Meet The Professor

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

Thomas E Hutson, DO, PharmD
Director, GU Oncology Program
Co-Director, Urologic Cancer Research and Treatment Center
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Charles A Sammons Cancer Center
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Professor of Medicine
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Dallas, Texas

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

Dr Hutson — Disclosures

No relevant conflicts of interest to disclose.

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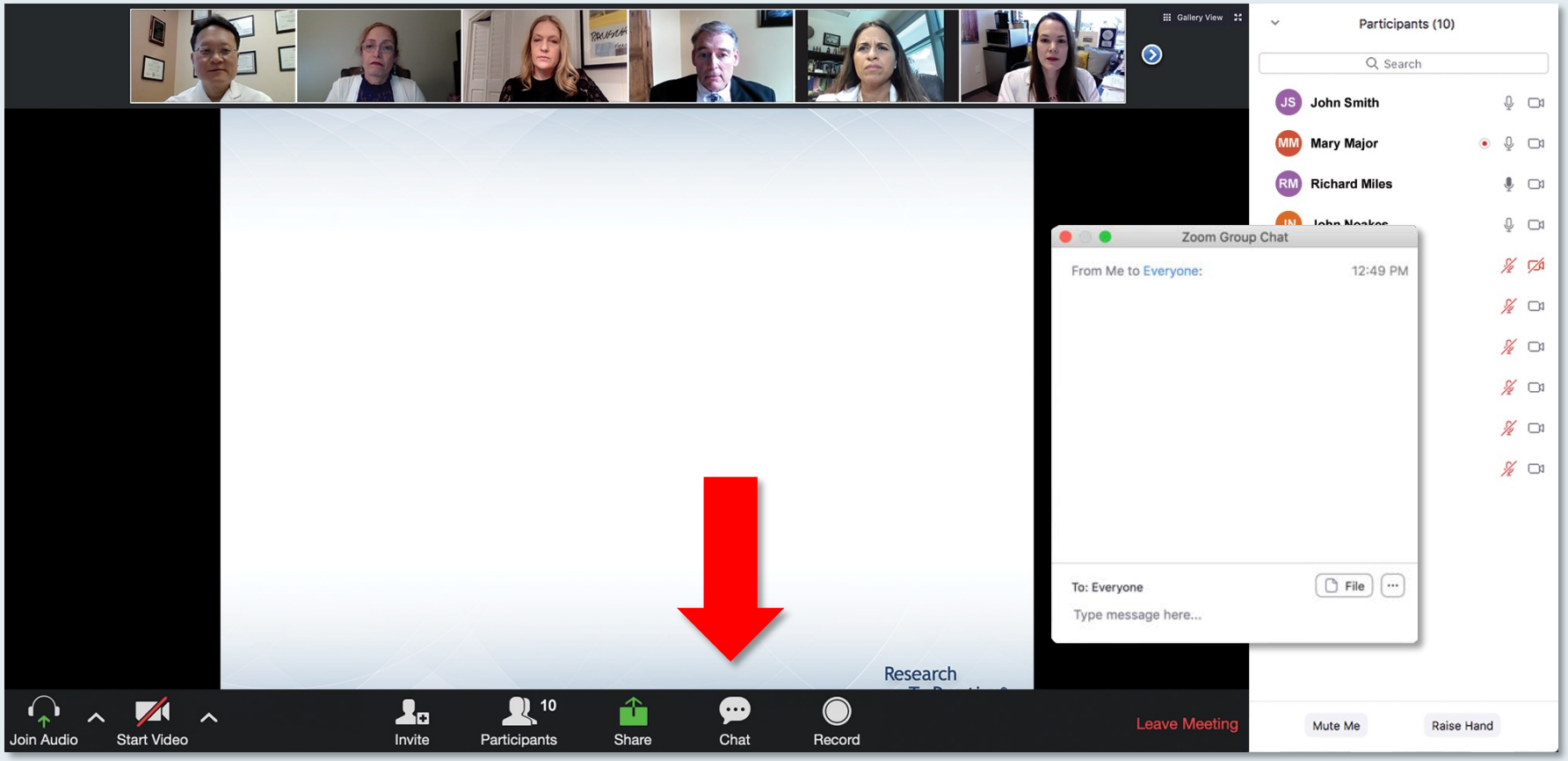
We Encourage Clinicians in Practice to Submit Questions



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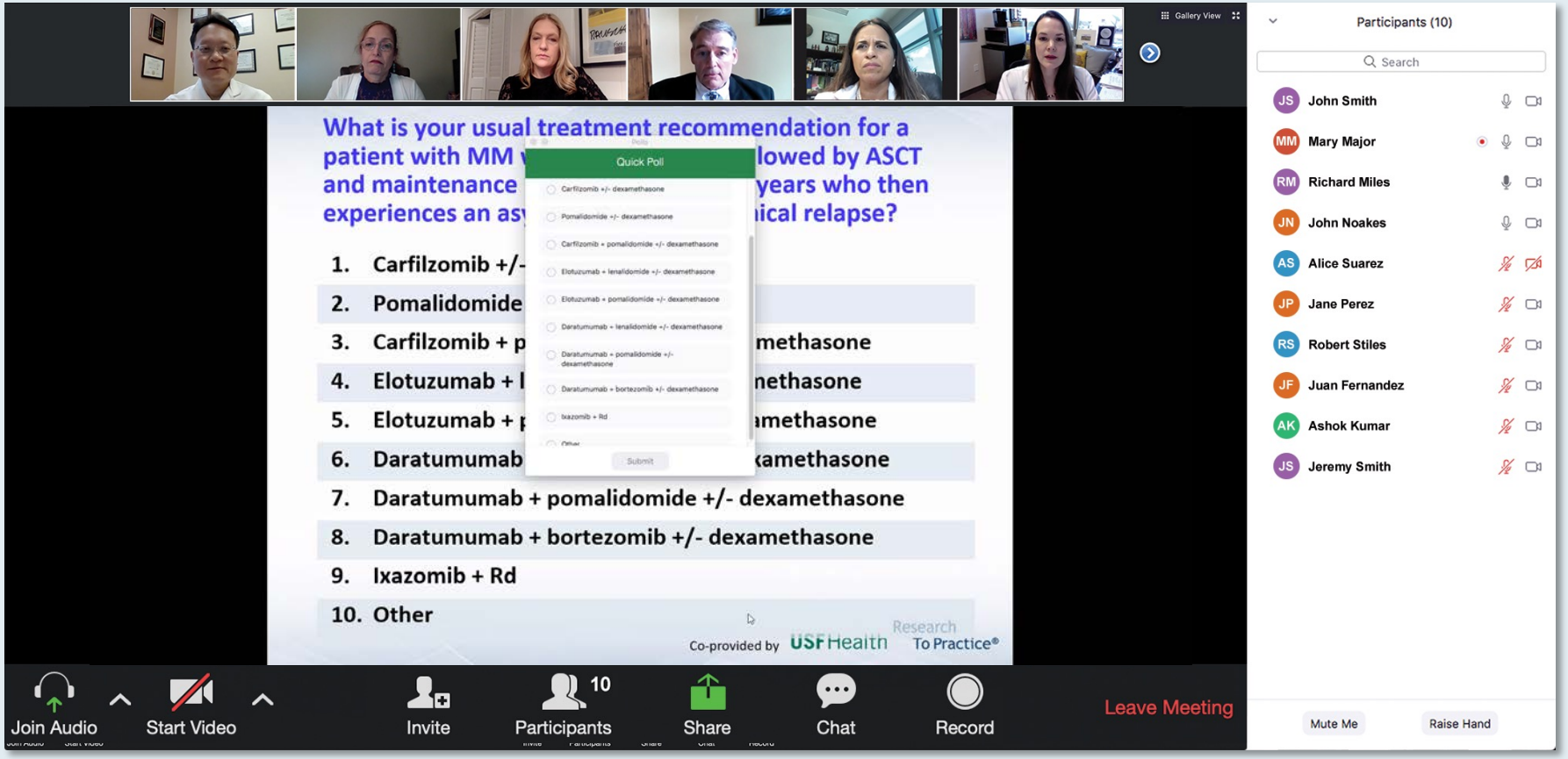

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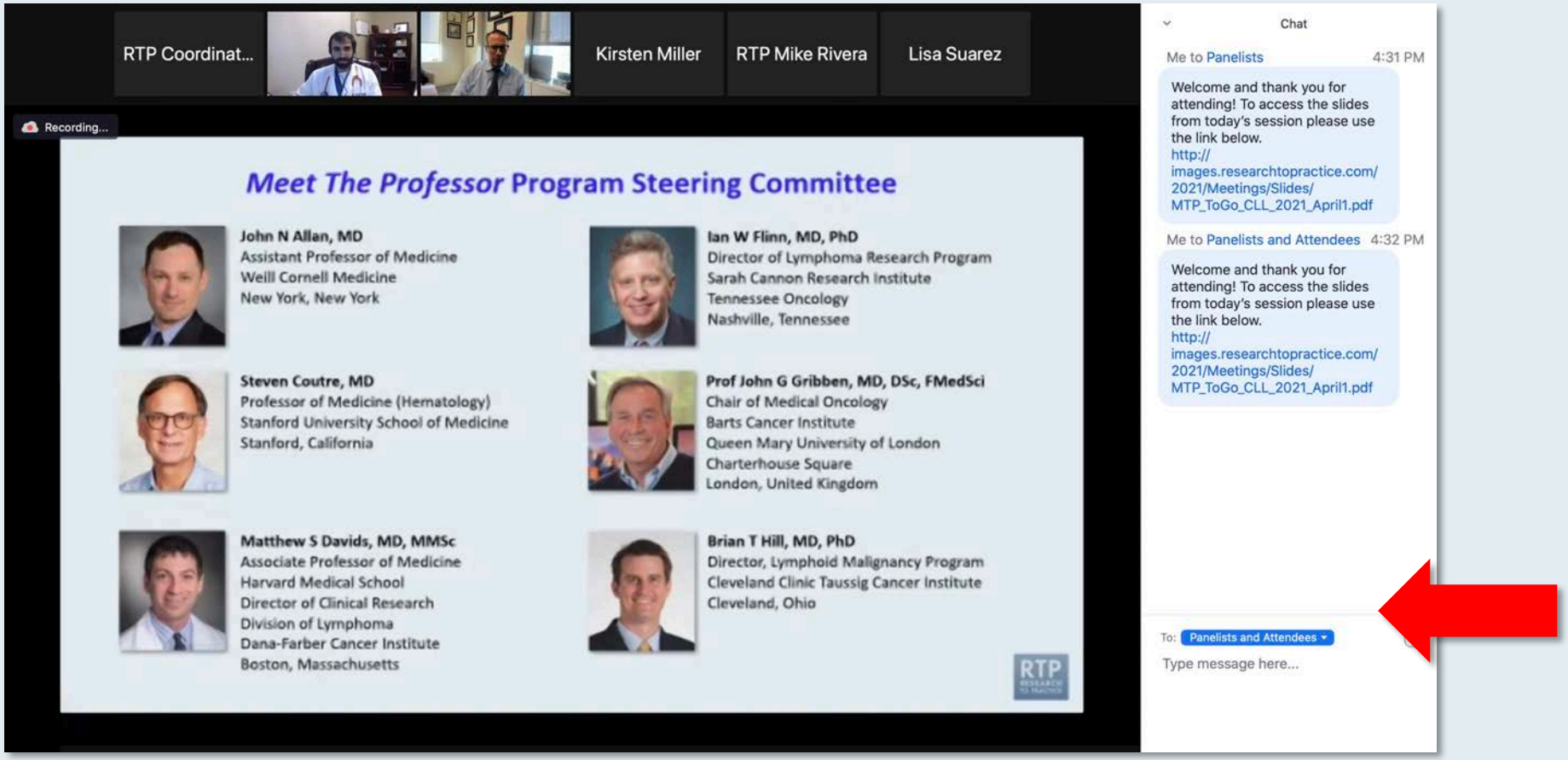

Drag the white line above the submission box up to create more space for your message.

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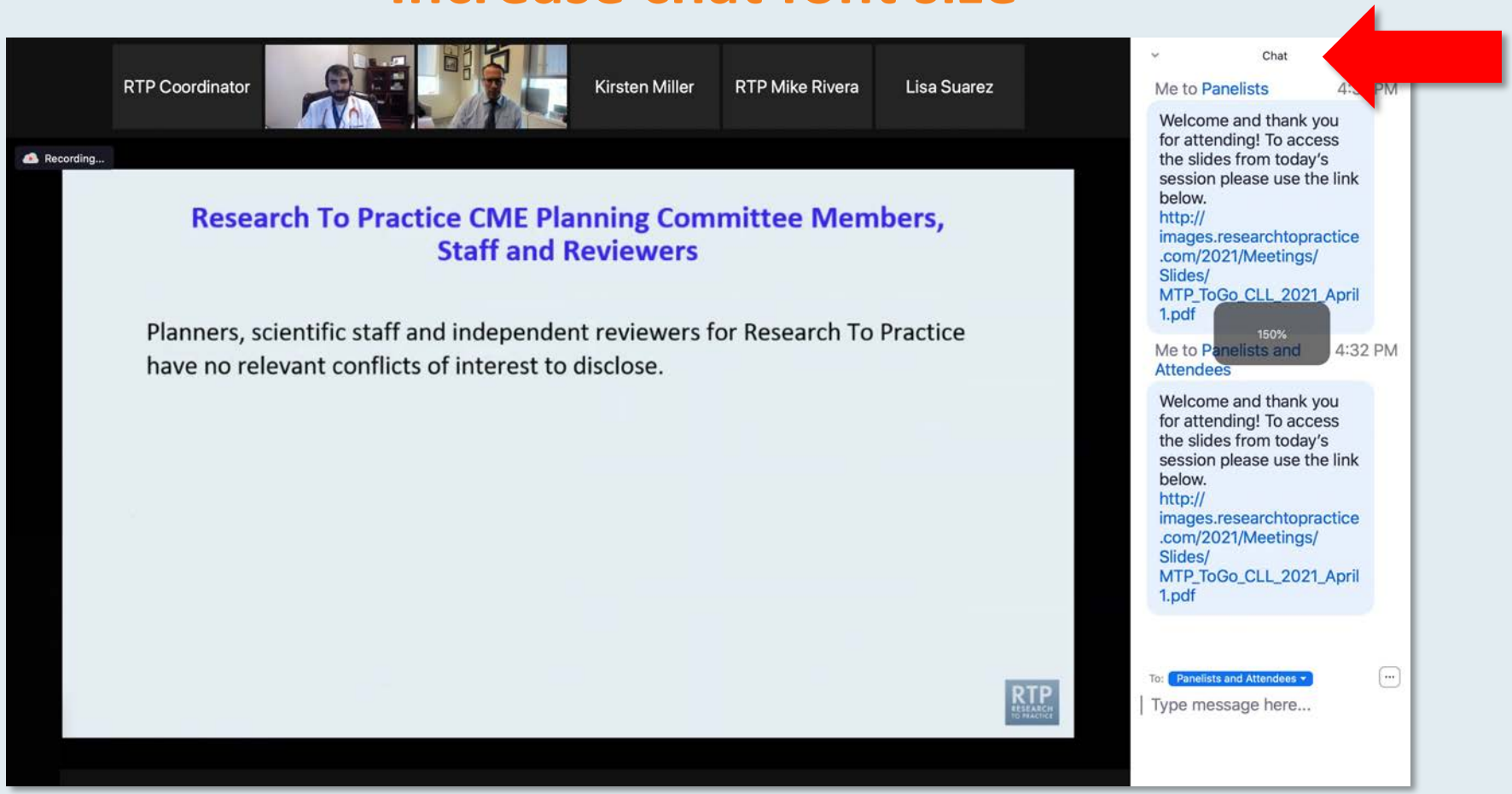

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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WITH DR NEIL LOVE

Renal Cell Carcinoma

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MEMORIAL SLOAN KETTERING CANCER CENTER

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Joyce O'Shaughnessy, MD

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RTP RESEARCH TO PRACTICE

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

In Partnership with Project Echo® and Florida Cancer Specialists

Tuesday, July 6, 2021
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Faculty

David I Quinn, MBBS, PhD

Moderator

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

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Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
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The University of Texas
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Beth Israel Deaconess Medical Center
Leader, Kidney Cancer Program
Dana-Farber/Harvard Cancer Center
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

William K Oh, MD
Clinical Professor of Medicine
Icahn School of Medicine at Mount Sinai
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New York, New York

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Chief of Clinical Trials
Vanderbilt-Ingram Cancer Center
Ingram Professor of Medicine
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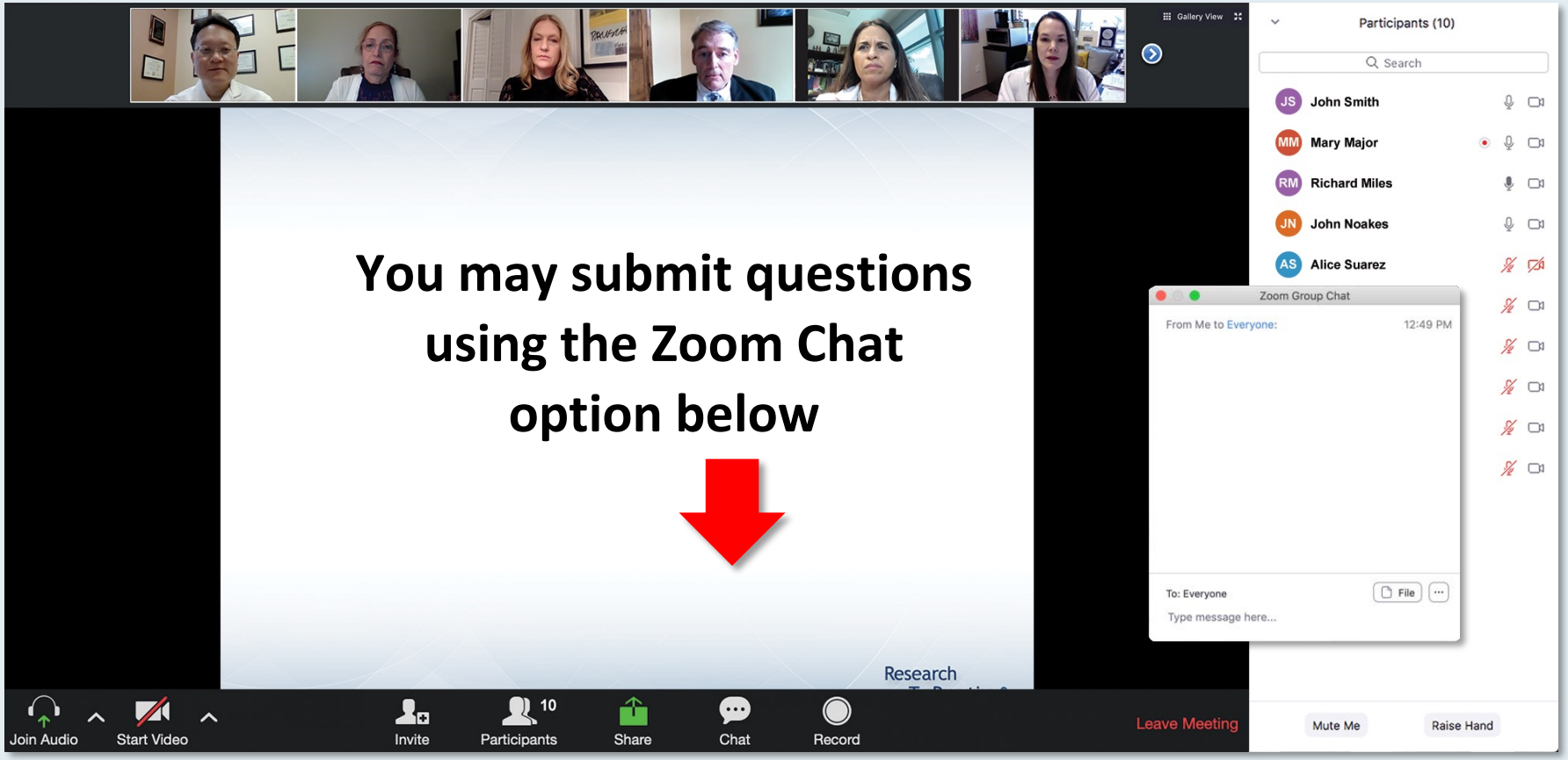

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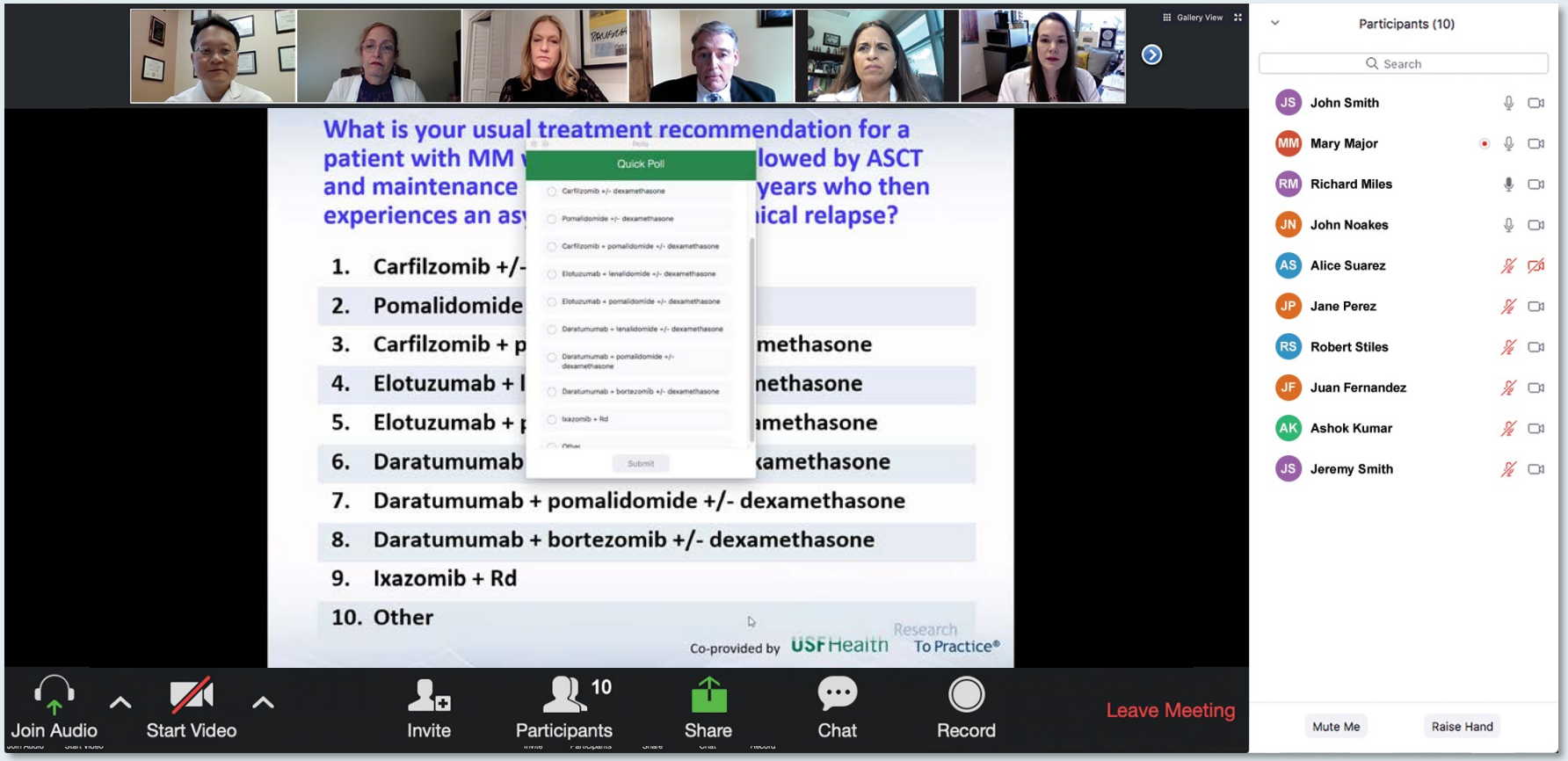

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Division of Hematology and Oncology
UT Southwestern Medical Center
Dallas, Texas

Yanjun Ma, MD
Tennessee Oncology
Murfreesboro, Tennessee

Meet The Professor with Dr Hutson

MODULE 1: Cases from Drs Hammers and Ma

- Dr Ma: A 56-year-old woman with recurrent metastatic clear cell renal cell carcinoma (ccRCC) and blood pressure dysregulation and weight gain on pembrolizumab/axitinib
- Dr Hammers: A 61-year-old man with ccRCC and a single site of metastatic progression in the pancreas
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MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Hutson

MODULE 4: Key Data Sets

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Regulatory and reimbursement issues aside, would you offer adjuvant pembrolizumab to a patient who is s/p nephrectomy for average-risk RCC and has a history of psoriasis that does not currently require systemic treatment?

1. Yes
2. No

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

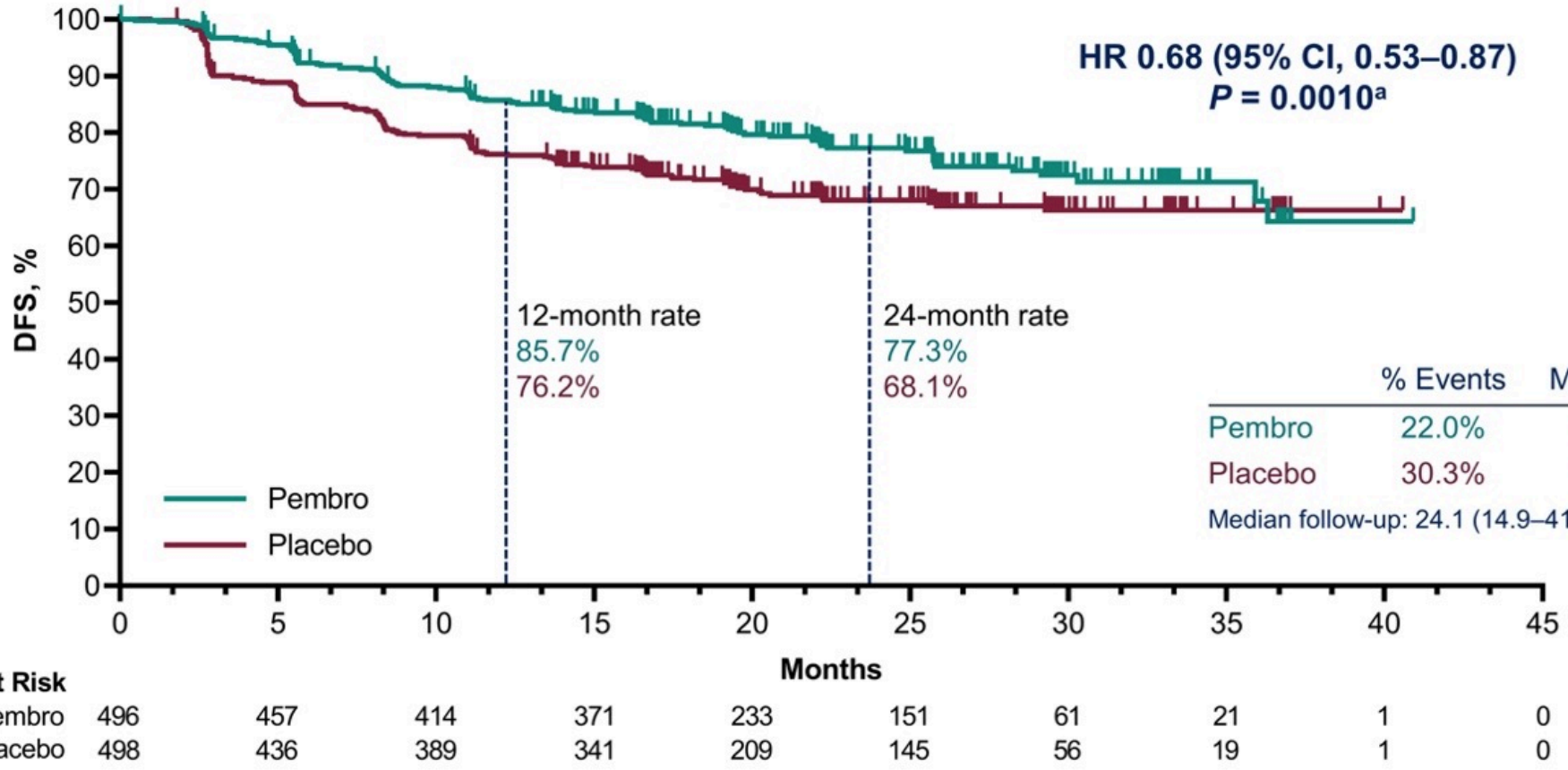
Toni K. Choueiri[1]; Piotr Tomczak[2]; Se Hoon Park[3]; Balaji Venugopal[4]; Thomas Ferguson[5]; Yen-Hwa Chang[6]; Jaroslav Hajek[7]; Stefan Symeonides[8]; Jae Lyun Lee[9]; Naveed Sarwar[10]; Antoine Thiery-Vuillemin[11]; Marine Gross-Goupil[12]; Mauricio Mahave[13]; Naomi Haas[14]; Piotr Sawrycki[15]; Rodolfo F. Perini[16]; Pingye Zhang[16]; Jaqueline Willemann-Rogerio[16]; Kentaro Imai[16]; David Quinn[17]; Thomas Powles[18]; on behalf of the KEYNOTE-564 investigators.

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

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

Choueiri TK et al. ASCO 2021;Abstract LBA5.

DFS by Investigator, ITT Population



	% Events	Median (95% CI)
Pembro	22.0%	NR (NR–NR)
Placebo	30.3%	NR (NR–NR)

Median follow-up: 24.1 (14.9–41.5) months.

No. at Risk

Pembro	496	457	414	371	233	151	61	21	1	0
Placebo	498	436	389	341	209	145	56	19	1	0

[a]Crossed prespecified p-value boundary for statistical significance of 0.0114.
ITT population included all randomized participants. NR, not reached. Data cutoff date: December 14, 2020.

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

Choueiri TK et al. ASCO 2021;Abstract LBA5.

Interim OS Results, ITT Population

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

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

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Case Presentation – Dr Ma: A 56-year-old woman with recurrent metastatic ccRCC and blood pressure dysregulation and weight gain on pembrolizumab/axitinib

Dr Yanjun Ma

- 2015: Left nephrectomy for clear cell renal carcinoma
- 7/2019: Recurrent/metastatic disease noted on restaging scan that involved bulky left adrenal gland, pancreatic head mass, as well as bilateral lung metastases
  - Pancreatic head mass has resulted in biliary obstruction that required ERCP and stent placement
- 9/2019: Pembrolizumab/axitinib
  - Diffuse arthralgia and malaise noted 1 month later
  - Adrenal insufficiency treated with hydrocortisone 5mg BID
  - Developed labile blood pressure resulting in episodes of fainting and of hyper- and hypotension
- Axitinib stopped and hypertension issues resolved
- Pembrolizumab discontinued for several months due to 70-lb weight gain in 5 months' time

Questions

- Have you experienced similar side effects with pembrolizumab/axitinib in your patients?

Case Presentation – Dr Hammers: A 61-year-old man with ccRCC and a single site of metastatic progression in the pancreas

Dr Hans Hammers

- Initially diagnosed with Stage II, Grade 2 ccRCC for which he underwent a nephrectomy
- 4 years later, he presents with a single enlarging and enhancing deposit in the tail of the pancreas
- No other sites of disease found on imaging

Questions

- What do you think when you see a patient with metastatic disease in the pancreas? How would you approach the treatment of such a patient?

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Case Presentation – Dr Hammers: A 61-year-old man with ccRCC and a single site of metastatic progression in the pancreas (continued)

Dr Hans Hammers

- Initially diagnosed with Stage II, Grade 2 ccRCC for which he underwent a nephrectomy
- 4 years later, he presents with a single enlarging and enhancing deposit in the tail of the pancreas
- No other sites of disease found on imaging
- ***Metastectomy/partial pancreatectomy, with no further recurrences over 1.5 years later***

Case Presentation – Dr Ma: A 58-year-old man with recurrent metastatic ccRCC and severe psoriasis

Dr Yanjun Ma

- 2014: Left kidney, stage I, T1b,N0,M0, 6.0 x 5.5 cm renal cell carcinoma primarily sarcomatoid arising out of clear cell histology
- PMH: Severe psoriasis and psoriatic arthritis
- 7/2015: Recurrence isolated in the left lung, LLL VATS wedge resection
- 4/2016 – 10/2018: Pazopanib → Cabozantinib → RLL tumor resection
- 3/2020: Lenvatinib/everolimus with tolerability issues
  - Everolimus is at 5 mg dose, lenvatinib dose cycles between 8 mg and 12 mg

Questions

- In your experience, do patients often tolerate the full dose of lenvatinib? Is this even considered a meaningful dose or am I just seeing everolimus efficacy here?

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Case Presentation – Dr Ma: A 58-year-old man with recurrent metastatic ccRCC and severe psoriasis (continued)

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  - Everolimus is at 5 mg dose, lenvatinib dose cycles between 8 mg and 12 mg
- Experienced resolution of psoriatic conditions while on cabozantinib
- ***Patient is willing to attempt immunotherapy but concerns exist regarding flare up of patient's severe psoriatic condition and its detrimental effects on quality of life***

Case Presentation – Dr Hammers: A 53-year-old man presenting with ccRCC and metastases to the brain

Dr Hans Hammers

- An otherwise healthy man presents to the ER with increasing SOB/malaise and headaches
- Workup reveals a large right-sided pleural effusion with pleural mass, multiple bilateral lung nodules (largest 1.7 cm), and a left-sided renal mass 12 cm
  - COVID-19 negative
  - Imaging for headaches reveals brain metastases with significant edema, 7 and 12 mm
  - Biopsy of renal mass: ccRCC, Grade 3
- Fluid was drained and dexamethasone administered for edema
- Radiation oncology consult for stereotactic radiation

Question

- What systemic therapy would you recommend next for this patient?

Case Presentation – Dr Hammers: A 53-year-old man presenting with ccRCC and metastases to the brain (continued)

Dr Hans Hammers

- An otherwise healthy man presents to the ER with increasing SOB/malaise and headaches
- Workup reveals a large right-sided pleural effusion with pleural mass, multiple bilateral lung nodules (largest 1.7 cm), and a left-sided renal mass 12 cm
  - Imaging for headaches reveals brain metastases with significant edema, 7 and 12 mm
  - Biopsy of renal mass: ccRCC, Grade 3
- Fluid was drained and dexamethasone administered for edema
- ***Treatment plan: begin with a TKI to promote resolution of pleural effusion and allowing for quick weaning off steroids, and then add immune checkpoint inhibition***
- ***Cabozantinib/nivolumab → patient is doing well***

Case Presentation – Dr Ma: A 60-year-old woman with recurrent metastatic RCC, chromophobe histology — PTEN mutation

Dr Yanjun Ma

- 11/2016: Left nephrectomy for Stage II, pT2b, pN0c, M0 renal cell carcinoma, chromophobe type
- 7/2018: Recurrence noted, located mainly in the surgical bed and retroperitoneum
- Ipilimumab/nivolumab initiated
  - Development of severe diarrhea 3 months later, several recurrent episodes requiring hospitalizations; therapy stopped and monitored for disease progression
- 5/2019: Cabozantinib; dose lowered to 40 mg in November
- 2/2020: Treatment stopped due to fistula/muscle abscess between descending colon and psoas muscle → diverting colostomy
- 9/2020: Everolimus initiated
- NGS: PTEN mutation

Questions

- What would you have recommended as first-line treatment? What would you recommend as her next-line of therapy if she experiences disease progression?

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Case Presentation – Dr Ma: A 53-year-old man with newly diagnosed metastatic ccRCC and transverse myelitis on pembrolizumab/axitinib

Dr Yanjun Ma

- Diagnosed with de novo metastatic ccRCC with brain metastases and systemic metastases
  - Aggressive tumor that doubled in size in a month's time
- Pembrolizumab/axitinib led to quick response and improvement in patient's symptoms
- Developed transverse myelitis and paralysis from waist down
  - High dose steroid with taper – no improvement
- Family is trying to decide to continue therapy or transition to hospice

Questions

- Have you experienced similar side effects with pembrolizumab/axitinib in your patients?

Question and Comments: Perspectives on the biology of RCC

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TO PRACTICE

Meet The Professor with Dr Hutson

MODULE 1: Cases from Drs Hammers and Ma

- Dr Ma: A 56-year-old woman with recurrent metastatic clear cell renal cell carcinoma (ccRCC) and blood pressure dysregulation and weight gain on pembrolizumab/axitinib
- Dr Hammers: A 61-year-old man with ccRCC and a single site of metastatic progression in the pancreas
- Dr Ma: A 58-year-old man with recurrent metastatic ccRCC and severe psoriasis
- Dr Hammers: A 53-year-old man presenting with ccRCC and metastases to the brain
- Dr Ma: A 60-year-old woman with recurrent metastatic RCC, chromophobe histology — PTEN mutation
- Dr Ma: A 53-year-old man with newly diagnosed metastatic ccRCC and transverse myelitis on pembrolizumab/axitinib

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Hutson

MODULE 4: Key Data Sets

RTP RESEARCH TO PRACTICE

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

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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

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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

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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 (R/R) RCC; Novel Approaches under Investigation

In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear-cell RCC who receives first-line ipilimumab/nivolumab and experiences disease progression after 12 months?

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

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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 Hutson

MODULE 1: Cases from Drs Hammers and Ma

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Hutson

- A single-arm, multicenter Phase II study of lenvatinib with everolimus for patients with advanced RCC
- Time to resolution of axitinib-related adverse events after treatment interruption for patients with advanced RCC

MODULE 4: Key Data Sets

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

European Association of Urology

Eur Urol 2021;[Online ahead of print].

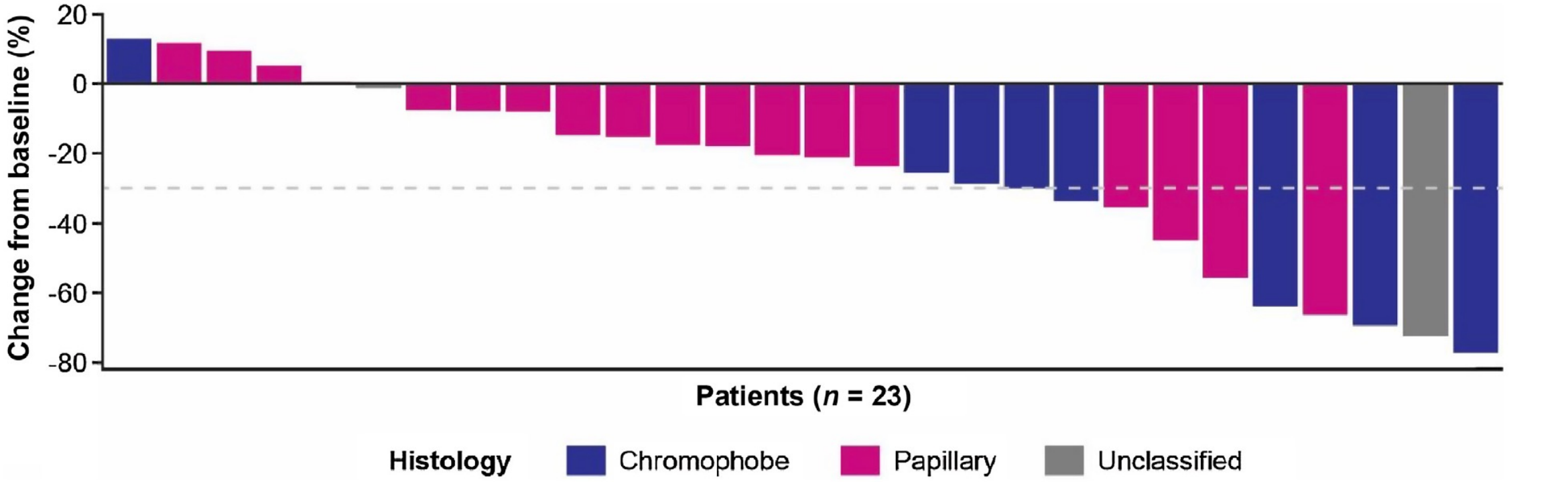
Platinum Priority – Kidney Cancer

A Single-arm, Multicenter, Phase 2 Study of Lenvatinib Plus Everolimus in Patients with Advanced Non-Clear Cell Renal Cell Carcinoma

Thomas E. Hutson[a,*], *M. Dror Michaelson*[b], *Timothy M. Kuzel*[c], *Neeraj Agarwal*[d], *Ana M. Molina*[e], *James J. Hsieh*[f], *Ulka N. Vaishampayan*[g], *Ran Xie*[h], *Urmi Bapat*[h], *Weifei Ye*[i], *Rohit K. Jain*[j], *Mayer N. Fishman*[k]

RTP RESEARCH TO PRACTICE

Tumor Response with Lenvatinib and Everolimus



Hutson TE et al. *Eur Urol* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

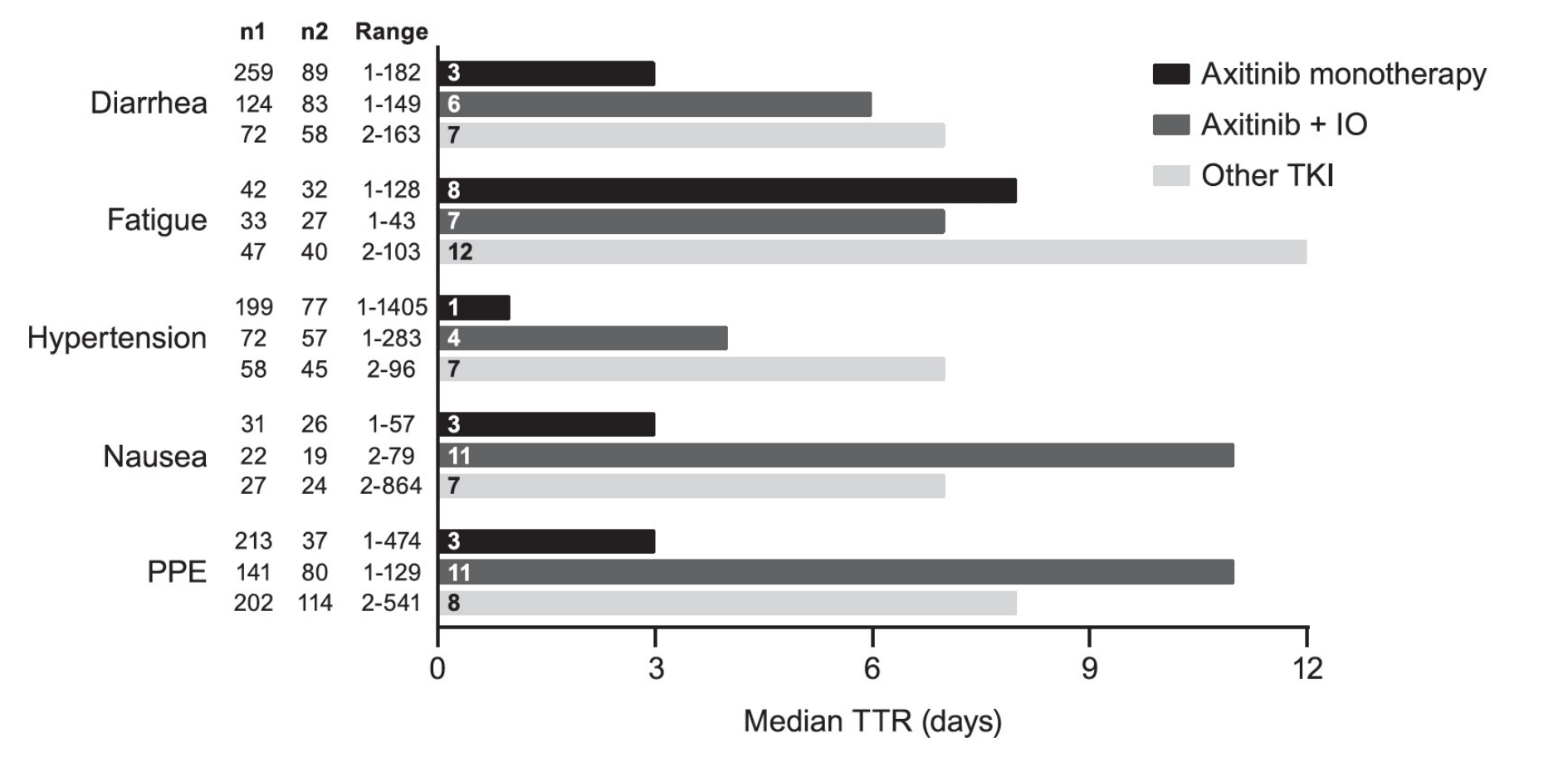
Original study

Time to Resolution of Axitinib-Related Adverse Events After Treatment Interruption in Patients With Advanced Renal Cell Carcinoma

Brian I. Rini,[1] Michael B. Atkins,[2] Toni K. Choueiri,[3] Despina Thomaidou,[4] Brad Rosbrook,[5] Maghull Thakur,[6] Thomas E. Hutson[7]

Clin Genitourin Cancer 2021;[Online ahead of print].

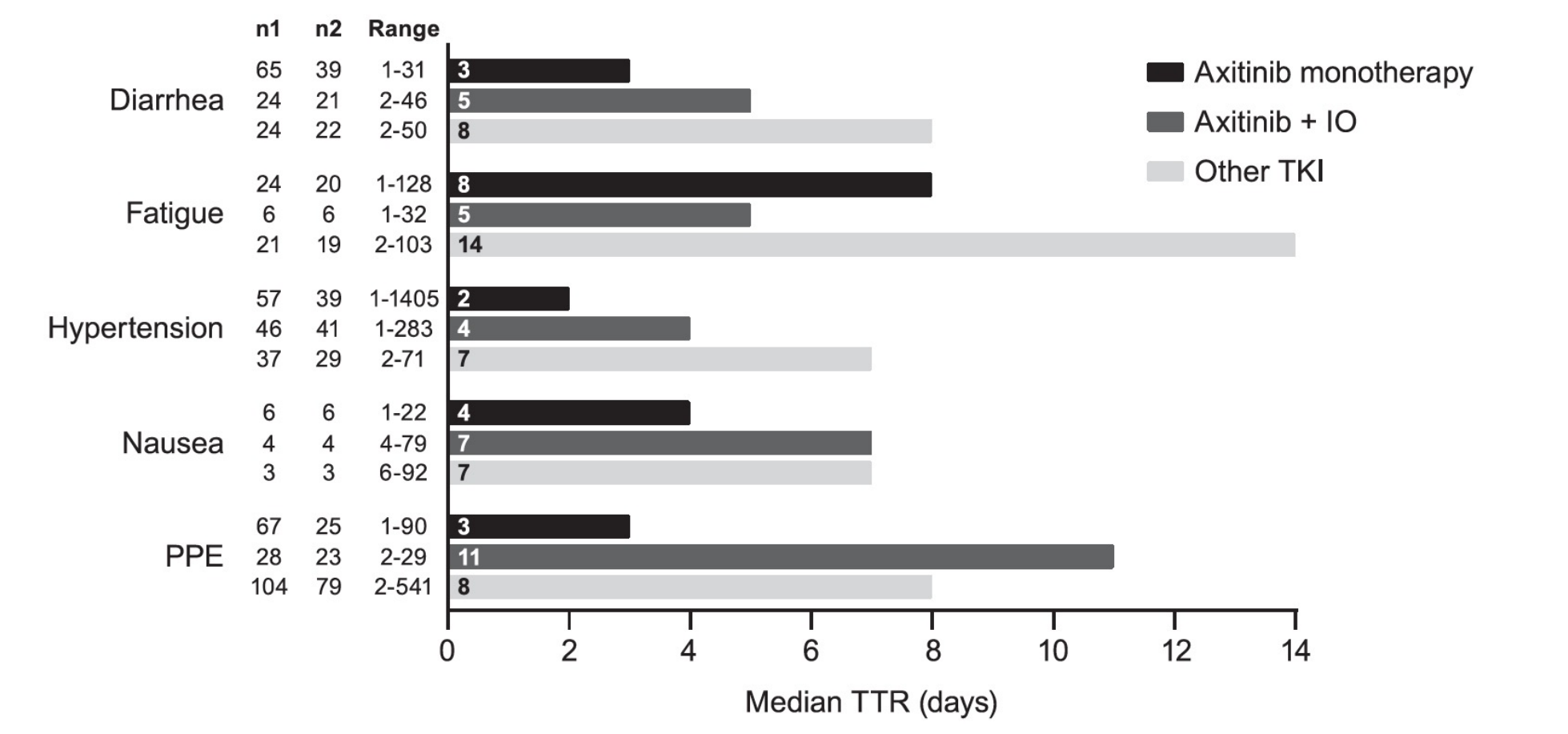
Time to Resolution (TTR) of Any-Grade Adverse Events After Interruption or Temporary Discontinuation of Treatment



n1 = number of events that resolved; n2 = number of patients

Rini BI et al. *Clin Genitourin Cancer* 2021;[Online ahead of print].

Time to Resolution (TTR) of Grade ≥3 Adverse Events After Interruption or Temporary Discontinuation of Treatment



n1 = number of events that resolved; n2 = number of patients

Rini BI et al. *Clin Genitourin Cancer* 2021;[Online ahead of print].

Meet The Professor with Dr Hutson

MODULE 1: Cases from Drs Hammers and Ma

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Dr Hutson

- A single-arm, multicenter Phase II study of lenvatinib with everolimus for patients with advanced RCC
- Time to resolution of axitinib-related adverse events after treatment interruption for patients with advanced RCC

MODULE 4: Key Data Sets

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

	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.

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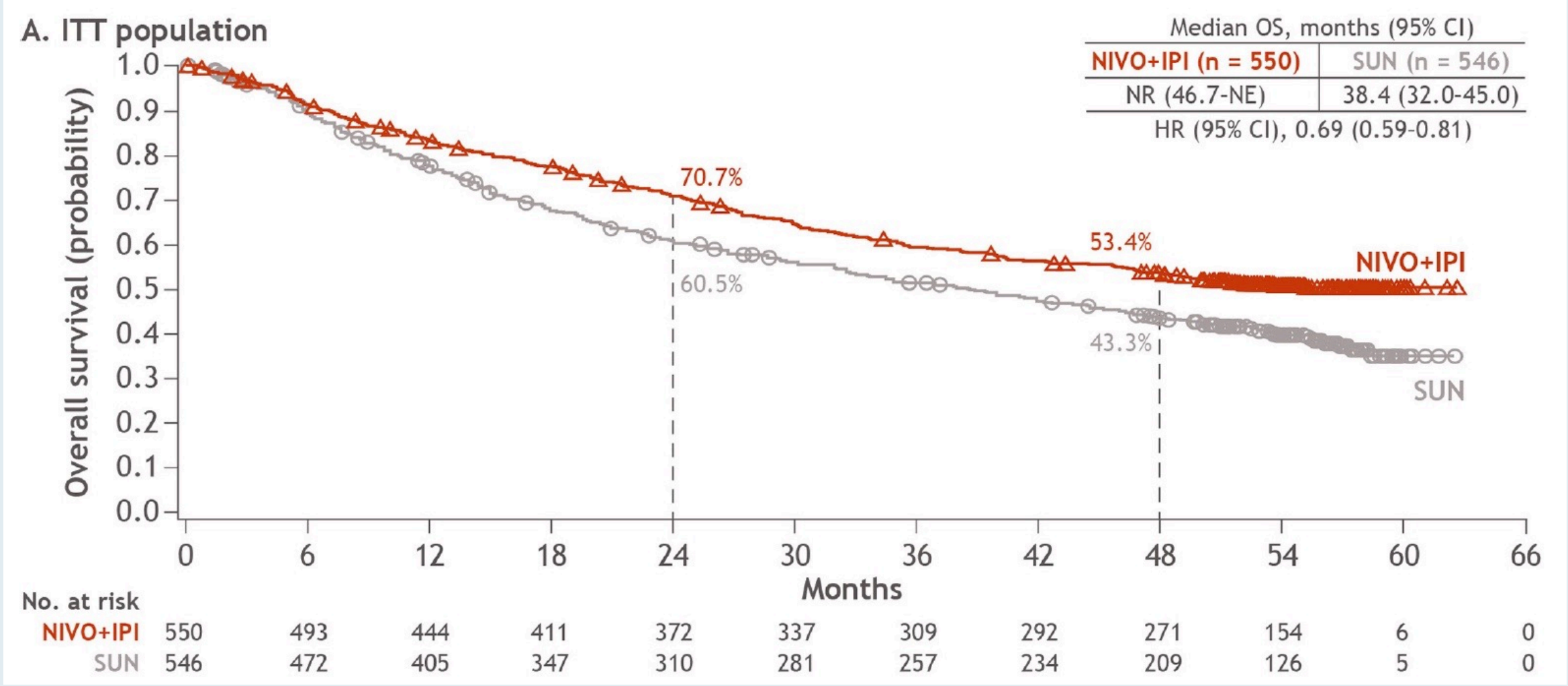
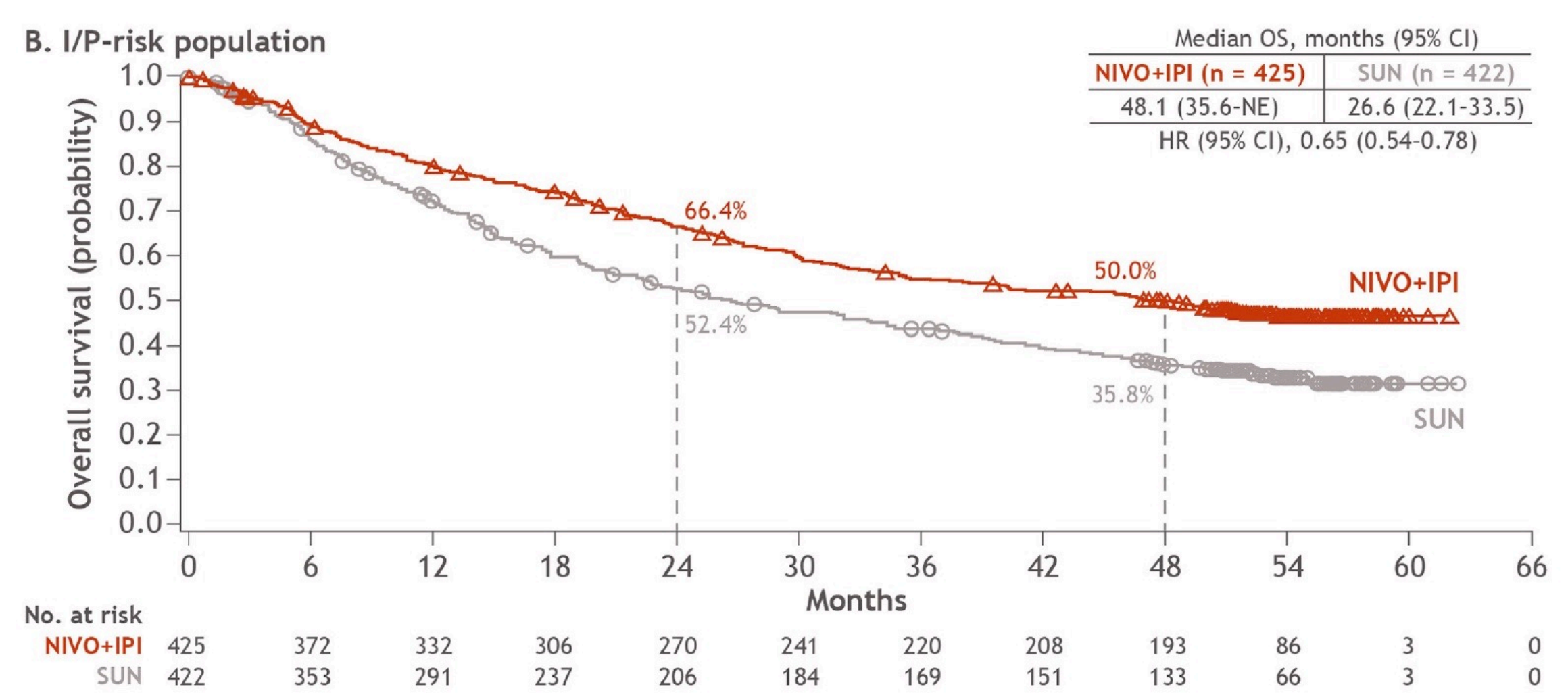
CheckMate 214: Overall Survival (ITT)



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.

FDA Approves Nivolumab with Cabozantinib for Advanced RCC

Press Release: January 22, 2021

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

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

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-nivolumab-plus-cabozantinib-advanced-renal-cell-carcinoma

RTP RESEARCH TO PRACTICE

ORIGINAL ARTICLE

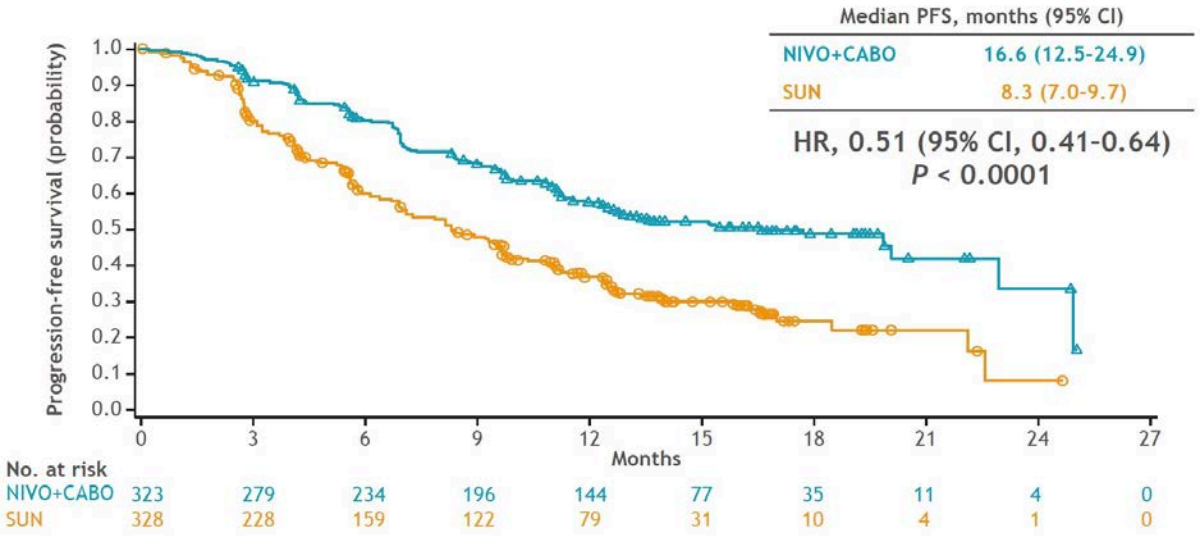
Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

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*

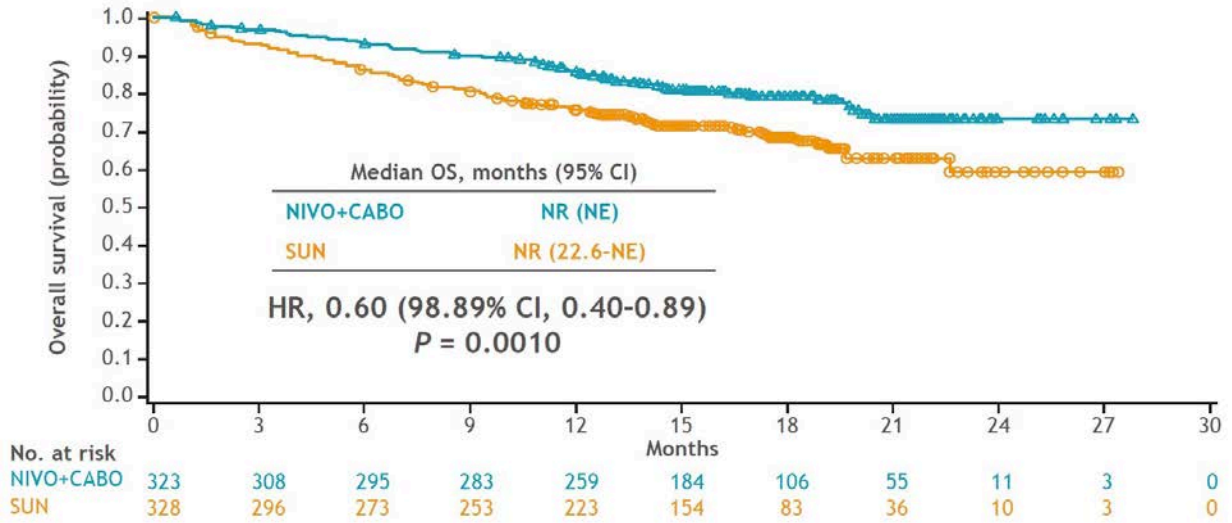
N Engl J Med 2021;384(9):829-41.

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

Progression-free survival per BICR



Overall survival



Choueiri TK et al. *N Engl J Med* 2021;384(9):829-41; ESMO 2020;Abstract 696O.

RTP RESEARCH TO PRACTICE

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

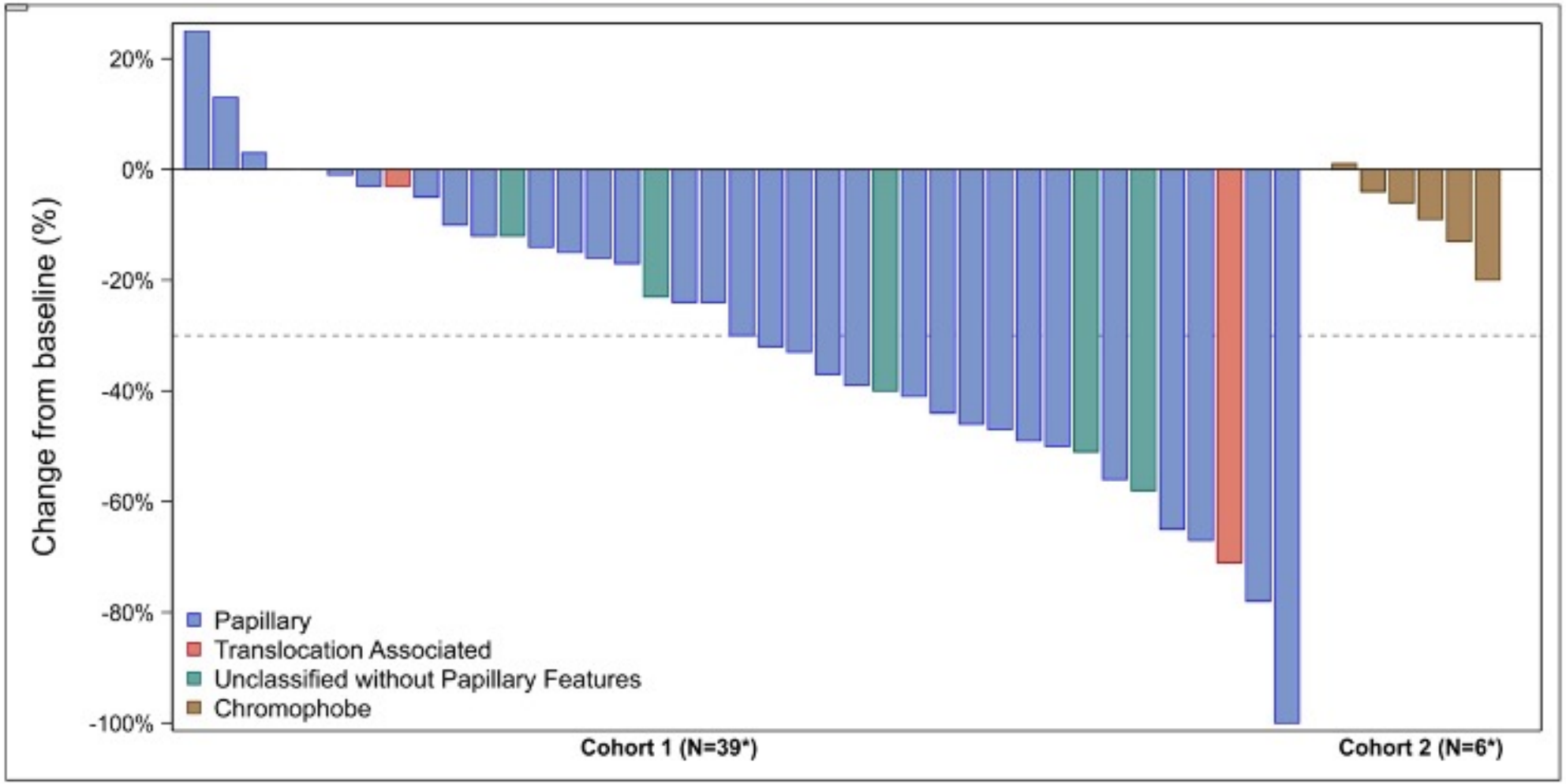
Chung-Han Lee, Martin H Voss, Maria Isabel Carlo, Ying-Bei Chen, Ed Reznik, Andrea Knezevic, Robert A Lefkowitz, Natalie Shapnik, Diana Tassone, Chloe Dadoun, Mark Zucker, Neil J. Shah, Colette Ngozi Owens, Deaglan Joseph McHugh, David Henry Aggen, Andrew Leonard Laccetti, Ritesh Kotecha, Darren R. Feldman,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

June 6, 2021

Corresponding Author Contact:
Dr. Chung-Han Lee

Lee CH et al. ASCO 2021;Abstract 4509.

Maximum Change in Target Lesions by Histology



Lee CH et al. ASCO 2021;Abstract 4509.

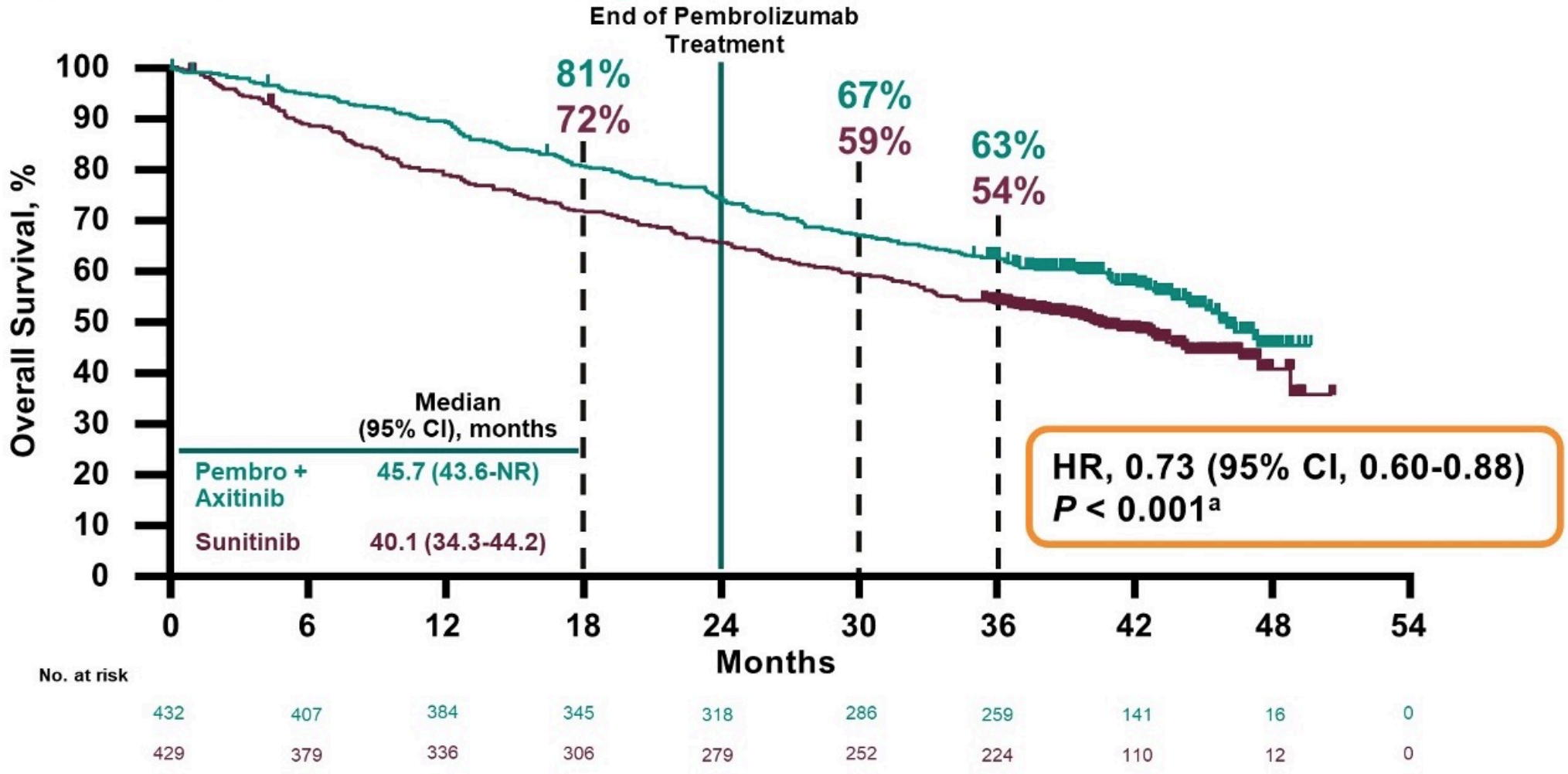
Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

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.

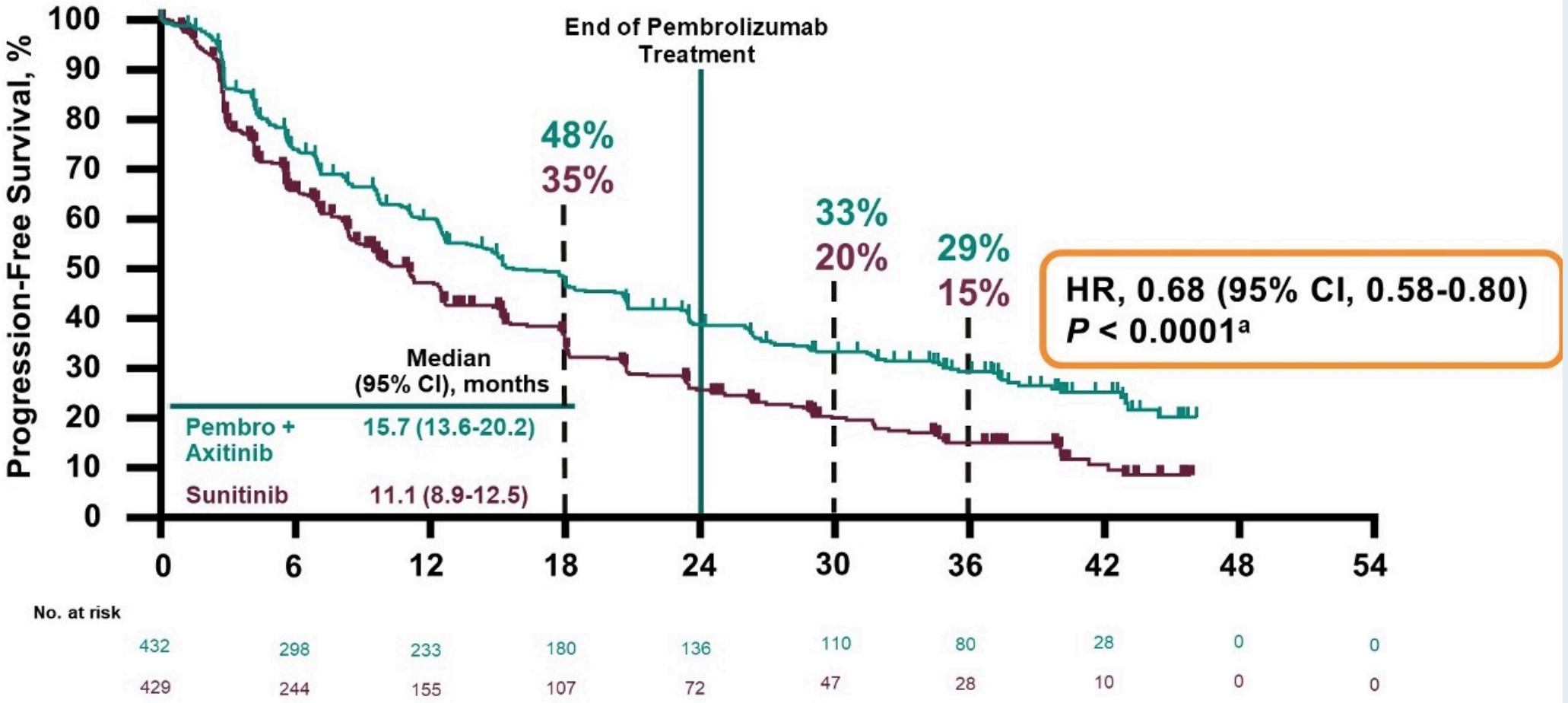
OS in the ITT Population



[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

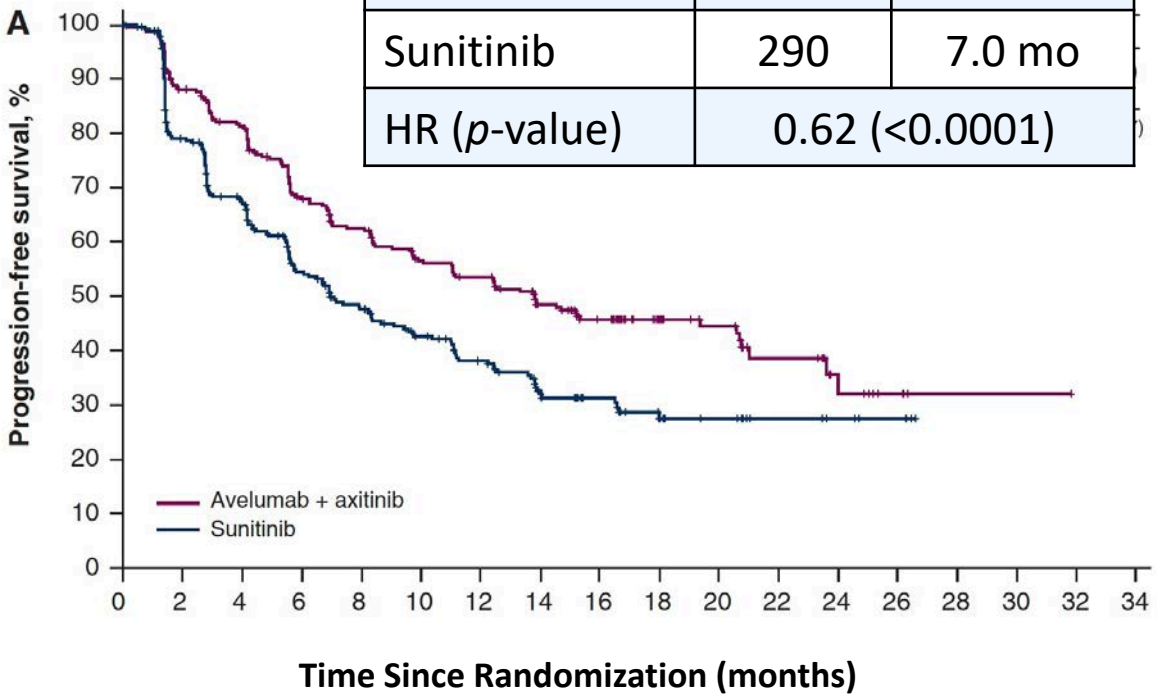
	PD-L1-Positive		Overall	
	Avelumab + Axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + Axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing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

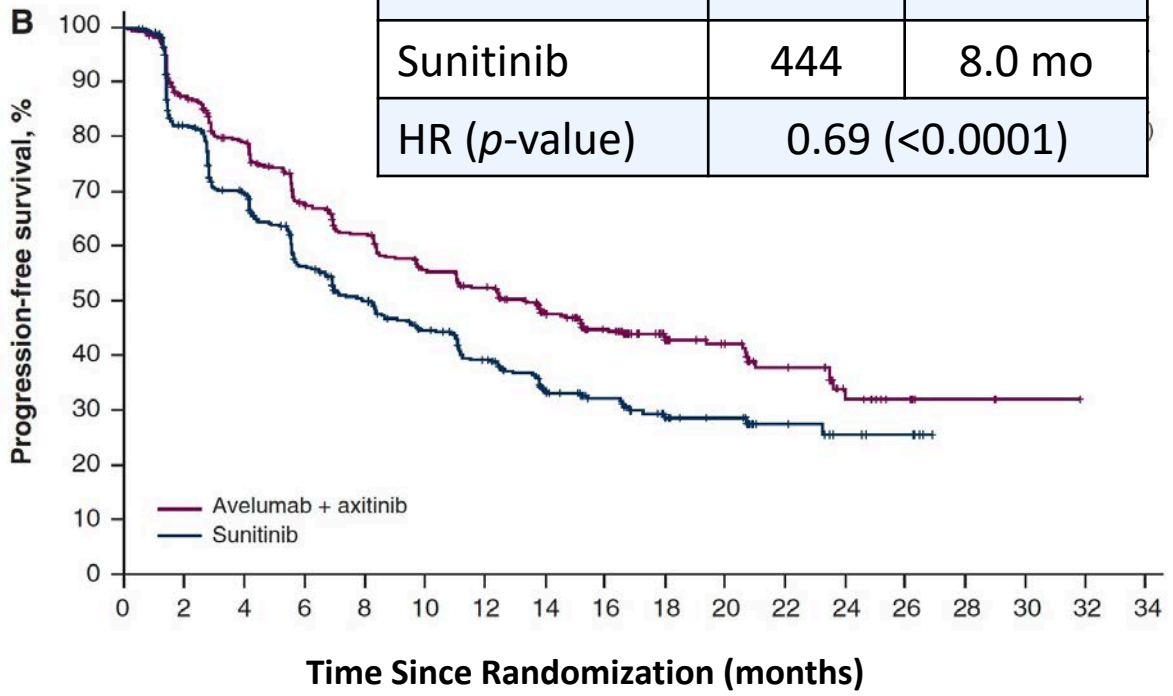
PD-L1 ≥ 1% Population

	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.

The NEW ENGLAND JOURNAL of MEDICINE

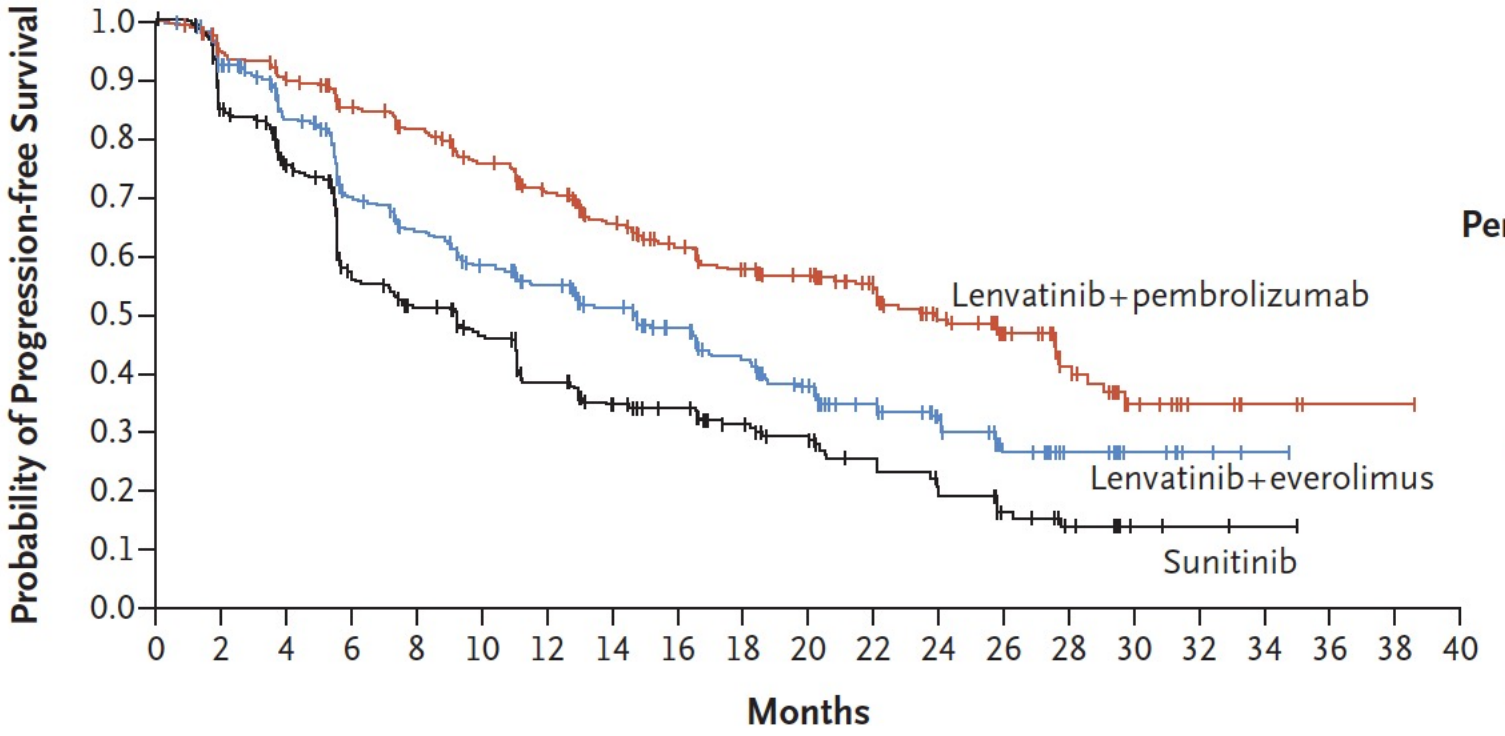
ORIGINAL ARTICLE

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)

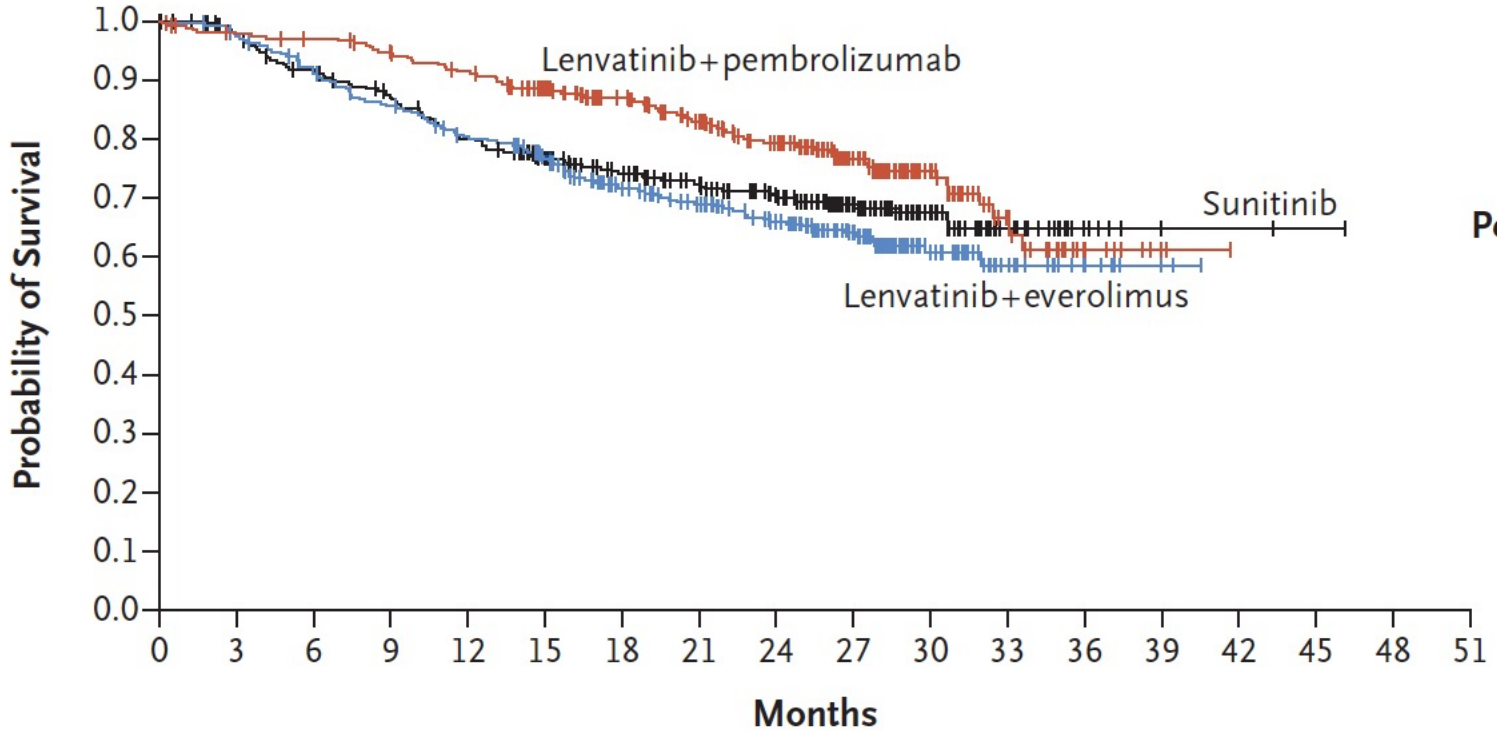
Hazard ratio for disease progression or death (lenvatinib+ pembrolizumab vs. sunitinib), 0.39 (95% CI, 0.32–0.49); P<0.001

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

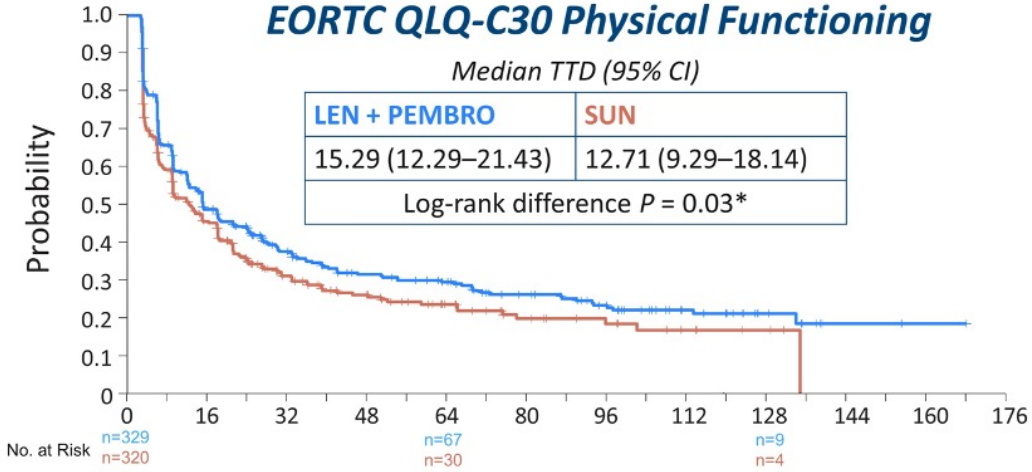
Health-Related Quality-of-life Analysis From the Phase 3 CLEAR Trial of Lenvatinib Plus Pembrolizumab or Everolimus vs Sunitinib for Patients With Advanced Renal Cell Carcinoma

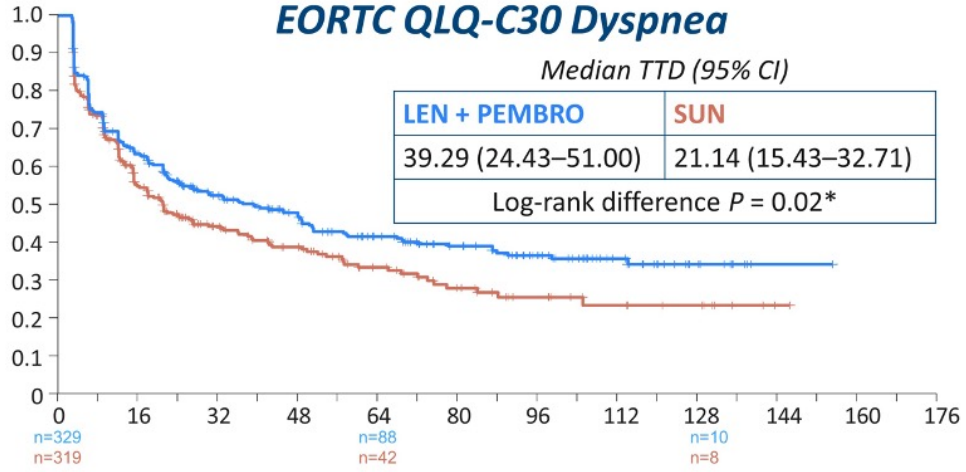
Robert Motzer[1], Camillo Porta[2], Boris Alekseev[3], Sun Young Rha[4], Toni Choueiri[5], Maria Jose Mendez-Vidal[6], Sung-Hoo Hong[7], Anil Kapoor[8], Jeffrey C. Goh[9], Masatoshi Eto[10], Jinyi Wang[11], Janice Pan[12], Alemseged Ayele Asfaw[13], Cixin Steven He[12], Kalgi Mody[12], David Cella[14]

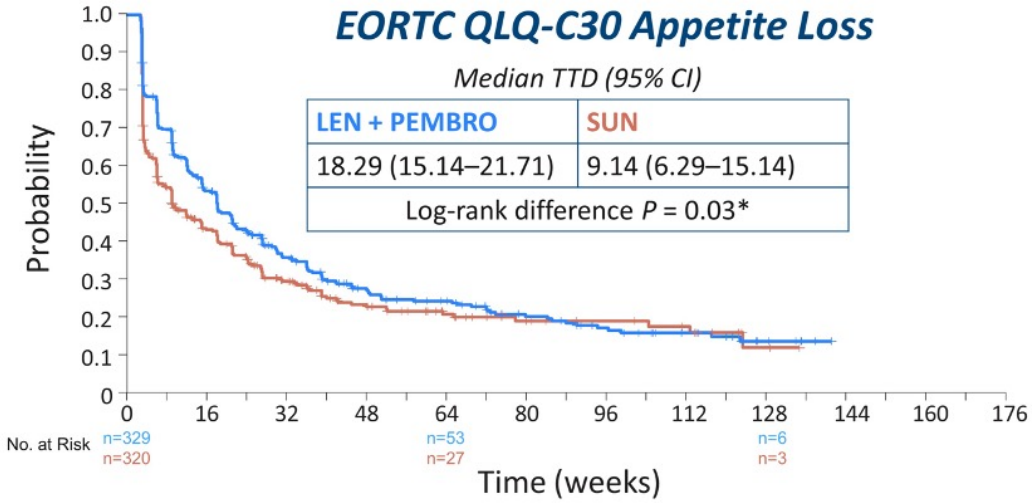
[1]Memorial Sloan Kettering Cancer Center; New York, NY, USA; [2]San Matteo University Hospital Foundation, Pavia, Italy; [3]P.A. Herzen Moscow Oncological Research Institute, Moscow, Russia; [4]Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Maimonides Institute for Biomedical Research of Cordoba (IMIBIC) Hospital Universitario Reina Sofía, Córdoba, Spain; [7]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, South Korea; [8]McMaster University Hamilton, Ontario, Canada; [9]ICON Research, South Brisbane & University of Queensland, St Lucia, Queensland, Australia; [10]Kyushu University, Fukuoka, Japan; [11]RTI Health Solutions, Research Triangle Park, NC, USA; [12]Eisai Inc., Woodcliff Lake, NJ, USA; [13]Merck & Co., Inc., Kenilworth, NJ, USA; [14]Northwestern University, Chicago, IL, USA.

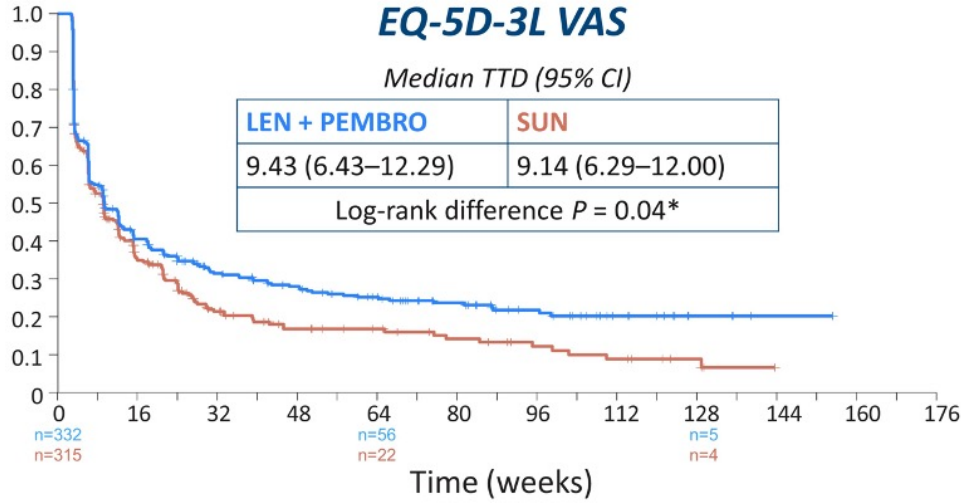
Motzer R et al. ASCO 2021;Abstract 4502.

Time to First Deterioration: Lenvatinib + Pembrolizumab versus Sunitinib









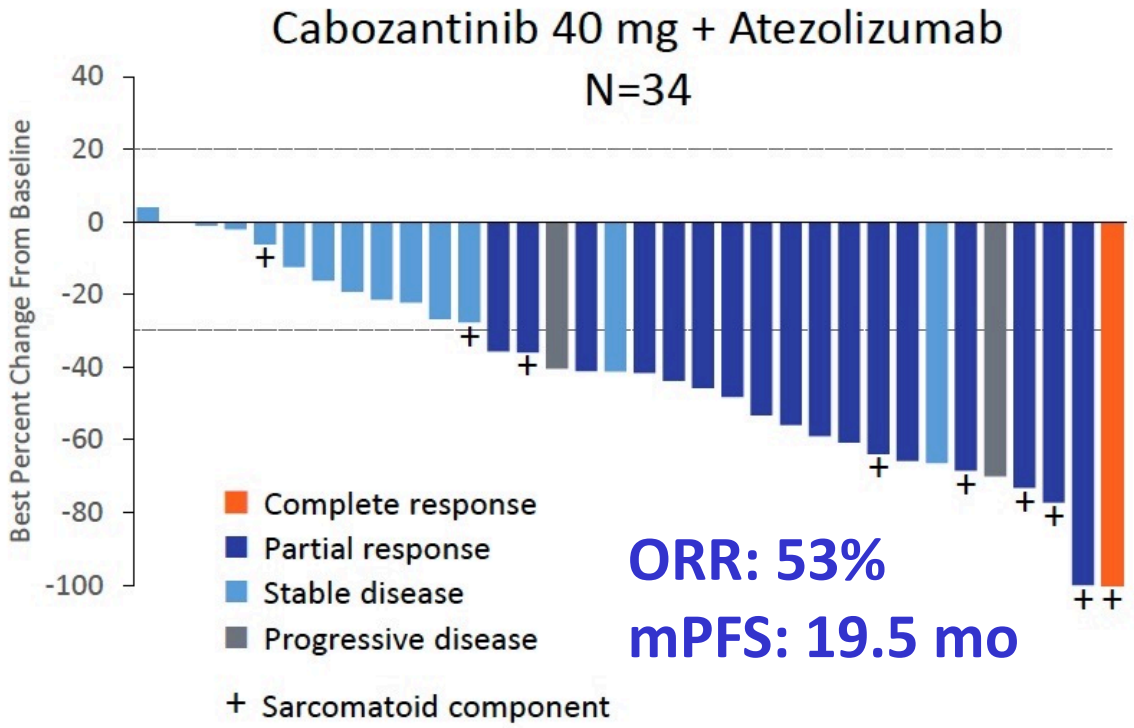
Motzer R et al. ASCO 2021;Abstract 4502.

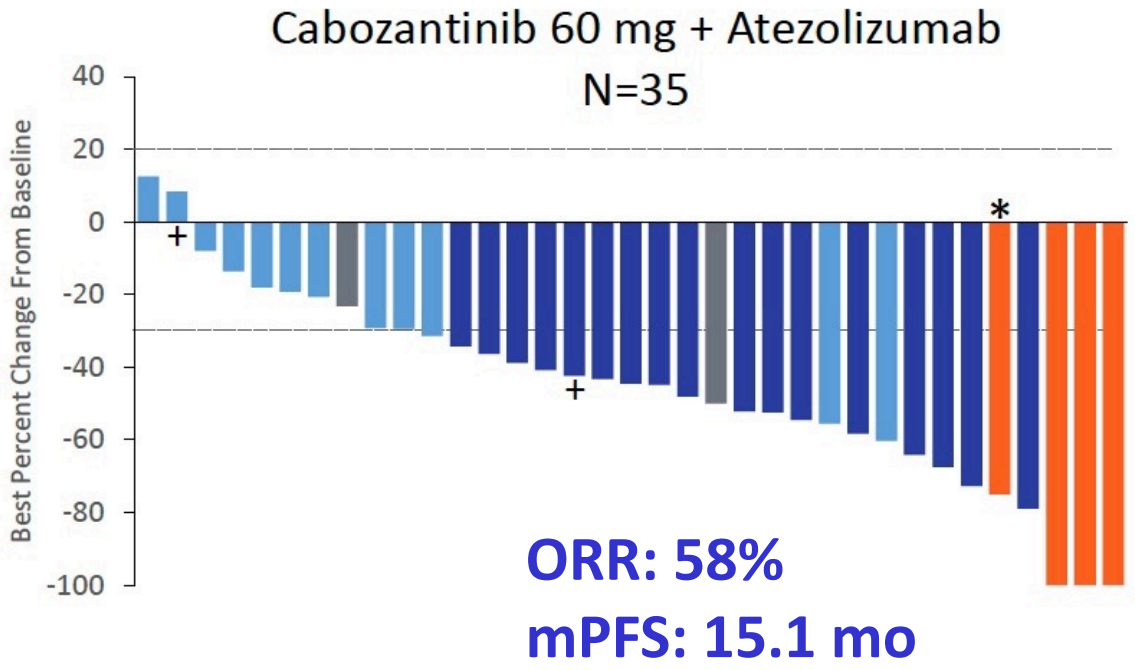
Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

Pal S et al.

ESMO 2020;Abstract 702O.

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





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

RTP RESEARCH TO PRACTICE

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

Study acronym	Target accrual	Randomization	Primary endpoint(s)	Estimated primary completion
COSMIC-313	840	• 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

RTP RESEARCH TO PRACTICE

Sequencing of Therapy for Patients with Relapsed/Refractory (R/R) 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."

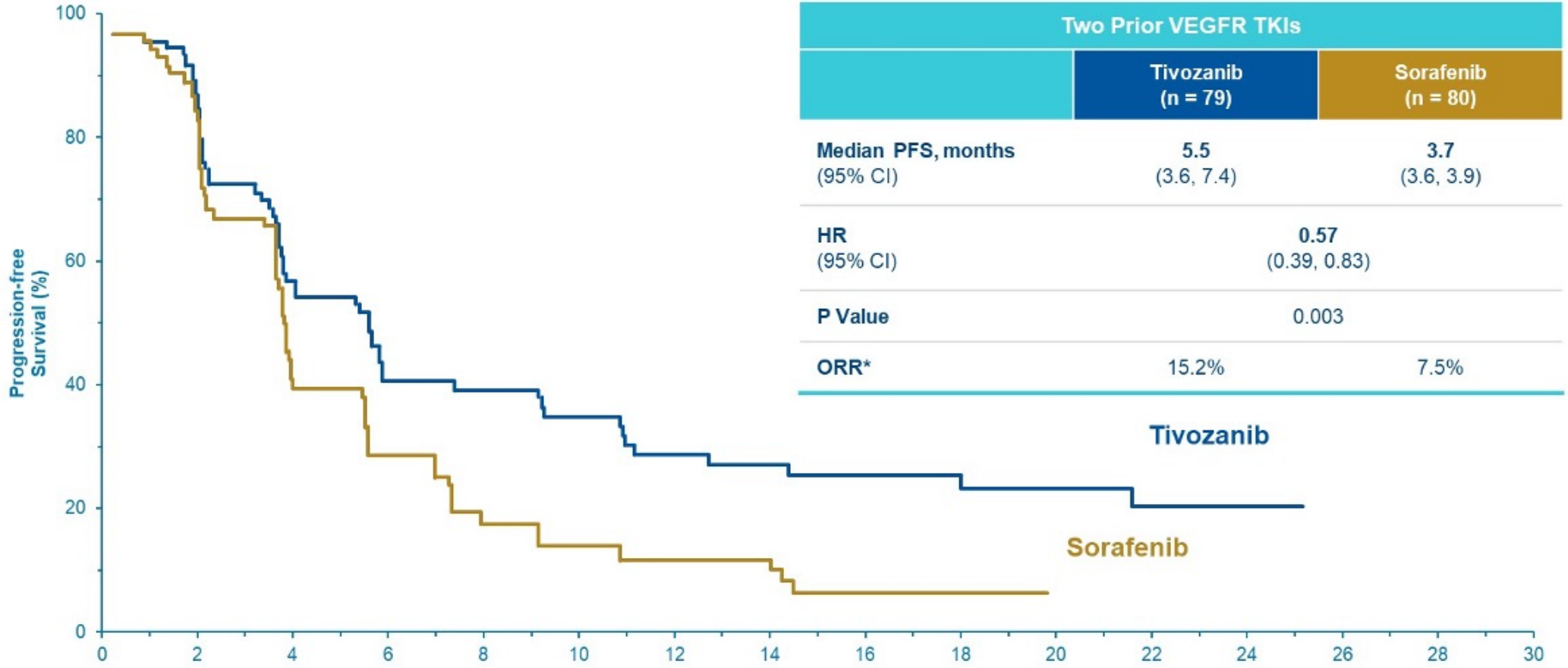
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

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 2 Prior TKIs Patient Subgroup



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

Press Release – March 16, 2021

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

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

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

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

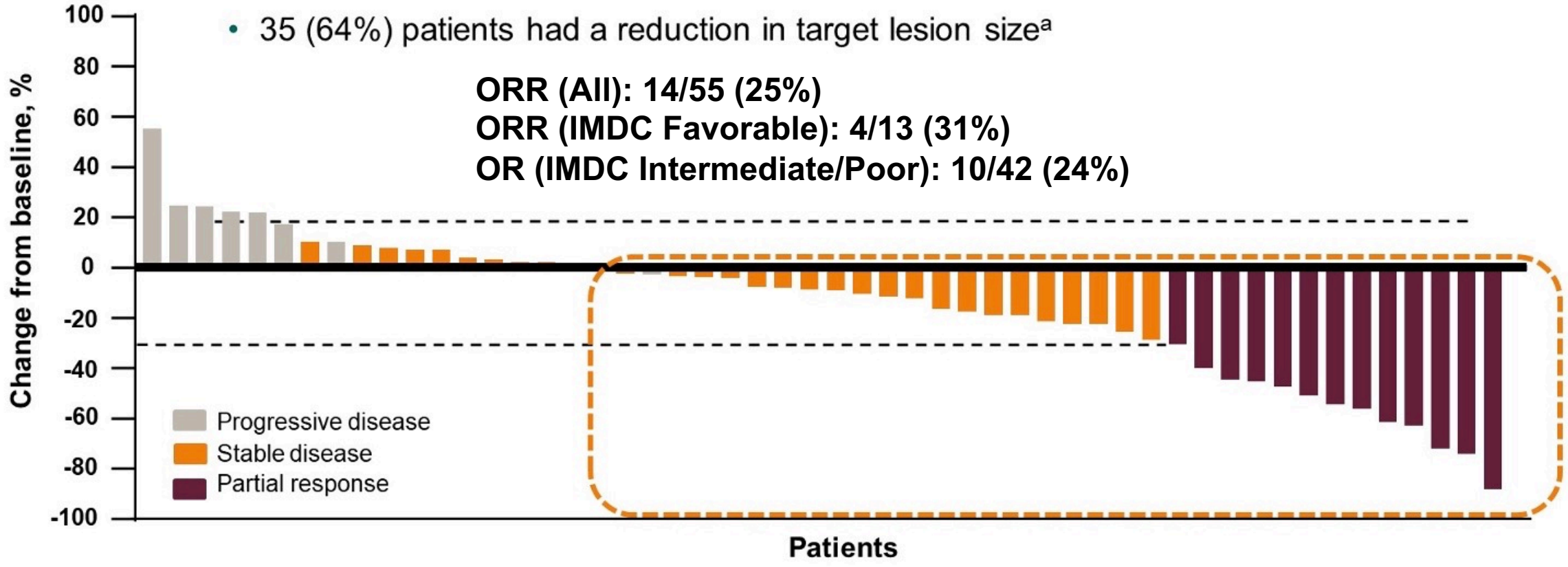
Genitourinary Cancers Symposium 2021;Abstract 273

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

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

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

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



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

Bauer TM et al. Genitourinary Cancers Symposium 2021;Abstract 273.

RTP RESEARCH TO PRACTICE

All-Cause Adverse Events ≥20% (ccRCC Cohort)

All cause AEs in ≥20% of patients, n (%)	Belzutifan N = 55			
	Any Grade	Grade 3	Grade 4[a]	Grade 5[b]
Any	55 (100)	33 (60)	2 (4)	4 (7)
Anemia	42 (76)	15 (27)	0 (0)	0 (0)
Fatigue	39 (71)	3 (5)	0 (0)	0 (0)
Dyspnea	27 (49)	3 (5)	0 (0)	0 (0)
Nausea	20 (36)	1 (2)	0 (0)	0 (0)
Cough	17 (31)	0 (0)	0 (0)	0 (0)
Hypoxia	17 (31)	9 (16)	0 (0)	0 (0)
Vomiting	16 (29)	0 (0)	0 (0)	0 (0)
Edema peripheral	15 (27)	0 (0)	0 (0)	0 (0)
Arthralgia	14 (25)	0 (0)	0 (0)	0 (0)
Blood creatinine increased	14 (25)	1 (2)	0 (0)	0 (0)
Headache	14 (25)	1 (2)	0 (0)	0 (0)
Dizziness	13 (24)	0 (0)	0 (0)	0 (0)
Back pain	12 (22)	1 (2)	0 (0)	0 (0)
Diarrhea	12 (22)	0 (0)	0 (0)	0 (0)
Hyperkalemia	12 (22)	1 (2)	0 (0)	0 (0)
Constipation	12 (22)	0 (0)	0 (0)	0 (0)
Dehydration	11 (20)	1 (2)	0 (0)	0 (0)

[a]2 patients experienced 4 grade 4 adverse events (sepsis [n = 2], hypercalcemia [n = 1], respiratory failure [n = 1]). [b]4 patients experienced grade 5 adverse events (disease progression [n = 1], malignant neoplasm progression [n = 1], acute kidney injury [n = 1], cardiac arrest [n = 1]). Data cutoff: June 1, 2020.

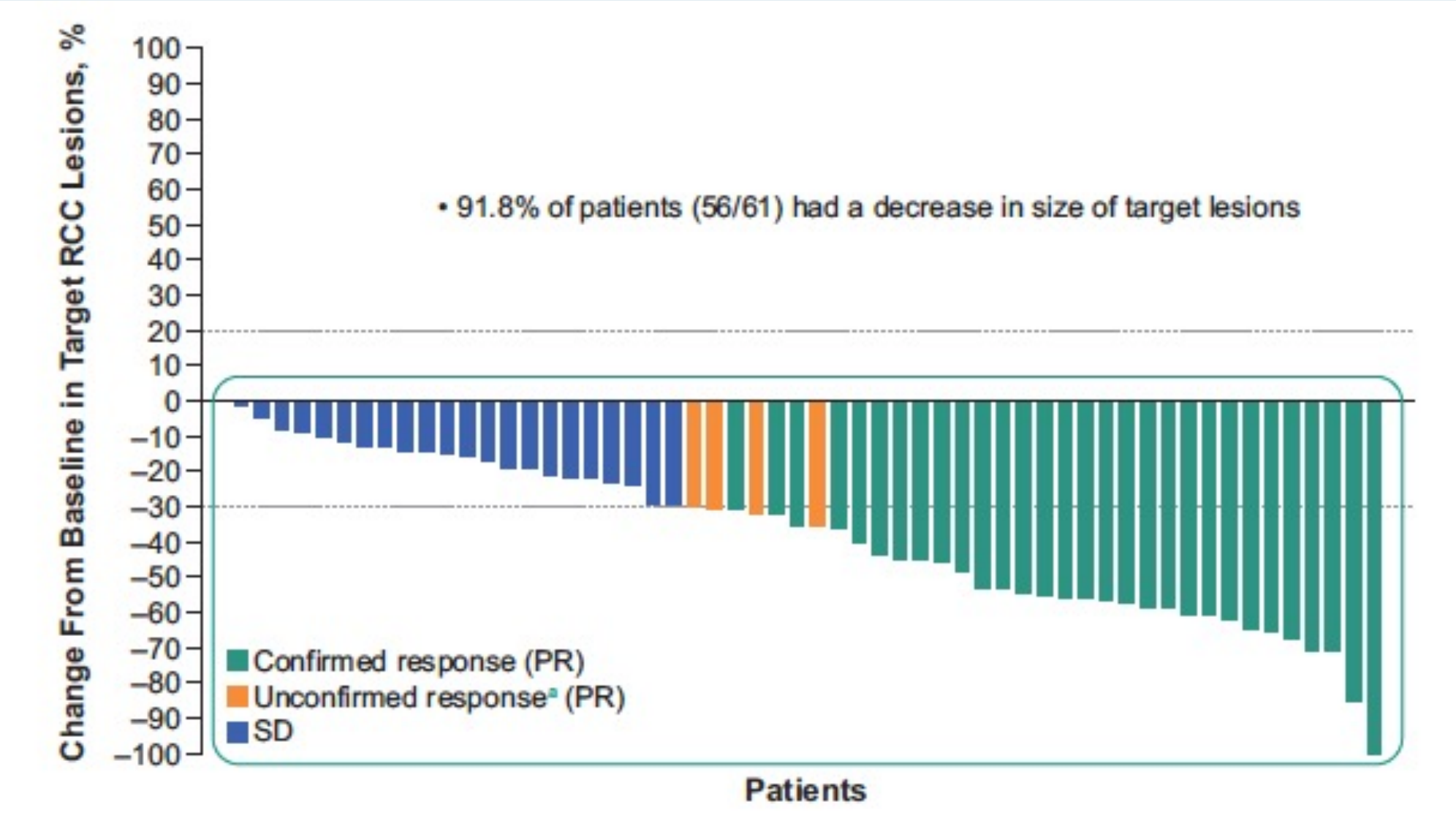
Bauer TM et al. Genitourinary Cancers Symposium 2021;Abstract 273.

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.

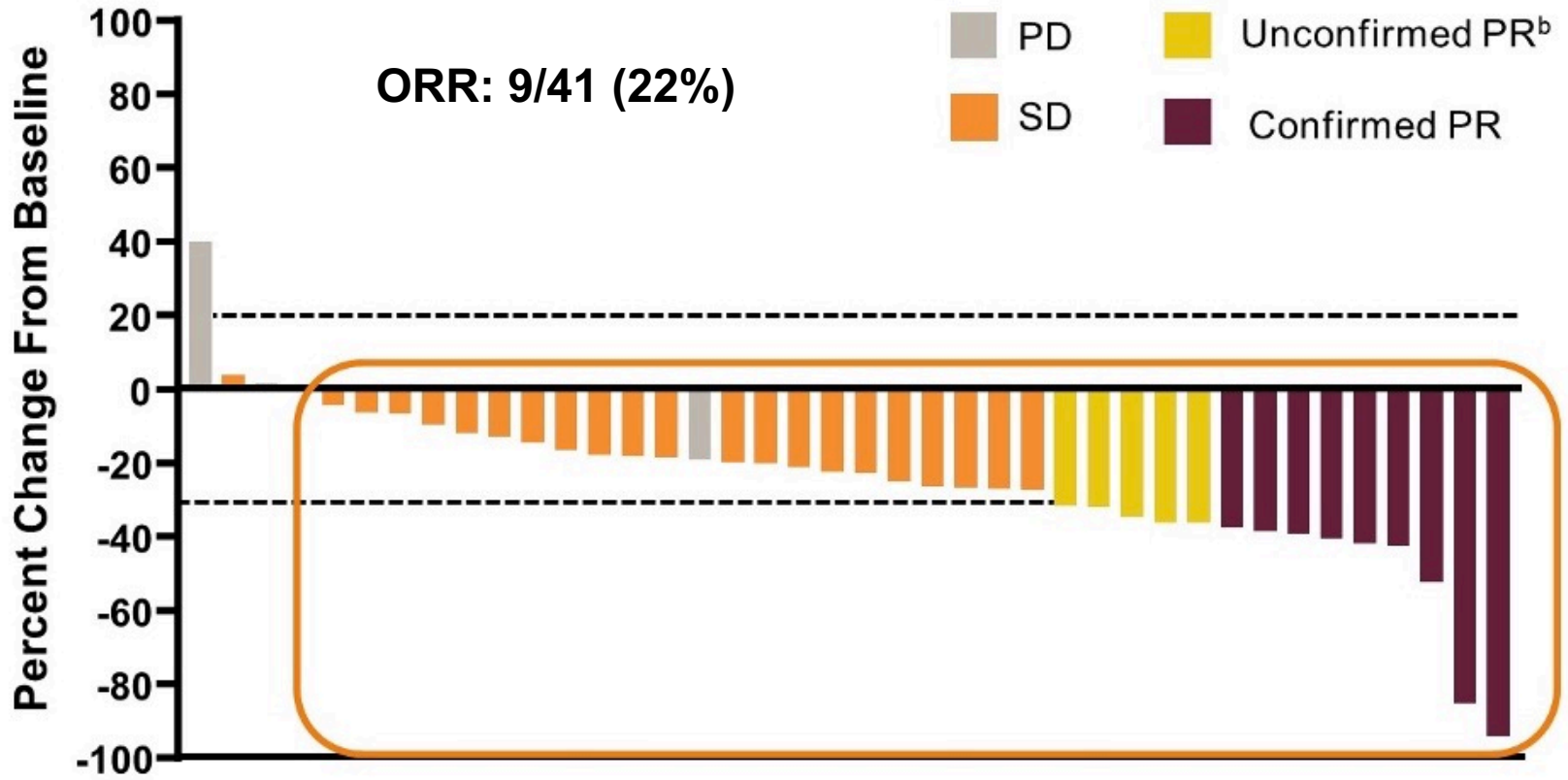
Phase 2 Study of the Oral Hypoxia-Inducible Factor 2α Inhibitor Belzutifan (MK-6482) in Combination With Cabozantinib in Patients With Advanced Clear Cell Renal Cell Carcinoma

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.

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Hodgkin and Non-Hodgkin Lymphomas

Thursday, June 17, 2021
5:00 PM – 6:00 PM ET

Faculty

Carla Casulo, MD
Jacklyn Gideon, MSN, AGPCNP-BC

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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