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

In Partnership with Project Echo® and Florida Cancer Specialists

Tuesday, April 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Sumanta K Pal, MD
Uday Dandamudi, MD

Moderator

Neil Love, MD

Faculty

Sumanta K Pal, MD
Clinical Professor, Department of
Medical Oncology
City of Hope Comprehensive Cancer Center
Duarte, California

Uday Dandamudi, MD
Florida Cancer Specialists and
Research Institute
New Port Richey, Florida

Steering Committee

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

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Head, Section of GU Cancer, Division of Oncology
Associate Professor of Medicine
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Fred C Buffett Professor of Medicine
Dean for Clinical Research
Deputy Director, Comprehensive Cancer Center
The University of Chicago
Chicago, Illinois

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Commercial Support

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Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

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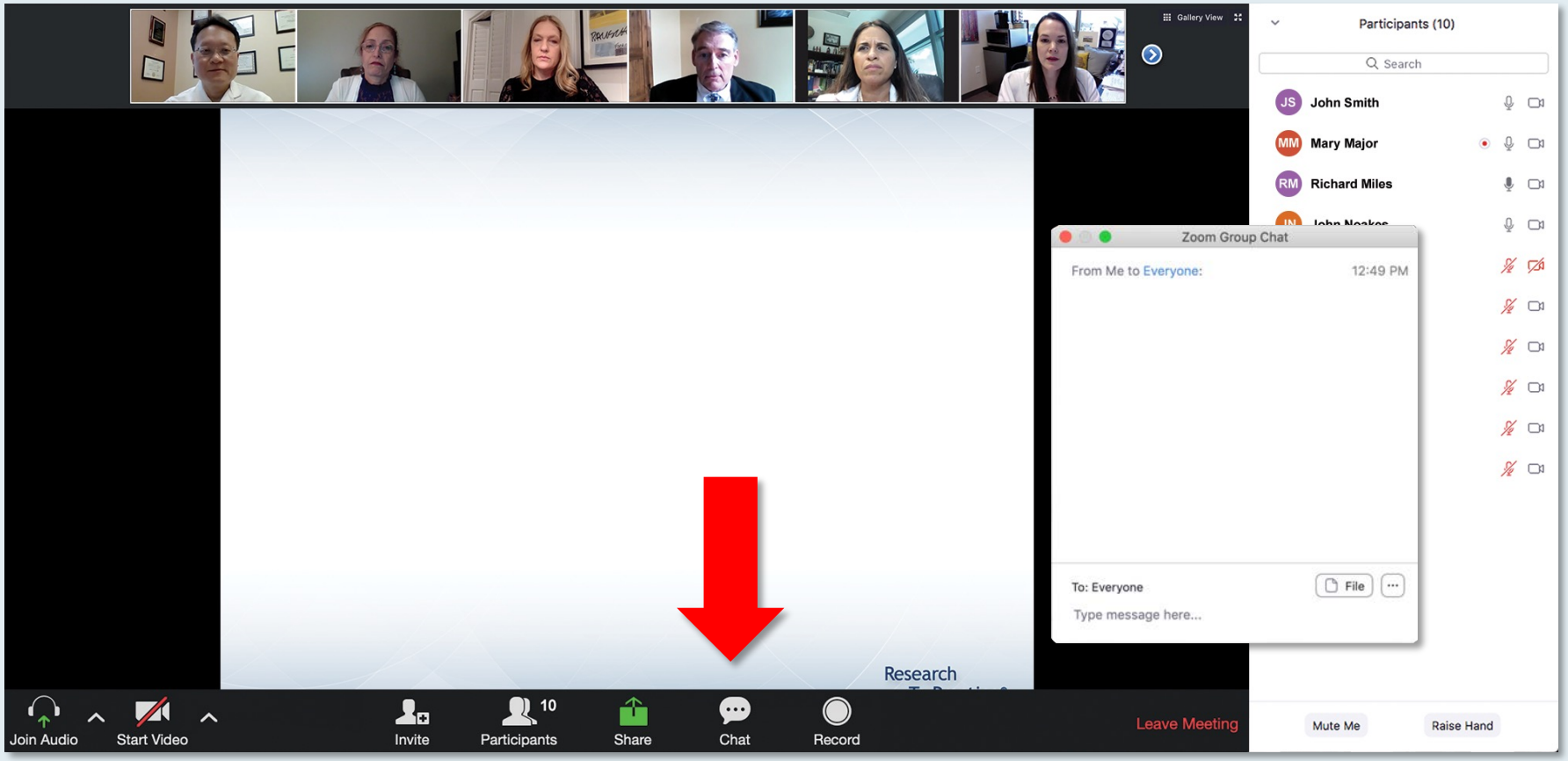
Dr Pal — Disclosures

No relevant conflicts of interest to disclose.

Dr Dandamudi — Disclosures

No relevant conflicts of interest to disclose.

We Encourage Clinicians in Practice to Submit Questions



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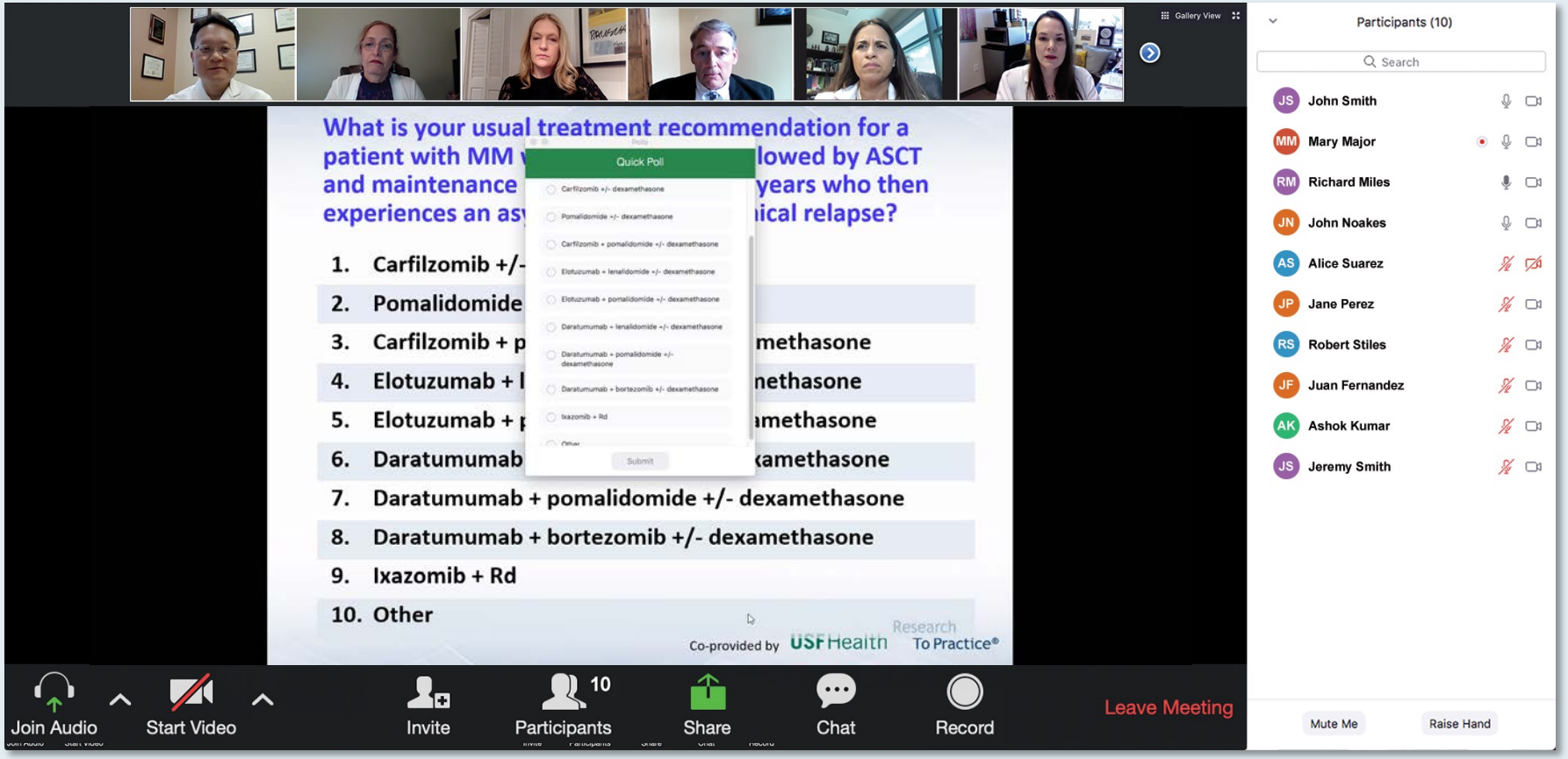
Familiarizing Yourself with the Zoom Interface

How to answer poll questions



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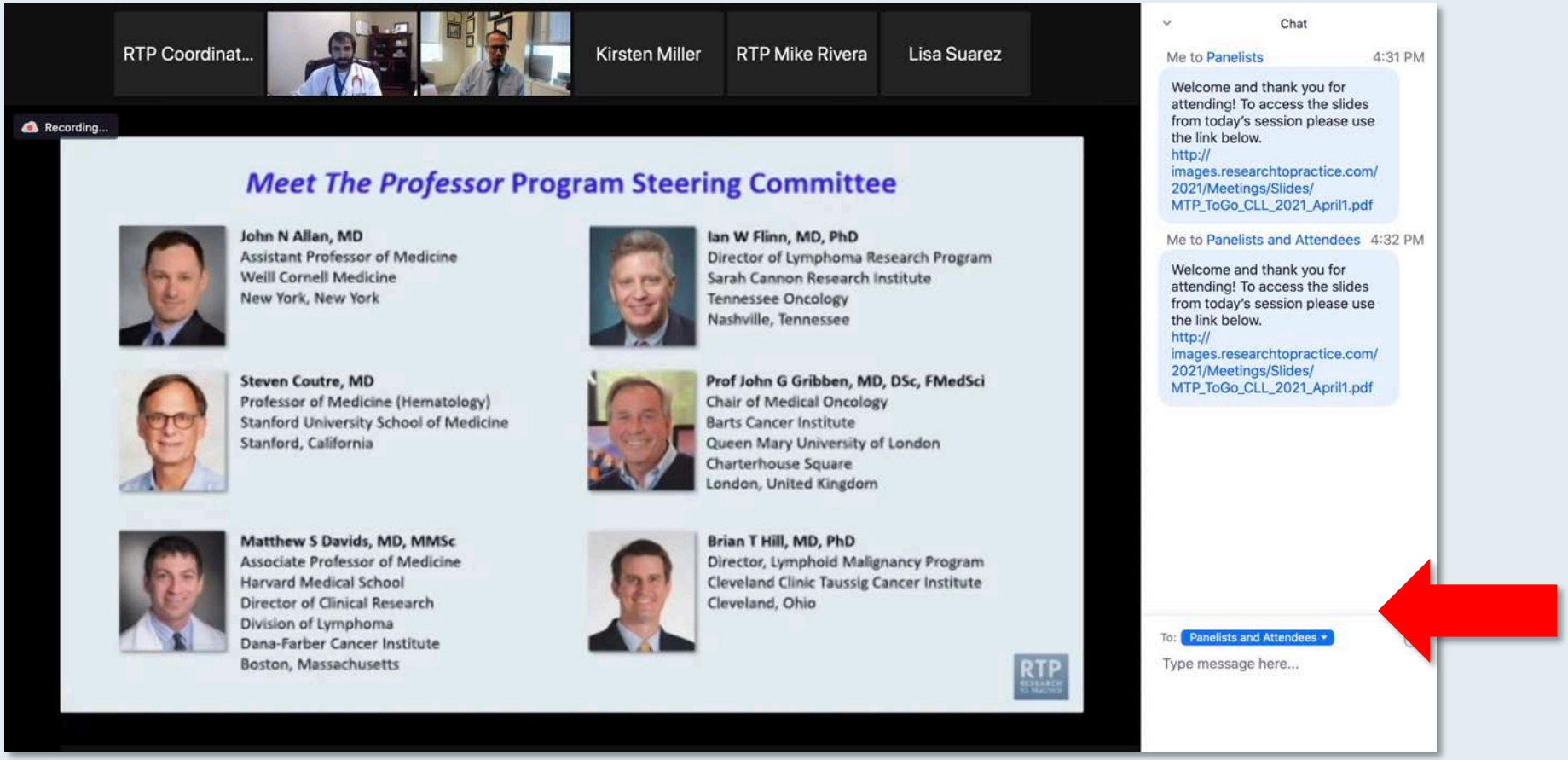
Familiarizing Yourself with the Zoom Interface

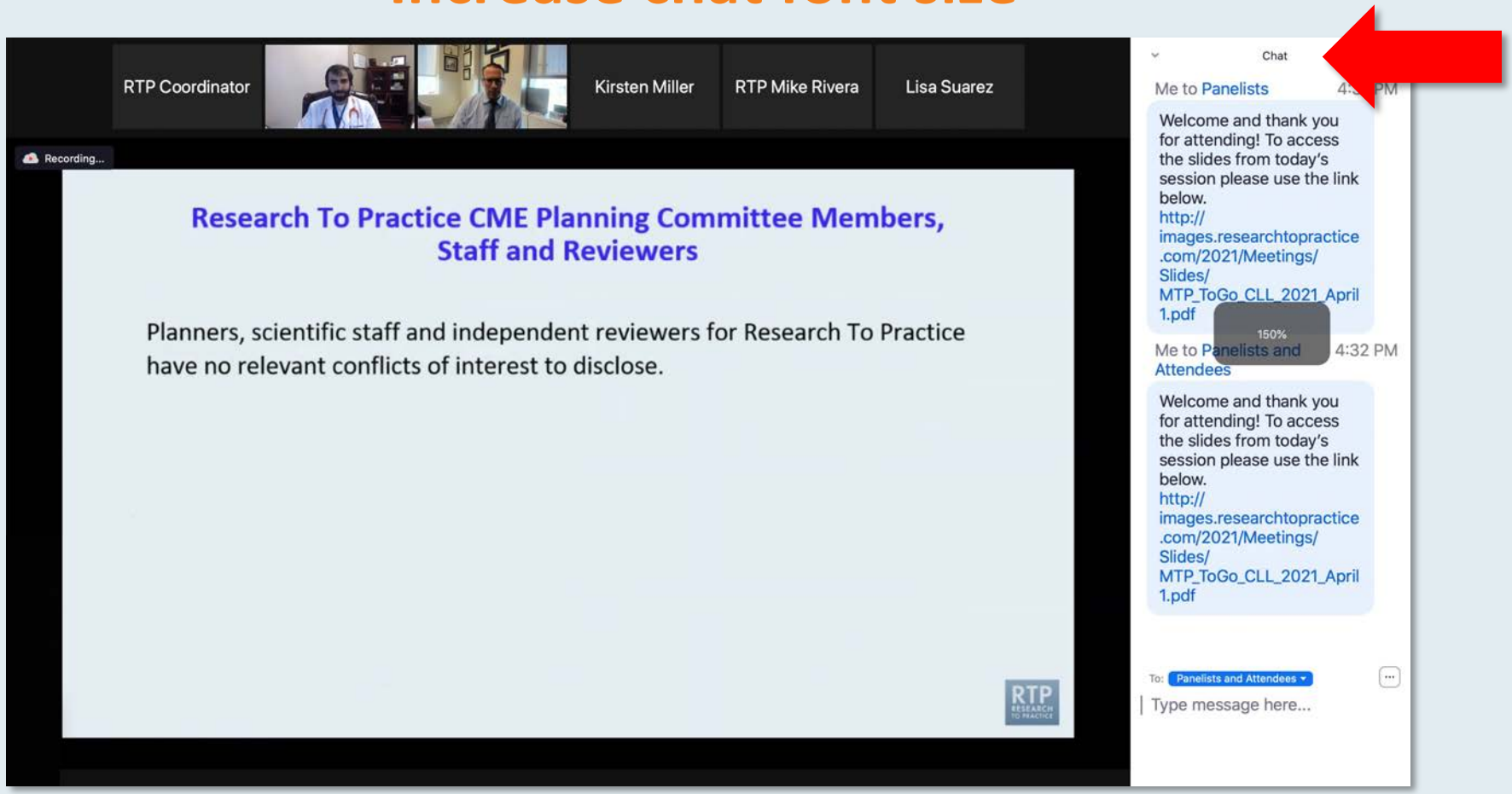
Expand chat submission box



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

MEMORIAL SLOAN KETTERING CANCER CENTER

NEW YORK, NEW YORK

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Thursday, April 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Dirk Arnold, MD, PhD

Moderator

Neil Love, MD

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Ask the Investigators: Applying Emerging Clinical Research to the Care of Patients with Gastroesophageal Cancers

A Satellite Educational Symposium Held in Conjunction with the 2021 AACR Virtual Annual Meeting

Monday, April 12, 2021
6:30 PM – 7:30 PM ET

Faculty

Joseph Chao, MD
Yelena Y Janjigian, MD

Moderator

Neil Love, MD

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RESEARCH
TO PRACTICE

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Thursday, April 15, 2021
5:00 PM – 6:00 PM ET

Faculty

John N Allan, MD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Dissecting the Decision: Investigator Perspectives on Key Issues in the Management of Common Cancers

A Complimentary NCPD Live Webinar Series Hosted in Conjunction with the 46th Annual ONS Congress

Breast Cancer
Tuesday, April 20, 2021
8:30 AM – 10:00 AM ET

Non-Small Cell Lung Cancer
Tuesday, April 20, 2021
5:00 PM – 6:30 PM ET

Acute Myeloid Leukemia
Wednesday, April 21, 2021
12:00 PM – 1:00 PM ET

Colorectal and Gastroesophageal Cancers
Wednesday, April 21, 2021
4:45 PM – 5:45 PM ET

Prostate Cancer
Thursday, April 22, 2021
8:30 AM – 10:00 AM ET

Hodgkin and Non-Hodgkin Lymphomas
Thursday, April 22, 2021
5:00 PM – 6:30 PM ET

Multiple Myeloma
Tuesday, April 27, 2021
8:30 AM – 10:00 AM ET

Gynecologic Cancers
Tuesday, April 27, 2021
5:00 PM – 6:30 PM ET

Urothelial Bladder Carcinoma
Wednesday, April 28, 2021
12:00 PM – 1:00 PM ET

Chronic Lymphocytic Lymphoma
Thursday, April 29, 2021
8:30 AM – 10:00 AM ET

Chimeric Antigen Receptor T-Cell Therapy
Thursday, April 29, 2021
5:00 PM – 6:30 PM ET

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RESEARCH TO PRACTICE

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In Partnership with Project Echo® and Florida Cancer Specialists

Webinar 1 – Tuesday, April 6, 2021

Faculty
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Webinar 2 – Tuesday, May 4, 2021

Faculty
Chung-Han Lee, MD, PhD

Webinar 3 – Tuesday, June 1, 2021

Faculty
Walter Stadler, MD

Webinar 4 – Tuesday, July 6, 2021

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SUBMIT A CASE OR QUESTION FOR OUR FACULTY TO PROVIDE THEIR FEEDBACK

http://www.ResearchToPractice.com/Webinars/RCC2021/Mar-Jun/Questions

This link is posted in our Zoom chat room

Thank you for joining us!

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

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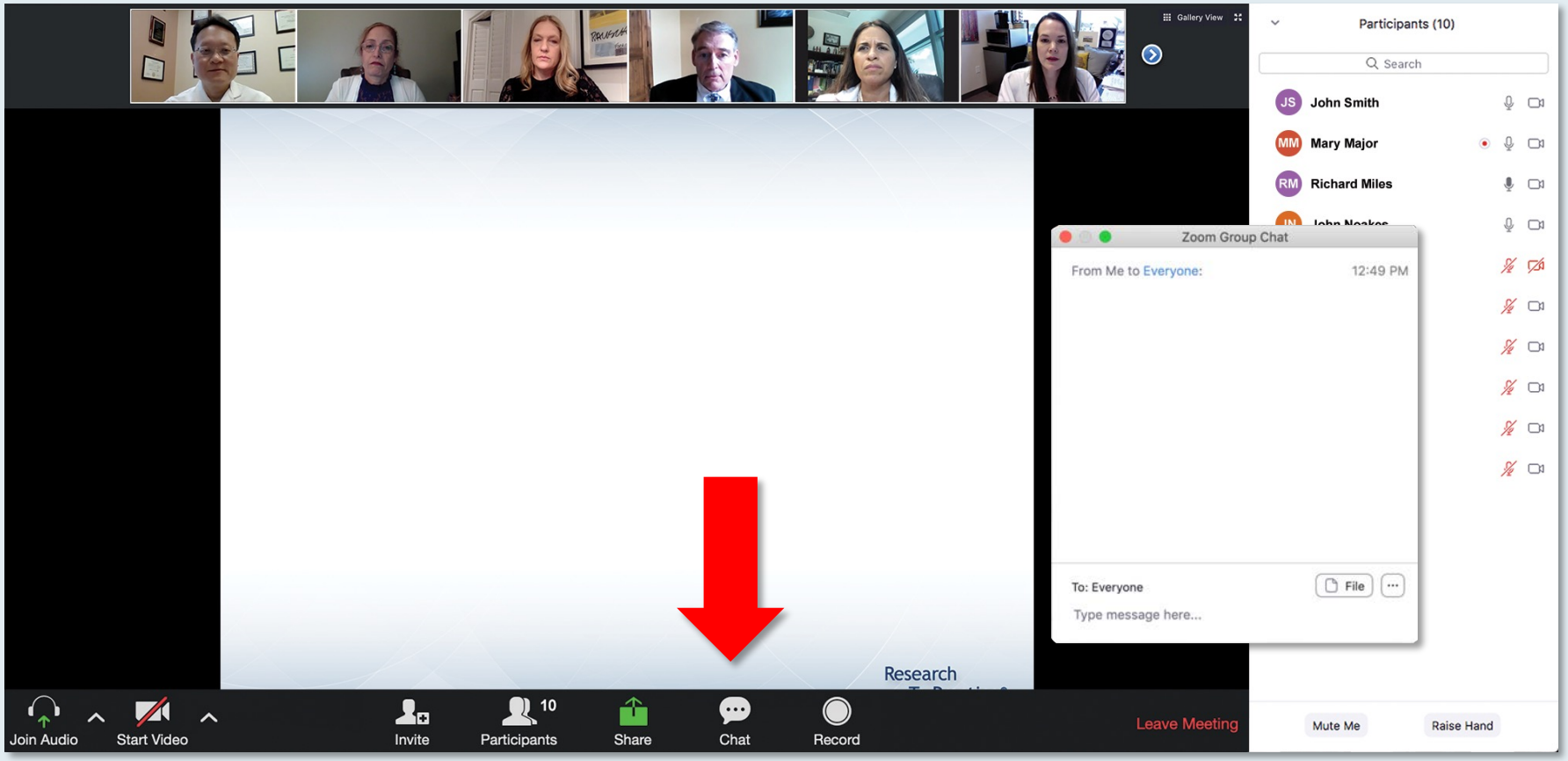

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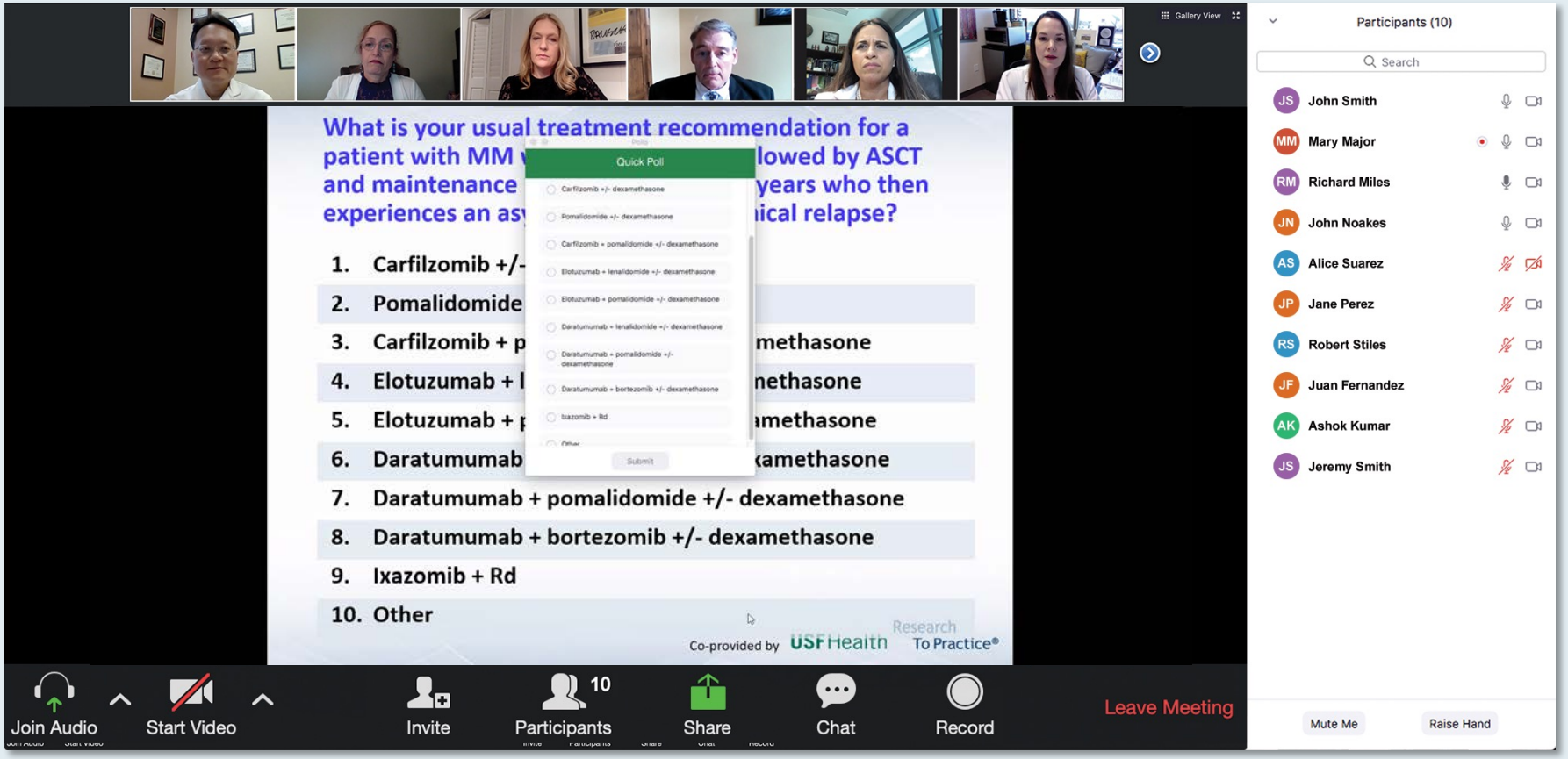

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Agenda

MODULE 1: Cases from the Practice of Dr Dandamudi

- A 60-year-old woman with renal cell carcinoma (RCC) and rhabdoid features who responded to ipilimumab/nivolumab
- A 68-year-old man with RCC and MET amplification
- A 42-year-old man with RCC and sarcomatoid differentiation

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

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Pal

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

Case Presentation: Dr Dandamudi – A 60-year-old woman with RCC and rhabdoid features who responded to ipilimumab/nivolumab and then developed autoimmune hepatitis

- A 60-year-old female was diagnosed with RCC with rhabdoid features in January 2019. IMDC high risk (KPS 90%, Hgb 10.8 g/dl, Ca 9.8 mg/dl, neutrophils 3 x 109/L, platelets 225 cell/microliter) and LDH was 552. Imaging showed right hilar lymph node of 2.4 x 1.9 cm, right upper lobe mass of 3.2 cm, bulky para-aortic lymphadenopathy with largest measuring 4.5 cm as well as left renal mass of 6 cm. Biopsy of the lung mass was consistent with RCC with rhabdoid features.
- Started on ipilimumab and nivolumab in January 2019 and had good response to the treatment. Follow-up scans showed very good response and was continued on maintenance nivolumab. Last scans done in December 2020 demonstrated 1.7 x 1.5 cm (stable since January 2020), heterogenous mass in the anterior aspect of left kidney measuring 2.7 x 2.1 cm (stable since October 2019).
- Needed multiple interruptions of nivolumab because of the autoimmune hepatitis, and patient also developed adrenal insufficiency for which patient is on hydrocortisone supplementation.

Questions

- Can we stop the treatment and follow closely?
- Do you get biopsy prior to making decision about stopping the immunotherapy?

Case Presentation: Dr Dandamudi – A 68-year-old man with RCC and MET amplification

- A 68-year-old male with no significant past medical history incidentally noted to have mass on the left kidney in October 2019 after patient presented to the ED with complaints of left flank pain. CT scan showed left kidney mass of 6 x 8 cm, clear cell type, Fuhrman grade 3, negative for renal vascular invasion and no extension outside the capsule. Stage IA (pT1b, pN0 cM0)
- He presented to the ED on 03/16/2021 with complaints of right hip pain and unable to bear weight. Work up showed large destructive mass over the acetabulum of the left pelvis with pathologic fracture. He was also noted to have bulky retroperitoneal lymph nodes, largest measuring 3 cm and noted to have mass over the left renal fossa measuring 5 x 6 cm. Biopsy showed mostly necrotic tumor and scanty clusters of atypical cell embedded in cellular fibrous stroma suggestive of renal cell carcinoma. IMDC intermediate risk. His LDH was 294. His CMP and CBC with diff were normal.
- Guardant CDx® showed MET amplification, Tp53 G282V.

Questions

- What regimen do you prefer in this patient?
- Does MET amplification influence the treatment decisions?

Case Presentation: Dr Dandamudi – A 42-year-old man with RCC and sarcomatoid differentiation

- A 42-year-old male with past medical history of hypertension and hyperlipidemia presented to the ED in March 2021 with complaints of SOB and hemoptysis. Work up showed bilateral pulmonary nodules, largest was 3 cm, mediastinal lymph nodes with subcarinal lymph node measuring 2.5 cm, liver lesions measuring 3 cm and 4 cm over the right lobe and 4 x 6 cm over the upper pole of the right kidney.
- Lytic lesions were noted on the T12 with compression fracture as well as right iliac bone. Biopsy of the pulmonary nodule was positive renal cell carcinoma with sarcomatoid differentiation. CBC with diff showed ANC 2.2, and platelets 480. CMP showed Alk phos of 380 and calcium of 10.8 mg/dl. LDH was 284.

Question

- What regimen do you prefer in sarcomatoid kidney cancers?

Agenda

MODULE 1: Cases from the Practice of Dr Dandamudi

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- A 42-year-old man with RCC and sarcomatoid differentiation

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MODULE 3: Renal Cell Carcinoma Journal Club with Dr Pal

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

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

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

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

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

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for 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)?

 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

Regulatory and reimbursement issues aside, 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 a Hb of 11.4 g/dL (PS = 1)?

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

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

 Dr Lee	Cabozantinib
 Dr Pal	Cabozantinib
 Dr Quinn	Cabozantinib
 Dr Stadler	Cabozantinib

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

 Dr Lee	No
 Dr Pal	No
 Dr Quinn	No
 Dr Stadler	No

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 pembrolizumab/axitinib and experiences disease progression after 12 months?

 Dr Lee	Cabozantinib
 Dr Pal	Cabozantinib
 Dr Quinn	Cabozantinib
 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

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)?

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


Dr Lee — I have


Dr Pal — I have


Dr Quinn — I have


Dr Stadler — I have

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 Dandamudi

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MODULE 3: Renal Cell Carcinoma Journal Club with Dr Pal

- Nivolumab with ipilimumab versus sunitinib in first-line treatment of advanced sarcomatoid RCC
- Cytoreductive nephrectomy for favorable-risk mRCC? Yes, cytoreductive nephrectomy should still be considered
- Deferred cytoreductive nephrectomy in newly diagnosed metastatic RCC (mRCC)
- Impact of probiotic supplementation on gut microbiome and clinical outcome from targeted therapy in mRCC
- Assessment of the stool microbiome in patients with mRCC receiving targeted therapy or immunotherapy
- Stool microbiome profiling of patients with mRCC receiving anti-PD-1 immune checkpoint inhibitors
- Evaluation of clear cell, papillary, and chromophobe RCC metastasis sites and association with survival
- SWOG 1500: Sunitinib versus cabozantinib, crizotinib or savolitinib in metastatic papillary RCC

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

Clin Cancer Res 2021;27(1):78-86

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Efficacy and Safety of Nivolumab Plus Ipilimumab versus Sunitinib in First-line Treatment of Patients with Advanced Sarcomatoid Renal Cell Carcinoma

Nizar M. Tannir[1], Sabina Signoretti[2,3], Toni K. Choueiri[4], David F. McDermott[5], Robert J. Motzer[6], Abdallah Flaifel[2], Jean-Christophe Pignon[2], Miriam Ficial[2], Osvaldo Arén Frontera[7], Saby George[8], Thomas Powles[9], Frede Donskov[10], Michael R. Harrison[11], Philippe Barthélémy[12], Scott S. Tykodi[13], Judit Kocsis[14,15], Alain Ravaud[16], Jeronimo R. Rodriguez-Cid[17], Sumanta K. Pal[18], Andre M. Murad[19], Yuko Ishii[20], Shruti Shally Saggi[20], M. Brent McHenry[21], and Brian I. Rini[22]

POINT-COUNTERPOINT

Cytoreductive nephrectomy for favorable risk patients with metastatic renal cell carcinoma? Yes, cytoreductive nephrectomy should still be considered

Luis Meza, Alexander Chehrazi-Raffle, and Sumanta Kumar Pal

Curr Opin Urol 2020;30(5):740-2

EUROPEAN UROLOGY 78 (2020) 615–623

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Kidney Cancer

Deferred Cytoreductive Nephrectomy in Patients with Newly Diagnosed Metastatic Renal Cell Carcinoma

Bimal Bhindi[a,b,*], *Jeffrey Graham*[c], *J. Connor Wells*[d], *Ziad Bakouny*[e], *Frede Donskov*[f], *Anna Fraccon*[g], *Felice Pasini*[h], *Jae Lyun Lee*[i], *Naveen S. Basappa*[j], *Aaron Hansen*[k], *Christian K. Kollmannsberger*[l], *Ravindran Kanesvaran*[m], *Takeshi Yuasa*[n], *D. Scott Ernst*[o], *Sandy Srinivas*[p], *Brian I. Rini*[q], *Isaac Bowman*[r], *Sumanta K. Pal*[s], *Toni K. Choueiri*[e], *Daniel Y.C. Heng*[d]

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Cancer Medicine Open Access WILEY

ORIGINAL RESEARCH

Randomized trial assessing impact of probiotic supplementation on gut microbiome and clinical outcome from targeted therapy in metastatic renal cell carcinoma

Nazli Dizman[1,2] | JoAnn Hsu[1] | Paulo G. Bergerot[1] | John D. Gillece[3] | Megan Folkerts[3] | Lauren Reining[3] | Jeffrey Trent[4] | Sarah K. Highlander[3] | Sumanta K. Pal[1]

First Assessment of the Stool Mycobiome in Patients (pts) with Metastatic Renal Cell Carcinoma (mRCC) Receiving Targeted Therapy (TT) or Immunotherapy (IO)

Dizman N et al.

Genitourinary Cancers Symposium 2021;Abstract 337.

EUROPEAN UROLOGY 78 (2020) 498–502

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Brief Correspondence – Editor's Choice

Stool Microbiome Profiling of Patients with Metastatic Renal Cell Carcinoma Receiving Anti–PD-1 Immune Checkpoint Inhibitors

Nicholas J. Salgia[a,†], *Paulo G. Bergerot*[a,†], *Manuel Caitano Maia*[b,†], *Nazli Dizman*[a], *JoAnn Hsu*[a], *John D. Gillece*[c], *Megan Folkerts*[c], *Lauren Reining*[c], *Jeffrey Trent*[d], *Sarah K. Highlander*[c,*], *Sumanta K. Pal*[a,*]

JAMA Netw Open 2021;4(1):e2021869

JAMA Network | Open™

Original Investigation | Oncology

Evaluation of Clear Cell, Papillary, and Chromophobe Renal Cell Carcinoma Metastasis Sites and Association With Survival

Shaan Dudani, MBChB; Guillermo de Velasco, MD; J. Connor Wells, MD; Chun Loo Gan, MBBS; Frede Donskov, MD; Camillo Porta, MD; Anna Fraccon, MD; Felice Pasini, MD; Jae Lyun Lee, MD; Aaron Hansen, MBBS; Georg A. Bjarnason, MD; Benoit Beuselinck, MD; Sumanta K. Pal, MD; Takeshi Yuasa, MD; Nils Kroeger, MD; Ravindran Kanesvaran, MD; M. Neil Reaume, MD; Christina Canil, MD; Toni K. Choueiri, MD; Daniel Y. C. Heng, MD

Sunitinib versus cabozantinib, crizotinib or savolitinib in metastatic papillary renal cell carcinoma (pRCC): Results from the randomized phase II SWOG 1500 study

Sumanta K. Pal,[1] Catherine Tangen,[2] Ian Murchie Thompson Jr.,[3] Naomi B. Haas,[4] Daniel J. George,[5] Daniel Yick Chin Heng,[6] Brian M. Shuch,[7] Mark N. Stein,[8] Maria S. Tretiakova,[9] Peter Humphrey,[10] Adebowale Adeniran,[10] Vivek Narayan,[11] Georg A. Bjarnason,[12] Ulka N. Vaishampayan,[13] Ajjai Shivaram Alva,[13] Tian Zhang,[14] Scott Wesley Cole,[15] Melissa Plets,[2] John Wright,[16] Primo N. Lara Jr.[17]

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PRESENTED AT: Genitourinary Cancers Symposium

#GU21

Abstract 270

Presented By Sumanta Pal at 2021 Genitourinary Cancers Symposium

Agenda

MODULE 1: Cases from the Practice of Dr Dandamudi

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

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Pal

- Nivolumab with ipilimumab versus sunitinib in first-line treatment of advanced sarcomatoid RCC
- Cytoreductive nephrectomy for favorable-risk mRCC? Yes, cytoreductive nephrectomy should still be considered
- Deferred cytoreductive nephrectomy in newly diagnosed metastatic RCC (mRCC)
- Impact of probiotic supplementation on gut microbiome and clinical outcome from targeted therapy in mRCC
- Assessment of the stool microbiome in patients with mRCC receiving targeted therapy or immunotherapy
- Stool microbiome profiling of patients with mRCC receiving anti-PD-1 immune checkpoint inhibitors
- Evaluation of clear cell, papillary, and chromophobe RCC metastasis sites and association with survival
- SWOG 1500: Sunitinib versus cabozantinib, crizotinib or savolitinib in metastatic papillary RCC

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

RTP RESEARCH TO PRACTICE

Project ECHO

Indirect comparison of the 4 regimens available.

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

Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

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 Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%			
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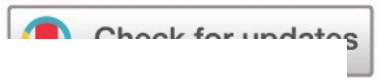
Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

Open access Original research

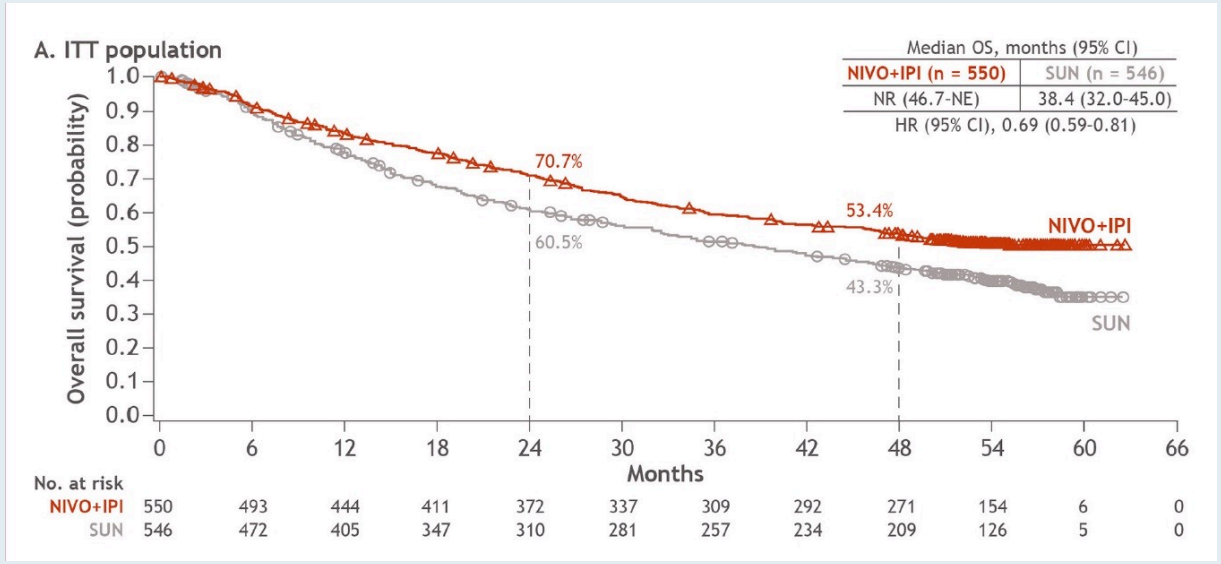


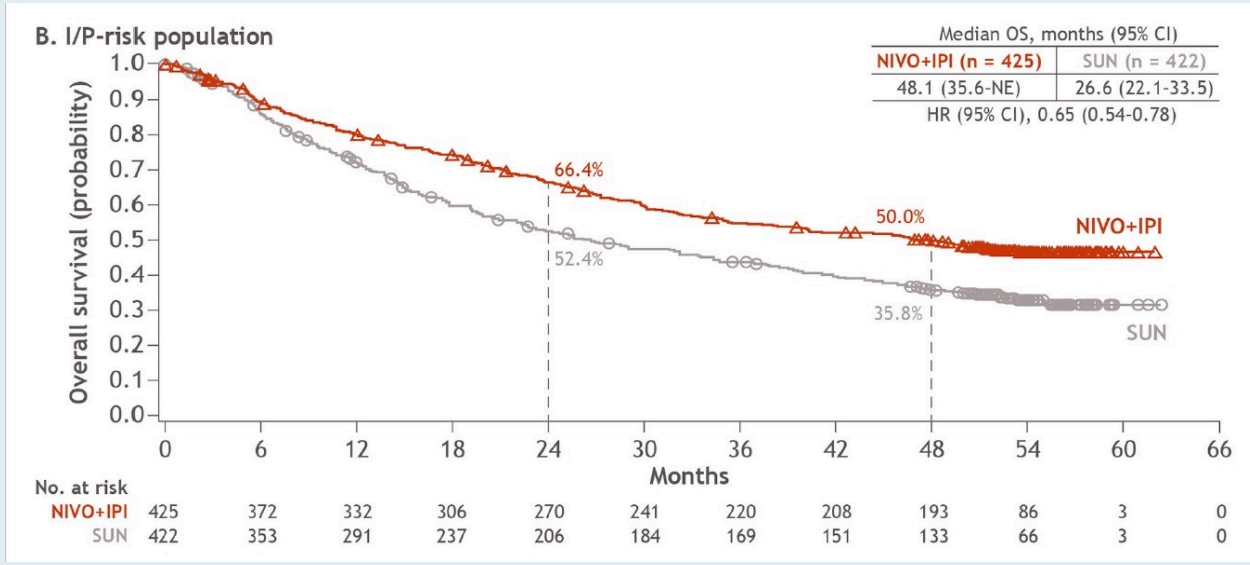
Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial

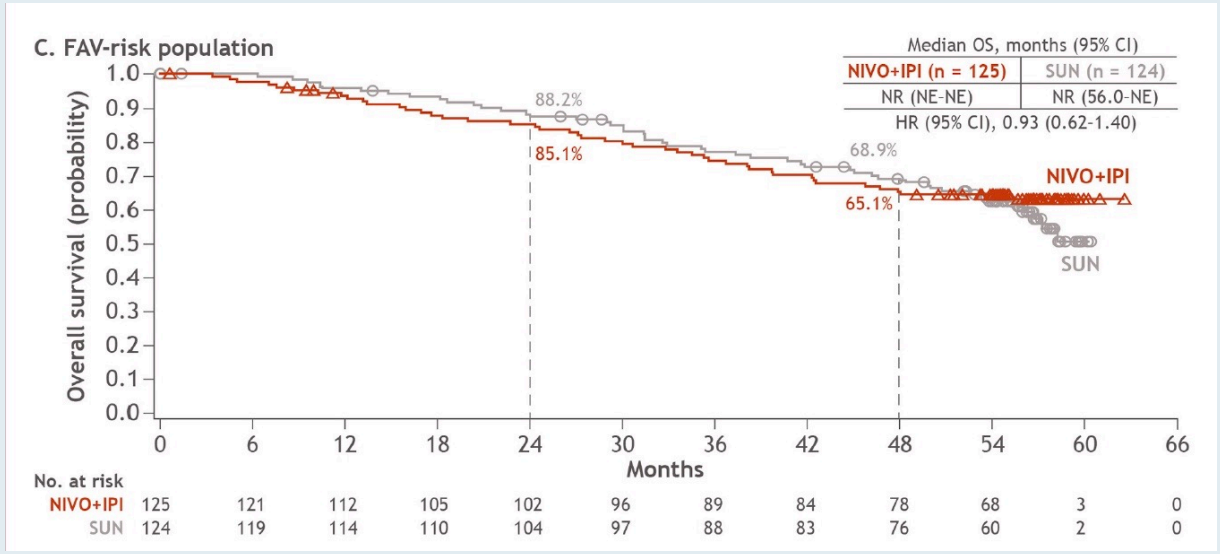
Laurence Albiges ,[1] Nizar M Tannir,[2] Mauricio Burotto,[3] David McDermott,[4,5] Elizabeth R Plimack,[6] Philippe Barthélémy,[7,8] Camillo Porta ,[9] Thomas Powles,[10,11] Frede Donskov,[12] Saby George,[13] Christian K Kollmannsberger,[14] Howard Gurney,[15,16] Marc-Oliver Grimm,[17] Yoshihiko Tomita,[18]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

ESMO Open 2020;5(6):e001079

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

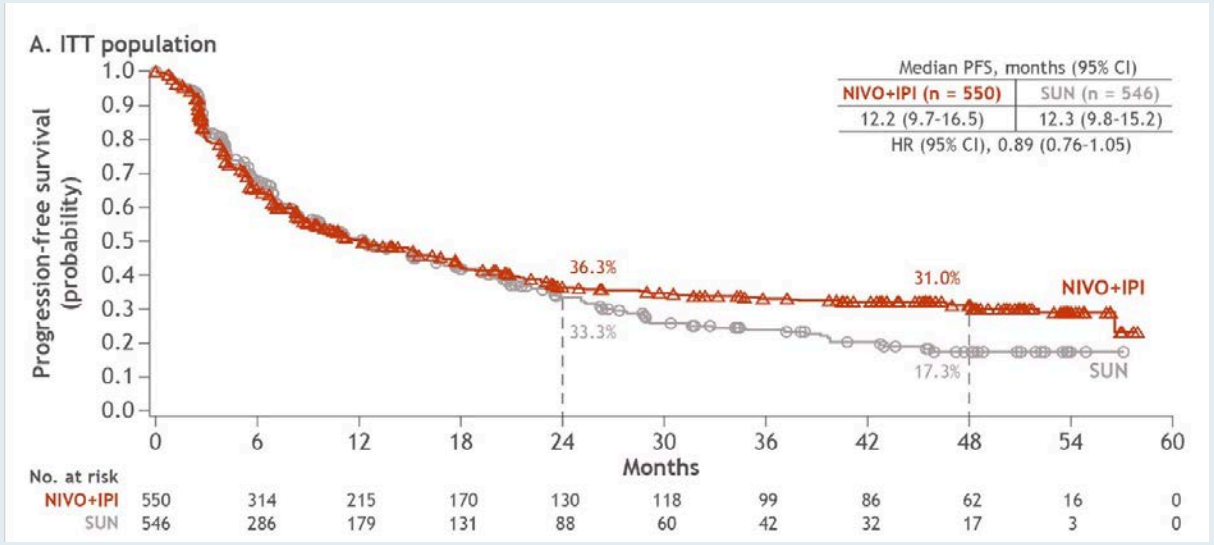


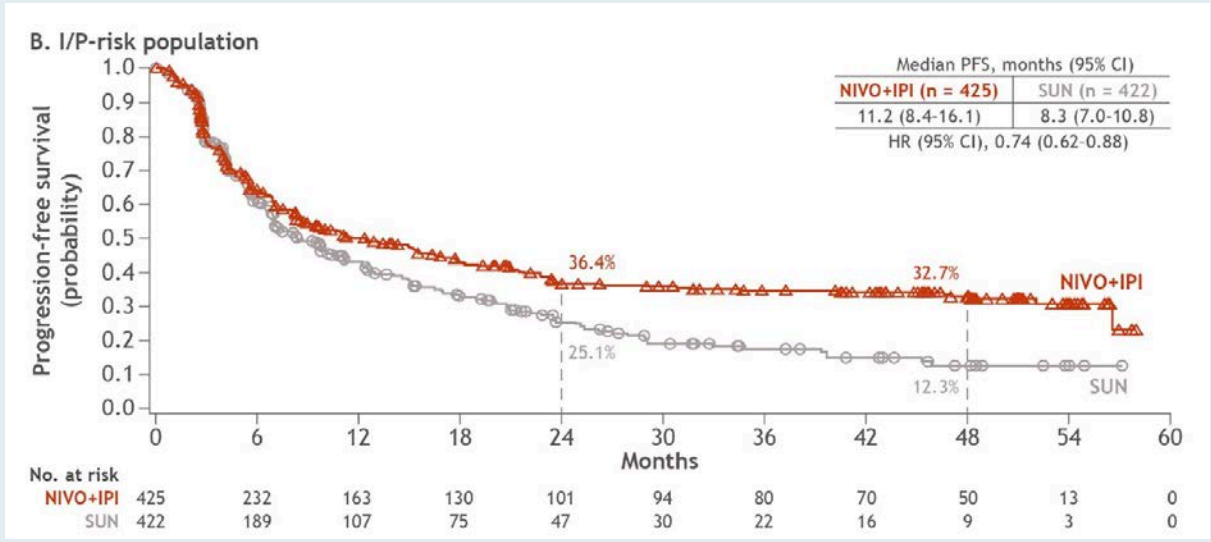


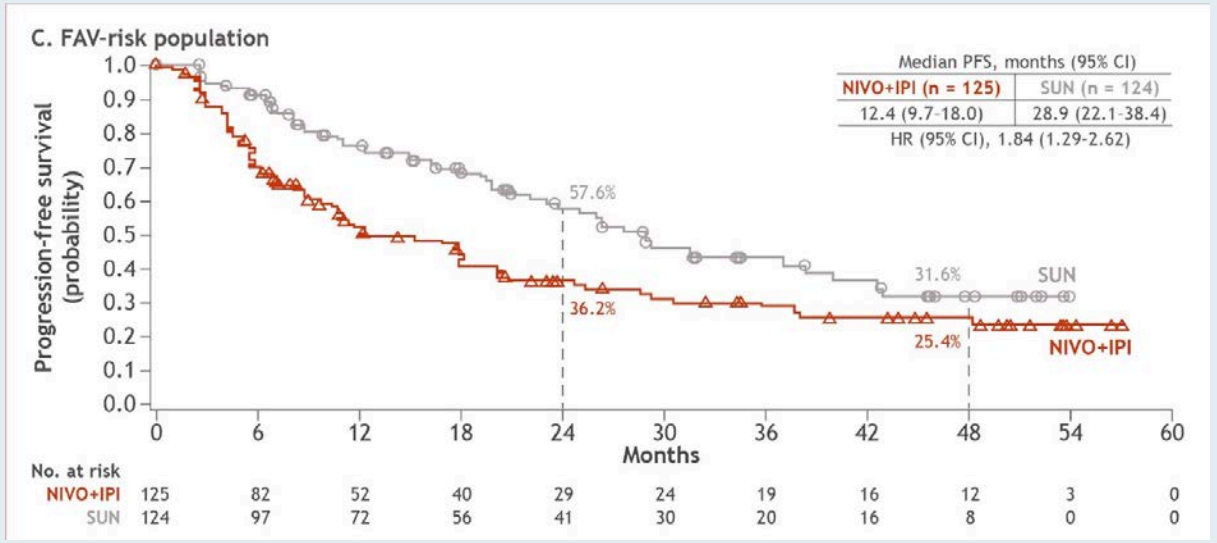


Albiges L et al. *ESMO Open* 2020;5(6):e001079.

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







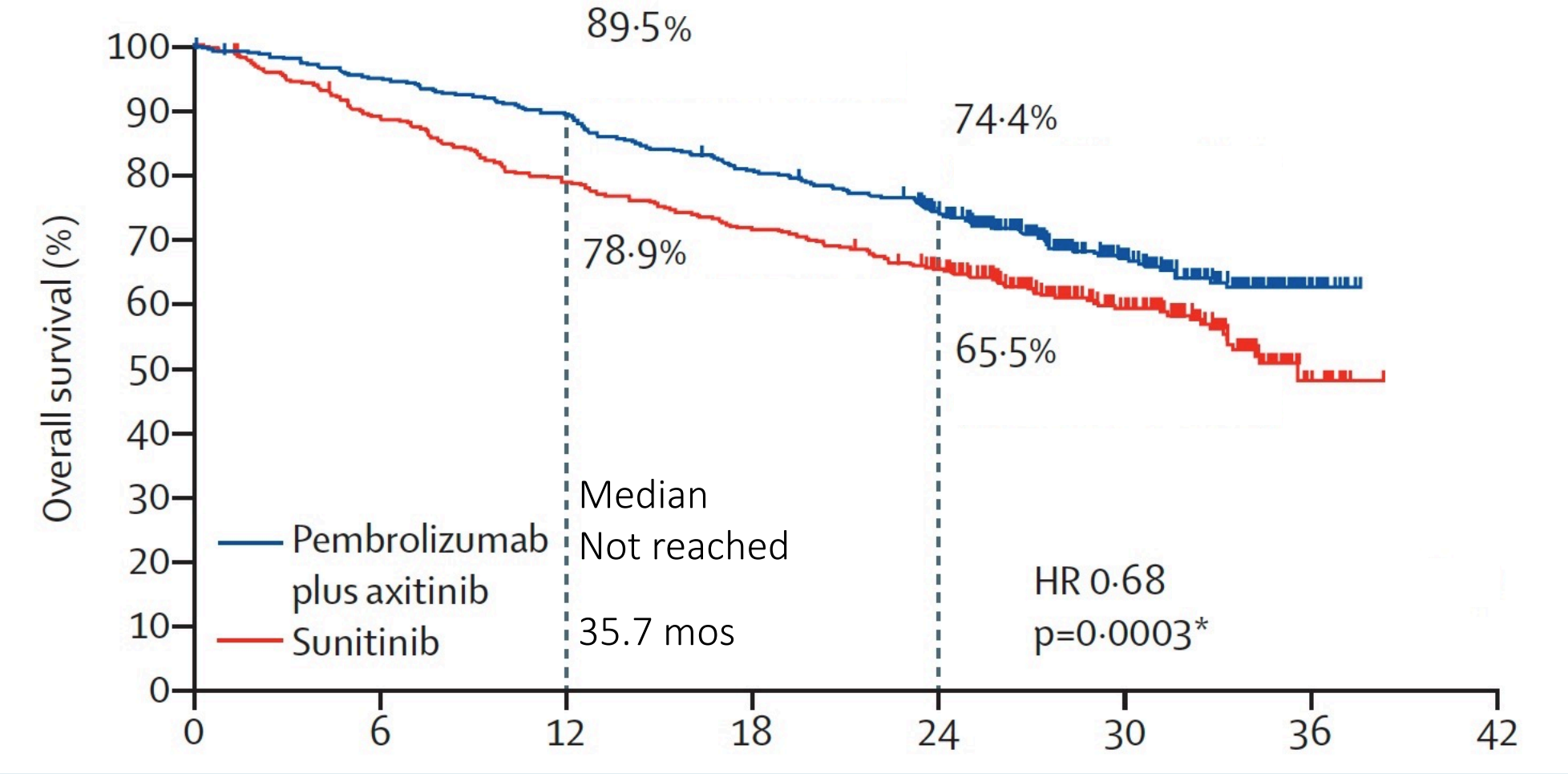
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

Lancet Oncol 2020;21:1563-73

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

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

KEYNOTE-426: Overall Survival with Extended Follow-Up



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

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

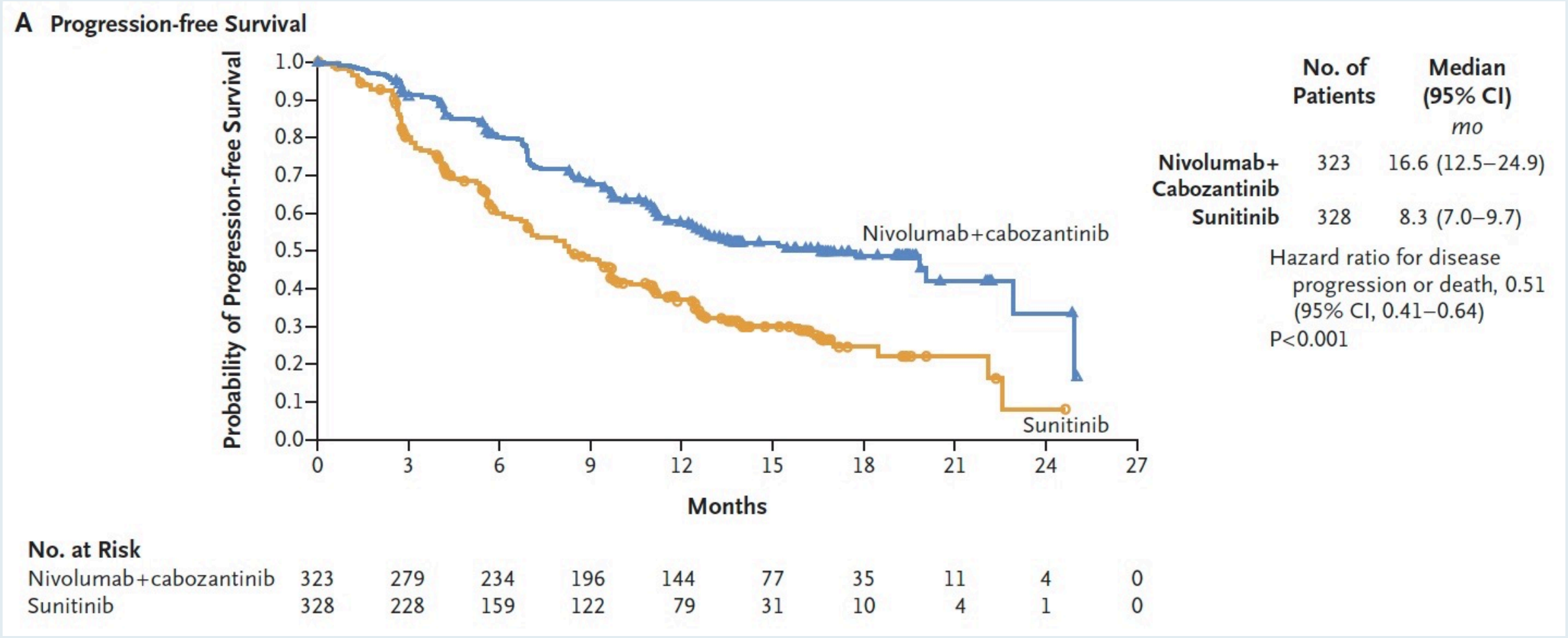
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

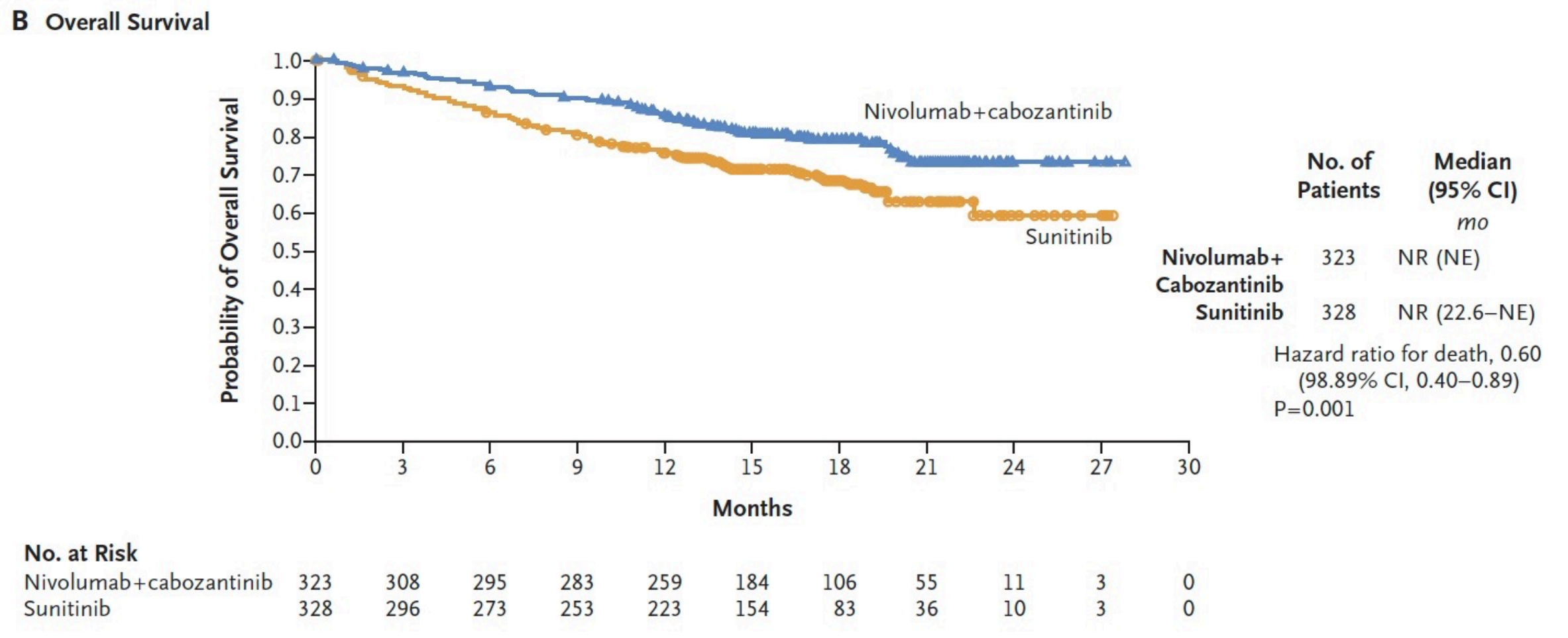
T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bourlon, B. Zurawski, V.M. Oyervides Juárez, J.J. Hsieh, U. Basso, A.Y. Shah, C. Suárez, A. Hamzaj, J.C. Goh, C. Barrios, M. Richardet, C. Porta, R. Kowalyszyn, J.P. Feregrino, J. Żołnierek, D. Pook, E.R. Kessler, Y. Tomita, R. Mizuno, J. Bedke,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

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



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

Overall Survival in the Intention-to-Treat Population



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

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

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

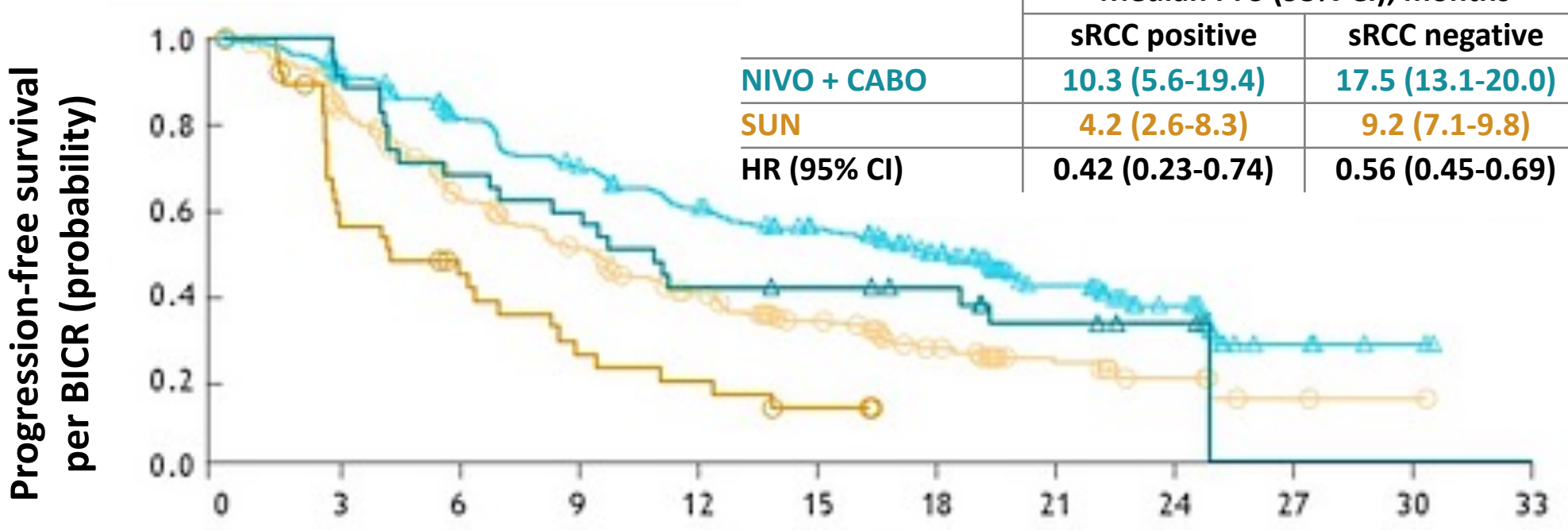
Nivolumab + Cabozantinib (NIVO + CABO) versus Sunitinib (SUN) for Advanced Renal Cell Carcinoma (aRCC): Outcomes by Sarcomatoid Histology and Updated Trial Results with Extended Follow-Up of CheckMate 9ER

Motzer RJ et al.

Genitourinary Cancers Symposium 2021;Abstract 308.

Progression-Free Survival per BICR by Sarcomatoid Histology

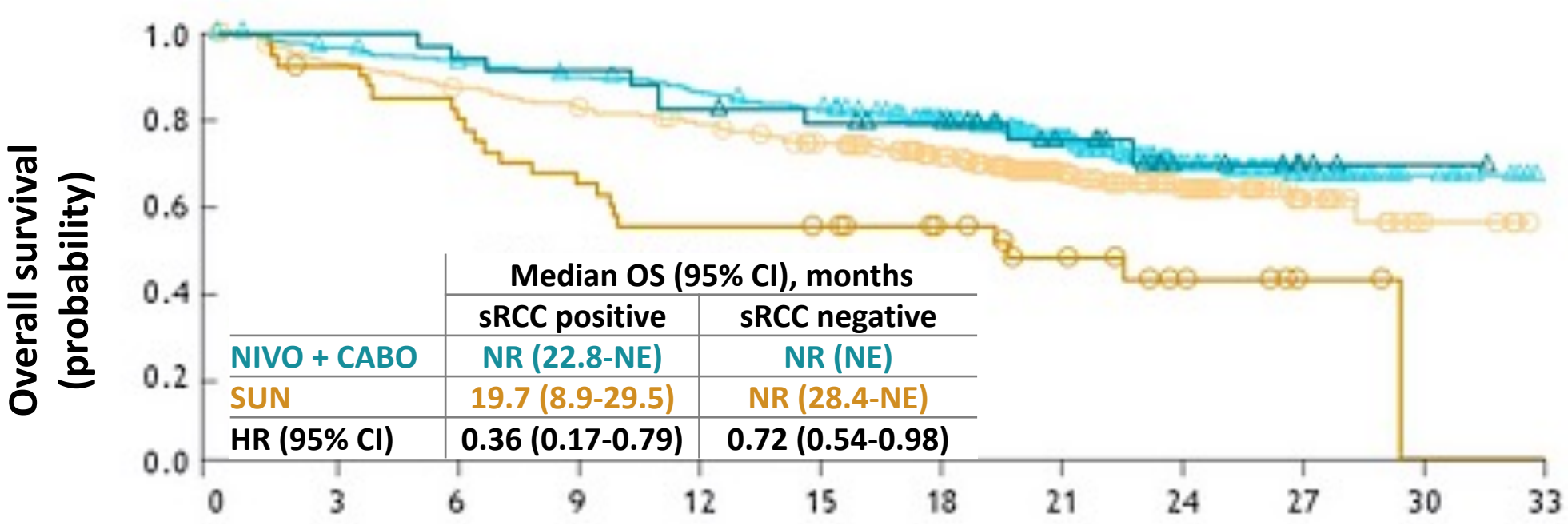
	Median PFS (95% CI), months	
	sRCC positive	sRCC negative
NIVO + CABO	10.3 (5.6-19.4)	17.5 (13.1-20.0)
SUN	4.2 (2.6-8.3)	9.2 (7.1-9.8)
HR (95% CI)	0.42 (0.23-0.74)	0.56 (0.45-0.69)



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

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

Overall Survival by Sarcomatoid Histology



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

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

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

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

The NEW ENGLAND JOURNAL of MEDICINE

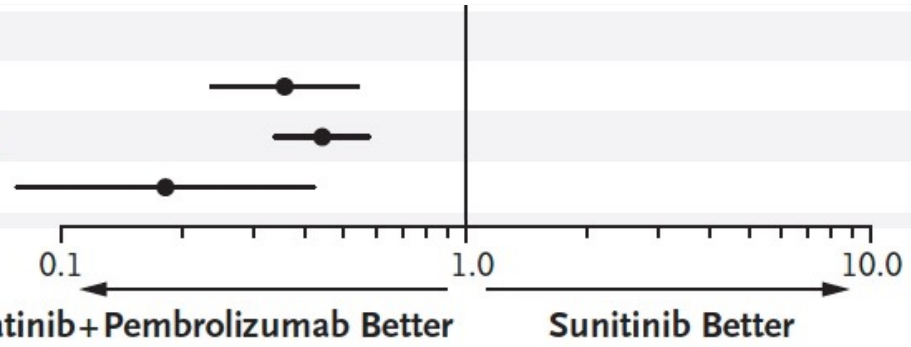
ORIGINAL ARTICLE

Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma

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

Subgroup Analysis of Progression-Free Survival: MSKCC Risk Group

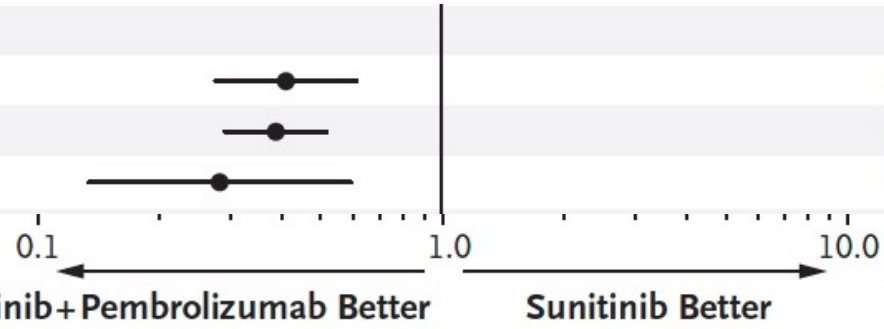
Subgroup	Lenvatinib+ Pembrolizumab	Sunitinib	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/no. of patients		
MSKCC risk group			
Favorable	39/96	60/97	0.36 (0.23–0.54)
Intermediate	101/227	126/228	0.44 (0.34–0.58)
Poor	20/32	19/32	0.18 (0.08–0.42)



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

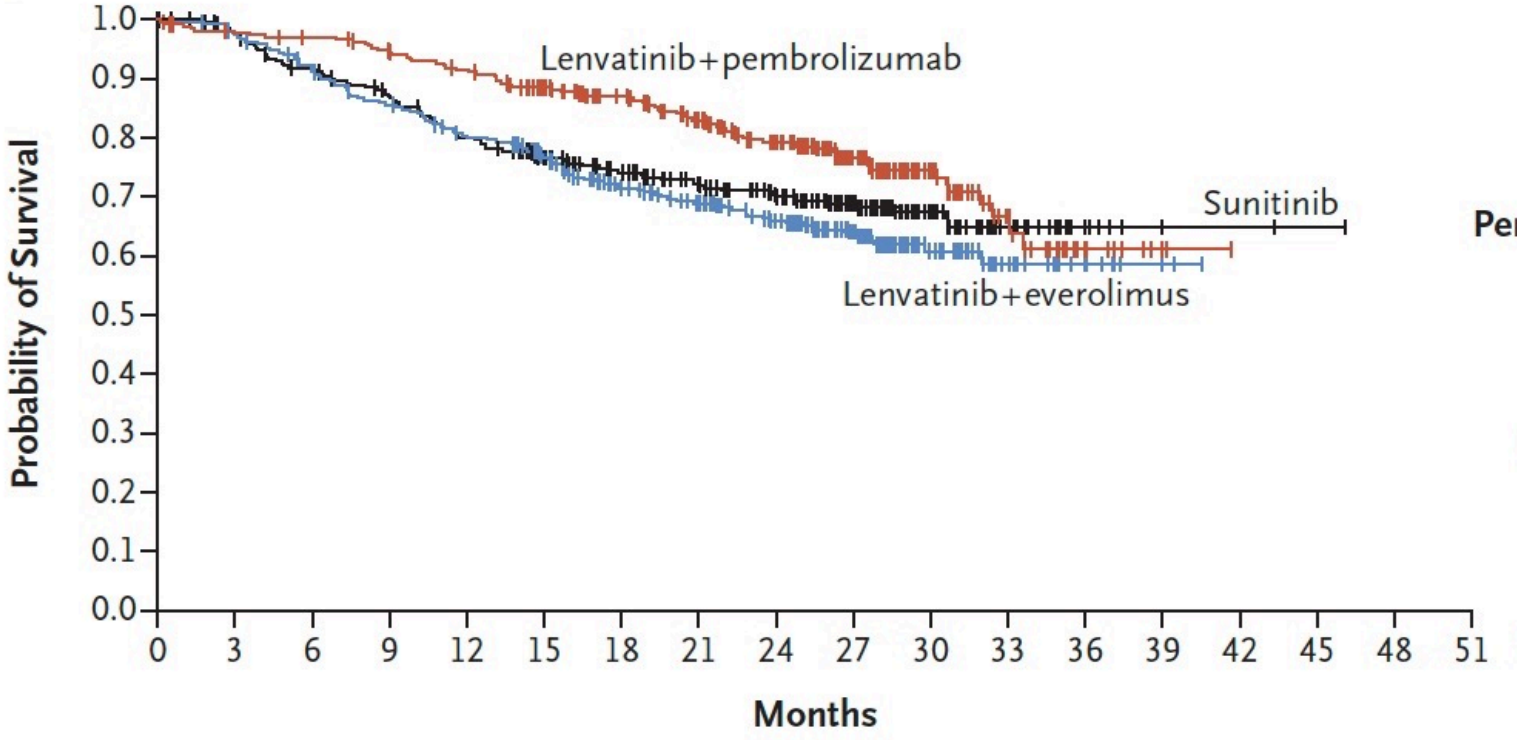
Subgroup Analysis of Progression-Free Survival: IMDC Risk Group

Subgroup	Lenvatinib+ Pembrolizumab	Sunitinib	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/no. of patients		
IMDC risk group			
Favorable	43/110	67/124	0.41 (0.28–0.62)
Intermediate	97/210	110/192	0.39 (0.29–0.52)
Poor	18/33	26/37	0.28 (0.13–0.60)



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

Kaplan-Meier Analysis of Overall Survival



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

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

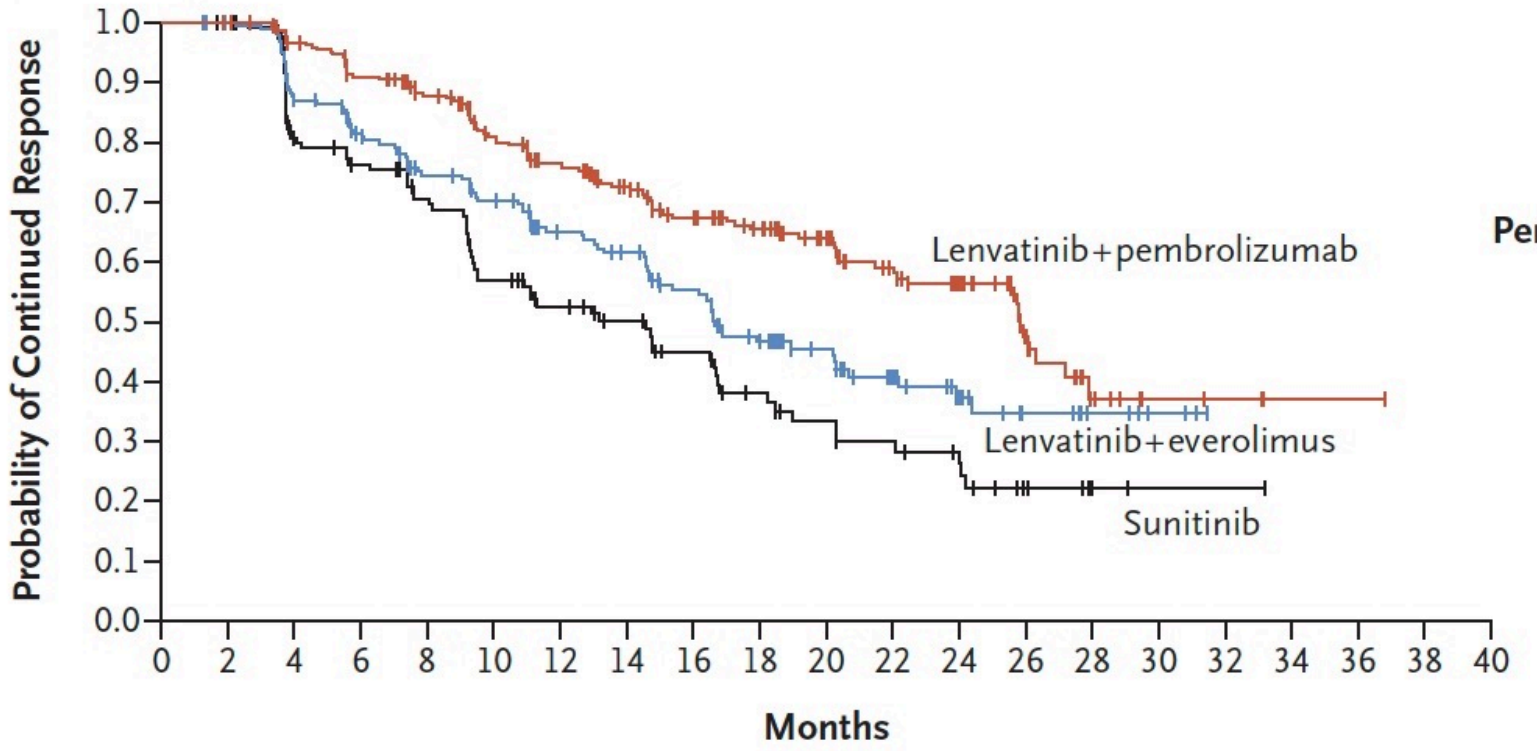
Hazard ratio for death (lenvatinib+ everolimus vs. sunitinib), 1.15 (95% CI, 0.88–1.50); P=0.30

No. at Risk

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

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

Kaplan-Meier Analysis of Response Duration



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

No. at Risk

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

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

Confirmed Tumor Responses

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

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

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

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

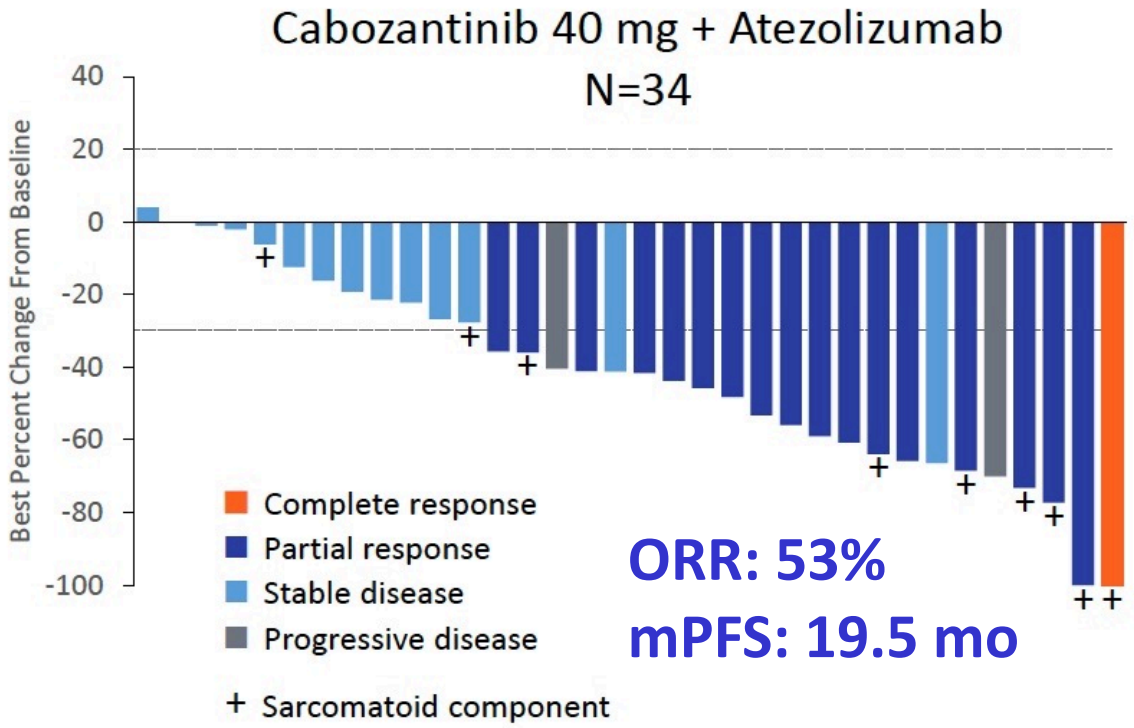
Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

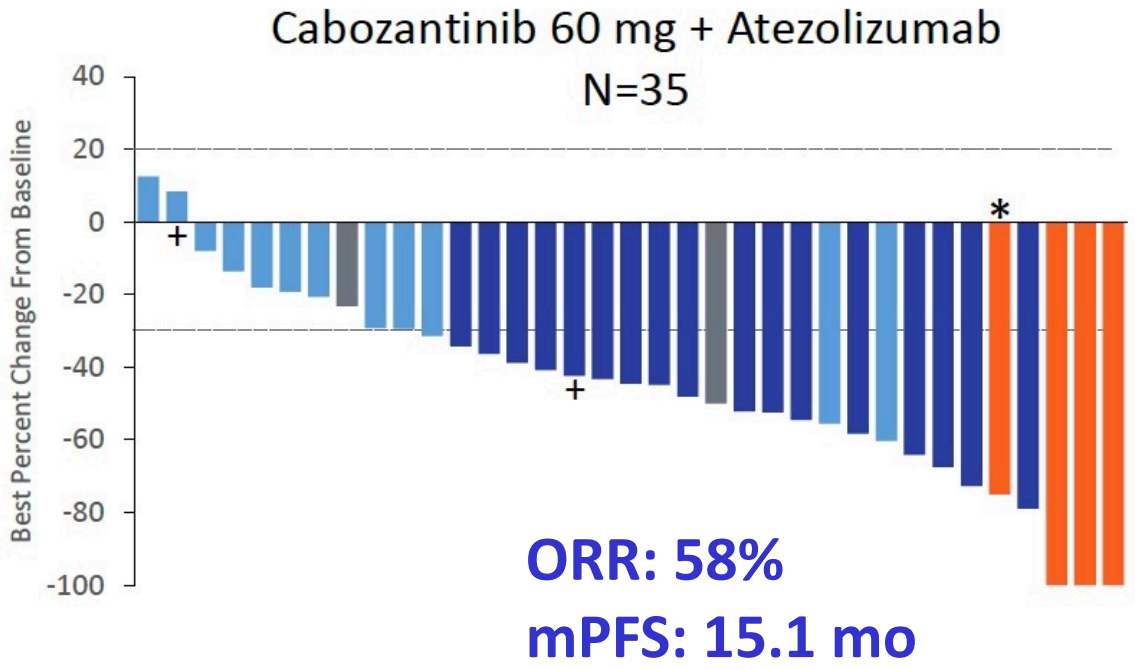
Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

Pal S et al.

ESMO 2020;Abstract 702O.

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





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

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

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

FDA Approves Tivozanib for Relapsed or Refractory Advanced RCC

Press Release: March 10, 2021

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

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

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

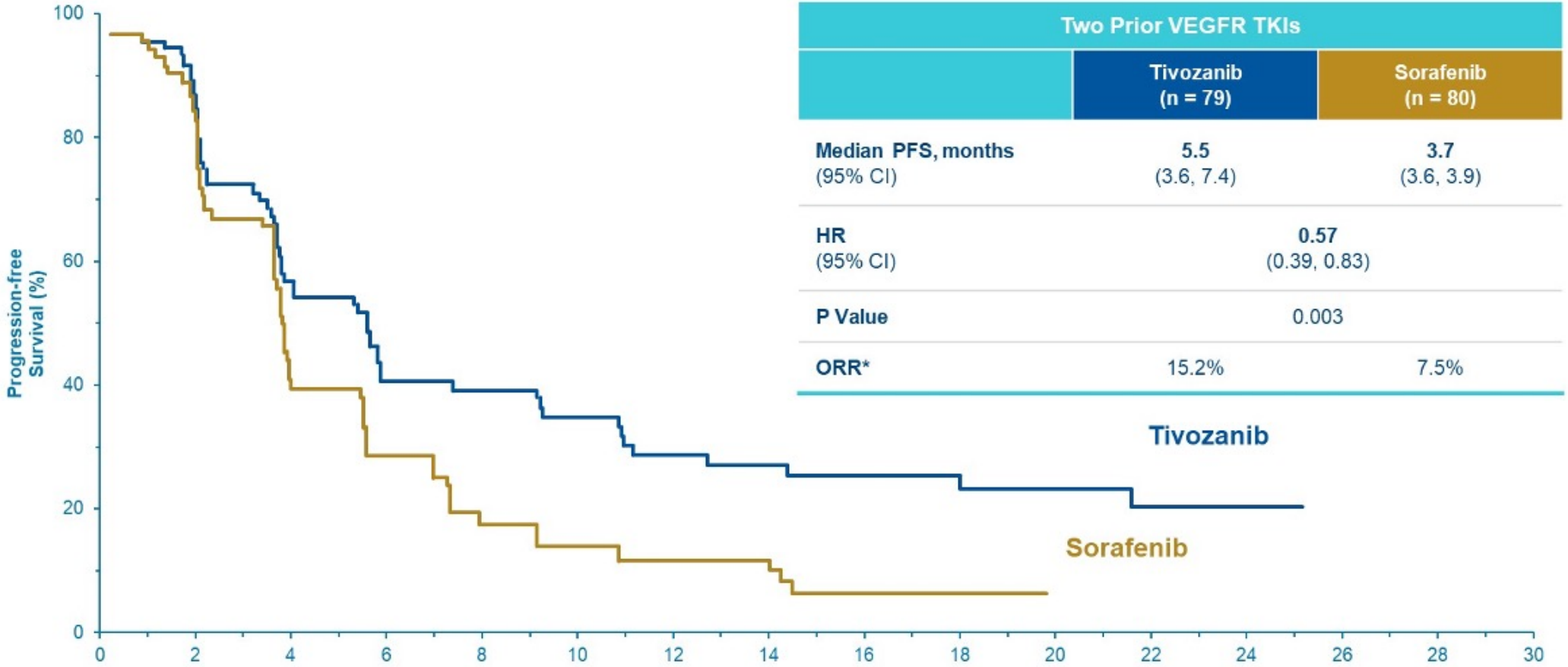
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

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

Rini BI et al.

Genitourinary Cancers Symposium 2021;Abstract 278.

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



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

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

TIVO-3: Tivozanib After Axitinib

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

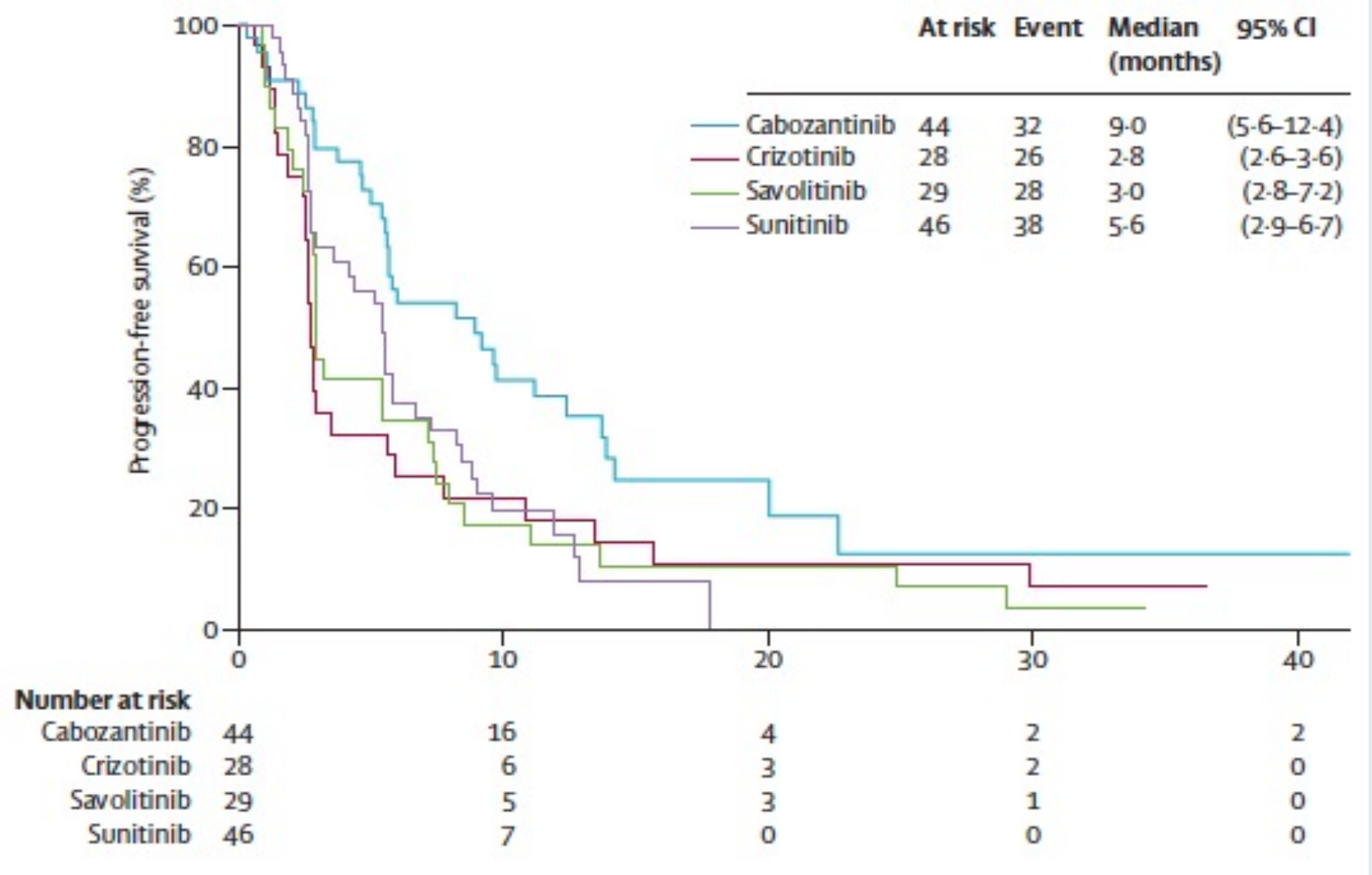
Rini BI et al. Genitourinary Cancers Symposium 2021;Abstract 278.

Lancet 2021;397:695-703

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

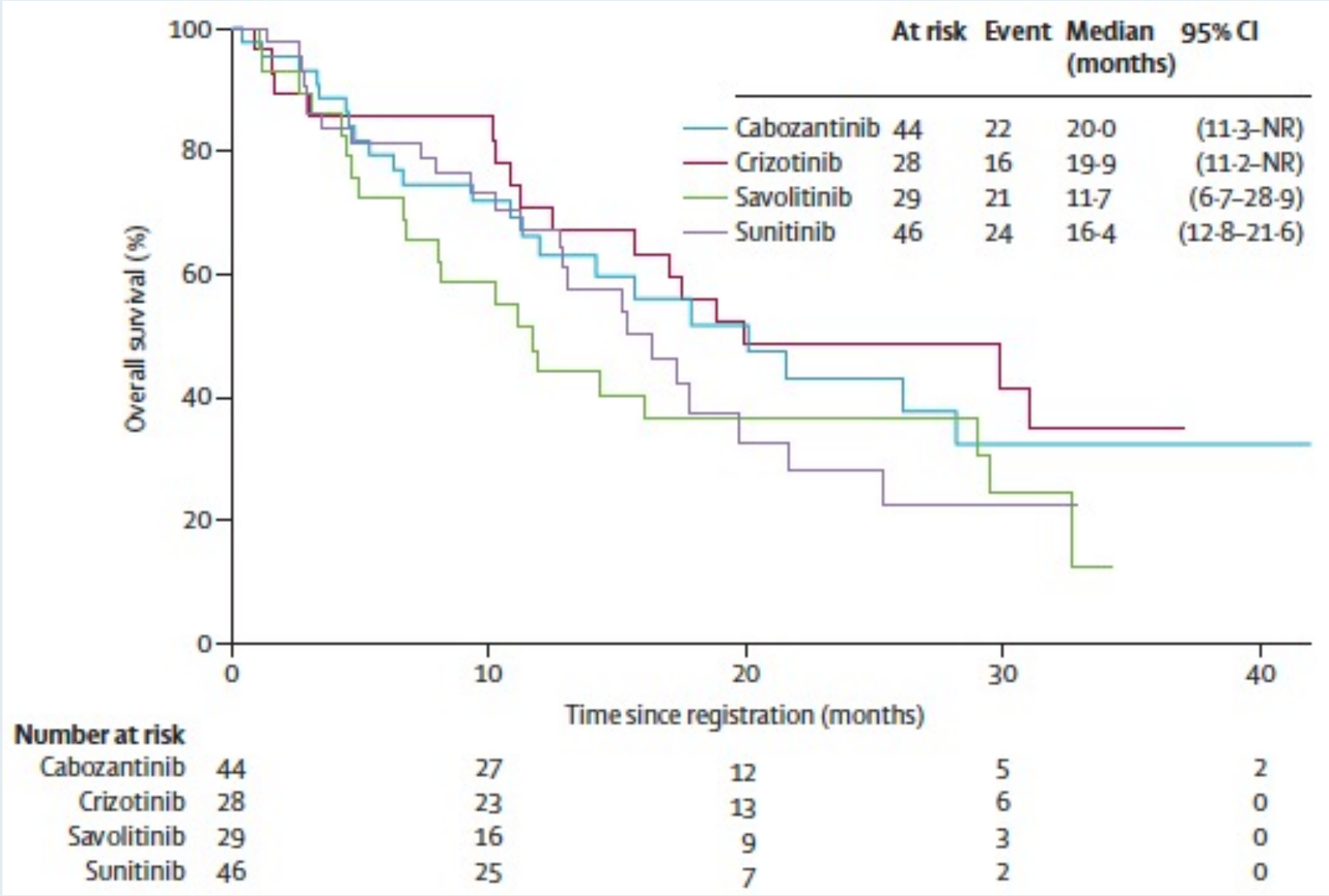
Sumanta K Pal, Catherine Tangen, Ian M Thompson Jr, Naomi Balzer-Haas, Daniel J George, Daniel Y C Heng, Brian Shuch, Mark Stein, Maria Tretiakova, Peter Humphrey, Adebowale Adeniran, Vivek Narayan, Georg A Bjarnason, Ulka Vaishampayan, Ajjai Alva, Tian Zhang, Scott Cole, Melissa Plets, John Wright,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

Kaplan-Meier Analysis of Progression-Free Survival



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

Kaplan-Meier Analysis of Overall Survival



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

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

Press Release – March 16, 2021

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

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

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

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

RTP RESEARCH TO PRACTICE

Project ECHO

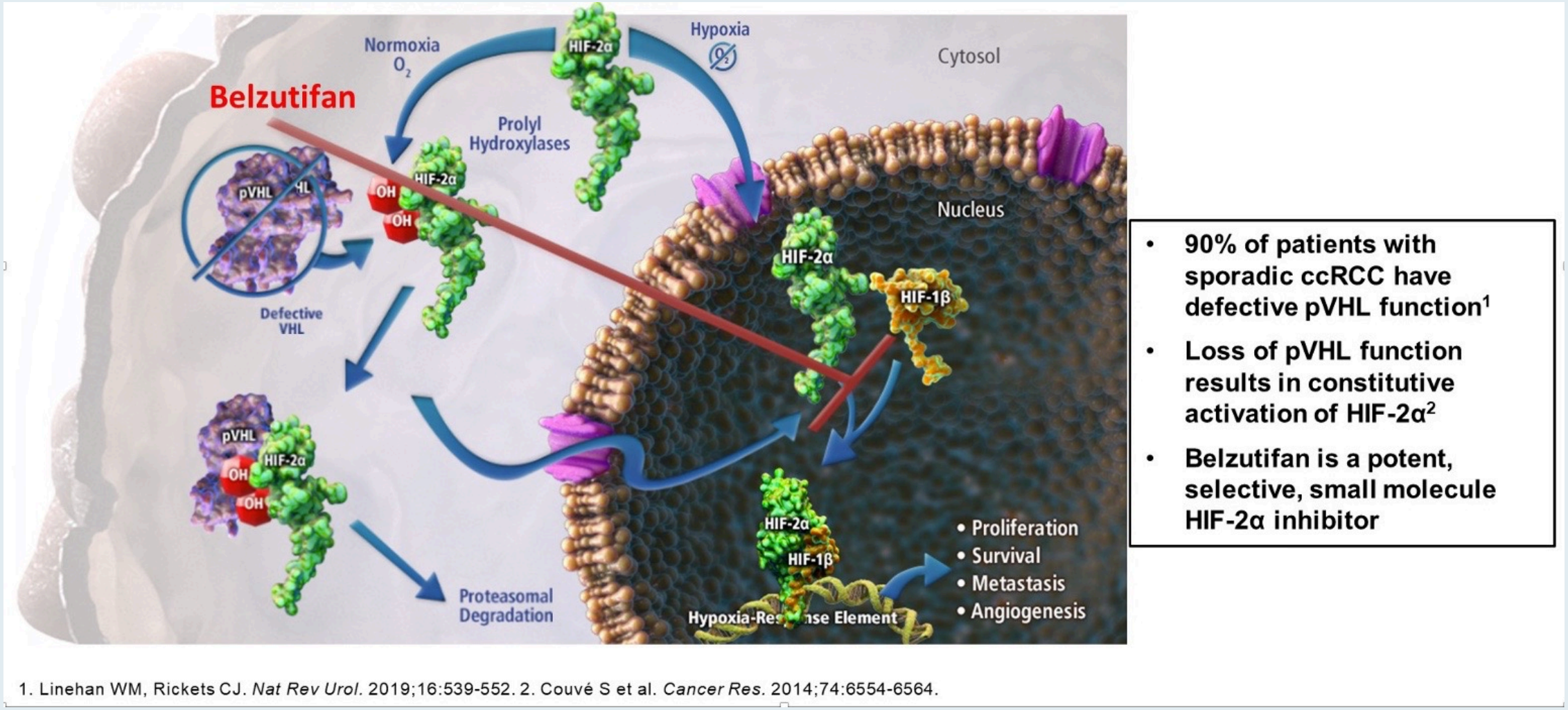
Genitourinary Cancers Symposium 2021;Abstract 273

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

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

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

pVHL Deficiency Results in HIF-2-alpha Activation

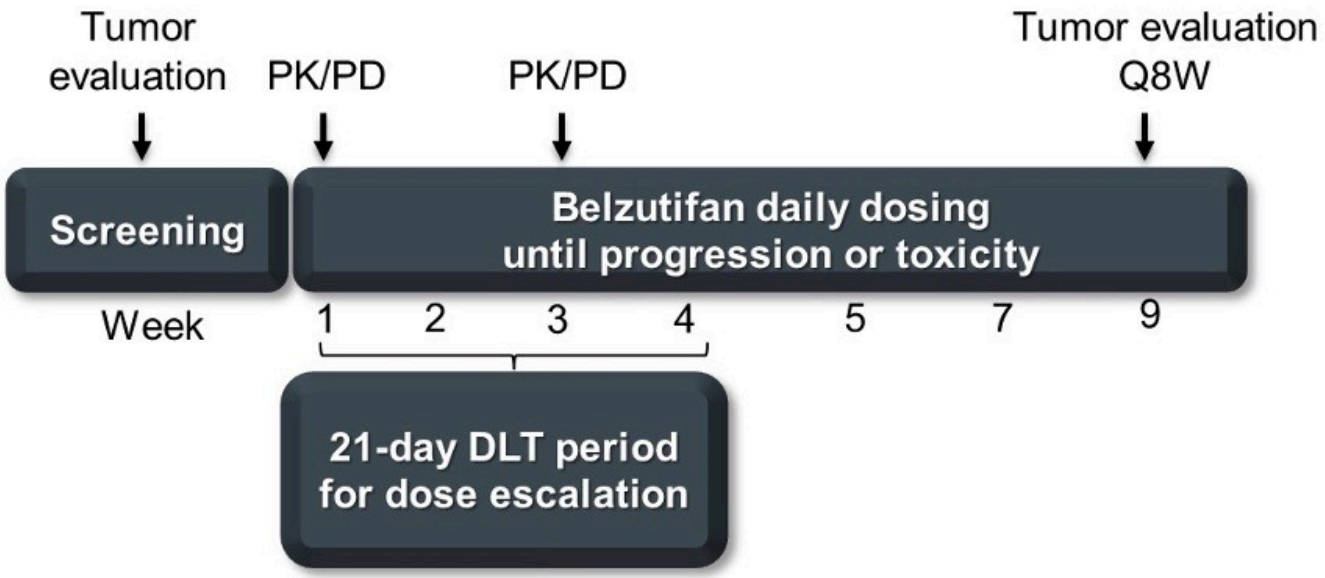


- 90% of patients with sporadic ccRCC have defective pVHL function[1]
- Loss of pVHL function results in constitutive activation of HIF-2α[2]
- Belzutifan is a potent, selective, small molecule HIF-2α inhibitor

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

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

Study Design

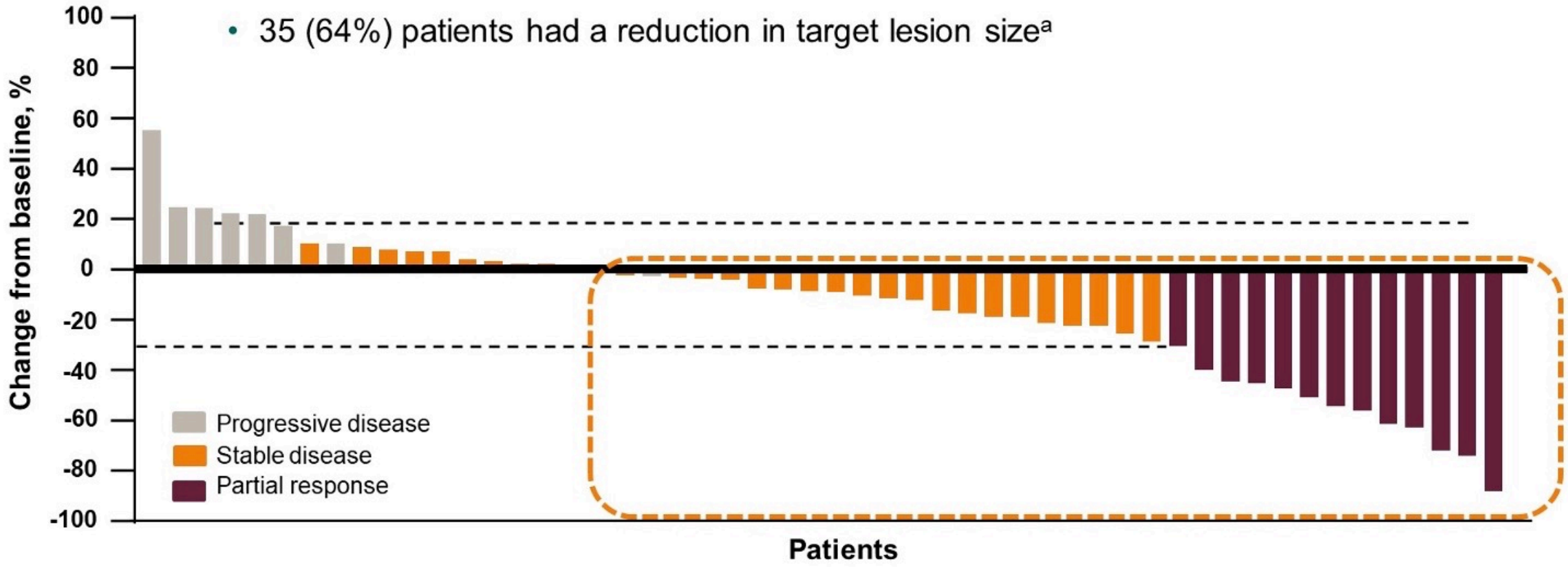


- Dose-escalation cohort for patients with advanced solid tumors
- Dose-expansion cohort for patients with advanced ccRCC who previously received ≥1 therapy
  - Key end points: Safety, objective response rate, duration of response

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

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

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



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

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

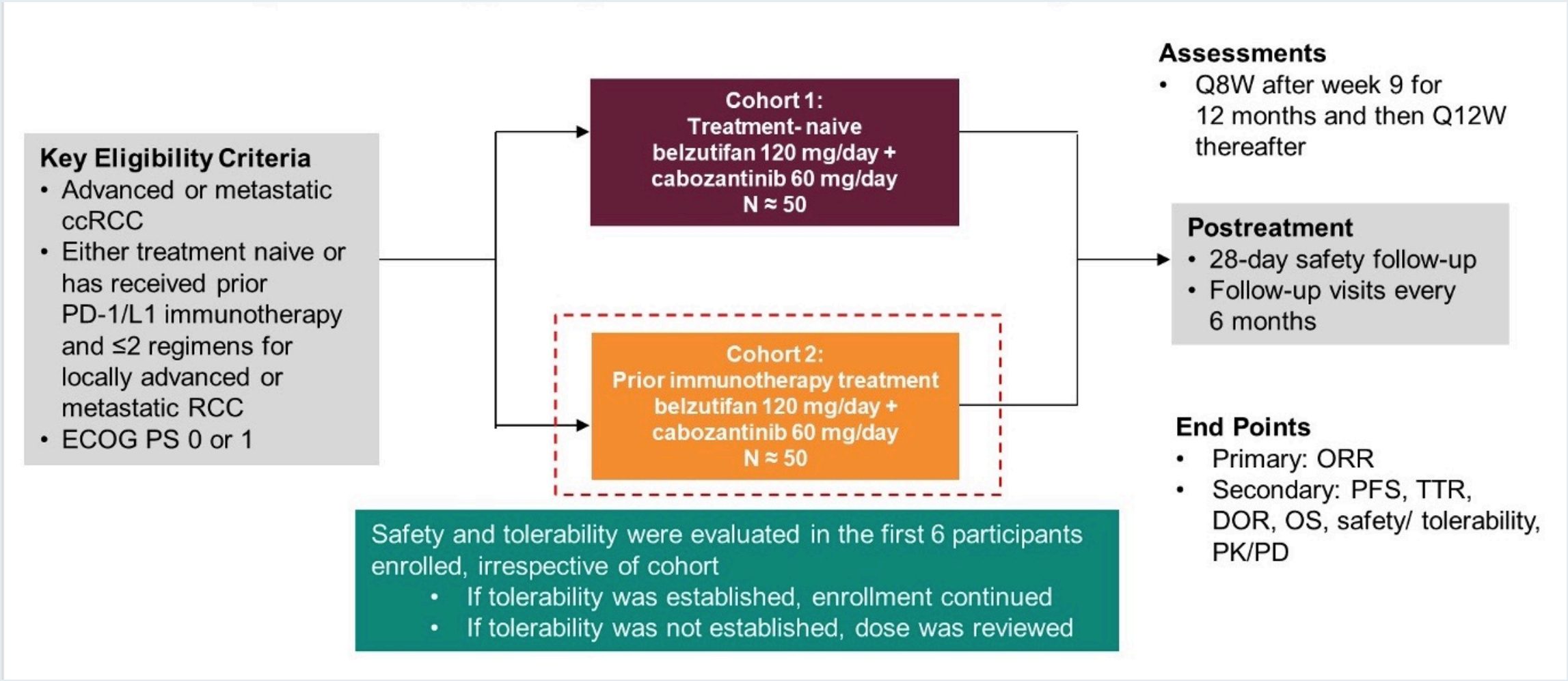
Genitourinary Cancers Symposium 2021;Abstract 272.

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

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

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

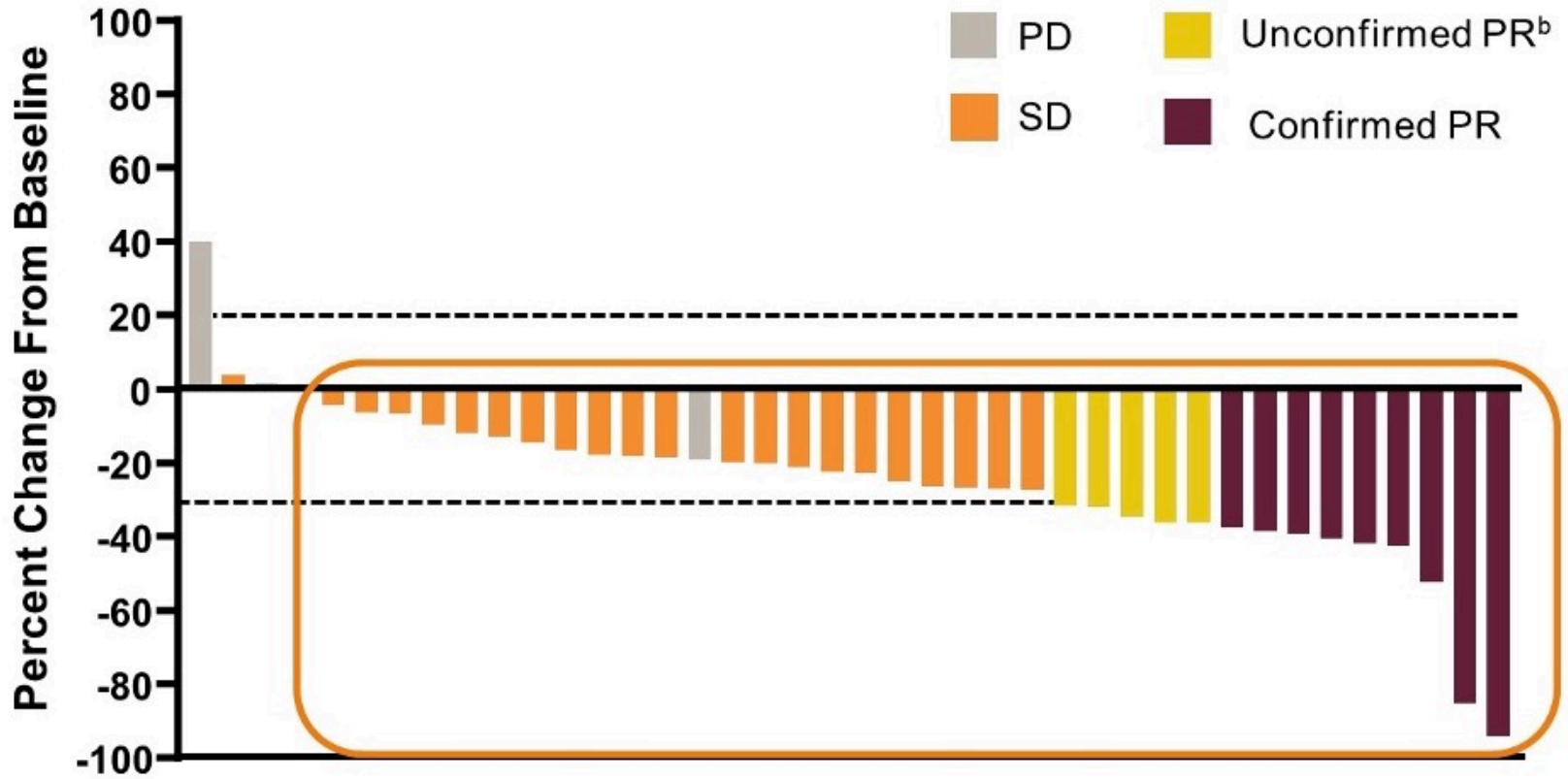
Study Design



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

Best Tumor Change from Baseline

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



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

Treatment-Related Adverse Events

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

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

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

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

Agenda

MODULE 1: Cases from the Practice of Dr Dandamudi

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

MODULE 3: Renal Cell Carcinoma Journal Club with Dr Pal

- Nivolumab with ipilimumab versus sunitinib in first-line treatment of advanced sarcomatoid RCC
- Cytoreductive nephrectomy for favorable-risk mRCC? Yes, cytoreductive nephrectomy should still be considered
- Deferred cytoreductive nephrectomy in newly diagnosed metastatic RCC (mRCC)
- Impact of probiotic supplementation on gut microbiome and clinical outcome from targeted therapy in mRCC
- Assessment of the stool microbiome in patients with mRCC receiving targeted therapy or immunotherapy
- Stool microbiome profiling of patients with mRCC receiving anti-PD-1 immune checkpoint inhibitors
- Evaluation of clear cell, papillary, and chromophobe RCC metastasis sites and association with survival
- SWOG 1500: Sunitinib versus cabozantinib, crizotinib or savolitinib in metastatic papillary RCC

MODULE 4: Key Data Sets

MODULE 5: Other Recent Data Sets

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

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

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

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

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

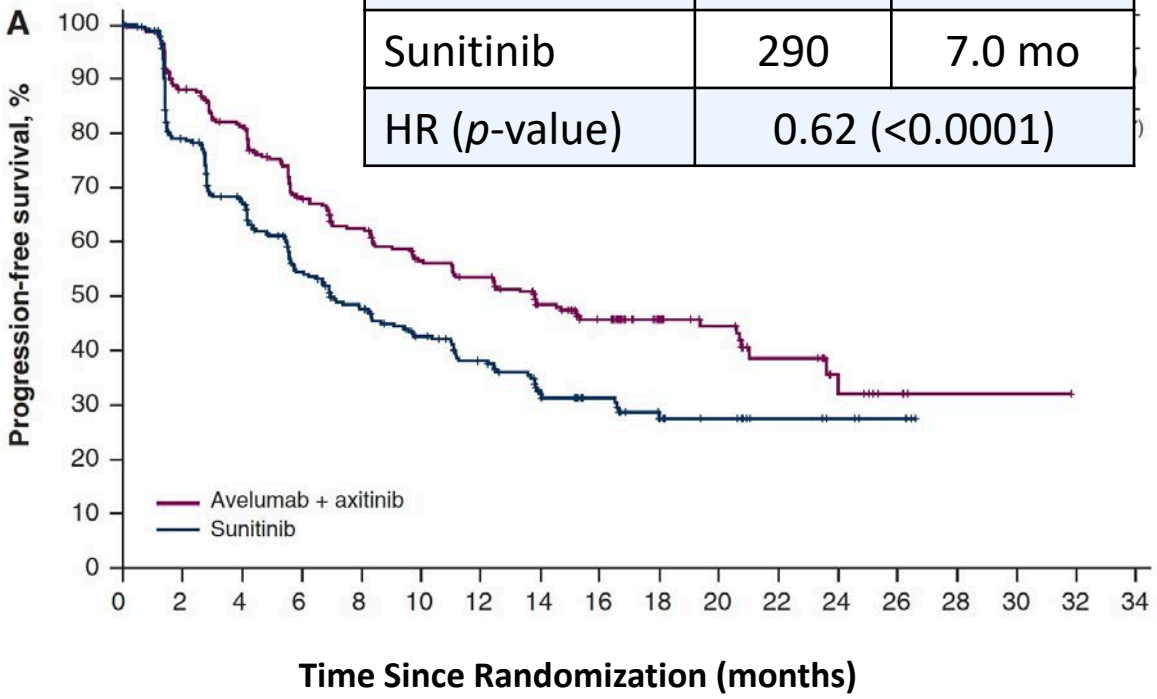
	PD-L1-positive		Overall	
	Avelumab + axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing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

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

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

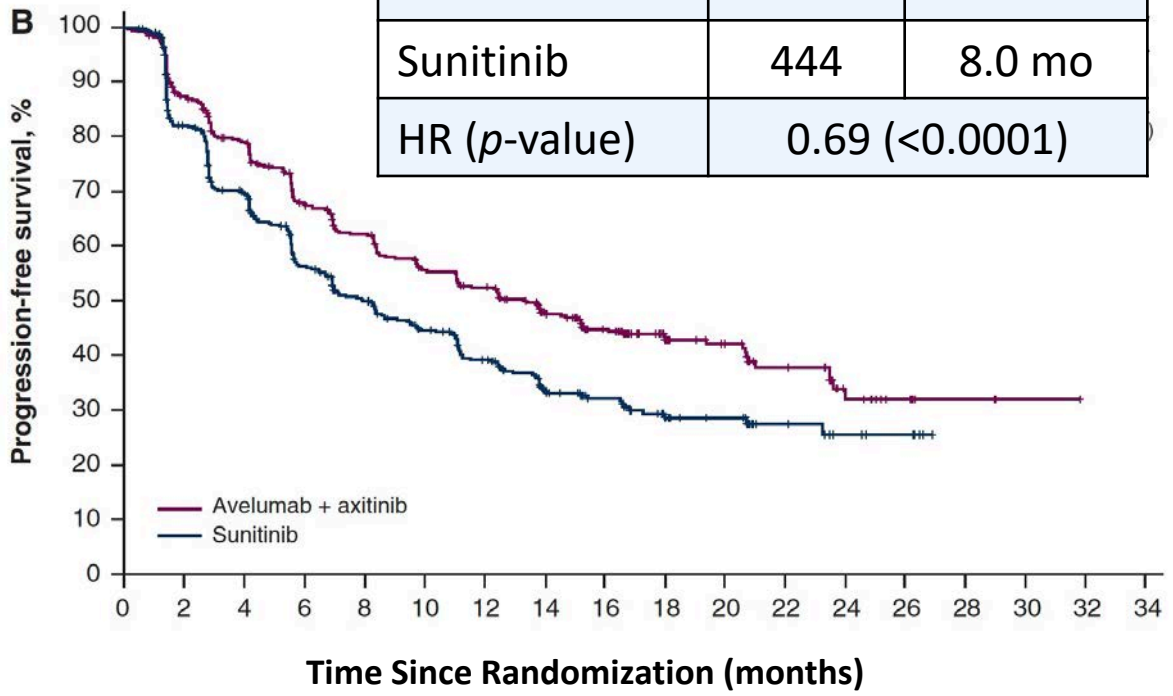
PD-L1 ≥ 1% Population

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



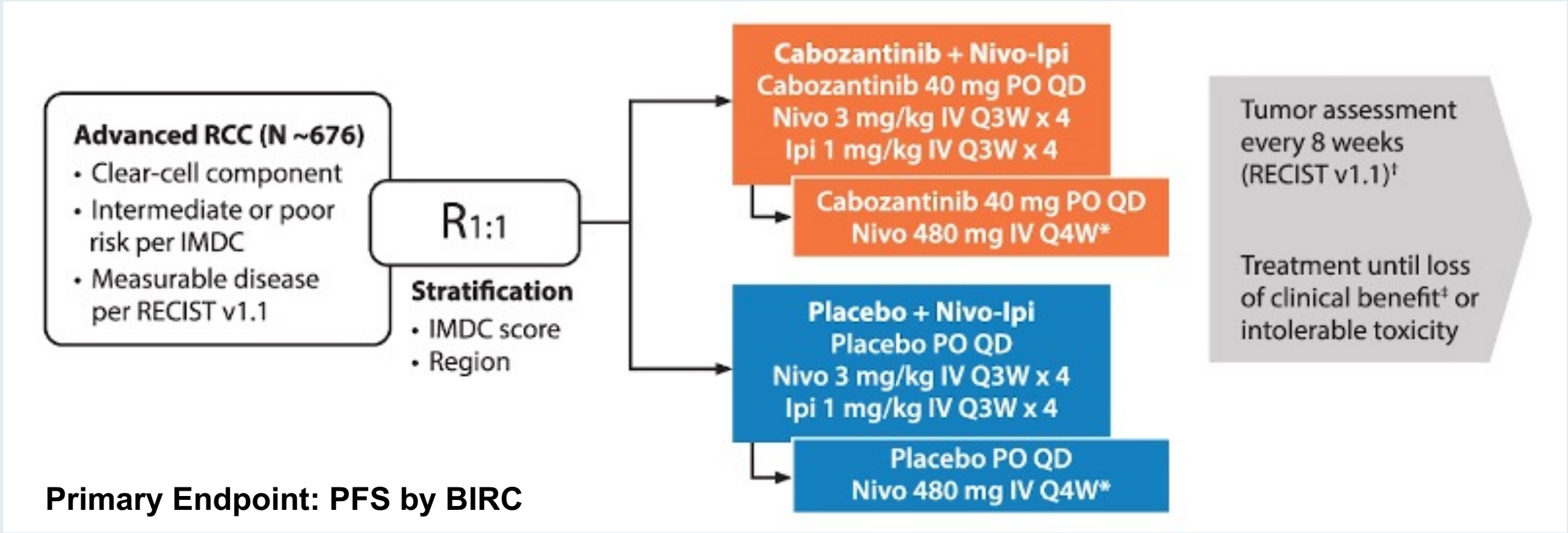
Overall Population

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



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

COSMIC-313 Phase III Schema



Primary Endpoint: PFS by BIRC

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

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

rapid communications

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

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

J Clin Oncol 2020;38:3088-94.

Salvage Ipilimumab/Nivolumab for mRCC After Prior ICI Therapy

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

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

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

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

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

Oya M et al.

ASCO 2020;Abstract 5089.

Efficacy of Cabozantinib with or without Prior Immunotherapy

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

Oya M et al. ASCO 2020;Abstract 5089.

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

Lee C-H et al.

ASCO 2020;Abstract 5008.

Efficacy of Lenvatinib/Pembrolizumab in Patients Previously Treated with Immunotherapy

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

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

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Thursday, April 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Dirk Arnold, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Thank you for joining us!

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