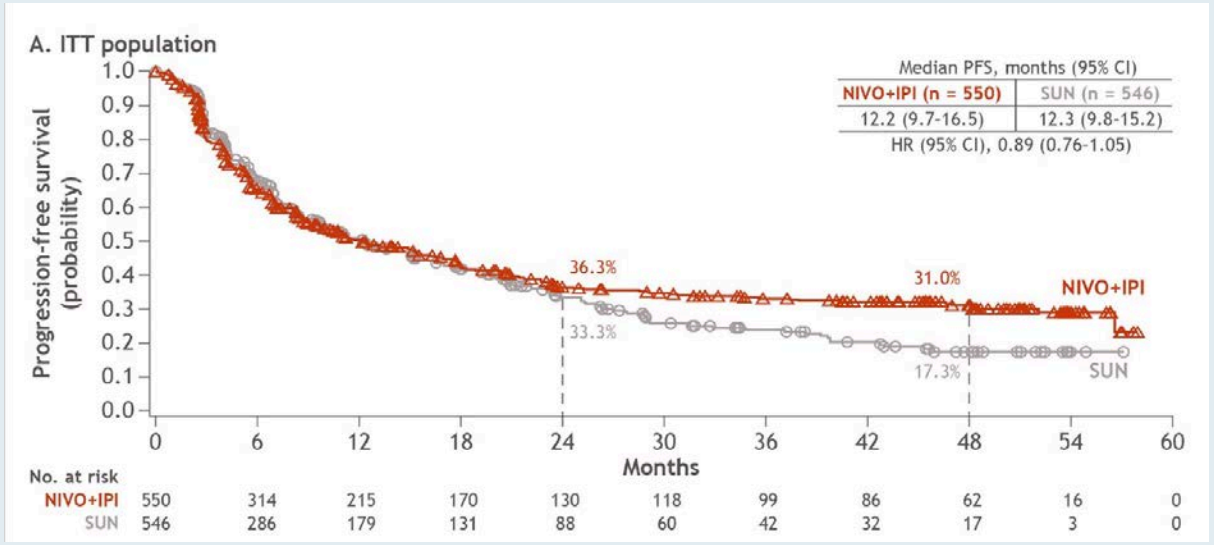


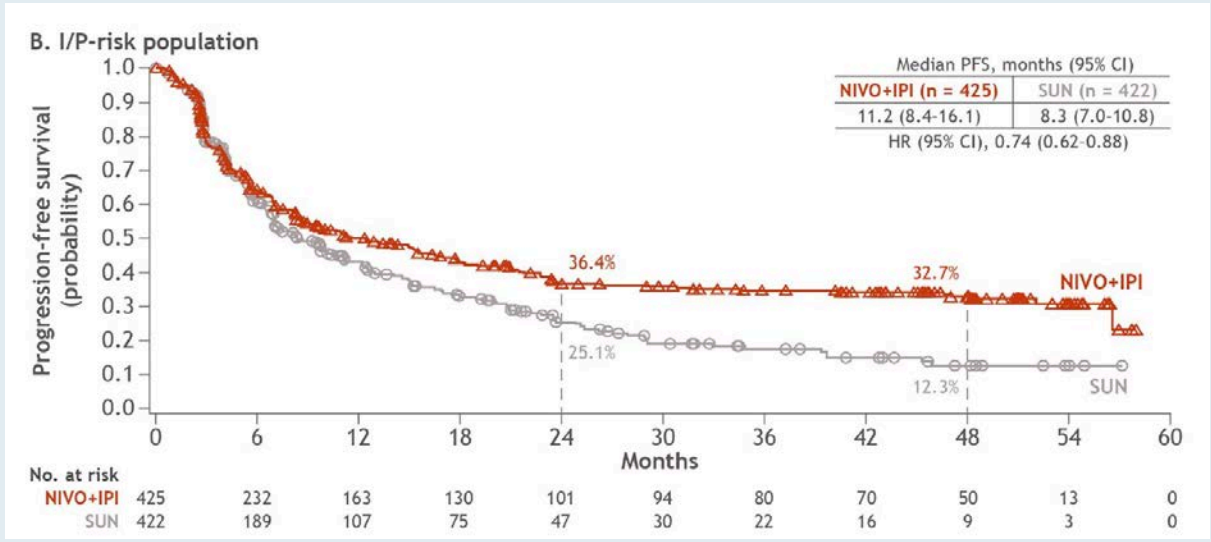


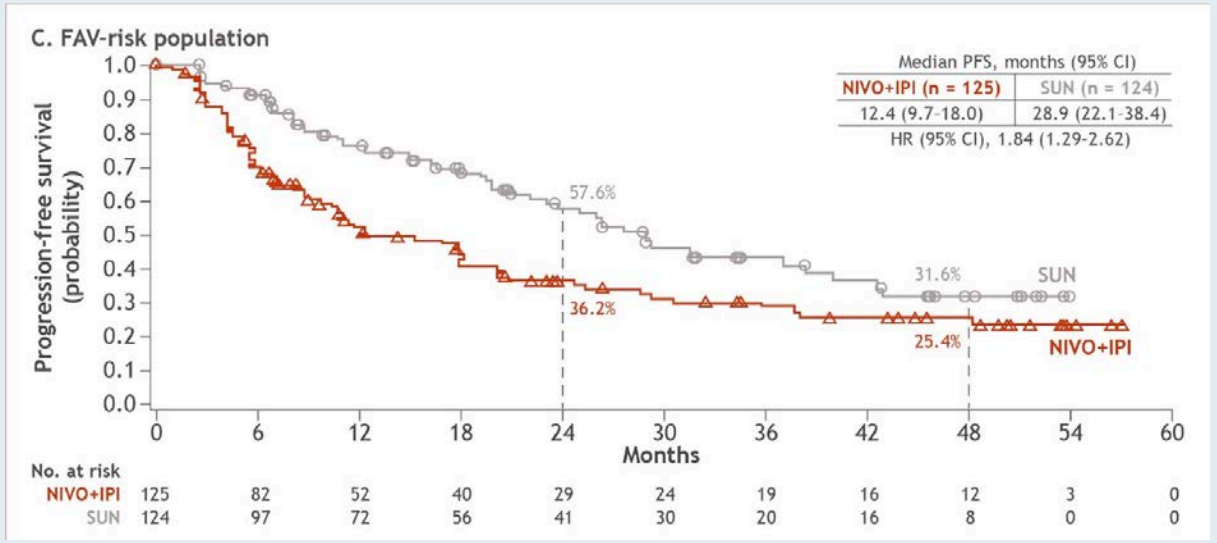


Albiges L et al. *ESMO Open* 2020;5(6):e001079.

CheckMate 214: PFS in ITT, Intermediate/Poor-Risk and Favorable-Risk Populations







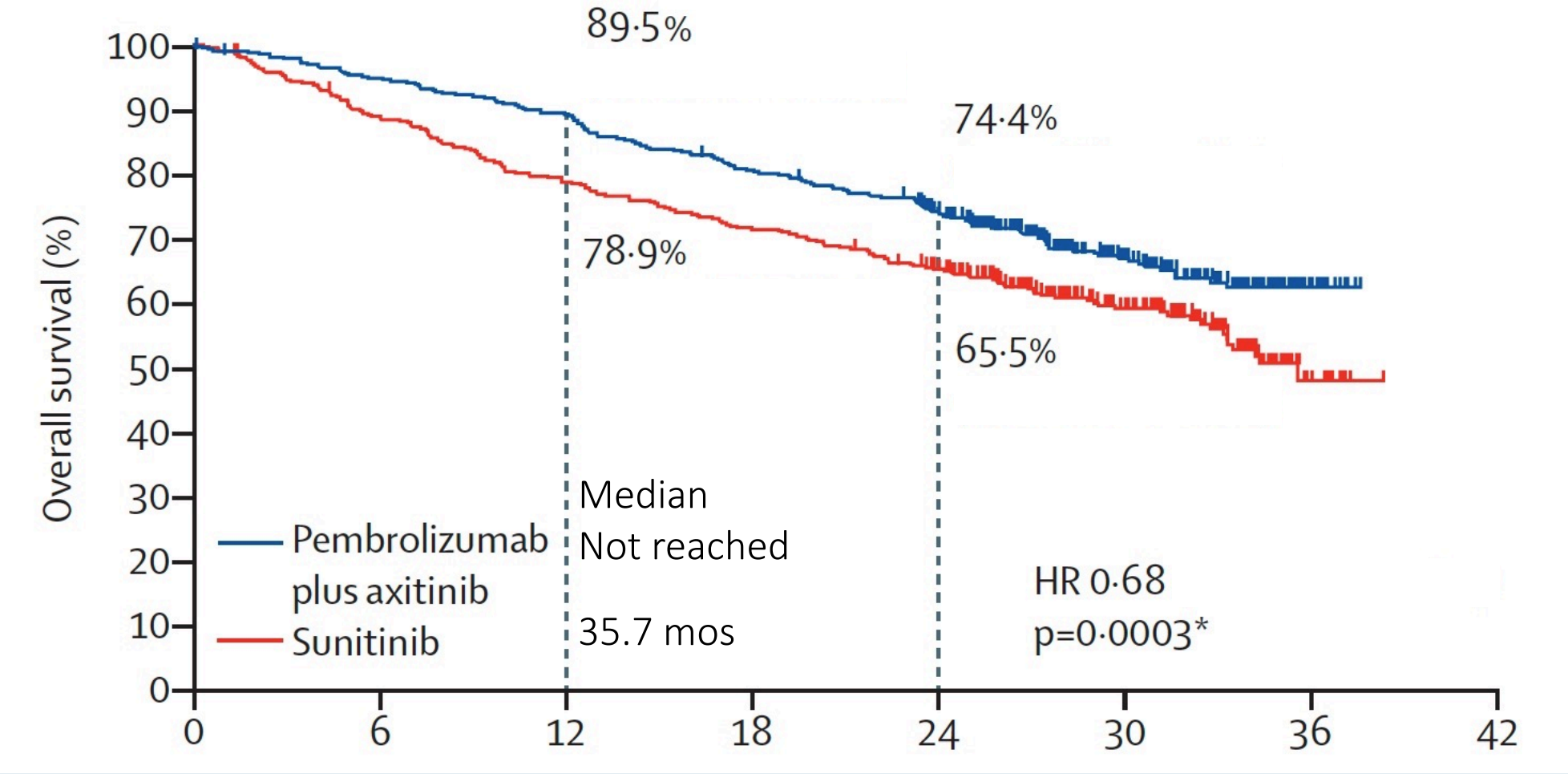
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

Lancet Oncol 2020;21:1563-73

Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial

Thomas Powles, Elizabeth R Plimack, Denis Soulières, Tom Waddell, Viktor Stus, Rustem Gafanov, Dmitry Nosov, Frédéric Pouliot, Bohuslav Melichar, Ihor Vynnychenko, Sergio J Azevedo, Delphine Borchiellini, Raymond S McDermott, Jens Bedke, Satoshi Tamada, Lina Yin, Mei Chen, L Rhoda Molife, Michael B Atkins, Brian I Rini

KEYNOTE-426: Overall Survival with Extended Follow-Up



Powles T et al. *Lancet Oncol* 2020;21:1563-73.

N Engl J Med 2021;384(9):829-41

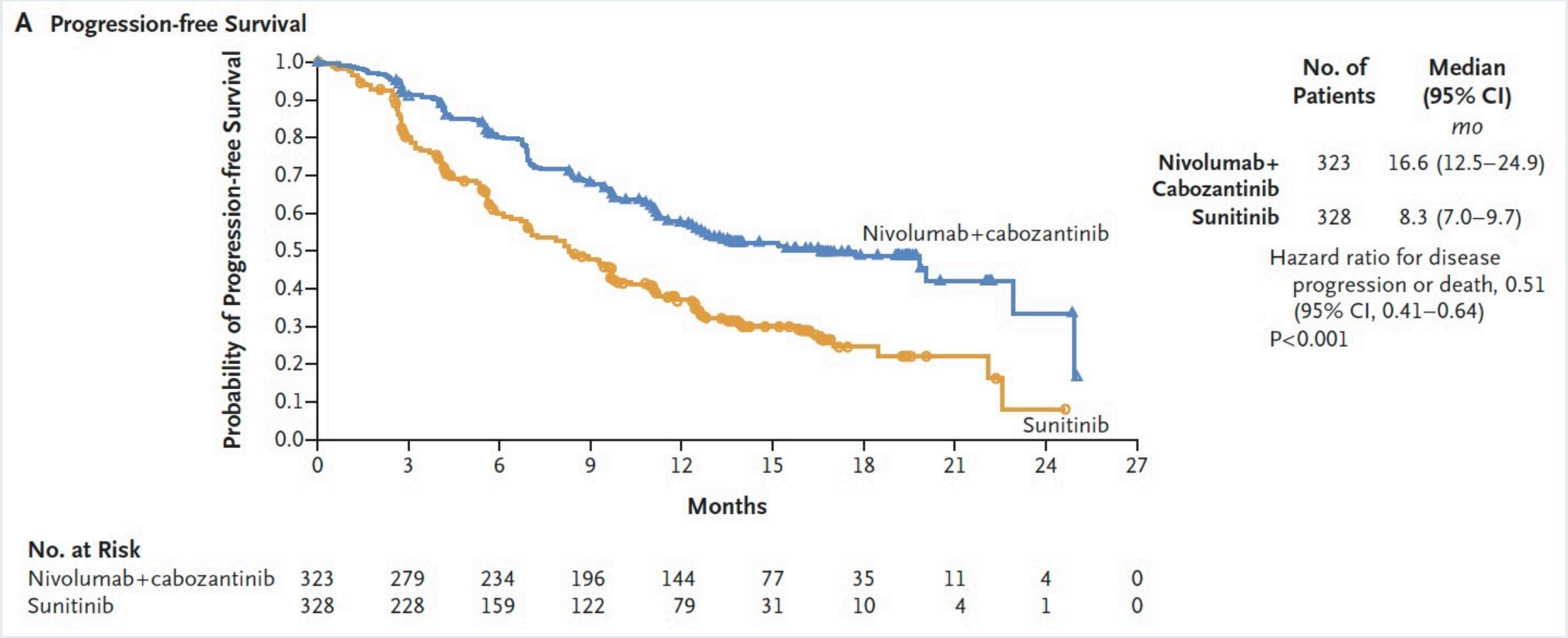
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

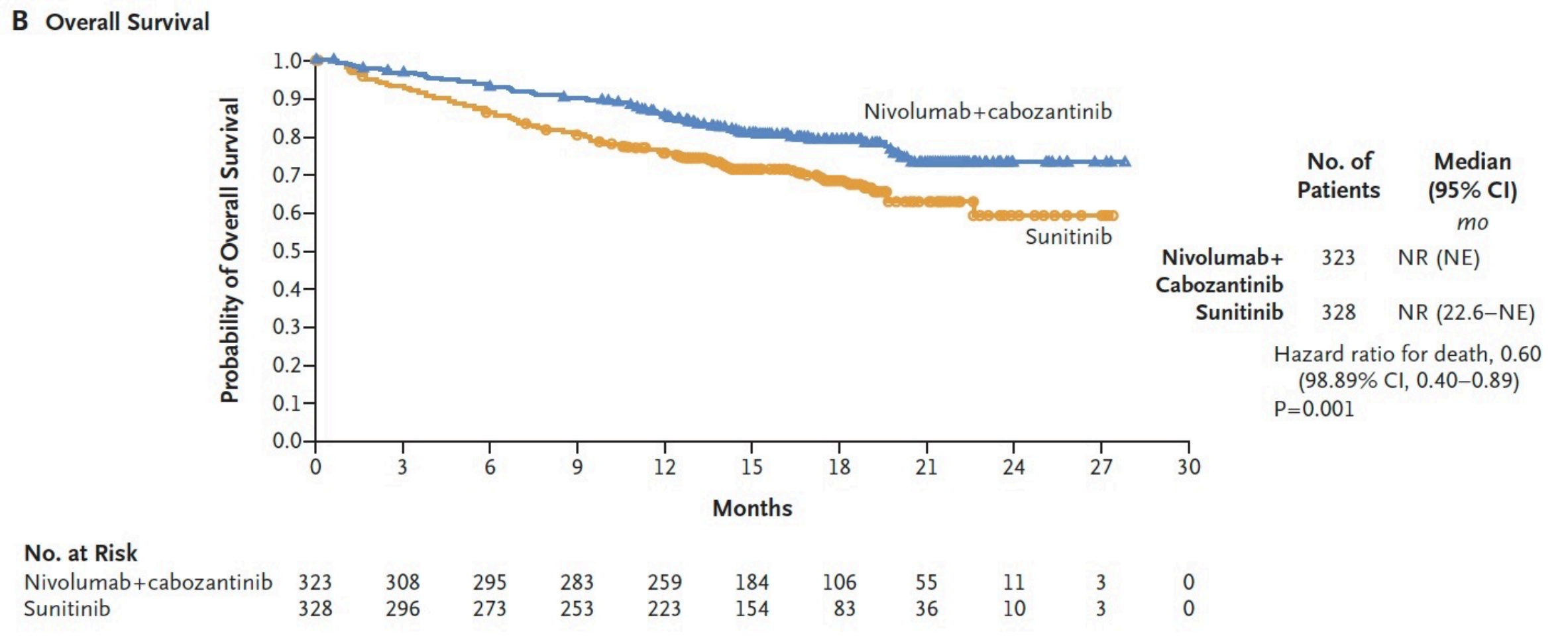
T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bourlon, B. Zurawski, V.M. Oyervides Juárez, J.J. Hsieh, U. Basso, A.Y. Shah, C. Suárez, A. Hamzaj, J.C. Goh, C. Barrios, M. Richardet, C. Porta, R. Kowalyszyn, J.P. Feregrino, J. Żołnierek, D. Pook, E.R. Kessler, Y. Tomita, R. Mizuno, J. Bedke, J. Zhang, M.A. Maurer, B. Simsek, F. Ejzykowicz, G.M. Schwab, A.B. Apolo, and R.J. Motzer, for the CheckMate 9ER Investigators*

Progression-Free Survival in the Intention-to-Treat Population



Choueiri TK et al. *N Engl J Med* 2021;384(9):829-41.

Overall Survival in the Intention-to-Treat Population



	No. of Patients	Median (95% CI) *mo*
Nivolumab+ Cabozantinib	323	NR (NE)
Sunitinib	328	NR (22.6–NE)

Hazard ratio for death, 0.60 (98.89% CI, 0.40–0.89)
P=0.001

Choueiri TK et al. *N Engl J Med* 2021;384(9):829-41.

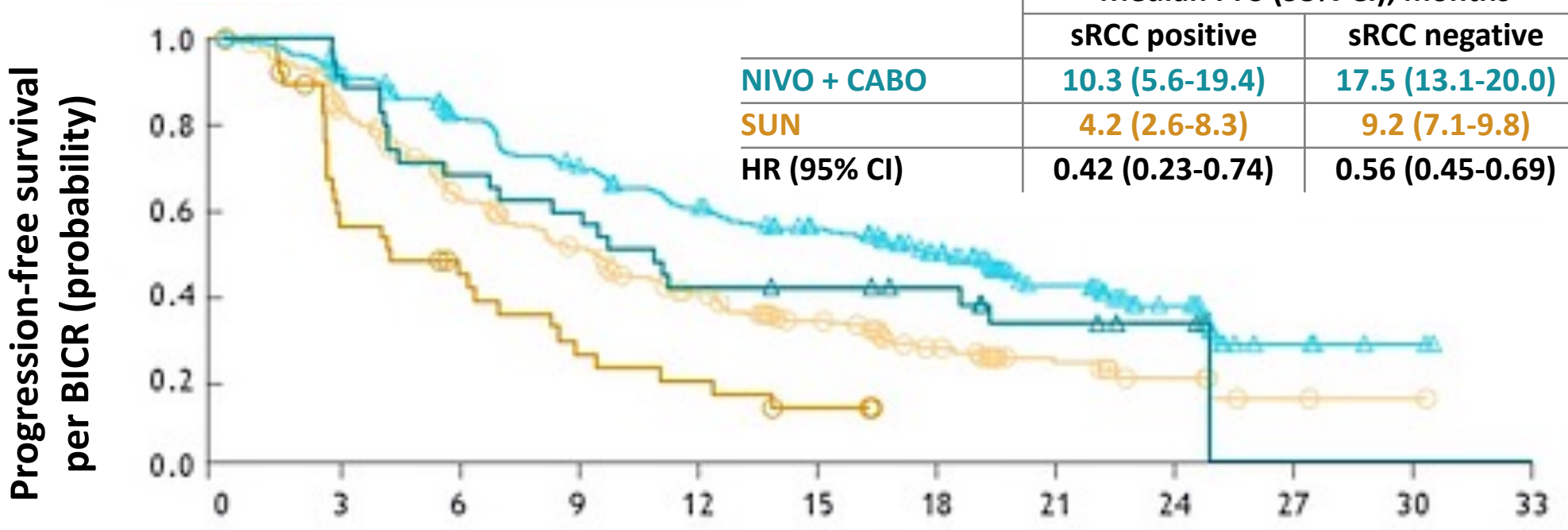
Nivolumab + Cabozantinib (NIVO + CABO) versus Sunitinib (SUN) for Advanced Renal Cell Carcinoma (aRCC): Outcomes by Sarcomatoid Histology and Updated Trial Results with Extended Follow-Up of CheckMate 9ER

Motzer RJ et al.

Genitourinary Cancers Symposium 2021;Abstract 308.

Progression-Free Survival per BICR by Sarcomatoid Histology

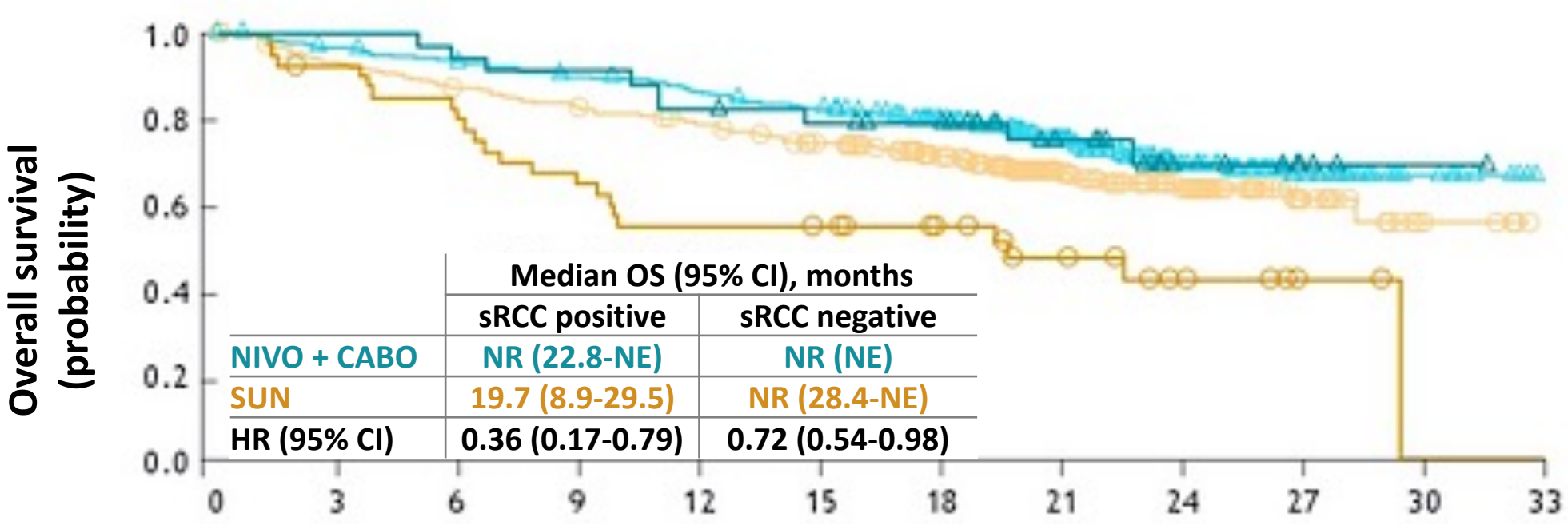
	Median PFS (95% CI), months	
	sRCC positive	sRCC negative
NIVO + CABO	10.3 (5.6-19.4)	17.5 (13.1-20.0)
SUN	4.2 (2.6-8.3)	9.2 (7.1-9.8)
HR (95% CI)	0.42 (0.23-0.74)	0.56 (0.45-0.69)



No. at risk												
NIVO + CABO sRCC positive	34	31	23	20	14	13	11	7	4	0	0	0
SUN sRCC positive	41	20	14	8	6	2	0	0	0	0	0	0
NIVO + CABO sRCC negative	289	249	213	181	152	132	91	49	22	5	2	0
SUN sRCC negative	287	210	146	114	81	59	37	17	7	2	1	0

Motzer RJ et al. Genitourinary Cancers Symposium 2021;Abstract 308.

Overall Survival by Sarcomatoid Histology



	Median OS (95% CI), months	
	sRCC positive	sRCC negative
NIVO + CABO	NR (22.8-NE)	NR (NE)
SUN	19.7 (8.9-29.5)	NR (28.4-NE)
HR (95% CI)	0.36 (0.17-0.79)	0.72 (0.54-0.98)

No. at risk												
NIVO + CABO sRCC positive	34	34	32	31	28	26	24	16	7	3	1	0
SUN sRCC positive	41	37	32	26	22	21	17	12	6	2	0	0
NIVO + CABO sRCC negative	289	274	263	252	241	229	196	131	77	37	9	0
SUN sRCC negative	287	258	240	228	214	196	172	106	56	20	4	0

Motzer RJ et al. Genitourinary Cancers Symposium 2021;Abstract 308.

N Engl J Med 2021;[Online ahead of print].

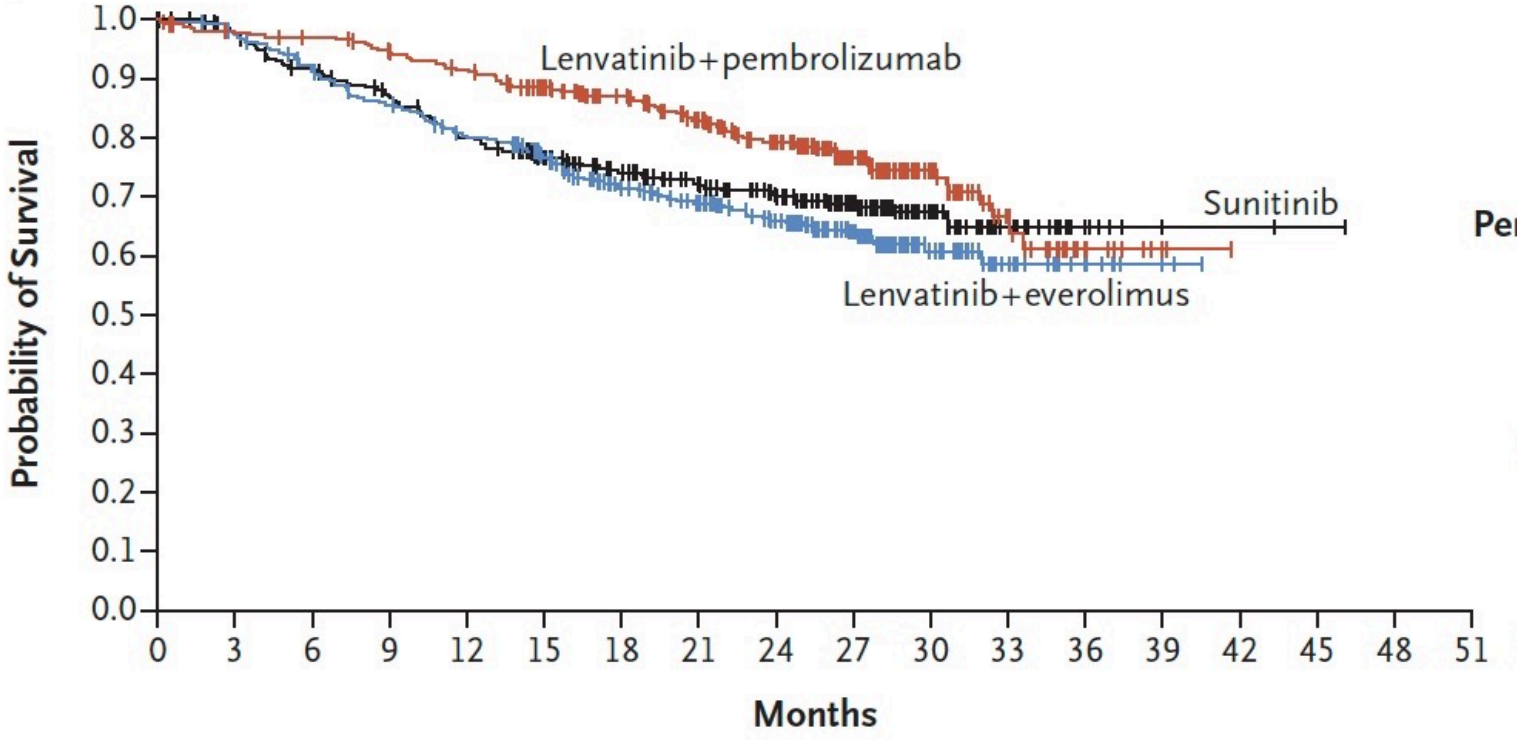
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma

R. Motzer, B. Alekseev, S.-Y. Rha, C. Porta, M. Eto, T. Powles, V. Grünwald, T.E. Hutson, E. Kopyltsov, M.J. Méndez-Vidal, V. Kozlov, A. Alyasova, S.-H. Hong, A. Kapoor, T. Alonso Gordoa, J.R. Merchan, E. Winquist, P. Maroto, J.C. Goh, M. Kim, H. Gurney, V. Patel, A. Peer, G. Procopio, T. Takagi, B. Melichar, F. Rolland, U. De Giorgi, S. Wong, J. Bedke, M. Schmidinger, C.E. Dutcus, A.D. Smith, L. Dutta, K. Mody, R.F. Perini, D. Xing, and T.K. Choueiri, for the CLEAR Trial Investigators*

Kaplan-Meier Analysis of Overall Survival



	Median Overall Survival (95% CI)
	mo
Lenvatinib+ Pembrolizumab	NR (33.6–NE)
Lenvatinib+ Everolimus	NR (NE–NE)
Sunitinib	NR (NE–NE)

Hazard ratio for death (lenvatinib+ pembrolizumab vs. sunitinib), 0.66 (95% CI, 0.49–0.88); P=0.005

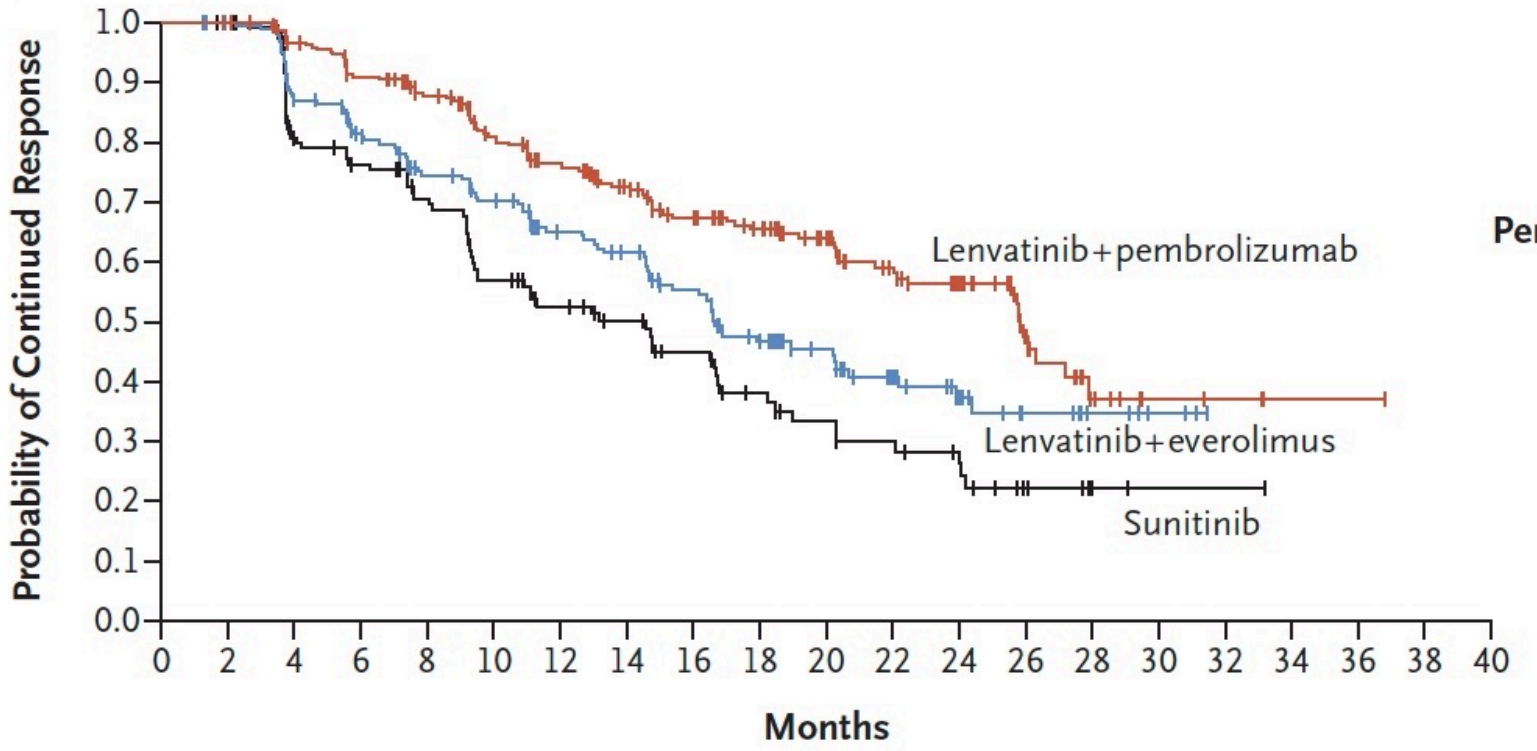
Hazard ratio for death (lenvatinib+ everolimus vs. sunitinib), 1.15 (95% CI, 0.88–1.50); P=0.30

No. at Risk

Lenvatinib+pembrolizumab	355	342	338	327	313	280	253	222	188	129	66	26	10	2	0		
Lenvatinib+everolimus	357	346	321	299	277	246	205	183	154	109	46	22	8	2	0		
Sunitinib	357	332	307	289	264	236	207	186	160	112	60	25	7	2	2	1	0

Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

Kaplan-Meier Analysis of Response Duration



Median Duration of Response (95% CI)	*mo*
Lenvatinib+ Pembrolizumab	25.8 (22.1–27.9)
Lenvatinib+ Everolimus	16.6 (14.6–20.6)
Sunitinib	14.6 (9.4–16.7)

No. at Risk

Lenvatinib+pembrolizumab	252	250	234	215	197	172	153	131	112	101	83	63	45	23	9	4	3	1	1	0
Lenvatinib+everolimus	191	186	159	142	125	113	93	83	65	50	39	27	18	11	6	3	0			
Sunitinib	129	125	91	82	73	57	47	40	33	25	20	17	13	7	2	1	1	0		

Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

Confirmed Tumor Responses

Measure	Lenvatinib plus Pembrolizumab (N = 355)	Lenvatinib plus Everolimus (N = 357)	Sunitinib (N = 357)
Objective response (95% CI) — %†	71.0 (66.3–75.7)	53.5 (48.3–58.7)	36.1 (31.2–41.1)
Relative risk vs. sunitinib (95% CI)	1.97 (1.69–2.29)	1.48 (1.26–1.74)	Reference
Best overall response — no. (%)			
Complete response	57 (16.1)	35 (9.8)	15 (4.2)
Partial response	195 (54.9)	156 (43.7)	114 (31.9)
Stable disease	68 (19.2)	120 (33.6)	136 (38.1)
Progressive disease	19 (5.4)	26 (7.3)	50 (14.0)
Unknown or could not be evaluated‡	16 (4.5)	20 (5.6)	42 (11.8)
Median time to response (range) — mo	1.94 (1.41–18.50)	1.91 (1.41–14.36)	1.94 (1.61–16.62)
Median duration of response (95% CI) — mo	25.8 (22.1–27.9)	16.6 (14.6–20.6)	14.6 (9.4–16.7)

Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

Selected Adverse Events of Any Cause That Emerged or Worsened During Treatment in at Least 25% of the Patients in Any Treatment Group

Event	Lenvatinib plus Pembrolizumab (N=352)		Lenvatinib plus Everolimus (N=355)		Sunitinib (N=340)	
	Any Grade	Grade ≥3†	Any Grade	Grade ≥3†	Any Grade	Grade ≥3†
	number of patients (percent)					
Any event	351 (99.7)	290 (82.4)	354 (99.7)	295 (83.1)	335 (98.5)	244 (71.8)
Diarrhea	216 (61.4)	34 (9.7)	236 (66.5)	41 (11.5)	168 (49.4)	18 (5.3)
Hypertension	195 (55.4)	97 (27.6)	162 (45.6)	80 (22.5)	141 (41.5)	64 (18.8)
Hypothyroidism‡	166 (47.2)	5 (1.4)	95 (26.8)	2 (0.6)	90 (26.5)	0
Decreased appetite	142 (40.3)	14 (4.0)	144 (40.6)	22 (6.2)	105 (30.9)	5 (1.5)
Fatigue	141 (40.1)	15 (4.3)	149 (42.0)	27 (7.6)	125 (36.8)	15 (4.4)

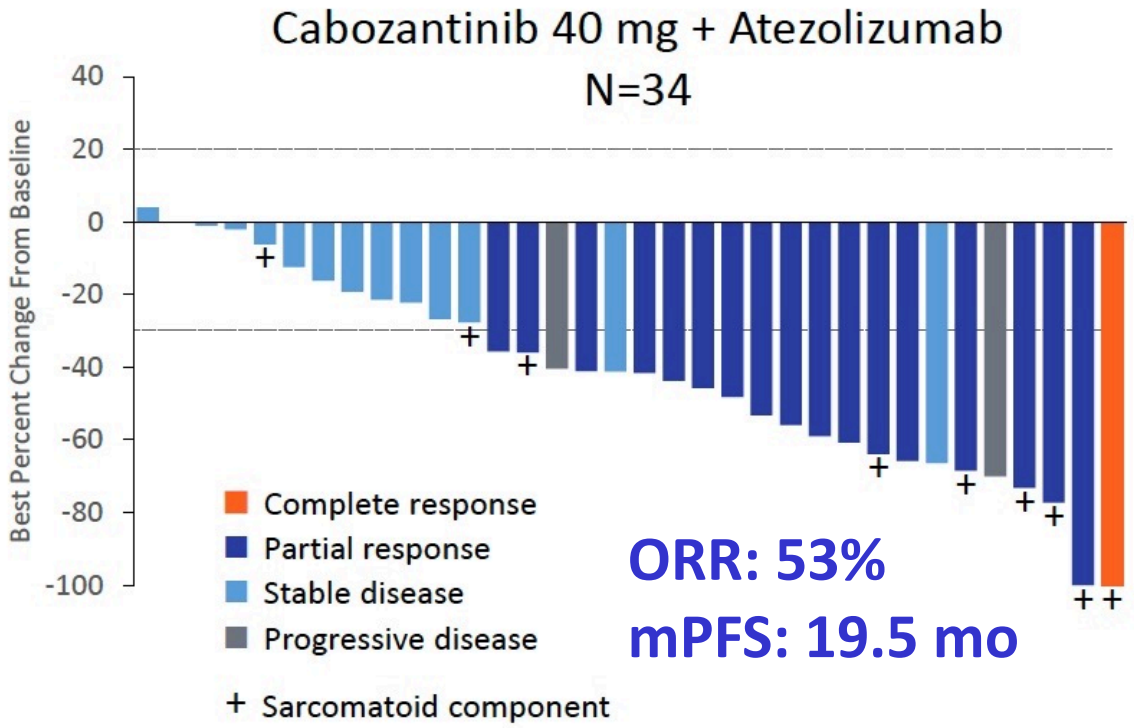
Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

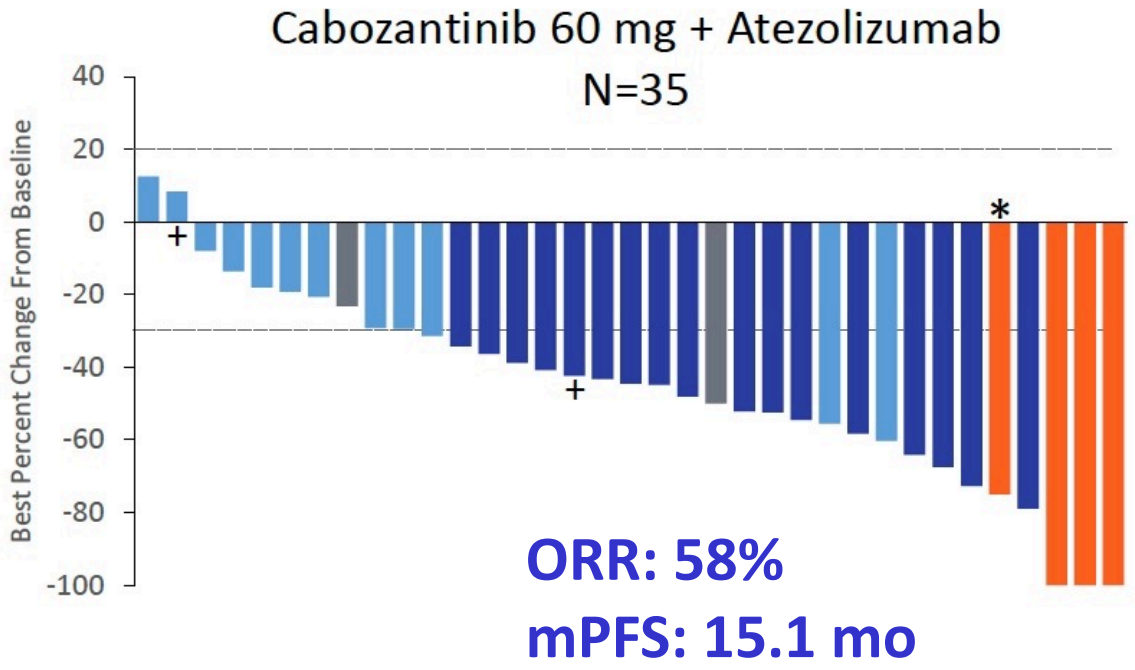
Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

Pal S et al.

ESMO 2020;Abstract 702O.

COSMIC-021: Cabozantinib/Atezolizumab for Previously Untreated Advanced ccRCC





Pal S et al. ESMO 2020;Abstract 702O.

Select, Ongoing Phase III Clinical Trials for Previously Untreated Metastatic Renal Cell Carcinoma

Study acronym	Target accrual	Randomization	Primary endpoint(s)	Estimated primary completion
COSMIC-313	840	• Cabozantinib + nivolumab + ipilimumab (4 doses) → cabozantinib + nivolumab • Placebo + nivolumab + ipilimumab (4 doses) → placebo + nivolumab	PFS	Nov 2021
PDIGREE	1,046	After Induction nivolumab/ipilimumab • Pts with CR → Nivolumab • Pts with non-CR or non-PD, *randomized* → Nivolumab → Nivolumab + Cabozantinib • Pts with PD → Cabozantinib	OS	Sept 2021

FDA Approves Tivozanib for Relapsed or Refractory Advanced RCC

Press Release: March 10, 2021

"On March 10, 2021, the Food and Drug Administration approved tivozanib, a kinase inhibitor, for adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

Efficacy was evaluated in TIVO-3 (NCT02627963), a randomized (1:1), open-label, multicenter trial of tivozanib versus sorafenib in patients with relapsed or refractory advanced RCC who received two or three prior systemic treatments, including at least one VEGFR kinase inhibitor other than sorafenib or tivozanib.

The recommended tivozanib dose is 1.34 mg once daily (with or without food) for 21 consecutive days every 28 days until disease progression or unacceptable toxicity."

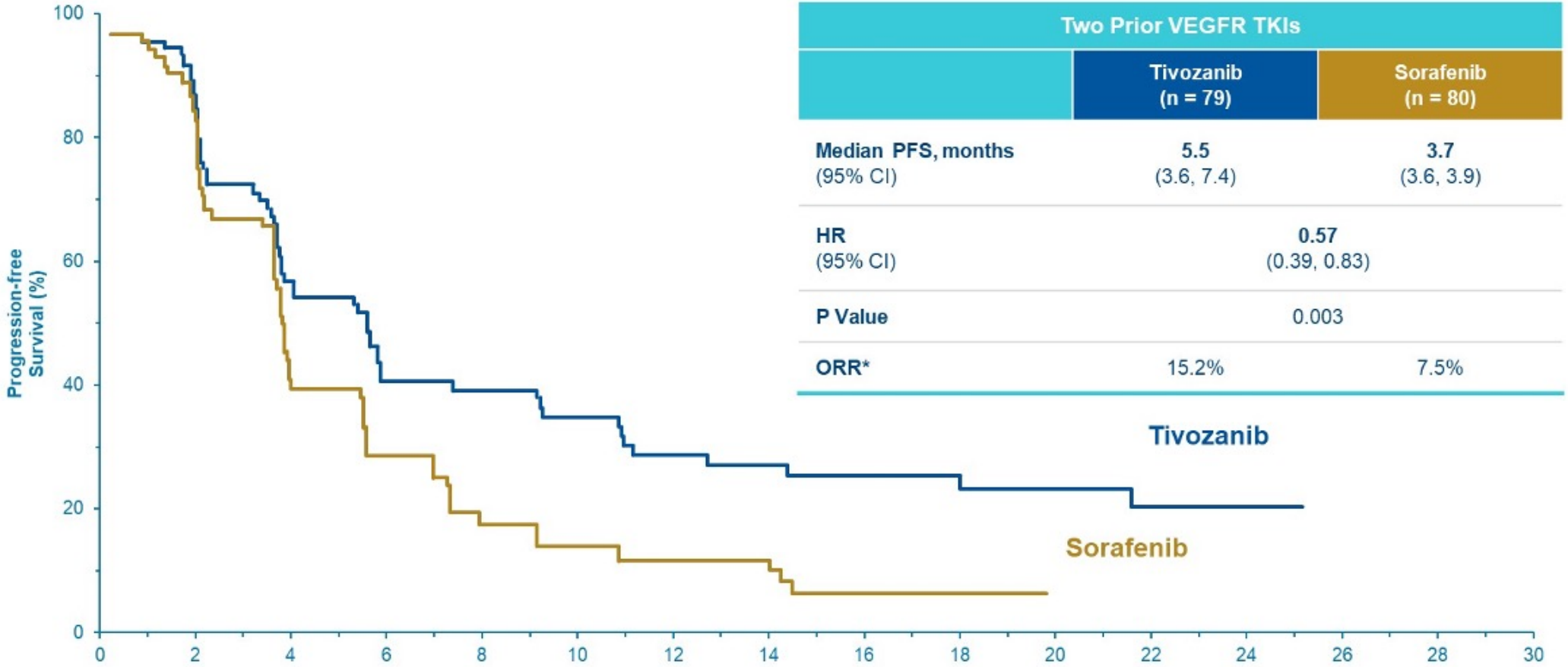
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

Tivozanib in Patients with Advanced Renal Cell Carcinoma (aRCC) Who Have Progressed After Prior Treatment of Axitinib: Results from TIVO-3

Rini BI et al.

Genitourinary Cancers Symposium 2021;Abstract 278.

TIVO-3: Progression-Free Survival and ORR in Patient Subgroup with 2 Prior TKIs



Two Prior VEGFR TKIs		
	Tivozanib (n = 79)	Sorafenib (n = 80)
Median PFS, months (95% CI)	5.5 (3.6, 7.4)	3.7 (3.6, 3.9)
HR (95% CI)	0.57 (0.39, 0.83)	
P Value	0.003	
ORR*	15.2%	7.5%

Rini BI et al. Genitourinary Cancers Symposium 2021;Abstract 278.

TIVO-3: Tivozanib After Axitinib

RCC Population	N (subjects)		mPFS (months)		HR	ORR	
	Tivo	Sor	Tivo	Sor		Tivo	Sor
ITT	175	175	5.6	3.9	0.73	18%	8%
3rd Line Any Prior Axitinib	47	46	5.5	3.9	0.71	16%	6%
4th Line Any Prior Axitinib	36	43	5.5	3.6	0.64	11%	10%
3rd and 4th Line Any Prior Axitinib	83	89	5.5	3.7	0.68	13%	8%

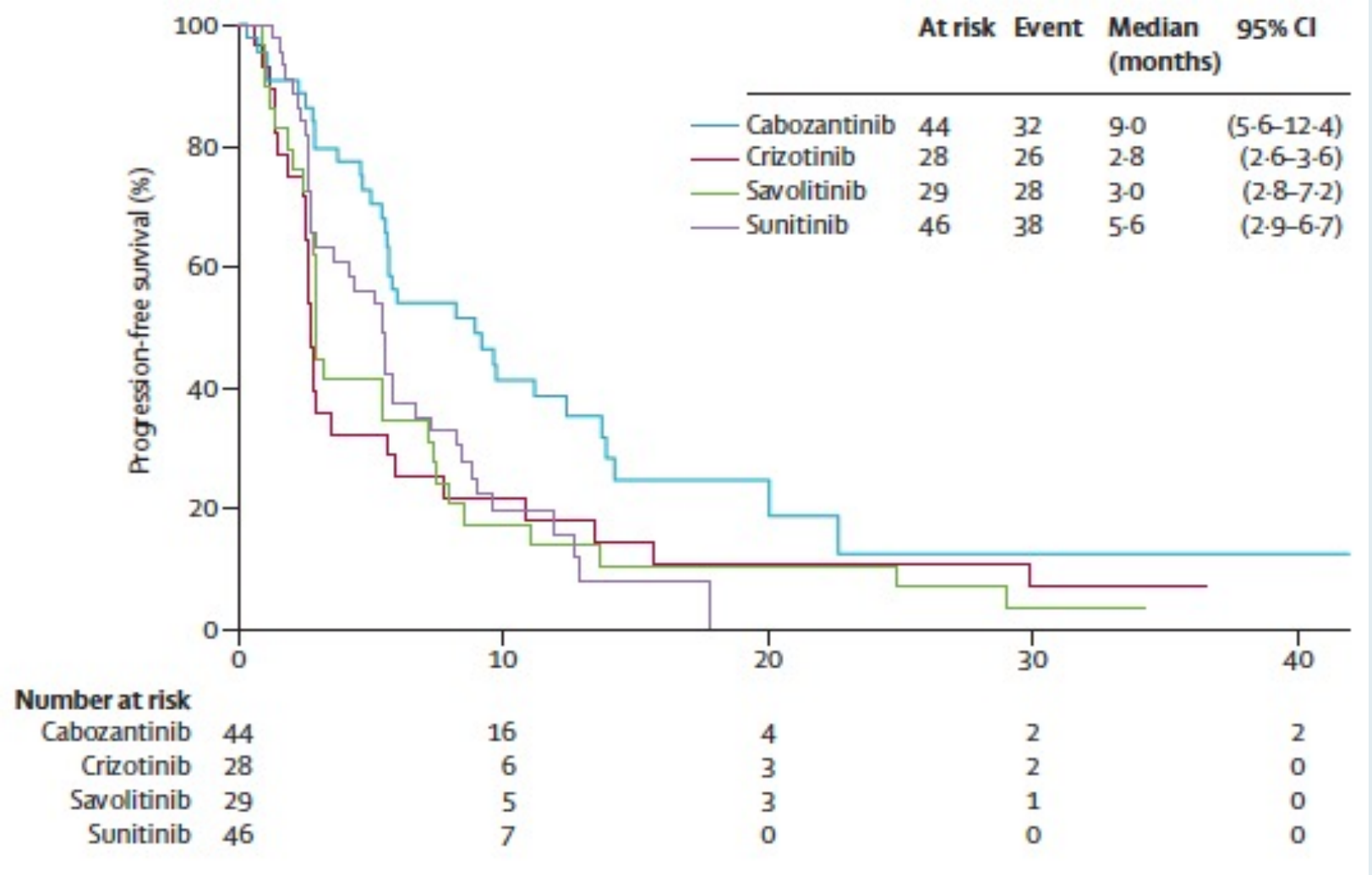
Rini BI et al. Genitourinary Cancers Symposium 2021;Abstract 278.

Lancet 2021;397:695-703

A comparison of sunitinib with cabozantinib, crizotinib, and savolitinib for treatment of advanced papillary renal cell carcinoma: a randomised, open-label, phase 2 trial

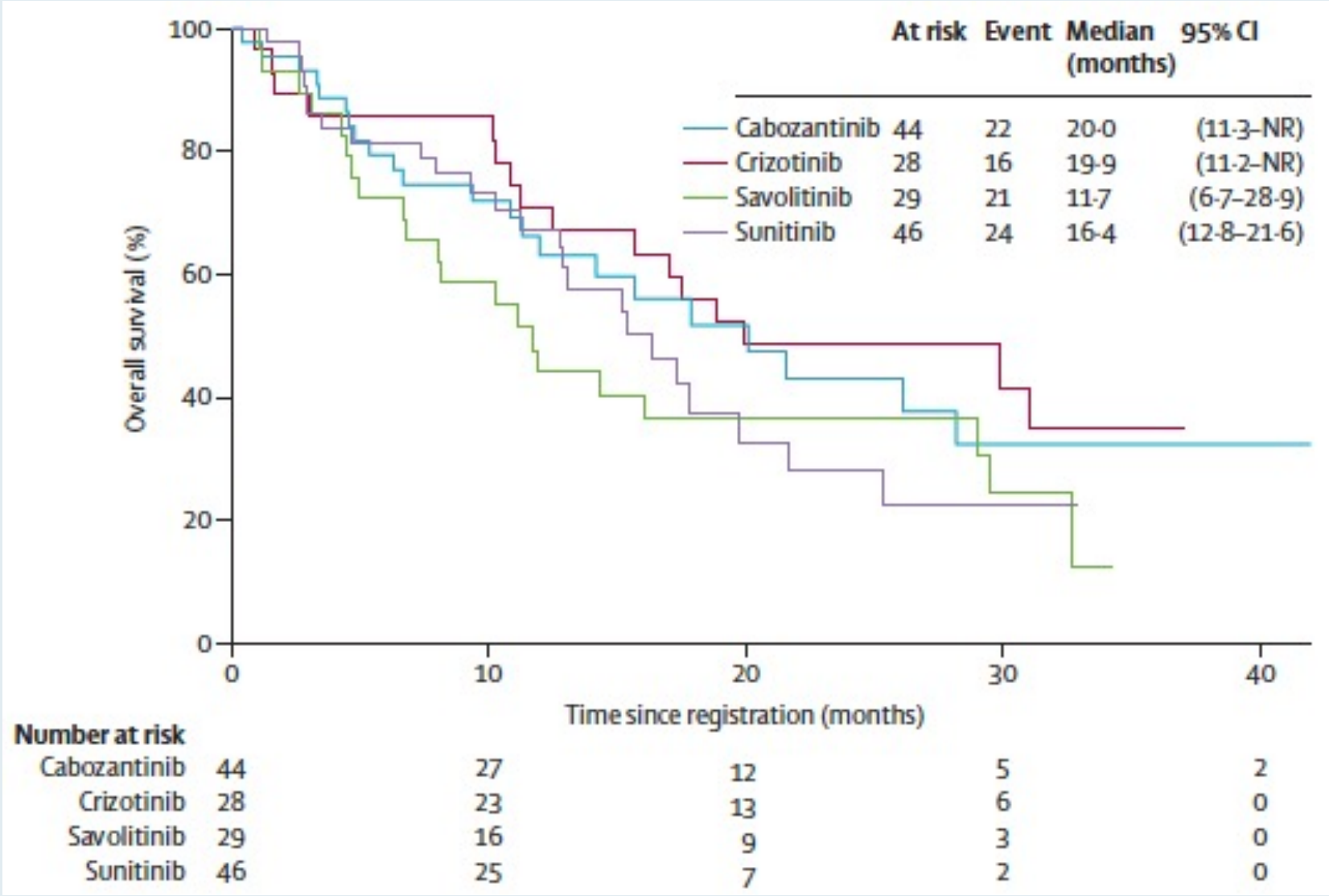
Sumanta K Pal, Catherine Tangen, Ian M Thompson Jr, Naomi Balzer-Haas, Daniel J George, Daniel Y C Heng, Brian Shuch, Mark Stein, Maria Tretiakova, Peter Humphrey, Adebowale Adeniran, Vivek Narayan, Georg A Bjarnason, Ulka Vaishampayan, Ajjai Alva, Tian Zhang, Scott Cole, Melissa Plets, John Wright, Primo N Lara Jr

Kaplan-Meier Analysis of Progression-Free Survival



Pal SK et al. *Lancet* 2021;397:695-703.

Kaplan-Meier Analysis of Overall Survival



Pal SK et al. *Lancet* 2021;397:695-703.

FDA Grants Priority Review to Belzutifan for von Hippel-Lindau Disease-Associated RCC

Press Release – March 16, 2021

"The FDA accepted a new drug application for belzutifan to treat von Hippel-Lindau disease-associated renal cell carcinoma and granted it priority review based on response rate results from a phase 2 trial.

A new drug application for belzutifan was accepted by the FDA and granted priority review for the treatment of patients with von Hippel-Lindau (VHL) disease-associated renal cell carcinoma (RCC), not requiring immediate surgery…

The application is based on results of a phase 2 trial, Study-004 (NCT03401788), of belzutifan in the treatment of VHL disease-associated RCC, with a primary end point of objective response rate and secondary measures of disease control rate, duration of response, time to response, progression-free survival, time to surgery, and safety. Patients treated on the trial must have had at least 1 measurable solid tumor localized to the kidneys and were not in need of immediate surgical intervention."

https://www.cancernetwork.com/view/fda-grants-priority-review-to-belzutifan-for-von-hippel-lindau-disease-associated-rcc

RTP RESEARCH TO PRACTICE

Project ECHO

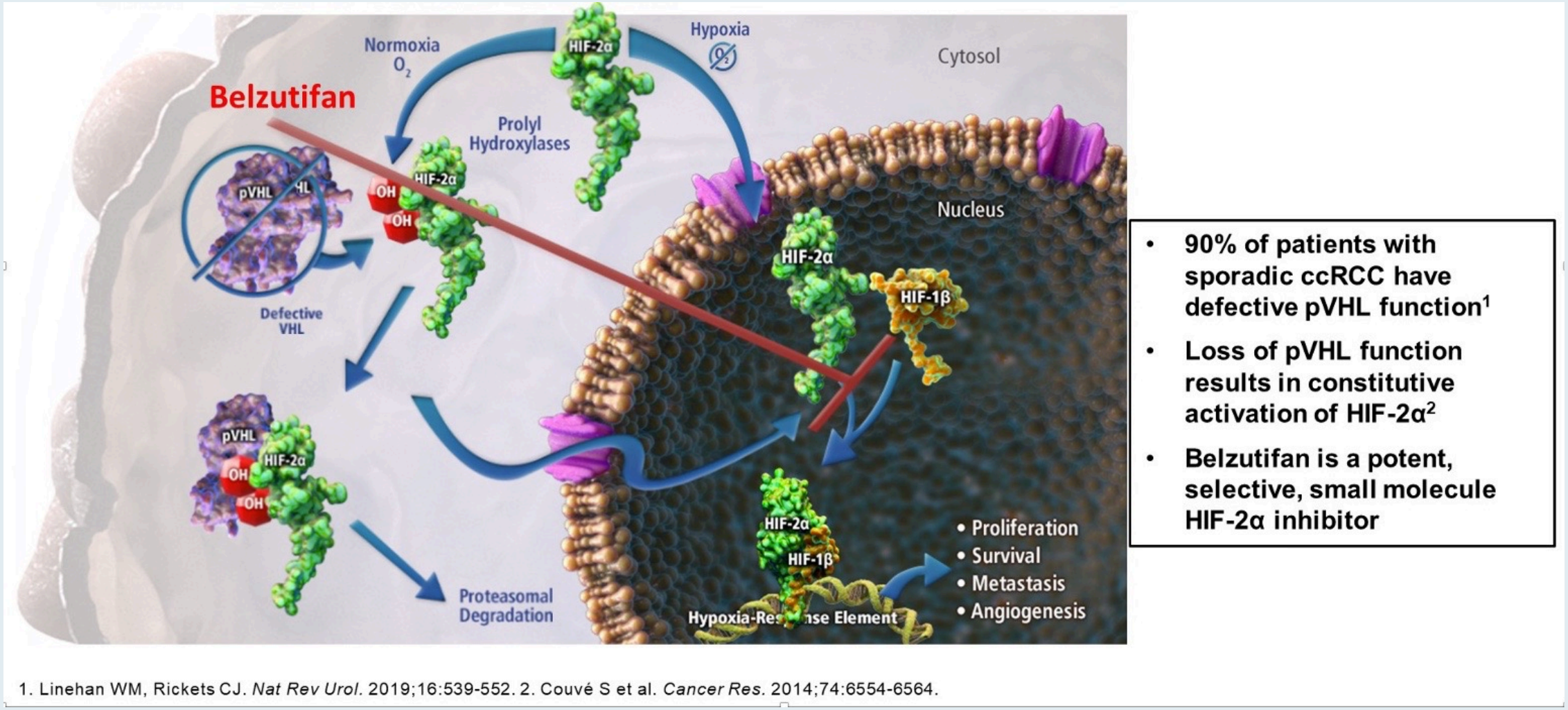
Genitourinary Cancers Symposium 2021;Abstract 273.

The Oral HIF-2α Inhibitor Belzutifan (MK-6482) in Patients With Advanced Clear Cell Renal Cell Carcinoma: Updated Follow-up of a Phase 1/2 Study

Todd Michael Bauer,[1] Toni K. Choueiri,[2] Kyriakos P. Papadopoulos,[3] Elizabeth R. Plimack,[4] Jaime R. Merchan,[5] David F. McDermott,[6] M. Dror Michaelson,[7] Leonard Joseph Appleman,[8] Sanjay Thamake,[9] Rodolfo F. Perini,[9] Eric Kristopher Park,[9] Eric Jonasch[10]

[1]Sarah Cannon Research Institute/Tennessee Oncology, PLLC, Nashville, TN, USA; [2]Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA; [3]South Texas Accelerated Research Therapeutics (START), San Antonio, TX, USA; [4]Fox Chase Cancer Center, Philadelphia, PA, USA; [5]University of Miami, Miami, FL, USA; [6]Beth Israel Deaconess Medical Center, Boston, MA, USA; [7]Massachusetts General Hospital, Boston, MA, USA; [8]University of Pittsburgh Medical Center, Pittsburgh, PA; [9]Merck & Co., Inc., Kenilworth, NJ, USA; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

pVHL Deficiency Results in HIF-2-alpha Activation

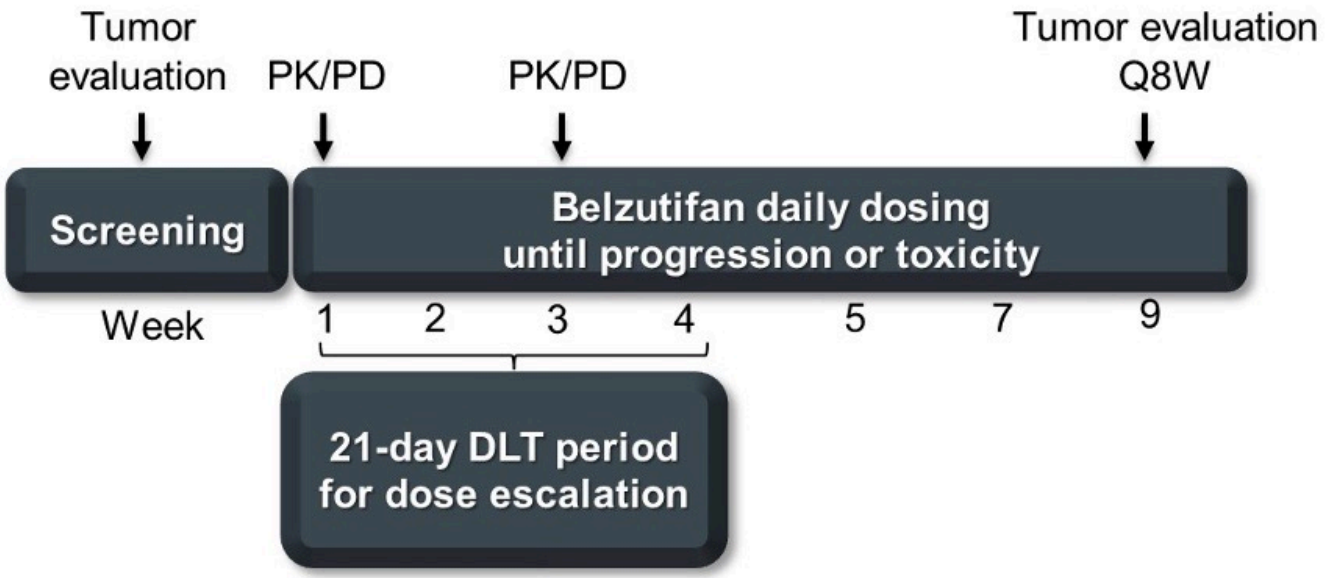


- 90% of patients with sporadic ccRCC have defective pVHL function[1]
- Loss of pVHL function results in constitutive activation of HIF-2α[2]
- Belzutifan is a potent, selective, small molecule HIF-2α inhibitor

1. Linehan WM, Rickets CJ. *Nat Rev Urol.* 2019;16:539-552. 2. Couvé S et al. *Cancer Res.* 2014;74:6554-6564.

Bauer TD et al. GU Cancers Symposium 2021;Abstract 273.

Study Design

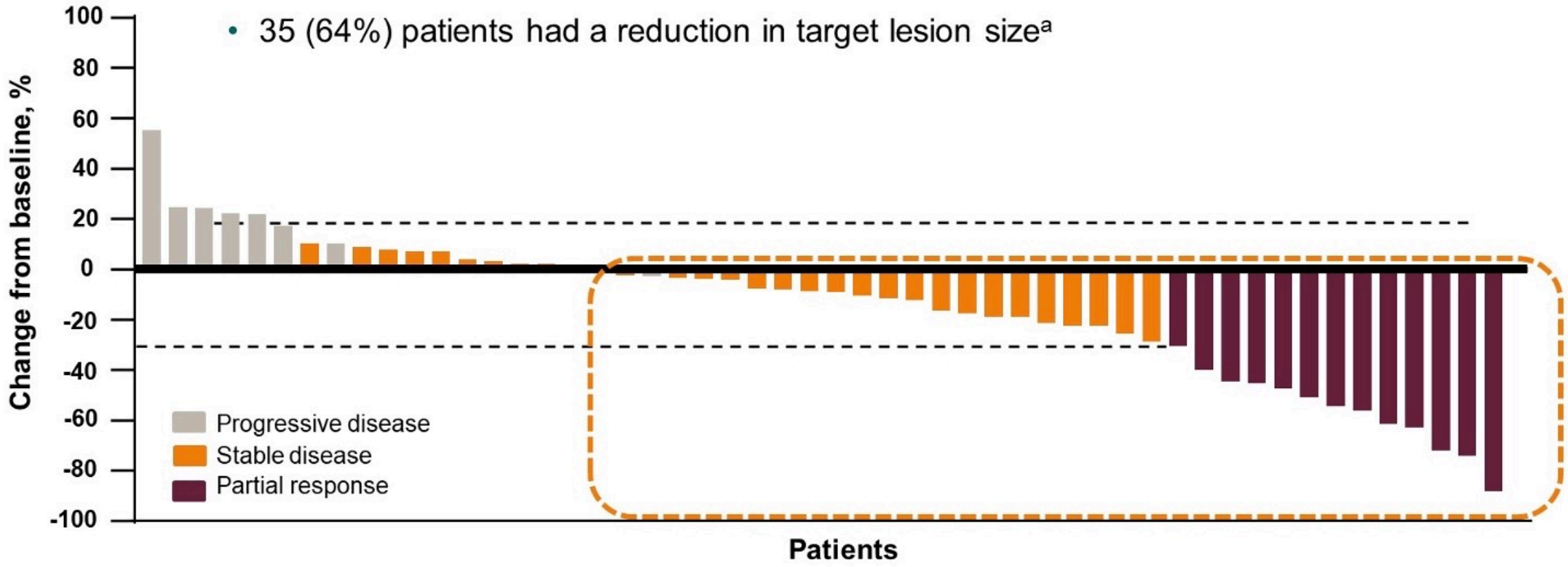


- Dose-escalation cohort for patients with advanced solid tumors
- Dose-expansion cohort for patients with advanced ccRCC who previously received ≥1 therapy
  - Key end points: Safety, objective response rate, duration of response

- Dose of 120 mg once daily selected for further clinical development from the dose-escalation cohort
- **55 patients with previously treated advanced ccRCC enrolled at 120 mg orally once daily in the dose-expansion cohort**
  - 44 (80%) discontinued
    - Most common reason was disease progression: 60%
  - 11 (20%) have treatment ongoing
- Median (range) follow-up:
  - 27.7 (24.8-34.3) months

Bauer TD et al. GU Cancers Symposium 2021;Abstract 273.

Best Tumor Change from Baseline (Investigator Assessment in the ccRCC Cohort)



[a]3 patients were nonevaluable. Data cutoff: June 1, 2020.

Bauer TD et al. GU Cancers Symposium 2021;Abstract 273.

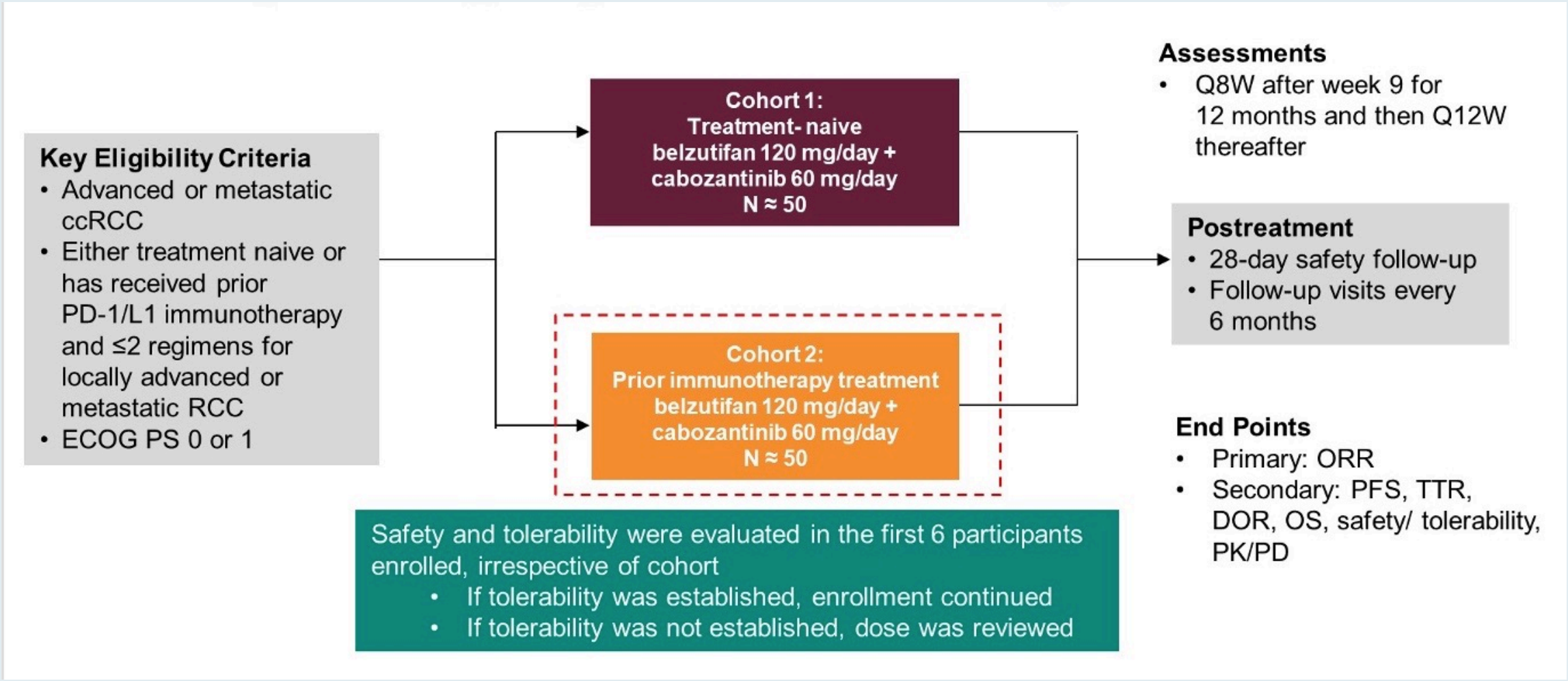
Genitourinary Cancers Symposium 2021;Abstract 272.

Phase 2 Study of the Oral Hypoxia-Inducible Factor 2α Inhibitor Belzutifan (MK-6482) in Combination With Cabozantinib in Patients With Advanced Clear Cell Renal Cell Carcinoma

Toni K. Choueiri[1]; Todd M. Bauer[2]; David F. McDermott[3]; Edward Arrowsmith[4]; Ananya Roy[5]; Rodolfo Perini[5]; Donna Vickery[5]; Scott S. Tykodi[6]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [3]Beth Israel Deaconess Medical Center, Boston, MA, USA; [4]Tennessee Oncology, Chattanooga, TN, USA; [5]Merck & Co., Inc., Kenilworth, NJ, USA; [6]University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA, USA

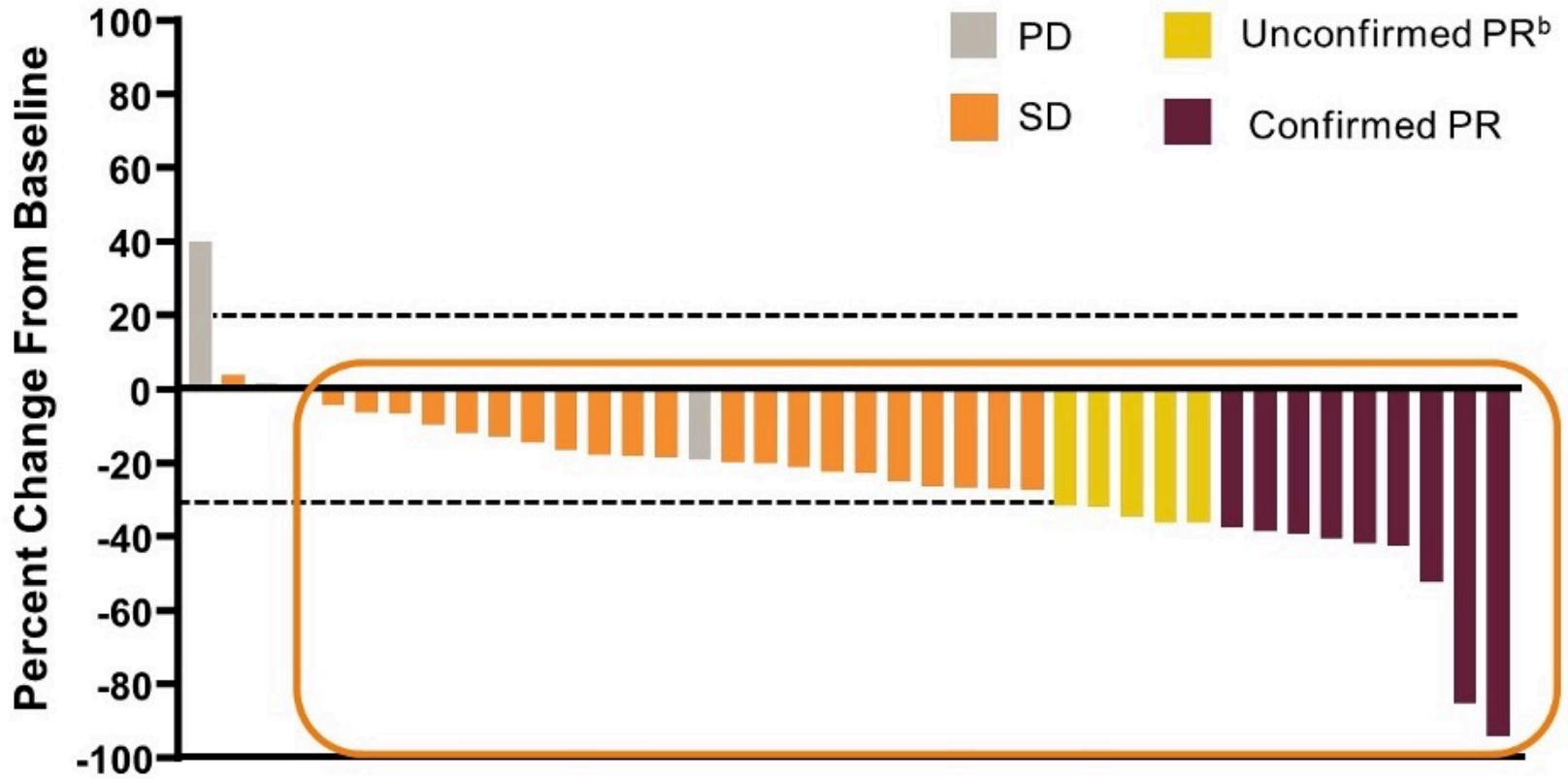
Study Design



Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

Best Tumor Change from Baseline

- 36 of 41 patients (88%) experienced a reduction in target lesion size[a]



Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

Treatment-Related Adverse Events

Treatment-Related AEs in ≥15% of Patients	Safety Analysis Set N = 52			
	Any Grade		Grade 3	
	Event, n	n (%)	Event, n	n (%)
Any	742	51 (98)	60	31 (60)
Anemia	92	40 (77)	8	6 (12)
Fatigue	67	35 (67)	10	6 (12)
Hand-foot syndrome	56	28 (54)	1	1 (2)
Diarrhea	49	23 (44)	2	2 (4)
Hypertension	52	23 (44)	15	12 (23)
Nausea	24	18 (35)	1	1 (2)
ALT increased	48	17 (33)	7	3 (6)
AST increased	34	17 (33)	2	2 (4)
Decreased appetite	22	15 (29)	1	1 (2)
Dysgeusia	19	12 (23)	1	1 (2)
Headache	12	10 (19)	0	0 (0)
Hypophosphatemia	18	9 (17)	2	2 (4)
Stomatitis	10	8 (15)	0	0 (0)

[a]All patients who received ≥1 dose of treatment. Data cutoff: October 15, 2020.

- There were no grade 4/5 treatment-related AEs
- Of all 742 AEs, 92% were grade 1 or 2 in severity
- Treatment-related hypoxia, considered an on-target AE for belzutifan, occurred in 2 patients (4%) (both were grade 3 AEs)

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

Agenda

MODULE 1: Cases from the Practice of Dr Choksi

MODULE 2: Consensus or Controversy – Clinical Investigator Approaches to Clinical Scenarios

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Lee

- Prevalence and landscape of actionable genomic alterations in renal cell carcinoma (RCC)
- FRACTION-RCC trial: Innovative, high-throughput assessment of nivolumab + ipilimumab for treatment-refractory metastatic RCC
- DNA damage repair pathway alterations in metastatic clear cell RCC and implications for systemic therapy
- Current role for adjuvant and neoadjuvant therapy in RCC
- Genomic biomarkers of response to lenvatinib/pembrolizumab (Len/Pembro) in patients with advanced RCC (aRCC)
- Phase IB/II trial of Len/Pembro in patients with aRCC, endometrial cancer and other advanced solid tumors
- Clinicogenomic predictors of extreme responses to anti-PD-1/PD-L1 checkpoint inhibitors in metastatic urothelial cancer

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

Ann Oncol 2020;31(8):1030-9

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

Updated efficacy results from the JAVELIN Renal 101 trial: first-line avelumab plus axitinib versus sunitinib in patients with advanced renal cell carcinoma

T. K. Choueiri[1*], R. J. Motzer[2], B. I. Rini[3†], J. Haanen[4], M. T. Campbell[5], B. Venugopal[6], C. Kollmannsberger[7], G. Gravis-Mescam[8], M. Uemura[9], J. L. Lee[10], M.-O. Grimm[11], H. Gurney[12], M. Schmidinger[13], J. Larkin[14], M. B. Atkins[15], S. K. Pal[16], J. Wang[17], M. Mariani[18], S. Krishnaswami[19], P. Cislo[20], A. Chudnovsky[21], C. Fowst[18], B. Huang[19], A. di Pietro[22] & L. Albiges[23]

JAVELIN Renal 101: Overall Response and Best Response Rate in the PD-L1-Positive and Overall Populations

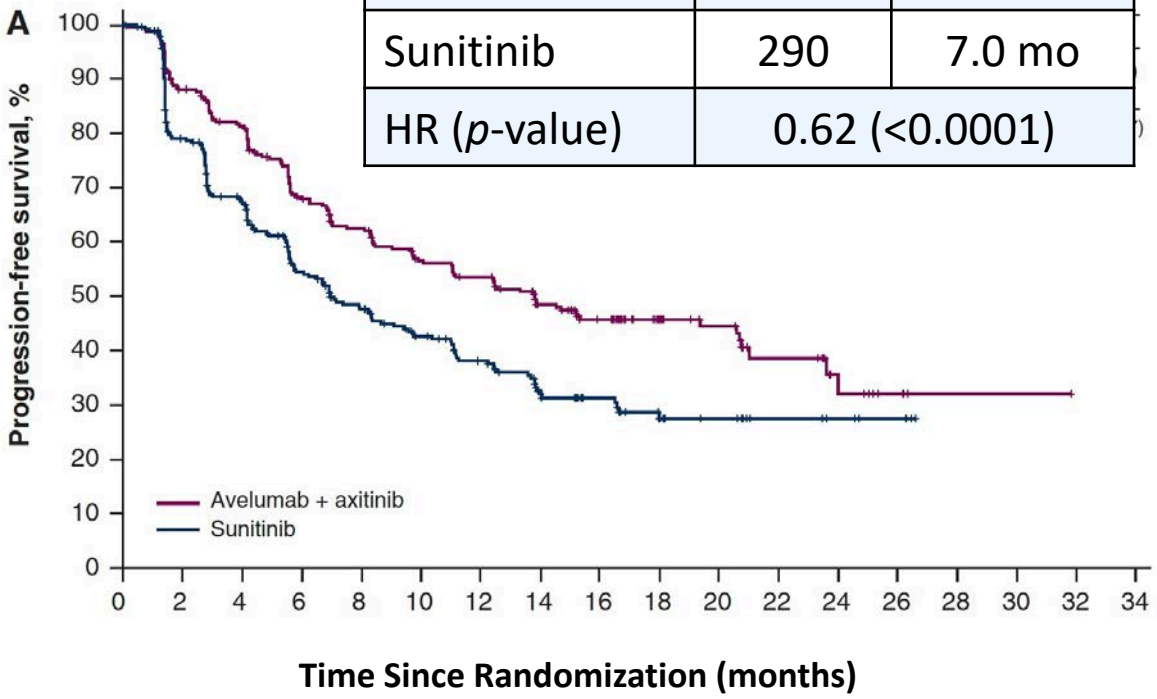
	PD-L1-positive		Overall	
	Avelumab + axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing response	55.6%	53.2%	54.3%	50.4%

Choueiri TK et al. *Ann Oncol* 2020;31(8):1030-9.

JAVELIN Renal 101: PFS in the PD-L1+ and Overall Populations

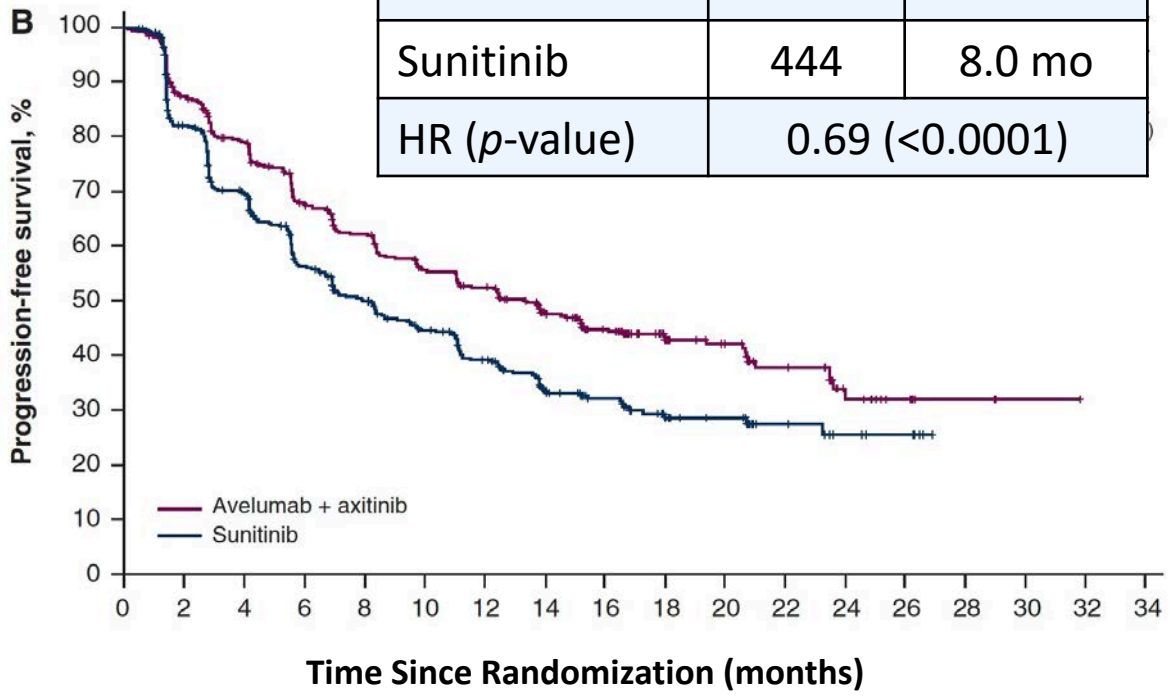
PD-L1 ≥ 1% Population

	N	mPFS
Avelumab + axitinib	270	13.8 mo
Sunitinib	290	7.0 mo
HR (*p*-value)	0.62 (<0.0001)	



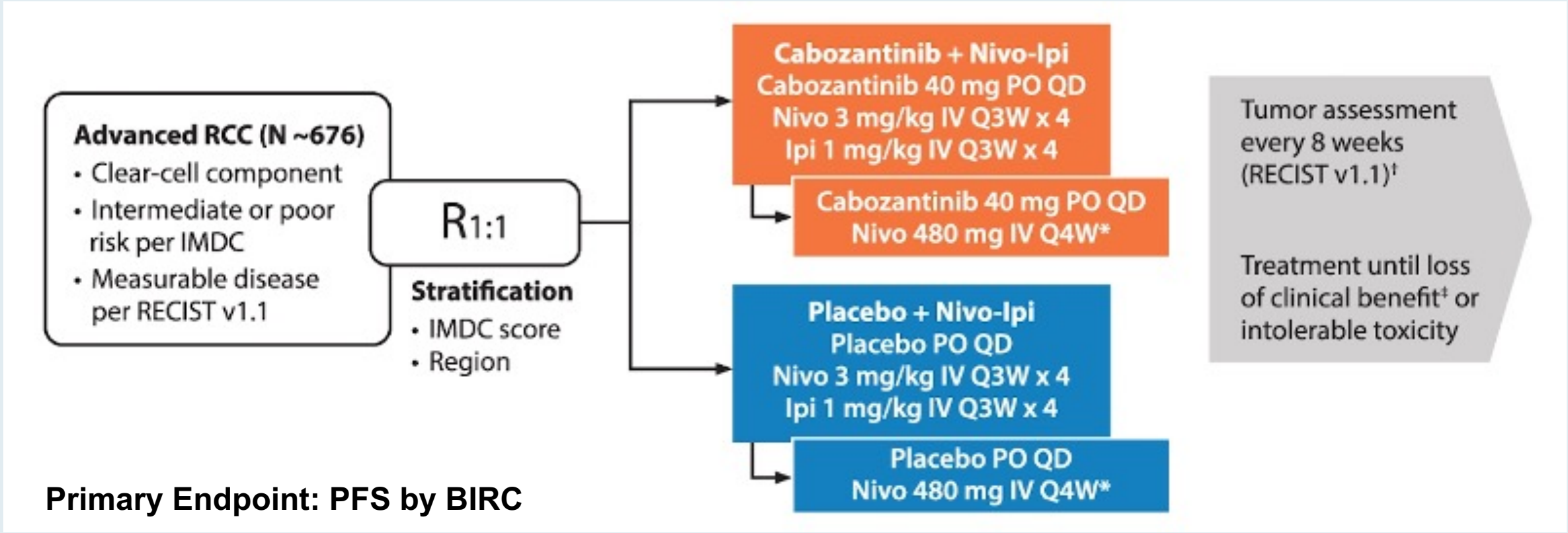
Overall Population

	N	mPFS
Avelumab + axitinib	442	13.3 mo
Sunitinib	444	8.0 mo
HR (*p*-value)	0.69 (<0.0001)	



Choueiri TK et al. *Ann Oncol* 2020;31(8):1030-9.

COSMIC-313 Phase III Schema



Primary Endpoint: PFS by BIRC

https://www.urotoday.com/conference-highlights/asco-2020/asco-2020-kidney-cancer/121877-asco-2020-cosmic-313-phase-iii-study-of-cabozantinib-in-combination-with-nivolumab-and-ipilimumab-in-patients-with-previously-untreated-advanced-renal-cell-carcinoma-of-intermediate-or-poor-risk.html

Sequencing of Therapy for Patients with Relapsed/Refractory (R/R) RCC; Novel Approaches Under Investigation

rapid communications

Salvage Ipilimumab and Nivolumab in Patients With Metastatic Renal Cell Carcinoma After Prior Immune Checkpoint Inhibitors

Anita Gul, MD[1]; Tyler F. Stewart, MD[2,3]; Charlene M. Mantia, MD[4]; Neil J. Shah, MD[5]; Emily Stern Gatof, MD[4]; Ying Long, PharmD[2]; Kimberly D. Allman, MSN, CNP[1]; Moshe C. Ornstein, MD, MA[1]; Hans J. Hammers, MD, PhD[6]; David F. McDermott, MD[4]; Michael B. Atkins, MD[5]; Michael Hurwitz, MD, PhD[2]; and Brian I. Rini, MD[1]

J Clin Oncol 2020;38:3088-94.

Salvage Ipilimumab/Nivolumab for mRCC After Prior ICI Therapy

Variable	No. (%)
No. of prior lines of systemic therapy	
1	9 (20)
2	12 (27)
3	8 (18)
4	6 (13)
> 4	10 (22)
Prior VEGF receptor inhibitor[a]	27 (60)
Prior immunotherapy	
Anti–PD-1[b]	34 (76)
Anti–PD-L1[b]	11 (24)
IL-2[c]	14 (31)
Best response to prior ICI	
PR	24 (53)
SD	12 (27)
PD	9 (20)

BOR to Prior ICI	No. (%)	BOR to Salvage Ipilimumab and Nivolumab	No. (%)
PR	24 (53)	PR	4 (17)
		SD	2 (8)
		PD	17 (71)
		NE	1 (4)
SD	12 (27)	PR	3 (25)
		SD	5 (42)
		PD	4 (33)
PD	9 (20)	PR	2 (22)
		PD	7 (78)

Abbreviations: BOR, best objective response; ICI, immune checkpoint inhibitor; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Gul A et al. *J Clin Oncol* 2020;38:3088-94.

A Pooled Analysis of the Efficacy and Safety of Cabozantinib Post Immunotherapy in Patients with Advanced Renal Cell Carcinoma

Oya M et al.

ASCO 2020;Abstract 5089.

Efficacy of Cabozantinib with or without Prior Immunotherapy

	Prior IO (N = 33)	No Prior IO (N = 332)
Objective response rate	21.2%	17.2%
Clinical benefit rate	75.8%	83.7%
Median PFS	Not reached	7.4 mo
6-months PFS	65.5%	58.3%
Median PFS	19.5 mo	21.9 mo
6-months OS	90.8%	90.6%

Oya M et al. ASCO 2020;Abstract 5089.

Phase II Trial of Lenvatinib (LEN) plus Pembrolizumab (PEMBRO) for Disease Progression After PD-1/PD-L1 Immune Checkpoint Inhibitor (ICI) in Metastatic Clear Cell Renal Cell Carcinoma (mccRCC)

Lee C-H et al.

ASCO 2020;Abstract 5008.

Efficacy of Lenvatinib/Pembrolizumab in Patients Previously Treated with Immunotherapy

	Anti-PD-1/PD-L1 (N = 104)	Anti-PD-1/PD-L1 and anti-VEGF (n = 68)	Nivolumab + ipilimumab (n = 38)
ORR	55%	59%	47%
Median DOR	12 mo	9 mo	Not reached
Median PFS (irRECIST)	11.7 mo	Not reported	Not reported
OS at 12 months	77%	Not reported	Not reported

Lee C-H et al. ASCO 2020;Abstract 5008.

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Wednesday, May 5, 2021
5:00 PM – 6:00 PM ET

Faculty

Jeremy Abramson, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

CME and ABIM MOC credit information will be emailed to each participant within 5 business days.