

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

In Partnership with Project Echo® and Florida Cancer Specialists

**Tuesday, July 6, 2021
5:00 PM – 6:00 PM ET**

Faculty

**David I Quinn, MBBS, PhD
Maria Regina Flores, MD**

Moderator

Neil Love, MD

Faculty



David I Quinn, MBBS, PhD

Medical Director, USC Norris Cancer Hospital and Clinics
Head, Section of GU Cancer, Division of Oncology
Associate Professor of Medicine
USC Norris Comprehensive Cancer Center
Keck School of Medicine of USC
Los Angeles, California



Maria Regina Flores, MD

Advent Health Orlando
Orlando Regional Hospital
HCA Oviedo Medical Center
UCF Lake Nona
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Steering Committee



Chung-Han Lee, MD, PhD

Assistant Attending Physician
Genitourinary Oncology Service
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New York, New York



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Medical Director, USC Norris Cancer Hospital and Clinics
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Sumanta K Pal, MD

Clinical Professor, Department of Medical Oncology
City of Hope Comprehensive Cancer Center
Duarte, California



Walter Stadler, MD

Fred C Buffett Professor of Medicine
Dean for Clinical Research
Deputy Director, Comprehensive Cancer Center
The University of Chicago
Chicago, Illinois

Commercial Support

This activity is supported by an educational grant from Pfizer Inc.

Dr Love — Disclosures

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Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Project ECHO® Disclosure

Project ECHO collects registration, participation, questions/answers, chat comments, and poll responses for some teleECHO® programs. Your individual data will be kept confidential. These data may be used for reports, maps, communications, surveys, quality assurance, evaluation, research, and to inform new initiatives.

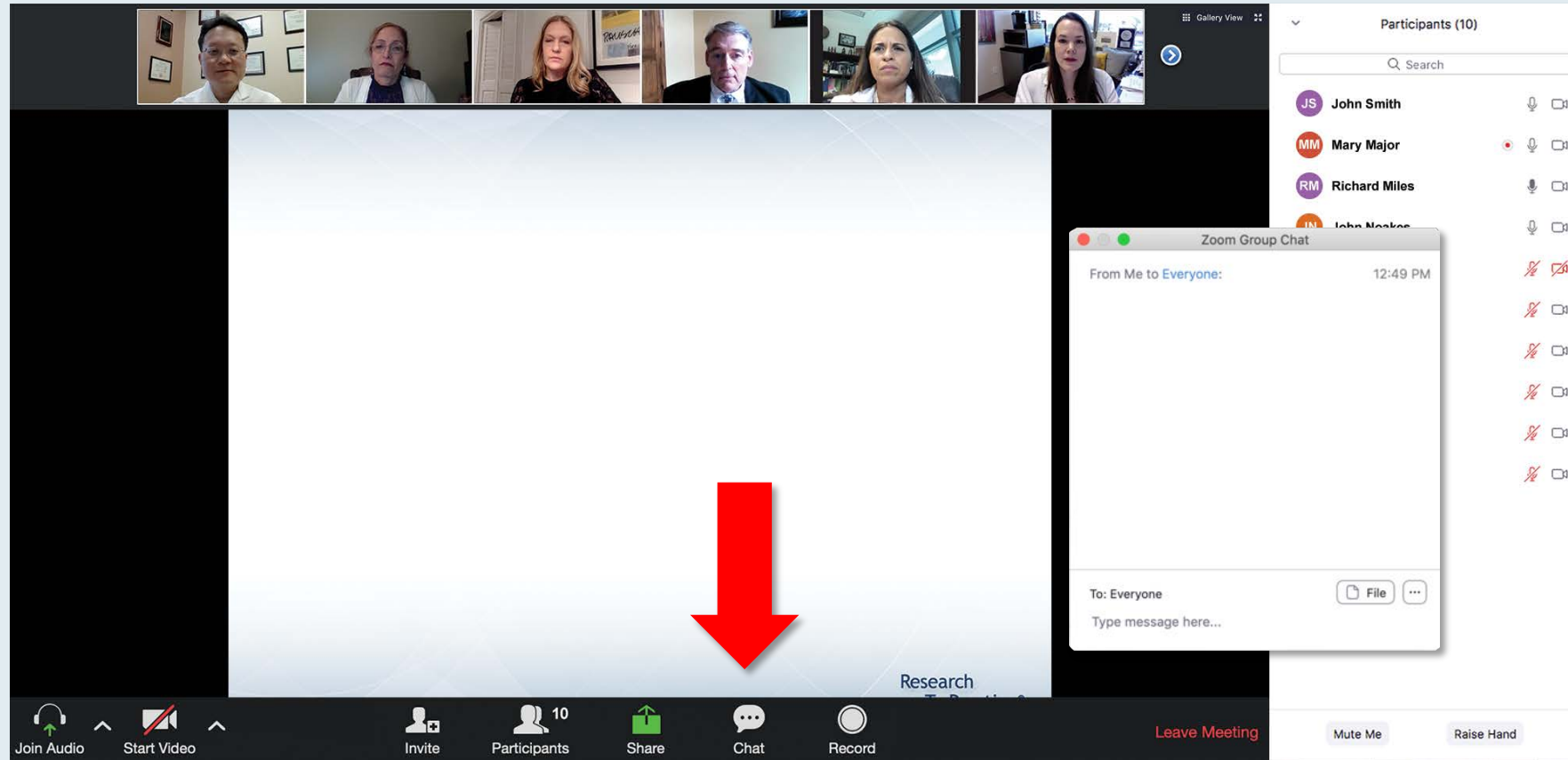
Dr Quinn — Disclosures

Advisory Committee and Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, EMD Serono Inc, Exelixis Inc, Genentech, a member of the Roche Group, Merck, Novartis, Pfizer Inc, Roche Laboratories Inc, Seagen Inc
Contracted Research	Bayer HealthCare Pharmaceuticals, Merck, Pfizer Inc
Data and Safety Monitoring Board/Committee	Eisai Inc

Dr Flores — Disclosures

No relevant conflicts of interest to disclose

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

Familiarizing Yourself with the Zoom Interface

How to answer poll questions

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What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
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6. Daratumumab + lenalidomide +/- dexamethasone
7. Daratumumab + pomalidomide +/- dexamethasone
8. Daratumumab + bortezomib +/- dexamethasone
9. Ixazomib + Rd
10. Other

Co-provided by USF Health Research To Practice®

Participants (10)

Name	Status
JS John Smith	Microphone On, Video On
MM Mary Major	Microphone On, Video On
RM Richard Miles	Microphone On, Video On
JN John Noakes	Microphone On, Video On
AS Alice Suarez	Microphone Off, Video Off
JP Jane Perez	Microphone Off, Video Off
RS Robert Stiles	Microphone Off, Video Off
JF Juan Fernandez	Microphone Off, Video Off
AK Ashok Kumar	Microphone Off, Video Off
JS Jeremy Smith	Microphone Off, Video Off

When a poll question pops up, click your answer choice from the available options.
Results will be shown after everyone has answered.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot shows a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below the thumbnails is a slide titled "Meet The Professor Program Steering Committee" featuring six members with their photos and titles:

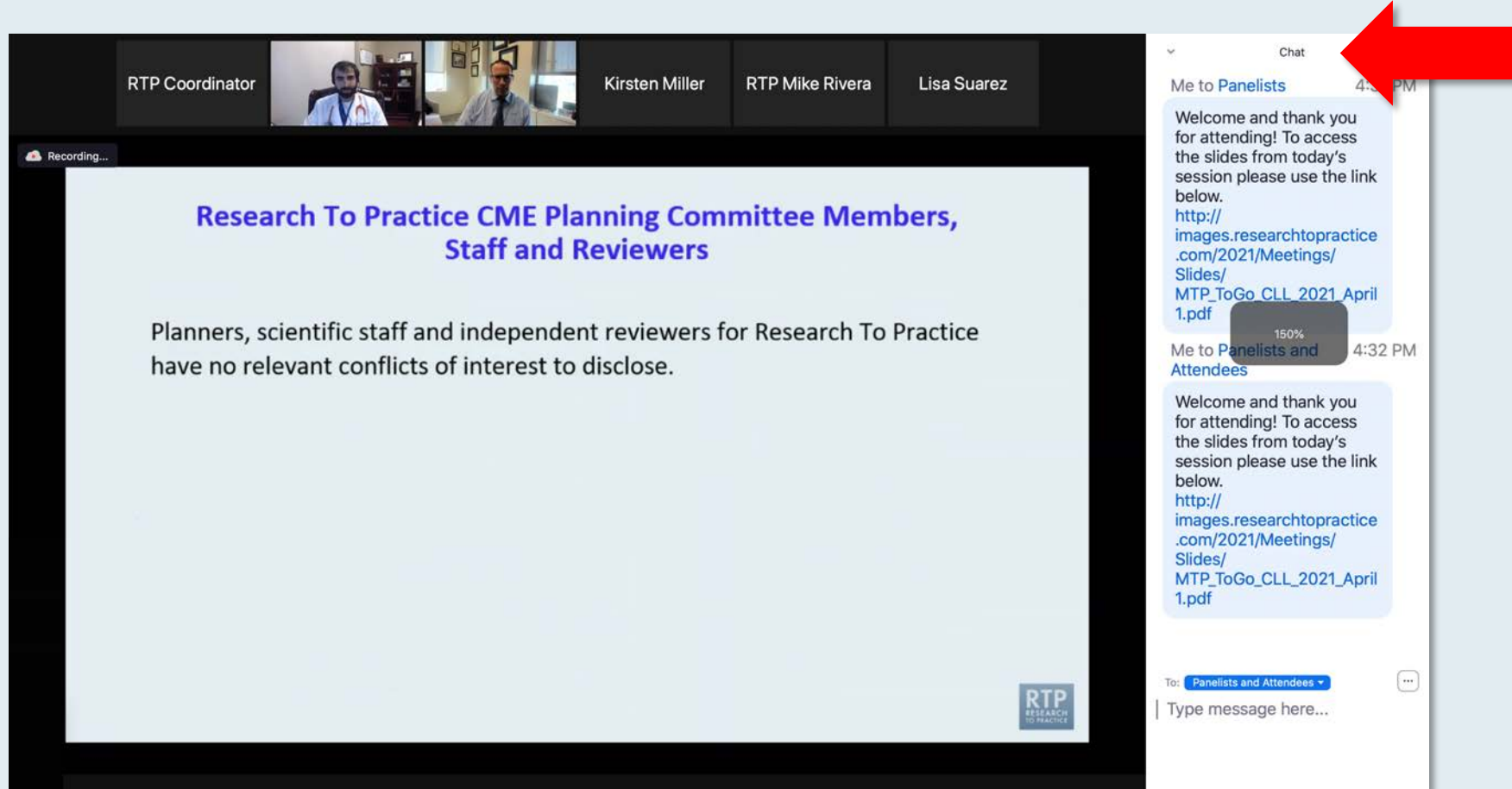
- John N Allan, MD**
Assistant Professor of Medicine
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- Ian W Flinn, MD, PhD**
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee
- Steven Coutre, MD**
Professor of Medicine (Hematology)
Stanford University School of Medicine
Stanford, California
- Prof John G Gribben, MD, DSc, FMedSci**
Chair of Medical Oncology
Barts Cancer Institute
Queen Mary University of London
Charterhouse Square
London, United Kingdom
- Matthew S Davids, MD, MMSc**
Associate Professor of Medicine
Harvard Medical School
Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts
- Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

At the bottom right of the slide is the RTP Research to Practice logo. To the right of the slide is a chat window titled "Chat". It shows two messages from "Me to Panelists" and "Me to Panelists and Attendees" at 4:31 PM and 4:32 PM respectively. The messages contain a welcome message and a link to a PDF file. Below the messages is a "To:" dropdown menu set to "Panelists and Attendees" and a text input field labeled "Type message here...". A large red arrow points to the white line above the text input field, indicating where to drag to expand the submission box.

Drag the white line above the submission box up to create more space for your message.

Familiarizing Yourself with the Zoom Interface

Increase chat font size



**Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.**

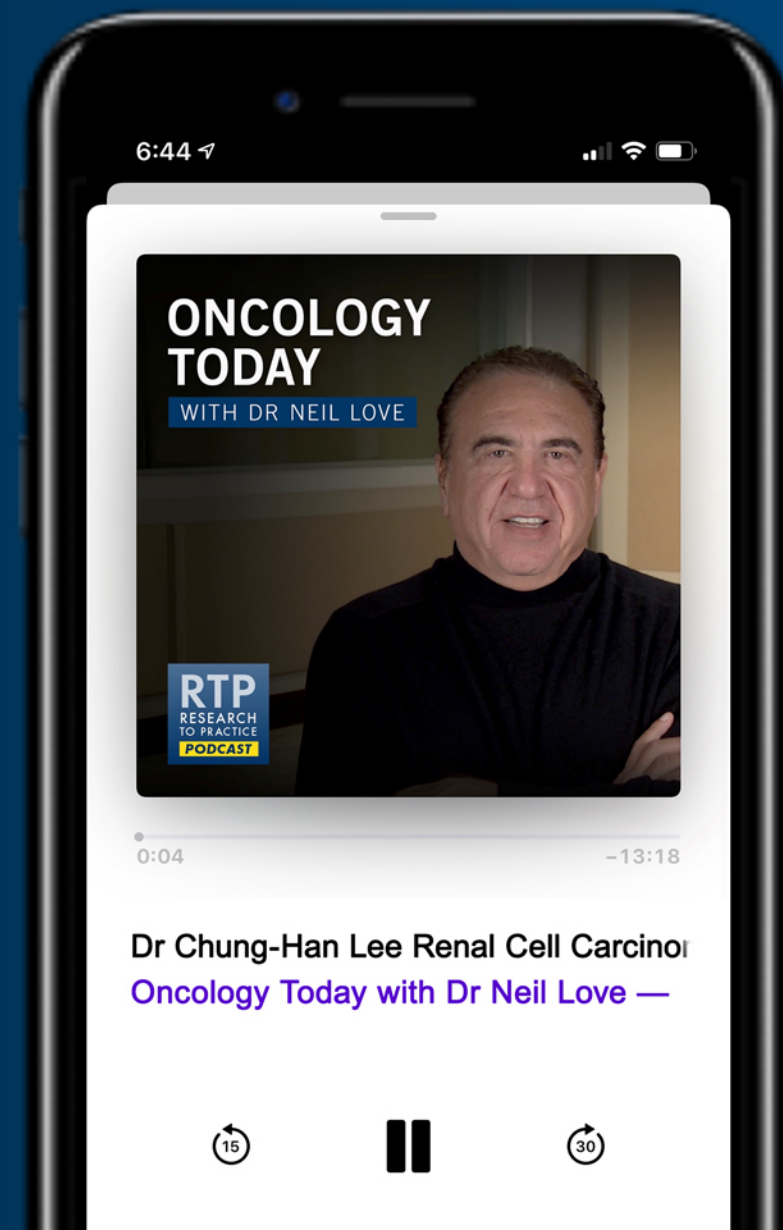
ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma



DR CHUNG-HAN LEE
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NEW YORK, NEW YORK



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Gail J Roboz, MD
Eytan M Stein, MD**

Moderator

Neil Love, MD

A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

**Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET**

Faculty

**Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD**

Moderator

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A Conversation with the Investigators: Bladder Cancer

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Daniel P Petrylak, MD
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Webinar 1 – Tuesday, April 6, 2021

Faculty

Sumanta K Pal, MD

Webinar 3 – Wednesday, June 2, 2021

Faculty

Walter Stadler, MD

Webinar 2 – Tuesday, May 4, 2021

Faculty

Chung-Han Lee, MD, PhD

Webinar 4 – Tuesday, July 6, 2021

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David I Quinn, MBBS, PhD

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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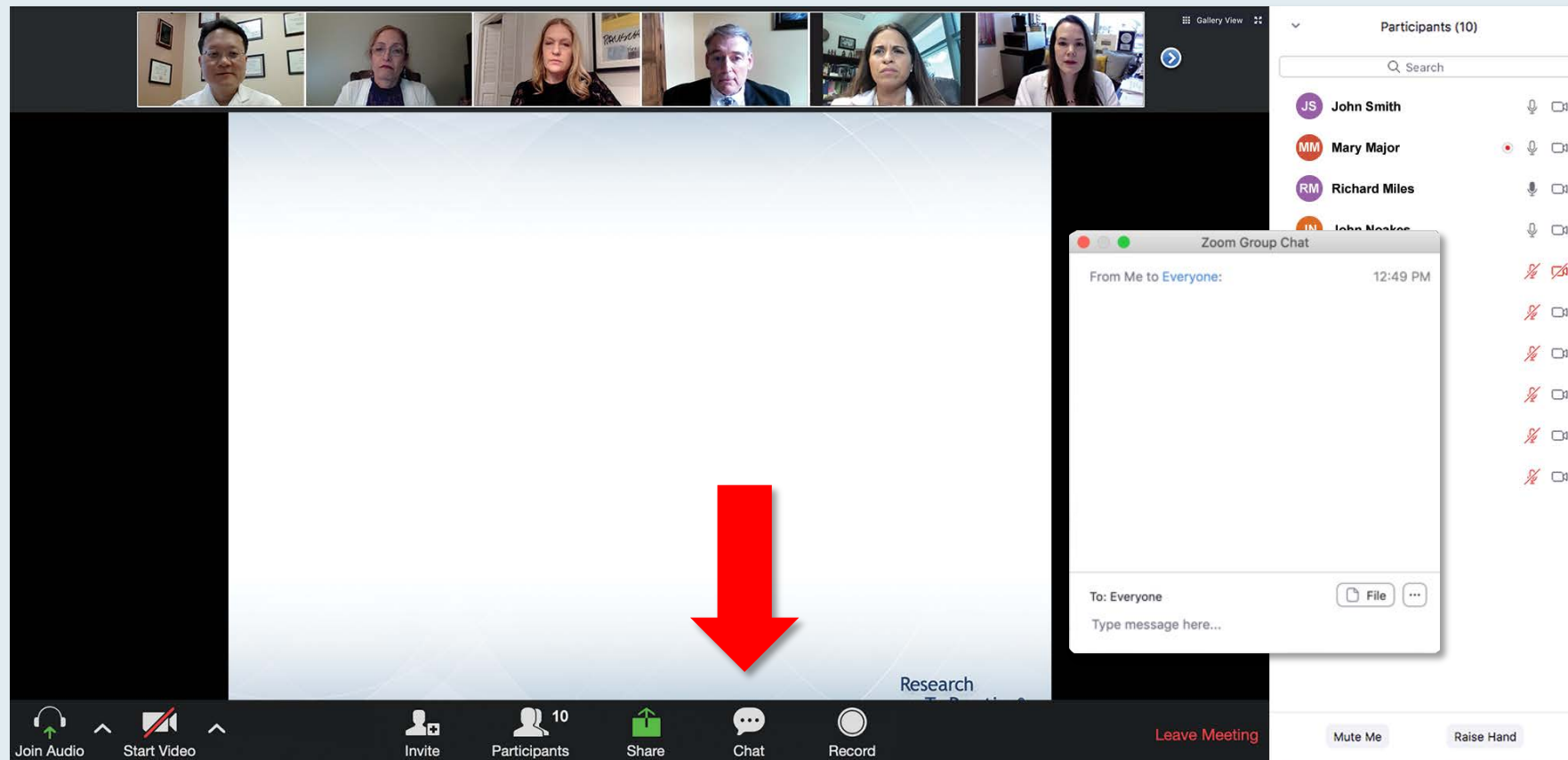
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What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

Quick Poll

- ☐ Carfilzomib +/- dexamethasone
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- ☐ Ixazomib + Rd
- ☐ Other

Submit

Participants (10)

Initials	Name	Mute	Video	Chat
JS	John Smith	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
MM	Mary Major	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
RM	Richard Miles	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
JN	John Noakes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
AS	Alice Suarez	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
JP	Jane Perez	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
RS	Robert Stiles	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
JF	Juan Fernandez	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
AK	Ashok Kumar	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
JS	Jeremy Smith	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

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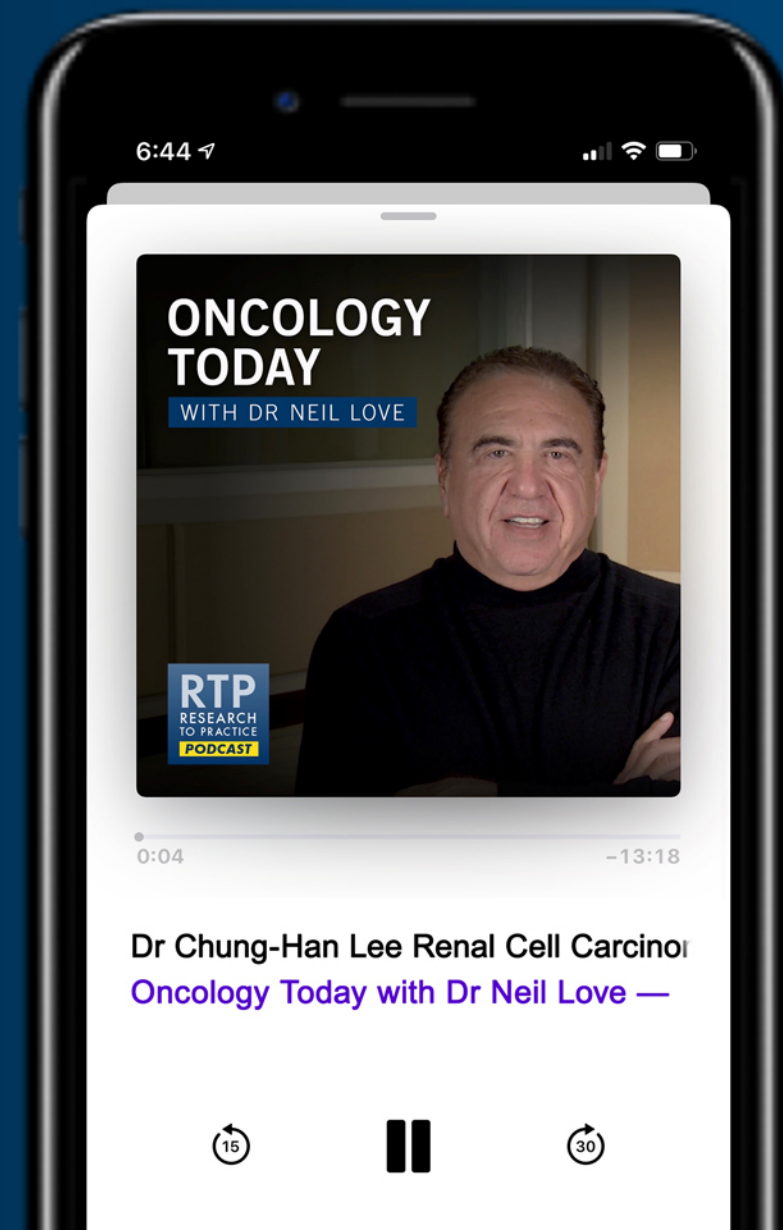
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Agenda

MODULE 1: Cases from the Practice of Dr Flores

- A 56-year-old man with recurrence of renal cell carcinoma (RCC) after nephrectomy
- A 37-year-old man with repeated kidney tumors and suspected hereditary RCC
- A 63-year-old man with non-clear cell RCC
- A 78-year-old man with newly diagnosed metastatic RCC (mRCC)
- A 61-year-old man with newly diagnosed mRCC and hypercalcemia

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

MODULE 3: Key Data Sets

MODULE 4: Other Recent Data Sets

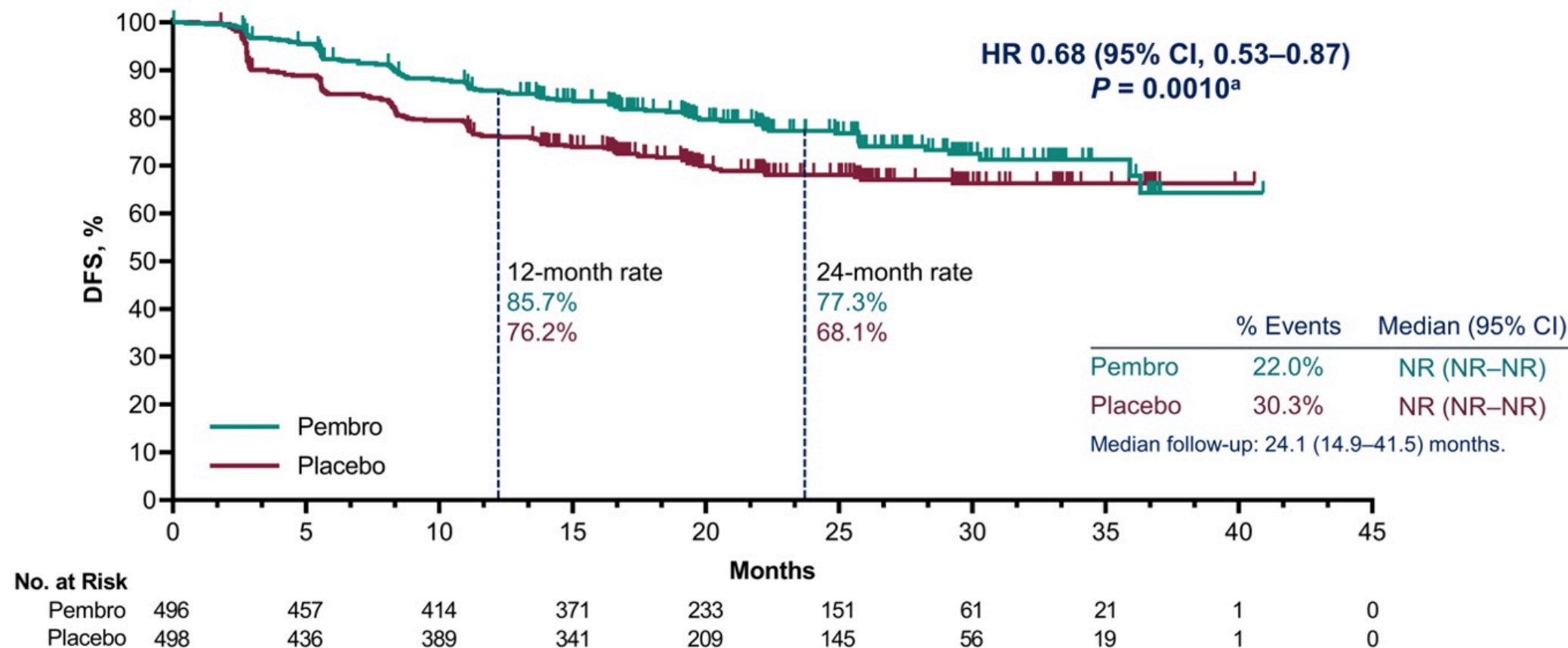
Pembrolizumab vs Placebo as Post Nephrectomy Adjuvant Therapy for Patients with Renal Cell Carcinoma: Randomized, Double-Blind, Phase 3 KEYNOTE-564 Study

Toni K. Choueiri¹; Piotr Tomczak²; Se Hoon Park³; Balaji Venugopal⁴; Thomas Ferguson⁵; Yen-Hwa Chang⁶; Jaroslav Hajek⁷; Stefan Symeonides⁸; Jae Lyun Lee⁹; Naveed Sarwar¹⁰; Antoine Thiery-Vuillemin¹¹; Marine Gross-Goupil¹²; Mauricio Mahave¹³; Naomi Haas¹⁴; Piotr Sawrycki¹⁵; Rodolfo F. Perini¹⁶; Pingye Zhang¹⁶; Jaqueline Willemann-Rogerio¹⁶; Kentaro Imai¹⁶; David Quinn¹⁷; Thomas Powles¹⁸; on behalf of the KEYNOTE-564 investigators.

¹Dana-Farber Cancer Institute, Boston, MA, USA; ²Poznań University of Medical Sciences, Poznań, Poland; ³Sungkyunkwan University, Samsung Medical Center, Seoul, South Korea; ⁴Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, UK; ⁵Fiona Stanley Hospital, Perth, Australia; ⁶Taipei Veterans General Hospital, Taipei, Taiwan; ⁷Fakultni Nemocnice Ostrava, Ostrava, Czech Republic; ⁸Edinburgh Cancer Center and University of Edinburgh, Edinburgh, UK; ⁹Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; ¹⁰Imperial College Healthcare NHS Trust, London, UK; ¹¹University Hospital Jean Minjoz, Besançon, France; ¹²University Hospital Bordeaux-Hôpital Saint-André, Bordeaux, France; ¹³Fundacion Arturo Lopez Perez FALP, Santiago, Chile; ¹⁴Abramson Cancer Center, Philadelphia, PA, USA; ¹⁵Wojewodzki Szpital Zespolony im. L. Rydygiera w Toruniu, Torun, Poland; ¹⁶Merck & Co., Inc., Kenilworth, NJ, USA; ¹⁷USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; ¹⁸Royal Free Hospital NHS Trust, University College London, London, UK.

Presented By: **Dr. Toni K. Choueiri**

DFS by Investigator, ITT Population

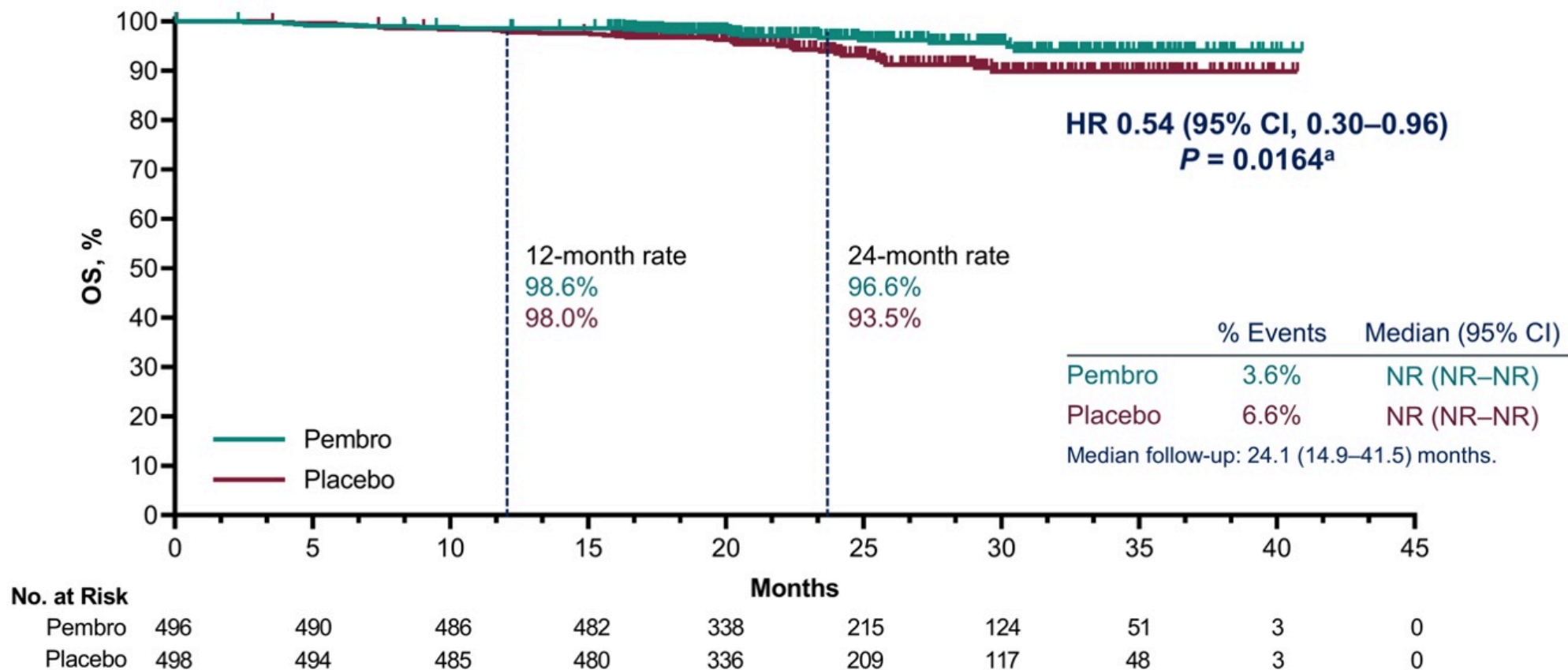


^aCrossed prespecified p-value boundary for statistical significance of 0.0114.

ITT population included all randomized participants. NR, not reached. Data cutoff date: December 14, 2020.

Presented By: Dr. Toni K. Choueiri

Interim OS Results, ITT Population



^aDid not cross prespecified p-value boundary for statistical significance of 0.0000093 for 51 events. Final analysis for OS to occur after approximately 200 OS events. ITT population included all randomized participants. NR, not reached. Data cutoff date: December 14, 2020.

Presented By: Dr. Toni K. Choueiri

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MODULE 3: Key Data Sets

MODULE 4: Other Recent Data Sets

Case Presentation — Dr Flores: A 56-year-old man with recurrence of RCC after nephrectomy

- June 2016: left radical nephrectomy for RCC
- Recurred in the renal bed; urologist excised a 10-cm retroperitoneal mass representing matted lymph nodes; appears to have a capsule
- Patient refused systemic therapy and had radiation to the renal bed

Questions

- If he agreed to systemic therapy, what would you give him at that point? How do you choose therapy for metastatic clear cell RCC: Immunotherapy doublet, single agent IO, IO plus TKI and which specific combination?
- What is your sequencing of therapy in the metastatic setting?
- What about adjuvant therapy? Can you comment on the older sunitinib data or the new pembrolizumab data?

Case Presentation — Dr Flores: A 37-year-old man with repeated kidney tumors and suspected hereditary RCC

- Referred for eosinophilia; has psoriasis
- Diagnosed with RCC at age 32 for which he underwent partial nephrectomy
- He also has had ablation of kidney tumors twice
- The patient was referred for genetic counseling

Questions

- How would you follow this patient as far as surveillance?
- Would you do a partial nephrectomy whenever feasible when he develops a recurrence, assuming that he has a hereditary syndrome?
- Would you favor radiofrequency ablation vs cryoablation vs microwave ablation?

Case Presentation — Dr Flores: A 63-year-old man with non-clear cell RCC

- PMH: ESRD on hemodialysis since 2017, CVA in 2010 without residual deficits
- Drastic 40-pound weight loss and was found to have a 5-cm left kidney mass
- Pre-op evaluation reveals pleural effusion and lung nodules, bronchoscopy with EBUS with FNA of mediastinal lymph node which showed metastatic carcinoma with oncocytic features that does not appear to be clear cell carcinoma

Questions

- How do you treat patients with non clear cell histology? What is your sequencing of treatment?
- Is there a role for nephrectomy in metastatic RCC, or is this a thing of the past in view of the new therapies? Do you put value to the old data of prolongation of survival with the use of nephrectomy?

Case Presentation (12-3-20) — Dr Flores: A 78-year-old man with newly diagnosed mRCC

- PMH: HTN, DM CKD, melanoma in situ, and gross hematuria
- Bilateral renal cyst L kidney with a complex mass and has bilateral lung nodules, indeterminate 1.8-cm liver nodule
- Non-diagnostic liver biopsy and L nephrectomy; pathology shows clear cell RCC with nuclear Gr 3 extensive lymphovascular invasion and IVC thrombus

Questions

- What treatment will you offer and why? Immunotherapy combination vs pembrolizumab/axitinib?

Case Presentation (12-3-20) — Dr Flores: A 78-year-old man with newly diagnosed mRCC (recent follow-up)

- He had a drop in his performance status and had a hard time recovering after the nephrectomy, and he decided that he does not want further treatment and went with hospice

Case Presentation (12-3-20) — Dr Flores: A 61-year-old man with newly diagnosed mRCC and hypercalcemia

- Hematuria which was self limiting
- Right renal mass 8.4 x 7.2 cm
- Chest CT showed bilateral pulmonary nodules
- In the process of being worked up, he developed a TIA and was noted to be hypercalcemic

Question

- Does nephrectomy still have a role in metastatic RCC in the absence of any significant hematuria?

Case Presentation (12-3-20) — Dr Flores: A 61-year-old man with newly diagnosed mRCC and hypercalcemia (recent follow-up)

- CVA after his nephrectomy and has been in rehab but has been stable and pursued further treatment.
- I gave him nivolumab/ipilimumab, but I had to stop IO due to liver toxicity after the third cycle. I treated him with prednisone and this has been tapered off.
- His calcium and LFTs are now normal and he is on nivolumab alone, which was re-introduced after 2 months of being off treatment, and he has had a partial response.

Agenda

MODULE 1: Cases from the Practice of Dr Flores

- A 56-year-old man with recurrence of renal cell carcinoma (RCC) after nephrectomy
- A 37-year-old man with repeated kidney tumors and suspected hereditary RCC
- A 63-year-old man with non-clear cell RCC
- A 78-year-old man with newly diagnosed metastatic RCC (mRCC)
- A 61-year-old man with newly diagnosed mRCC and hypercalcemia

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

MODULE 3: Key Data Sets

MODULE 4: 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 Flores

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

MODULE 3: Key Data Sets

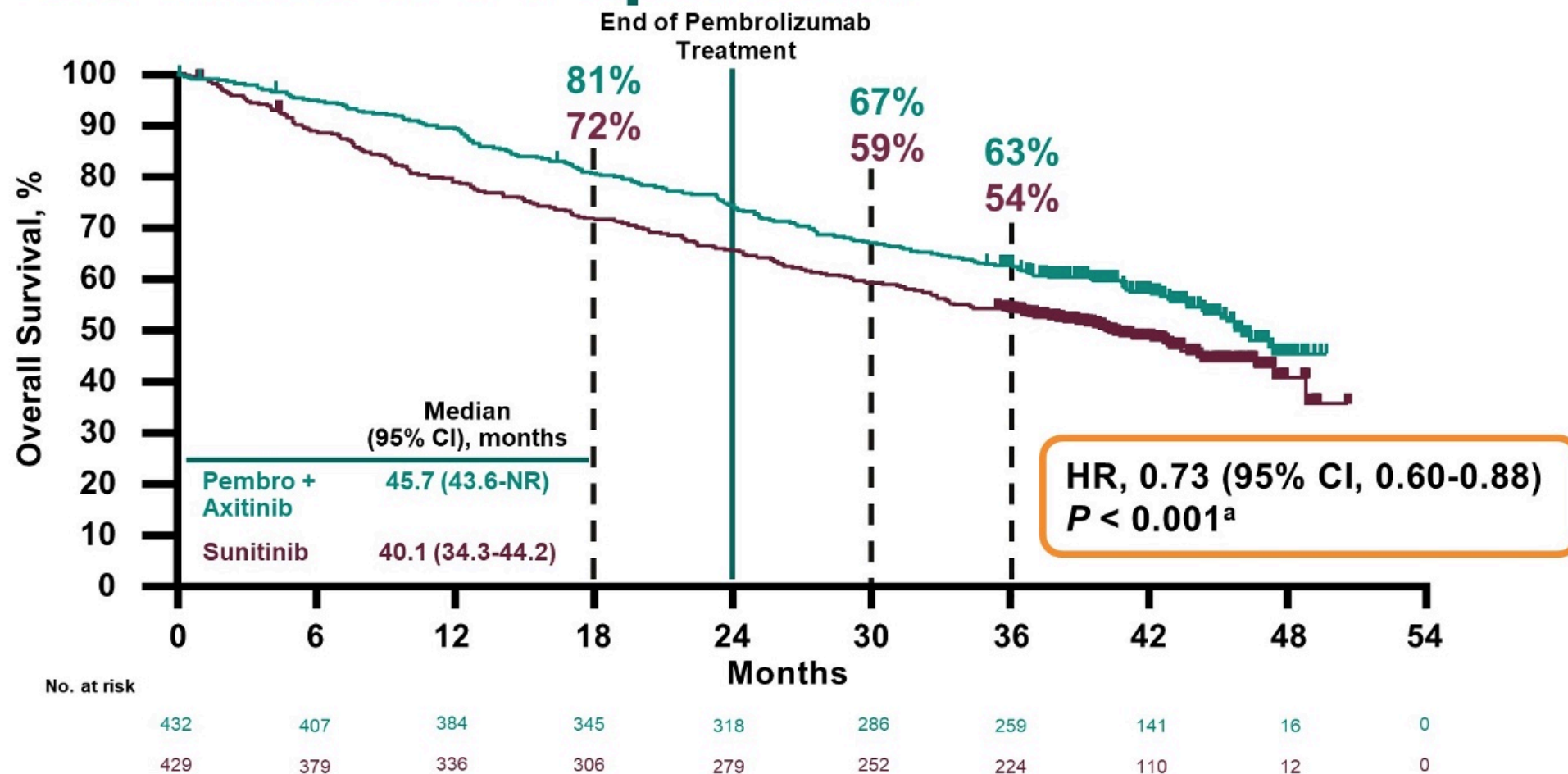
MODULE 4: Other Recent Data Sets

Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

B. I. Rini¹; E. R. Plimack²; V. Stus³; T. Waddell⁴; R. Gafanov⁵; F. Pouliot⁶; D. Nosov⁷; B. Melichar⁸; D. Soulieres⁹; D. Borchellini¹⁰; I. Vynnychenko¹¹; R. S. McDermott¹²; S. J. Azevedo¹³; S. Tamada¹⁴; A. Kryzhanivska¹⁵; C. Li¹⁶; J. E. Burgents¹⁶; L. R. Molife¹⁷; J. Bedke¹⁸; T. Powles¹⁹

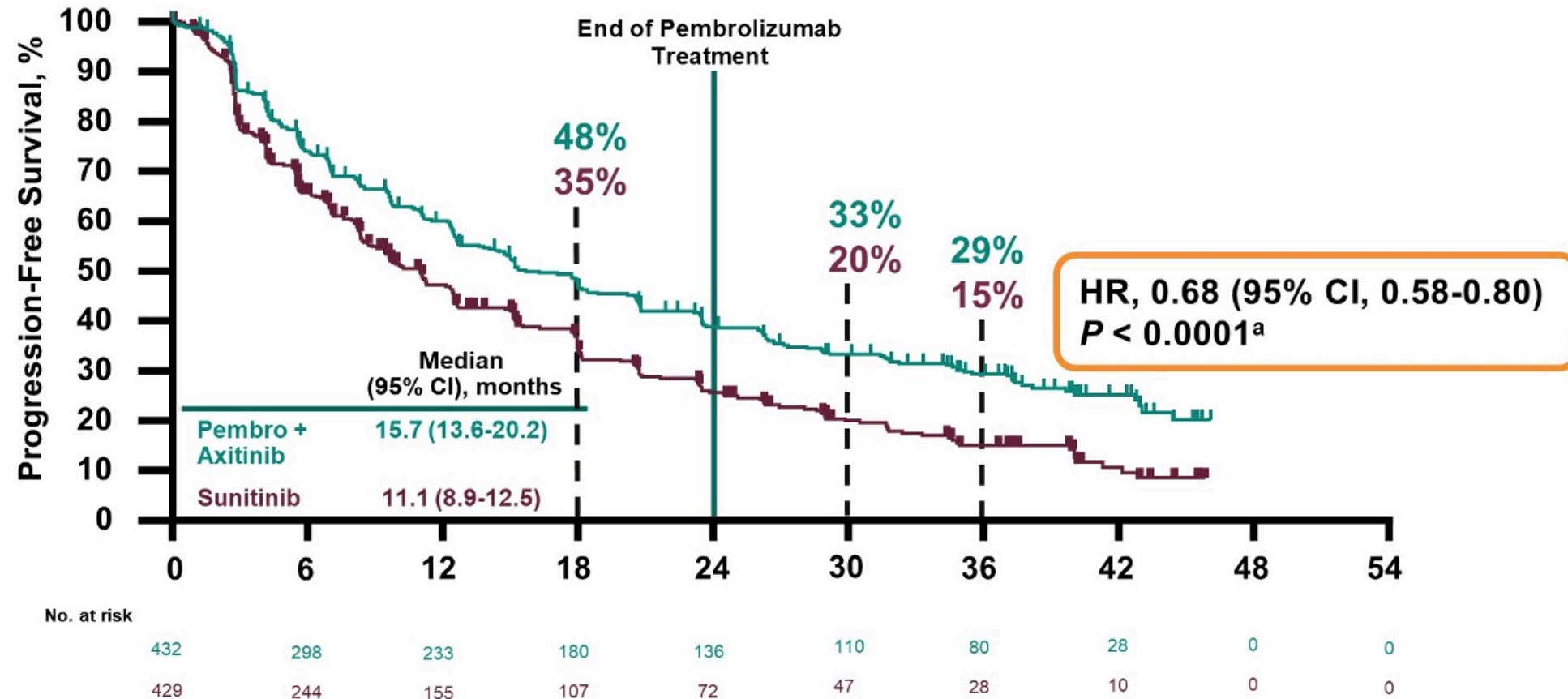
¹Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; ²Fox Chase Cancer Center, Philadelphia, PA, USA; ³Dnipropetrovsk Medical Academy of Ministry of Health of Ukraine, Dnipro, Ukraine; ⁴The Christie NHS Foundation Trust, Manchester, United Kingdom; ⁵Russian Scientific Center of Roentgenoradiology, Moscow, Russia; ⁶CHU of Québec and Laval University, Québec City, QC, Canada; ⁷Central Clinical Hospital With Outpatient Clinic, Moscow, Russia; ⁸Palacky University Medical School and Teaching Hospital, Olomouc, Czech Republic; ⁹Centre Hospitalier de l'Universitaire de Montréal, Montréal, QC, Canada; ¹⁰Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; ¹¹Sumy State University, Sumy Regional Oncology Center, Sumy, Ukraine; ¹²Adelaide and Meath Hospital and University College Dublin, Dublin, Ireland; ¹³Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; ¹⁴Osaka City University Hospital, Osaka, Japan; ¹⁵Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine; ¹⁶Merck & Co., Inc., Kenilworth, NJ, USA; ¹⁷MSD UK, London, United Kingdom; ¹⁸Eberhard Karls Universität Tübingen, Tübingen, Germany; ¹⁹Barts Health NHS Trust and the Royal Free NHS Foundation Trust, Barts Cancer Institute, and Queen Mary University of London, London, United Kingdom

OS in the ITT Population



^aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to OS; only nominal *P* values are reported. Data cutoff: January 11, 2021.

PFS in the ITT Population



^aBecause superiority of pembrolizumab + axitinib was shown at the first interim analysis, no alpha was allocated to PFS; only nominal P values are reported. Data cutoff: January 11, 2021.


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	83% vs. 78%	90% vs. 79%	87% vs. 78% (est)	90% vs 79% (est.)
Landmark OS 24 mo	71% vs. 61%	74% vs. 66%	74% vs 60% (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	23	32	23	31
Intermediate	61	55	58	59
Poor	17	13	19	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....

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);			
Landmark OS 12 mo	83% vs. 78%			
Landmark OS 24 mo	71% vs. 61%			
mPFS, months HR (CI)	12.2 vs 12.3 0.89 (0.76–1.05)			
ORR, %	39 vs 32			
CR, %	11 vs 3			
Med f/u, months	55			
Prognostic risk, %				
Favorable	23			
Intermediate	61			
Poor	17			
Prior nephrectomy	82%			
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)			



Please handle with care....

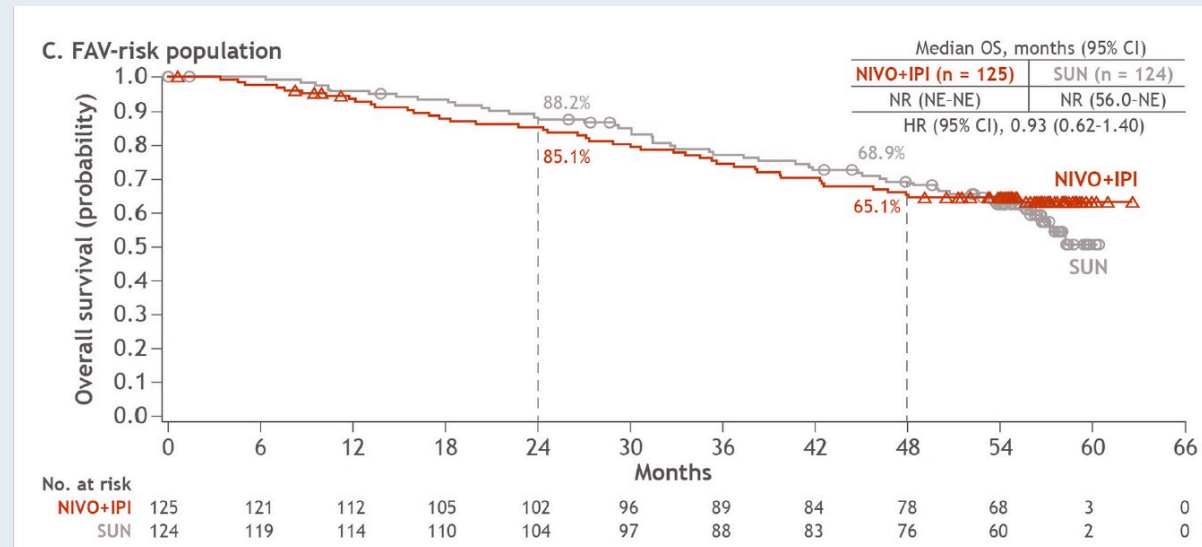
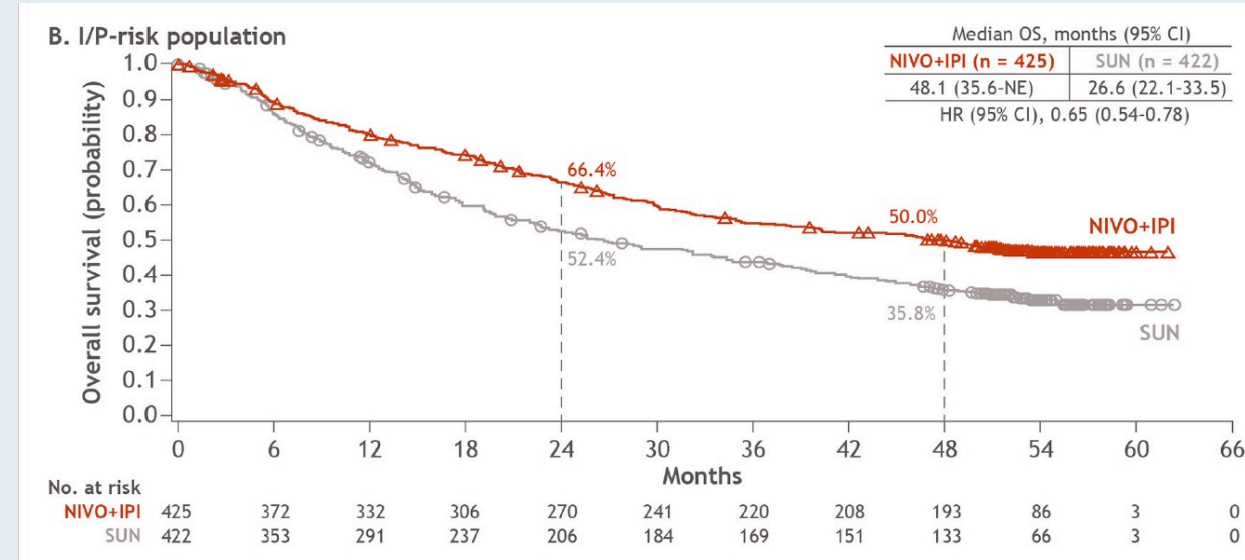
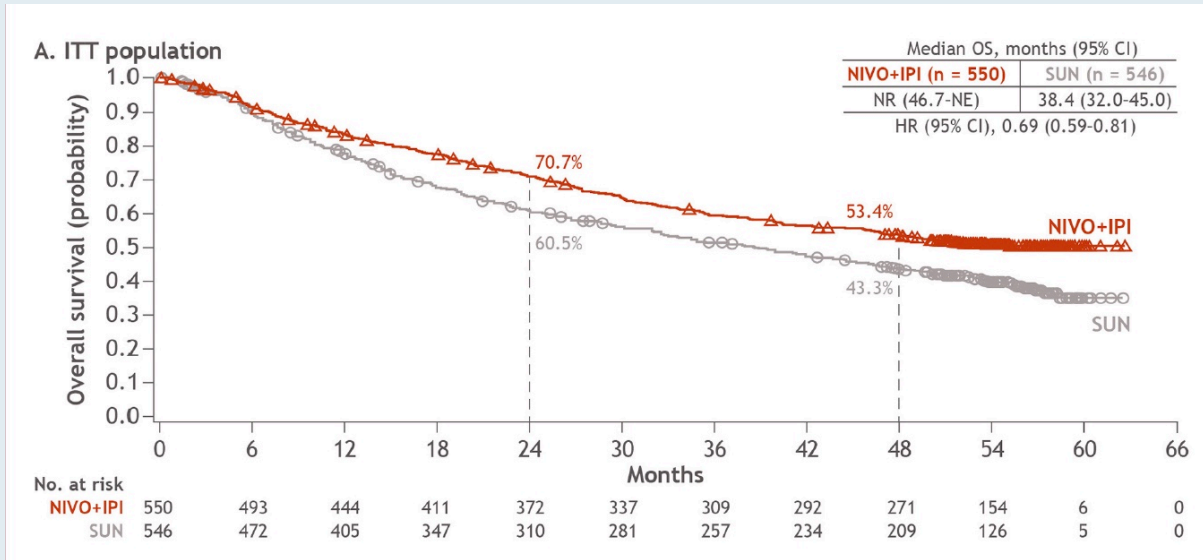


Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial

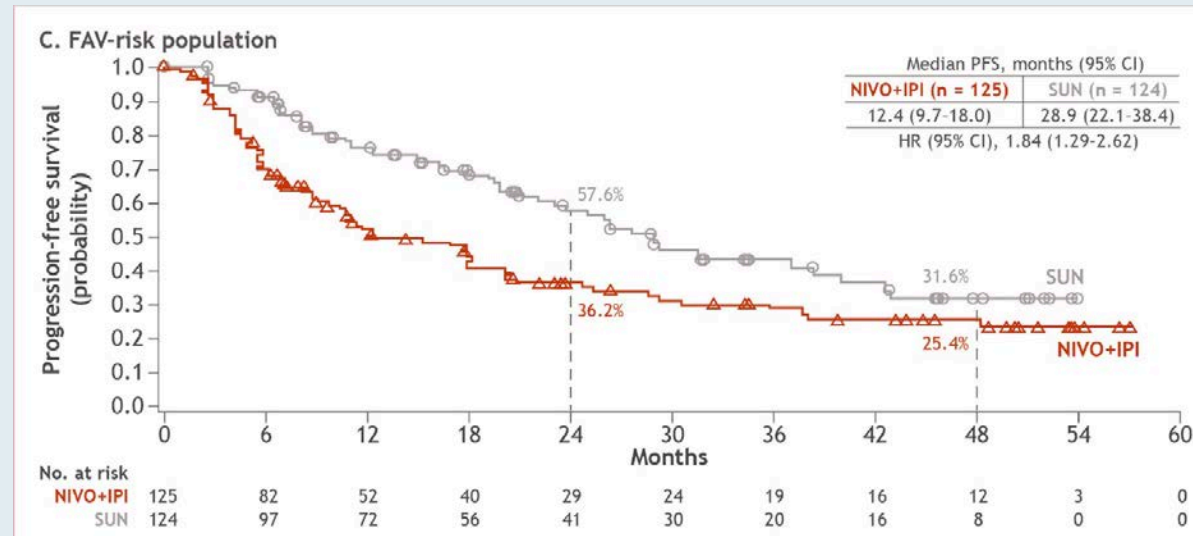
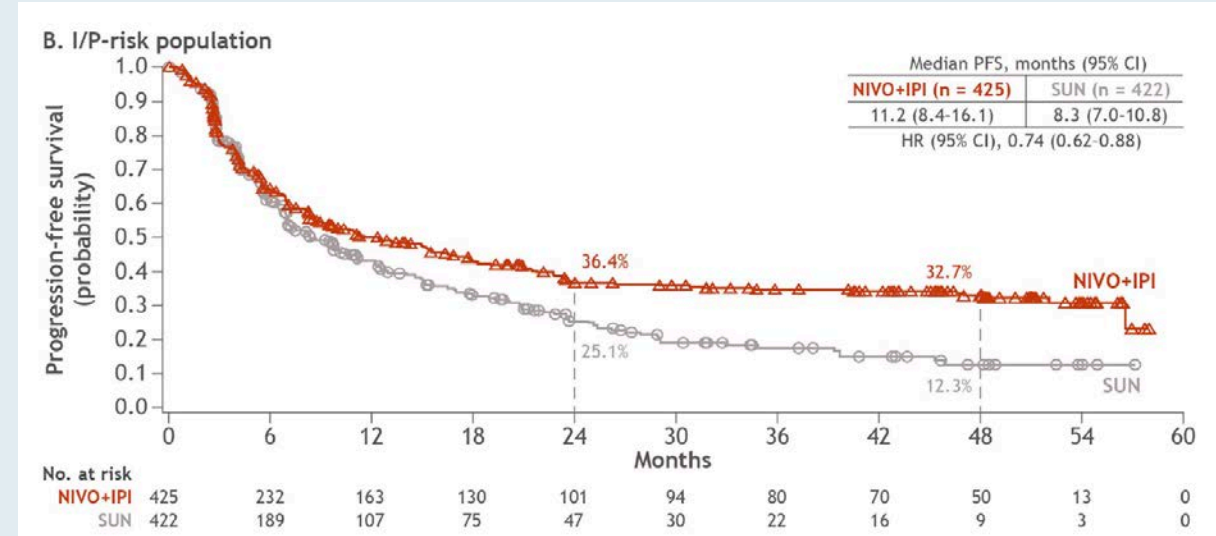
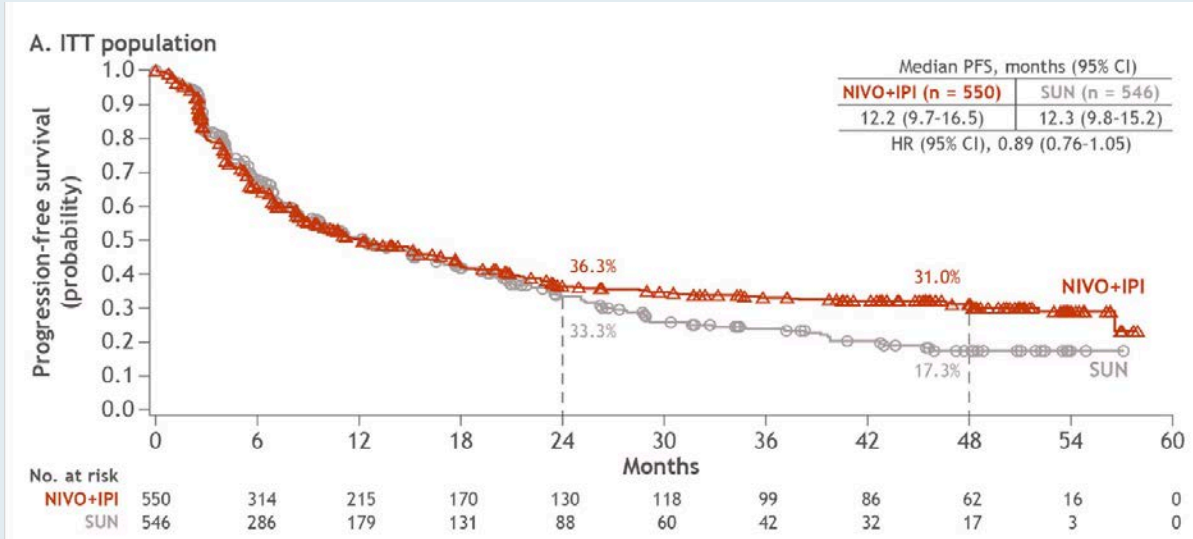
Laurence Albiges ¹, Nizar M Tannir,² Mauricio Burotto,³ David McDermott,^{4,5} Elizabeth R Plimack,⁶ Philippe Barthélémy,^{7,8} Camillo Porta ⁹, Thomas Powles,^{10,11} Frede Donskov,¹² Saby George,¹³ Christian K Kollmannsberger,¹⁴ Howard Gurney,^{15,16} Marc-Oliver Grimm,¹⁷ Yoshihiko Tomita,¹⁸ Daniel Castellano,¹⁹ Brian I Rini,²⁰ Toni K Choueiri,²¹ Shruti Shally Saggi,²² M Brent McHenry,²³ Robert J Motzer²⁴

ESMO Open 2020;5(6):e001079

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



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



FDA Approves Nivolumab with Cabozantinib for Advanced RCC

Press Release: January 22, 2021

“On January 22, 2021, the Food and Drug Administration approved the combination of nivolumab and cabozantinib as first-line treatment for patients with advanced renal cell carcinoma (RCC).

Efficacy was evaluated in CHECKMATE-9ER (NCT03141177), a randomized, open-label trial in patients with previously untreated advanced RCC. Patients were randomized to receive either nivolumab 240 mg over 30 minutes every 2 weeks in combination with cabozantinib 40 mg orally once daily (n=323) or sunitinib 50 mg orally daily for the first 4 weeks of a 6-week cycle (4 weeks on treatment followed by 2 weeks off) (n=328).”

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

The NEW ENGLAND JOURNAL of MEDICINE

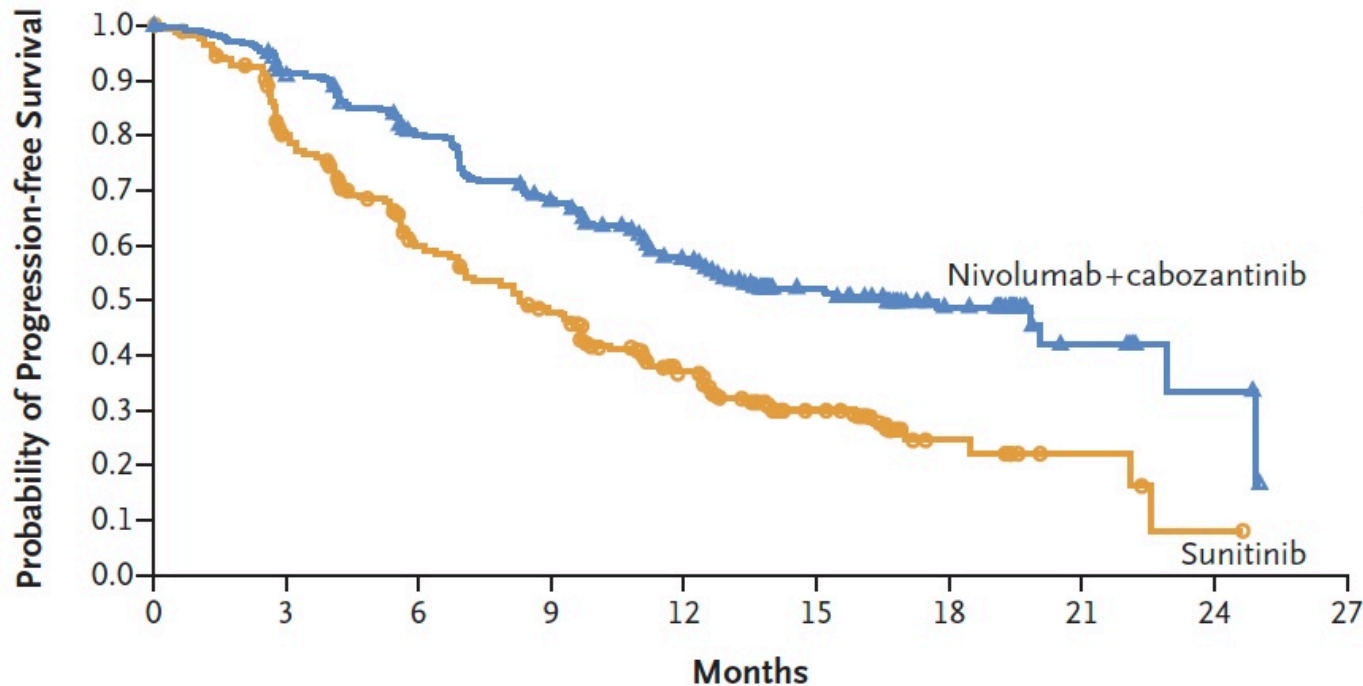
ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bours, 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. Żołnierak, 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

A Progression-free Survival



	No. of Patients	Median (95% CI) mo
Nivolumab+ Cabozantinib	323	16.6 (12.5–24.9)
Sunitinib	328	8.3 (7.0–9.7)

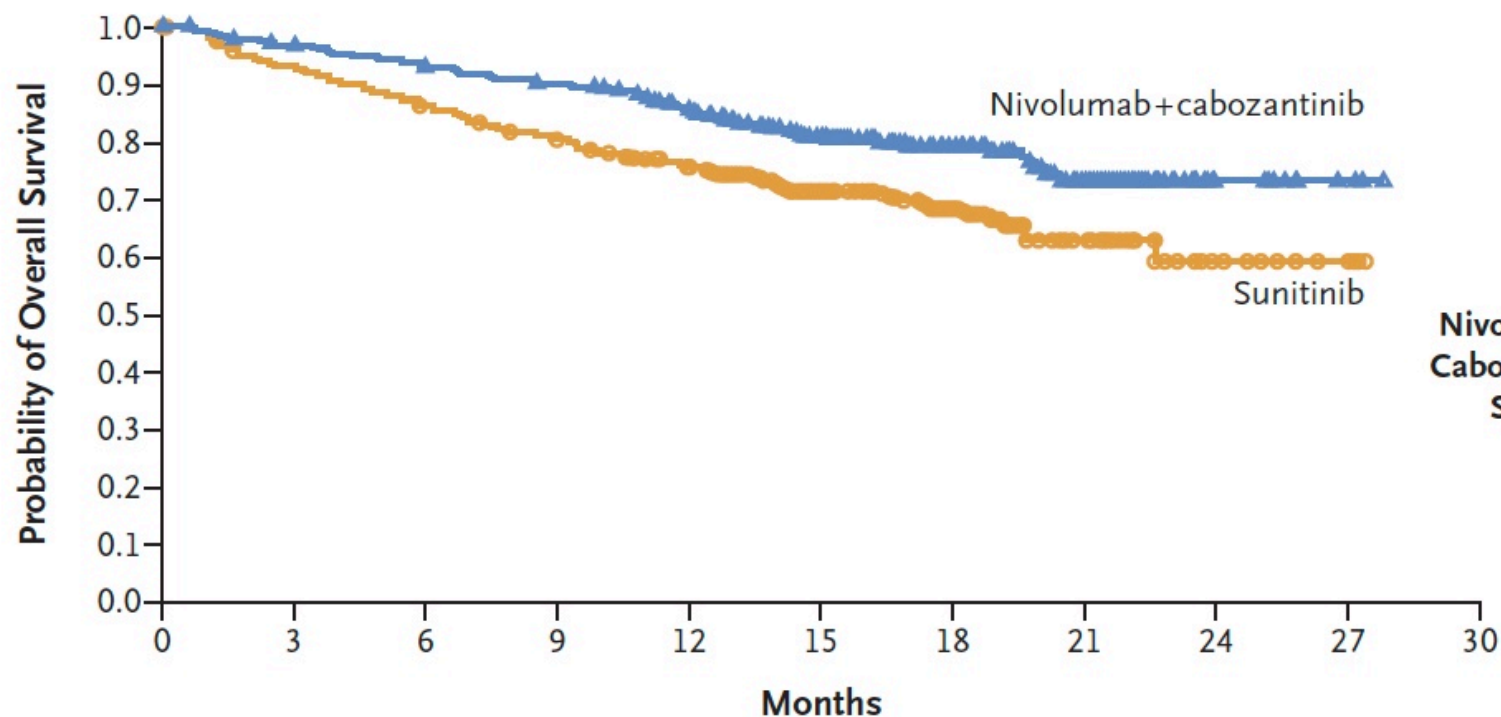
Hazard ratio for disease progression or death, 0.51 (95% CI, 0.41–0.64)
P<0.001

No. at Risk

Nivolumab+cabozantinib	323	279	234	196	144	77	35	11	4	0
Sunitinib	328	228	159	122	79	31	10	4	1	0

Overall Survival in the Intention-to-Treat Population

B Overall Survival



	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

No. at Risk

Nivolumab+cabozantinib	323	308	295	283	259	184	106	55	11	3	0
Sunitinib	328	296	273	253	223	154	83	36	10	3	0

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

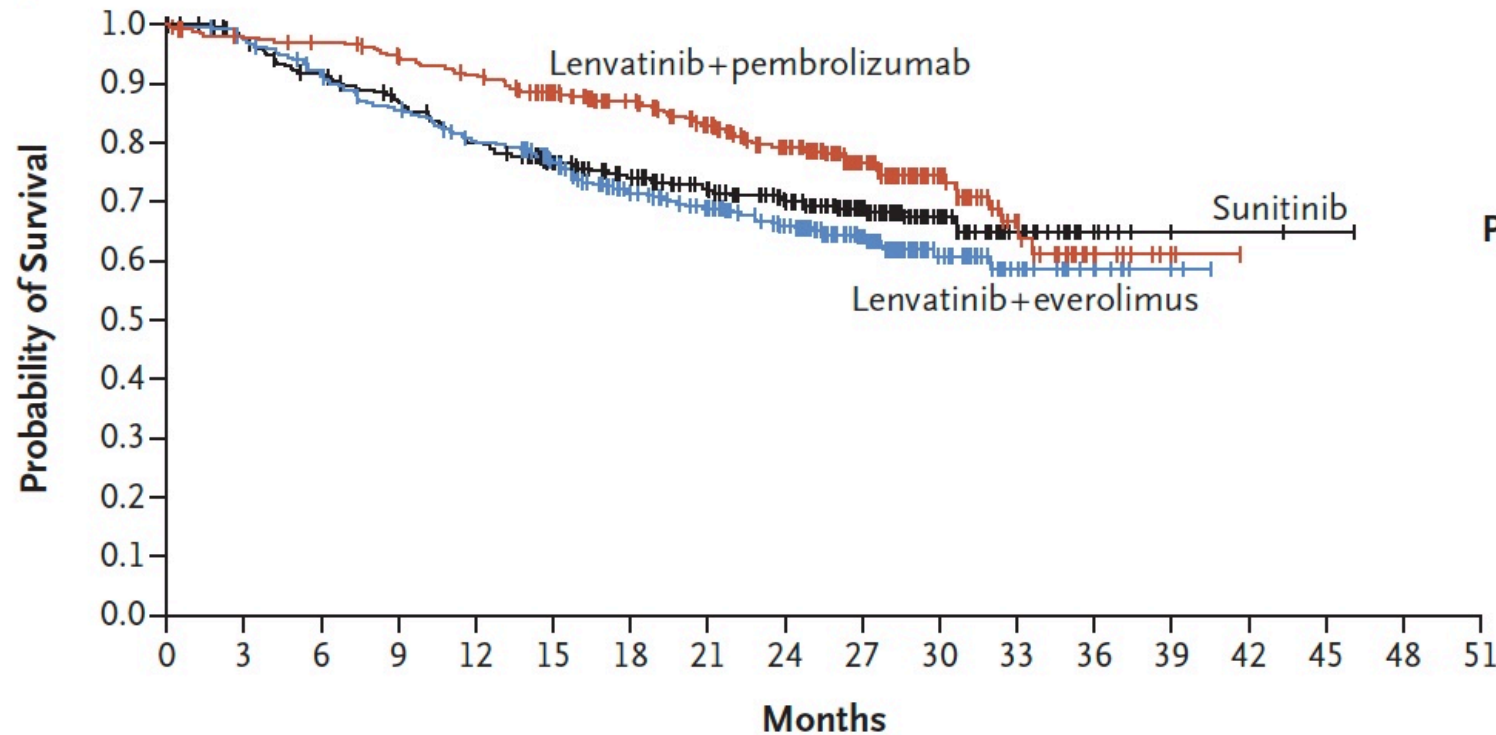
The NEW ENGLAND JOURNAL of MEDICINE

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 Gordo, J.R. Merchan, E. Winkquist, 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



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

Median Overall Survival (95% CI)

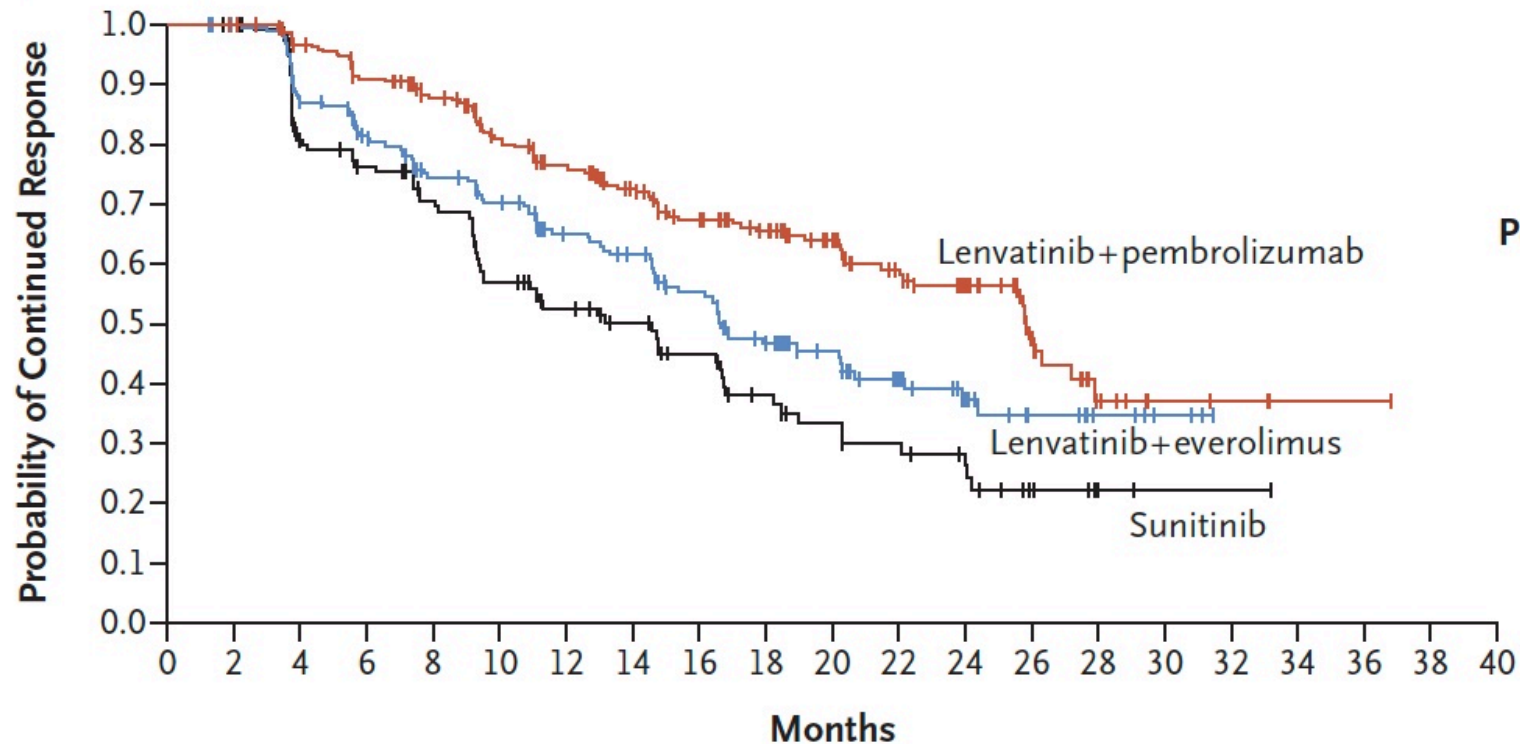
mo

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

Kaplan-Meier Analysis of Response Duration



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		

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)

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

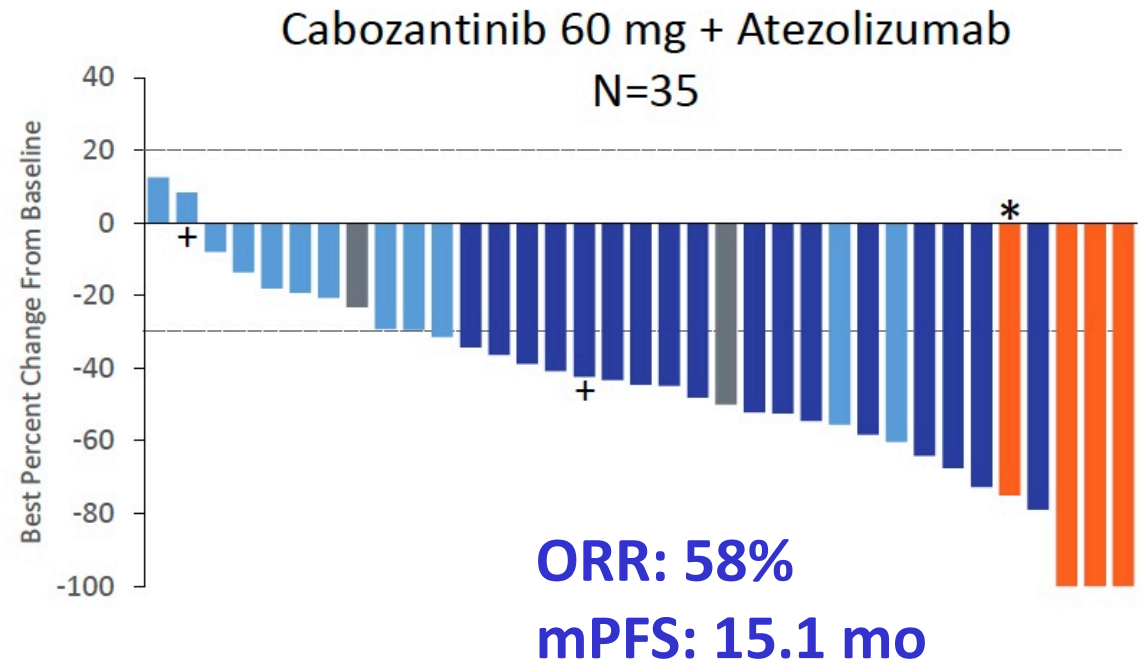
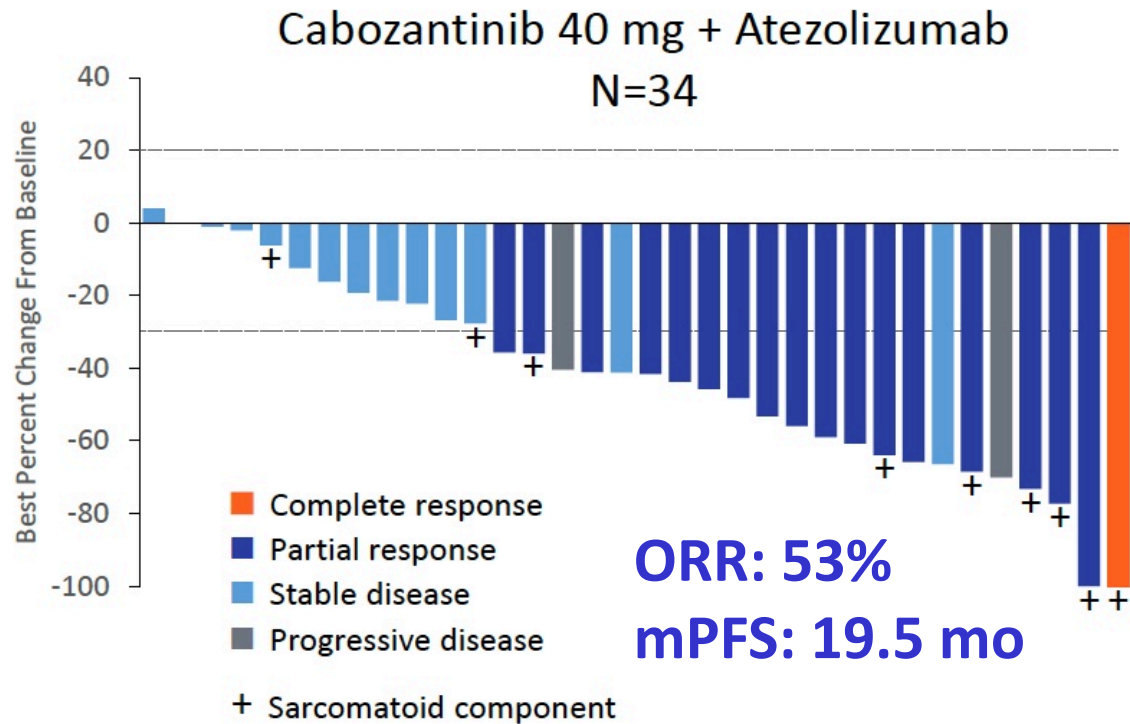
Event	Lenvatinib plus Pembrolizumab (N = 352)		Lenvatinib plus Everolimus (N = 355)		Sunitinib (N = 340)	
	Any Grade	Grade ≥ 3 [†]	Any Grade	Grade ≥ 3 [†]	Any Grade	Grade ≥ 3 [†]
	<i>number of patients (percent)</i>					
Any event	351 (99.7)	290 (82.4)	354 (99.7)	295 (83.1)	335 (98.5)	244 (71.8)
Diarrhea	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)

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 7020.

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



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	<ul style="list-style-type: none"> Cabozantinib + nivolumab + ipilimumab (4 doses) → cabozantinib + nivolumab Placebo + nivolumab + ipilimumab (4 doses) → placebo + nivolumab 	PFS	Nov 2021
PDIGREE	1,046	After Induction nivolumab/ipilimumab <ul style="list-style-type: none"> Pts with CR → Nivolumab <ul style="list-style-type: none"> Pts with non-CR or non-PD, <i>randomized</i> <ul style="list-style-type: none"> → 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.

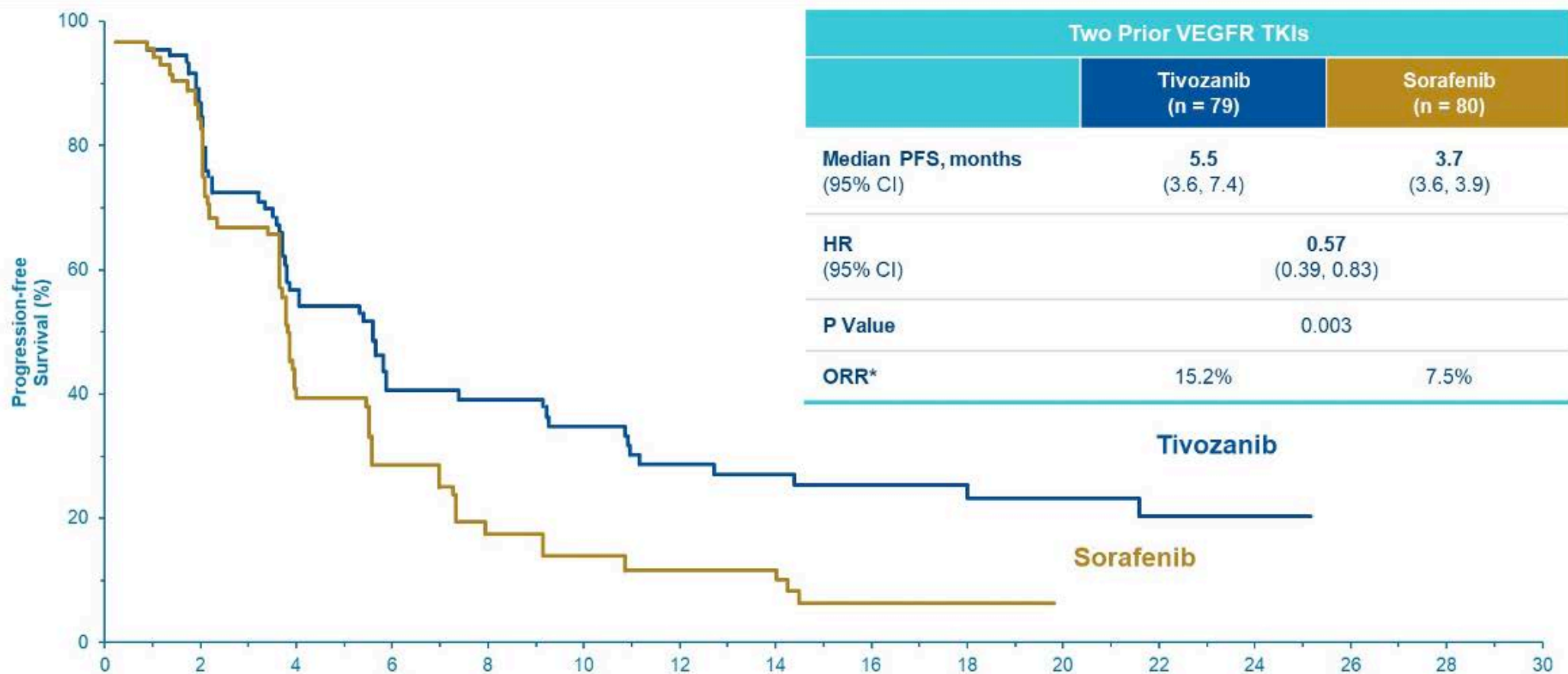
The recommended tivozanib dose is 1.34 mg once daily (with or without food) for 21 consecutive days every 28 days until disease progression or unacceptable toxicity.”

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



Tivozanib

Sorafenib

TIVO-3: Tivozanib After Axitinib

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

TIVO-3: Durability of Response and Updated Overall Survival of Tivozanib versus Sorafenib in Metastatic Renal Cell Carcinoma (mRCC)

Verzoni et al.

ASCO 2021;Abstract 4546.

“Tivozanib demonstrated clinically meaningful and statistically significant improvement in ORR and DoR with similar OS to sorafenib in patients with highly relapsed or refractory mRCC”

- *Median DoR was 20.3 months with tivozanib, twice that observed with sorafenib*

Lancet 2021;397:695-703

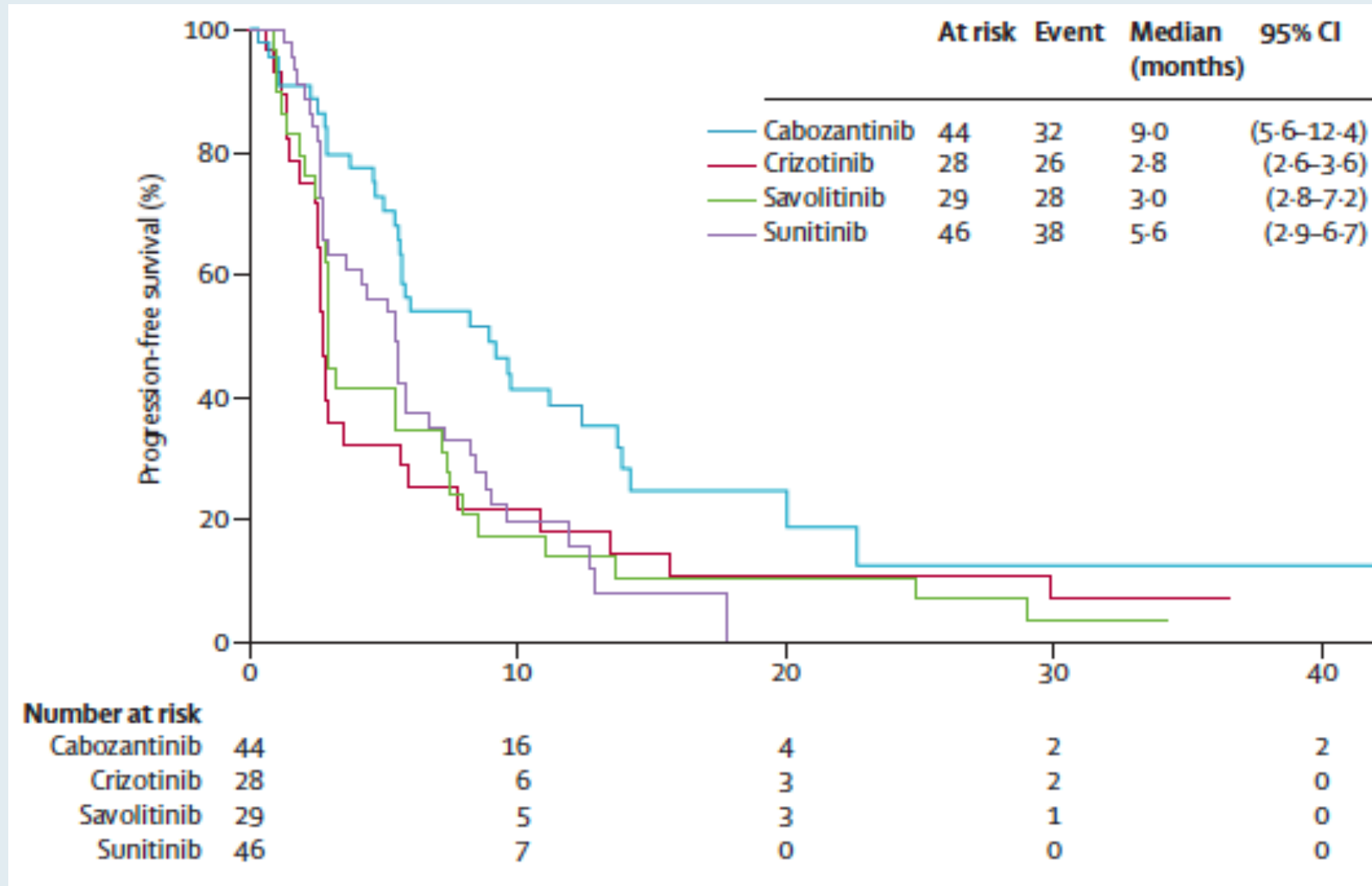
Articles

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

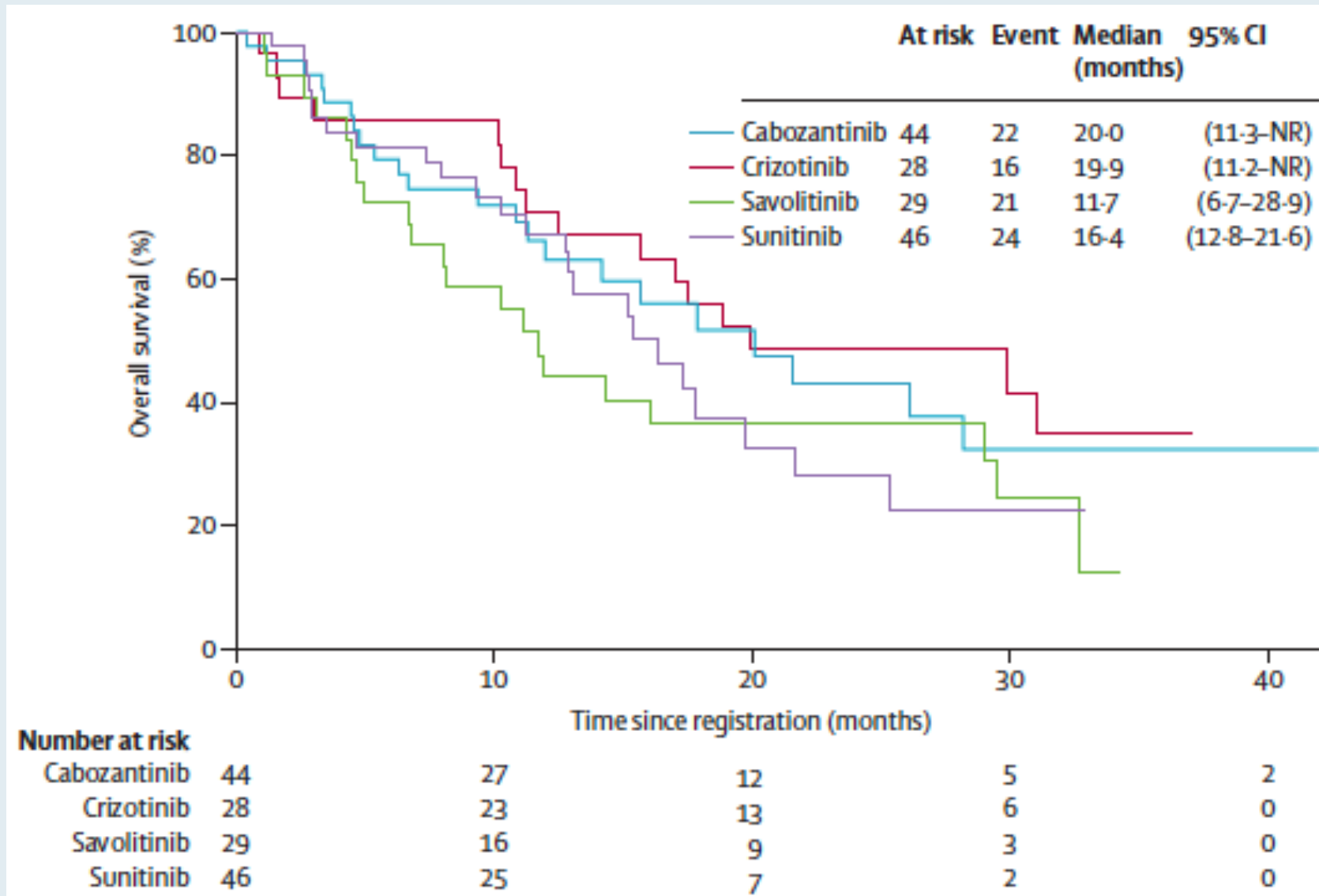


Sumanta K Pal, Catherine Tangen, Ian M Thompson Jr, Naomi Balzer-Haas, Daniel J George, Daniel Y C Heng, Brian Shuch, Mark Stein, Maria Tretiakova, Peter Humphrey, Adebowale Adeniran, Vivek Narayan, Georg A Bjarnason, Ulka Vaishampayan, Ajjai Alva, Tian Zhang, Scott Cole, Melissa Plets, John Wright,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

Kaplan-Meier Analysis of Progression-Free Survival



Kaplan-Meier Analysis of Overall Survival



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...

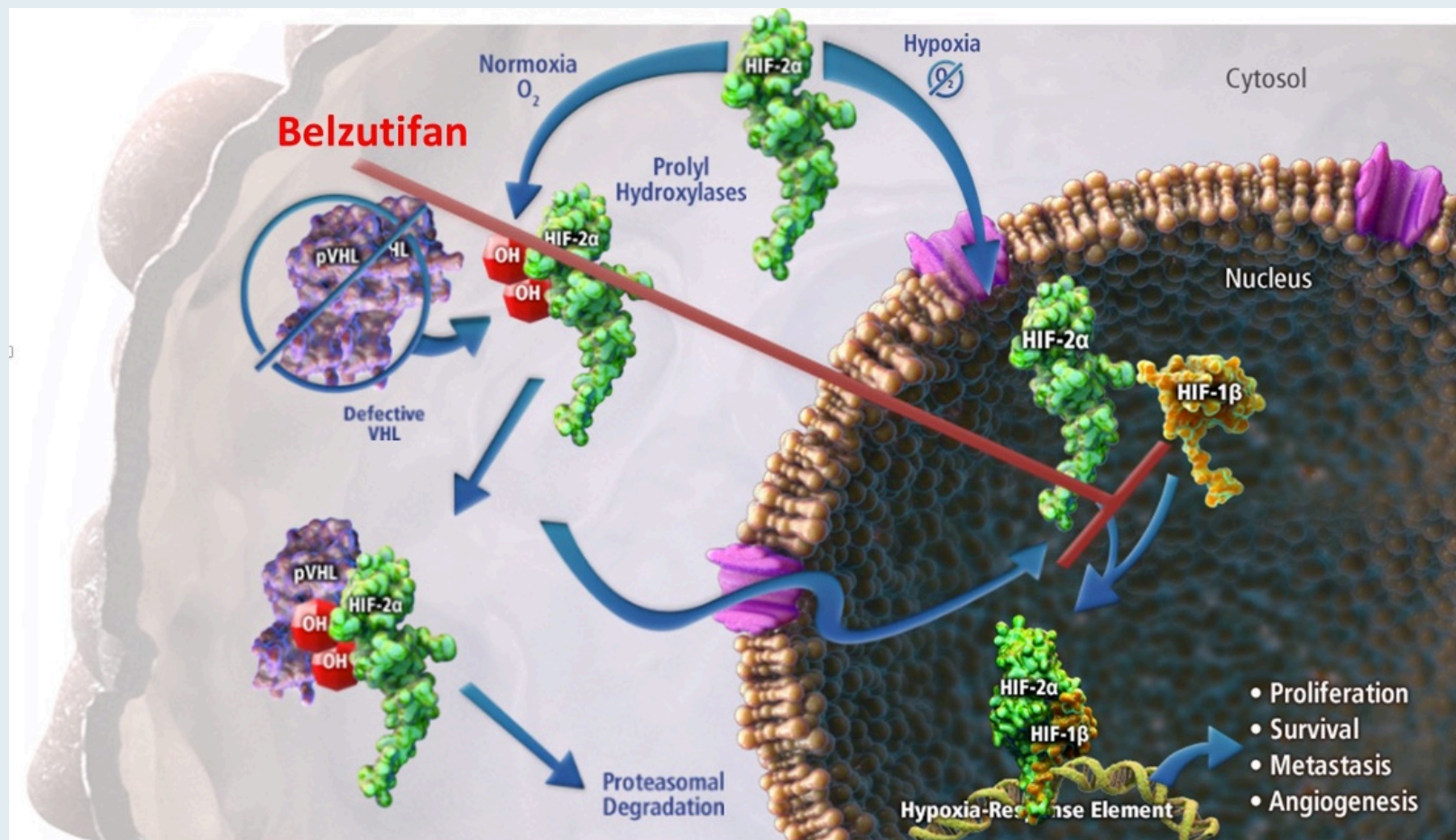
The application is based on results of a phase 2 trial, Study-004 (NCT03401788), of belzutifan in the treatment of VHL disease-associated RCC, with a primary end point of objective response rate and secondary measures of disease control rate, duration of response, time to response, progression-free survival, 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.”

The Oral HIF-2 α 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 Jonasch¹⁰

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

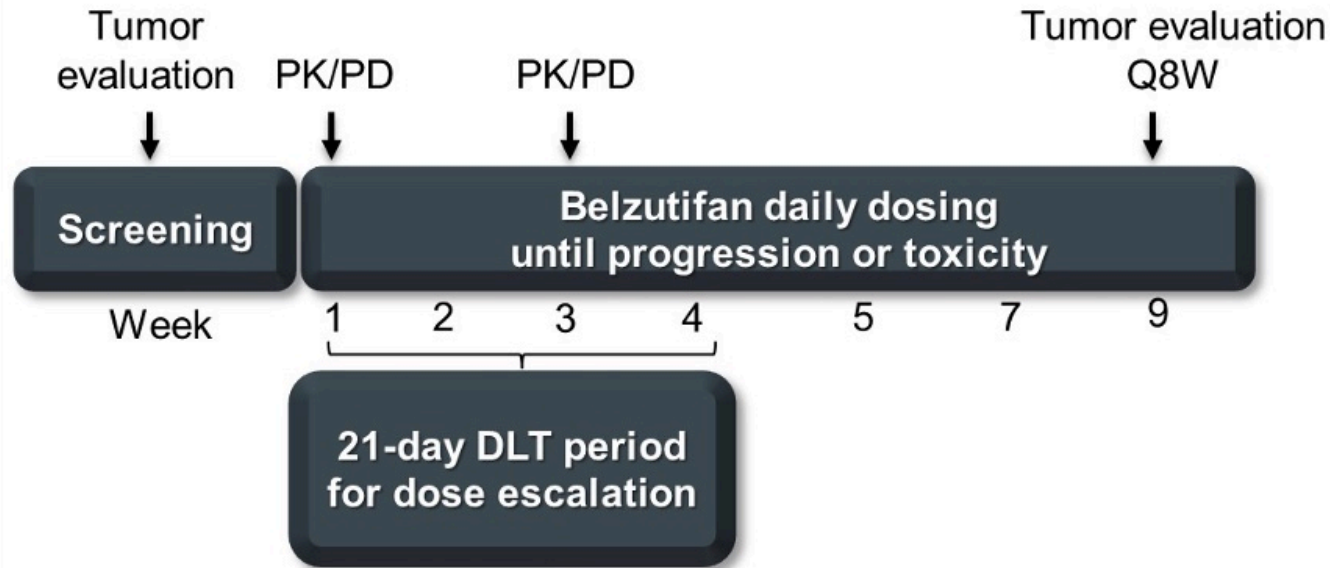
pVHL Deficiency Results in HIF-2-alpha Activation



- 90% of patients with sporadic ccRCC have defective pVHL function¹
- Loss of pVHL function results in constitutive activation of HIF-2α²
- 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.

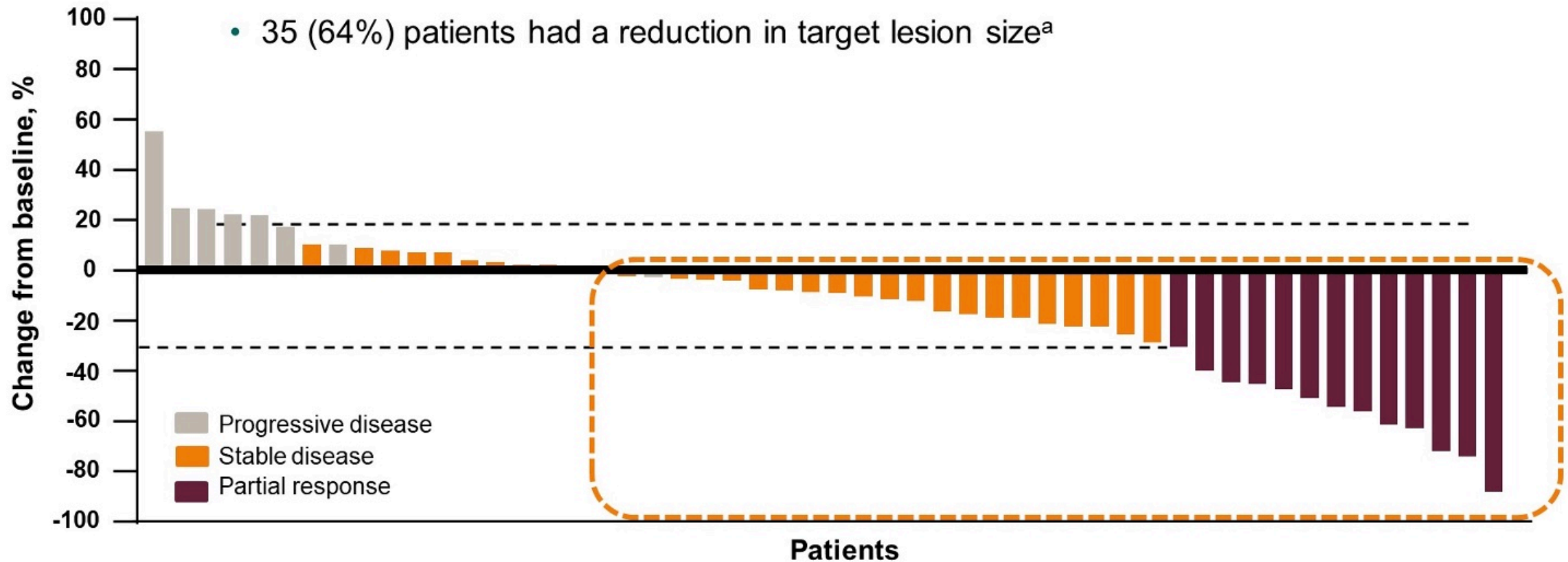
Study Design



- 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

- 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

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



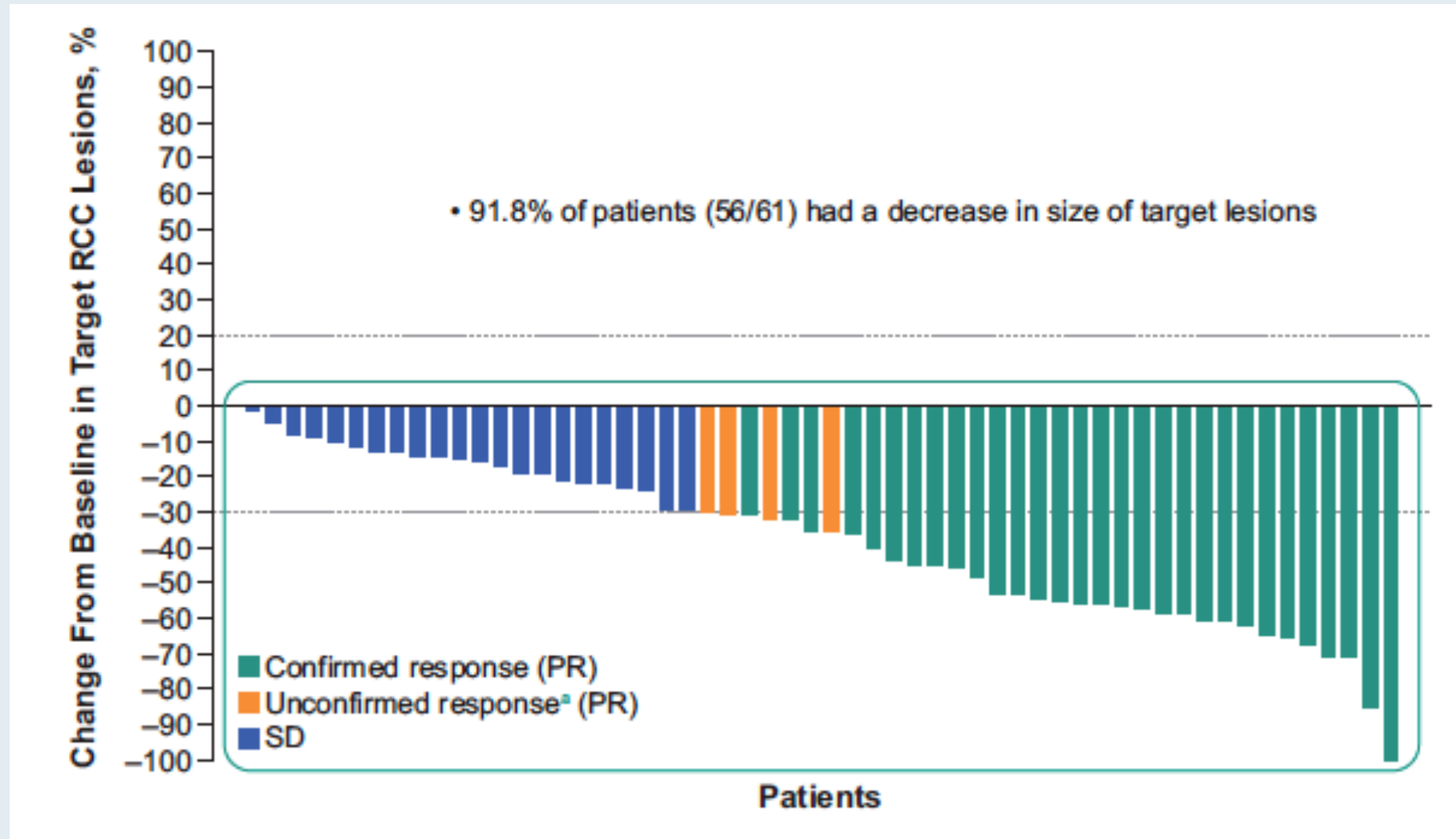
^a3 patients were nonevaluable. Data cutoff: June 1, 2020.

Phase 2 Study of Belzutifan (MK-6482), an Oral Hypoxia-Inducible Factor 2 α (HIF-2 α) Inhibitor, for Von Hippel-Lindau (VHL) Disease-Associated Clear Cell Renal Cell Carcinoma (ccRCC)

Srinivasan R et al.

ASCO 2021;Abstract 4555.

Maximum Change from Baseline in Sum of Target RCC Lesions



Genitourinary Cancers Symposium 2021;Abstract 272.

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

Toni K. Choueiri¹; Todd M. Bauer²; David F. McDermott³; Edward Arrowsmith⁴; Ananya Roy⁵; Rodolfo Perini⁵; Donna Vickery⁵; Scott S. Tykodi⁶

¹Dana-Farber Cancer Institute, Boston, MA, USA; ²Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA;

³Beth Israel Deaconess Medical Center, Boston, MA, USA; ⁴Tennessee Oncology, Chattanooga, TN, USA;

⁵Merck & Co., Inc., Kenilworth, NJ, USA; ⁶University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Study Design

Key Eligibility Criteria

- Advanced or metastatic ccRCC
- Either treatment naive or has received prior PD-1/L1 immunotherapy and ≤ 2 regimens for locally advanced or metastatic RCC
- ECOG PS 0 or 1

Cohort 1:
Treatment-naïve
belzutifan 120 mg/day +
cabozantinib 60 mg/day
N \approx 50

Cohort 2:
Prior immunotherapy treatment
belzutifan 120 mg/day +
cabozantinib 60 mg/day
N \approx 50

Safety and tolerability were evaluated in the first 6 participants enrolled, irrespective of cohort

- If tolerability was established, enrollment continued
- If tolerability was not established, dose was reviewed

Assessments

- Q8W after week 9 for 12 months and then Q12W thereafter

Posttreatment

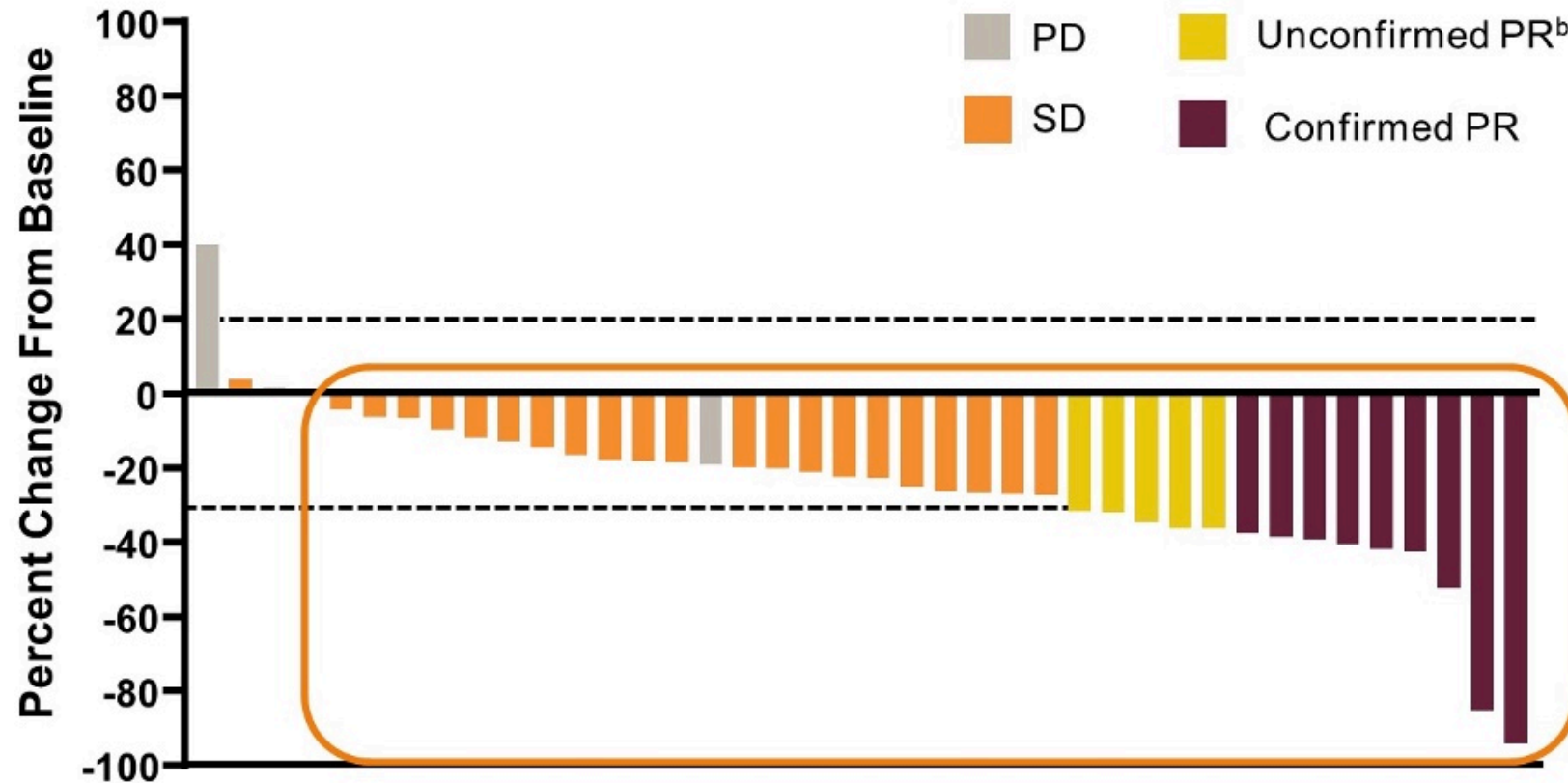
- 28-day safety follow-up
- Follow-up visits every 6 months

End Points

- Primary: ORR
- Secondary: PFS, TTR, DOR, OS, safety/ tolerability, PK/PD

Best Tumor Change from Baseline

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



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)

^aAll 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)

Agenda

MODULE 1: Cases from the Practice of Dr Flores

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

MODULE 3: Key Data Sets

MODULE 4: Other Recent Data Sets

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. Motzer², B. I. Rini^{3†}, J. Haanen⁴, M. T. Campbell⁵, B. Venugopal⁶, C. Kollmannsberger⁷, G. Gravis-Mescam⁸, M. Uemura⁹, J. L. Lee¹⁰, M.-O. Grimm¹¹, H. Gurney¹², M. Schmidinger¹³, J. Larkin¹⁴, M. B. Atkins¹⁵, S. K. Pal¹⁶, J. Wang¹⁷, M. Mariani¹⁸, S. Krishnaswami¹⁹, P. Cislo²⁰, A. Chudnovsky²¹, C. Fowst¹⁸, B. Huang¹⁹, A. di Pietro²² & L. Albiges²³

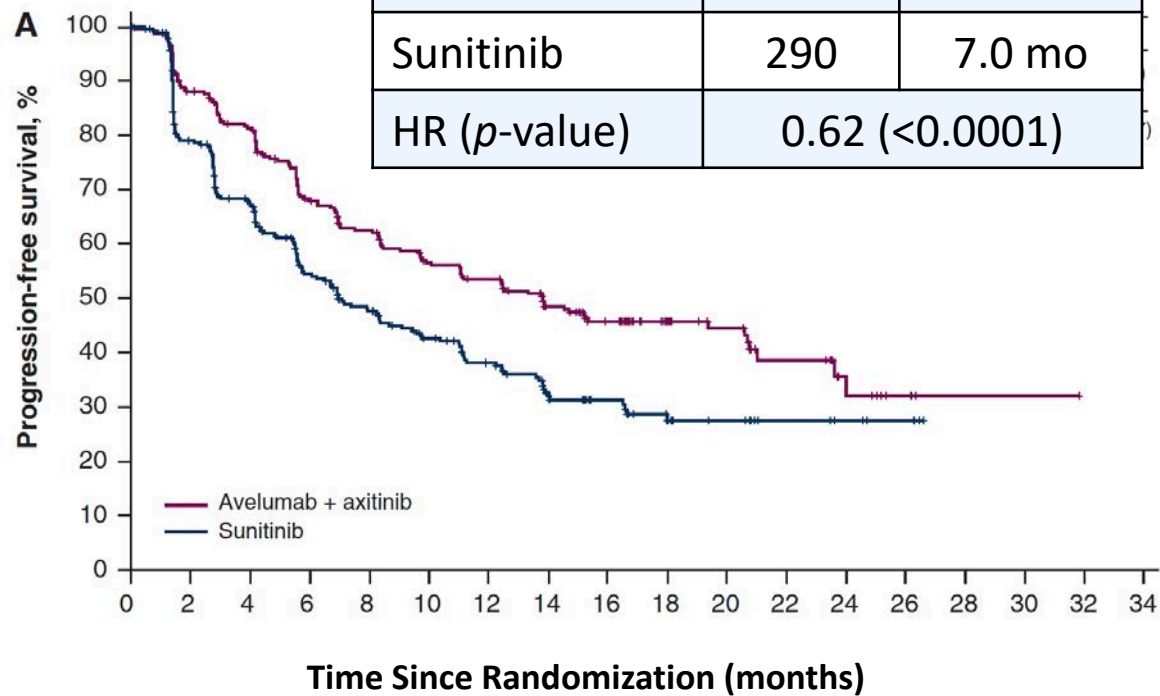
JAVELIN Renal 101: Overall Response and Best Response Rate in the PD-L1-Positive and Overall Populations

	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%

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

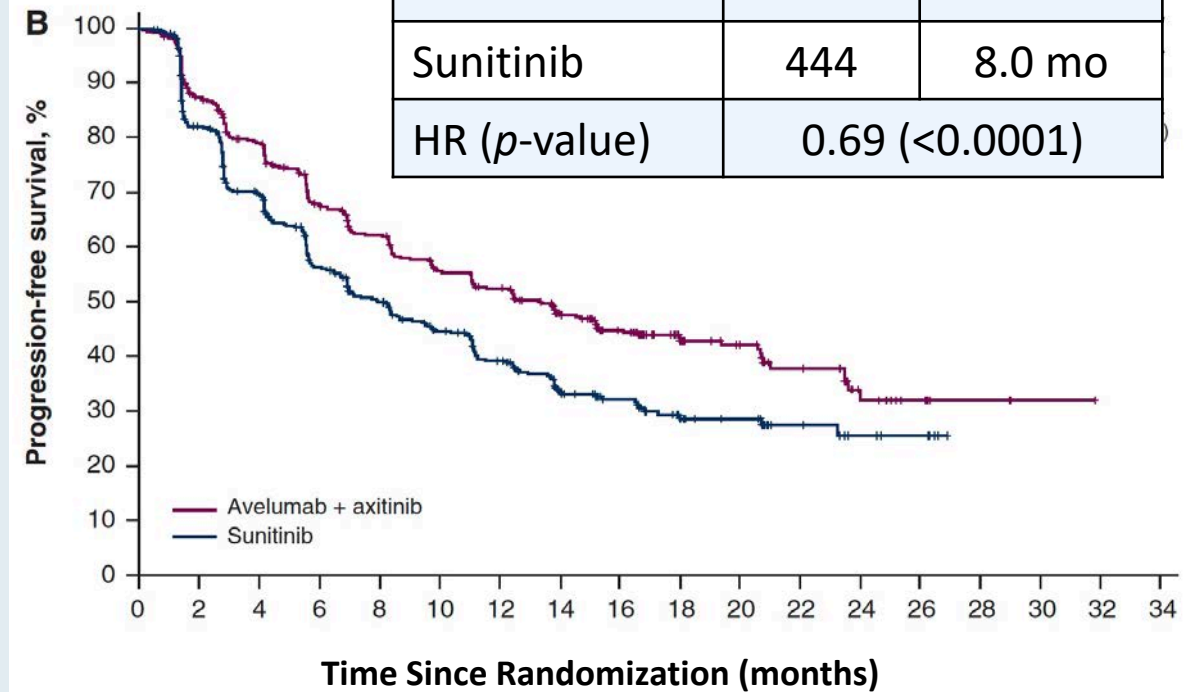
PD-L1 $\geq 1\%$ Population

	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)	



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

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

Anita Gul, MD¹; Tyler F. Stewart, MD^{2,3}; Charlene M. Mantia, MD⁴; Neil J. Shah, MD⁵; Emily Stern Gatof, MD⁴; Ying Long, PharmD²; Kimberly D. Allman, MSN, CNP¹; Moshe C. Ornstein, MD, MA¹; Hans J. Hammers, MD, PhD⁶; David F. McDermott, MD⁴; Michael B. Atkins, MD⁵; Michael Hurwitz, MD, PhD²; and Brian I. Rini, MD¹

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.

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 OS	19.5 mo	21.9 mo
6-months OS	90.8%	90.6%

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

A Conversation with the Investigators: Ovarian Cancer

**Wednesday, July 7, 2021
5:00 PM – 6:00 PM ET**

Faculty

**Michael J Birrer, MD, PhD
Kathleen Moore, MD
Richard T Penson, MD, MRCP**

Moderator

Neil Love, MD

Thank you for joining us!

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