Meet The Professor

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

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Director, Genitourinary Clinical Research
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Commercial Support

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Dr Love — Disclosures

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

Dr Plimack — Disclosures

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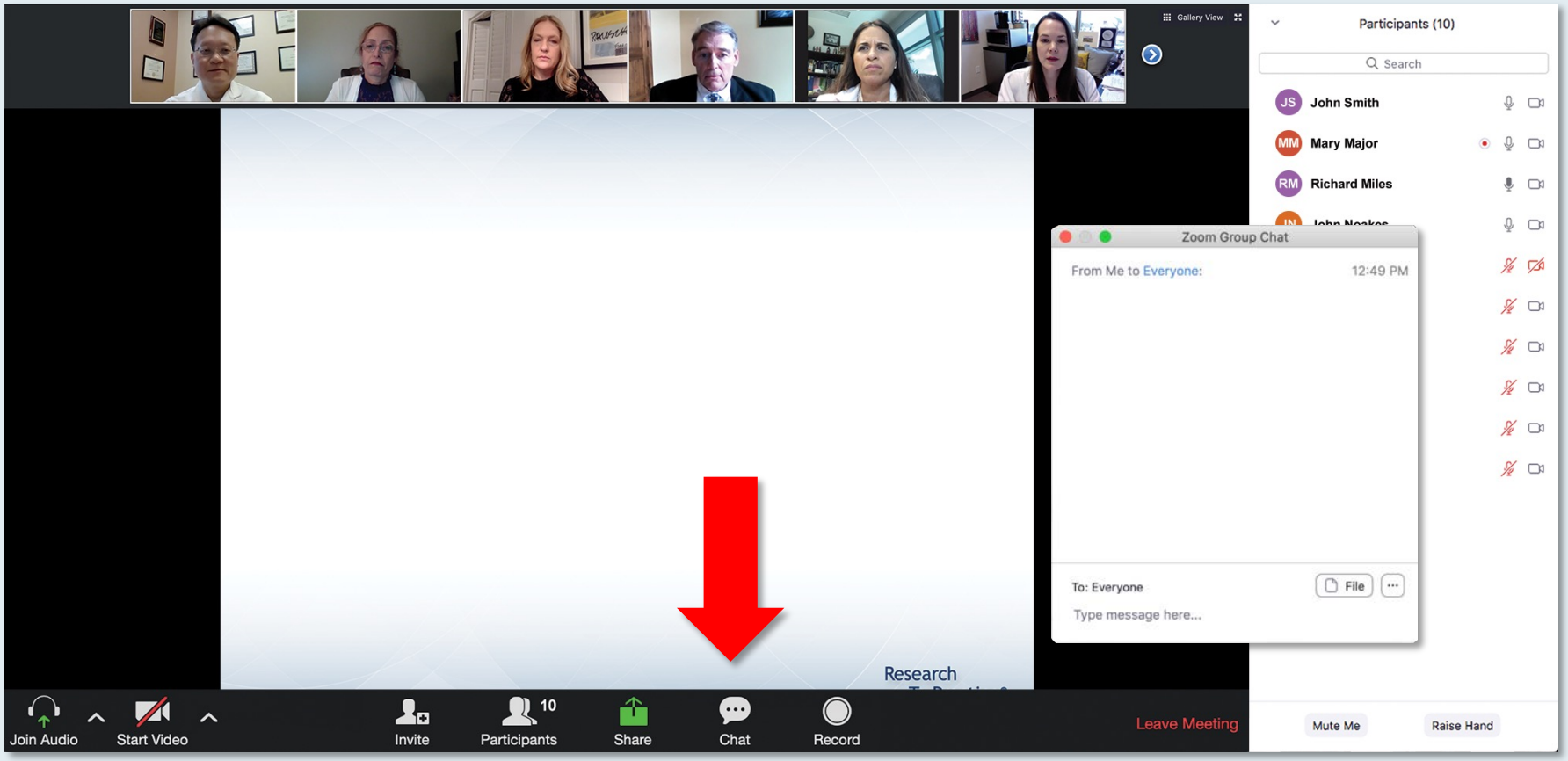
We Encourage Clinicians in Practice to Submit Questions



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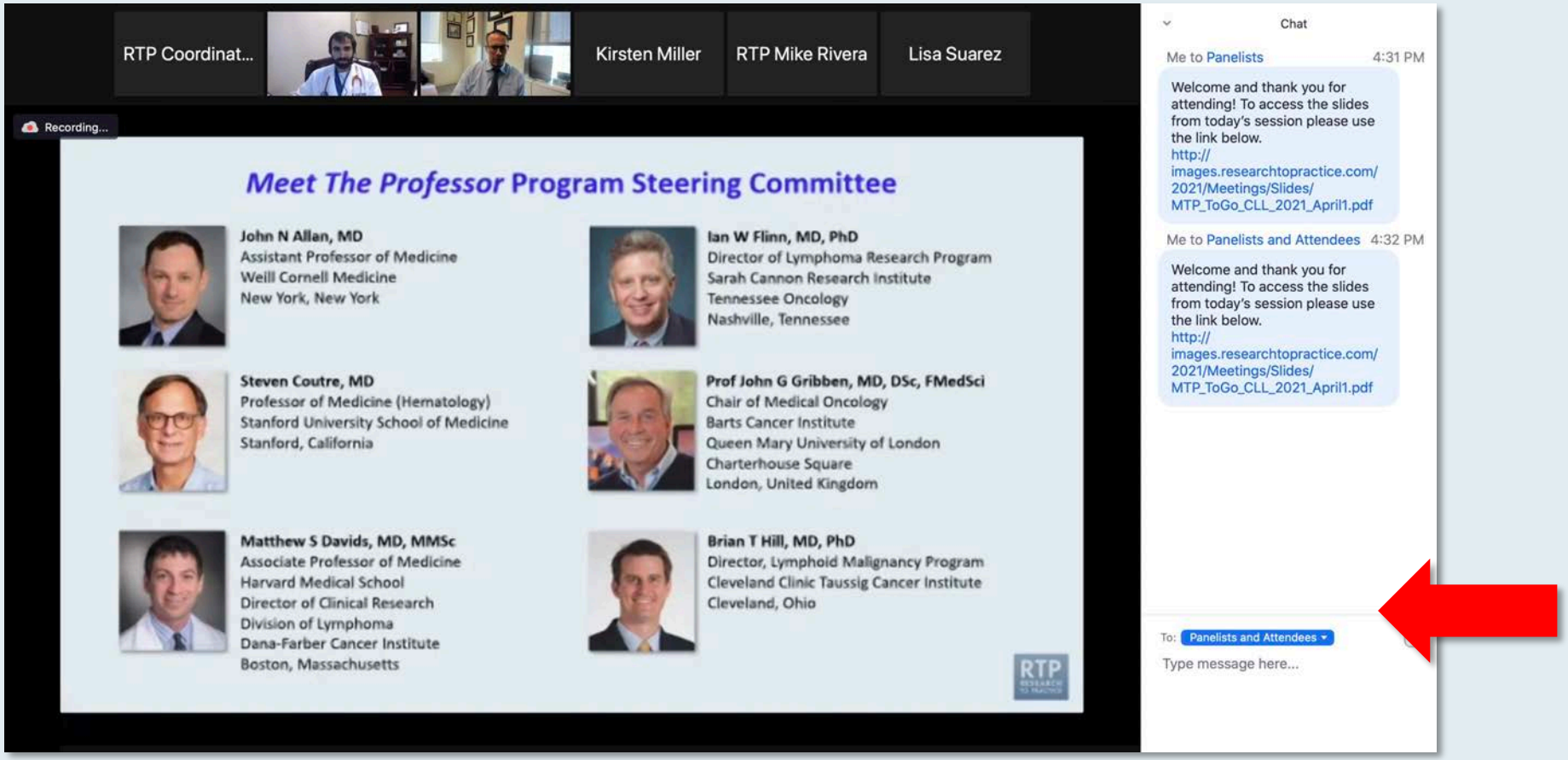

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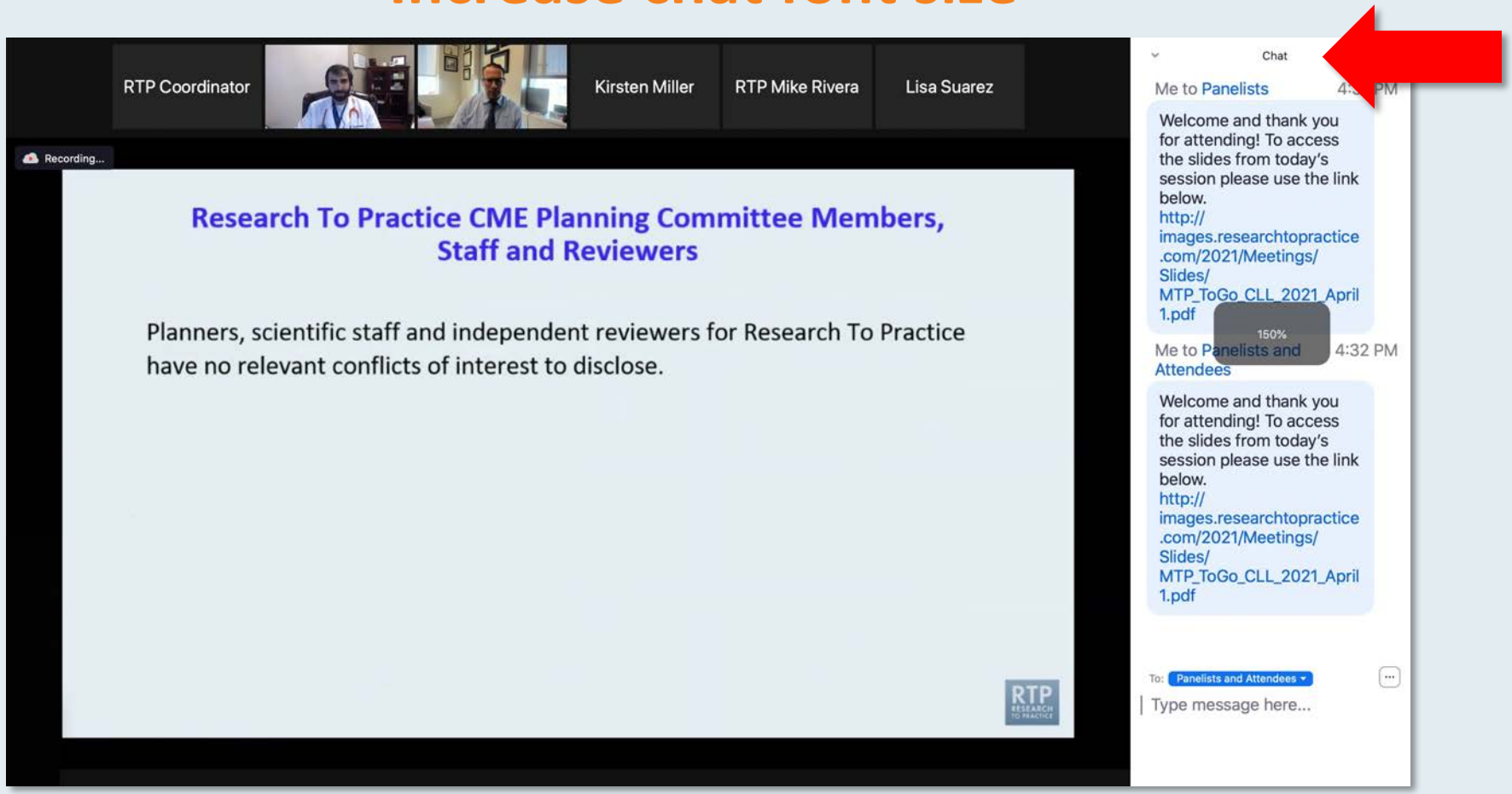

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma

DR SUMANTA PAL

CITY OF HOPE COMPREHENSIVE CANCER CENTER

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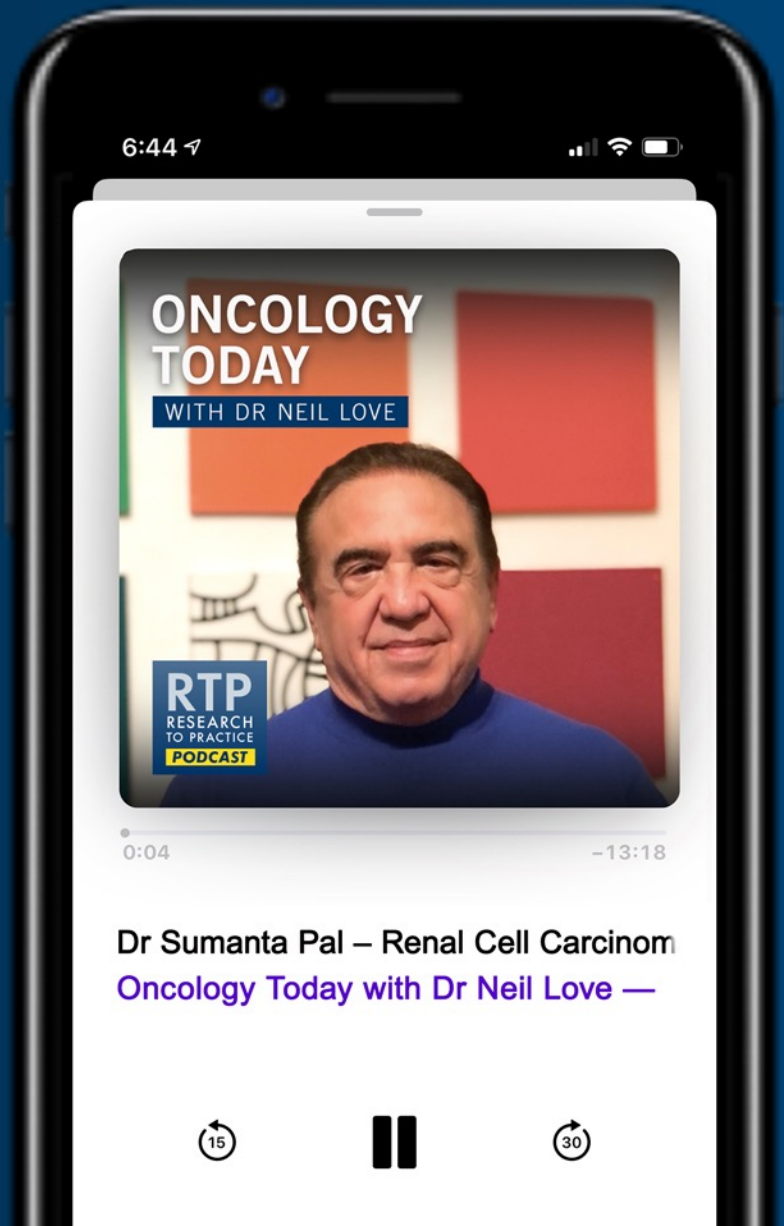

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Tuesday, October 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, October 13, 2021
5:00 PM – 6:00 PM ET

Faculty

Erika Hamilton, MD

Moderator

Neil Love, MD

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Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Triple-Negative Breast Cancer

Wednesday, October 20, 2021
5:00 PM – 6:00 PM ET

Faculty

Aditya Bardia, MD, MPH

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

A CME-MOC/NCPD Accredited Virtual Event

Saturday, October 23, 2021
9:30 AM – 4:30 PM ET

Faculty

Neeraj Agarwal, MD
Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH
David R Spigel, MD
Saad Zafar Usmani, MD, MBA
Andrew D Zelenetz, MD, PhD
Additional faculty to be announced.

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Professor, Department of Hematology/Oncology
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Philadelphia, Pennsylvania

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Huntsman Cancer Institute Presidential Endowed Chair of Cancer Research
Director, Center of Investigational Therapeutics
Director, Genitourinary Oncology Program
Huntsman Cancer Institute, University of Utah
Salt Lake City, Utah

Hans Hammers, MD, PhD
Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
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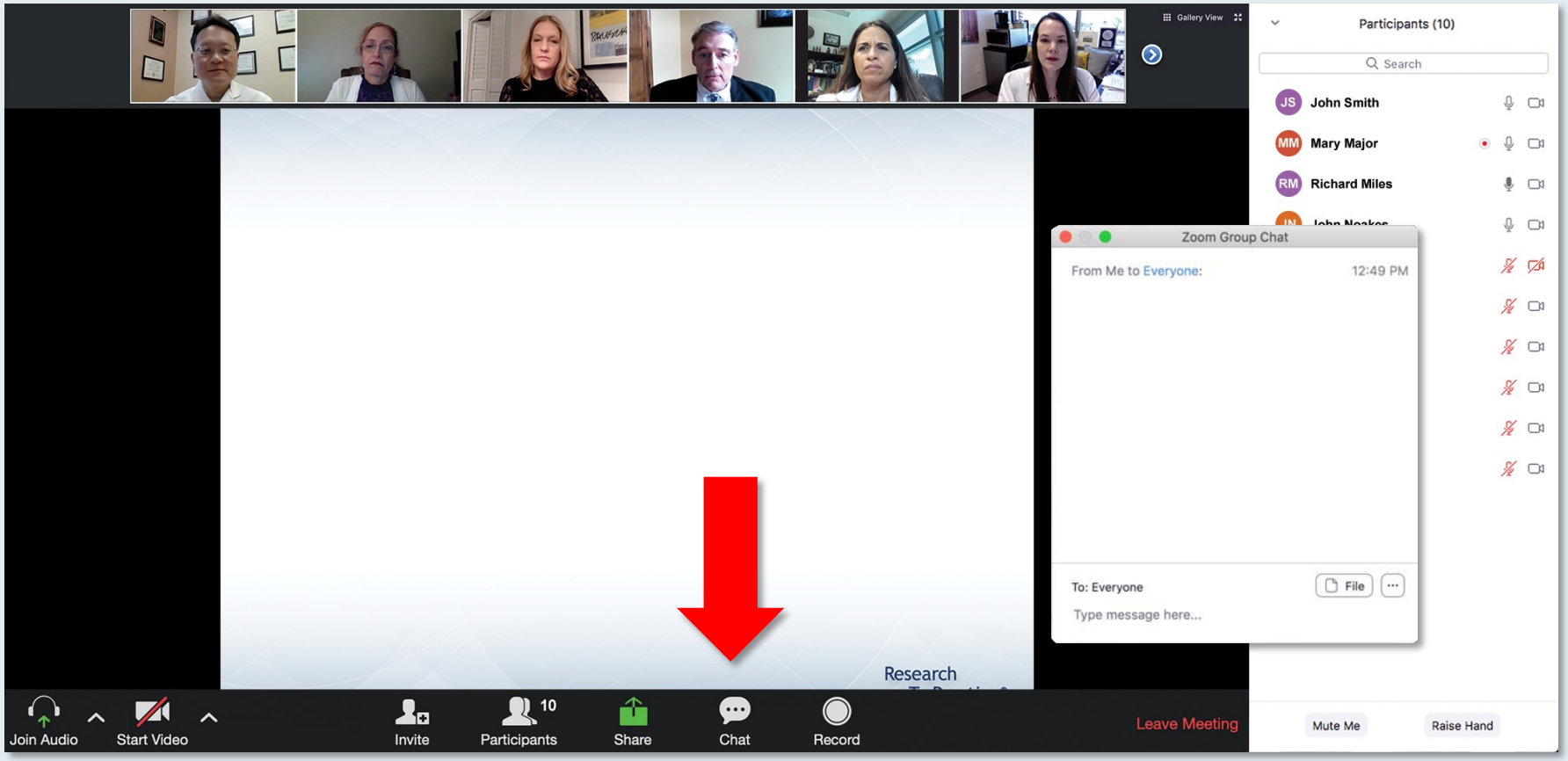

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Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

Module 1: Breast Cancer – 9:30 AM – 10:20 AM

Module 2: Lung Cancer – 10:30 AM – 11:20 AM

Module 3: Gastrointestinal Cancers – 11:30 AM – 12:20 PM

Module 4: Genitourinary Cancers – 12:30 PM – 1:20 PM

Module 5: CLL and Lymphomas – 1:30 PM – 2:20 PM

Module 6: Multiple Myeloma – 2:30 PM – 3:20 PM

Module 7: AML and MDS – 3:30 PM – 4:20 PM

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Florida Cancer Specialists and
Research Institute
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Hans Hammers, MD, PhD
Eugene P Frenkel, MD Scholar in
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Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
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Greensboro, North Carolina

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Meet The Professor with Dr Plimack

Introduction

MODULE 1: Case Presentations

- Dr Gupta: A 71-year-old man with highly symptomatic MSS metastatic non-clear-cell RCC – MET and MYC amplification, PD-L1 low
- Dr Ma: A 60-year-old woman with relapsed chromophobe RCC and a PTEN mutation
- Dr Hammers: A man in his 60s with recurrent RCC after renal transplant
- Dr Malik: A 63-year-old man with metastatic RCC and no actionable mutations, PD-L1 <1%
- Dr Mohamed: A 55-year-old man with metastatic RCC
- Dr Jasani: A 69-year-old man with metastatic clear cell RCC
- Dr Deutsch: A 64-year-old woman with metastatic RCC
- Dr Dandamudi: A 68-year-old man with metastatic clear cell RCC

MODULE 2: Journal Club with Dr Plimack

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

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Meet The Professor Renal Cell Carcinoma Series
February 17, 2021 to October 11, 2021

RCC webinar	Faculty	Total attendees
10/01/2021	Hans Hammers, MD, PhD	123
9/14/2021	Neeraj Agarwal, MD	144
8/23/201	Toni K Choueiri, MD	226
8/06/2021	Thomas Powles, MBBS, MRCP, MD	94
7/22/2021	David F McDermott, MD	151
6/16/2021	Thomas E Hutson, DO, PharmD	151
5/19/2021	Brian I Rini, MD	242
3/25/2021	Robert J Motzer, MD	239
2/17/2021	Eric Jonasch, MD	206
TOTAL		**1,576**

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European Association of Urology

Platinum Priority – Editorial

Referring to the article published on pp. 442–449 of this issue

The *European Urology* Commitment to Gender Equity and Diversity: Expanding Cognitive Diversity through Inclusivity at the Podium

Sarah P. Psutka [a,b,], Todd Morgan [b,c], Maarten Albersen [b,d], Jean-Nicolas Cornu [b,e], Giacomo Novara [b,f], Elizabeth Plimack [b,g], Piet Ost [b,h,i], James W.F. Catto [j,k]*

Introduction

"Inclusivity means not just 'we're allowed to be there,' but we are valued. I've always said, Smart teams will do amazing things, but truly diverse teams will do impossible things."

Claudia Brind-Woody,
Vice President and Managing Director of Intellectual Property at IBM

Meet The Professor with Dr Plimack

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MODULE 2: Journal Club with Dr Plimack

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Case Presentation – Dr Gupta: A 71-year-old man with highly symptomatic MSS metastatic non-clear-cell RCC – MET and MYC amplification, PD-L1 low

Dr Ranju Gupta

- PMH: HTN, DM
- Very symptomatic metastatic non-clear-cell RCC, with lung and liver metastases
- NGS: MET amplification, MYC amplification, MSS, PD-L1 low

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Case Presentation – Dr Gupta: A 71-year-old man with highly symptomatic MSS metastatic non-clear-cell RCC – MET and MYC amplification, PD-L1 low (cont)

Dr Ranju Gupta

- PMH: HTN, DM
- Very symptomatic metastatic non-clear-cell RCC, with lung and liver metastases
- NGS: MET amplification, MYC amplification, MSS, PD-L1 low
- ***Axitinib/pembrolizumab***
  - ***Severe fatigue, mucositis and hand-foot syndrome secondary to axitinib***
  - ***Axitinib dose reduced to 3 mg BID and symptoms resolved***
  - ***Excellent response***

Questions

- ***In the elderly should we rather be starting axitinib at 3 mg BID instead of the full dose of 5 mg BID?***
- ***What second-line treatment would you recommend? Would cabozantinib be an option due to the MET amplification?***
- ***If you had known about the MET amplification earlier, would you have started him on cabozantinib rather than axitinib/pembrolizumab?***

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Case Presentation – Dr Ma: A 60-year-old woman with relapsed chromophobe RCC and a PTEN mutation

Dr Yanjun Ma

- 11/2016: S/p left nephrectomy for Stage II RCC, chromophobe subtype
- 7/2018: Recurrence in tumor bed and in retroperitoneum
- Nivolumab/ipilimumab, with severe, recurrent diarrhea → Discontinued → Monitored off treatment
- 5/2019: Cabozantinib, with intolerance at 60 mg qd → Reduced dose to 40 mg qd
- 9/2020: Everolimus
- NGS: No actionable mutations

Questions

- For chromophobe histology, would you recommend a different first-line option?
- Since this patient received immunotherapy, a VEGF TKI, is currently on an mTOR inhibitor and is in great shape, what treatment would you recommend next?

Case Presentation – Dr Hammers: A man in his 60s with recurrent RCC after renal transplant

Dr Hans Hammers

- Recipient of kidney from his daughter
  - Immunosuppressive therapy with cyclosporine, prednisone and mycophenolate mofetil
  - He has done well with renal transplant
- Recurrent disease involving the lung as well as a lesion in the abdomen close to the bowel

Question

- What would you recommend as systemic therapy for his metastatic RCC?

Case Presentation – Dr Hammers: A man in his 60s with recurrent RCC after renal transplant (continued)

Dr Hans Hammers

- Recipient of kidney from his daughter
- Immunosuppressive therapy with cyclosporine, prednisone and mycophenolate mofetil
- He has done well with renal transplant
- Recurrent disease involving the lung as well as a lesion in the abdomen close to the bowel
- ***Patient wanted to retain graft as long as possible***
- ***Treated with various lines of TKI therapies and lenvatinib/everolimus***
- ***Nivolumab → no response, lost graft within the month***
- ***Patient succumbed to progressive disease***

Case Presentation – Dr Malik: A 63-year-old man with metastatic RCC and no actionable mutations, PD-L1 <1%

Dr Henna Malik

- Presents with severe back pain → 8 cm renal mass identified but lost to f/u x 1 year
- Returns to hospital with a 10 cm renal mass with sacral lytic lesion that was causing excruciating back pain
- Palliative radiation therapy, with significant improvement in pain
- Patient is hesitant to start chemotherapy due to concerns about side effects and cost
- NGS: No actionable mutations, PD-L1 <1%
- Axitinib/pembrolizumab, with excellent response after 3 months and improvement in functional status

Questions

- With all of the newly emerging first-line treatments, what are the second-line treatment options?
- Could we use ipilimumab and nivolumab as second-line therapy options after failure of axitinib and pembrolizumab?

Case Presentation – Dr Mohamed: A 55-year-old man with metastatic RCC

Dr Mohamed Mohamed

- S/p nephrectomy, staging workup revealed bilateral pulmonary nodules and mass under his right breast that were metastatic RCC
- Bone lesion in left femur detected and treated with radiation
- Initiated nivolumab/ipilimumab x 4
- Patient achieved partial response and is faring well on maintenance nivolumab

Question

- Should we “risk everything” up front or just sequence treatments gradually?

Case Presentation – Dr Jasani: A 69-year-old man with metastatic clear cell RCC

Dr Nikesh Jasani

- Presented with shortness of breath and weakness
- PMH: Waldenström macroglobulinemia in 2011
- Diagnosed with Stage IV ccRCC with bulky right renal mass with renal vein involvement, left pleural effusion with pleural-based metastases
- VATS/catheterization
- Ipilimumab/nivolumab x 4 cycles → nivolumab maintenance
- During assessment for nephrectomy was found to have brain metastases and progression

Questions

- What is the role of nephrectomy in the current era of TKI and immunotherapy?
- What is the best second-line therapy in these individuals who have received dual checkpoint inhibitors?

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Case Presentation – Dr Deutsch: A 64-year-old woman with metastatic RCC

Dr Margaret Deutsch

- 10/2003: pT1N0 RCC, s/p right nephrectomy
- 10/2014 CT: Biopsy-proven lung, liver and pancreatic metastases
- 11/2014: Pazopanib, with improvement in metastases
  - Severe nausea, vomiting and weight loss that persisted after dose reduction
  - 4/2019: Pazopanib discontinued
- 4/2019: Nivolumab, with PD over 2 consecutive image studies
  - Palmar rash and pruritus
- Lenvatinib/everolimus, cb hypertension, mucositis, nausea/vomiting, palpitations
  - Patient refused to continue
- Cabozantinib initially 40 mg PO qd but hand-foot syndrome, nausea/vomiting
  - Now receiving 40 mg PO qd 2 weeks on, 2 weeks off
  - Liver lesions significantly reduced in size

Question

- What would you have used as first-line therapy now after such a long disease-free interval?

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Case Presentation – Dr Dandamudi: A 68-year-old man with metastatic RCC

Dr Uday Dandamudi

- Stage IA renal cell carcinoma → left nephrectomy, with vascular invasion (outside institution)
  - No adjuvant therapy
- 2/2018: Presented to ER unable to walk
  - Imaging: Large iliac sclerotic lesion 4 x 5 cm and soft tissue nodules over nephrectomy fossa
- 2/2019 - 12/2019: Pembrolizumab/lenvatinib on clinical trial x 18 months → PD
  - Objective response, improvement in bone pain, well tolerated
- Cabozantinib 60 mg
  - Fatigue, weakness, calluses on upper/lower extremities → dose reduced to 40 mg
  - After 8 months, increased size of soft tissue nodules, new lymph nodes

Question

- Would you recommend an IO/IO combination for this patient or would you try another sequential TKI?

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Plimack

Introduction

MODULE 1: Case Presentations

- Dr Gupta: A 71-year-old man with highly symptomatic MSS metastatic non-clear-cell RCC – MET and MYC amplification, PD-L1 low
- Dr Ma: A 60-year-old woman with relapsed chromophobe RCC and a PTEN mutation
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- Dr Mohamed: A 55-year-old man with metastatic RCC
- Dr Jasani: A 69-year-old man with metastatic clear cell RCC
- Dr Deutsch: A 64-year-old woman with metastatic RCC
- Dr Dandamudi: A 68-year-old man with metastatic clear cell RCC

MODULE 2: Journal Club with Dr Plimack

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

Journal Club with Dr Plimack – Part 1

- Choueiri TK et al. **Inhibition of hypoxia-inducible factor-2α in renal cell carcinoma with belzutifan: A phase 1 trial and biomarker analysis**. *Nat Med* 2021;22(27):802-05.
- Rini BI et al. **Randomized, open-label, 3-arm phase III study comparing MK-1308A + lenvatinib and pembrolizumab (pembro) + belzutifan + lenvatinib versus pembro + lenvatinib as first-line (1L) treatment for advanced clear cell renal cell carcinoma (ccRCC).** ESMO 2021;Abstract 717TiP.
- Geynisman DM et al. **Systemic therapy for advanced non-clear-cell renal cell carcinoma: Slow but definite progress.** *Eur Urol* 2021;80(2):171-173. *Editorial:*
  - Hutson TE et al. **A single-arm, multicenter, phase 2 study of lenvatinib plus everolimus in patients with advanced non–clear-cell renal cell carcinoma.** *Eur Urol* 2021;80:162-70.

RTP RESEARCH TO PRACTICE

Journal Club with Dr Plimack – Part 2

- Plimack ER et al. **A phase 1b/2 umbrella study of investigational immune and targeted combination therapies as first-line therapy for patients with advanced renal cell carcinoma (RCC).** ASCO 2021;Abstract TPS4594.
- Rini BI et al. **Characterization and management of treatment-emergent hepatic toxicity in patients with advanced renal cell carcinoma receiving first-line pembrolizumab plus axitinib. Results from the KEYNOTE-426 trial.** *Eur Urol Oncol* 2021;[Online ahead of print].
- Zarrabi K et al. **Real-world outcomes in patients with metastatic clear cell renal cell carcinoma receiving front-line axitinib plus pembrolizumab versus ipilimumab plus nivolumab.** ASCO 2021;Abstract 4551.

RTP
RESEARCH
TO PRACTICE

Meet The Professor with Dr Plimack

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RTP RESEARCH TO PRACTICE

Optimizing Front-Line Decision-Making for Advanced RCC

RTP
RESEARCH
TO PRACTICE

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 Choueiri	Nivolumab/ cabozantinib	 Dr Motzer	Nivolumab/ cabozantinib
 Dr Hutson	Nivolumab/ cabozantinib	 Dr Plimack	Pembrolizumab/ axitinib
 Dr Jonasch	Nivolumab/ cabozantinib	 Prof Powles	Pembrolizumab/ lenvatinib
 Dr McDermott	Nivolumab/ipilimumab	 Dr Rini	Pembrolizumab/ lenvatinib

RTP RESEARCH TO PRACTICE

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 hemoglobin (Hb) of 11.4 g/dL (PS = 1)?

 Dr Choueiri	Nivolumab/ cabozantinib	 Dr Motzer	Nivolumab/ipilimumab
 Dr Hutson	Nivolumab/ cabozantinib	 Dr Plimack	Pembrolizumab/ lenvatinib
 Dr Jonasch	Nivolumab/ cabozantinib	 Prof Powles	Pembrolizumab/ axitinib
 Dr McDermott	Pembrolizumab/ lenvatinib	 Dr Rini	Pembrolizumab/ lenvatinib

RTP RESEARCH TO PRACTICE

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?

 Dr Choueiri	Cabozantinib	 Dr Motzer	Cabozantinib
 Dr Hutson	Cabozantinib	 Dr Plimack	Pazopanib
 Dr Jonasch	Sunitinib	 Prof Powles	Pazopanib
 Dr McDermott	Cabozantinib	 Dr Rini	Cabozantinib

RTP RESEARCH TO PRACTICE

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?

 Dr Choueiri	I don't know (likely same as axitinib)	 Dr Motzer	I don't know
 Dr Hutson	Efficacy is about the same	 Dr Plimack	Efficacy is about the same
 Dr Jonasch	Efficacy is about the same	 Prof Powles	Efficacy is about the same
 Dr McDermott	Efficacy is about the same	 Dr Rini	Efficacy is about the same

RTP RESEARCH TO PRACTICE

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?

 Dr Choueiri	Tivozanib is more tolerable	 Dr Motzer	Tivozanib is more tolerable
 Dr Hutson	Tivozanib is more tolerable	 Dr Plimack	Tivozanib is more tolerable
 Dr Jonasch	Tivozanib is more tolerable	 Prof Powles	Tolerability is about the same
 Dr McDermott	Tivozanib is more tolerable	 Dr Rini	Tivozanib is more tolerable

RTP RESEARCH TO PRACTICE

Sequencing of Therapy for Patients with Relapsed/Refractory 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?

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Axitinib
5. Avelumab/axitinib
6. Pembrolizumab/axitinib
7. Nivolumab/cabozantinib
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 Choueiri	Cabozantinib	 Dr Motzer	Axitinib
 Dr Hutson	Cabozantinib	 Dr Plimack	Pembrolizumab/ axitinib
 Dr Jonasch	Cabozantinib	 Prof Powles	Cabozantinib
 Dr McDermott	Cabozantinib	 Dr Rini	Axitinib

RTP RESEARCH TO PRACTICE

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?

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Sorafenib
5. Lenvatinib/everolimus
6. Nivolumab/ipilimumab
7. Nivolumab/cabozantinib
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 pembrolizumab/axitinib and experiences disease progression after 12 months?

 Dr Choueiri	Cabozantinib	 Dr Motzer	Cabozantinib
 Dr Hutson	Cabozantinib	 Dr Plimack	Cabozantinib
 Dr Jonasch	Cabozantinib	 Prof Powles	Cabozantinib
 Dr McDermott	Cabozantinib	 Dr Rini	Cabozantinib

RTP RESEARCH TO PRACTICE

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 Choueiri	Lenvatinib + everolimus	 Dr Motzer	Lenvatinib + everolimus
 Dr Hutson	Lenvatinib + everolimus	 Dr Plimack	Lenvatinib + everolimus
 Dr Jonasch	Lenvatinib + everolimus	 Prof Powles	Axitinib
 Dr McDermott	Nivolumab/ipilimumab	 Dr Rini	Axitinib

RTP RESEARCH TO PRACTICE

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RTP RESEARCH TO PRACTICE

Open access Original research

ESMO Open
Cancer Horizons

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]

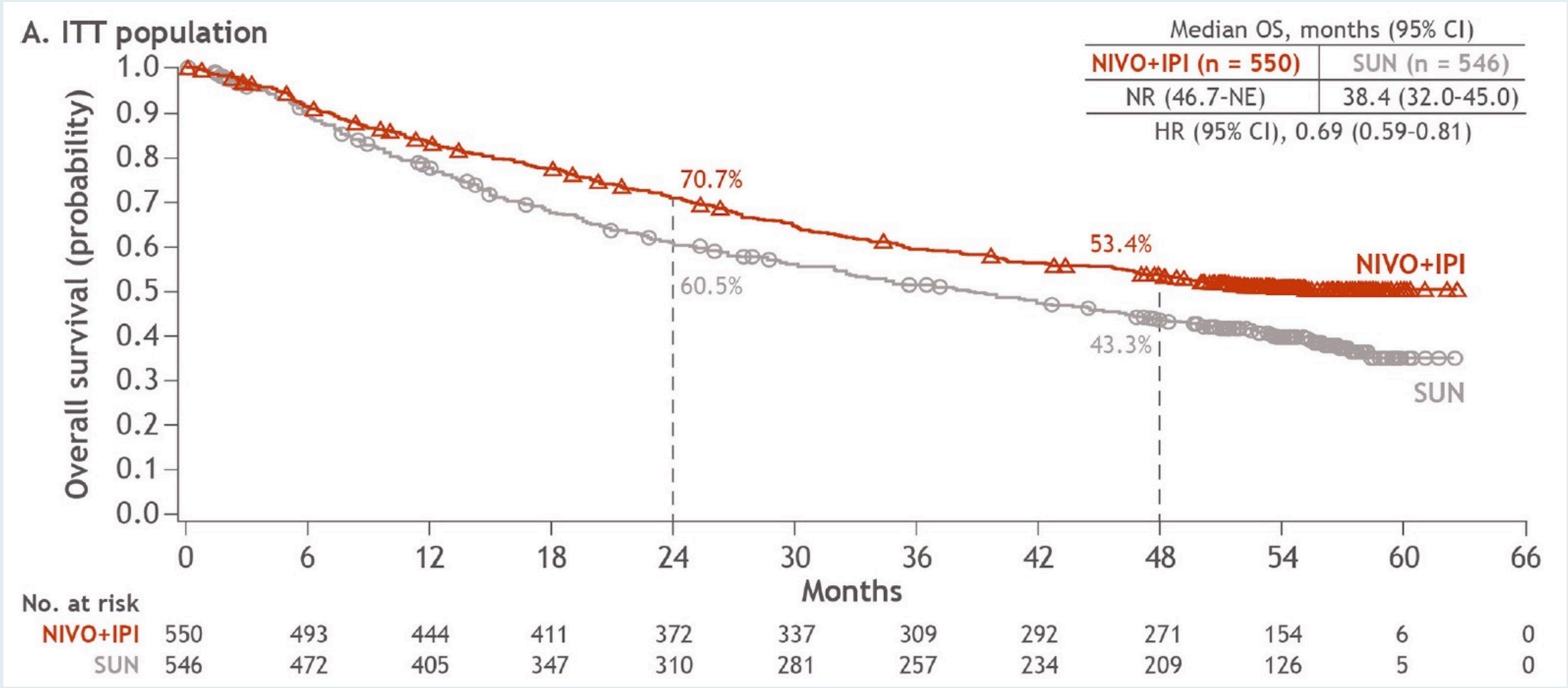
ESMO Open 2020;5(6):e001079.

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

	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%

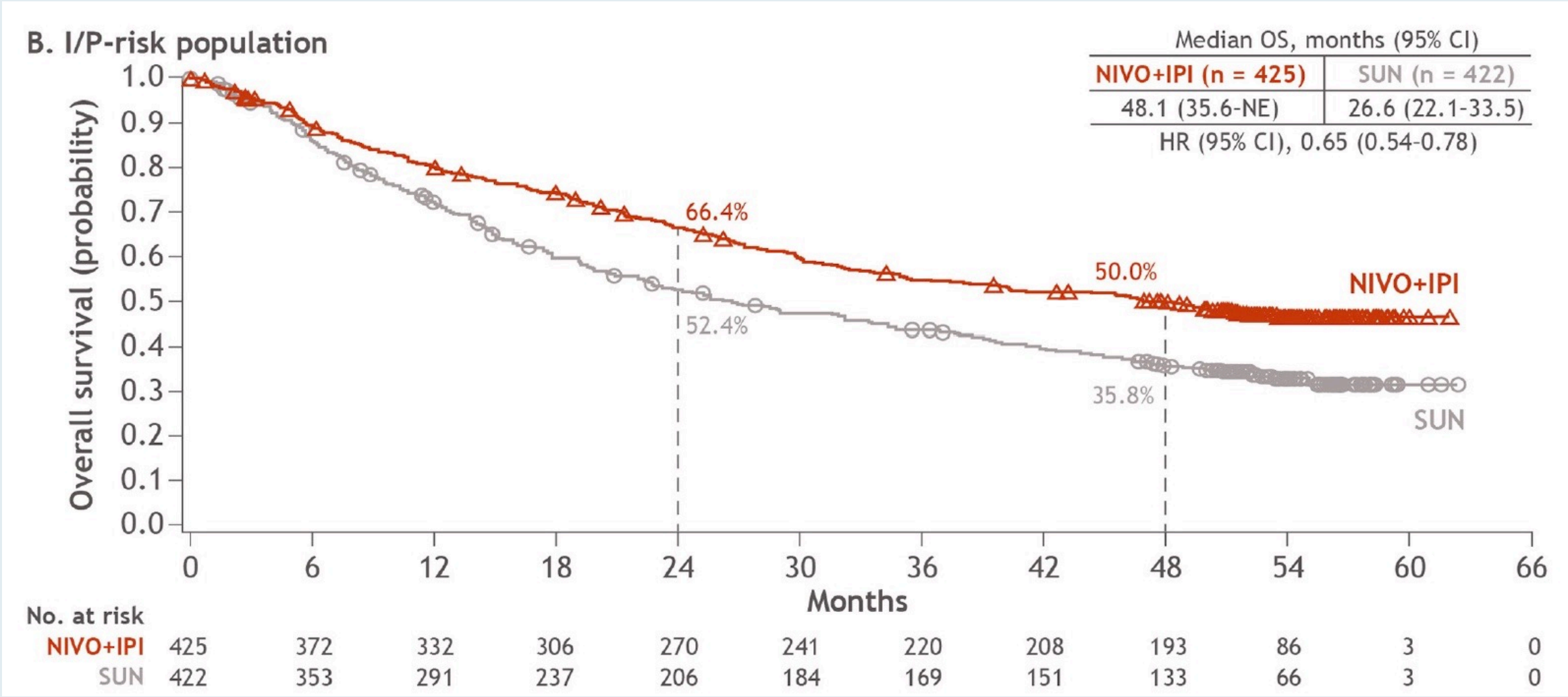
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

CheckMate 214: Overall Survival (ITT)



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

CheckMate 214: Overall Survival (Intermediate/Poor Risk)



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

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

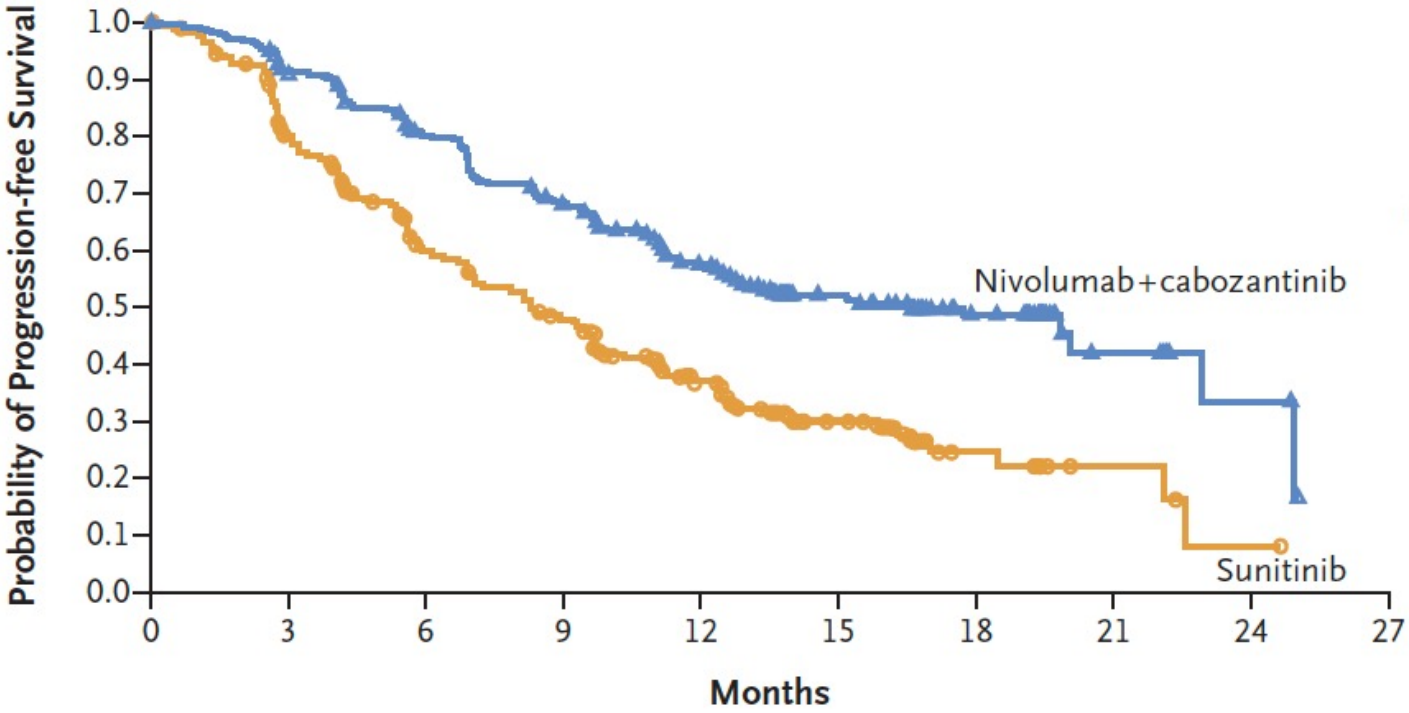
The NEW ENGLAND JOURNAL of MEDICINE

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*

CheckMate 9ER: Progression-Free Survival



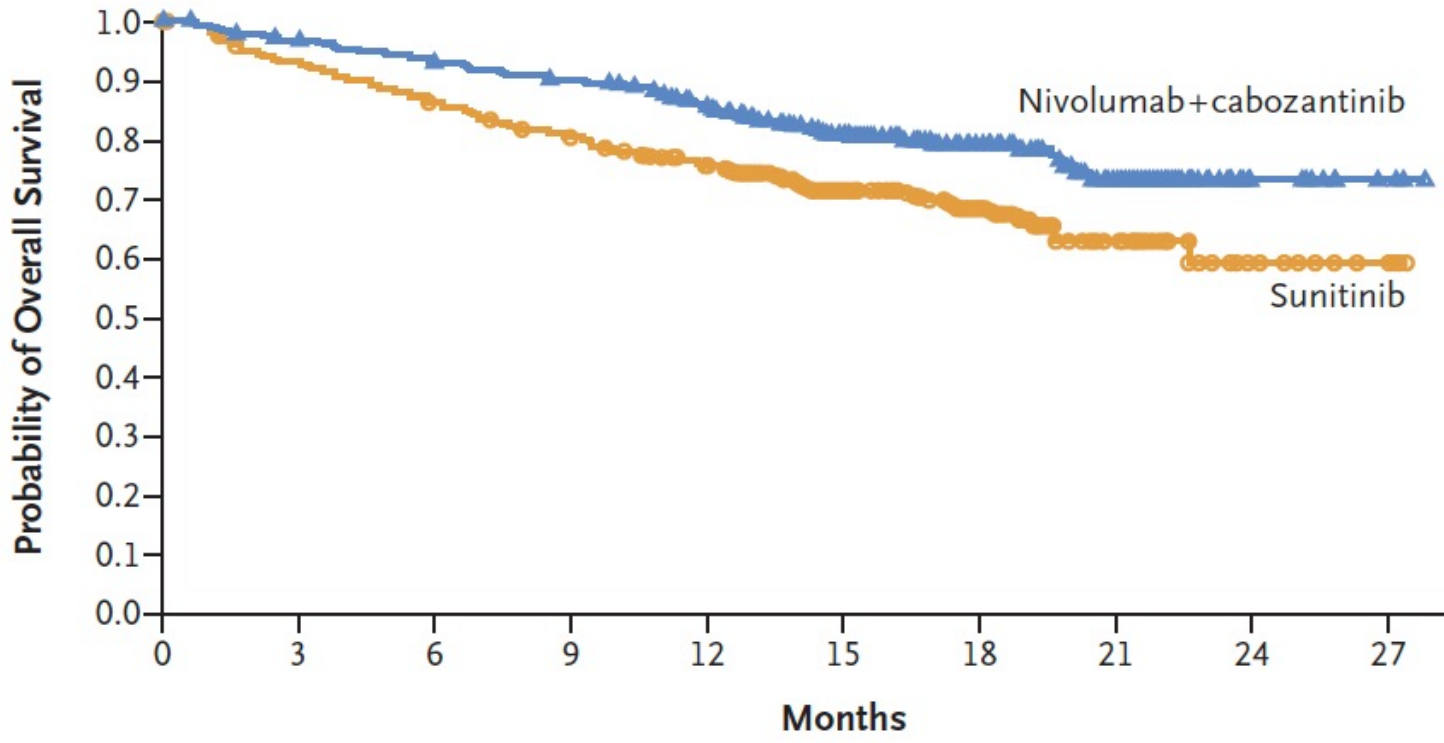
	No. of Patients	Median (95% CI) *mo*
Nivolumab+ Cabozantinib	323	16.6 (12.5–24.9)
Sunitinib	328	8.3 (7.0–9.7)

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

No. at Risk										
Nivolumab+cabozantinib	323	279	234	196	144	77	35	11	4	0
Sunitinib	328	228	159	122	79	31	10	4	1	0

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

CheckMate 9ER: Overall Survival



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

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

No. at Risk

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

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

ABSTRACT 4509: NIVOLUMAB PLUS CABOZANTINIB IN PATIENTS WITH NON-CLEAR CELL RENAL CELL CARCINOMA: RESULTS OF A PHASE 2 TRIAL

Chung-Han Lee, Martin H Voss, Maria Isabel Carlo, Ying-Bei Chen, Ed Reznik, Andrea Knezevic, Robert A Lefkowitz, Natalie Shapnik, Diana Tassone, Chloe Dadoun, Mark Zucker, Neil J. Shah, Colette Ngozi Owens, Deaglan Joseph McHugh, David Henry Aggen, Andrew Leonard Laccetti, Ritesh Kotecha, Darren R. Feldman, Robert J. Motzer

June 6, 2021

Memorial Sloan Kettering Cancer Center™

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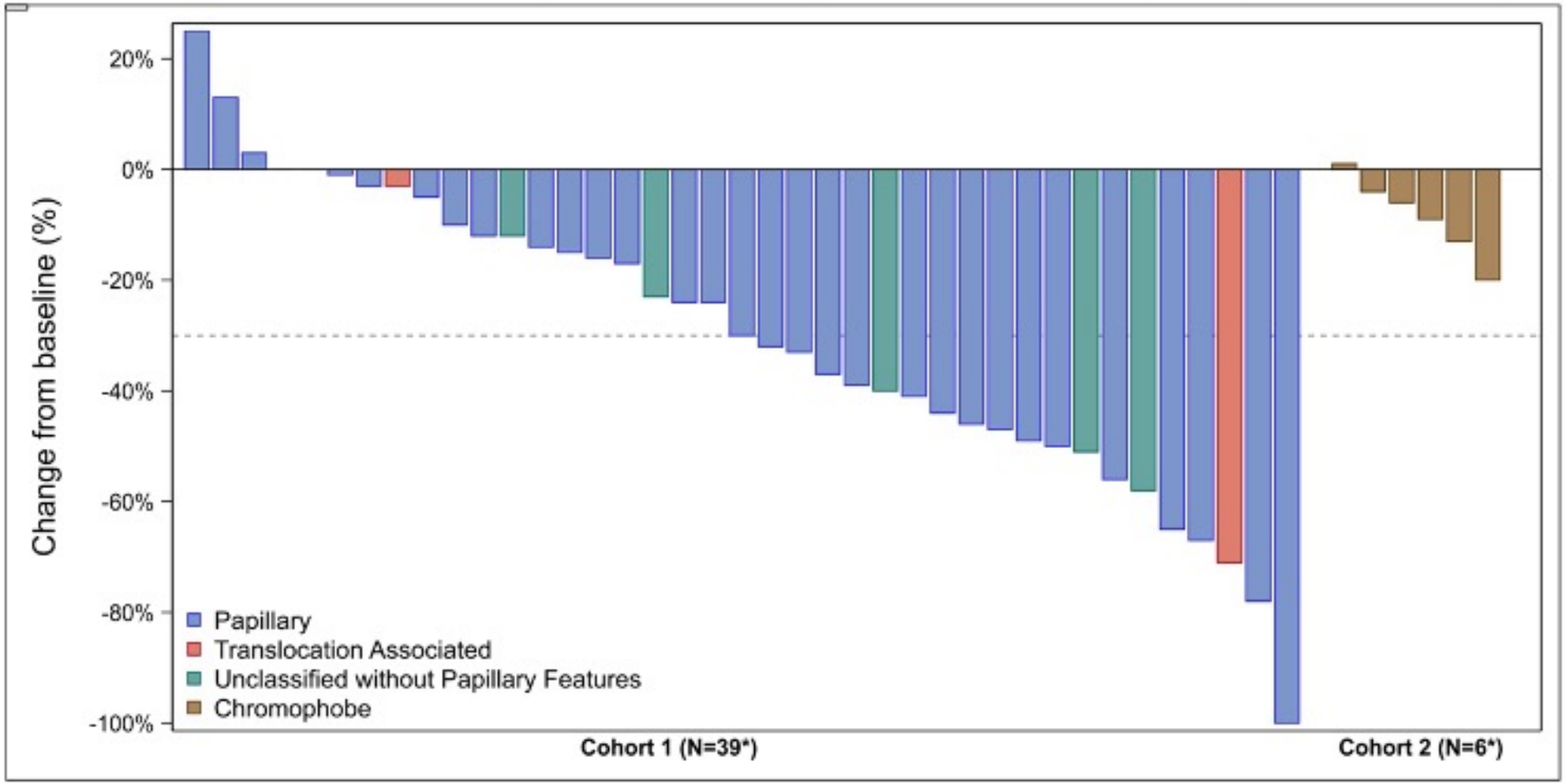
Lee CH et al. ASCO 2021;Abstract 4509.

RTP RESEARCH TO PRACTICE

Maximum Change in Target Lesions by Histology



Lee CH et al. ASCO 2021;Abstract 4509.

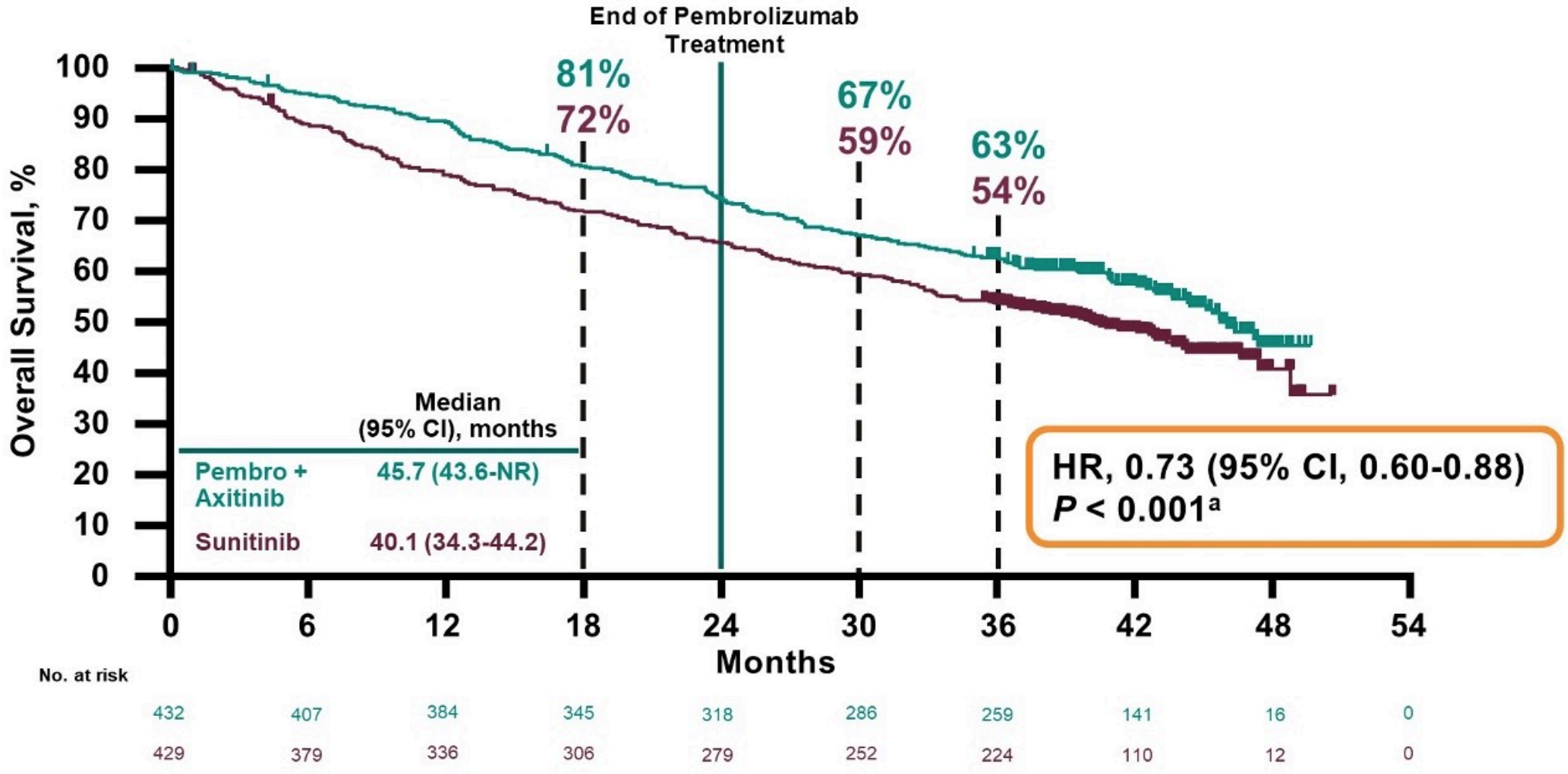
Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

B. I. Rini[1]; E. R. Plimack[2]; V. Stus[3]; T. Waddell[4]; R. Gafanov[5]; F. Pouliot[6]; D. Nosov[7]; B. Melichar[8]; D. Soulieres[9]; D. Borchiellini[10]; I. Vynnychenko[11]; R. S. McDermott[12]; S. J. Azevedo[13]; S. Tamada[14]; A. Kryzhanivska[15]; C. Li[16]; J. E. Burgents[16]; L. R. Molife[17]; J. Bedke[18]; T. Powles[19]

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

Rini BI et al. ASCO 2021;Abstract 4500.

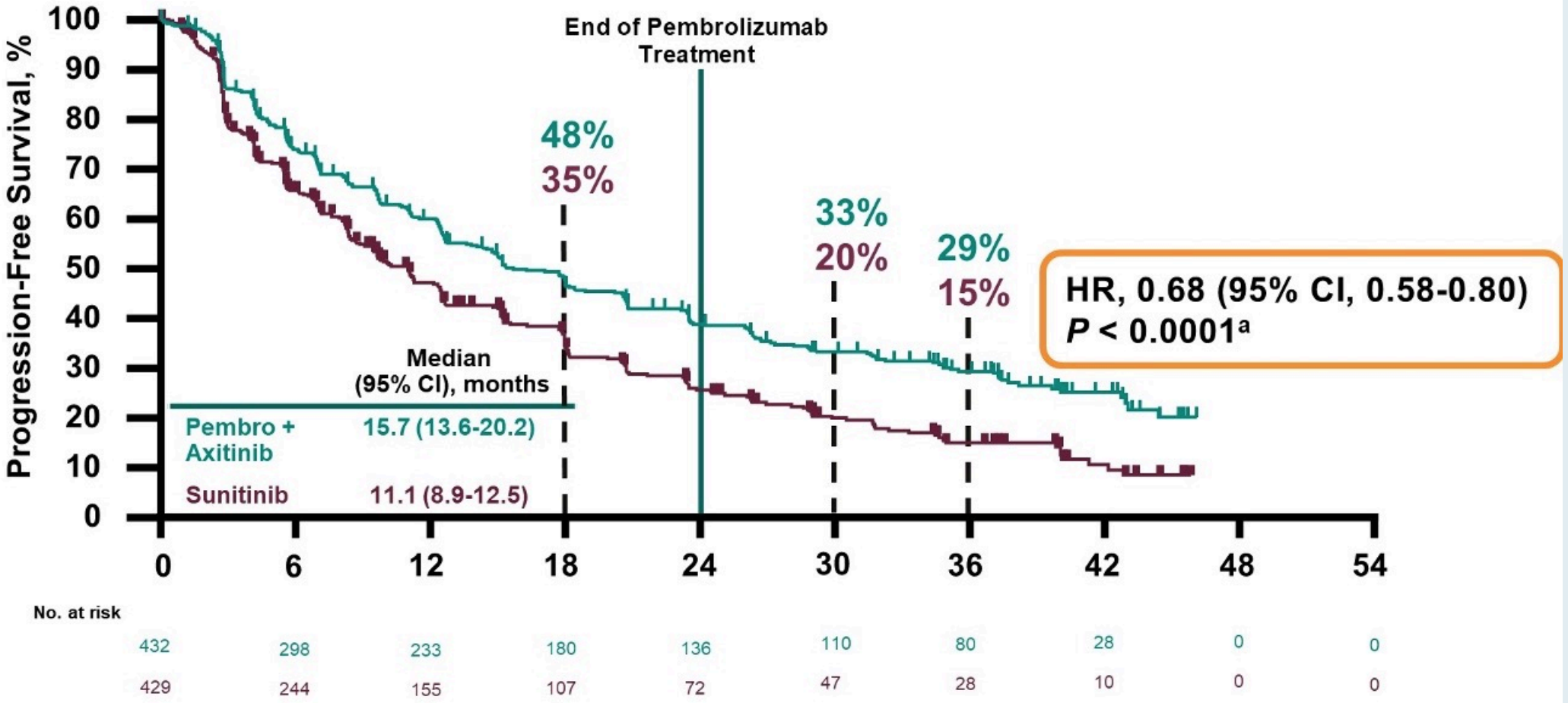
OS in the ITT Population



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

Rini BI et al. ASCO 2021;Abstract 4500.

PFS in the ITT Population



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

Rini BI et al. ASCO 2021;Abstract 4500.

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

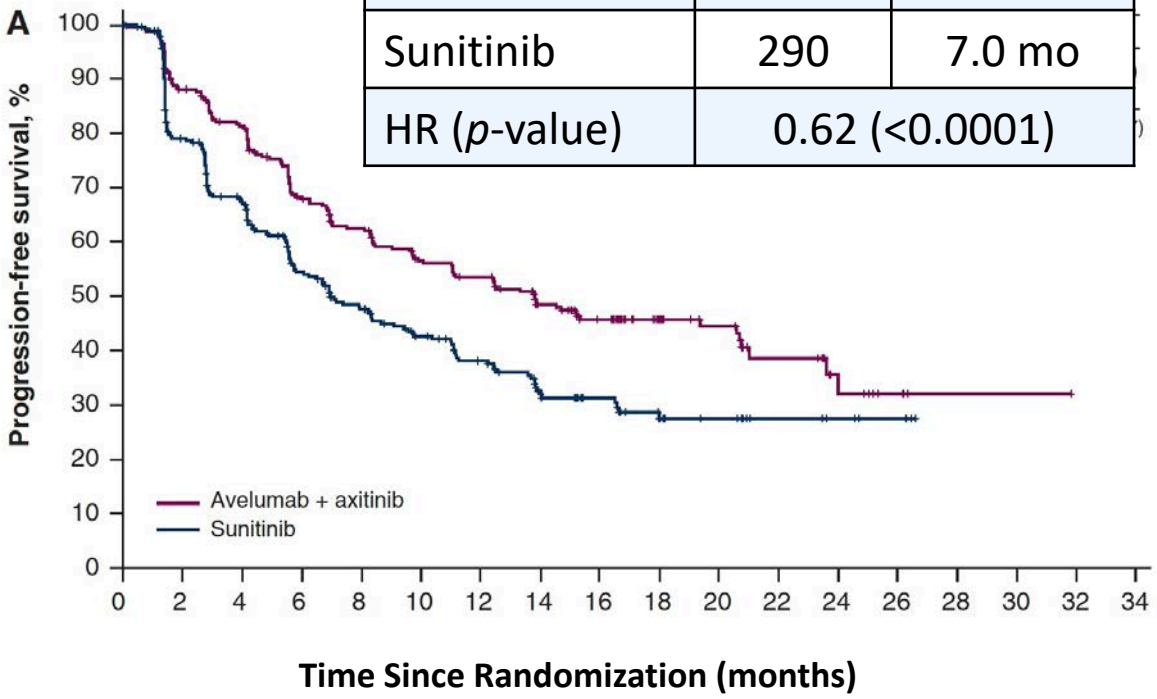
	PD-L1-positive		Overall	
	Avelumab + axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing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

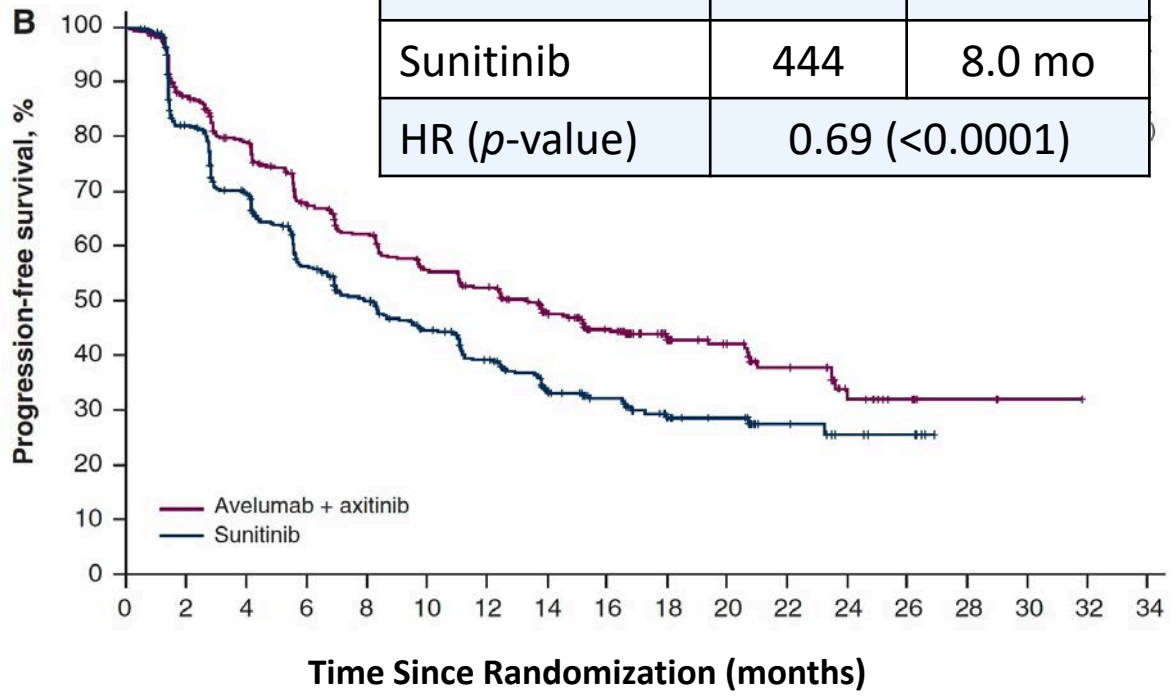
PD-L1 ≥ 1% Population

	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.

RTP RESEARCH TO PRACTICE

FDA Approves Lenvatinib with Pembrolizumab for Advanced RCC

Press Release – August 10, 2021

"The Food and Drug Administration approved the combination of lenvatinib plus pembrolizumab for first-line treatment of adult patients with advanced renal cell carcinoma (RCC).

The efficacy of this combination was investigated in CLEAR (Study 307/KEYNOTE-581; NCT02811861), a multicenter, open-label, randomized phase 3 trial in patients with advanced RCC in the first-line setting. Patients were enrolled regardless of PD-L1 tumor expression status.

The recommended dosages for patients with advanced RCC are lenvatinib 20 mg orally once daily with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks or 400 mg administered as an intravenous infusion over 30 minutes every 6 weeks up to 2 years, until disease progression or until unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lenvatinib-plus-pembrolizumab-advanced-renal-cell-carcinoma

The NEW ENGLAND JOURNAL of MEDICINE

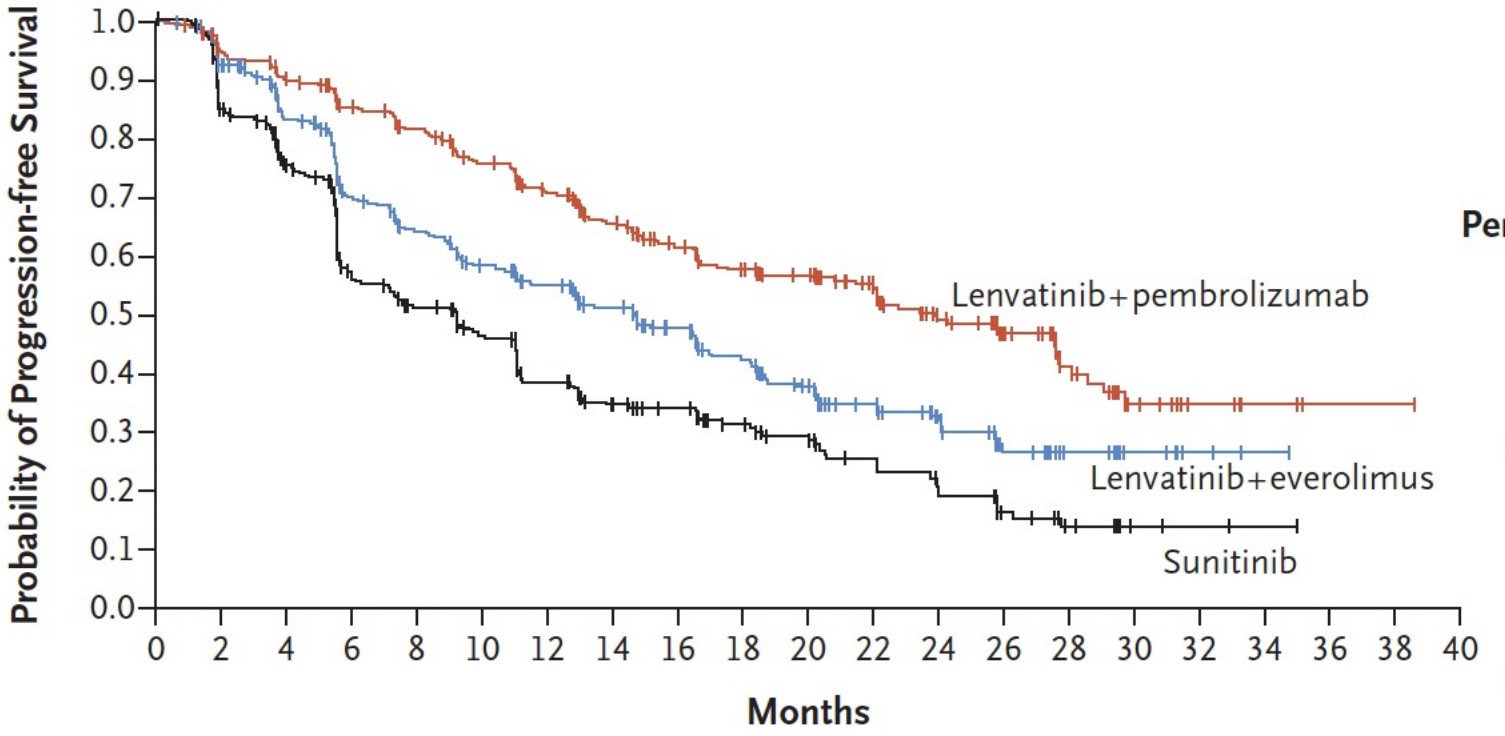
ORIGINAL ARTICLE

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*

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

CLEAR: Progression-Free Survival



No. at Risk

Lenvatinib+pembrolizumab	355	321	300	276	259	235	213	186	160	136	126	106	80	56	30	14	6	3	1	1	0
Lenvatinib+everolimus	357	305	259	207	185	163	149	125	105	85	70	53	37	20	13	7	3	1	0		
Sunitinib	357	262	218	145	124	107	85	69	62	49	42	32	25	16	9	3	2	1	0		

Median Progression-free Survival (95% CI)

	mo
Lenvatinib+ Pembrolizumab	23.9 (20.8–27.7)
Lenvatinib+ Everolimus	14.7 (11.1–16.7)
Sunitinib	9.2 (6.0–11.0)

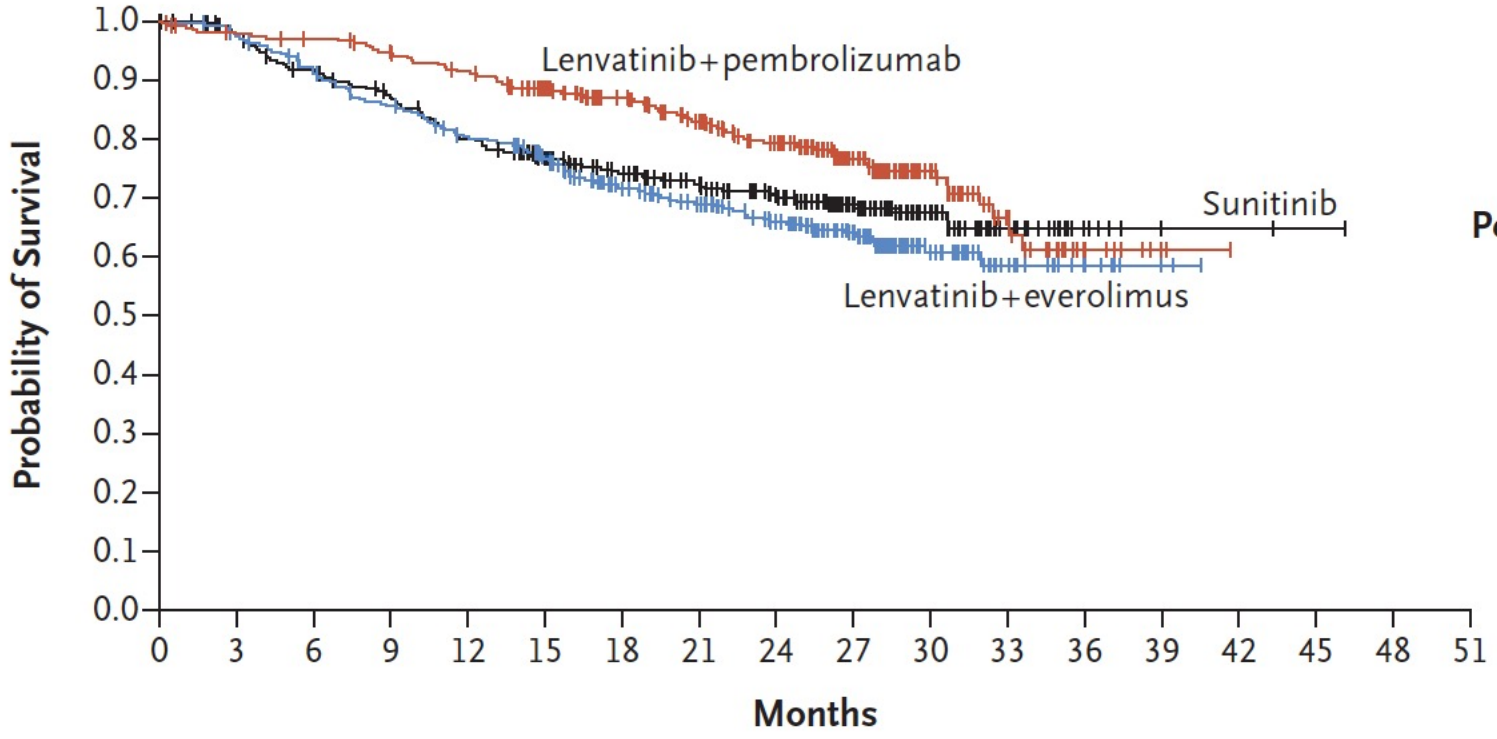
Hazard ratio for disease progression or death (lenvatinib+ pembrolizumab vs. sunitinib), 0.39 (95% CI, 0.32–0.49); P<0.001

Hazard ratio for disease progression or death (lenvatinib+ everolimus vs. sunitinib), 0.65 (95% CI, 0.53–0.80); P<0.001

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

RTP RESEARCH TO PRACTICE

CLEAR: 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].

RTP RESEARCH TO PRACTICE

ANALYSIS OF THE CLEAR STUDY IN PATIENTS WITH ADVANCED RENAL CELL CARCINOMA: DEPTH OF RESPONSE AND EFFICACY FOR SELECTED SUBGROUPS IN THE LENVATINIB-PLUS-PEMBROLIZUMAB AND SUNITINIB TREATMENT ARMS

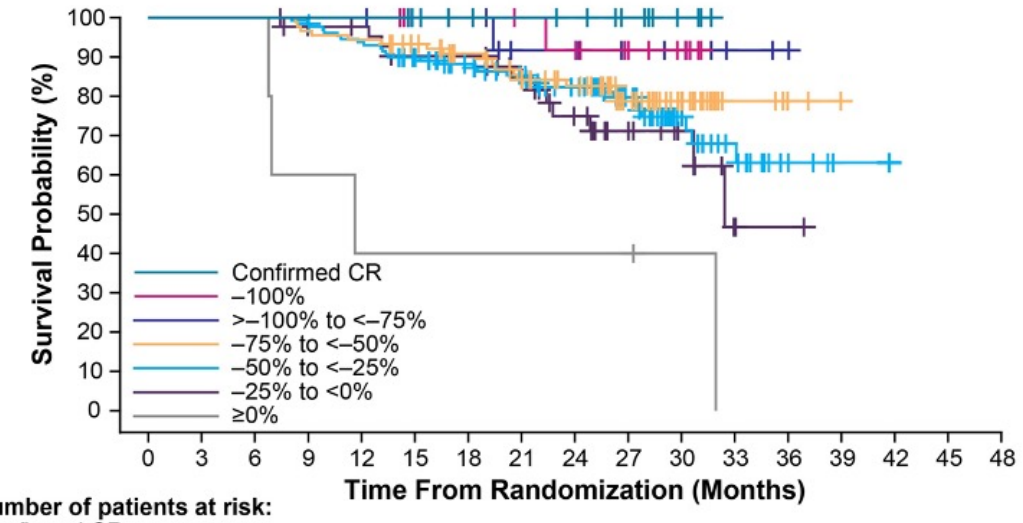
Viktor Grünwald[1], Thomas Powles[2], Evgeny Kopyltsov[3], Vadim Kozlov[4], Teresa Alonso Gordoa[5], Masatoshi Eto[6], Thomas Hutson[7], Robert Motzer[8], Eric Winquist[9], Pablo Maroto[10], Bhumsuk Keam[11], Giuseppe Procopio[12], Shirley Wong[13], Bohuslav Melichar[14], Frederic Rolland[15], Mototsugu Oya[16], Karla Rodriguez-Lopez[17], Kenichi Saito[18], Alan Smith[19], Camillo Porta[20]

[1]University Hospital Essen, Essen, Germany; [2]The Royal Free NHS Trust, London, England, UK; [3]State Institution of Healthcare "Regional Clinical Oncology Dispensary", Omsk, Russia; [4]State Budgetary Health Care Institution "Novosibirsk Regional Clinical Oncology Dispensary", Novosibirsk, Russia; [5]Hospital Universitario Ramón y Cajal, Madrid, Spain; [6]Kyushu University, Fukuoka, Japan; [7]Texas Oncology, Dallas, TX, USA; [8]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [9]Western University, London, Ontario, Canada; [10]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [11]Seoul National University Hospital, Seoul, Korea; [12]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milan, Italy; [13]Western Health, VIC, Australia; [14]Palacký University Medical School and Teaching Hospital, Olomouc, Czech Republic; [15]Centre René Gauducheau Centre de Lutte Contre Le Cancer Nantes, Saint-Herblain, France; [16]Keio University School of Medicine, Tokyo, Japan; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]Eisai Inc., Woodcliff Lake, NJ, USA; [19]Eisai Ltd., Hatfield, England, UK; [20]San Matteo University Hospital Foundation, Pavia, Italy.

Grunwald V et al. ASCO 2021;Abstract 4560.

CLEAR: 6-Month OS Analysis by Depth of Response

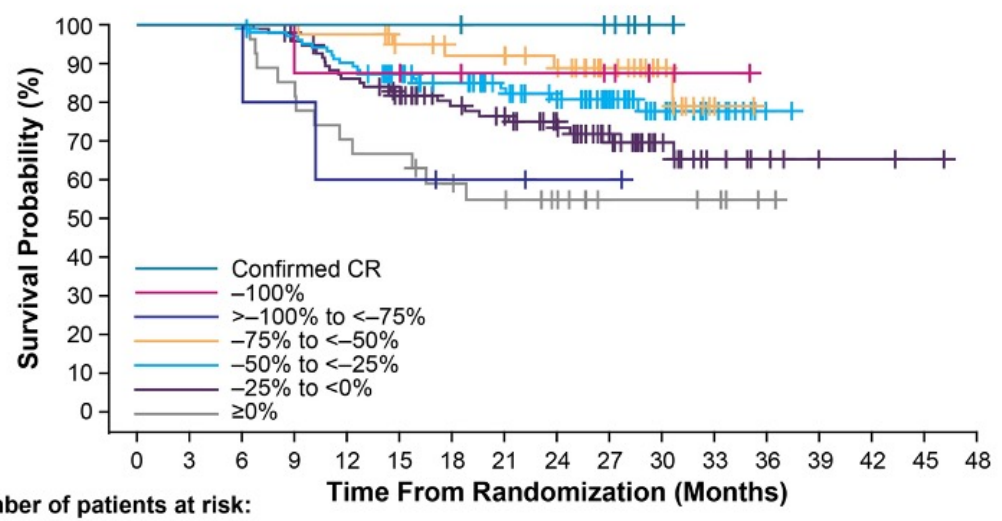
Lenvatinib plus Pembrolizumab



Number of patients at risk:

Confirmed CR	16	16	16	14	12	11	10	7	3	0	0	0	0	0	0
–100%	20	20	20	17	14	12	11	8	5	0	0	0	0	0	0
>–100% to <–75%	16	16	16	13	13	9	9	6	5	2	1	0	0	0	0
–75% to <–50%	89	86	84	78	70	61	54	37	20	5	2	0	0	0	0
–50% to <–25%	129	128	120	108	96	88	76	53	23	14	5	1	0	0	0
–25% to <0%	44	40	39	35	35	29	21	13	8	2	1	0	0	0	0
≥0%	5	3	2	2	2	2	2	2	1	0	0	0	0	0	0

Sunitinib



Number of patients at risk:

Confirmed CR	7	7	7	7	7	6	6	5	1	0	0	0	0	0	0
–100%	8	8	7	7	6	5	5	4	2	1	0	0	0	0	0
>–100% to <–75%	5	4	3	3	2	2	1	1	0	0	0	0	0	0	0
–75% to <–50%	40	40	39	35	32	32	28	19	10	2	0	0	0	0	0
–50% to <–25%	103	99	92	80	71	61	53	39	21	9	1	0	0	0	0
–25% to <0%	96	90	80	71	60	56	47	34	17	9	5	2	2	1	0
≥0%	27	23	19	18	15	13	10	5	5	4	1	0	0	0	0

Among patients treated with lenvatinib plus pembrolizumab, all those who had a complete response were alive at 2 years; survival rates were similar for patients who had more than 75% reduction in target lesions.

Tumors assessed by Independent Review Committee per RECIST v1.1

Grunwald V et al. ASCO 2021;Abstract 4560.

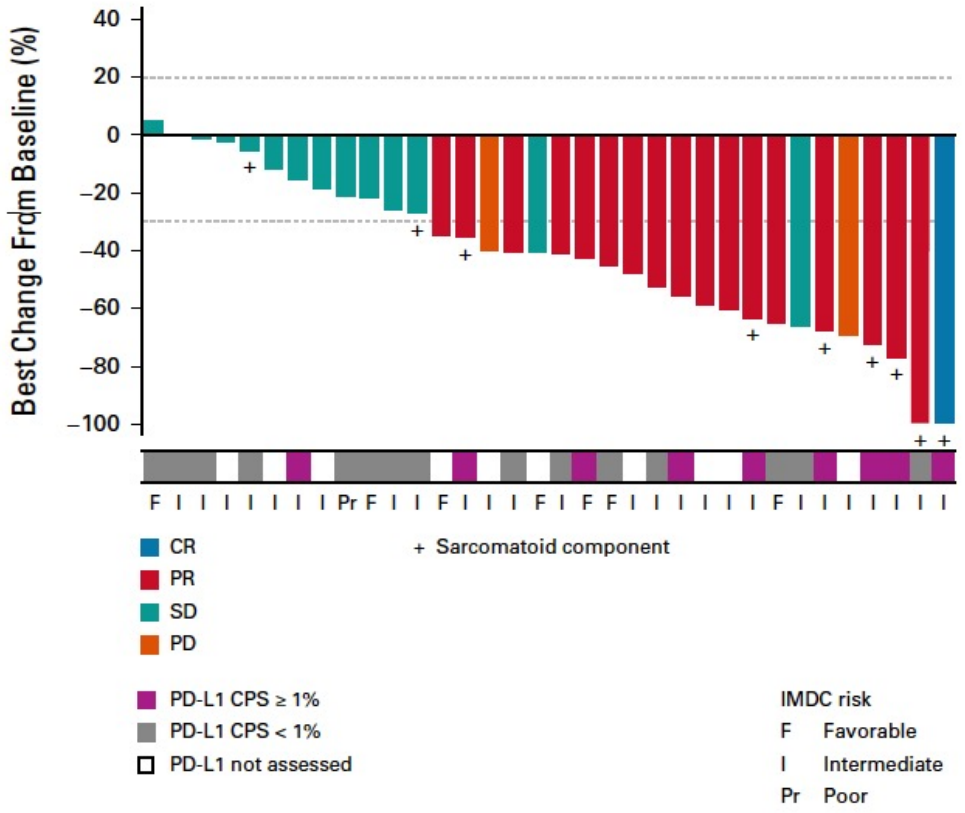
Cabozantinib in Combination With Atezolizumab for Advanced Renal Cell Carcinoma: Results From the COSMIC-021 Study

Sumanta K. Pal, MD[1]; Bradley McGregor, MD[2]; Cristina Suárez, MD[3]; Che-Kai Tsao, MD[4]; William Kelly, DO[5]; Ulka Vaishampayan, MD[6,7]; Lance Pagliaro, MD[8]; Benjamin L. Maughan, MD[9]; Yohann Loriot, MD[10]; Daniel Castellano, MD[11]; Sandy Srinivas, MD[12]; Rana R. McKay, MD[13]; Robert Dreicer, MD[14]; Thomas Hutson, DO[15]; Sarita Dubey, MD[16]; Scott Werneke, PhD[17]; Ashok Panneerselvam, PhD[17]; Dominic Curran, MBChB[17]; Christian Scheffold, MD[17]; Toni K. Choueiri, MD[2]; and Neeraj Agarwal, MD[9]

J Clin Oncol 2021;[Online ahead of print].

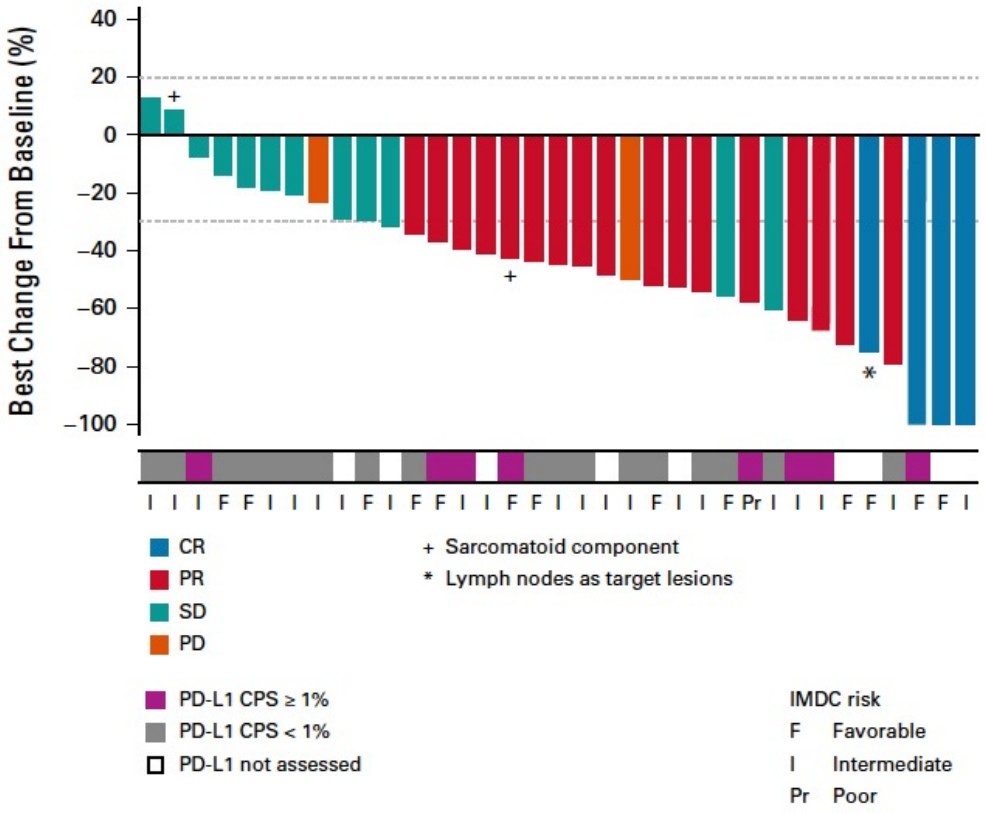
COSMIC-021: Cabozantinib/Atezolizumab for Previously Untreated Advanced ccRCC

Cabozantinib 40mg + Atezolizumab (n = 34)



ORR: 53%
mPFS: 19.5 mo

Cabozantinib 60mg + Atezolizumab (n = 35)



ORR: 58%
mPFS: 15.1 mo

Pal SK et al. *J Clin Oncol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Select Ongoing Phase III Clinical Trials for Previously Untreated Metastatic RCC

Study acronym	Target accrual	Randomization	Primary endpoint	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

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

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."

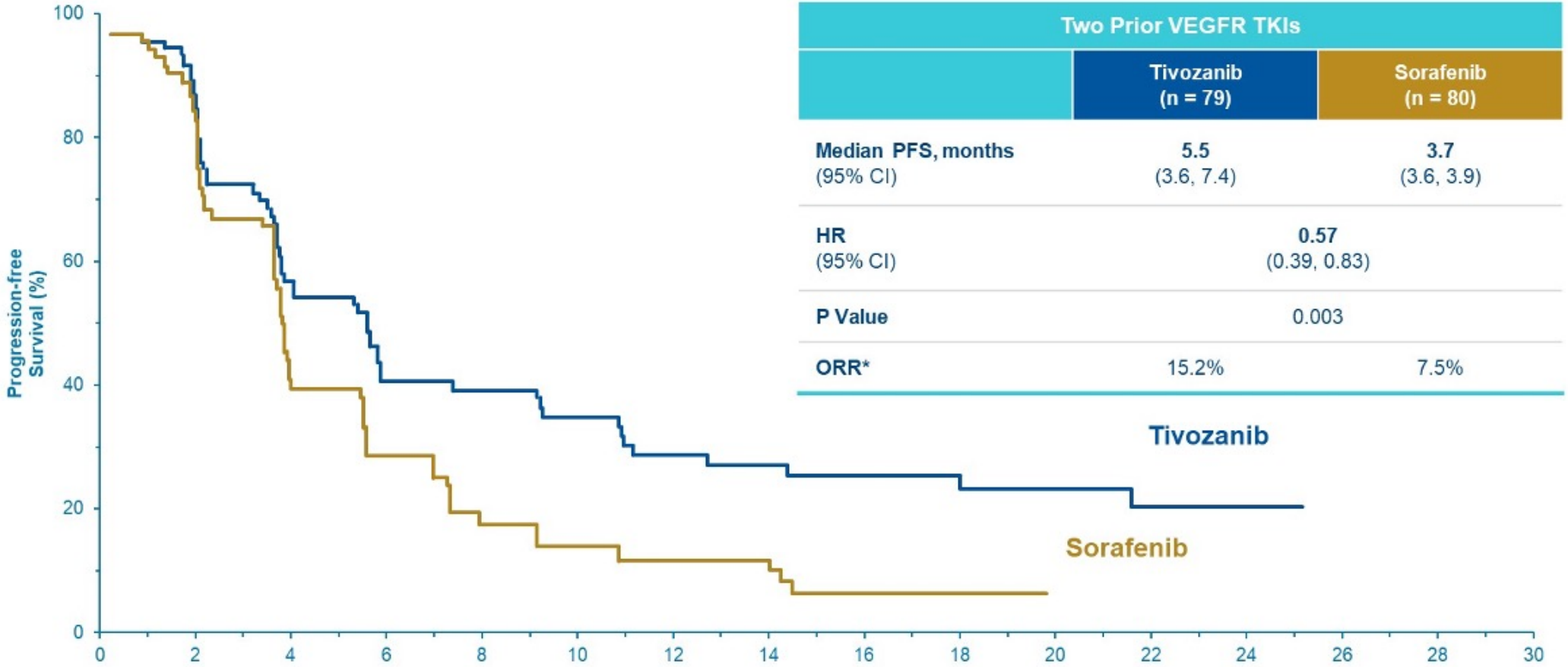
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

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.

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

Verzoni et al.
ASCO 2021;Abstract 4546.

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

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

FDA Approves Belzutifan for Cancers Associated with von Hippel-Lindau Disease

Press Release – August 13, 2021

"The Food and Drug Administration approved belzutifan, a hypoxia-inducible factor inhibitor for adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

Belzutifan was investigated in the ongoing Study 004 (NCT03401788), an open-label clinical trial in 61 patients with VHL-associated RCC (VHL-RCC) diagnosed based on a VHL germline alteration and with at least one measurable solid tumor localized to the kidney. Enrolled patients had other VHL-associated tumors, including CNS hemangioblastomas and pNET. Patients received belzutifan 120 mg once daily until disease progression or unacceptable toxicity."

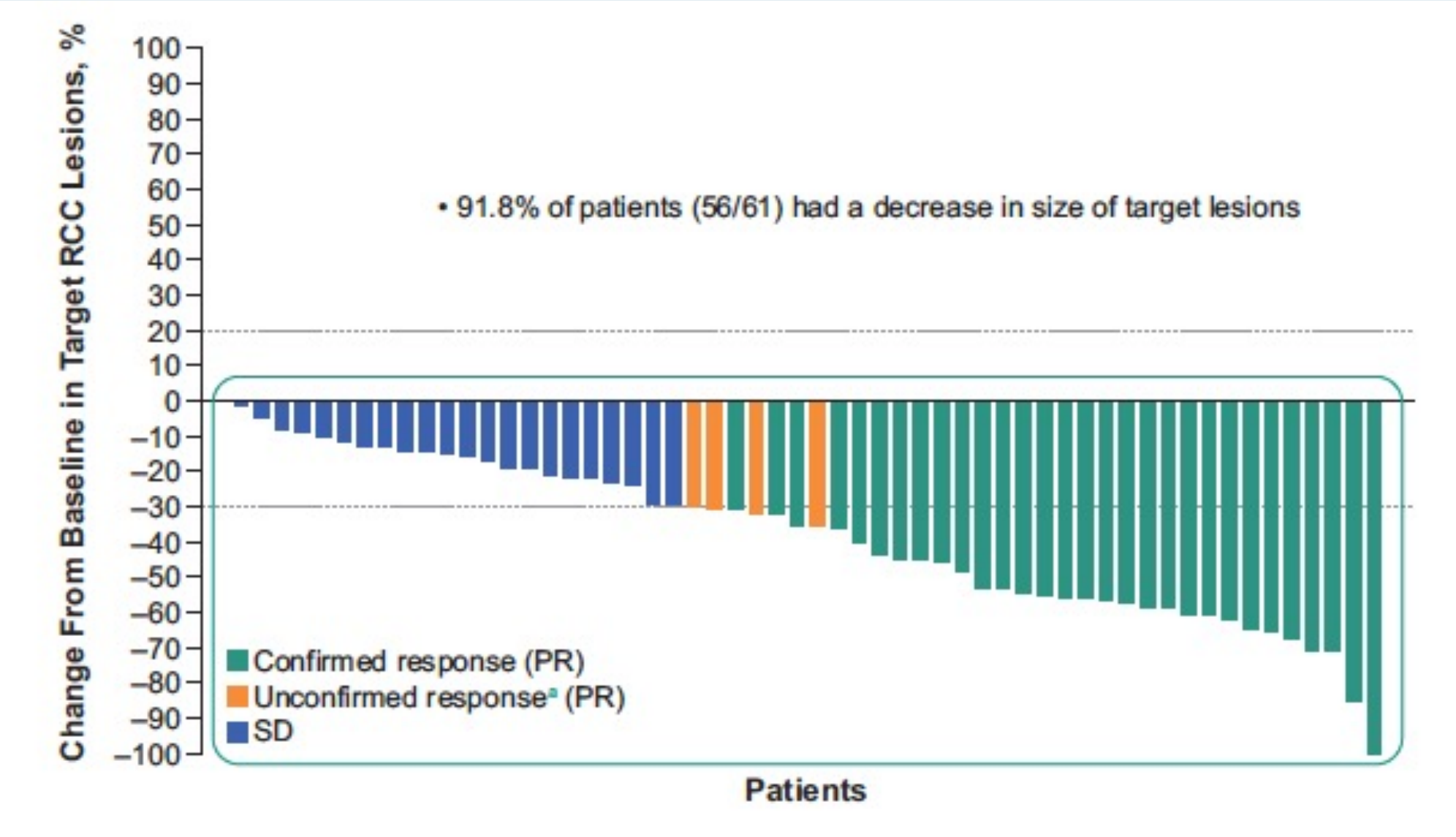
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belzutifan-cancers-associated-von-hippel-lindau-disease

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

Srinivasan R et al.

ASCO 2021;Abstract 4555.

Maximum Change from Baseline in Sum of Target RCC Lesions



Srinivasan R et al. ASCO 2021;Abstract 4555.

RTP RESEARCH TO PRACTICE

Genitourinary Cancers Symposium 2021;Abstract 272.

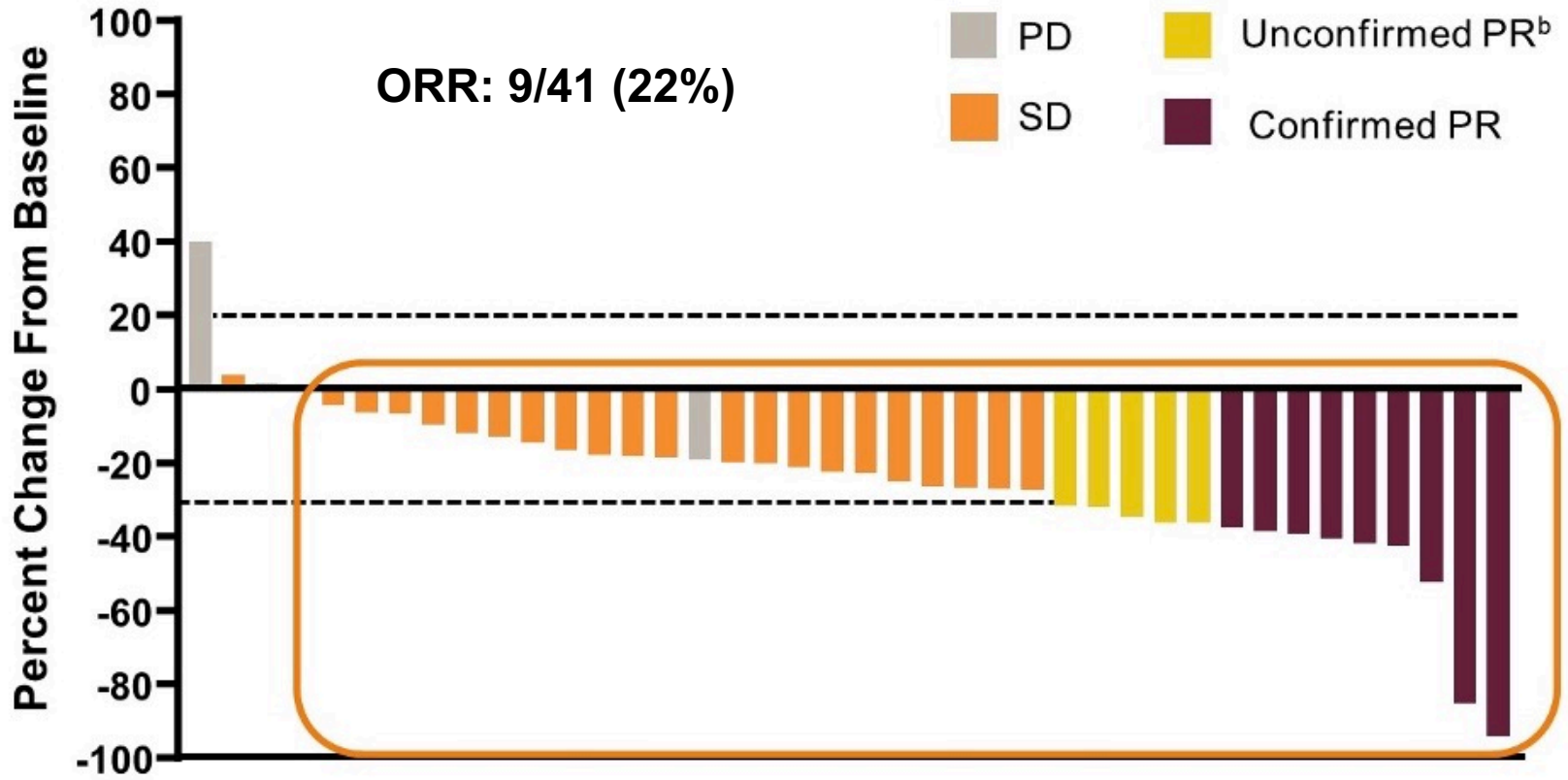
Phase 2 Study of the Oral Hypoxia-Inducible Factor 2α Inhibitor Belzutifan (MK-6482) in Combination With Cabozantinib in Patients With Advanced Clear Cell Renal Cell Carcinoma

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

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.

Summary of Adverse Events

n (%)	N = 52
Any grade treatment-emergent AE	52 (100)
Any grade treatment-related AE	51 (98)
Related to belzutifan	51 (98)
Related to cabozantinib	51 (98)
Grade 3-5 treatment-emergent AEs	35 (67)
Grade 3[b] treatment-related AEs	31 (60)
Related to belzutifan	17 (33)
Related to cabozantinib	28 (54)
Serious treatment-emergent AEs	16 (31)
Serious treatment-related AEs	7 (13)
Related to belzutifan	4 (8)
Related to cabozantinib	4 (8)

n (%)	N = 52
Deaths due to a treatment-emergent AE	1 (2)[c]
Deaths due to a treatment-related AE	0 (0)
Belzutifan dose reduced[d]	10 (19)
Cabozantinib dose reduced[e]	25 (48)
Discontinued any drug due to a treatment-emergent AE	8 (15)
Discontinued belzutifan[f]	6 (12)
Discontinued cabozantinib[g]	8 (15)

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.

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Tuesday, October 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Shannon N Westin, MD, MPH

Moderator

Neil Love, MD

RTP
RESEARCH TO PRACTICE

Recent Advances and Future Directions in Oncology: A Daylong Multitumor Educational Webinar in Partnership with Florida Cancer Specialists

A CME-MOC/NCPD Accredited Virtual Event

Saturday, October 23, 2021
9:30 AM – 4:30 PM ET

Faculty

Neeraj Agarwal, MD
Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD
Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH
David R Spigel, MD
Saad Zafar Usmani, MD, MBA
Andrew D Zelenetz, MD, PhD
Additional faculty to be announced.

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma

DR SUMANTA PAL

CITY OF HOPE COMPREHENSIVE CANCER CENTER

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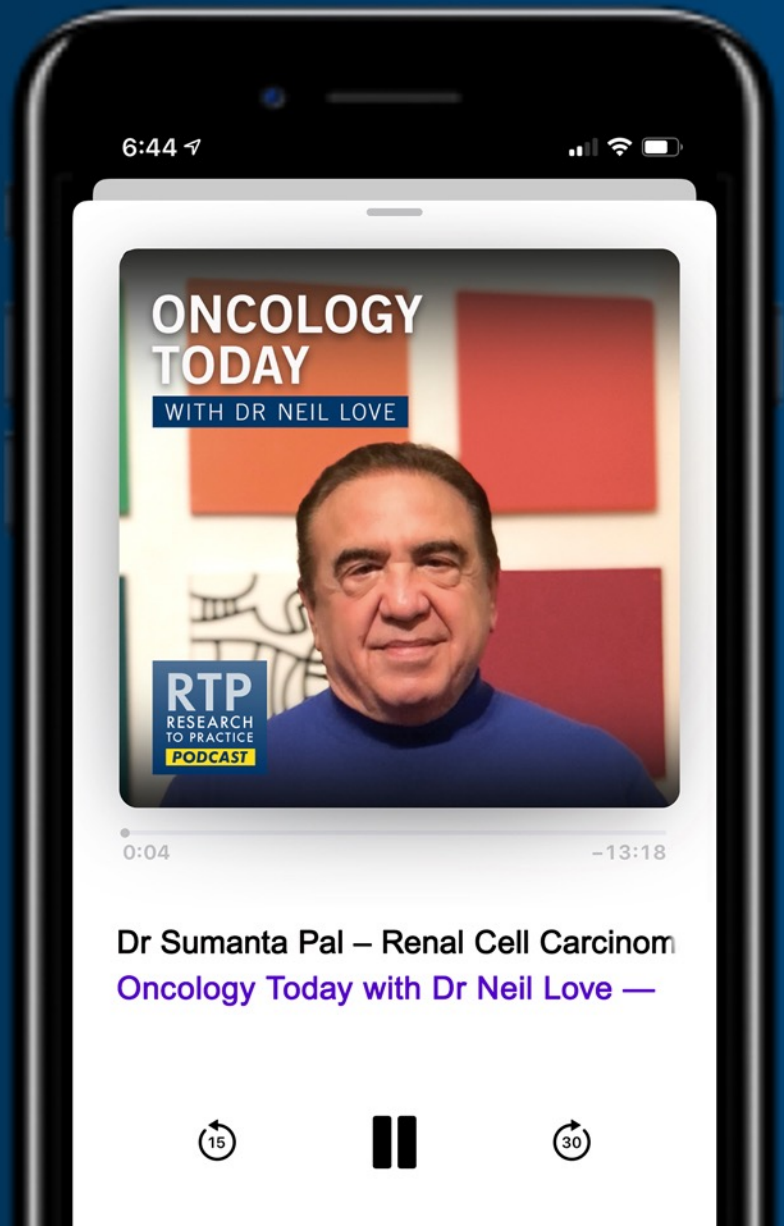

Thank you for joining us!

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

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