

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Eric Jonasch, MD

Professor of Medicine

Department of Genitourinary Medical Oncology
The University of Texas MD Anderson Cancer Center
Houston, Texas

Commercial Support

This activity is supported by educational grants from Aveo Pharmaceuticals, Bristol-Myers Squibb Company, Eisai Inc and Exelixis Inc.

Dr Love — Disclosures

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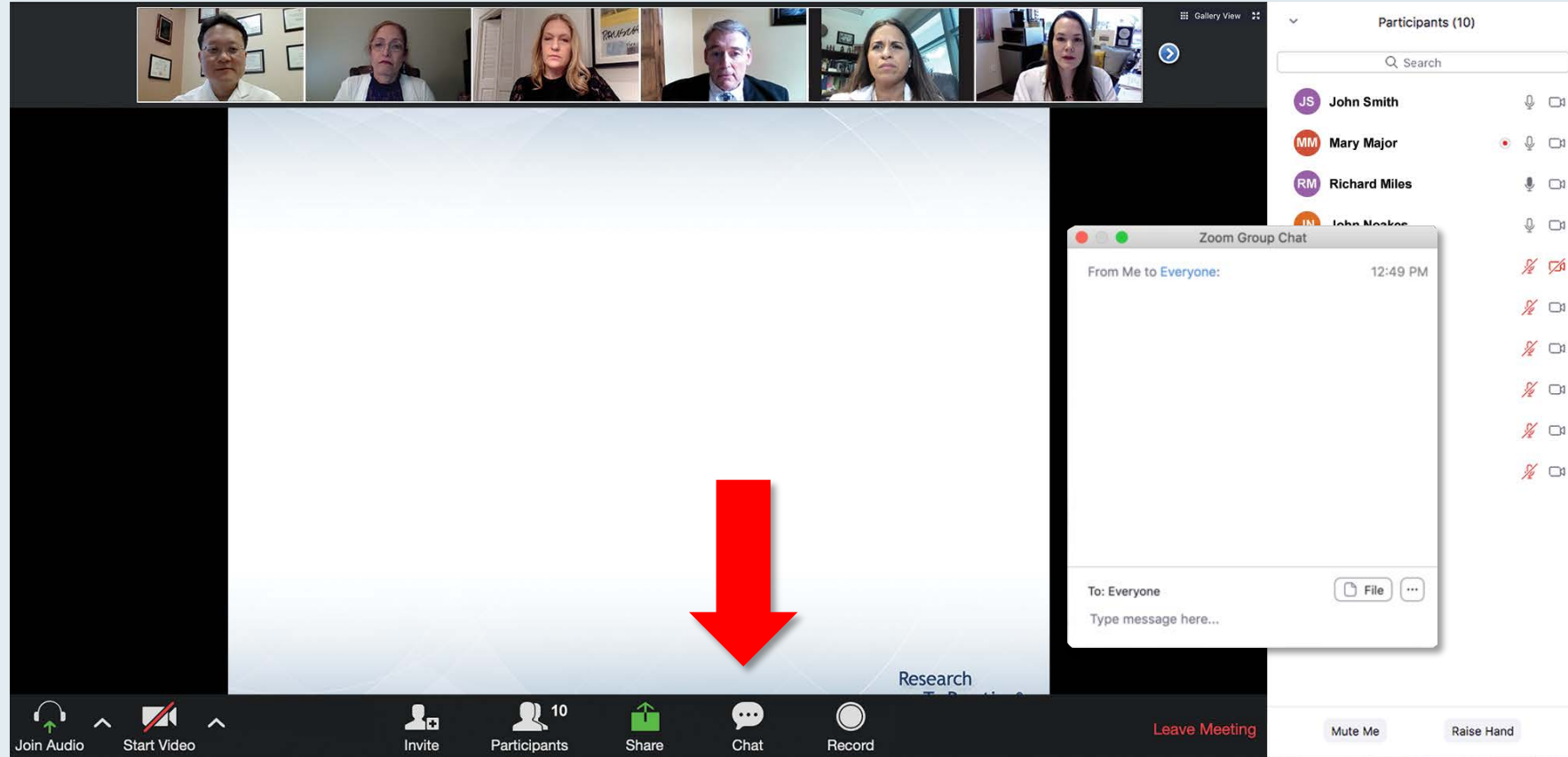
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Dr Jonasch — Disclosures

Consulting Agreements	Aveo Pharmaceuticals, Eisai Inc, Exelixis Inc, Merck, Novartis, Pfizer Inc
Contracted Research	Merck, Telix Pharmaceuticals
Data and Safety Monitoring Board/Committee	Pfizer Inc

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

The screenshot shows a Zoom meeting interface. At the top, there are six video thumbnails of participants. Below them is a slide with a poll question: "What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-2 years who then experiences an asymptomatic relapse?". The slide lists ten options, including combinations of Carfilzomib, Pomalidomide, Elotuzumab, Daratumumab, and Ixazomib with or without dexamethasone. A "Quick Poll" window is overlaid on the slide, showing the same options with radio buttons for selection. The Zoom interface includes a "Participants (10)" list on the right, a "Join Audio" button, and a "Start Video" button at the bottom.

Participants (10)

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-2 years who then experiences an asymptomatic relapse?

Quick Poll

- Carfilzomib +/- dexamethasone
- Pomalidomide +/- dexamethasone
- Carfilzomib + pomalidomide +/- dexamethasone
- Elotuzumab + lenalidomide +/- dexamethasone
- Elotuzumab + pomalidomide +/- dexamethasone
- Daratumumab + lenalidomide +/- dexamethasone
- Daratumumab + pomalidomide +/- dexamethasone
- Daratumumab + bortezomib +/- dexamethasone
- Ixazomib + Rd
- Other

Submit

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Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

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

What Clinicians Want to Know: Understanding the Factors Affecting the Optimal Diagnosis and Management of Ovarian Cancer

**Thursday, February 18, 2021
5:00 PM – 6:00 PM ET**

Faculty

Michael J Birrer, MD, PhD

Kathleen Moore, MD

David M O'Malley, MD

Moderator

Neil Love, MD

Meet The Professor

Management of Multiple Myeloma

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Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Management of Triple-Negative Breast Cancer

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A 4-Part Live Webinar Series Reviewing Key Data and
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**Paul M Barr, MD
Matthew S Davids, MD, MMSc
Kerry Rogers, MD**

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Prostate Cancer (Part 1 of a 3-Part Series)

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Fred Saad, MD
A Oliver Sartor, MD
Matthew R Smith, MD, PhD

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Neil Love, MD

Thank you for joining us!

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

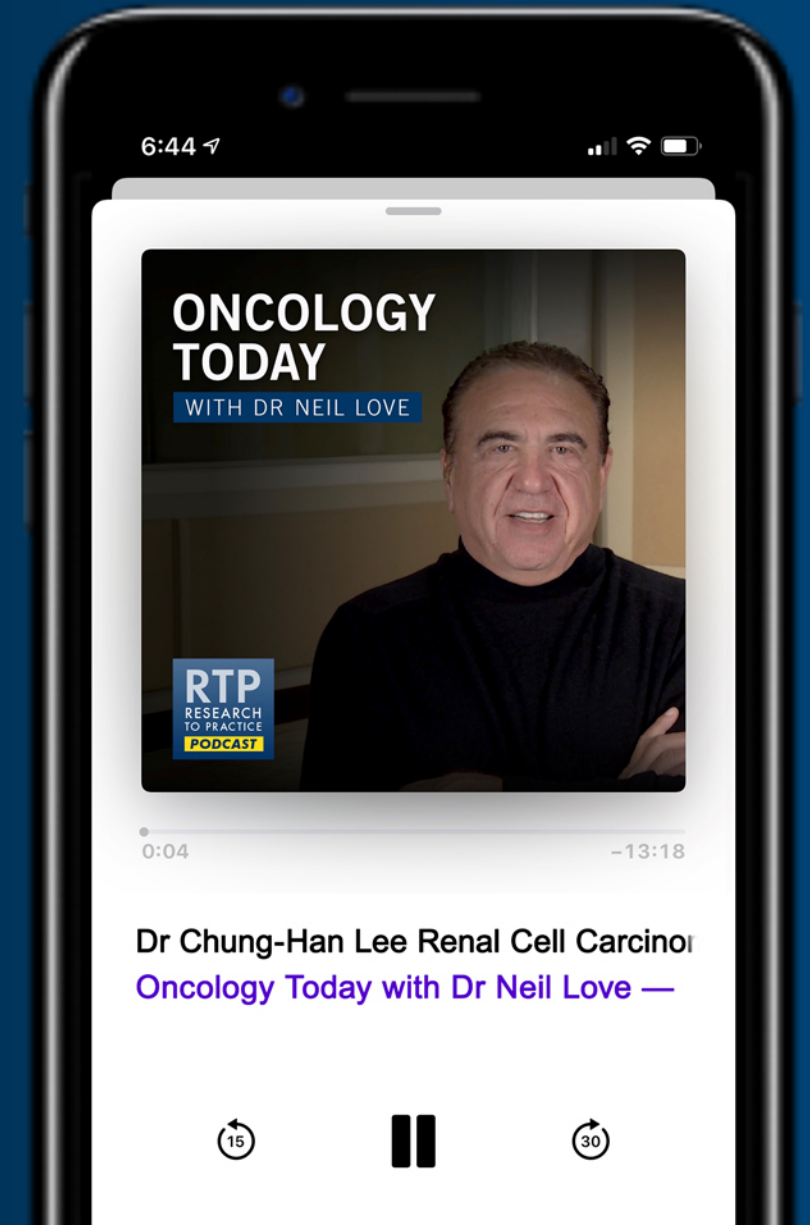
ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma



DR CHUNG-HAN LEE
MEMORIAL SLOAN KETTERING CANCER CENTER
NEW YORK, NEW YORK





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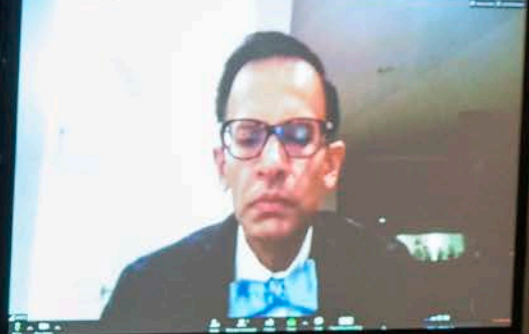
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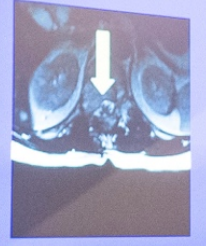
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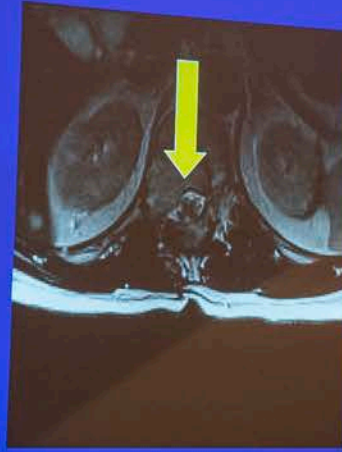
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PPE = personal protective equipment
 Miller R, et al. Guidelines for COVID-19 Infection





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Meet The Professor Program Participating Faculty



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Director, Lank Center for Genitourinary Oncology
Department of Medical Oncology
Dana-Farber Cancer Institute
The Jerome and Nancy Kohlberg Professor of Medicine
Harvard Medical School
Boston, Massachusetts



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Co-Director, Urologic Cancer Research
and Treatment Center
Texas Oncology
Charles A Sammons Cancer Center
Baylor University Medical Center
Professor of Medicine
Texas A&M HSC College of Medicine
Dallas, Texas



Hans Hammers, MD, PhD
Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
Division of Hematology and Oncology
UT Southwestern
Dallas, Texas



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Department of Genitourinary Medical Oncology
The University of Texas
MD Anderson Cancer Center
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David F McDermott, MD
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Beth Israel Deaconess Medical Center
Leader, Kidney Cancer Program
Dana-Farber/Harvard Cancer Center
Professor of Medicine
Harvard Medical School
Boston, Massachusetts



William K Oh, MD
Clinical Professor of Medicine
Icahn School of Medicine at Mount Sinai
The Tisch Cancer Institute
Mount Sinai Health System
New York, New York



Robert J Motzer, MD
Attending Physician, Department of Medicine
Jack and Dorothy Byrne Chair in Clinical Oncology
Memorial Sloan Kettering Cancer Center
New York, New York



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Professor, Department of Hematology/Oncology
Fox Chase Cancer Center, Temple Health
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Professor of Genitourinary Oncology
Barts Cancer Institute
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Queen Mary University of London
London, United Kingdom



Brian I Rini, MD
Chief of Clinical Trials
Vanderbilt-Ingram Cancer Center
Ingram Professor of Medicine
Division of Hematology/Oncology
Vanderbilt University Medical Center
Nashville, Tennessee

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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

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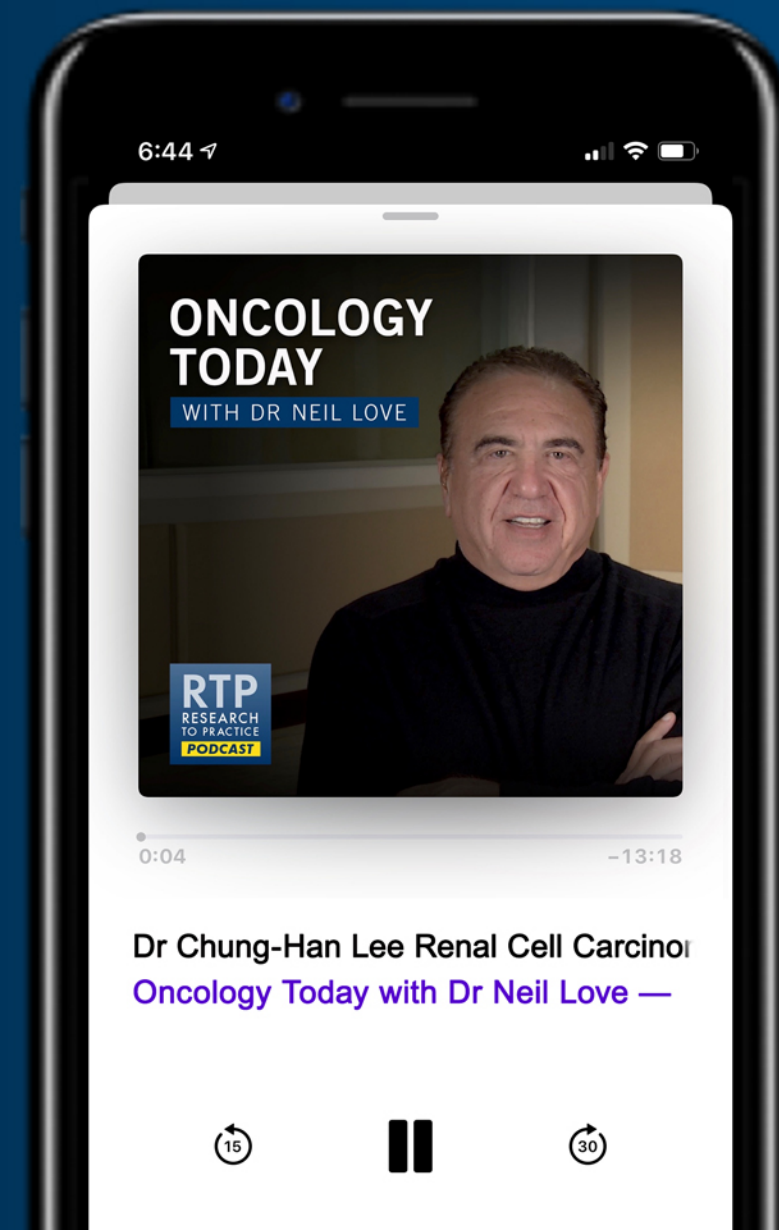
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Maria Regina Flores, MD

Physician Partner for Florida Cancer
Specialists and Research Institute
Orlando, Florida



Spencer Henick Bachow, MD

Hematologist/Oncologist at Lynn Cancer Institute
Affiliate Assistant Professor of Medicine at FAU
Schmidt College of Medicine
Boca Raton, Florida

Meet The Professor with Dr Jonasch

MODULE 1: Cases and Questions from Drs Bachow and Flores

- Dr Bachow: A 71-year-old man with metastatic clear cell renal cell carcinoma (ccRCC)
 - Parts 1 and 2
- Dr Flores: An obese 61-year-old man with metastatic RCC
- Dr Flores: A 63-year-old Asian woman with metastatic ccRCC
- Dr Bachow: A 53-year-old woman with metastatic non-clear-cell RCC
- Dr Flores: A 58-year-old man with metastatic ccRCC

MODULE 2: Renal Cell Carcinoma Journal Club with Dr Jonasch

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

Case Presentation – Dr Bachow: A 71-year-old man with metastatic ccRCC – Part 1



Dr Spencer Henick Bachow

- Presents with neurologic deficits
- CT brain: 4-cm left cerebellar hemorrhage → craniotomy (pathology: Clear cell RCC)
- MRI abdomen: 9.7-cm mass on lower pole of left kidney

Question

- Should this patient proceed directly to a cytoreductive nephrectomy or should we place this patient on systemic therapy?

Case Presentation – Dr Bachow: A 71-year-old man with metastatic ccRCC – Part 2



Dr Spencer Henick Bachow

- Presents with neurologic decline → CT brain: 4-cm left cerebellar hemorrhage → craniotomy (pathology: clear cell RCC)
- MRI abdomen: 9.7-cm mass on lower pole of left kidney
- **2/2019: Radical nephrectomy (T3aNx, clear cell type), with adrenal gland involvement**
- **7/2019 PET CT: 3.4-cm pectoralis major encased mass biopsy-proven mRCC**
- **NGS on primary tumor: von Hippel-Lindau exon 3 mutation, SETD2 mutation, TMB-low, mismatch repair proficient, PD-L1: 0%**
- **Ipilimumab/nivolumab x 4 → PD, with new brain metastases → SBRT, chest wall mass and other lesions**
- **11/2019: Cabozantinib, with dose reduction due to diarrhea**

Question

- **Does the von Hippel-Lindau gene mutation or the SETD2 mutation have implications for treatment in patients with metastatic ccRCC?**

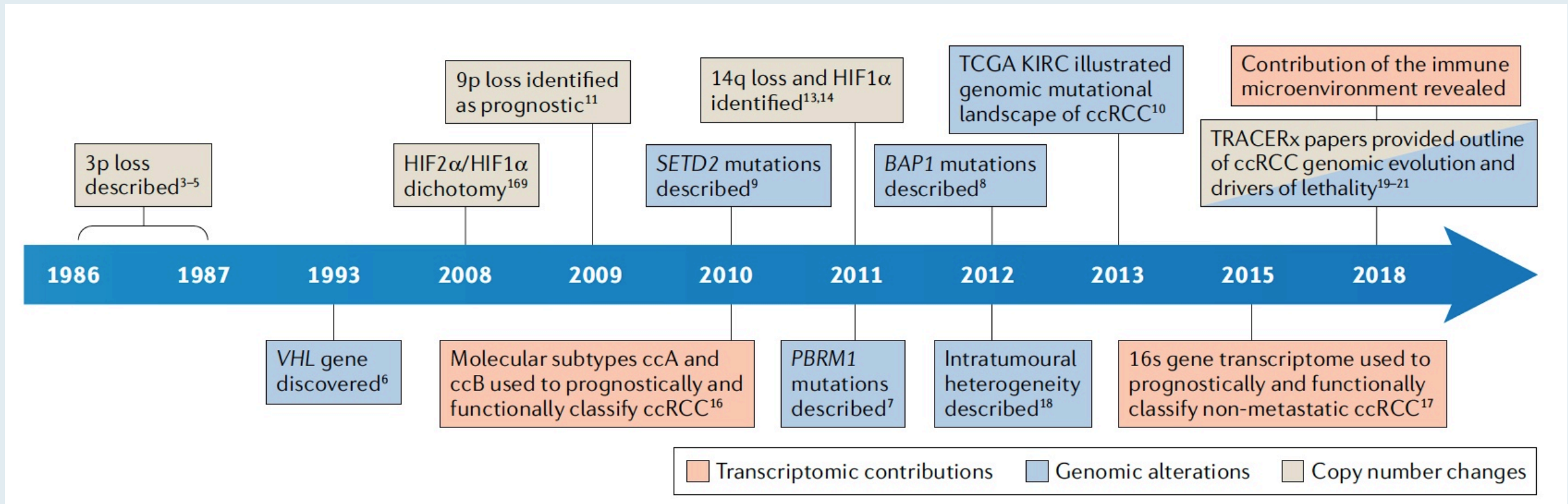
Nat Rev Nephrol 2020;[Online ahead of print]

REVIEWS

Clear cell renal cell carcinoma ontogeny and mechanisms of lethality

Eric Jonasch ¹ ✉, Cheryl Lyn Walker² and W. Kimryn Rathmell ³

Key Discoveries in ccRCC Genomics



Key Events in Clear Cell Renal Cell Carcinoma Progression

Tumour initiators

- 3p loss/5q gain
- *VHL* mutation
- *VHL* methylation



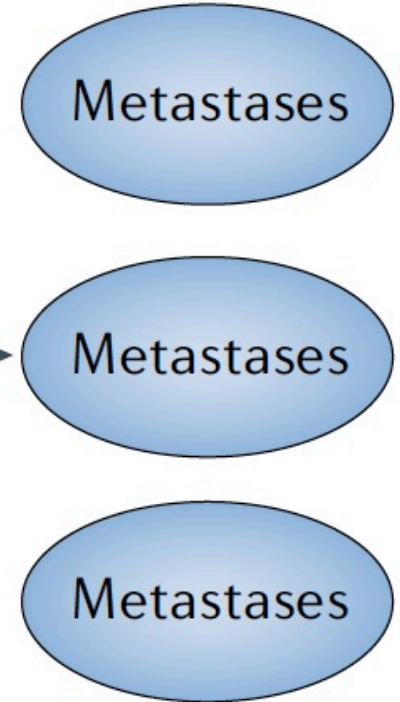
Drivers of evolution

- *PBRM1*, *SETD2* or *BAP1* mutations
- Defects in DNA repair
- Defects in mitosis

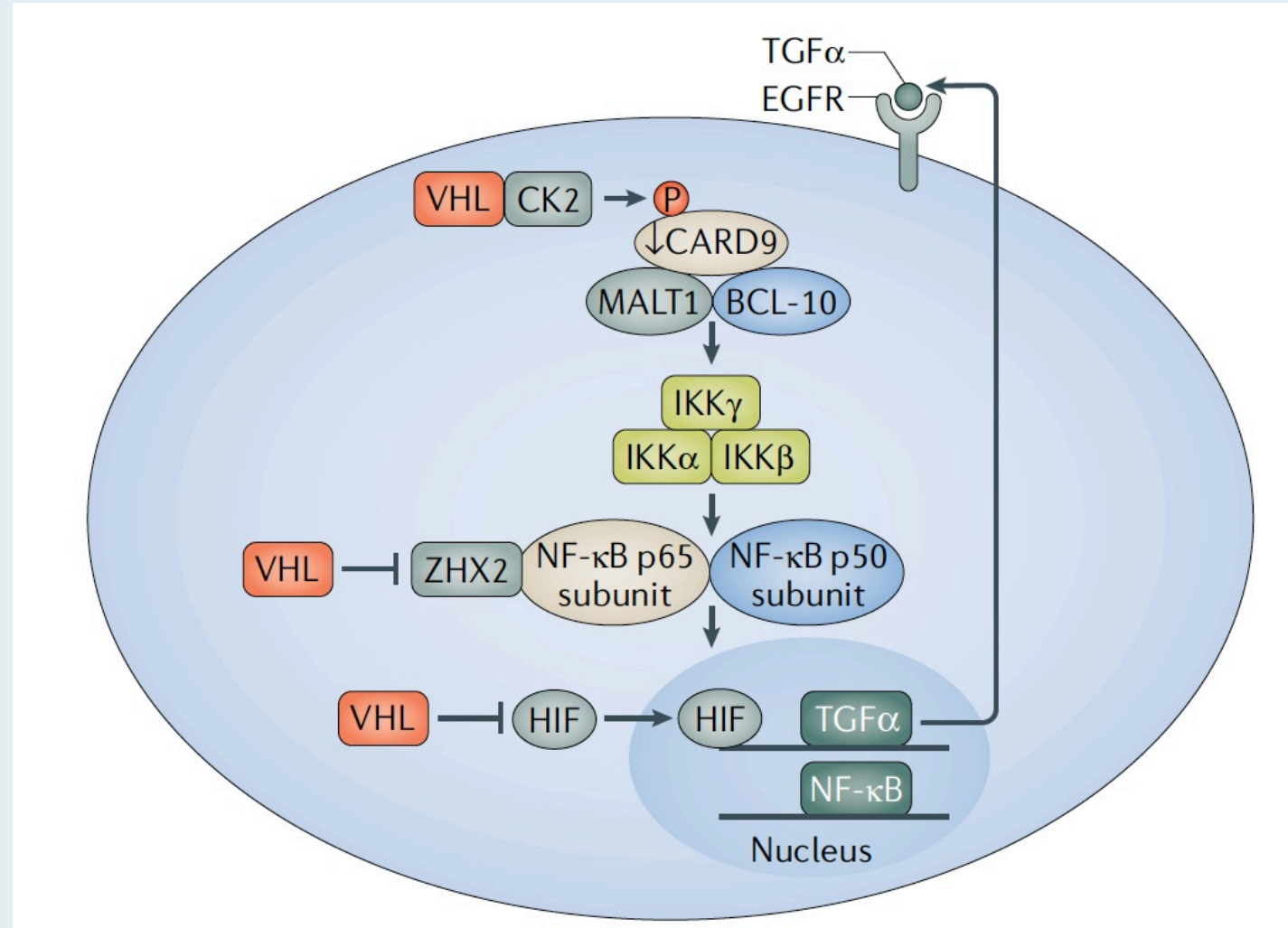


Lethal events

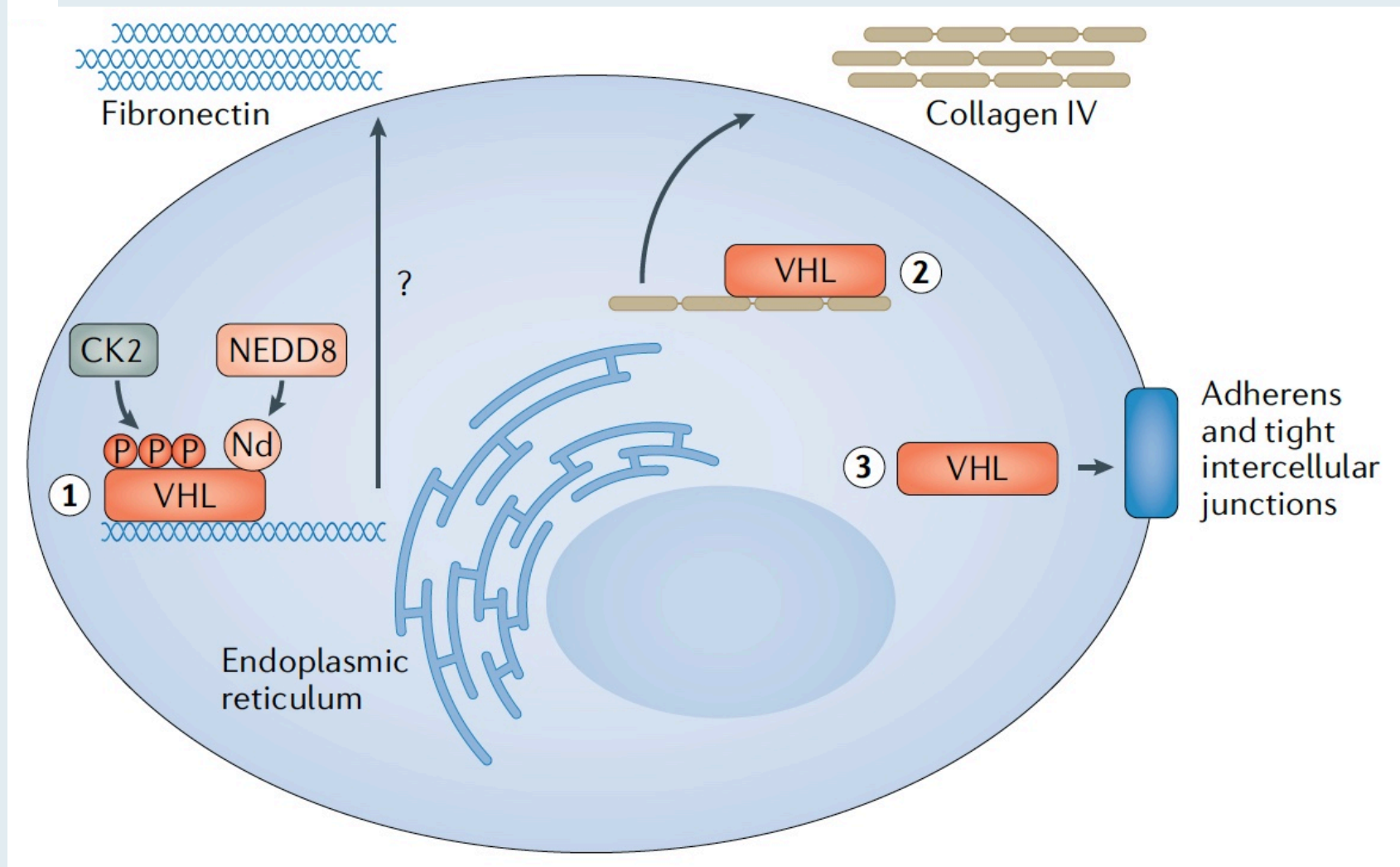
- PI3K pathway activation
- 9p, 14q loss, 8q gain
- Other oncogenic drivers



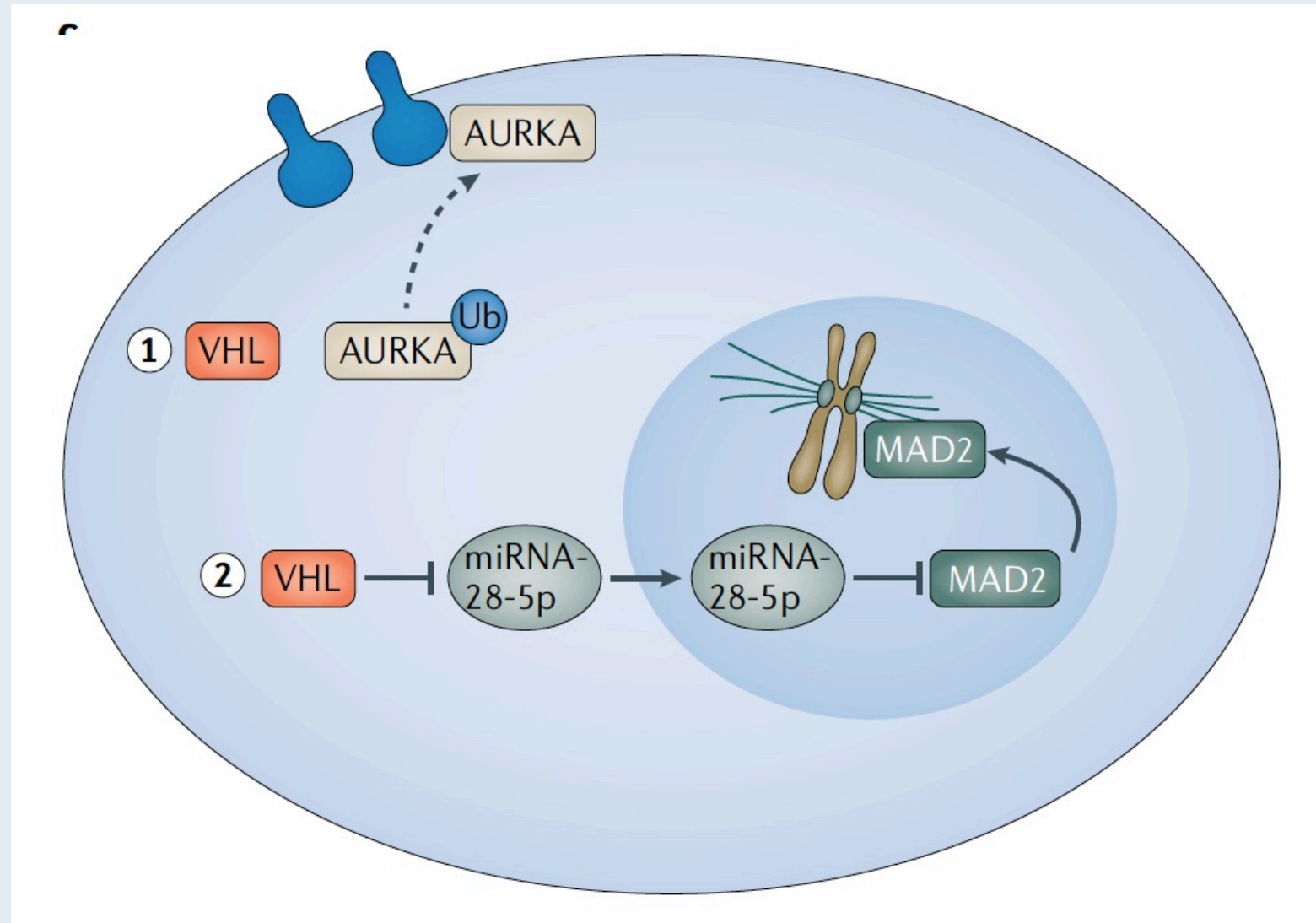
Non-HIF Targets of VHL: von Hippel–Lindau (VHL) Regulates NF- κ B Through Hypoxia-Inducible Factor (HIF)-Dependent and Independent Mechanisms



Non-HIF Targets of VHL: Extracellular Matrix Homeostasis Is Dependent on the Interaction Between VHL and Fibronectin and Requires CK2-Mediated Phosphorylation and Neddylation of VHL

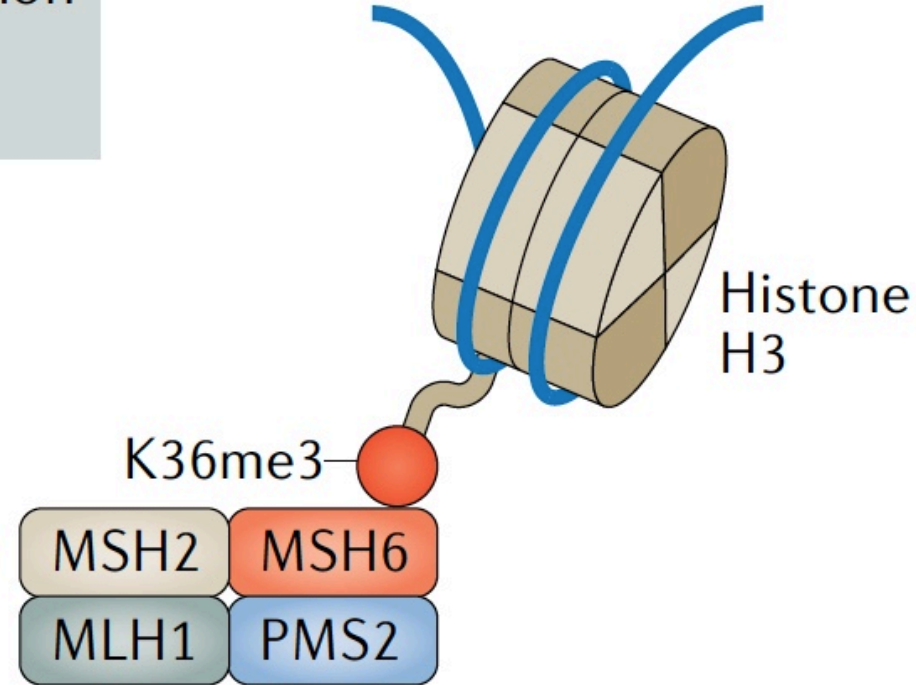


Non-HIF Targets of VHL: VHL Regulates the Primary Cilium and Mitosis



Factors Influencing Mismatch Repair in ccRCC

Enhanced degradation of MSH2 in the absence of VHL



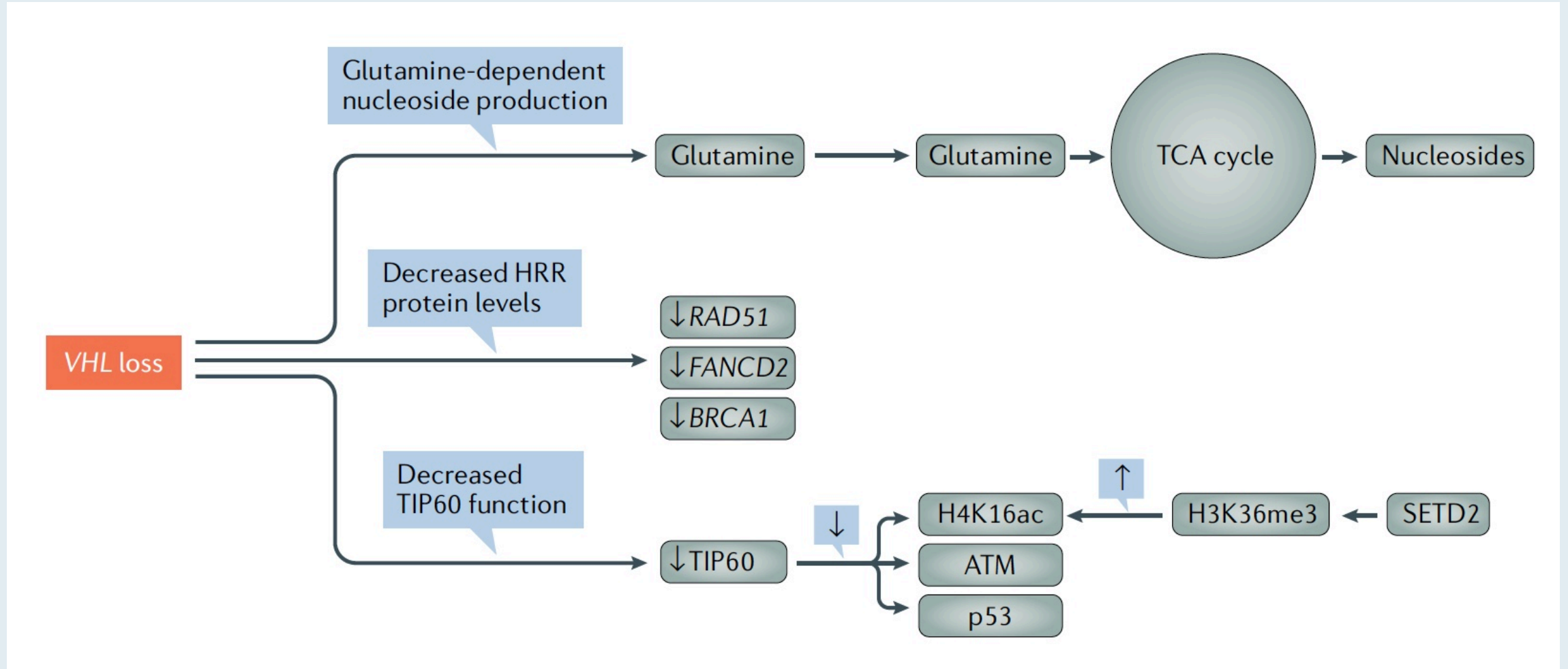
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Obligate loss of one copy of *MLH1*

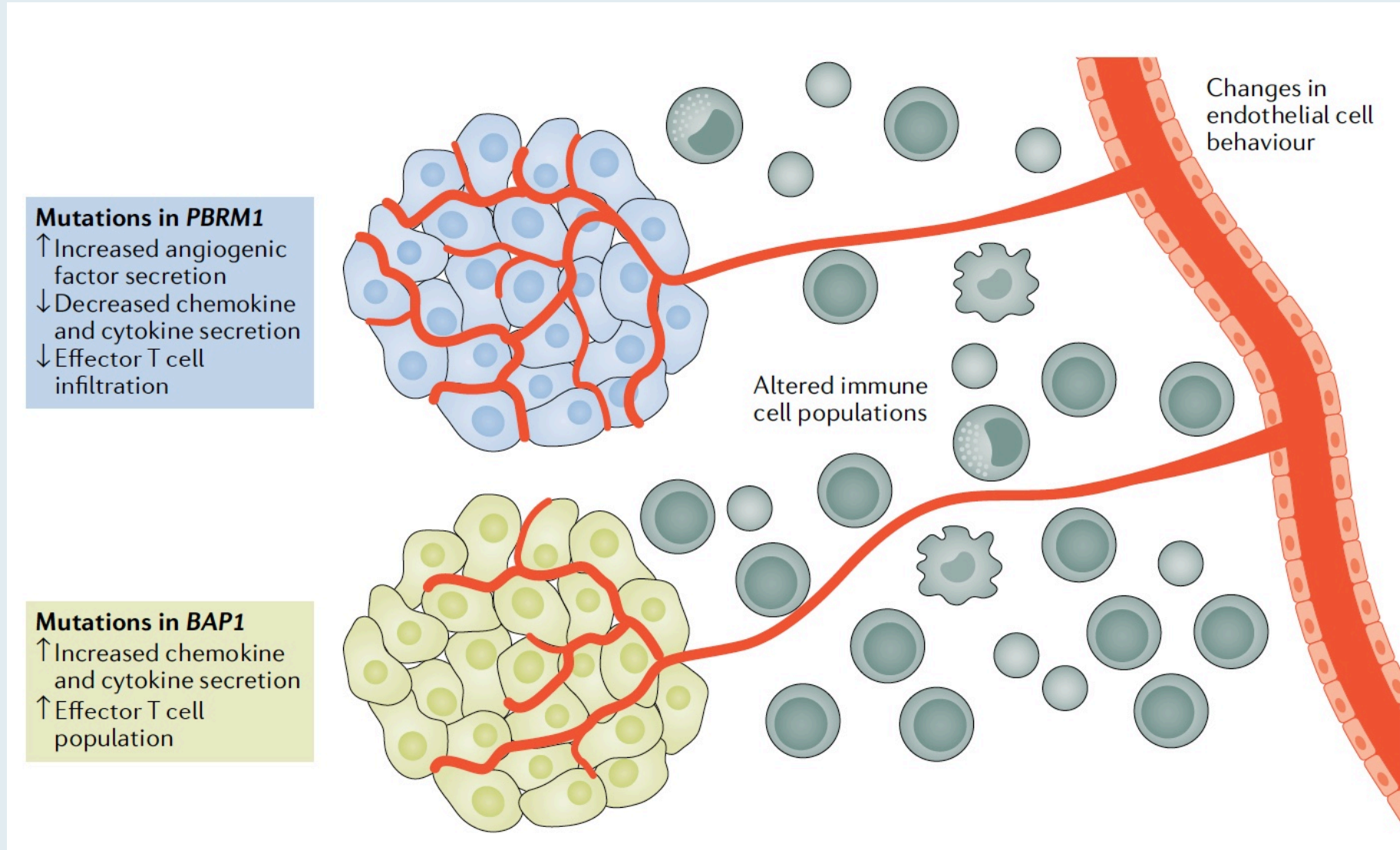
c

Decreased engagement via H3K36me3

Factors Influencing Homologous Recombination Repair in Clear Cell Renal Cell Carcinoma



Alterations in the Immune Microenvironment in Clear Cell Renal Cell Carcinoma



Case Presentation – Dr Flores: An obese 61-year-old man with metastatic RCC



Dr Maria Regina Flores

- History of hematuria that was self-limiting, obesity, HTN and atrial fibrillation (apixaban)
- Right renal mass 8.4 x 7.2-cm and bilateral pulmonary nodules
- Developed a TIA while being worked up and also found to be hypercalcemic, which was treated
- Plan: Discuss pros and cons of single-agent immunotherapy versus pembrolizumab/axitinib

Question

- What are your thoughts about the pros and cons of single-agent immunotherapy versus pembrolizumab/axitinib for this patient?

Case Presentation – Dr Flores: A 63-year-old Asian woman with metastatic ccRCC



Dr Maria Regina Flores

- 5/2015: Diagnosed with ccRCC, Fuhrman Grade 4, with sarcomatoid differentiation 40% and rhabdoid features 50%
- Developed lung metastasis that required decortication 5 months after her nephrectomy
- Clinical trial with bevacizumab and atezolizumab → PR, with stable disease for at least 2 years
 - Occasional proteinuria prompting drug hold but no nephrotic syndrome
 - Study ended in 2020 but continued treatment via compassionate use

Questions

- Would you stop treatment, given the stability of her disease for over 2 years?
- If she progresses on bevacizumab/atezolizumab, what drug sequencing would you use?
- How do you approach RCC with sarcomatoid histology outside of a clinical trial?
- If she were not enrolled on this clinical trial, what treatment would you have recommended?

Case Presentation – Dr Bachow: A 53-year-old woman with metastatic non-clear cell RCC



Dr Spencer Henick Bachow

- 10/2019: Diagnosed with RCC and multiple osseous metastases affecting the spine and several other bones, requiring surgical and radiologic interventions
- 11/2019: Cytoreductive nephrectomy for left 12.2-cm chromophobe RCC, with sarcomatoid features
- 12/2019: New bone metastases and bilateral pulmonary nodules
- Axitinib/pembrolizumab x 2 → florid PD
- Cabozantinib → florid PD throughout all vertebral bodies
- 3/2020: Everolimus/lenvatinib, with marked improvement x 3 months → PD
- ECOG PS 3-4 but patient and family desired treatment: Ipilimumab/nivolumab x 1 → brain metastases

Questions

- How do you approach up-front therapy in patients with metastatic non-clear cell RCC?
- Is there ever a role in re-treating with an immune checkpoint inhibitor or a combination of immune checkpoint inhibitors in patients with metastatic RCC who had prior progression on an immune checkpoint inhibitor?

Case Presentation – Dr Flores: A 58-year-old man with metastatic ccRCC



Dr Maria Regina Flores

- 11/2016: Right papillary RCC s/p nephrectomy
- 8/2018: Bone and soft tissue metastases, biopsy-proven clear cell carcinoma
- Nivolumab/ipilimumab → PD
- Clinical trial of cabozantinib plus CB-839 or placebo but discontinued after 1 cycle due to toxicity
- Patient desired re-challenge with immunotherapy, or potentially interleukin-2 (IL-2)/interferon
- Pembrolizumab/axitinib x 5 months → PD
- Lenvatinib/everolimus

Questions

- What would be your next line of treatment, given what he has received so far?
- Does IL-2/interferon still have a role in RCC?

Meet The Professor with Dr Jonasch

MODULE 1: Cases and Questions from Drs Bachow and Flores

MODULE 2: Renal Cell Carcinoma Journal Club with Dr Jonasch

- A review on von Hippel-Lindau disease
- Exposure-response modeling of cabozantinib: Implications for patient care
- Nivolumab for metastatic non-clear cell RCC
- Outcomes for patients with metastatic RCC with sarcomatoid dedifferentiation to immune checkpoint inhibitors (ICIs)
- Macrophage HIF-1 α : An independent prognostic indicator in RCC
- Combination therapy with nivolumab and tyrosine kinase inhibitors for metastatic RCC (mRCC)
- Axitinib with ICIs: Consensus recommendation for treatment optimization and management of related AEs
- Clear cell RCC ontogeny and mechanisms of lethality
- Oral HIF-2 α inhibitor MK-6482 for von Hippel-Lindau disease-associated RCC
- Society for Immunotherapy of Cancer consensus statement on immunotherapy for advanced RCC

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

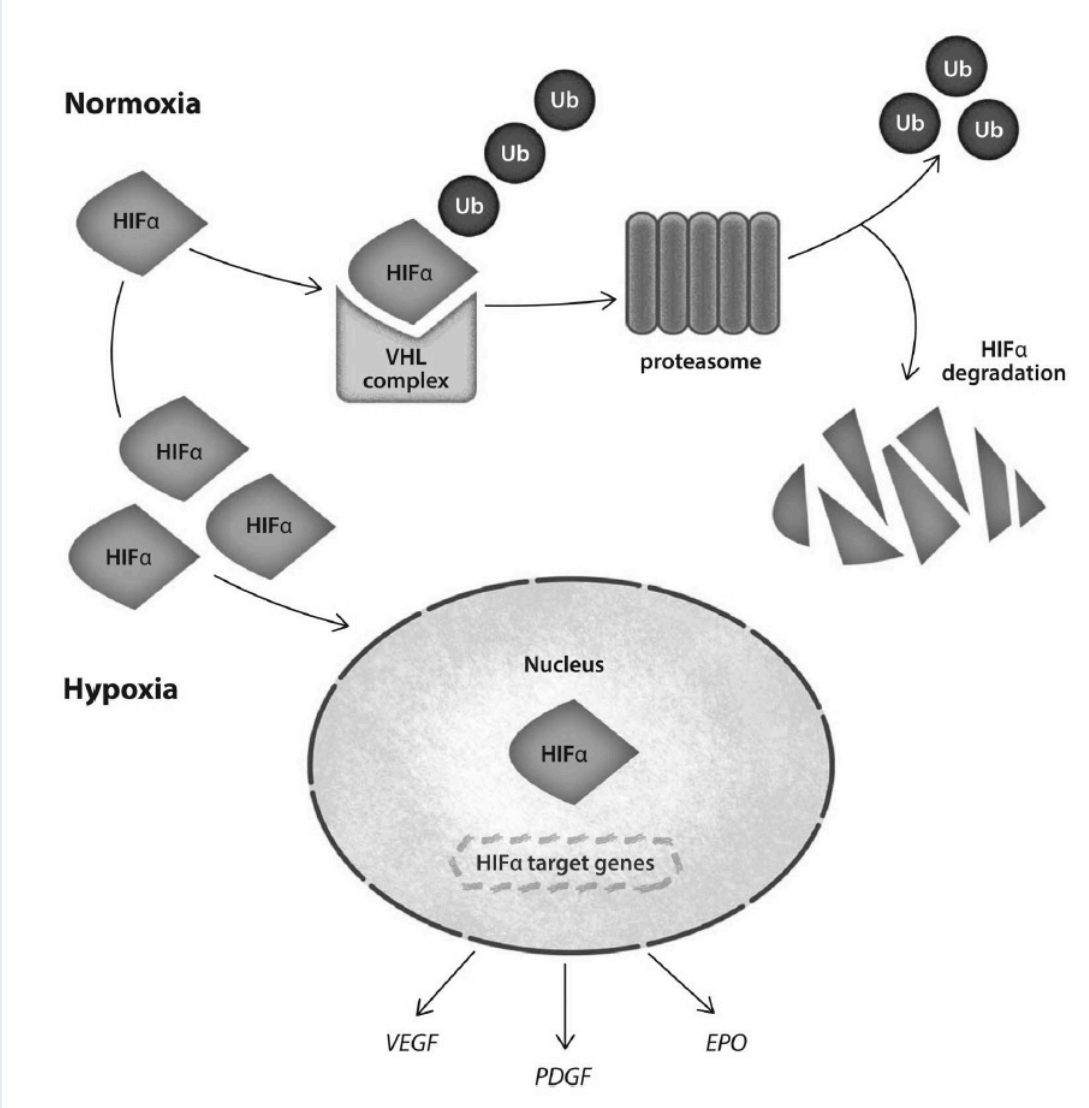
Review

VON HIPPEL-LINDAU DISEASE

Update on Pathogenesis and Systemic Aspects

MARY E. ARONOW, MD,* HENRY E. WILEY, MD,† ALAIN GAUDRIC, MD,‡ VALERIE KRIVOSIC, MD,‡
MICHAEL B. GORIN, MD, PhD,§ CAROL L. SHIELDS, MD,¶ JERRY A. SHIELDS, MD,¶
ERIC W. JONASCH, MD,** ARUN D. SINGH, MD,†† EMILY Y. CHEW, MD†

Role of pVHL in the Adaptive Response to Hypoxic Conditions



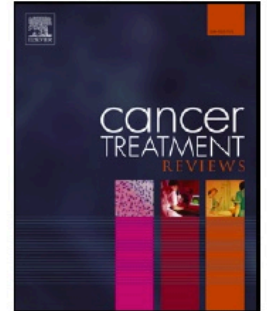


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Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv



Anti-tumour Treatment

Exposure-response modeling of cabozantinib in patients with renal cell carcinoma: Implications for patient care

Daniel Castellano^{a,*}, Jose Pablo Maroto^b, Fawzi Benzaghrou^c, Naila Taguieva^c, Linh Nguyen^d, Douglas O. Clary^d, Eric Jonasch^e

Oncologist 2020;25(3):252-8

Genitourinary Cancer

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Nivolumab for the Treatment of Patients with Metastatic Non-Clear Cell Renal Cell Carcinoma (nccRCC): A Single-Institutional Experience and Literature Meta-Analysis

JAD CHAHOUD,^a PAVLOS MSAOUEL,^b MATTHEW T. CAMPBELL,^b THARAKESWARA BATHALA,^b LIANCHUN XIAO,^b JIANJUN GAO,^b AMADO J. ZURITA,^b
AMISHI YOGESH SHAH,^b ERIC JONASCH,^b PADMANEE SHARMA,^b NIZAR M. TANNIR^b



Clinical-Kidney cancer

Outcomes of patients with metastatic renal cell carcinoma with sarcomatoid dedifferentiation to immune checkpoint inhibitors

Jad Chahoud, M.D.[#], Pavlos Msaouel, M.D.[#], Jeremy A. Ross, M.D.[#],
Barrett Z. McCormick, M.D., Tharakeswara K. Bathala, M.D., Jianjun Gao, M.D.,
Robert Horn, M.D., Lianchun Xiao, M.S., Kanishka Sircar, M.D., Matthew T. Campbell, M.D.,
Amishi Y. Shah, M.D., Sangeeta Goswami, M.D., Amado J. Zurita, M.D., Eric Jonasch, M.D.,
Surena F. Matin, M.D., Christopher G. Wood, M.D., Jose A. Karam, M.D.,
Padmanee Sharma, M.D., Nizar M. Tannir, M.D.*

Macrophage HIF-1 α Is an Independent Prognostic Indicator in Kidney Cancer

Sophie J. Cowman¹, Daniel G. Fuja¹, Xian-De Liu², Rebecca S. Slack Tidwell², Neelima Kandula¹, Deepika Sirohi¹, Archana M. Agarwal¹, Lyska L. Emerson³, Sheryl R. Tripp⁴, Jeffrey S. Mohlman¹, Miekian Stonhill¹, Guillermina Garcia⁵, Christopher J. Conley³, Adam A. Olalde⁵, Timothy Sargis⁵, Adela Ramirez-Torres⁵, Jose A. Karam², Christopher G. Wood², Kanishka Sircar², Pheroze Tamboli², Kenneth Boucher³, Benjamin Maughan³, Benjamin T. Spike³, Thai H. Ho⁶, Neeraj Agarwal³, Eric Jonasch², and Mei Yee Koh¹


Combination Therapy with Nivolumab and Tyrosine Kinase Inhibitors in Patients with Metastatic Renal Cell Carcinoma

Garmezy B et al.

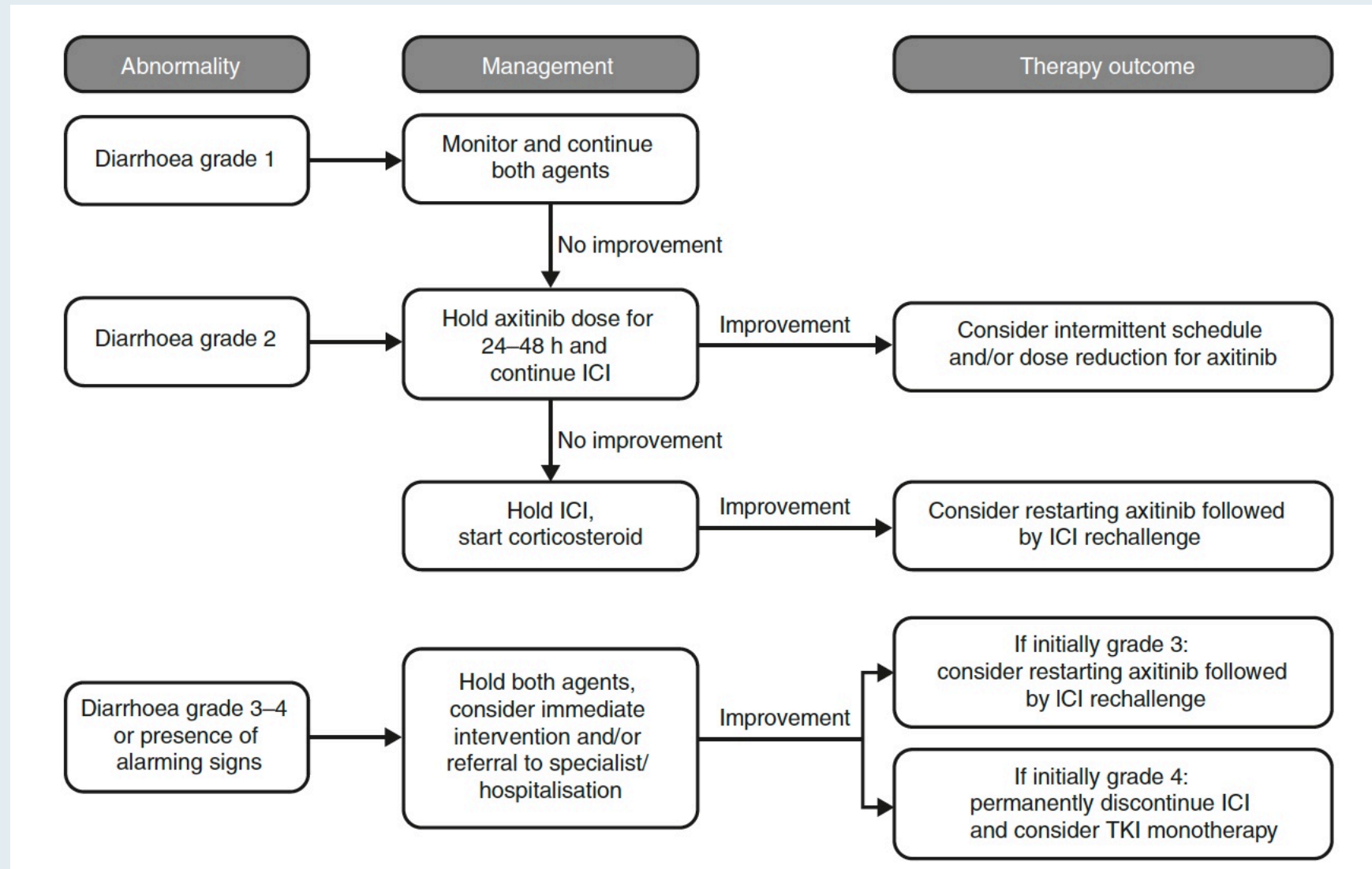
ASCO 2020;Abstract e17090.

CONSENSUS STATEMENT

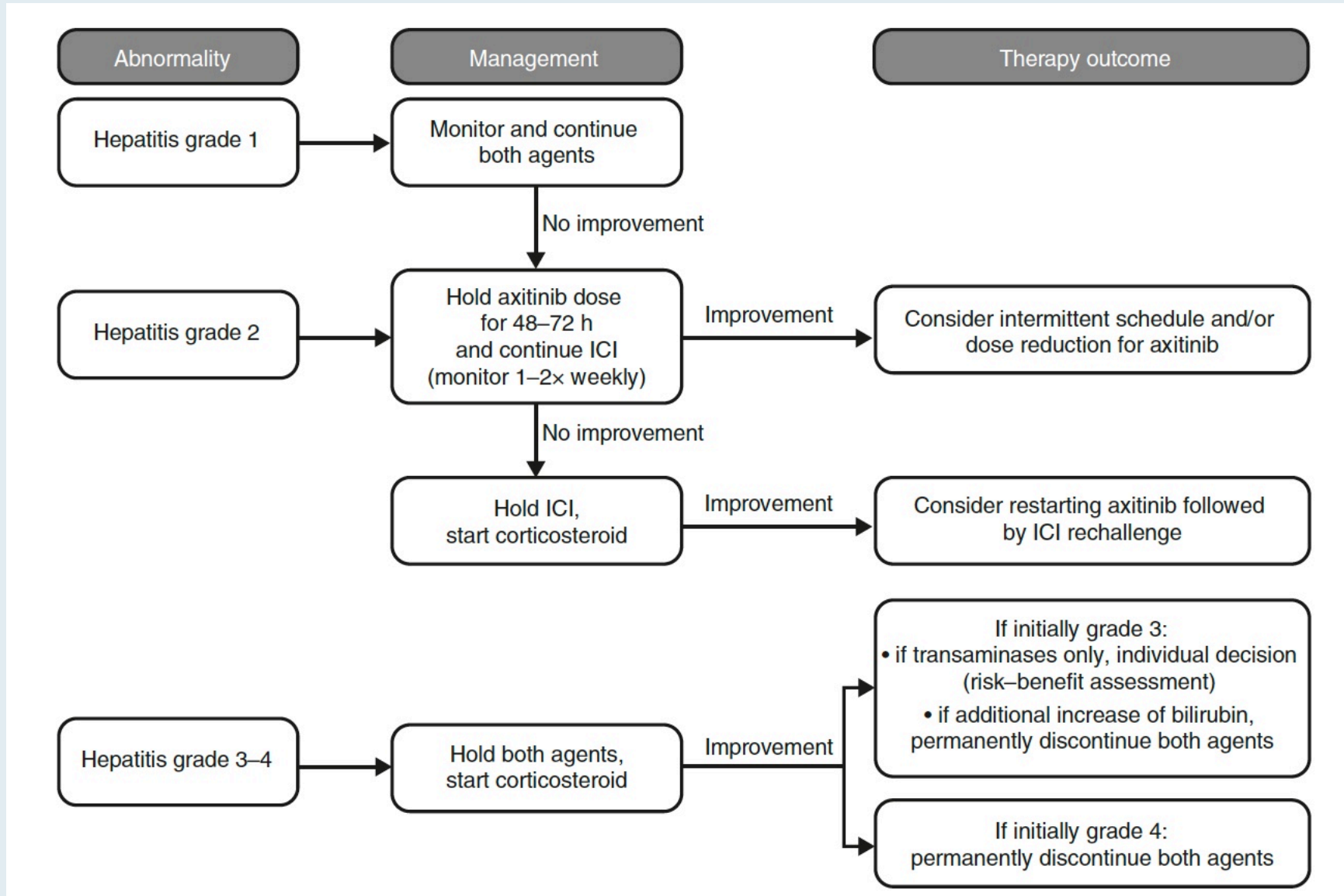
Axitinib plus immune checkpoint inhibitor: evidence- and expert-based consensus recommendation for treatment optimisation and management of related adverse events

Viktor Grünwald ¹, Martin H. Voss², Brian I. Rini³, Thomas Powles⁴, Laurence Albiges⁵, Rachel H. Giles⁶ and Eric Jonasch⁷

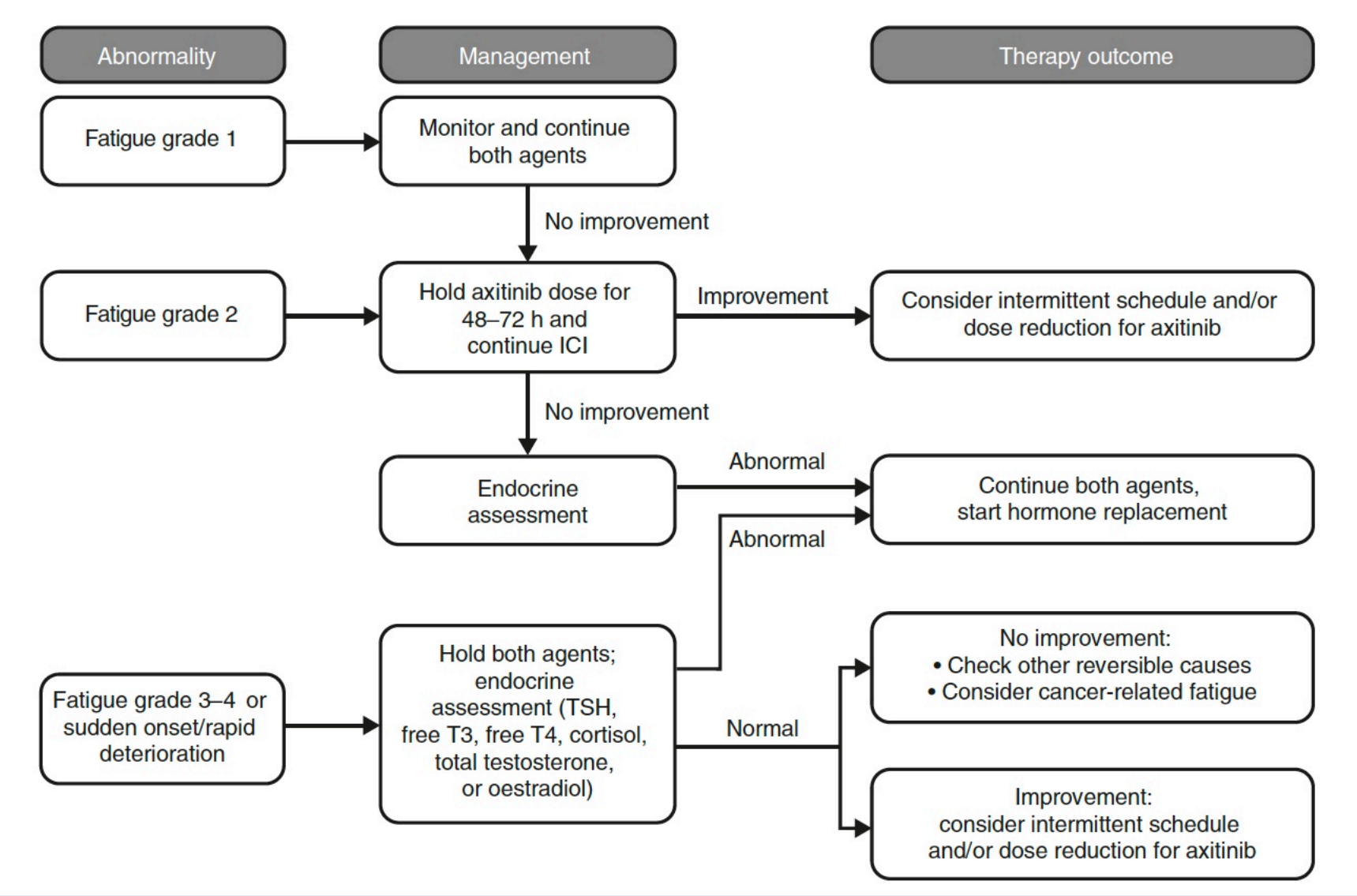
Managing Treatment-Induced Diarrhea



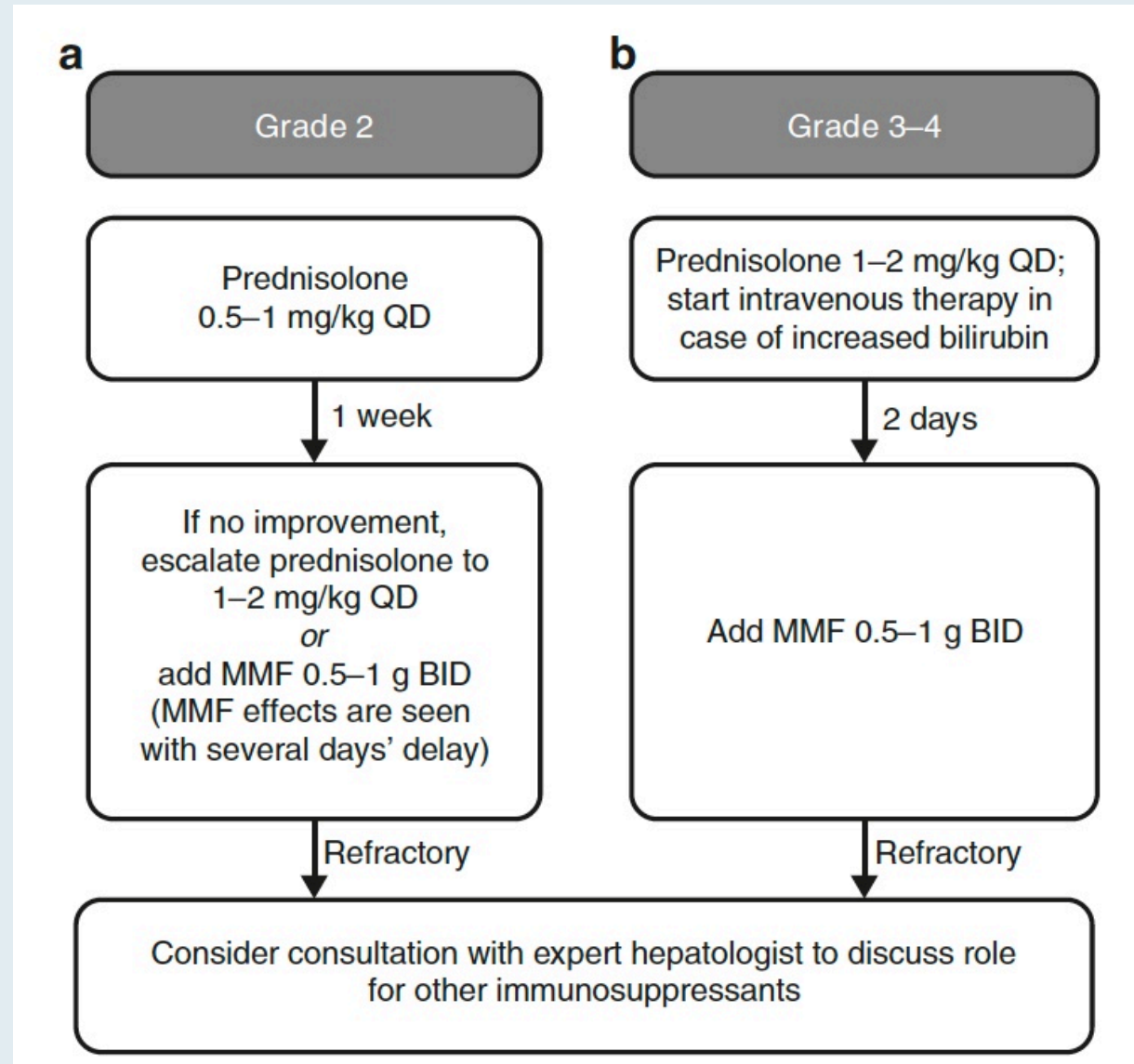
Managing Treatment-Induced Hepatitis



Managing Fatigue



Escalation Schema for Immunosuppressive Treatment of Immune-Related Hepatic Toxicity



Phase II Study of the Oral HIF-2 α Inhibitor MK-6482 for von Hippel-Lindau Disease-Associated Renal Cell Carcinoma


Jonasch E et al.

ASCO 2020;Abstract 5003.

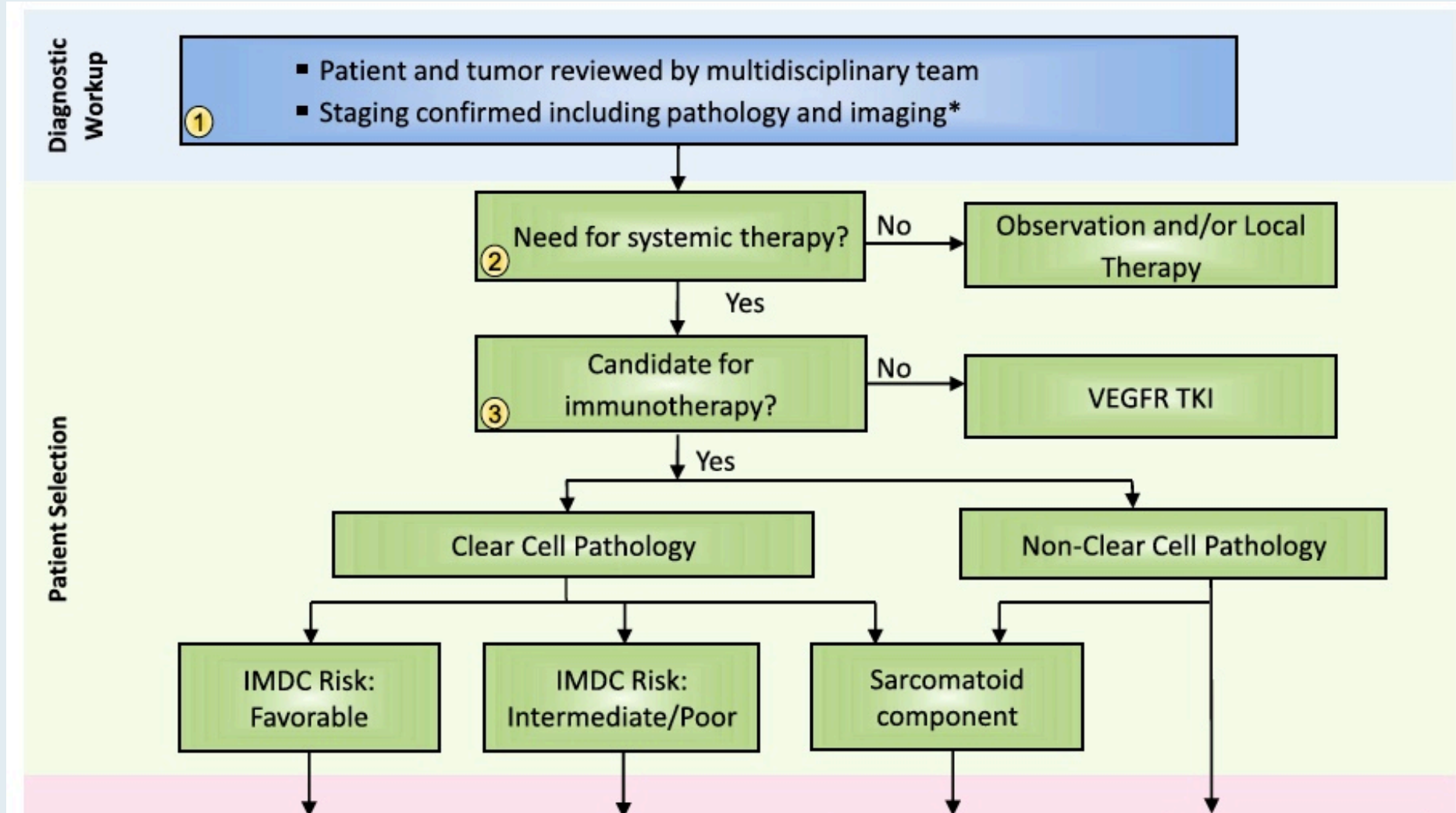
POSITION ARTICLE AND GUIDELINES

Open Access

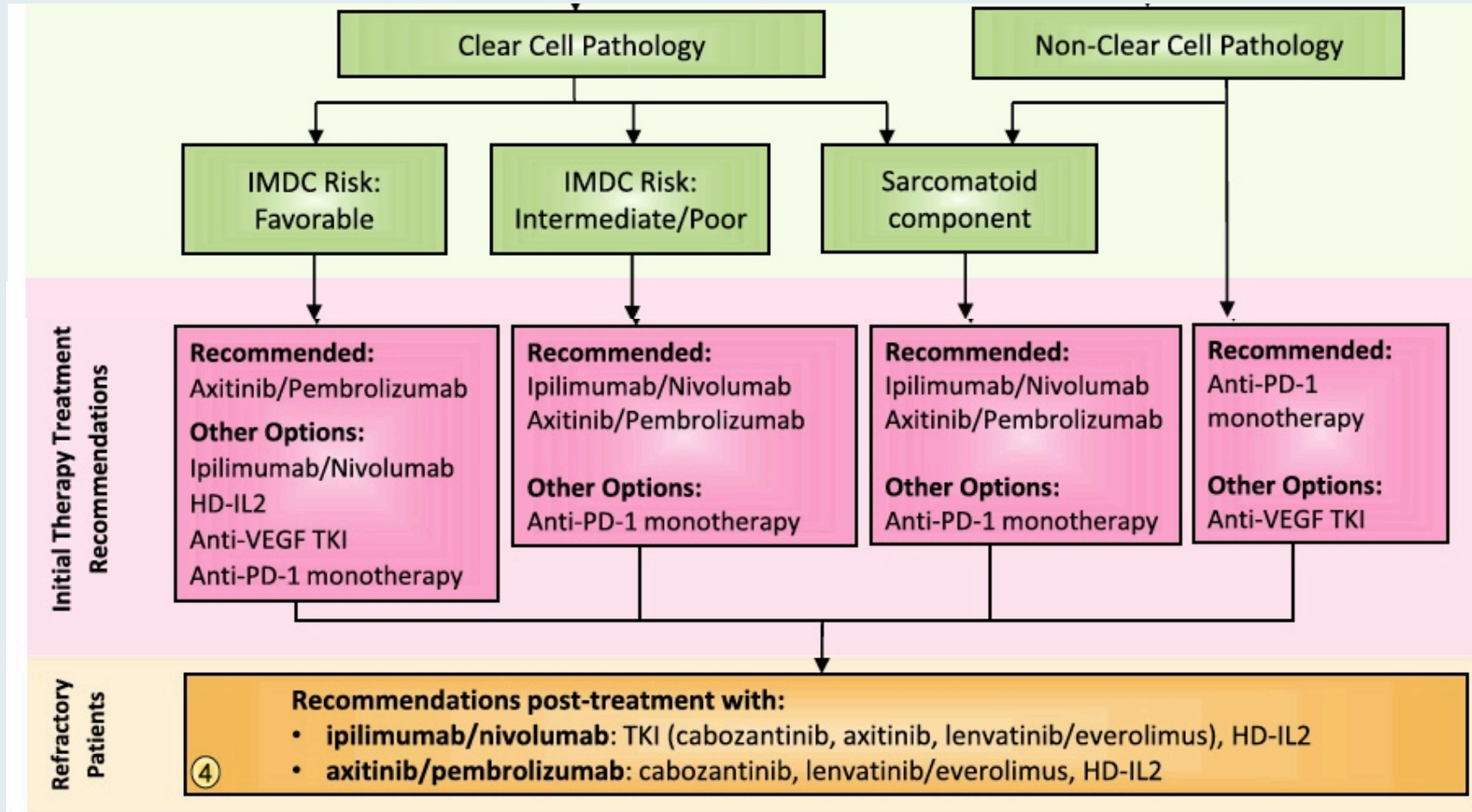
The society for immunotherapy of cancer consensus statement on immunotherapy for the treatment of advanced renal cell carcinoma (RCC)

Brian I. Rini¹, Dena Battle², Robert A. Figlin³, Daniel J. George⁴, Hans Hammers⁵, Tom Hutson⁶, Eric Jonasch⁷, Richard W. Joseph⁸, David F. McDermott⁹, Robert J. Motzer¹⁰, Sumanta K. Pal¹¹, Allan J. Pantuck¹², David I. Quinn¹³, Virginia Seery⁹, Martin H. Voss¹⁰, Christopher G. Wood⁷, Laura S. Wood¹ and Michael B. Atkins^{14*} 

Immunotherapy Treatment Algorithm for Patients with Advanced Renal Cell Carcinoma – Part 1



Immunotherapy Treatment Algorithm for Patients with Advanced Renal Cell Carcinoma – Part 2



*Baseline imaging recommendations discussed in figure legend.

Notes: 1) Clinical Trials are always an option for any patient, in any category. 2) This recommendation may change as data mature.

Meet The Professor with Dr Jonasch

MODULE 1: Cases and Questions from Drs Bachow and Flores

MODULE 2: Renal Cell Carcinoma Journal Club with Dr Jonasch

- A review on von Hippel-Lindau disease
- Exposure-response modeling of cabozantinib: Implications for patient care
- Nivolumab for metastatic non-clear cell RCC
- Outcomes for patients with metastatic RCC with sarcomatoid dedifferentiation to immune checkpoint inhibitors (ICIs)
- Macrophage HIF-1 α : An independent prognostic indicator in RCC
- Combination therapy with nivolumab and tyrosine kinase inhibitors for metastatic RCC (mRCC)
- Axitinib with ICIs: Consensus recommendation for treatment optimization and management of related AEs
- Clear cell RCC ontogeny and mechanisms of lethality
- Oral HIF-2 α inhibitor MK-6482 for von Hippel-Lindau disease-associated RCC
- Society for Immunotherapy of Cancer consensus statement on immunotherapy for advanced RCC

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios











MODULE 4: Key Recent Data Sets

Optimizing Front-Line Decision-Making for Advanced Renal Cell Carcinoma (RCC)











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. Nivolumab/cabozantinib
5. Tyrosine kinase inhibitor (TKI) monotherapy
6. Anti-PD-1/PD-L1 monotherapy
7. Other

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)?

 TONI K CHOU EI RI, MD	Cabozantinib	 ROBERT J MOTZER, MD	Nivolumab/cabozantinib
 HANS HAMMERS, MD, PHD	Nivolumab/ipilimumab	 WILLIAM K OH, MD	Nivolumab/cabozantinib
 THOMAS E HUTSON, DO, PHARM D	Nivolumab/cabozantinib	 ELIZABETH R PLIMACK, MD, MS	Pembrolizumab/axitinib
 ERIC JONASCH, MD	Nivolumab/cabozantinib	 THOMAS POWLES, MBBS, MRCP, MD	Pembrolizumab/axitinib
 DAVID F MCDERMOTT, MD	Nivolumab/ipilimumab	 BRIAN I RINI, MD	Pembrolizumab/axitinib











Which first-line therapy would you recommend for an 80-year-old patient with a history of nephrectomy for clear cell RCC who on routine follow-up 3 years later is found to have asymptomatic bone metastases (PS = 0)?

 TONI K CHOU EI RI, MD	Nivolumab/cabozantinib	 ROBERT J MOTZER, MD	Nivolumab/cabozantinib
 HANS HAMMERS, MD, PHD	Nivolumab/ipilimumab	 WILLIAM K OH, MD	Cabozantinib
 THOMAS E HUTSON, DO, PHARM D	Nivolumab/cabozantinib	 ELIZABETH R PLIMACK, MD, MS	Pembrolizumab/axitinib
 ERIC JONASCH, MD	Nivolumab/cabozantinib	 THOMAS POWLES, MBBS, MRCP, MD	Pembrolizumab/axitinib
 DAVID F MCDERMOTT, MD	Nivolumab	 BRIAN I RINI, MD	Pembrolizumab/axitinib











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. Nivolumab/cabozantinib
5. TKI monotherapy
6. Anti-PD-1/PD-L1 monotherapy
7. Other

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)?

 <p>TONI K CHOUERI, MD</p>	Nivolumab/cabozantinib	 <p>ROBERT J MOTZER, MD</p>	Nivolumab/ipilimumab
 <p>HANS HAMMERS, MD, PHD</p>	Nivolumab/ipilimumab	 <p>WILLIAM K OH, MD</p>	Nivolumab/ipilimumab
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Nivolumab/cabozantinib	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Pembrolizumab/axitinib and radiation therapy
 <p>ERIC JONASCH, MD</p>	Nivolumab/cabozantinib	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Pembrolizumab/axitinib
 <p>DAVID F MCDERMOTT, MD</p>	Nivolumab/ipilimumab	 <p>BRIAN I RINI, MD</p>	Pembrolizumab/axitinib



Which first-line therapy would you recommend for an 80-year-old patient who presents with clear cell RCC with multiple painful bone metastases and Hb of 11.4 g/dL (PS = 1)?

 <p>TONI K CHOUERI, MD</p>	Nivolumab/cabozantinib	 <p>ROBERT J MOTZER, MD</p>	Nivolumab/ipilimumab
 <p>HANS HAMMERS, MD, PHD</p>	Nivolumab/ipilimumab	 <p>WILLIAM K OH, MD</p>	Nivolumab/ipilimumab
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Nivolumab/cabozantinib	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Pembrolizumab/axitinib and radiation therapy
 <p>ERIC JONASCH, MD</p>	Nivolumab/cabozantinib	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Pembrolizumab/axitinib
 <p>DAVID F MCDERMOTT, MD</p>	Nivolumab/cabozantinib	 <p>BRIAN I RINI, MD</p>	Pembrolizumab/axitinib











In general, which first-line therapy would you recommend for a 65-year-old patient who presents with metastatic clear cell RCC and for whom the use of immune checkpoint inhibitors is contraindicated?

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Axitinib
5. Other

In general, which first-line therapy would you recommend for a 65-year-old patient who presents with metastatic clear cell RCC and for whom the use of immune checkpoint inhibitors is contraindicated?

 <p>TONI K CHOUERI, MD</p>	Cabozantinib	 <p>ROBERT J MOTZER, MD</p>	Cabozantinib
 <p>HANS HAMMERS, MD, PHD</p>	Axitinib	 <p>WILLIAM K OH, MD</p>	Cabozantinib
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Cabozantinib	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Pazopanib
 <p>ERIC JONASCH, MD</p>	Sunitinib	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Pazopanib
 <p>DAVID F MCDERMOTT, MD</p>	Cabozantinib	 <p>BRIAN I RINI, MD</p>	Cabozantinib

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

 <p>TONI K CHOUERI, MD</p>	I don't know (likely same as axitinib)	 <p>ROBERT J MOTZER, MD</p>	I don't know
 <p>HANS HAMMERS, MD, PHD</p>	I don't know	 <p>WILLIAM K OH, MD</p>	Efficacy is about the same
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Efficacy is about the same	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Efficacy is about the same
 <p>ERIC JONASCH, MD</p>	Efficacy is about the same	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Efficacy is about the same
 <p>DAVID F MCDERMOTT, MD</p>	Efficacy is about the same	 <p>BRIAN I RINI, MD</p>	Efficacy is about the same


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

 <p>TONI K CHOUERI, MD</p>	Tivozanib is more tolerable	 <p>ROBERT J MOTZER, MD</p>	Tivozanib is more tolerable
 <p>HANS HAMMERS, MD, PHD</p>	Tivozanib is more tolerable	 <p>WILLIAM K OH, MD</p>	Tolerability is about the same
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Tivozanib is more tolerable	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Tivozanib is more tolerable
 <p>ERIC JONASCH, MD</p>	Tivozanib is more tolerable	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Tolerability is about the same
 <p>DAVID F MCDERMOTT, MD</p>	Tivozanib is more tolerable	 <p>BRIAN I RINI, MD</p>	Tivozanib is more tolerable

Do you consider PD-L1 levels or tumor mutational burden (TMB) at any point in the treatment decision-making process for your patients with metastatic RCC?











 <p>TONI K CHOUERI, MD</p>	No	 <p>ROBERT J MOTZER, MD</p>	No
 <p>HANS HAMMERS, MD, PHD</p>	No	 <p>WILLIAM K OH, MD</p>	No
 <p>THOMAS E HUTSON, DO, PHARM D</p>	No	 <p>ELIZABETH R PLIMACK, MD, MS</p>	No
 <p>ERIC JONASCH, MD</p>	No	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	No
 <p>DAVID F MCDERMOTT, MD</p>	No	 <p>BRIAN I RINI, MD</p>	No

For a patient with metastatic RCC who experiences a complete response to checkpoint inhibitor-based therapy and is tolerating it well, for how long would you continue treatment? Partial response?











 <p>TONI K CHOUERI, MD</p>	2 years / 2 years	 <p>ROBERT J MOTZER, MD</p>	2 years / nivo indefinitely, pembro 2 years
 <p>HANS HAMMERS, MD, PHD</p>	2 years / 2 years	 <p>WILLIAM K OH, MD</p>	Indefinitely / Indefinitely
 <p>THOMAS E HUTSON, DO, PHARM D</p>	About 1 year / About 1 year	 <p>ELIZABETH R PLIMACK, MD, MS</p>	2 years / 2 years
 <p>ERIC JONASCH, MD</p>	1 year / Indefinitely	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	At least 1 year / At least 2 years
 <p>DAVID F MCDERMOTT, MD</p>	3 months / 2 years	 <p>BRIAN I RINI, MD</p>	Usually 1 year / Usually 1 year

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











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?

 TONI K CHOUERI, MD	Cabozantinib	 ROBERT J MOTZER, MD	Axitinib
 HANS HAMMERS, MD, PHD	Axitinib	 WILLIAM K OH, MD	Cabozantinib
 THOMAS E HUTSON, DO, PHARM D	Cabozantinib	 ELIZABETH R PLIMACK, MD, MS	Pembrolizumab/axitinib
 ERIC JONASCH, MD	Cabozantinib	 THOMAS POWLES, MBBS, MRCP, MD	Cabozantinib
 DAVID F MCDERMOTT, MD	Cabozantinib	 BRIAN I RINI, MD	Axitinib











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 pembrolizumab/axitinib and experiences disease progression after 12 months?

 <p>TONI K CHOUERI, MD</p>	Cabozantinib	 <p>ROBERT J MOTZER, MD</p>	Cabozantinib
 <p>HANS HAMMERS, MD, PHD</p>	Cabozantinib	 <p>WILLIAM K OH, MD</p>	Cabozantinib
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Cabozantinib	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Cabozantinib
 <p>ERIC JONASCH, MD</p>	Cabozantinib	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Cabozantinib
 <p>DAVID F MCDERMOTT, MD</p>	Cabozantinib	 <p>BRIAN I RINI, MD</p>	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?

 <p>TONI K CHOUERI, MD</p>	Lenvatinib + everolimus	 <p>ROBERT J MOTZER, MD</p>	Lenvatinib + everolimus
 <p>HANS HAMMERS, MD, PHD</p>	Lenvatinib + everolimus	 <p>WILLIAM K OH, MD</p>	Nivolumab/ipilimumab
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Lenvatinib + everolimus	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Lenvatinib + everolimus
 <p>ERIC JONASCH, MD</p>	Lenvatinib + everolimus	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Axitinib
 <p>DAVID F MCDERMOTT, MD</p>	Nivolumab/ipilimumab	 <p>BRIAN I RINI, MD</p>	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)?

 <p>TONI K CHOUERI, MD</p>	Lenvatinib + everolimus	 <p>ROBERT J MOTZER, MD</p>	Lenvatinib + everolimus
 <p>HANS HAMMERS, MD, PHD</p>	Lenvatinib + everolimus	 <p>WILLIAM K OH, MD</p>	Lenvatinib + everolimus
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Lenvatinib + everolimus	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Lenvatinib + everolimus
 <p>ERIC JONASCH, MD</p>	Lenvatinib + everolimus	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Lenvatinib + everolimus
 <p>DAVID F MCDERMOTT, MD</p>	Clinical trial with HIF2a inhibitor	 <p>BRIAN I RINI, MD</p>	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 ipilimumab/nivolumab and second-line cabozantinib (PS 0)?

 <p>TONI K CHOUEIRI, MD</p>	Lenvatinib + everolimus	 <p>ROBERT J MOTZER, MD</p>	Lenvatinib + everolimus
 <p>HANS HAMMERS, MD, PHD</p>	Lenvatinib + everolimus	 <p>WILLIAM K OH, MD</p>	Lenvatinib + everolimus
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Lenvatinib + everolimus	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Lenvatinib + everolimus
 <p>ERIC JONASCH, MD</p>	Lenvatinib + everolimus	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Lenvatinib + everolimus
 <p>DAVID F MCDERMOTT, MD</p>	Clinical trial with HIF2a inhibitor	 <p>BRIAN I RINI, MD</p>	Axitinib

Have you administered or would you administer nivolumab/ipilimumab to a patient with metastatic RCC who had received a prior checkpoint inhibitor either alone or in combination with an anti-angiogenic agent?






 <p>TONI K CHOUERI, MD</p>	I have	 <p>ROBERT J MOTZER, MD</p>	I have
 <p>HANS HAMMERS, MD, PHD</p>	I have	 <p>WILLIAM K OH, MD</p>	I have
 <p>THOMAS E HUTSON, DO, PHARM D</p>	I have not and would not	 <p>ELIZABETH R PLIMACK, MD, MS</p>	I have
 <p>ERIC JONASCH, MD</p>	I have	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	I have not but would for the right patient
 <p>DAVID F MCDERMOTT, MD</p>	I have	 <p>BRIAN I RINI, MD</p>	I have

Practical Considerations with the Use of Immune Checkpoint Inhibitors and TKIs for Advanced RCC











A patient who is experiencing a good response to ICI-based therapy for metastatic RCC presents with mild shortness of breath and cough and is found to have radiographic evidence of pneumonitis in both lungs. What would you recommend?

 <p>TONI K CHOUZEIRI, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>ROBERT J MOTZER, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved
 <p>HANS HAMMERS, MD, PHD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>WILLIAM K OH, MD</p>	Hold the ICI, resume when toxicity improved
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved
 <p>ERIC JONASCH, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved
 <p>DAVID F MCDERMOTT, MD</p>	Hold the ICI and do not restart until PD	 <p>BRIAN I RINI, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved

A patient who is experiencing a good response to ICI-based therapy for metastatic RCC reports experiencing an increase of 6 stools over baseline per day. What would you recommend?

 <p>TONI K CHOUERI, MD</p>	HOLD ICI and get a colonoscopy	 <p>ROBERT J MOTZER, MD</p>	Hold the ICI and resume when toxicity has improved
 <p>HANS HAMMERS, MD, PHD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>WILLIAM K OH, MD</p>	Hold the ICI and resume when toxicity has improved
 <p>THOMAS E HUTSON, DO, PHARM D</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>ELIZABETH R PLIMACK, MD, MS</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved
 <p>ERIC JONASCH, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved
 <p>DAVID F MCDERMOTT, MD</p>	Hold the ICI, administer corticosteroids, resume when PD	 <p>BRIAN I RINI, MD</p>	Hold the ICI, administer corticosteroids, resume when toxicity improved

In your clinical experience, what is the most effective way to manage the fatigue associated with TKI treatment in patients with metastatic RCC?

 <p>TONI K CHOUERI, MD</p>	<p>Dose reduction, hold or discontinuation Supportive care measures</p>	 <p>ROBERT J MOTZER, MD</p>	<p>Dose reduction, hold or discontinuation</p>
 <p>HANS HAMMERS, MD, PHD</p>	<p>Dose reduction, hold or discontinuation Supportive care measures</p>	 <p>WILLIAM K OH, MD</p>	<p>Dose reduction, hold or discontinuation</p>
 <p>THOMAS E HUTSON, DO, PHARM D</p>	<p>Dose reduction, hold or discontinuation Supportive care measures</p>	 <p>ELIZABETH R PLIMACK, MD, MS</p>	<p>Dose reduction, hold or discontinuation</p>
 <p>ERIC JONASCH, MD</p>	<p>Dose reduction, hold or discontinuation</p>	 <p>THOMAS POWLES, MBBS, MRCP, MD</p>	<p>Dose reduction, hold or discontinuation</p>
 <p>DAVID F MCDERMOTT, MD</p>	<p>Dose reduction, hold or discontinuation Supportive care measures</p>	 <p>BRIAN I RINI, MD</p>	<p>Dose reduction, hold or discontinuation Schedule modification</p>

Meet The Professor with Dr Jonasch

MODULE 1: Cases and Questions from Drs Bachow and Flores

MODULE 2: Renal Cell Carcinoma Journal Club with Dr Jonasch



- A review on von Hippel-Lindau disease
- Exposure-response modeling of cabozantinib: Implications for patient care
- Nivolumab for metastatic non-clear cell RCC
- Outcomes for patients with metastatic RCC with sarcomatoid dedifferentiation to immune checkpoint inhibitors (ICIs)
- Macrophage HIF-1 α : An independent prognostic indicator in RCC
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- Axitinib with ICIs: Consensus recommendation for treatment optimization and management of related AEs
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- Oral HIF-2 α inhibitor MK-6482 for von Hippel-Lindau disease-associated RCC
- Society for Immunotherapy of Cancer consensus statement on immunotherapy for advanced RCC

MODULE 3: Beyond the Guidelines – Clinical Investigator Approaches to Common Clinical Scenarios

MODULE 4: Key Recent Data Sets

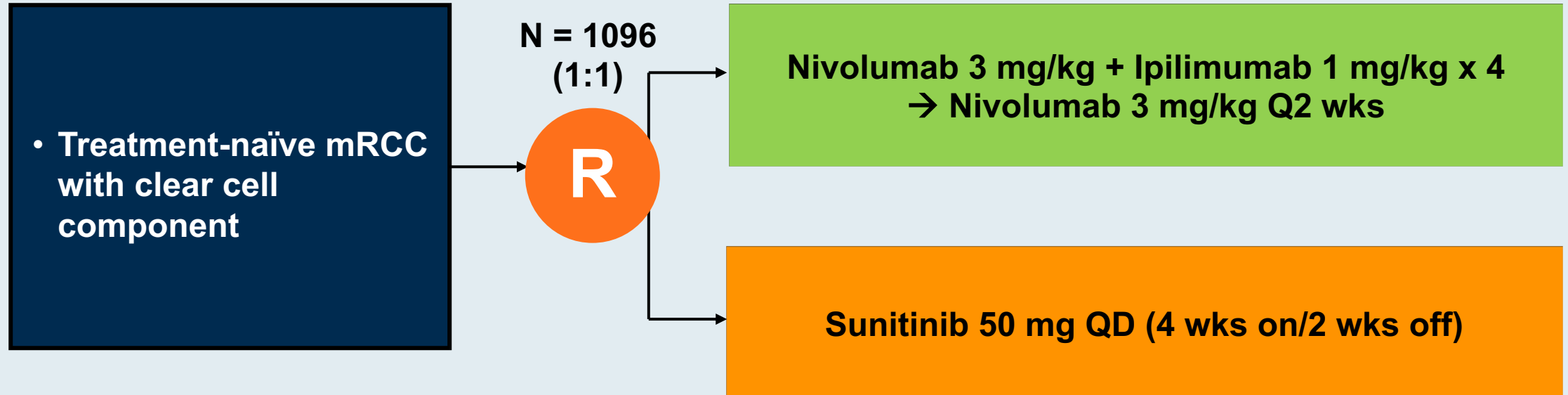


Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial

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 Phase III Schema



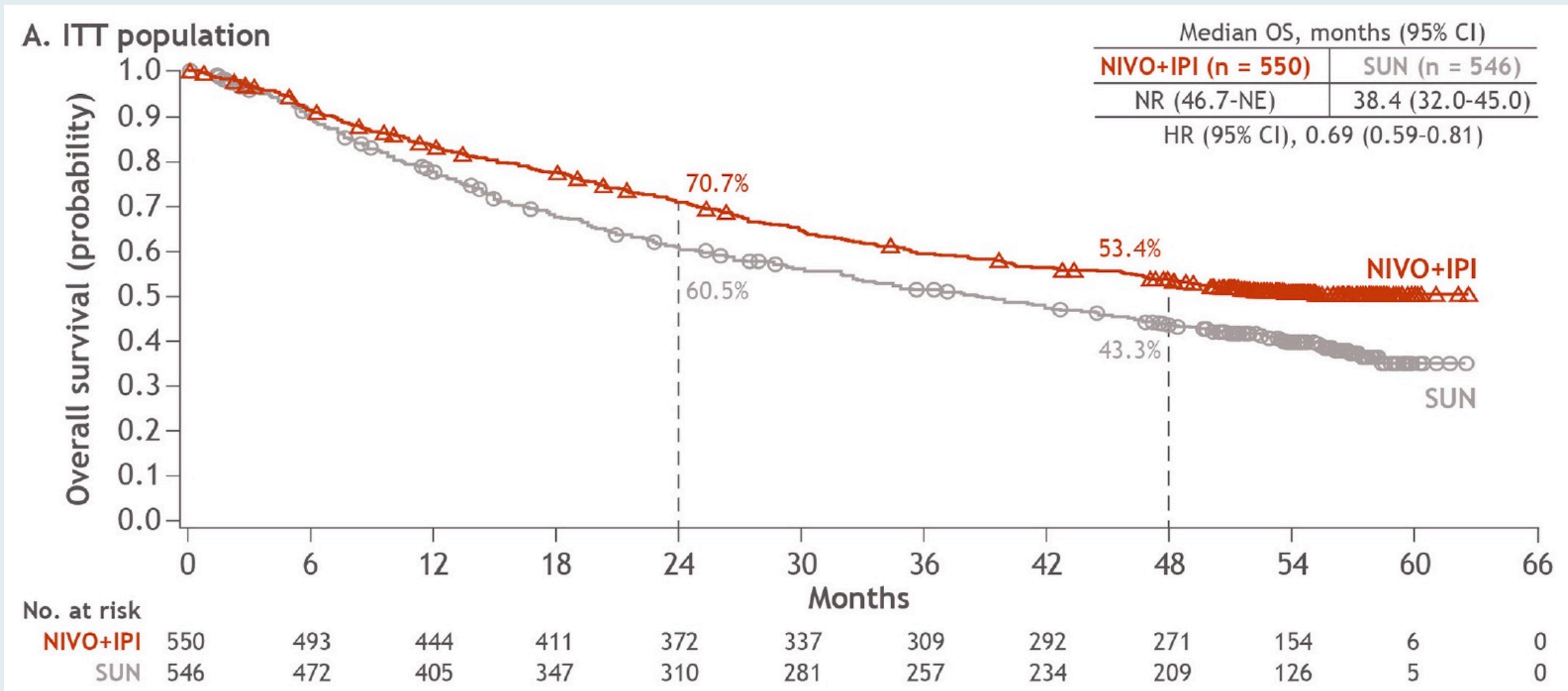
Co-Primary Endpoints

Objective response rate (ORR),
Progression-free survival (PFS),
Overall survival in intermediate- and poor-risk patients

CheckMate 214: Overall Response and Best Response Rate per IRRC at 4 Years, Minimum Follow-Up in ITT

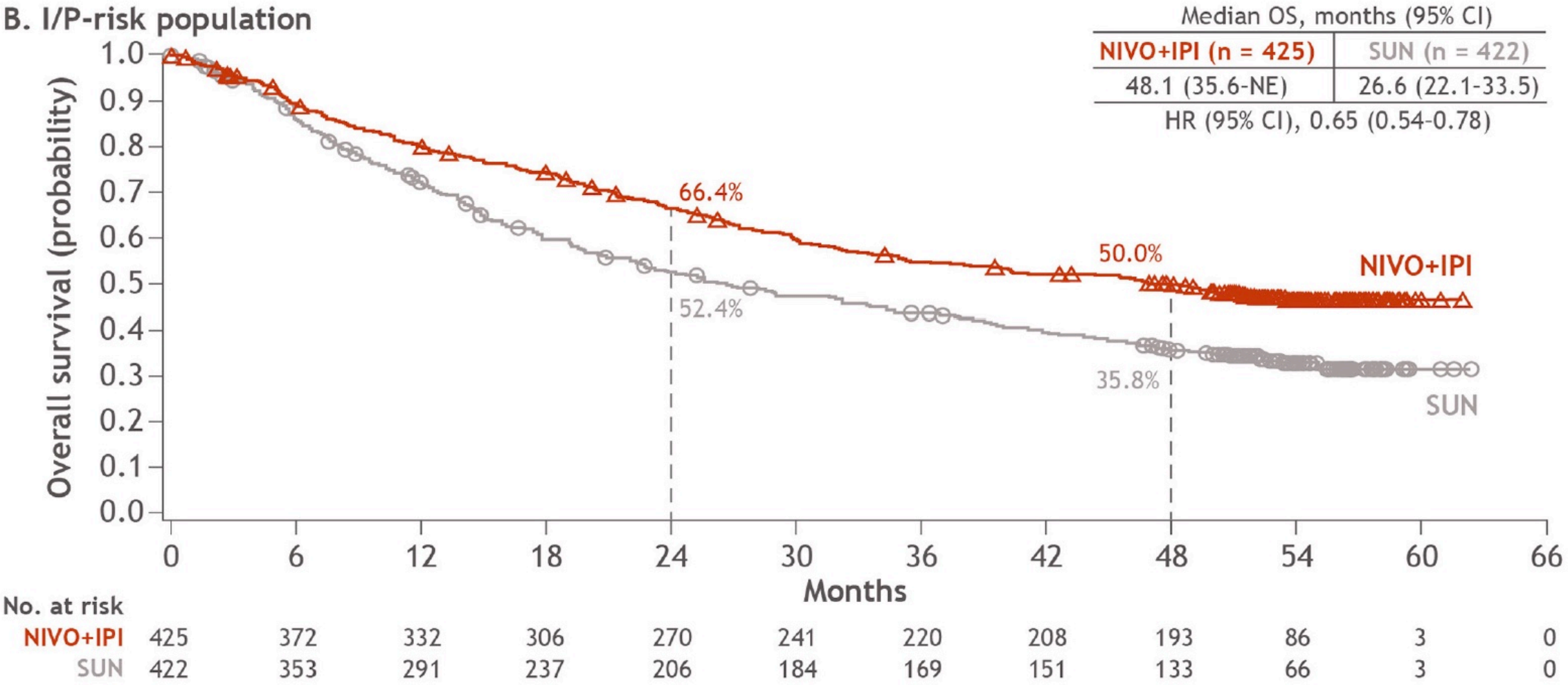
	Intent-to-Treat		Intermediate/Poor Risk		Favorable Risk	
	Nivo + Ipi (n = 550)	Sunitinib (n = 546)	Nivo + Ipi (n = 425)	Sunitinib (n = 422)	Nivo + Ipi (n = 125)	Sunitinib (n = 124)
Confirmed ORR	39.1%	32.4%	41.9%	26.8%	29.6%	51.6%
CR	10.7%	2.6%	10.4%	1.4%	12.0%	6.5%
PR	28.4%	29.9%	31.5%	25.4%	17.6%	45.2%
Stable disease	36.0%	42.1%	30.8%	44.3%	53.6%	34.7%
Progressive disease	17.6%	14.1%	19.3%	16.8%	12.0%	4.8%
Ongoing response	65.1%	52.0%	65.2%	49.6%	64.9%	56.3%

CheckMate 214: Overall Survival (ITT)



CheckMate 214: Overall Survival (Intermediate/Poor Risk)

B. I/P-risk population



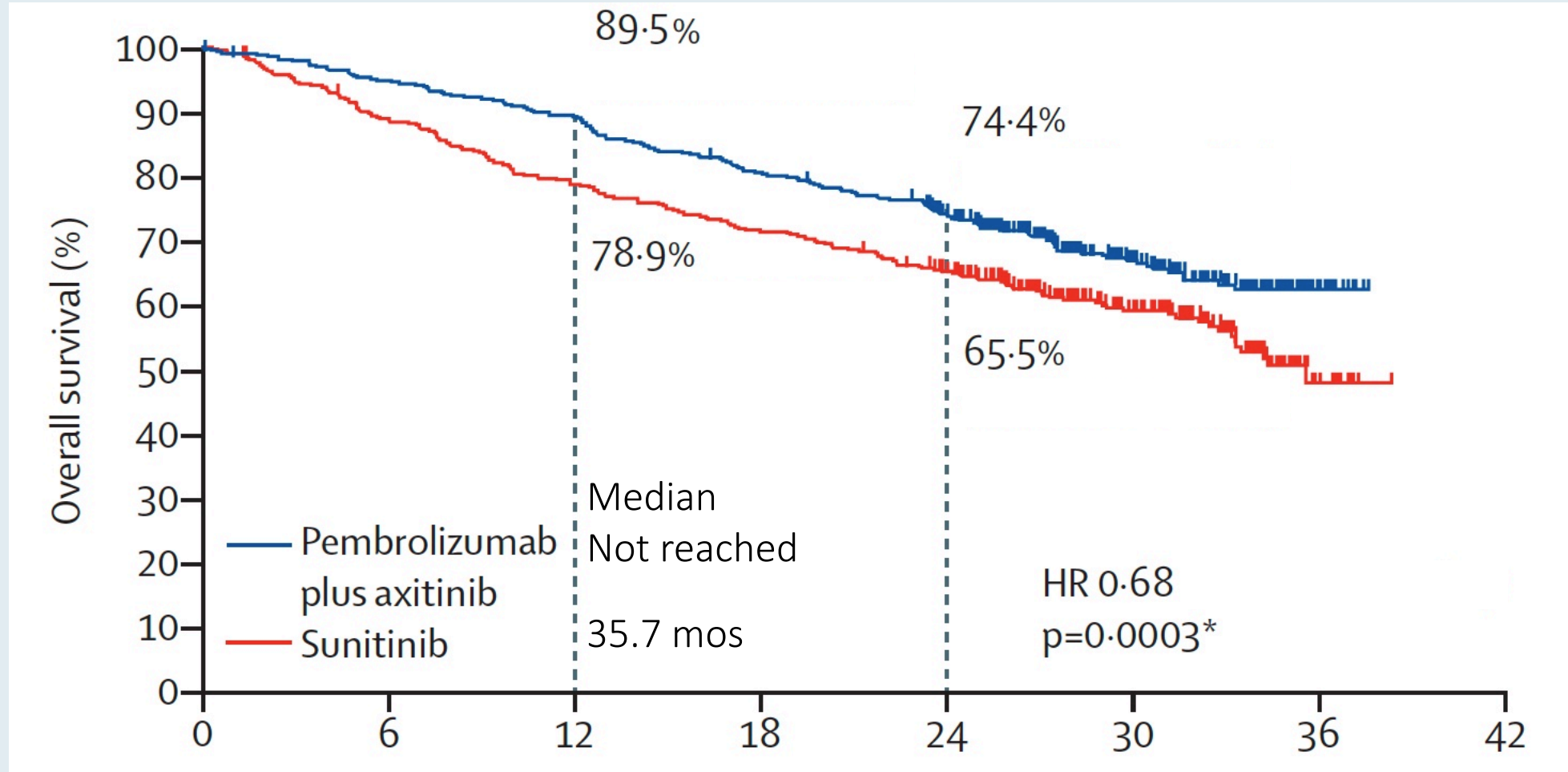
Lancet Oncol 2020;21:1563-73

**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



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

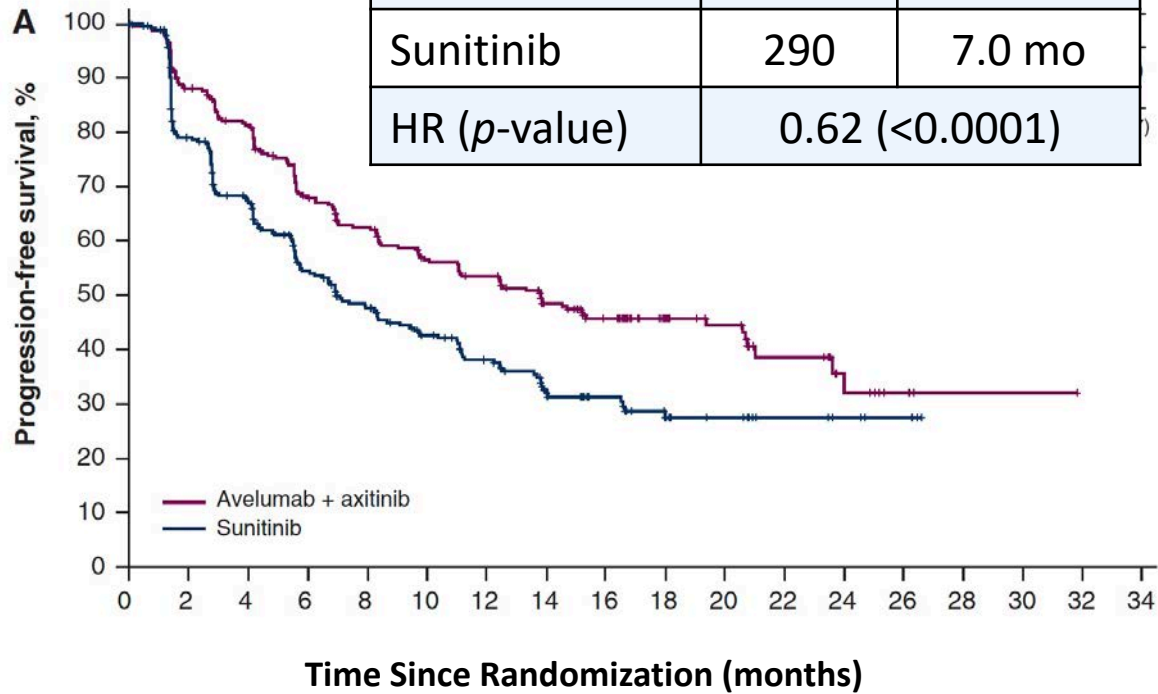
JAVELIN Renal 101: Overall Response and Best Response Rate in the PD-L1-Positive and Overall Populations

	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

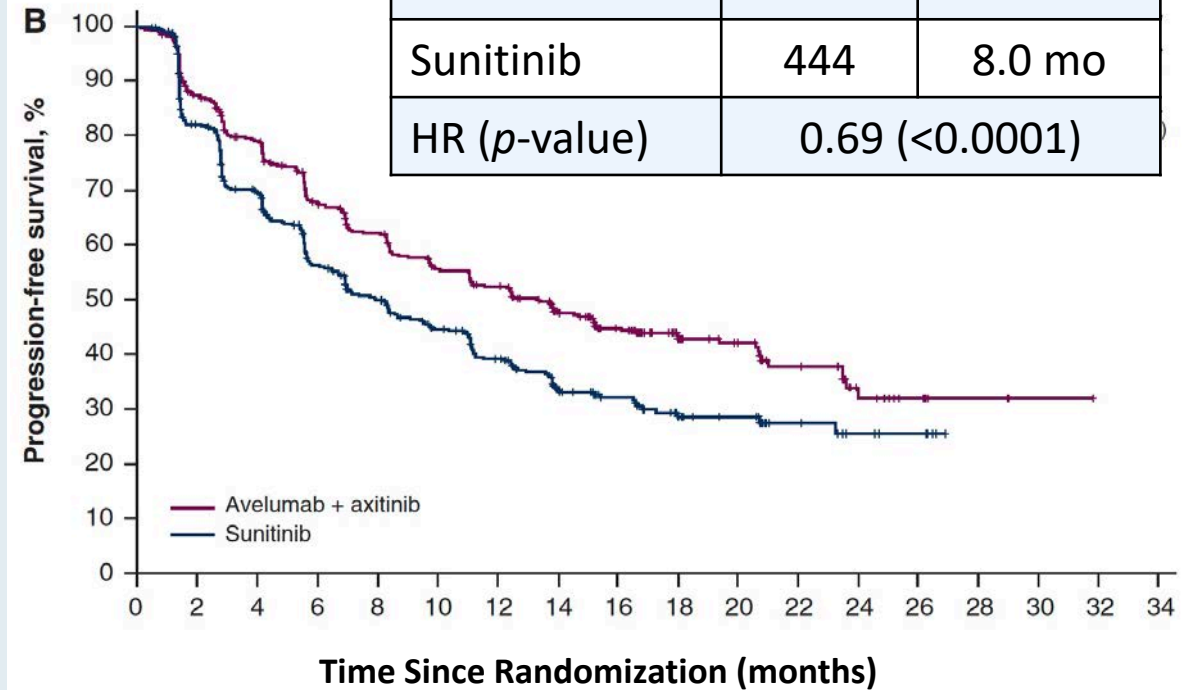
PD-L1 \geq 1% Population

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



Overall Population

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



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).”

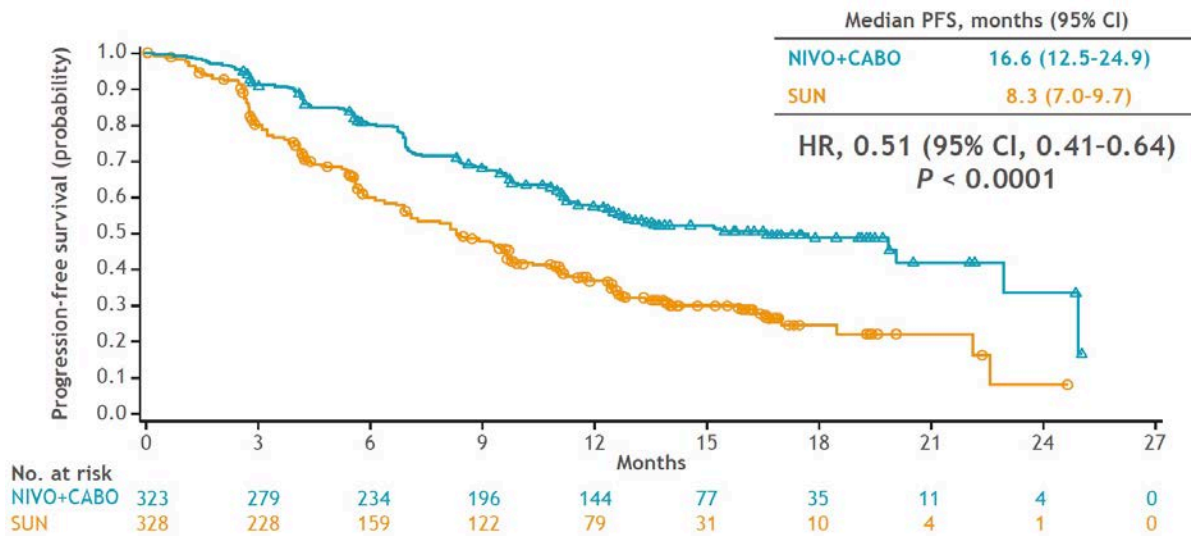
Nivolumab plus Cabozantinib versus Sunitinib in First-Line Treatment for Advanced Renal Cell Carcinoma: First Results from the Randomized Phase 3 CheckMate 9ER Trial

Choueiri TK et al.

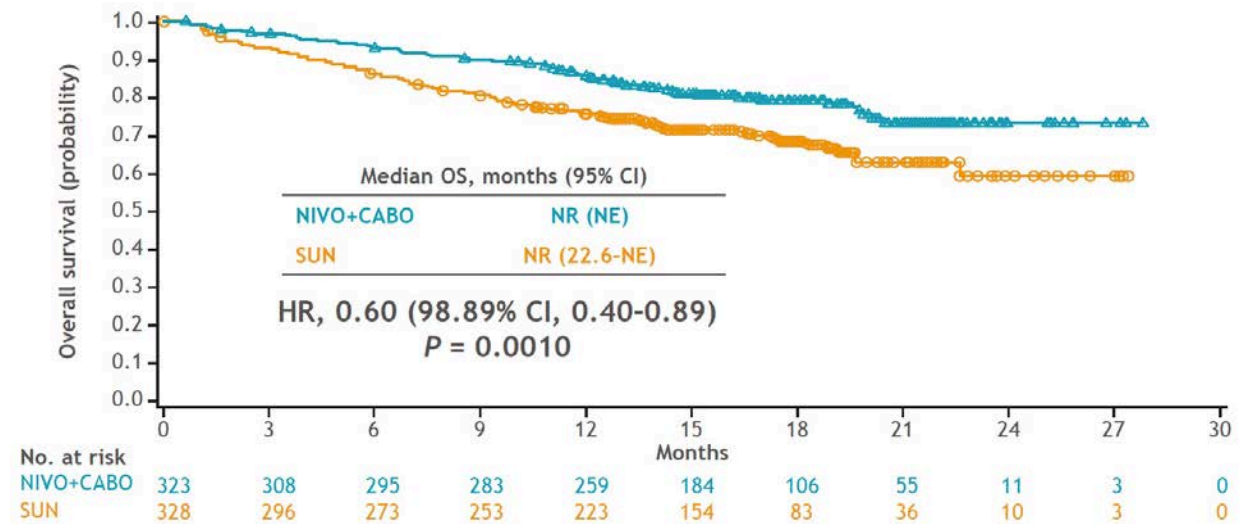
ESMO 2020;Abstract 6960.

CheckMate 9ER Survival Analyses: Nivolumab/Cabozantinib for Previously Untreated Advanced RCC

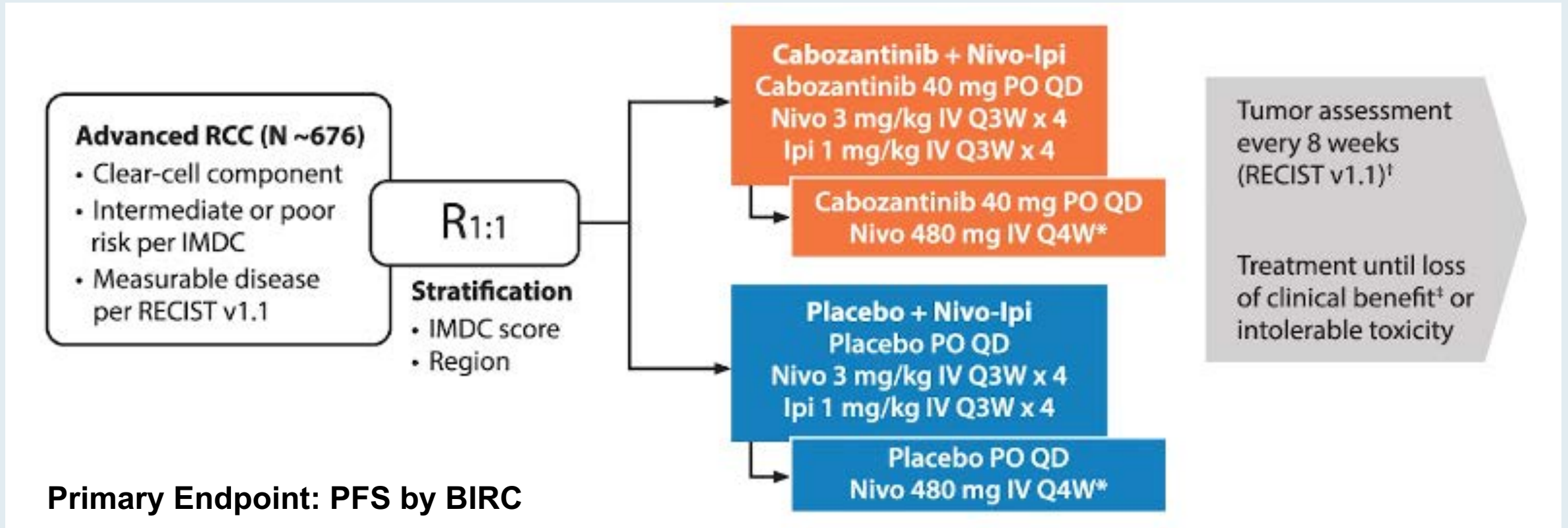
Progression-free survival per BICR



Overall survival

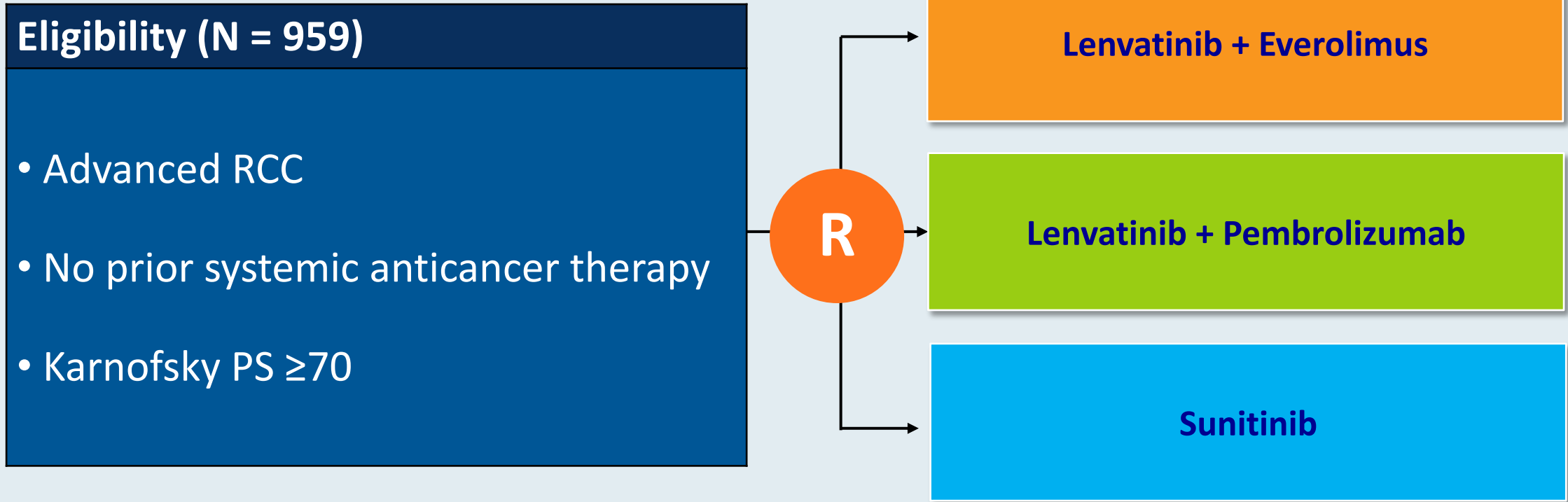


COSMIC-313 Phase III Schema



<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>

Ongoing Phase III KEYNOTE-581/CLEAR (Study 307) Trial Design



Primary endpoint: PFS

Secondary endpoints include: OS, Objective Response, Safety

Top-Line Results from the Pivotal Phase III KEYNOTE-581 (CLEAR) Trial

Press Release: November 10, 2020

“New investigational data were announced demonstrating positive top-line results from the pivotal Phase 3 KEYNOTE-581/CLEAR trial (Study 307). In the trial, the combinations of pembrolizumab plus lenvatinib, the orally available multiple receptor tyrosine kinase inhibitor, and LENVIMA plus everolimus were evaluated versus sunitinib for the first-line treatment of patients with advanced RCC. Pembrolizumab plus lenvatinib met the trial’s primary endpoint of PFS and its key secondary endpoints of OS and objective response rate (ORR), demonstrating a statistically significant and clinically meaningful improvement in PFS, OS and ORR versus sunitinib in the intention-to-treat (ITT) study population.

Lenvatinib plus everolimus also met the trial’s primary endpoint of PFS and a key secondary endpoint of ORR, demonstrating a statistically significant and clinically meaningful improvement in PFS and ORR versus sunitinib in the ITT study population. The ITT population included patients across all Memorial Sloan Kettering Cancer Center (MSKCC) risk groups (favorable, intermediate and poor).

The safety profiles of both pembrolizumab plus lenvatinib and lenvatinib plus everolimus were consistent with previously reported studies.”

Phase 3 Trial of Lenvatinib (LEN) plus Pembrolizumab (PEMBRO) or Everolimus (EVE) versus Sunitinib (SUN) Monotherapy as a First-Line Treatment for Patients (pts) with Advanced Renal Cell Carcinoma (RCC) (CLEAR study)

Motzer RJ et al.

Genitourinary Cancers Symposium 2021;Abstract 269.

CLEAR: Response and Survival Analyses

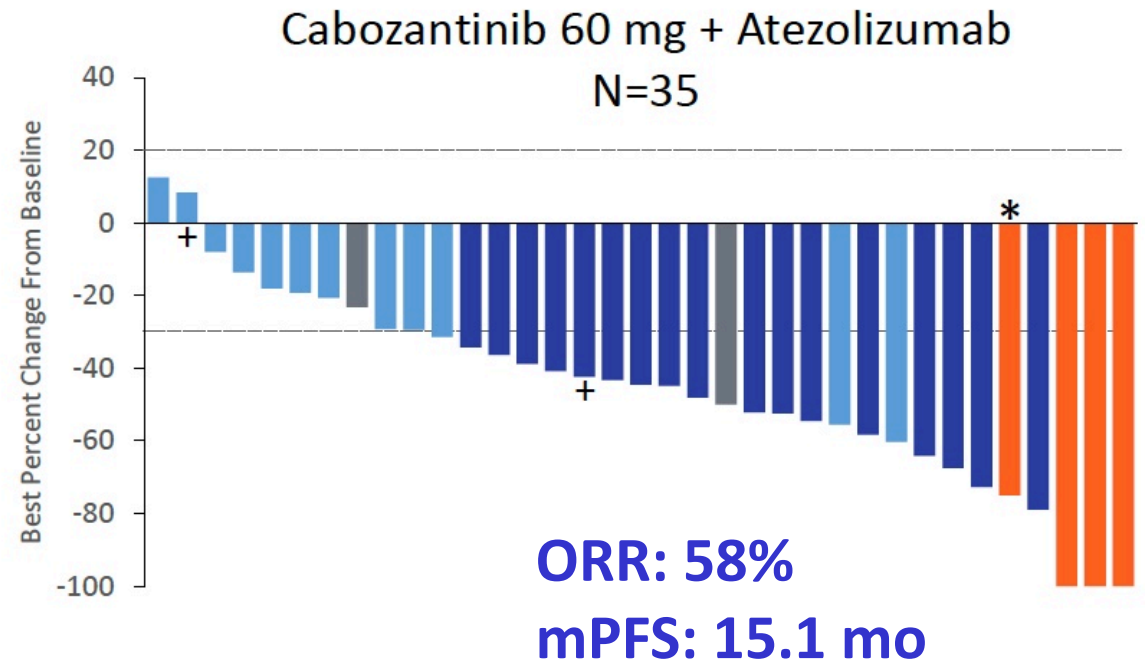
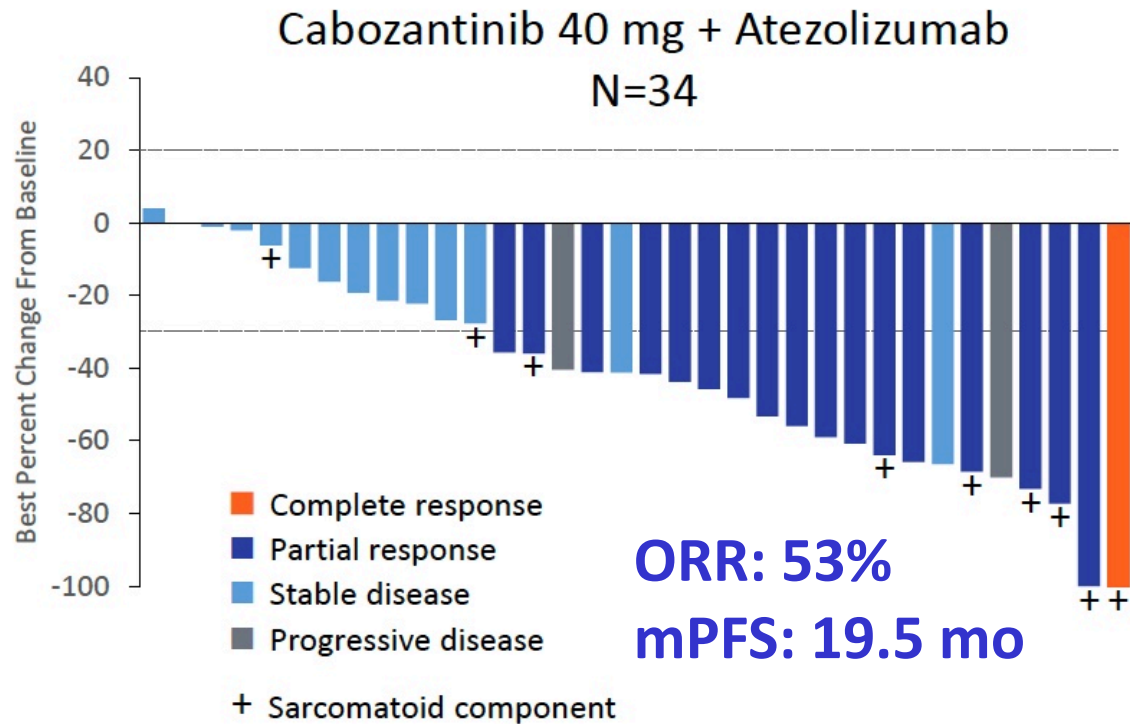
	LEN + PEMBRO (n = 355)	LEN + EVE (n = 357)	SUNITINIB (n = 357)
Median PFS	24 mo	15 mo	9 mo
PFS HR vs SUN; <i>p</i> -value	0.39 <i>p</i> < 0.0001	0.65 <i>p</i> < 0.0001	—
Median OS	NR	NR	NR
OS HR vs SUN; <i>p</i> -value	0.66 <i>p</i> = 0.0049	1.15 <i>p</i> = 0.2975	—
24-month OS rate	79%	66%	70%
ORR	71%	54%	36%
ORR odds ratio vs SUN; Descriptive <i>p</i> -value	4.35 <i>p</i> < 0.0001	2.15 <i>p</i> < 0.0001	—
Complete response	16%	10%	4%
Median DOR	26 mo	17 mo	15 mo

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 in Previously Untreated Advanced ccRCC



Select, Ongoing Phase III Clinical Trials in 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	<p>After Induction nivolumab/ipilimumab</p> <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> → Nivolumab → Nivolumab + Cabozantinib Pts with PD → Cabozantinib 	OS	Sept 2021

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 in 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)

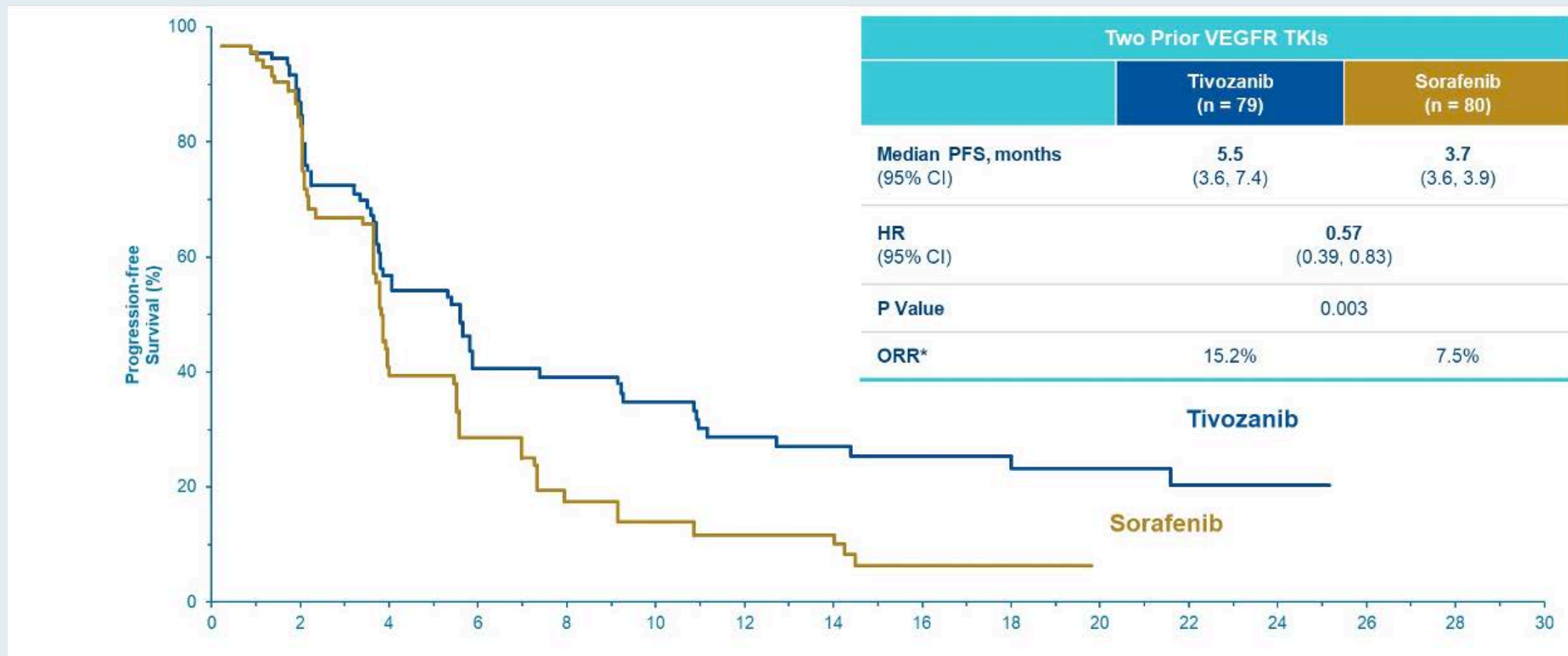
Abbreviations: BOR, best objective response; ICI, immune checkpoint inhibitor; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

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 2 Prior TKIs Patient Subgroup



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%

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 Group (N = 33)	No Prior IO Group (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

What Clinicians Want to Know: Understanding the Factors Affecting the Optimal Diagnosis and Management of Ovarian Cancer

**Thursday, February 18, 2021
5:00 PM – 6:00 PM ET**

Faculty

Michael J Birrer, MD, PhD

Kathleen Moore, MD

David M O'Malley, MD

Moderator

Neil Love, MD

Thank you for joining us!

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