# *Meet The Professor*

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

**Neeraj Agarwal, MD**
Professor of Medicine
Senior Director for Clinical Research Innovation
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

# Commercial Support

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

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# Dr Love — Disclosures

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# Dr Agarwal — Disclosures

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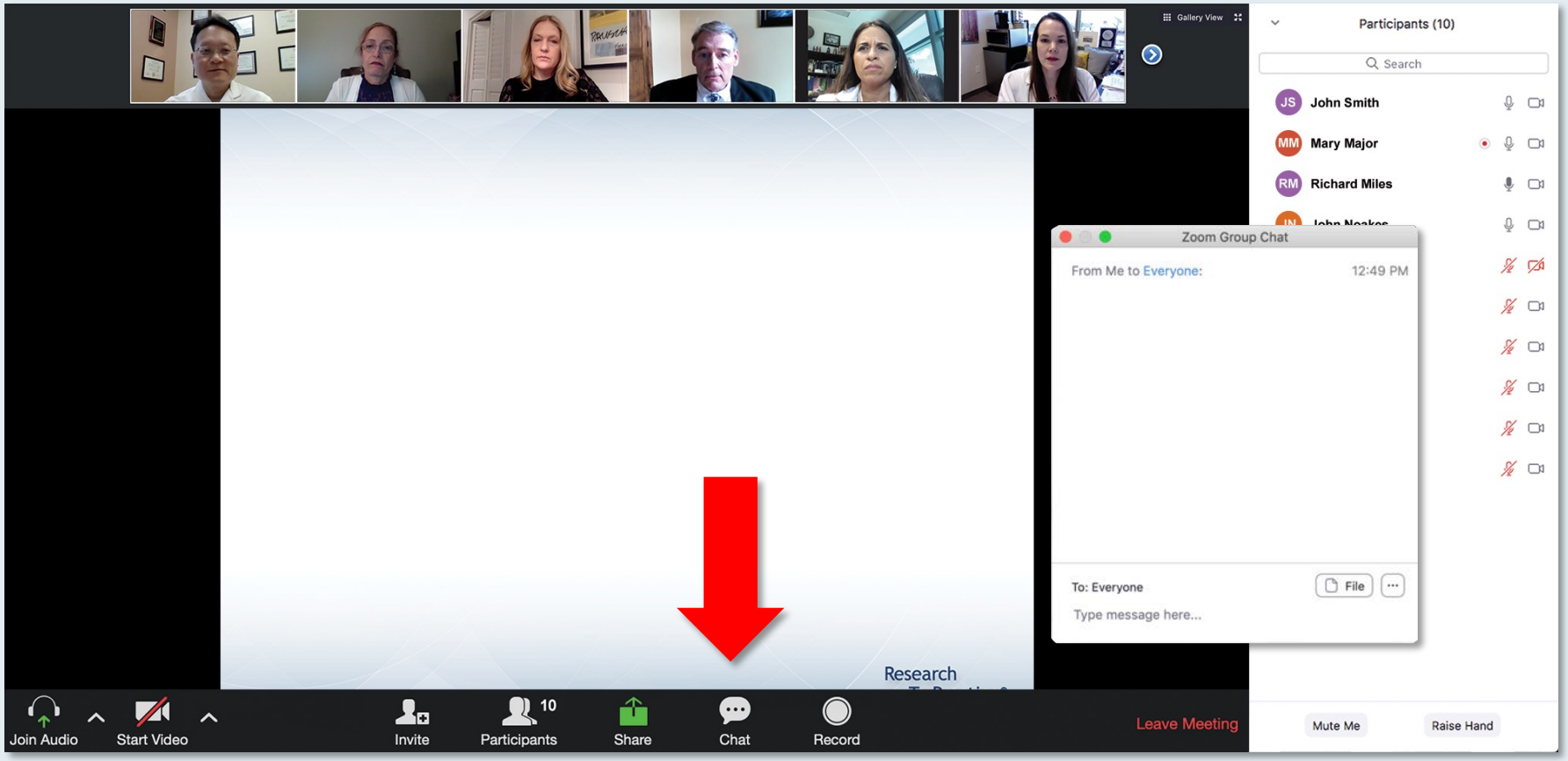
# We Encourage Clinicians in Practice to Submit Questions

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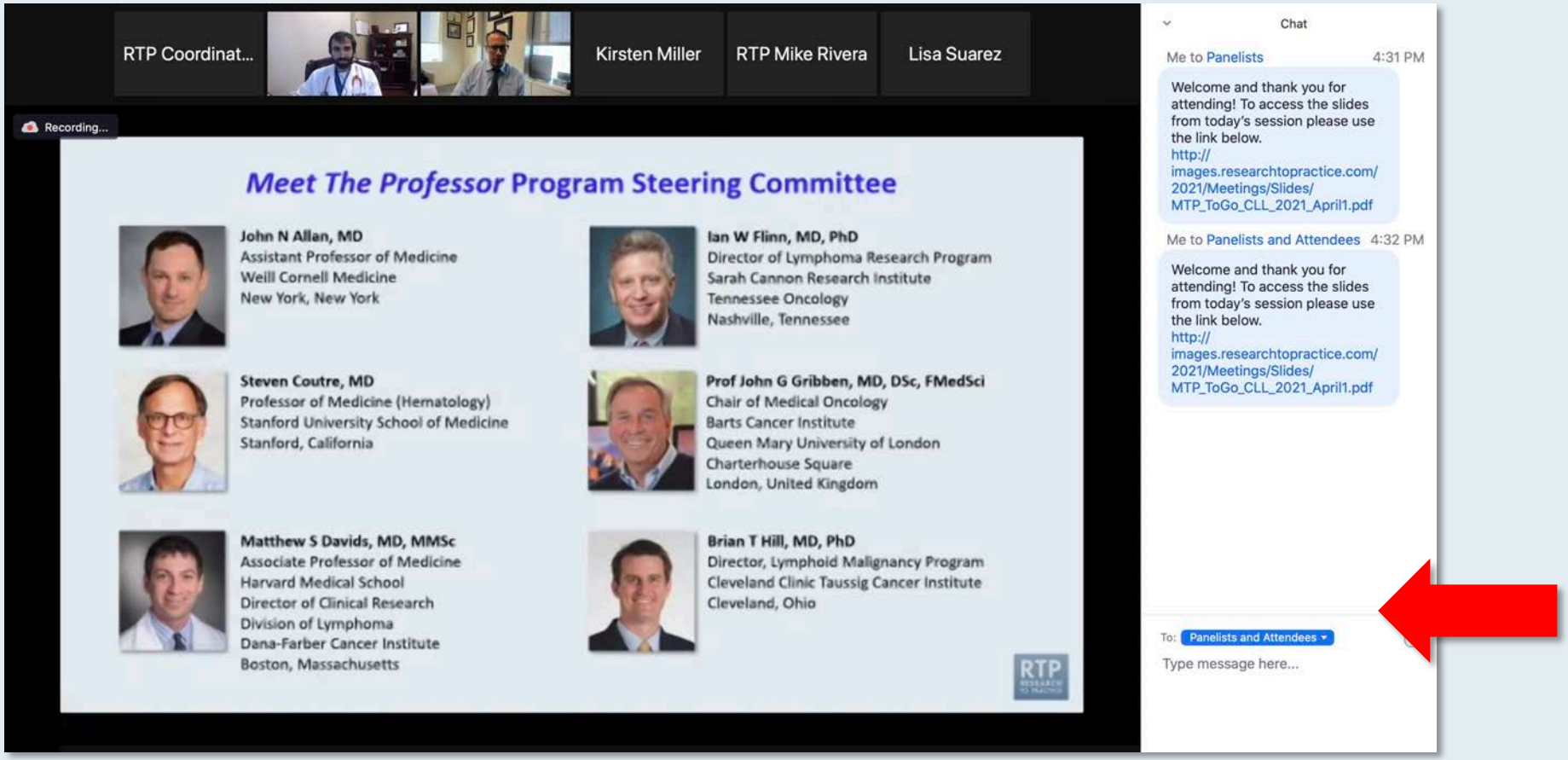
# Familiarizing Yourself with the Zoom Interface

## Expand chat submission box




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

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# Familiarizing Yourself with the Zoom Interface

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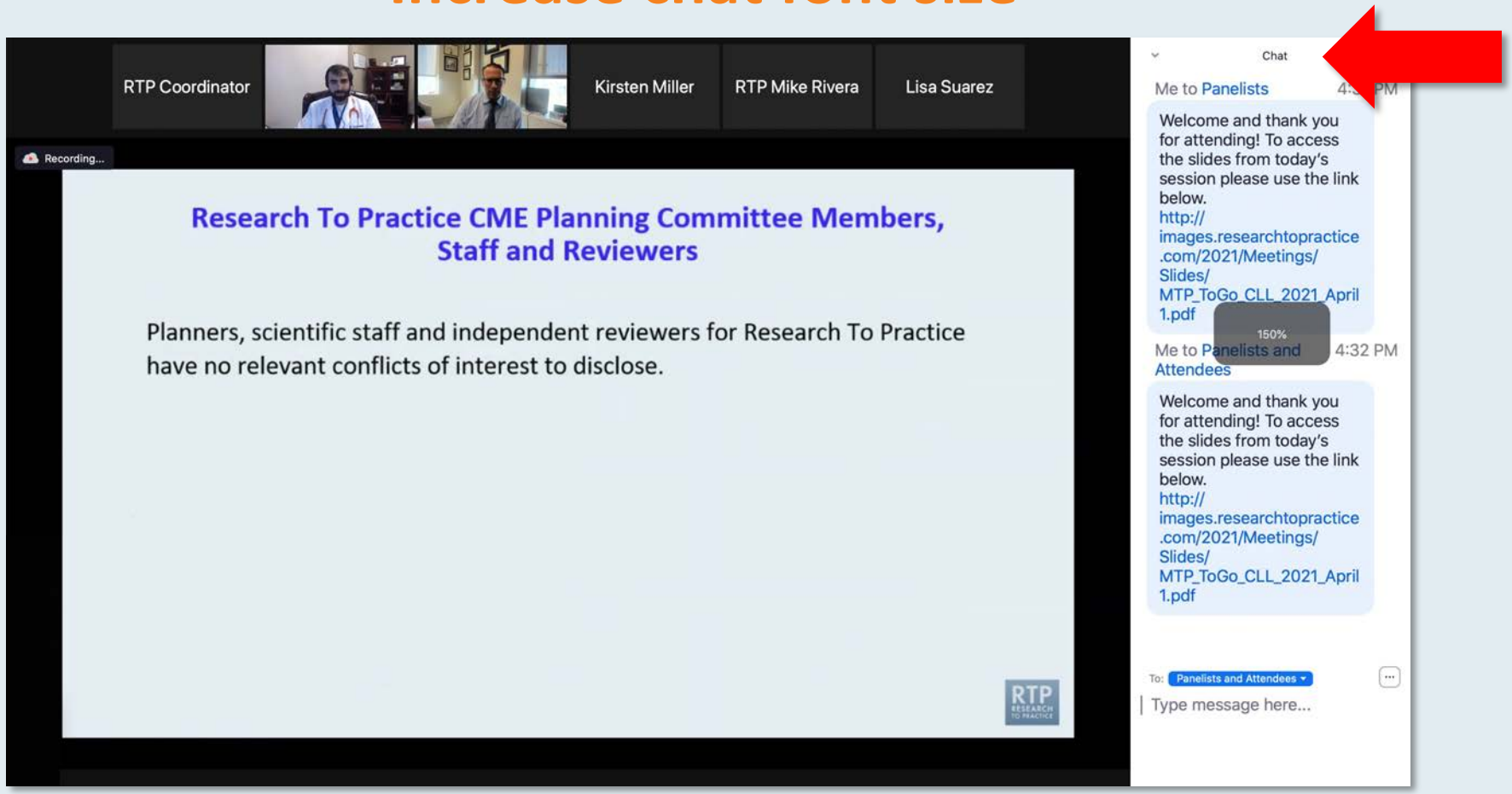


**Press Command (for Mac) or Control (for PC) and the + symbol.**
**You may do this as many times as you need for readability.**

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# Key Presentations on Genitourinary Cancers from the 2021 ASCO Annual Meeting

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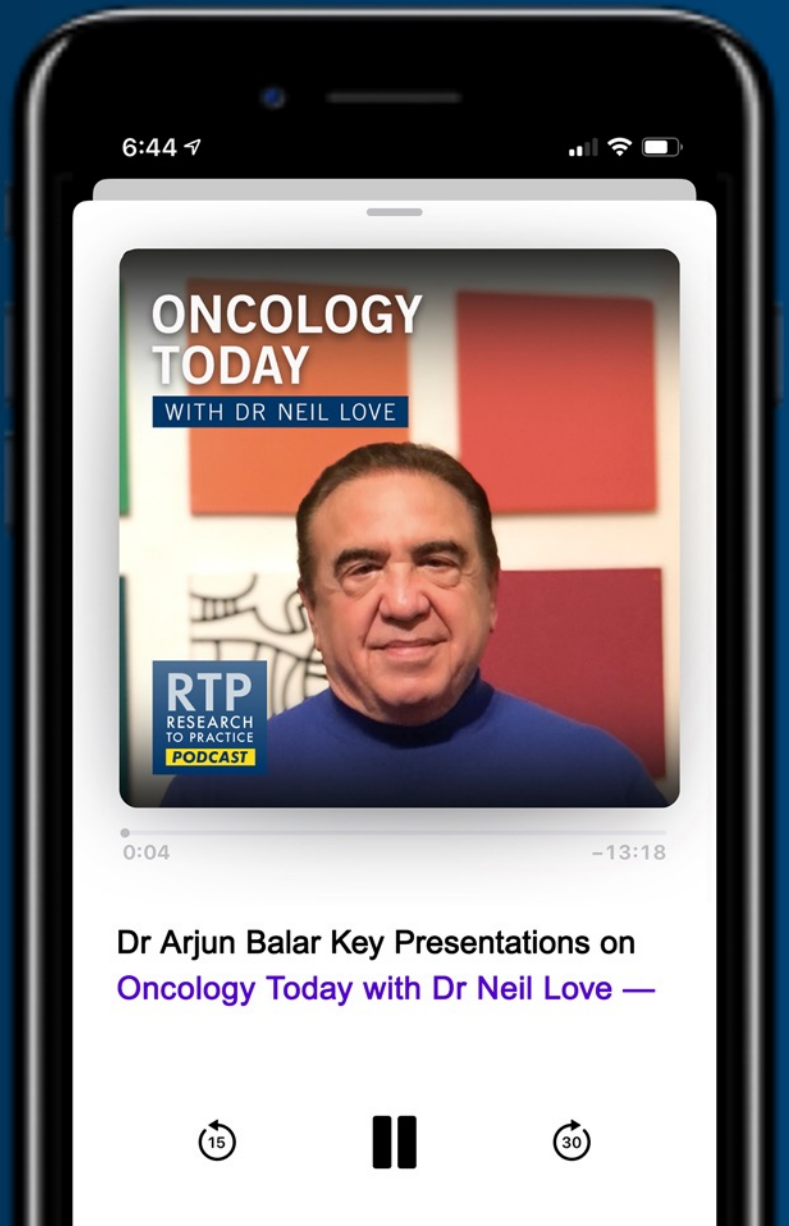

# *Meet The Professor*

# Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

**Thursday, September 16, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Loretta J Nastoupil, MD**

## Moderator

**Neil Love, MD**

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

**Friday, September 17, 2021**
**12:00 PM – 1:00 PM ET**

## Faculty

**Philip A Philip, MD, PhD, FRCP**

## Moderator

**Neil Love, MD**

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## Optimizing the Selection and Sequencing of Therapy for Patients with Urothelial Bladder Carcinoma

**Tuesday, September 21, 2021**
**5:00 PM – 6:00 PM ET**

### Faculty

**Jonathan E Rosenberg, MD**

### 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, September 22, 2021**
**5:00 PM – 6:00 PM ET**

### Faculty

**Sara M Tolaney, MD, MPH**

### Moderator

**Neil Love, MD**

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# *Meet The Professor*

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

**Monday, September 27, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Zev Wainberg, MD, MSc**

## 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

**Tuesday, September 28, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Professor Peter Schmid, MD, PhD**

## 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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Dana-Farber Cancer Institute
The Jerome and Nancy Kohlberg Professor of Medicine
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Boston, Massachusetts

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

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Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
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Beth Israel Deaconess Medical Center
Leader, Kidney Cancer Program
Dana-Farber/Harvard Cancer Center
Professor of Medicine
Harvard Medical School
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**William K Oh, MD**
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Icahn School of Medicine at Mount Sinai
The Tisch Cancer Institute
Mount Sinai Health System
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**Robert J Motzer, MD**
Attending Physician, Department of Medicine
Jack and Dorothy Byrne Chair in Clinical Oncology
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**Elizabeth R Plimack, MD, MS**
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Director, Genitourinary Clinical Research
Professor, Department of Hematology/Oncology
Fox Chase Cancer Center, Temple Health
Philadelphia, Pennsylvania

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Research To Practice
Miami, Florida

**Brian I Rini, MD**
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Ingram Professor of Medicine
Division of Hematology/Oncology
Vanderbilt University Medical Center
Nashville, Tennessee

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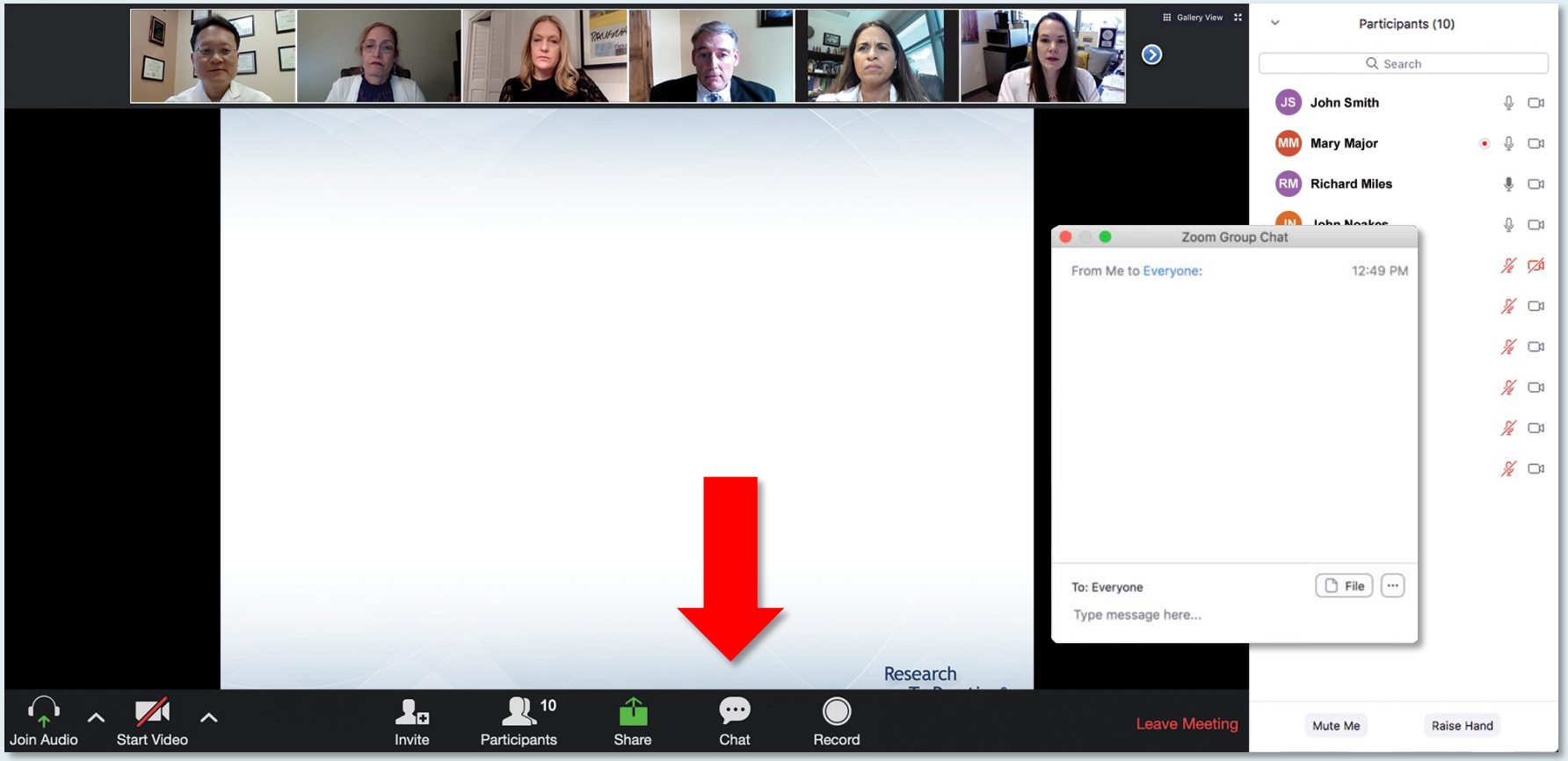


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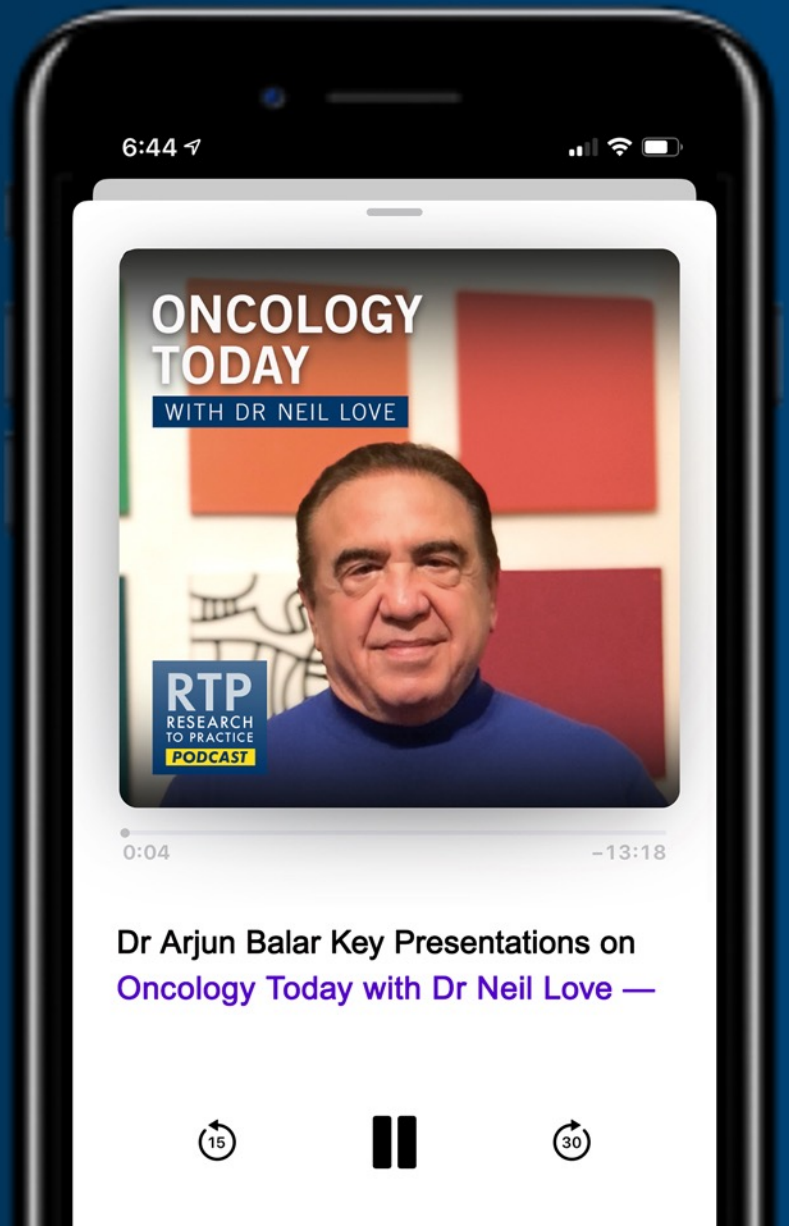

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Philadelphia, Pennsylvania

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MD Anderson Cancer Center
Houston, Texas

**Thomas Powles, MBBS, MRCP, MD**
Professor of Genitourinary Oncology
Barts Cancer Institute
Director of Barts Cancer Centre
Queen Mary University of London
London, United Kingdom

# Meet The Professor with Dr Agarwal

**MODULE 1: Case Presentations**

- Dr Plimack: A 61-year-old woman with metastatic clear cell RCC
- Dr Hammers: A 59-year-old man with intermediate/poor-risk ccRCC with metastases to the bone and lung
- Prof Powles: A 69-year-old man with metastatic sarcomatoid RCC to the liver
- Dr Hammers: A man in his 60s with recurrent RCC who is s/p renal transplant
- Dr Hammers: A man in his 70s with metastatic RCC and a long-standing history of Crohn's disease
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease

**MODULE 2: Journal Club with Dr Agarwal**

**MODULE 3: Beyond the Guidelines**

**MODULE 4: Key Data Sets**

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# At what point in your oncology career were you in 2016?

1. Clinical practice for 10 years or more
2. Clinical practice for 5 to 10 years
3. Clinical practice for less than 5 years
4. Residency or fellowship
5. Medical school
6. College
7. Other

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# Meet The Professor with Dr Agarwal

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# Case Presentation – Dr Plimack: A 61-year-old woman with metastatic clear cell RCC

**Dr Elizabeth Plimack**

- Presented with a large, painful RCC primary and lung and liver metastases

**Question**

- What would you do for this patient?

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# Case Presentation – Dr Plimack: A 61-year-old woman with metastatic clear cell RCC (continued)

Dr Elizabeth Plimack

- Presented with a large, painful RCC primary and lung and liver metastases
- ***Right radical cytoreductive nephrectomy with adrenalectomy, cholecystectomy and partial hepatectomy***
- ***Axitinib/pembrolizumab, with rapid disease progression***

**Question**

- ***What would you choose as her next line of therapy?***

# Case Presentation – Dr Plimack: A 61-year-old woman with metastatic clear cell RCC (continued)

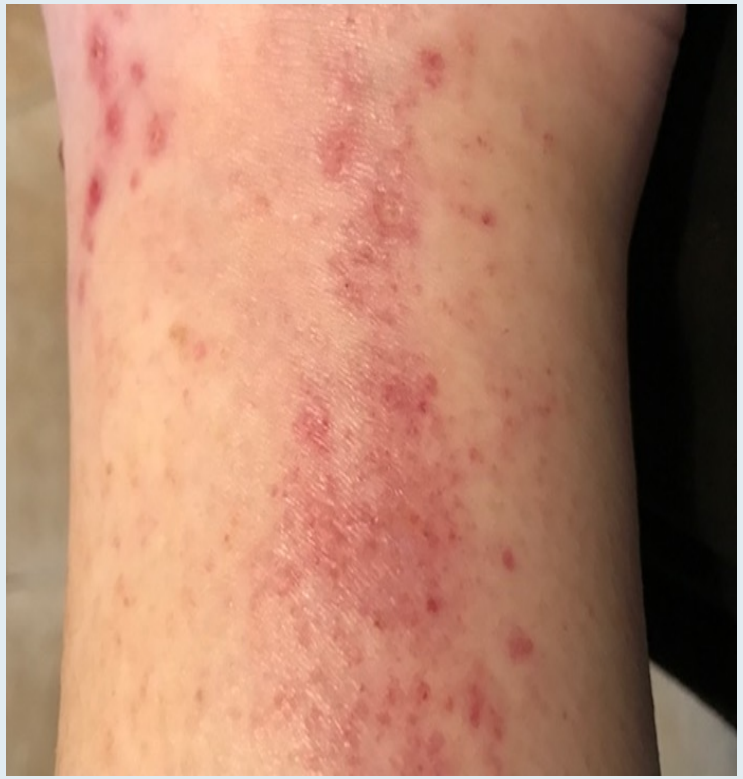
Dr Elizabeth Plimack

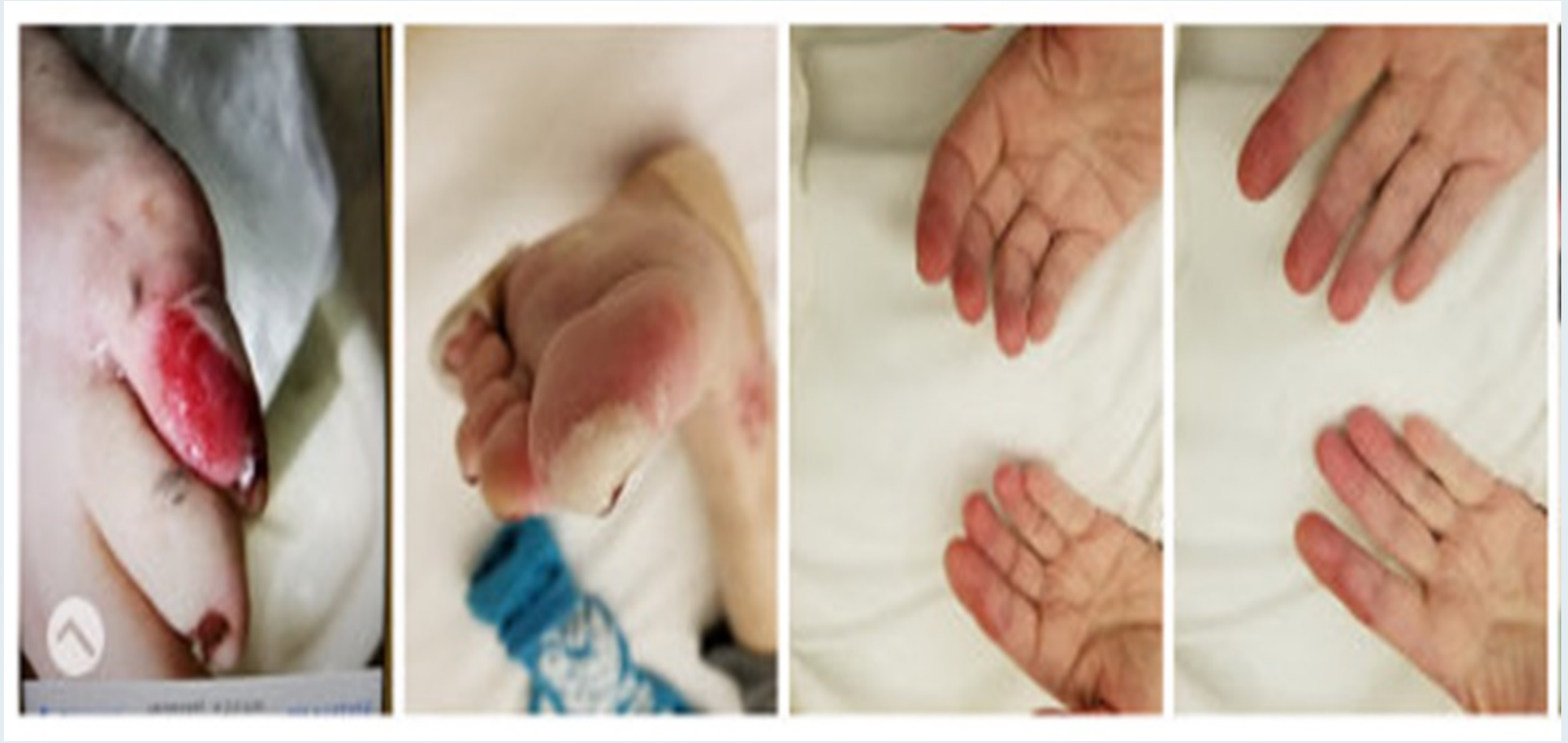
- Presented with a large, painful RCC primary and lung and liver metastases
- Right radical cytoreductive nephrectomy with adrenalectomy, cholecystectomy and partial hepatectomy
- Axitinib/pembrolizumab, with rapid disease progression
- ***Dose-reduced cabozantinib (40 mg daily)***
  - ***After 7 months, developed cutaneous toxicity, HFS***

# Case Presentation – Dr Plimack: A 61-year-old woman with metastatic clear cell RCC (continued)

Dr Elizabeth Plimack

## Cabozantinib-associated cutaneous toxicity





# Case Presentation – Dr Plimack: A 61-year-old woman with metastatic clear cell RCC (continued)

Dr Elizabeth Plimack

- Presented with a large, painful RCC primary and lung and liver metastases
- Right radical cytoreductive nephrectomy with adrenalectomy, cholecystectomy and partial hepatectomy
- Axitinib/pembrolizumab, with rapid disease progression
- Dose-reduced cabozantinib (40 mg daily)
  - After 7 months, developed cutaneous toxicity, HFS
  - ***Held treatment until fully healed, then re-challenged at a lower dose***

# Case Presentation – Dr Hammers: A 59-year-old man with intermediate/poor-risk ccRCC with metastases to the bone and lung

**Dr Hans Hammers**

- Patient initially diagnosed with stage III ccRCC, Grade 4, non-sarcomatoid
- Within the year, he presents with metastatic recurrence in the bone and lung
  - Pelvic osseous metastasis, 2-cm
  - Multiple lung metastases, the largest measuring 1.4-cm
- PMH: controlled HTN, controlled diabetes

**Question**

- What would you recommend as first-line therapy for this patient?

# Case Presentation – Dr Hammers: A 59-year-old man with intermediate/poor-risk ccRCC with metastases to the bone and lung (continued)

Dr Hans Hammers

- Patient initially diagnosed with stage III ccRCC, Grade 4, non-sarcomatoid
- Within the year, he presents with metastatic recurrence in the bone and lung
  - Pelvic osseous metastasis, 2-cm
  - Multiple lung metastases, the largest measuring 1.4-cm
- PMH: controlled HTN, controlled diabetes
- ***Nivolumab/ipilimumab, with a major response***
  - ***Grade 3 diarrhea after third dose of nivolumab***
  - ***Significant microscopic inflammatory changes on colonoscopy***

**Question**

- ***What would you do at this time?***

# Case Presentation – Dr Hammers: A 59-year-old man with intermediate/poor-risk ccRCC with metastases to the bone and lung (continued)

Dr Hans Hammers

- PMH: Controlled hypertension, DM
- Stage III, Grade 4 clear cell RCC, with no sarcomatoid or rhabdoid component
- One year later, 2-cm pelvic lytic osseous metastasis, multiple lung metastases
- Nivolumab/ipilimumab, with a major response
  - Grade 3 diarrhea after third dose of nivolumab
  - Significant microscopic inflammatory changes on colonoscopy
- ***Initiated steroids, dropped the last dose of the combination, continued nivolumab***
- ***One year later, progression in one lung nodule while on nivolumab***

**Question**

- ***What would you do next? With limited disease progression, would you consolidate with either surgery or stereotactic radiation therapy?***

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# Case Presentation – Prof Powles: A 69-year-old man with metastatic sarcomatoid RCC to the liver

**Prof Thomas Powles**

- PMH: Heavy smoker, airway disease (PS 1)
- Lung biopsy: Sarcomatoid mass

**Question**

- For sarcomatoid kidney cancer we know immune therapy has a really important role, but is this another group of patients that should get ipilimumab/nivolumab or actually pembrolizumab/cabozantinib/nivolumab?

# Case Presentation – Prof Powles: A 69-year-old man with metastatic sarcomatoid RCC to the liver (continued)

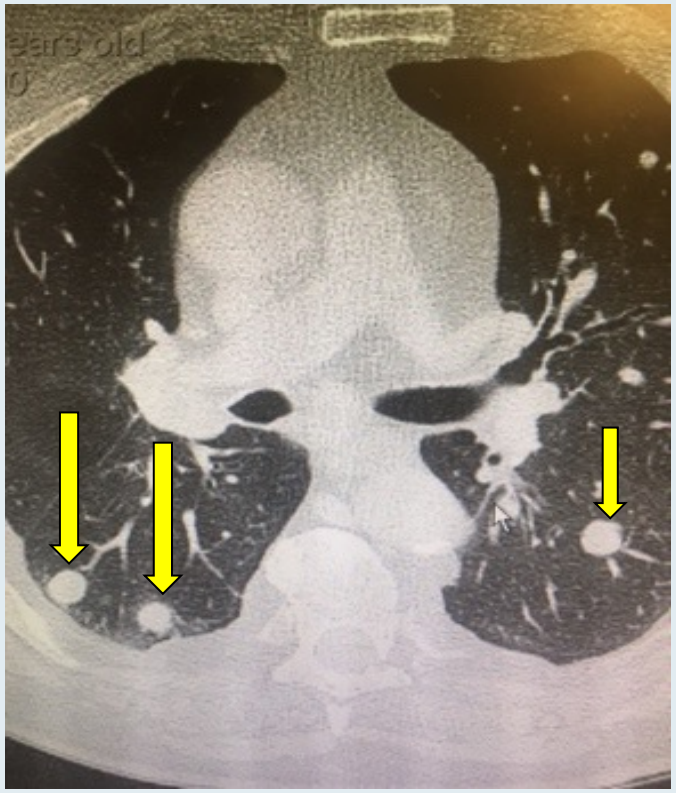
**Prof Thomas Powles**

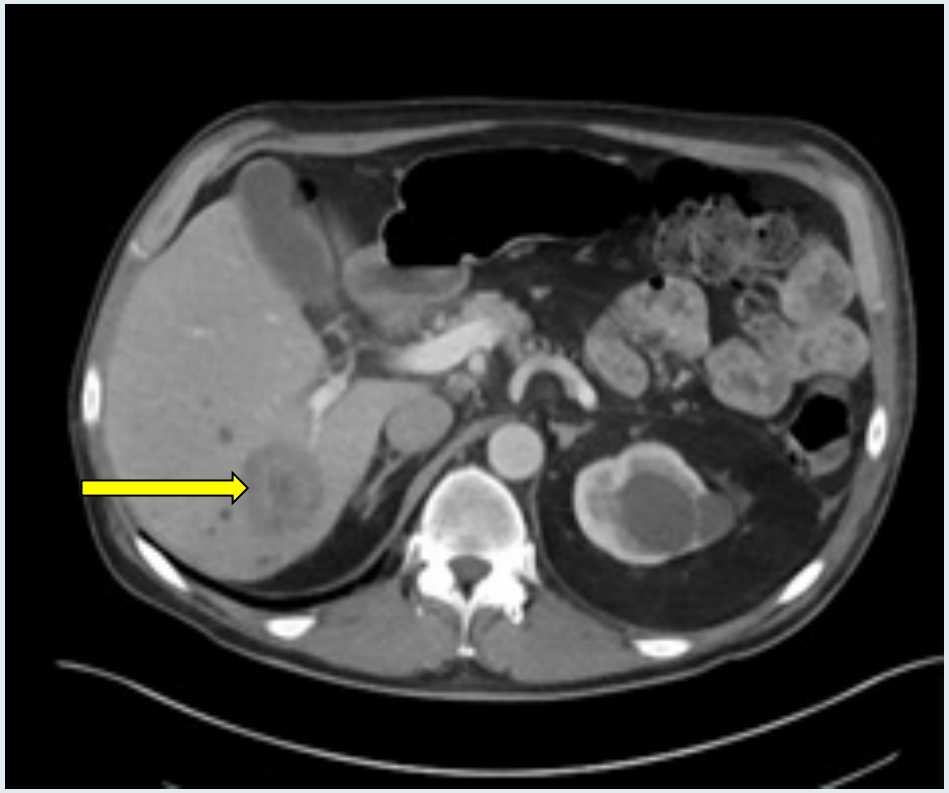
- PMH: Heavy smoker, airway disease (PS 1)
- Lung biopsy: Sarcomatoid mass
- ***CT scan: liver metastases and large renal mass***
- ***Cabozantinib and nivolumab***

# Case Presentation – Prof Powles: A 69-year-old man with metastatic sarcomatoid RCC to the liver (continued)

Prof Thomas Powles

## Baseline CT scans





# Case Presentation – Dr Hammers: A man in his 60s with recurrent RCC who is s/p 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 for this patient on immunosuppressive therapy?

# Case Presentation – Dr Hammers: A man in his 60s with recurrent RCC who is s/p 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 Hammers: A man in his 70s with metastatic RCC and a long-standing history of Crohn's disease

**Dr Hans Hammers**

- PMH: Crohn's disease that was well-controlled with a TNF agonist, HLA-B27 spondylitis
- Recurrent disease in lungs and abdomen, suboptimal PS
- TNF agonist held for several weeks
- Nivolumab/ipilimumab → beautiful response in lung lesions, lymph nodes, and abdominal implant
- Significant flare of spondylitis
- TNF agonist restarted with steroids
- Response has been maintained for over a year

# Case Presentation – Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease

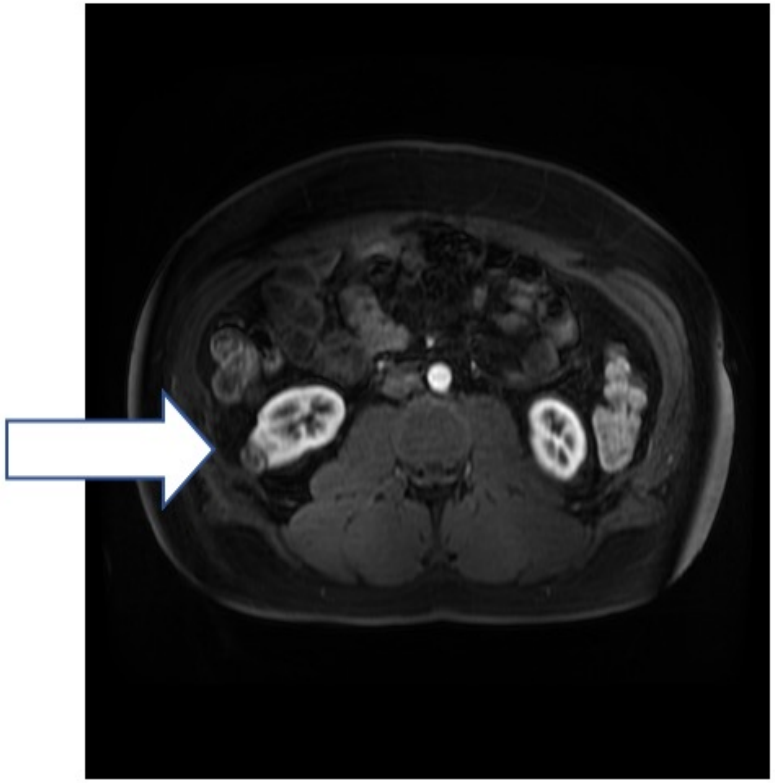
**Dr Eric Jonasch**

- PMH: hemangioblastoma, small renal cell mass
- Treated his father for VHL disease; Patient began surveillance in his early 20s

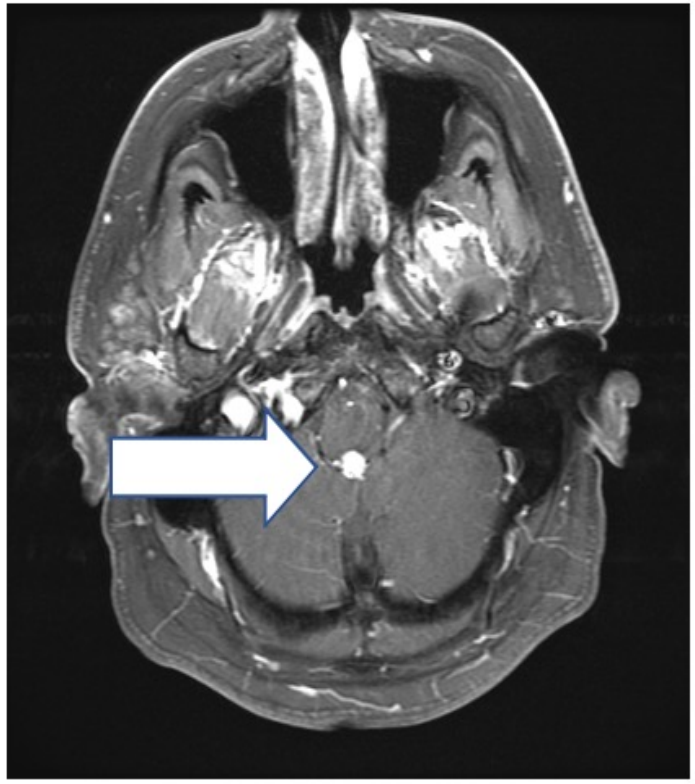
# Case Presentation – Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease (continued)

Dr Eric Jonasch

Small renal mass



Hemangioblastoma



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# Journal Club with Dr Agarwal – Part 1

- Duarte C et al. **Treatment outcomes in renal cell carcinoma patients with metastases to the pancreas and other sites.** ASCO 2021;Abstract 4557.
- Bakouny Z et al al. **Cytoreductive nephrectomy (CN) for metastatic renal cell carcinoma (mRCC) treated with immune checkpoint inhibitors (ICI) or targeted therapy (TT): A propensity score-based analysis.** Genitourinary Cancers Symposium 2020;Abstract 608.
- Ravi P et al. **Evaluation of the safety and efficacy of immunotherapy rechallenge in patients with renal cell carcinoma.** *JAMA Oncol* 2020;6(10):1606-10.
- Ravi et al. **Use of immune checkpoint inhibitors (ICIs) after prior ICI in metastatic renal cell carcinoma (mRCC): Results from a multicenter collaboration.** ASCO 2020;Abstract 5077.
- Dudani S et al. **Application of IMDC criteria across first-line (1L) and second-line (2L) therapies in metastatic renal-cell carcinoma (mRCC): New and updated benchmarks of clinical outcomes.** ASCO 2020;Abstract 5063.
- Schmidt AL et al. **The very favorable metastatic renal cell carcinoma (mRCC) risk group.** Genitourinary Cancers Symposium 2021;Abstract 339.

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# Journal Club with Dr Agarwal – Part 2


- Zengin ZB et al. **Illustration of temporal evolution in patients with metastatic renal cell carcinoma (mRCC) using both circulating tumor DNA (ctDNA) and tissue-based genomic data.** Genitourinary Cancers Symposium 2021;Abstract 347.
- Zengin ZB et al. **Complementary role of circulating tumor DNA assessment and tissue genomic profiling in metastatic renal cell carcinoma.** *Clin Cancer Res* 2021;27(17):4807-13.
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- 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(2):162-70.
- Li H et al. **Combination therapy with avelumab (Ave) and cabozantinib (Cabo) in patients (pts) with newly diagnosed metastatic clear cell renal cell carcinoma (mccRCC).** Genitourinary Cancers Symposium 2021;Abstract 334.


JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

# Meet The Professor with Dr Agarwal

**MODULE 1: Case Presentations**

- Dr Plimack: A 61-year-old woman with metastatic clear cell RCC
- Dr Hammers: A 59-year-old man with intermediate/poor-risk ccRCC with metastases to the bone and lung
- Prof Powles: A 69-year-old man with metastatic sarcomatoid RCC to the liver
- Dr Hammers: A man in his 60s with recurrent RCC who is s/p renal transplant
- Dr Hammers: A man in his 70s with metastatic RCC and a long-standing history of Crohn's disease
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease

**MODULE 2: Journal Club with Dr Agarwal**

**MODULE 3: Beyond the Guidelines**

**MODULE 4: Key Data Sets**

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

# Meet The Professor with Dr Agarwal

**MODULE 1: Case Presentations**

- Dr Plimack: A 61-year-old woman with metastatic clear cell RCC
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**MODULE 2: Journal Club with Dr Agarwal**

**MODULE 3: Beyond the Guidelines**

**MODULE 4: Key Data Sets**

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]

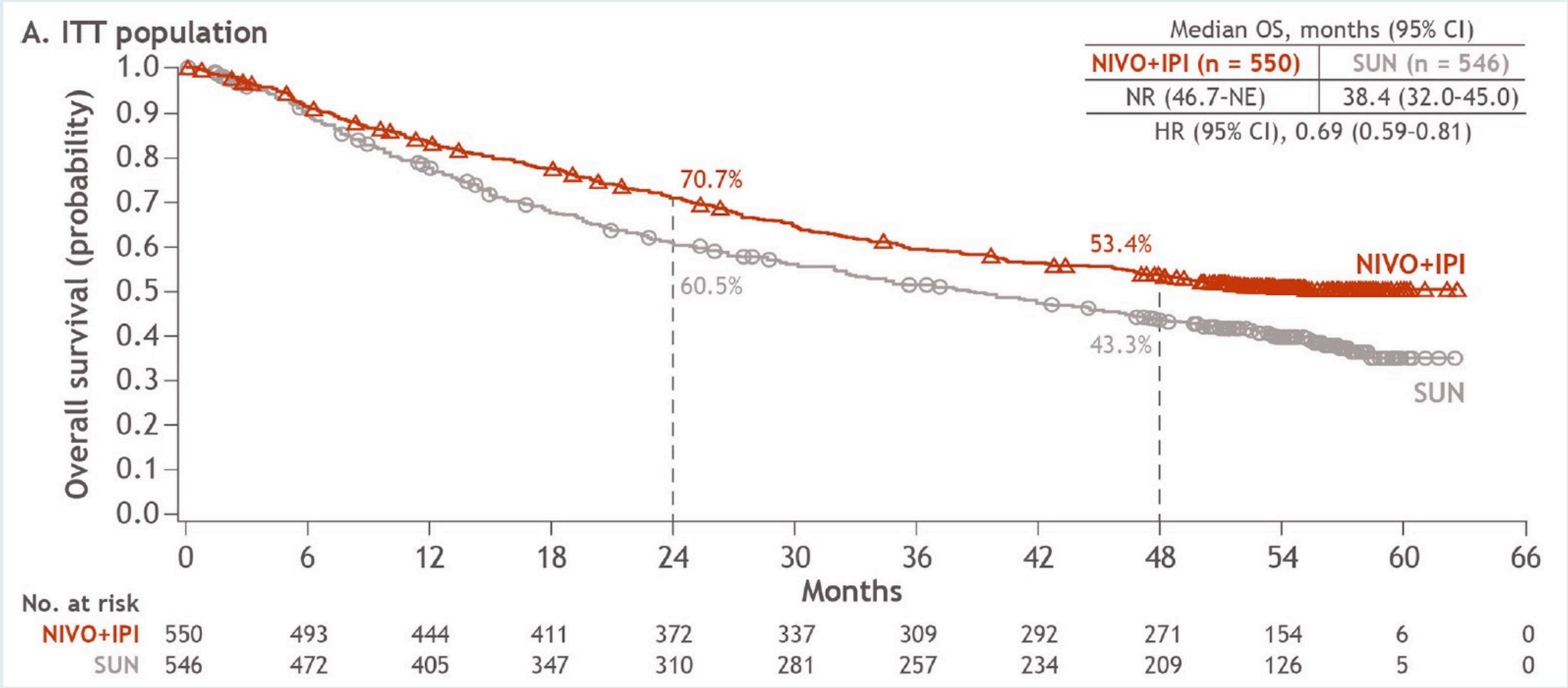
*ESMO Open* 2020;5(6):e001079.

# 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% |

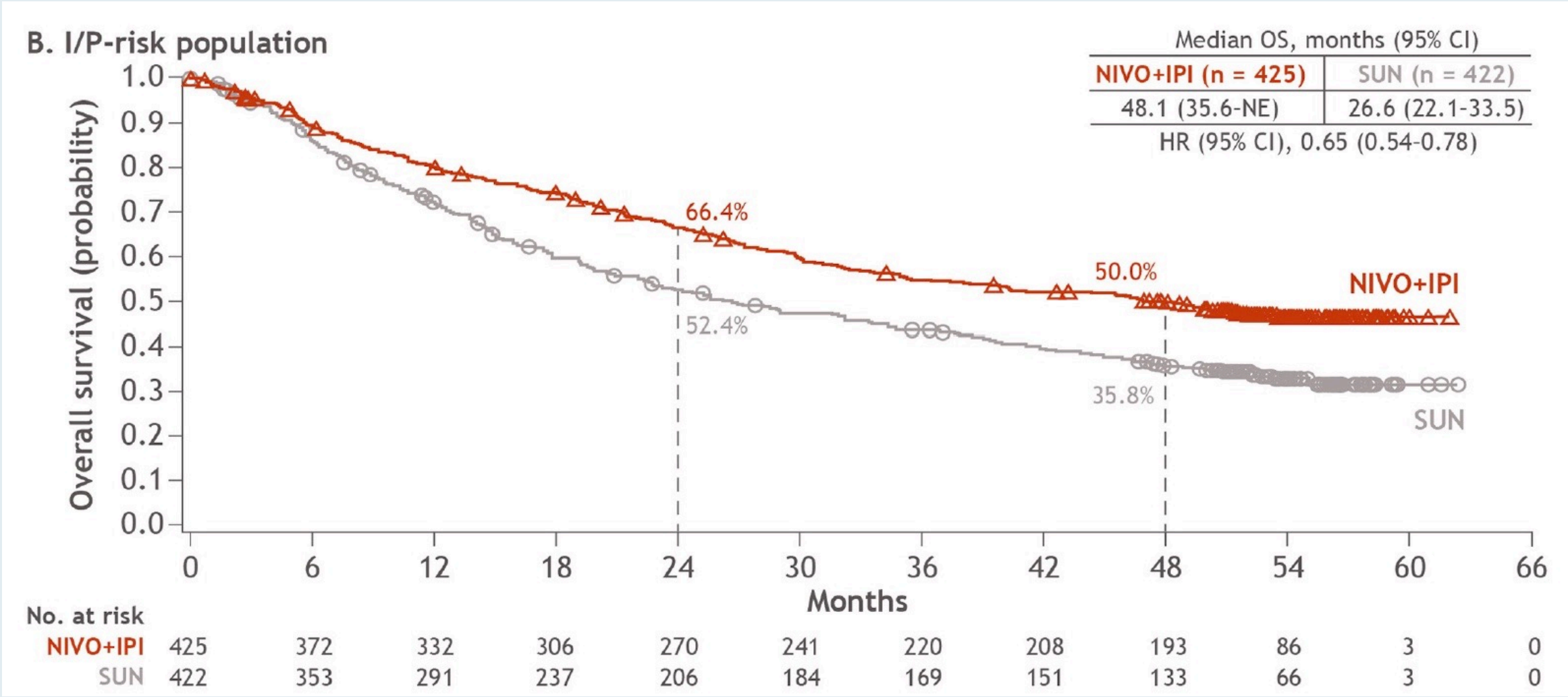
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

# 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

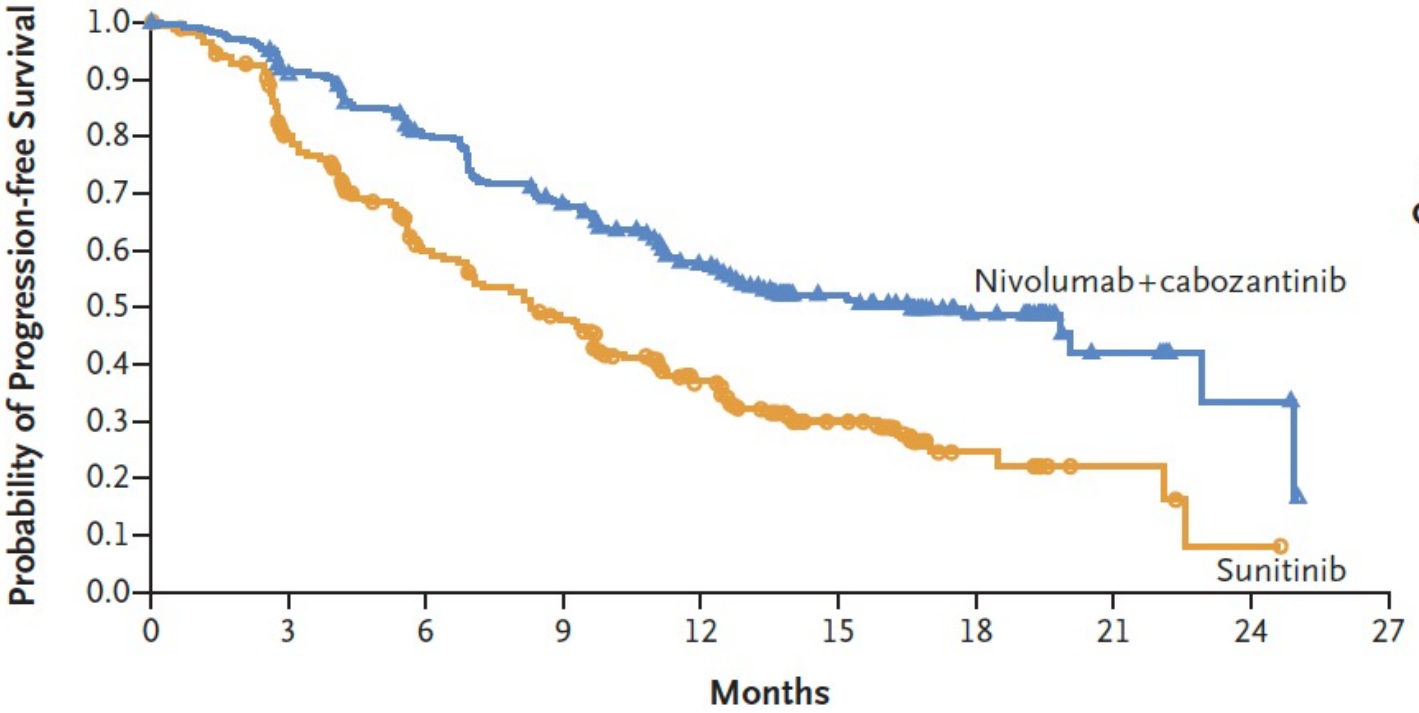
The NEW ENGLAND JOURNAL of MEDICINE

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) |

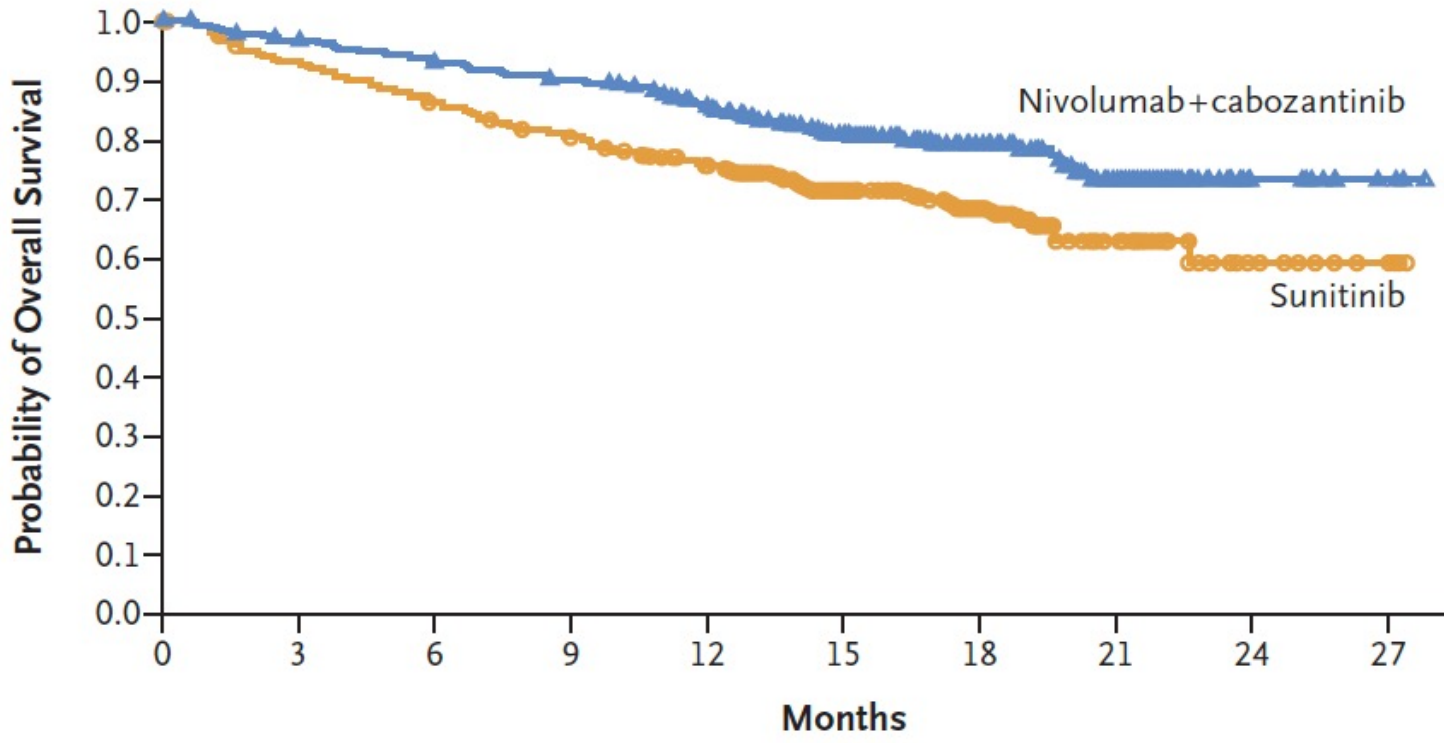
Hazard ratio for disease progression or death, 0.51 (95% CI, 0.41–0.64)
P<0.001

**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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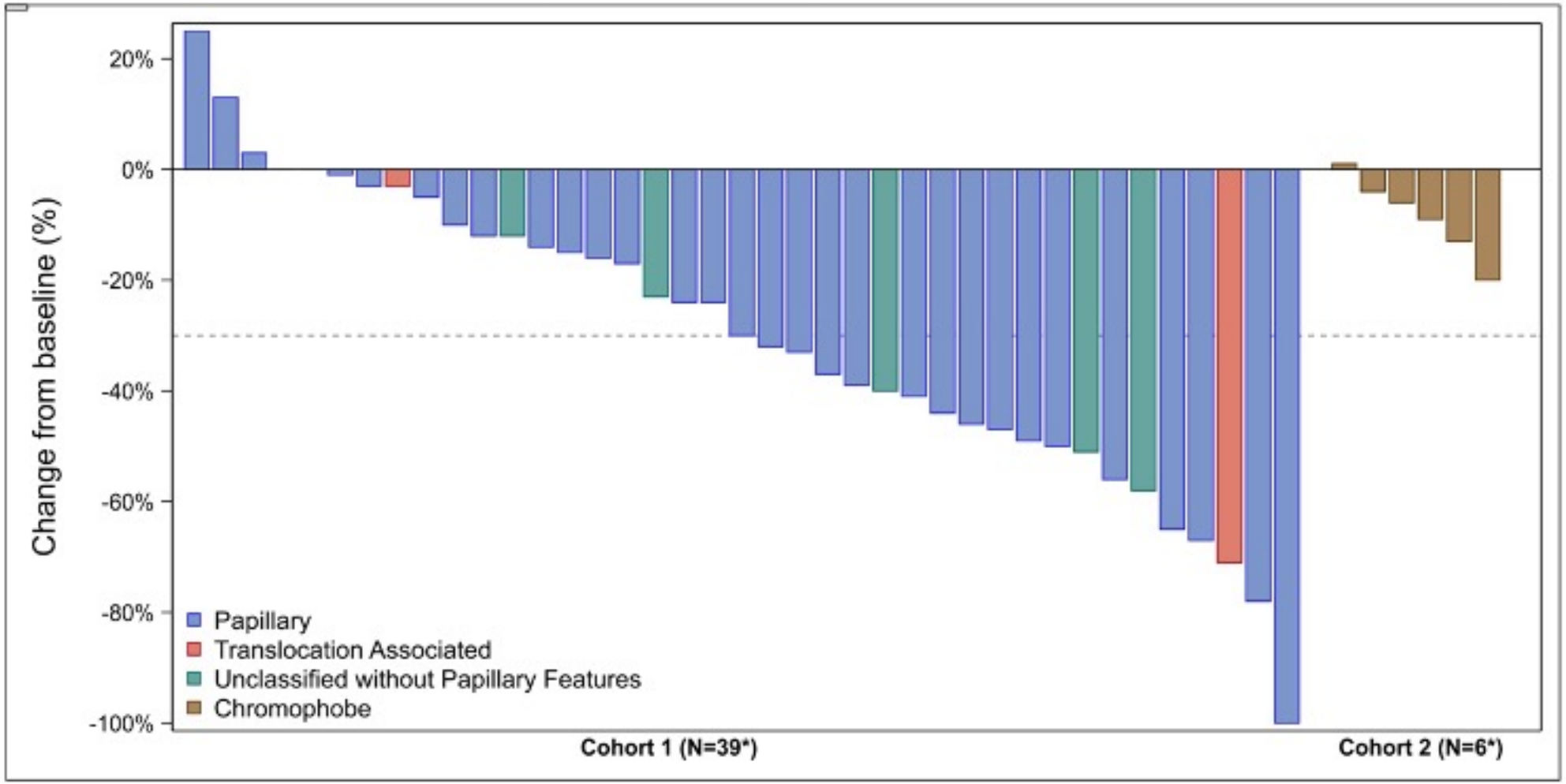
leec4@mskcc.org

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.

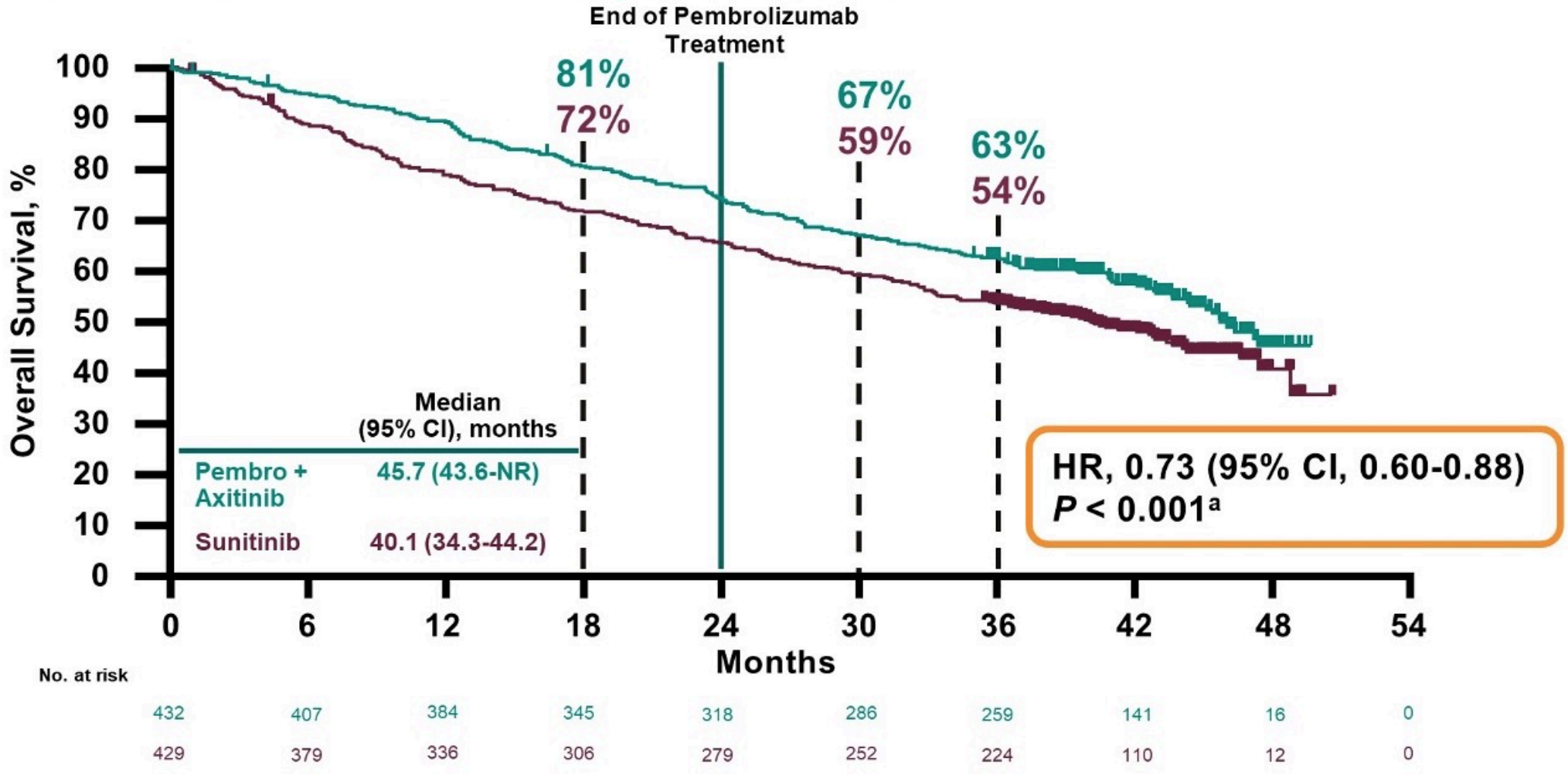
# Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

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.

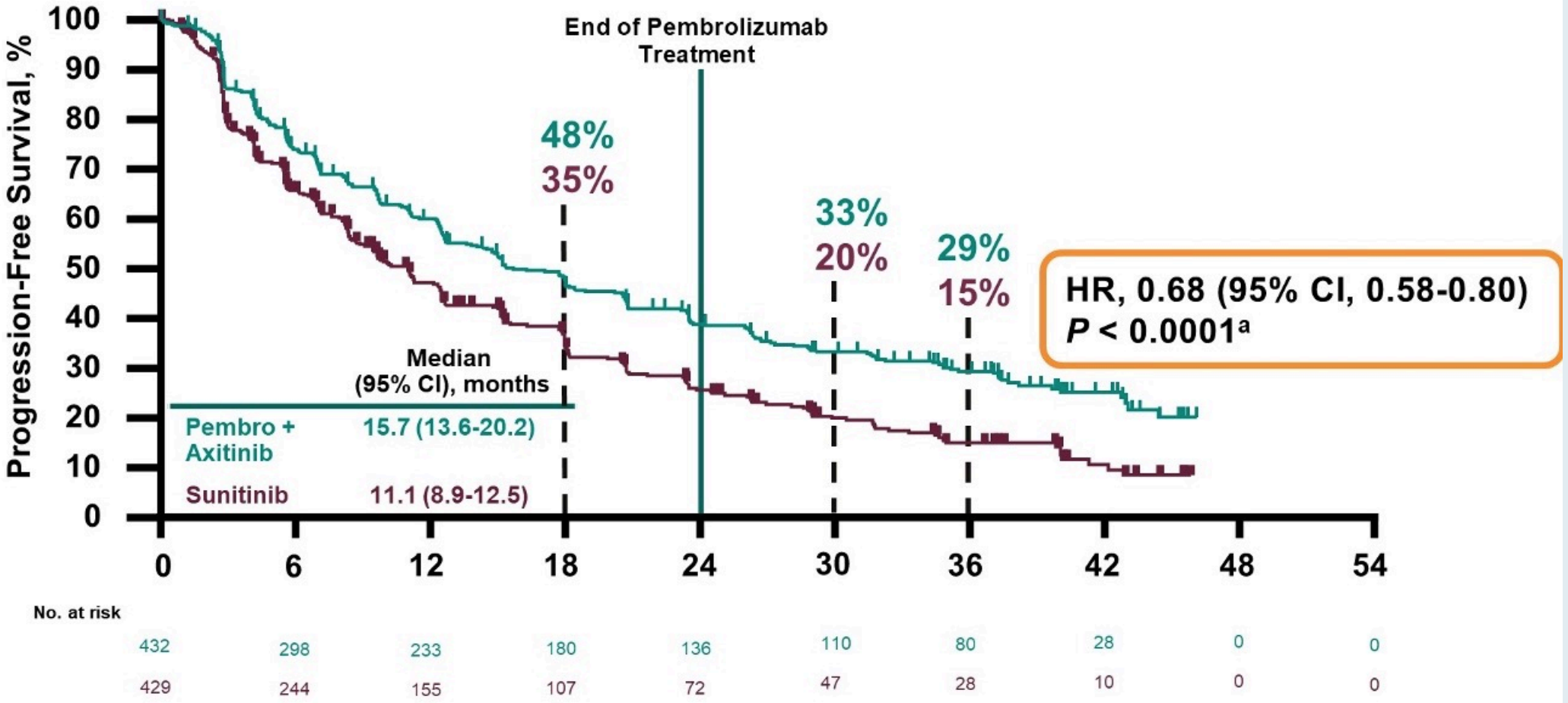
# OS in the ITT Population




[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

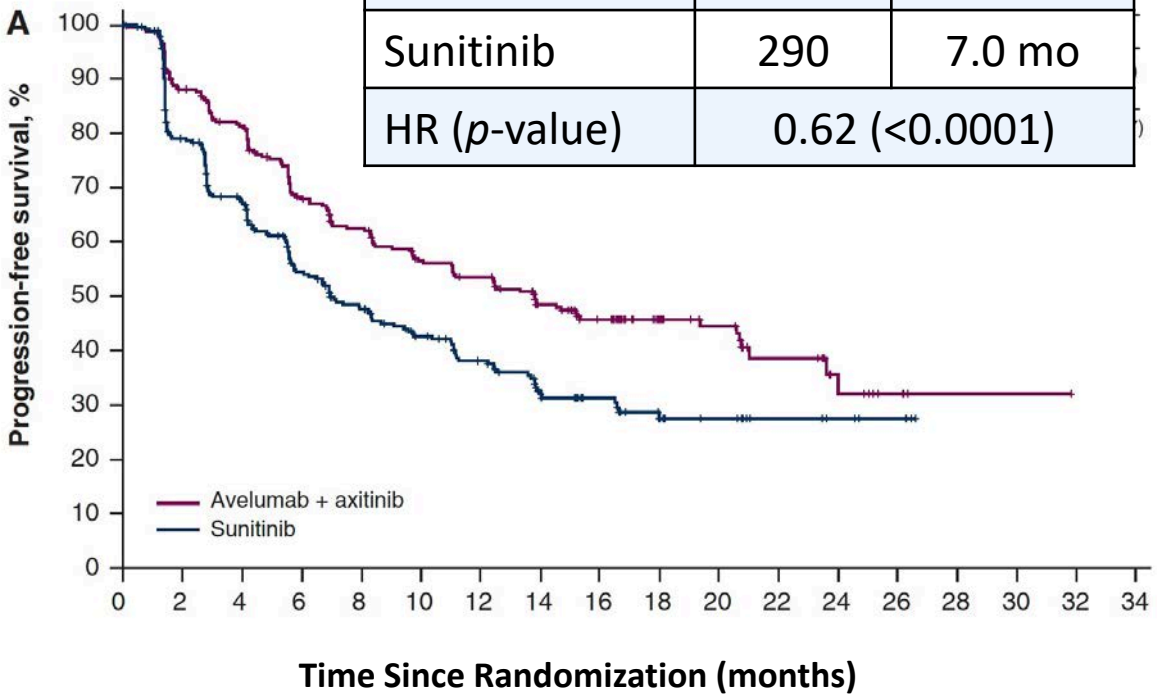
| | PD-L1-positive | | Overall | |
|---|---|---|---|---|
| | Avelumab + axitinib (n = 270) | Sunitinib (n = 290) | Avelumab + axitinib (n = 442) | Sunitinib (n = 444) |
| Confirmed ORR | 55.9% | 27.2% | 52.5% | 27.3% |
| CR | 5.6% | 2.4% | 3.8% | 2.0% |
| PR | 50.4% | 24.8% | 48.6% | 25.2% |
| Stable 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

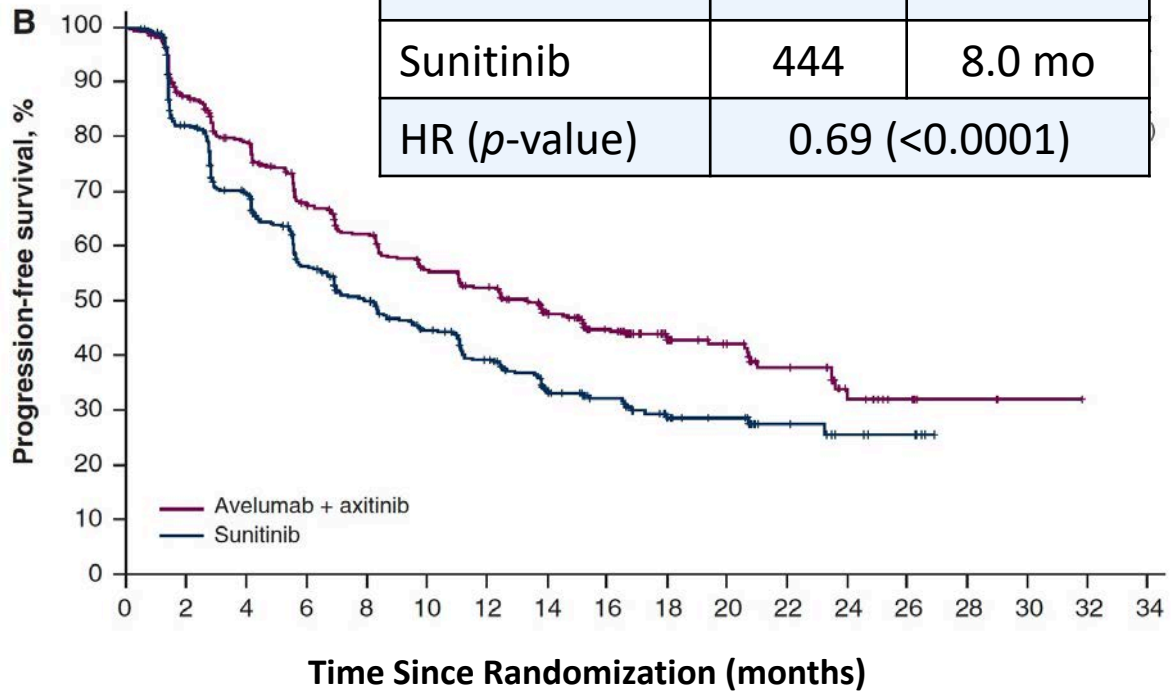
## PD-L1 ≥ 1% Population

| | 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

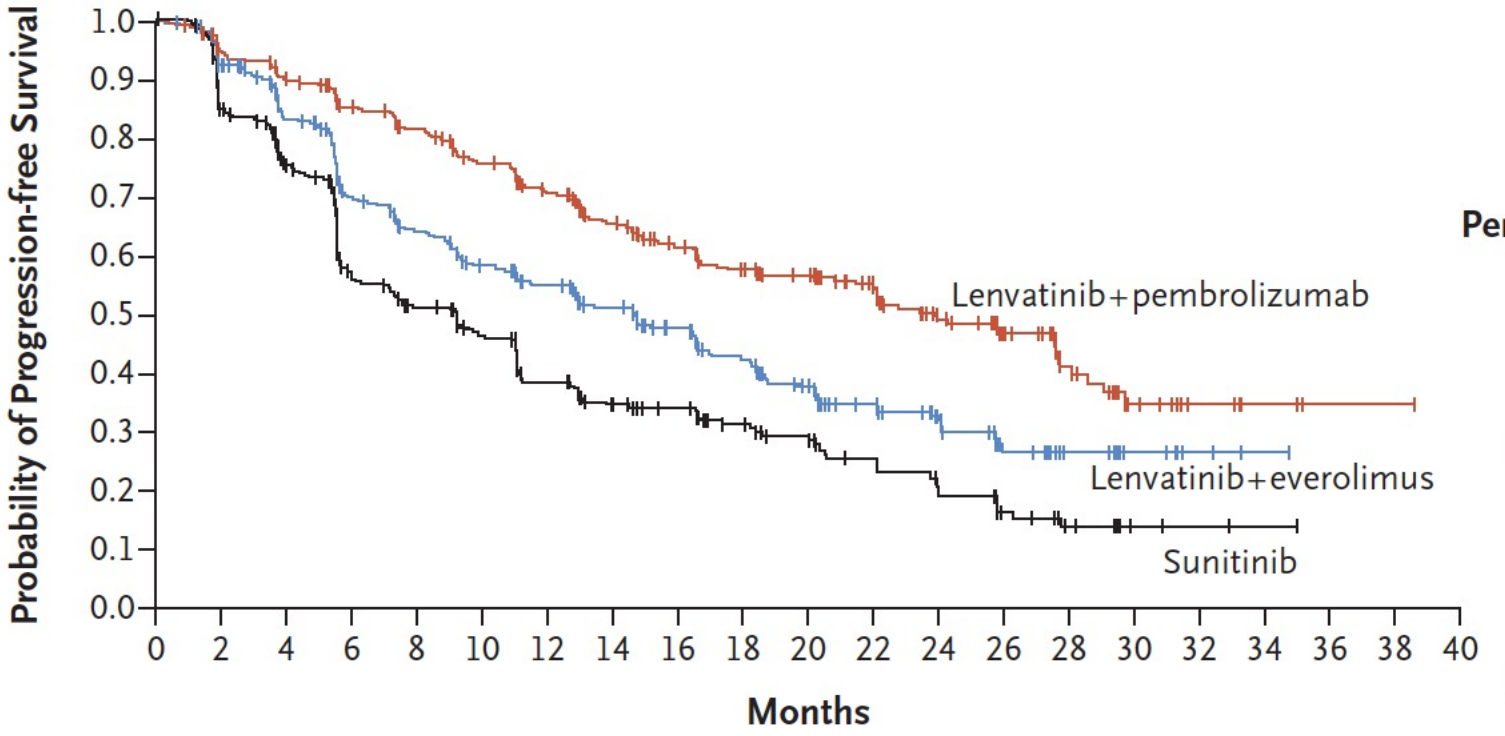
ORIGINAL ARTICLE

# 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) |

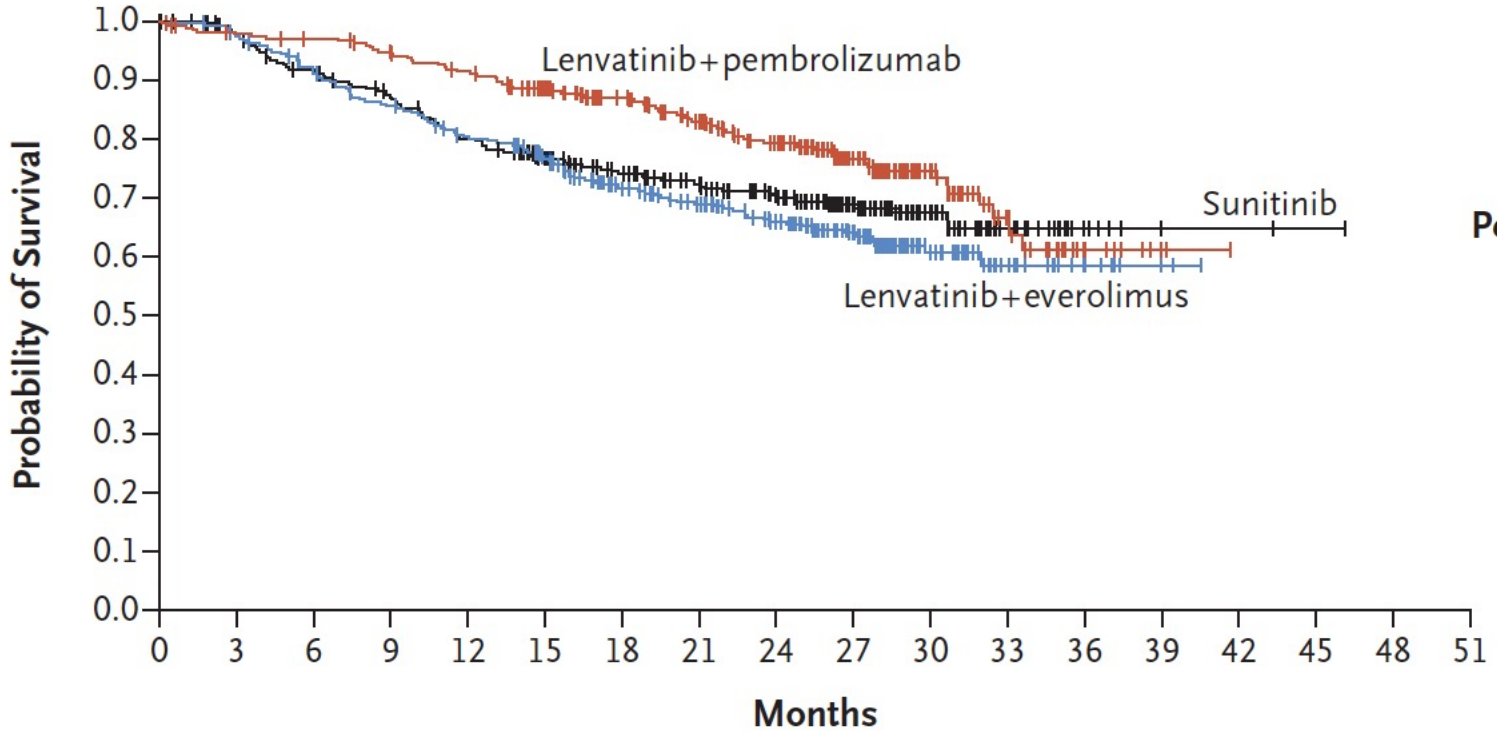
Hazard ratio for disease progression or death (lenvatinib+ pembrolizumab vs. sunitinib), 0.39 (95% CI, 0.32–0.49); P<0.001

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

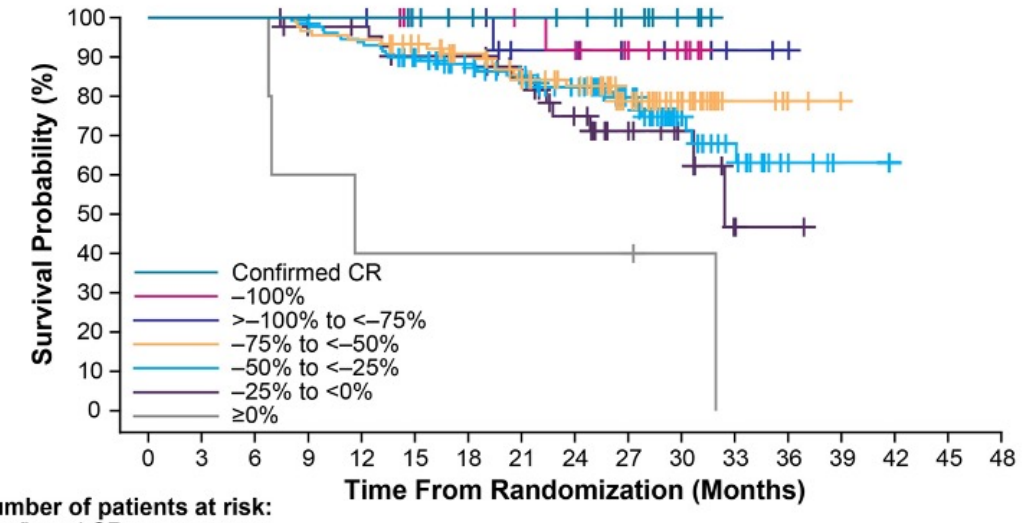
**Viktor Grünwald**[1], Thomas Powles[2], Evgeny Kopyltsov[3], Vadim Kozlov[4], Teresa Alonso Gordoa[5], Masatoshi Eto[6], Thomas Hutson[7], Robert Motzer[8], Eric Winquist[9], Pablo Maroto[10], Bhumsuk Keam[11], Giuseppe Procopio[12], Shirley Wong[13], Bohuslav Melichar[14], Frederic Rolland[15], Mototsugu 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

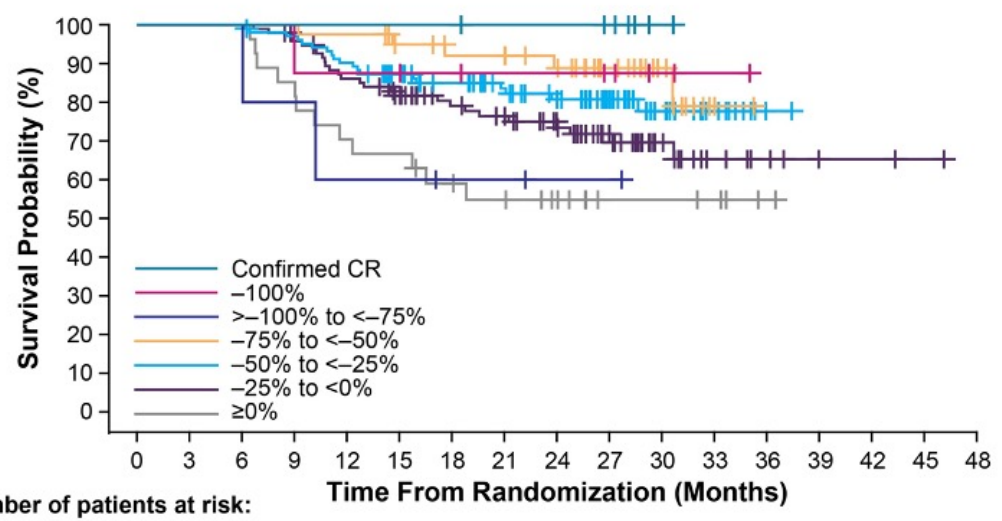
## Lenvatinib plus Pembrolizumab




**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

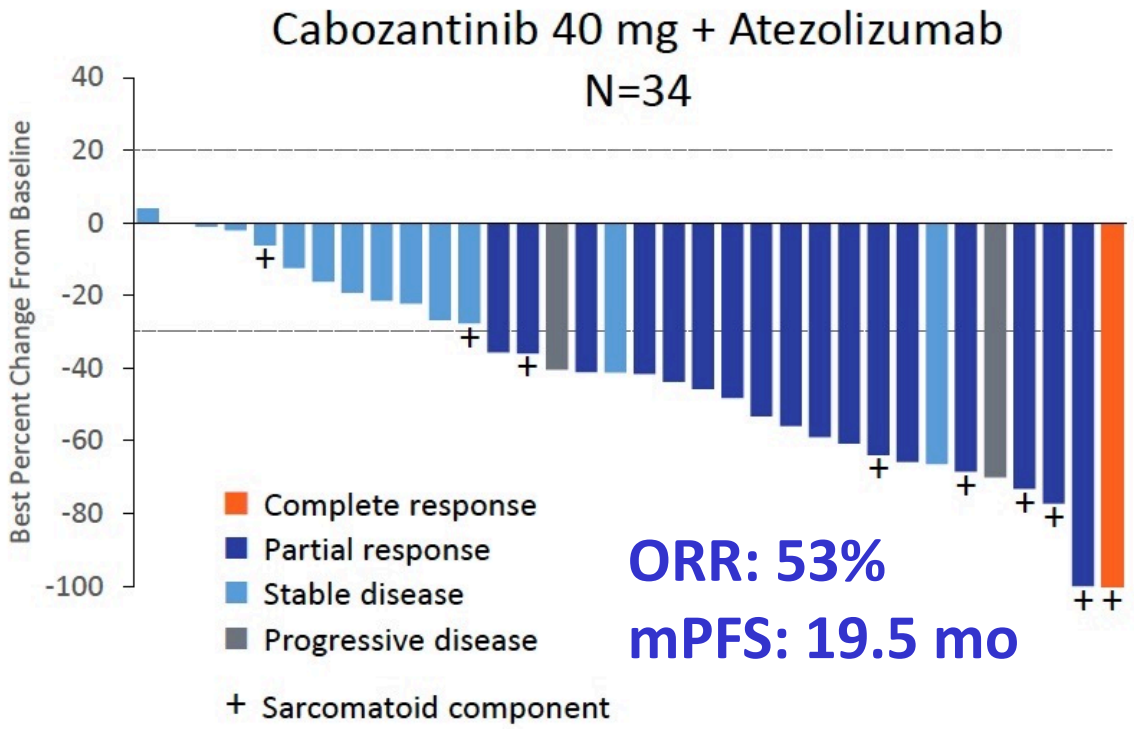
Grunwald V et al. ASCO 2021;Abstract 4560.

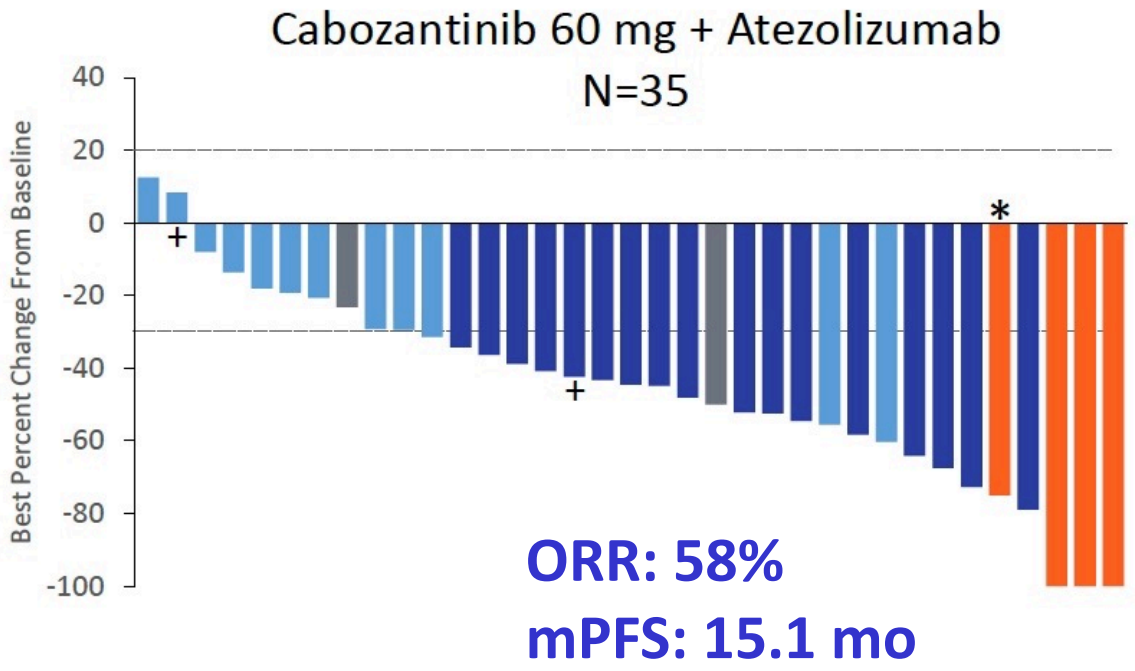
# Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

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.

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<br>• Placebo + nivolumab + ipilimumab (4 doses) → placebo + nivolumab | PFS | Nov 2021 |
| PDIGREE | 1,046 | After induction nivolumab/ipilimumab<br>• Pts with CR → Nivolumab<br>• Pts with non-CR or non-PD, *randomized*<br>→ Nivolumab<br>→ Nivolumab + cabozantinib<br>• 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."

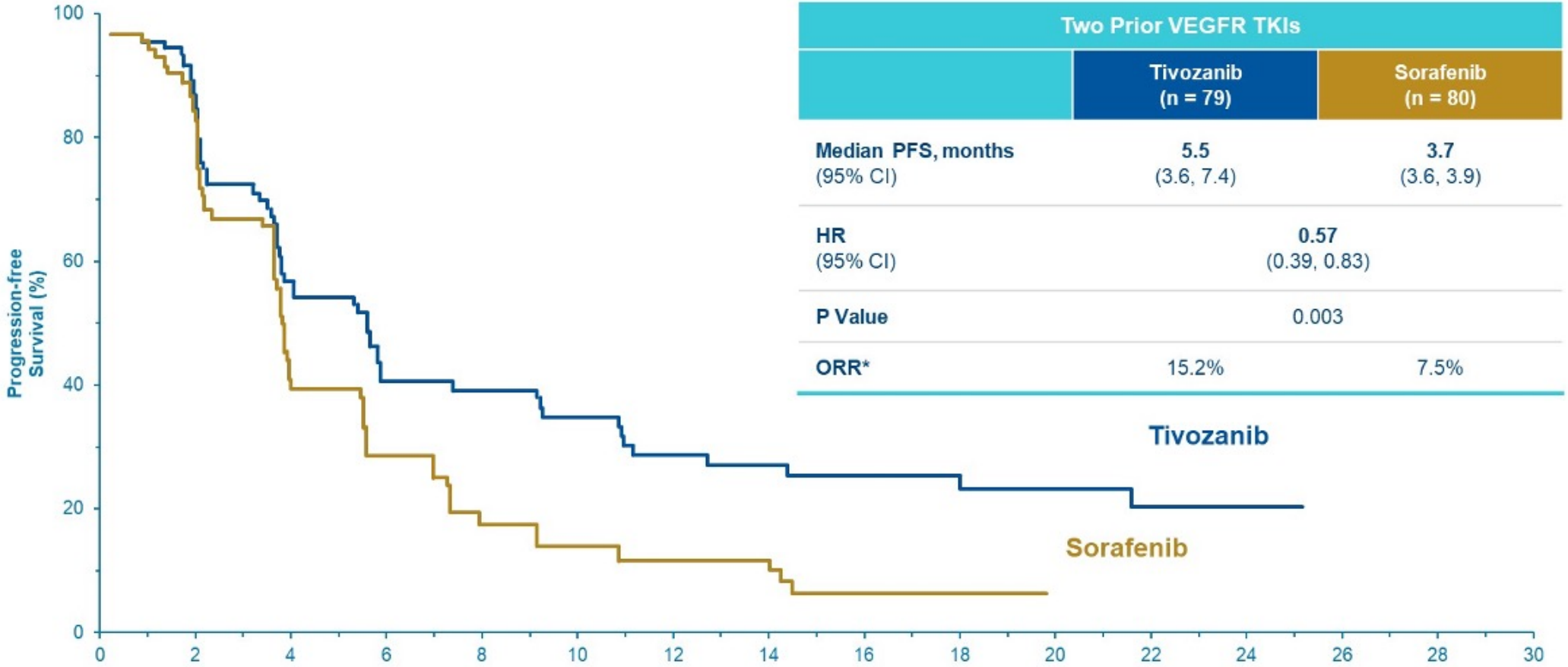
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

# 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."

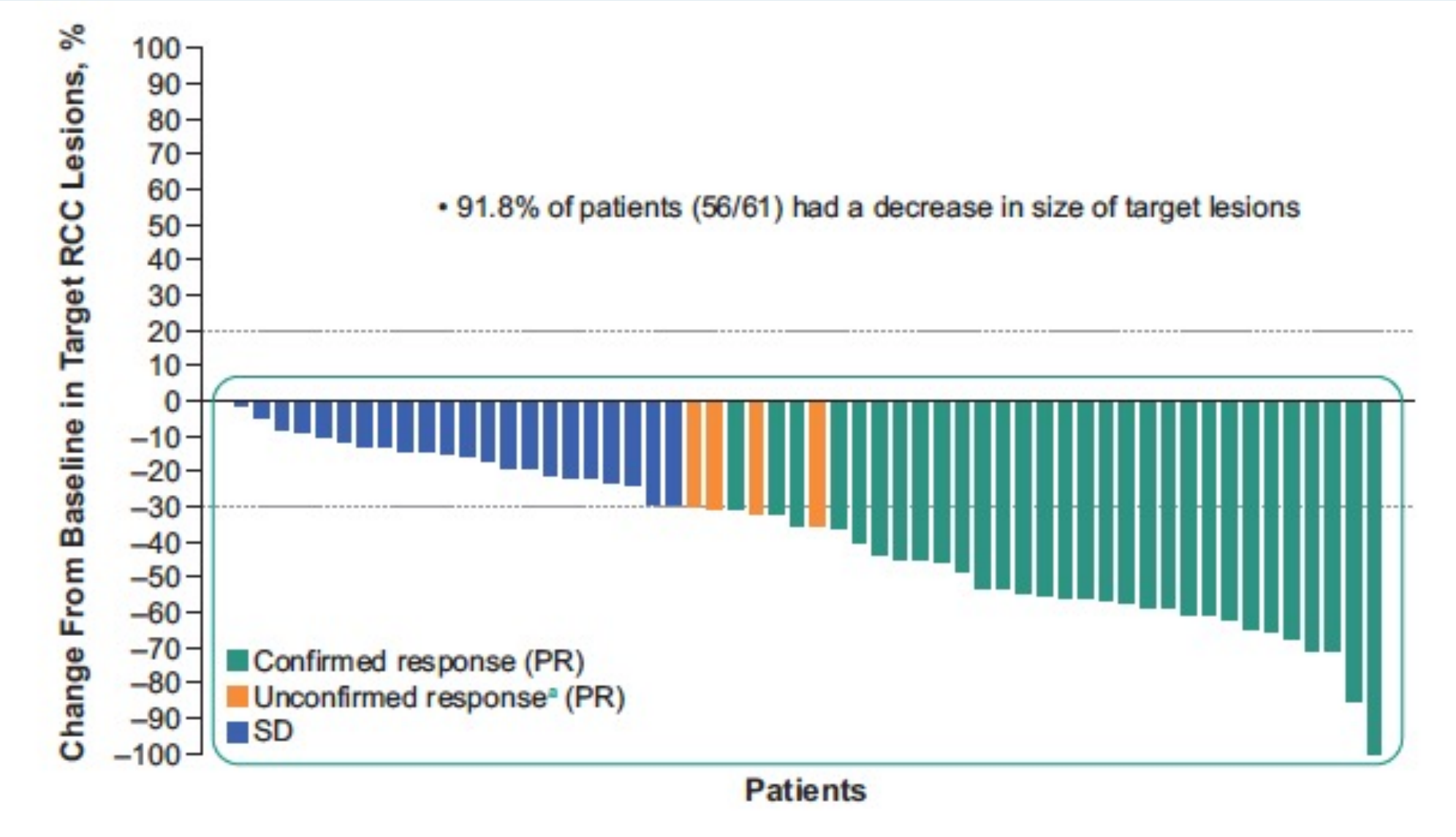
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belzutifan-cancers-associated-von-hippel-lindau-disease

# 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.

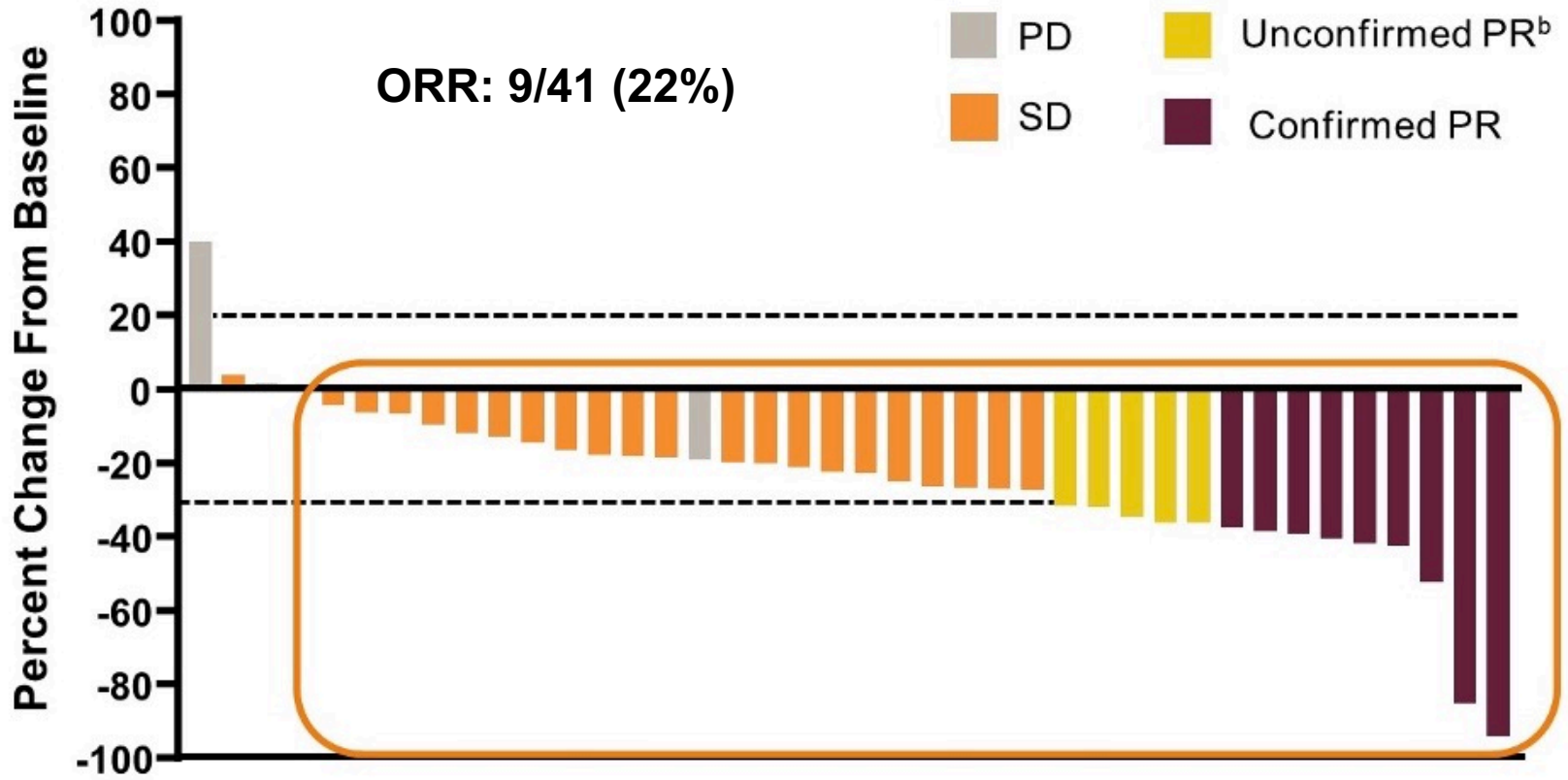
# Phase 2 Study of the Oral Hypoxia-Inducible Factor 2α Inhibitor Belzutifan (MK-6482) in Combination With Cabozantinib in Patients With Advanced Clear Cell Renal Cell Carcinoma

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*

# Optimizing the Clinical Management of Hodgkin and Non-Hodgkin Lymphomas

**Thursday, September 16, 2021**
**5:00 PM – 6:00 PM ET**

## Faculty

**Loretta J Nastoupil, MD**

## 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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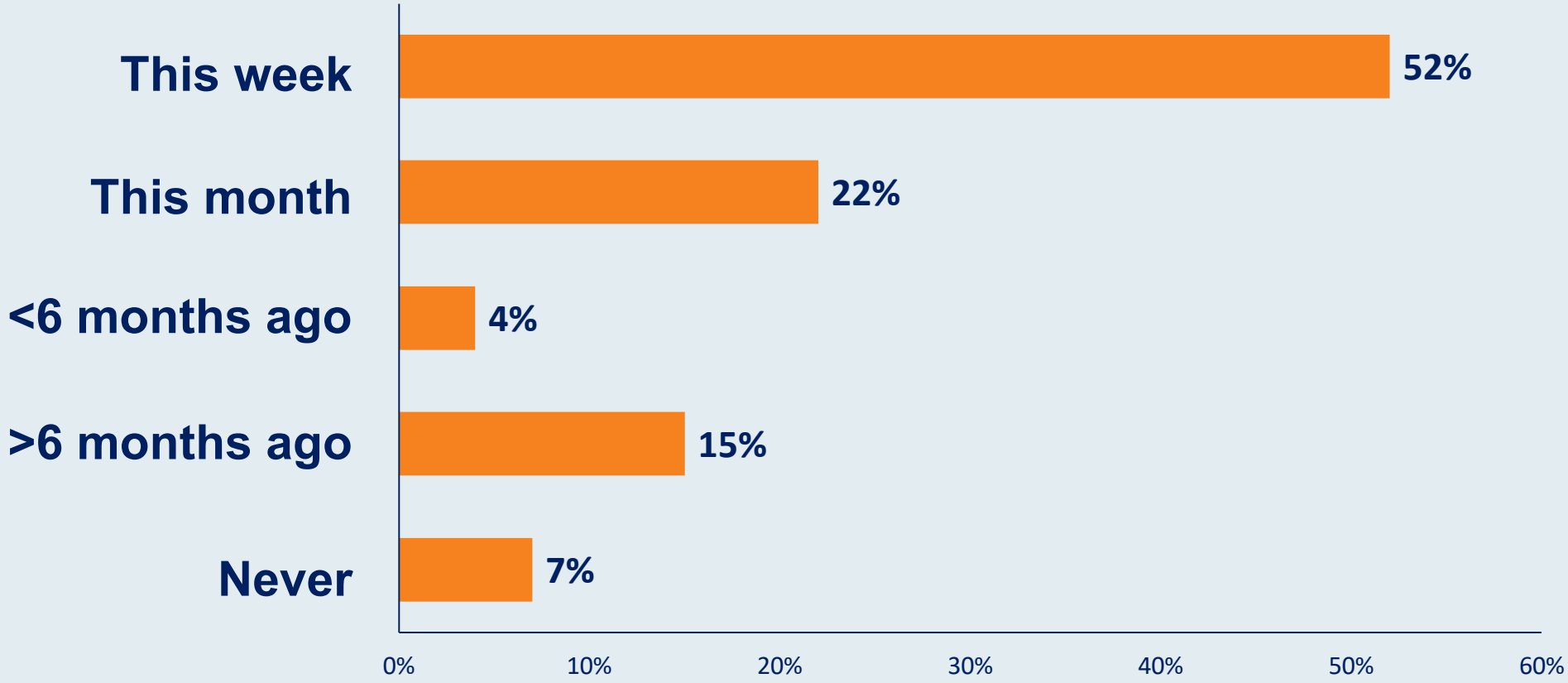
TO PRACTICE

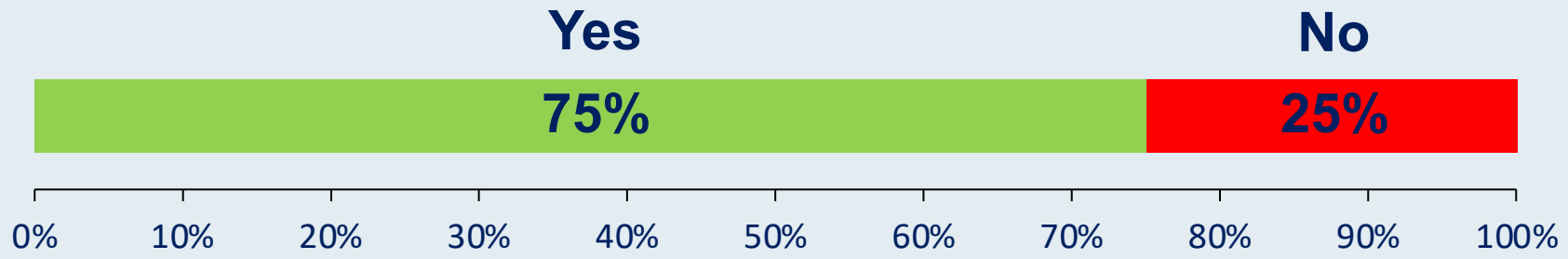
# When was the last time that you presented, or had a case presented for you, at a local tumor board meeting?




Premeeting survey: July 2021

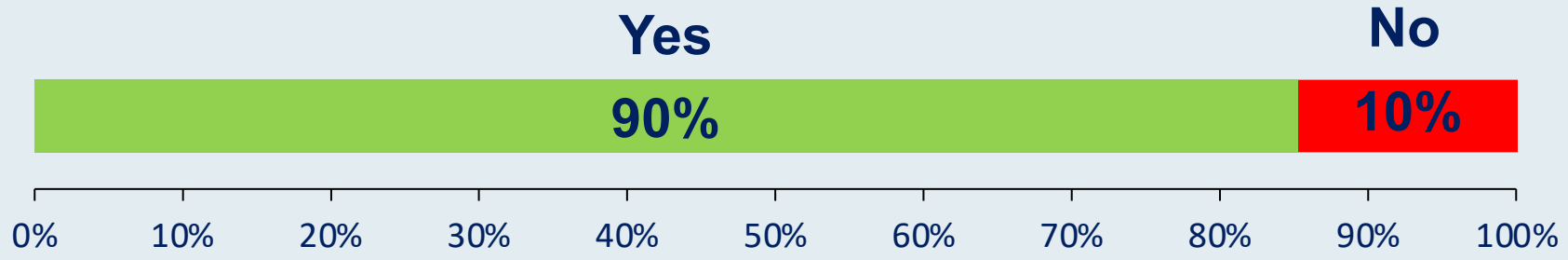
RTP RESEARCH TO PRACTICE

## In the past month have you listened to audio podcasts not related to medicine?



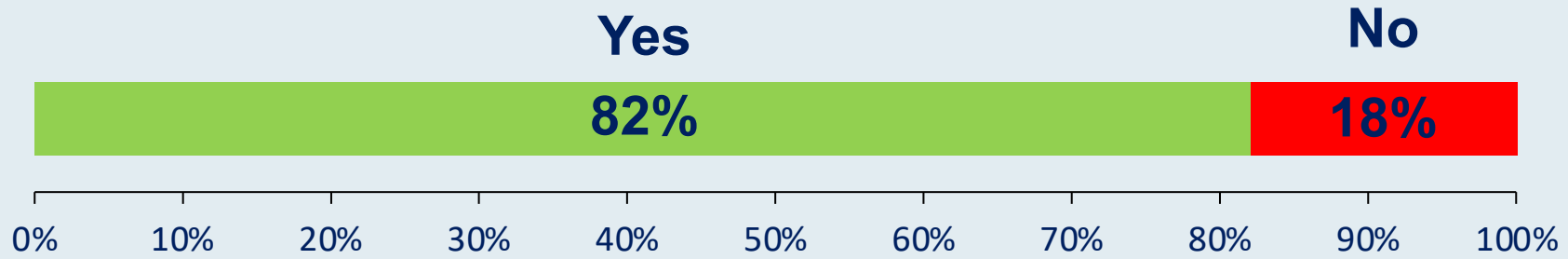

**Median: 5 hours**
**Range: 1-60**

## In the past month have you listened to oncology-related audio podcasts?




**Median: 5 hours**
**Range: 1-40**

## In the past month have you listened to RTP audio podcasts?




**Median: 4 hours**
**Range: 1-66**

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE