Meet The Professor

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

Thomas Powles, MBBS, MRCP, MD
Professor of Genitourinary Oncology
Barts Cancer Institute
Director of Barts Cancer Centre
Queen Mary University of London
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Commercial Support

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Dr Love — Disclosures

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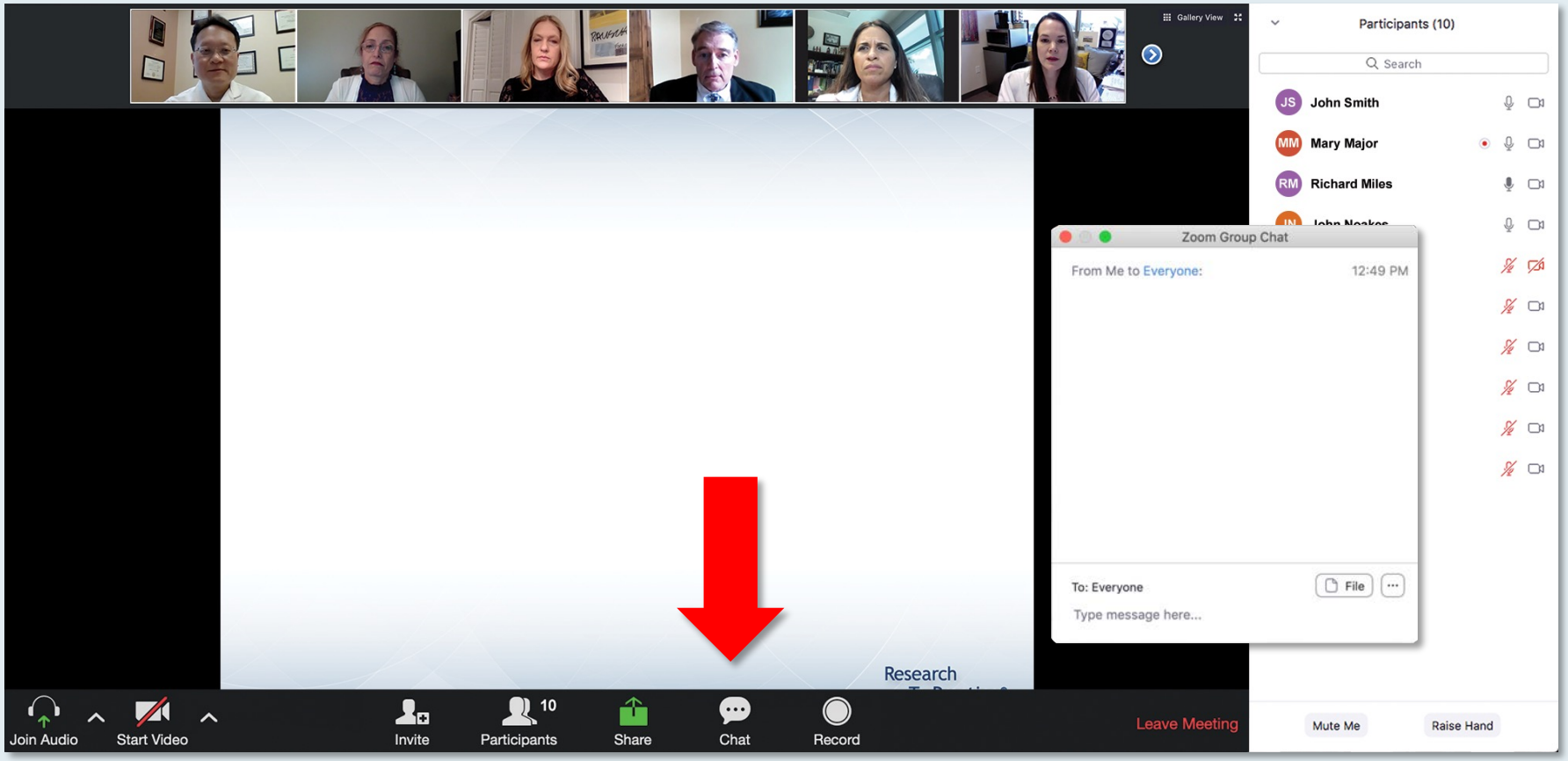

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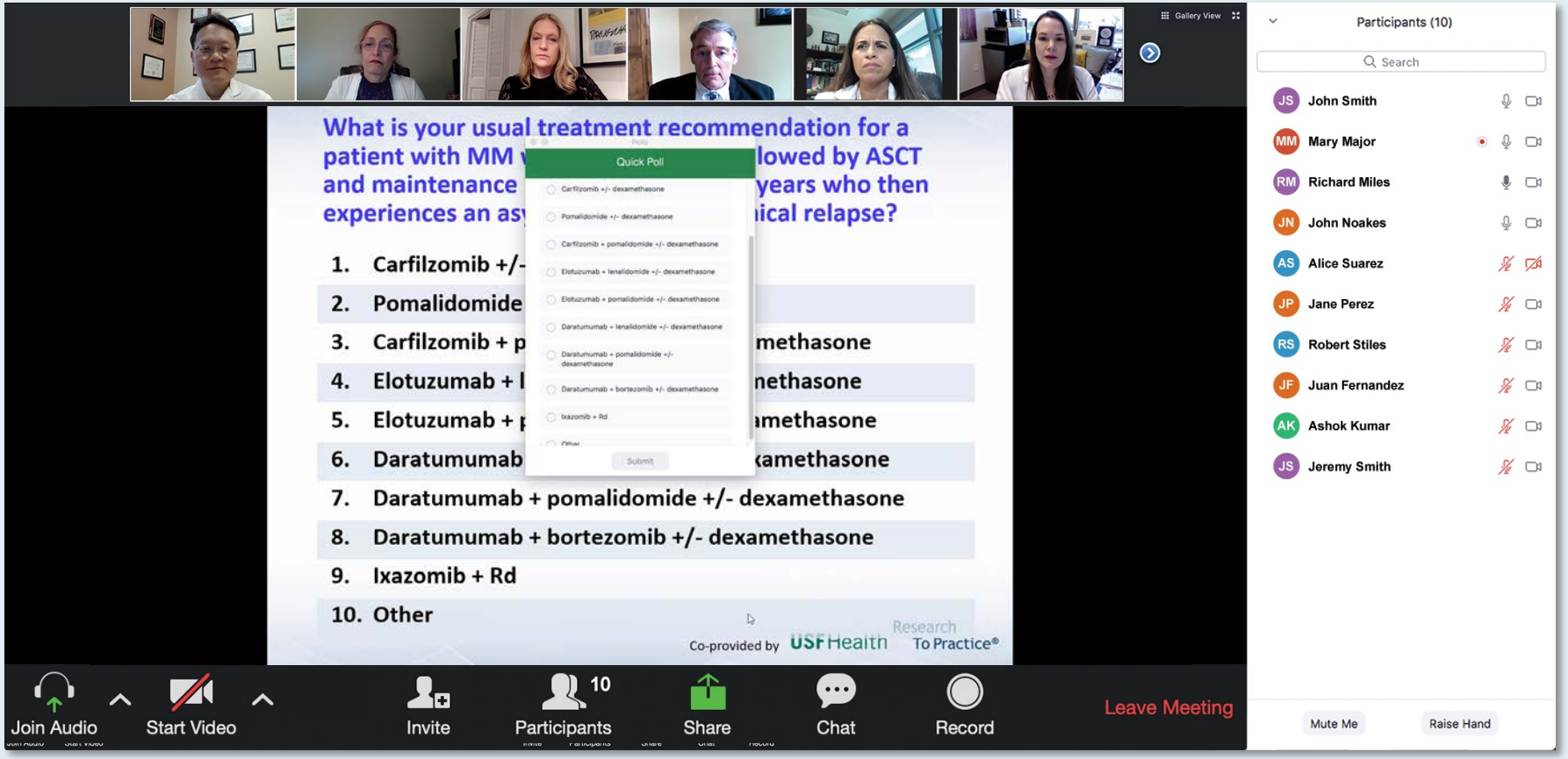

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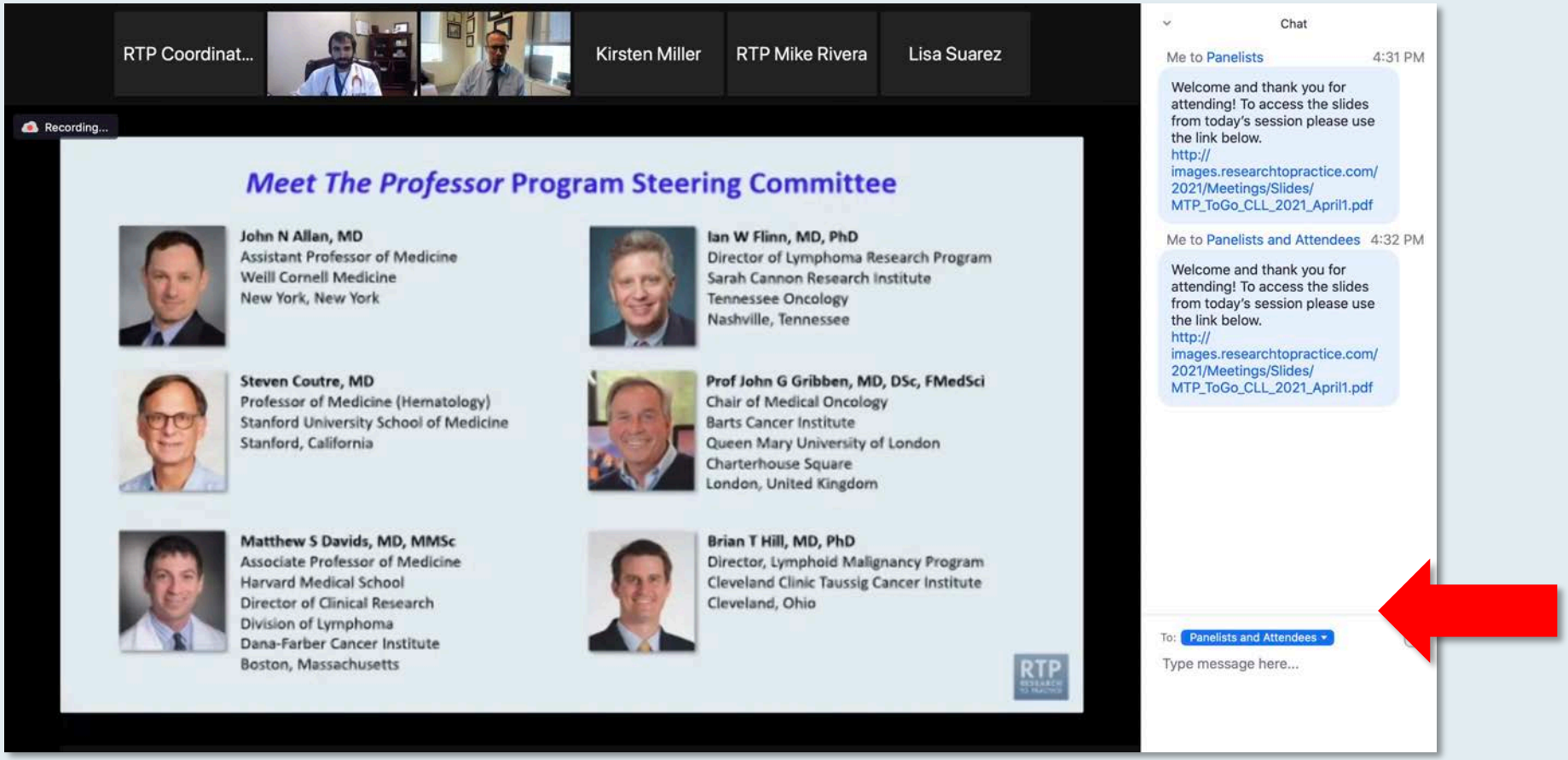

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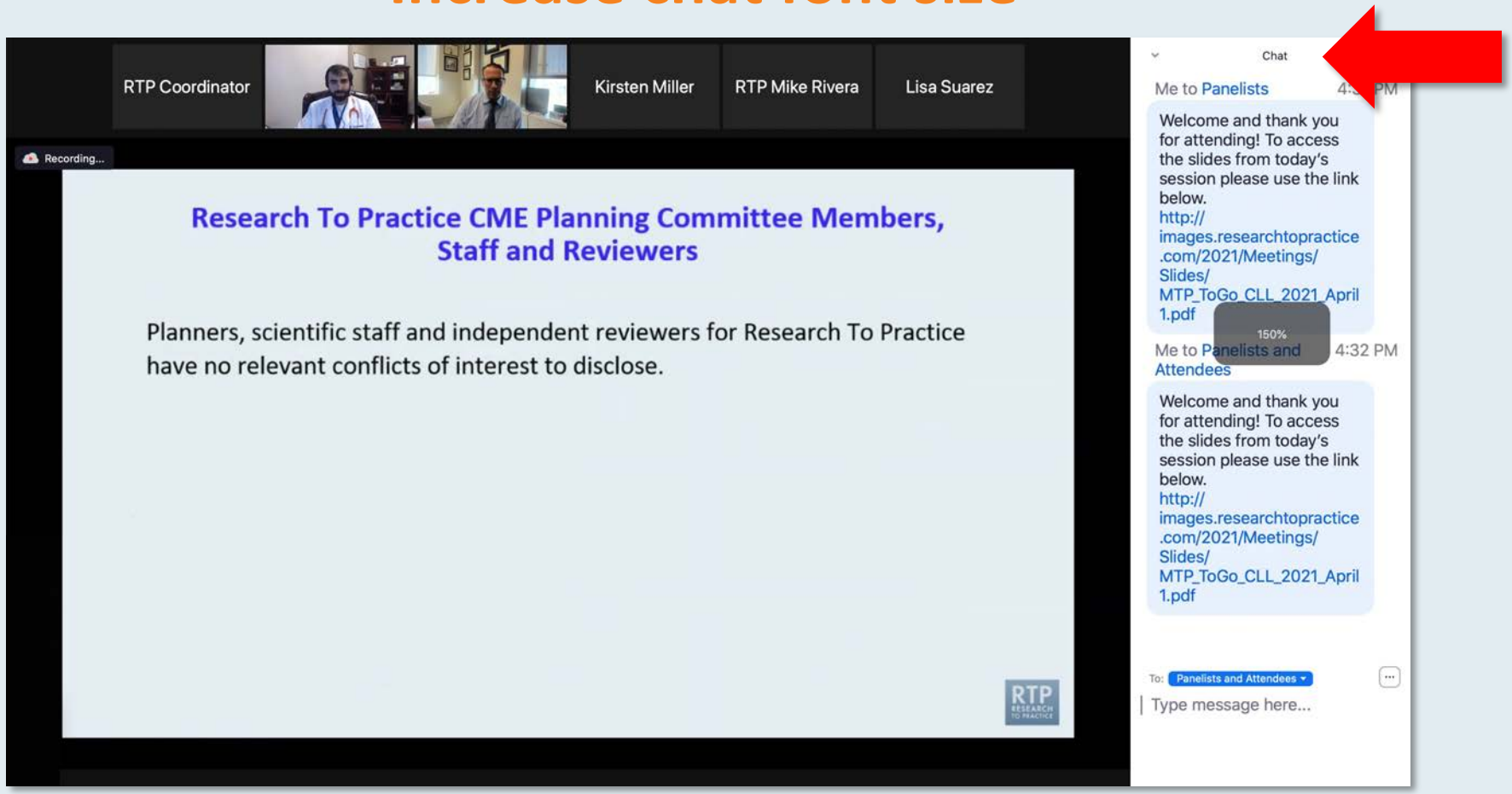

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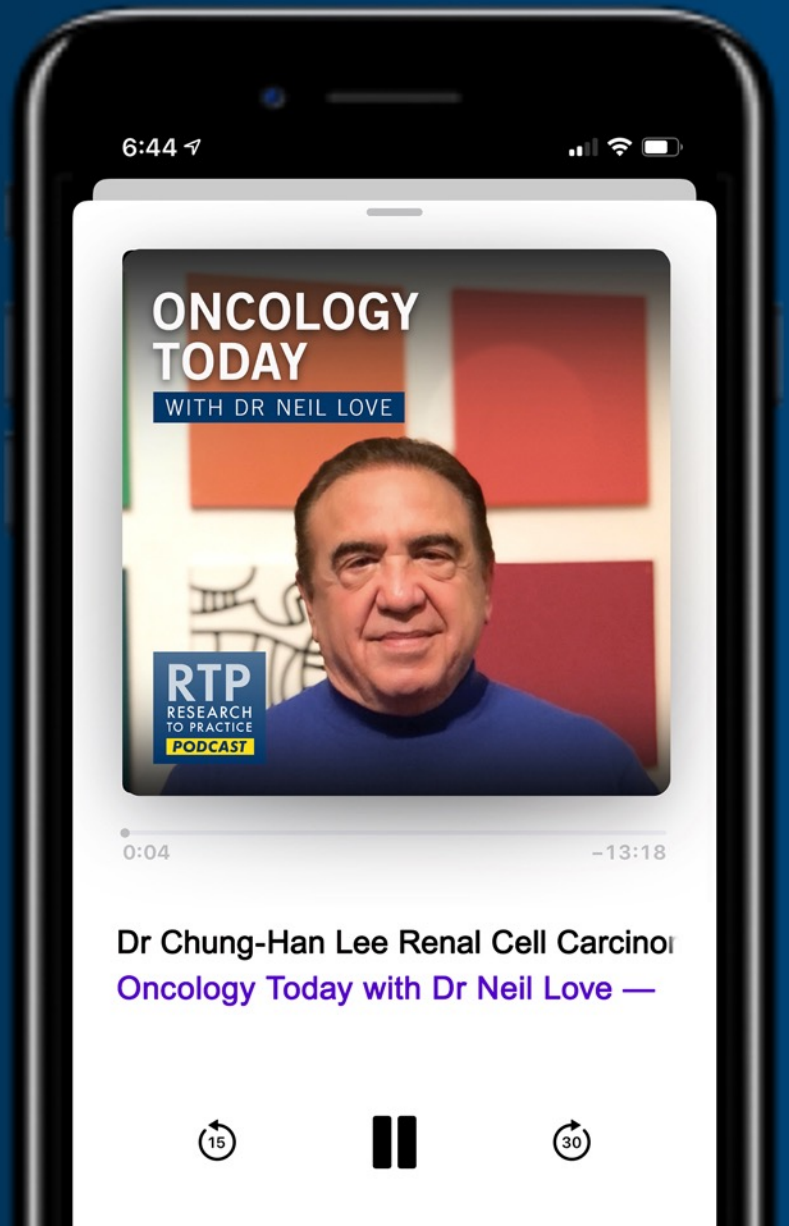

Three Exciting Educational Events Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

In Partnership with the University of Nebraska Medical Center

Expert Second Opinion — Acute Myeloid Leukemia and Myelodysplastic Syndromes

Monday, August 9, 2021
7:00 PM – 8:30 PM ET

Faculty
Krishna Gundabolu, MD
Richard M Stone, MD
Eunice S Wang, MD

Moderator
Harry Paul Erba, MD, PhD

Beyond the Guidelines — Chronic Lymphocytic Leukemia

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Cases from the Community — Multiple Myeloma

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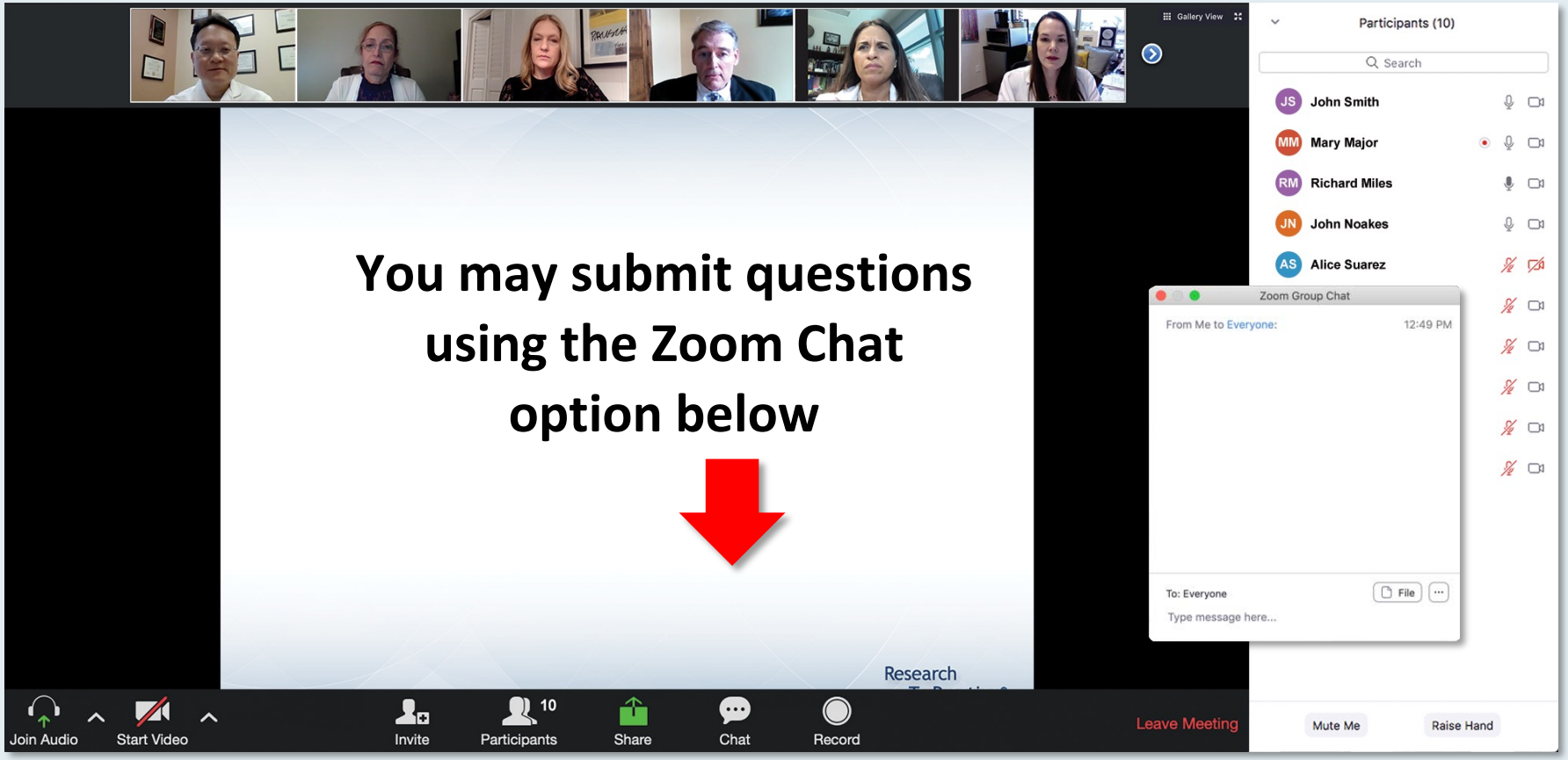

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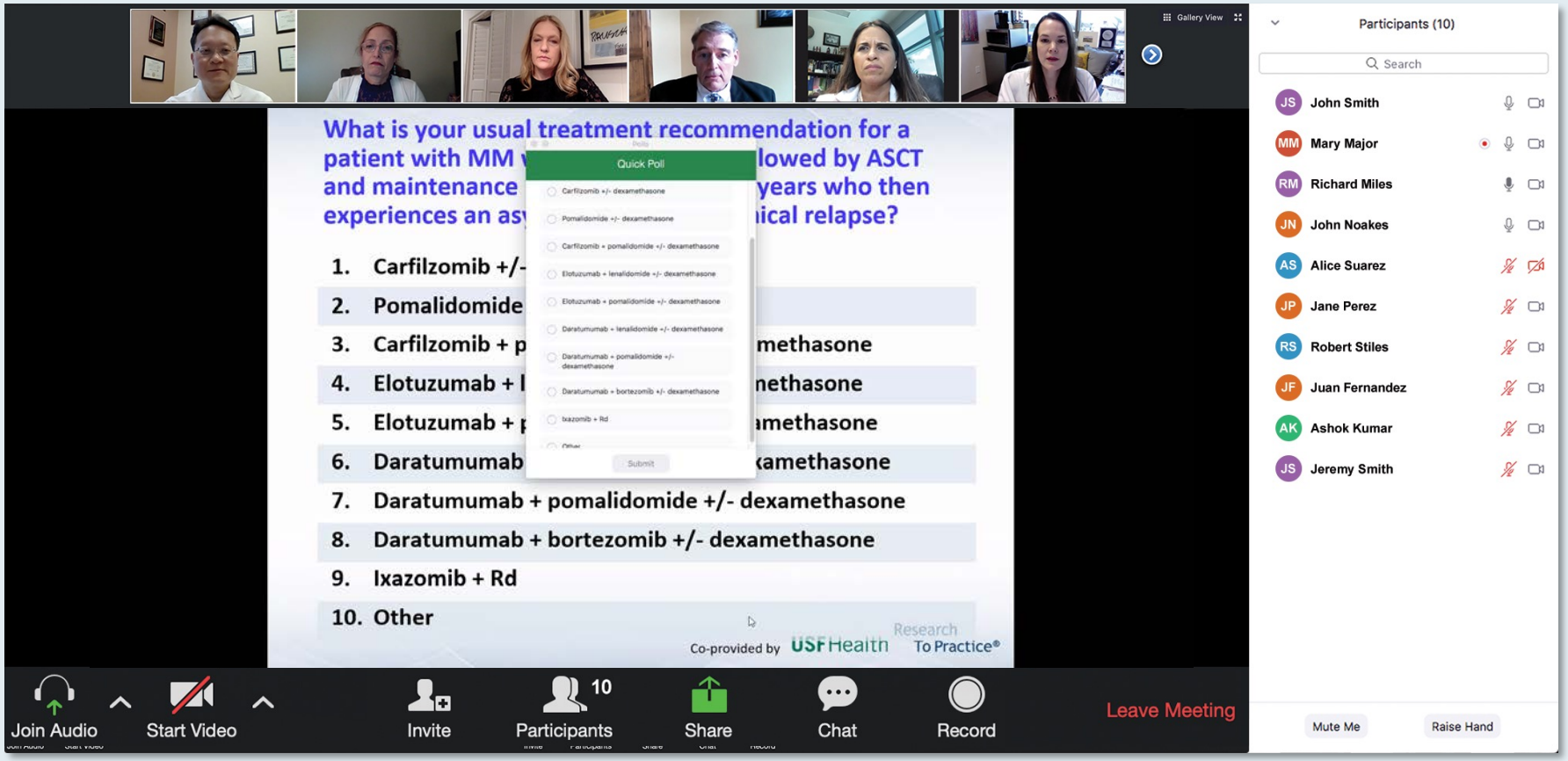

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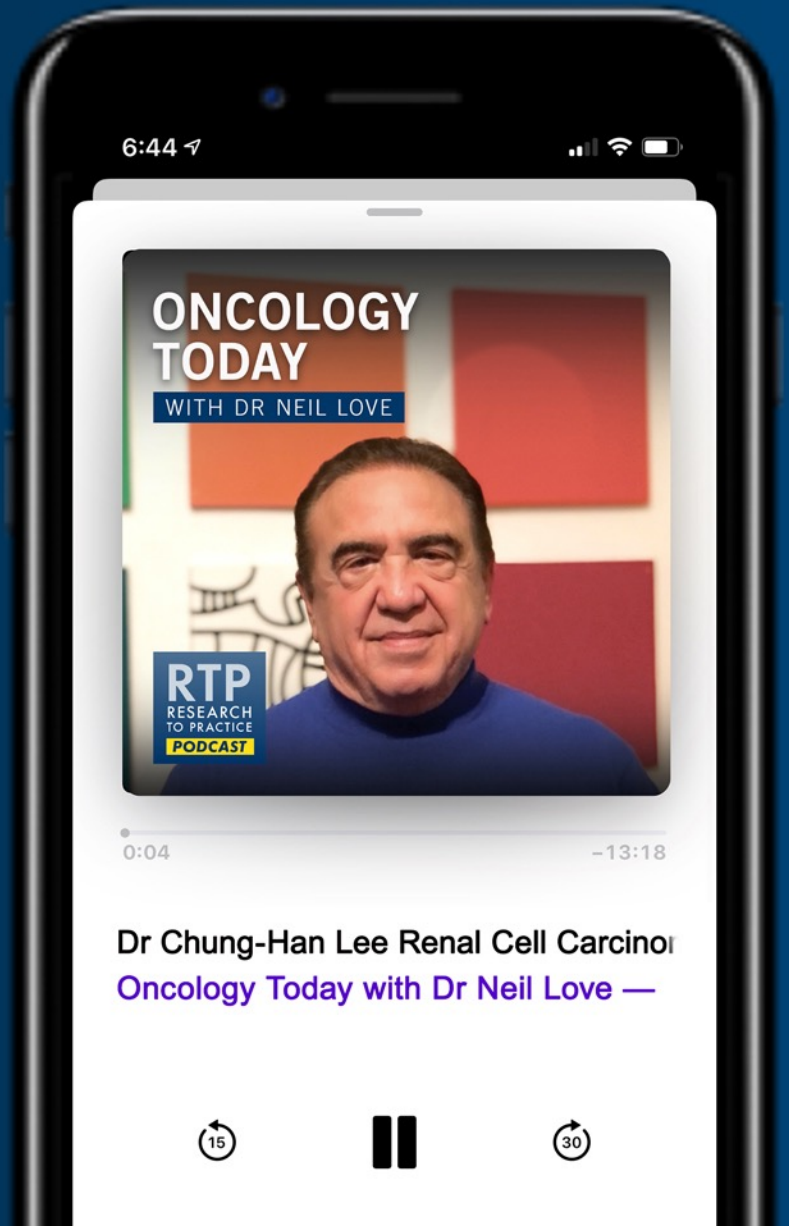

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Naples, Florida

Ranju Gupta, MD
Attending Physician
Co-Director
Cardio-Oncology Program
LVPG Hematology Oncology Associates
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Meet The Professor with Prof Powles

MODULE 1: Case Presentations

- Dr Lamar: A 64-year-old woman with metastatic clear cell RCC
- Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis
- Dr Gupta: A 61-year-old woman with metastatic papillary RCC
- Dr Jonasch: A 67-year-old man with metastatic RCC
- Dr Flores: An obese 61-year-old man with metastatic RCC
- Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein
- Dr Brooks: A 61-year-old man with metastatic clear cell RCC

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Prof Powles

MODULE 4: Key Data Sets

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Case Presentation – Dr Lamar: A 64-year-old woman with metastatic clear cell RCC

Dr Zanetta Lamar

- PMH: Rheumatoid arthritis treated by hydroxychloroquine
- 2019: Diagnosed with clear-cell RCC, s/p radical nephrectomy
- 9/2020: Rapidly growing scalp lesion; perihepatic/pancreatic, retroperitoneal, hilar and mediastinum adenopathy. Biopsy confirmed RCC, intermediate risk
  - Resolution of scalp lesions and adenopathy
- Ipilimumab/nivolumab, with resolution of scalp lesions after 3 cycles
  - Cycle 4: Bilateral parotid swelling requiring inpatient admission and IV steroids, several months to resolution

Questions

- What would you recommend if her disease progresses?

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Case Presentation – Dr Lamar: A 64-year-old woman with metastatic clear cell RCC (continued)

Dr Zanetta Lamar

- PMH: Rheumatoid arthritis treated by hydroxychloroquine
- 2019: Diagnosed with clear-cell RCC, s/p radical nephrectomy
- 9/2020: Rapidly growing scalp lesion; perihepatic/pancreatic, retroperitoneal, hilar and mediastinum adenopathy. Biopsy confirmed RCC, intermediate risk
  - Resolution of scalp lesions and adenopathy
- Ipilimumab/nivolumab, with resolution of scalp lesions after 3 cycles
  - Cycle 4: Bilateral parotid swelling requiring inpatient admission and IV steroids, several months to resolution
- ***She experienced the same facial and bilateral parotid swelling when she received the COVID-19 vaccine***
  - ***Again, treated with steroids***

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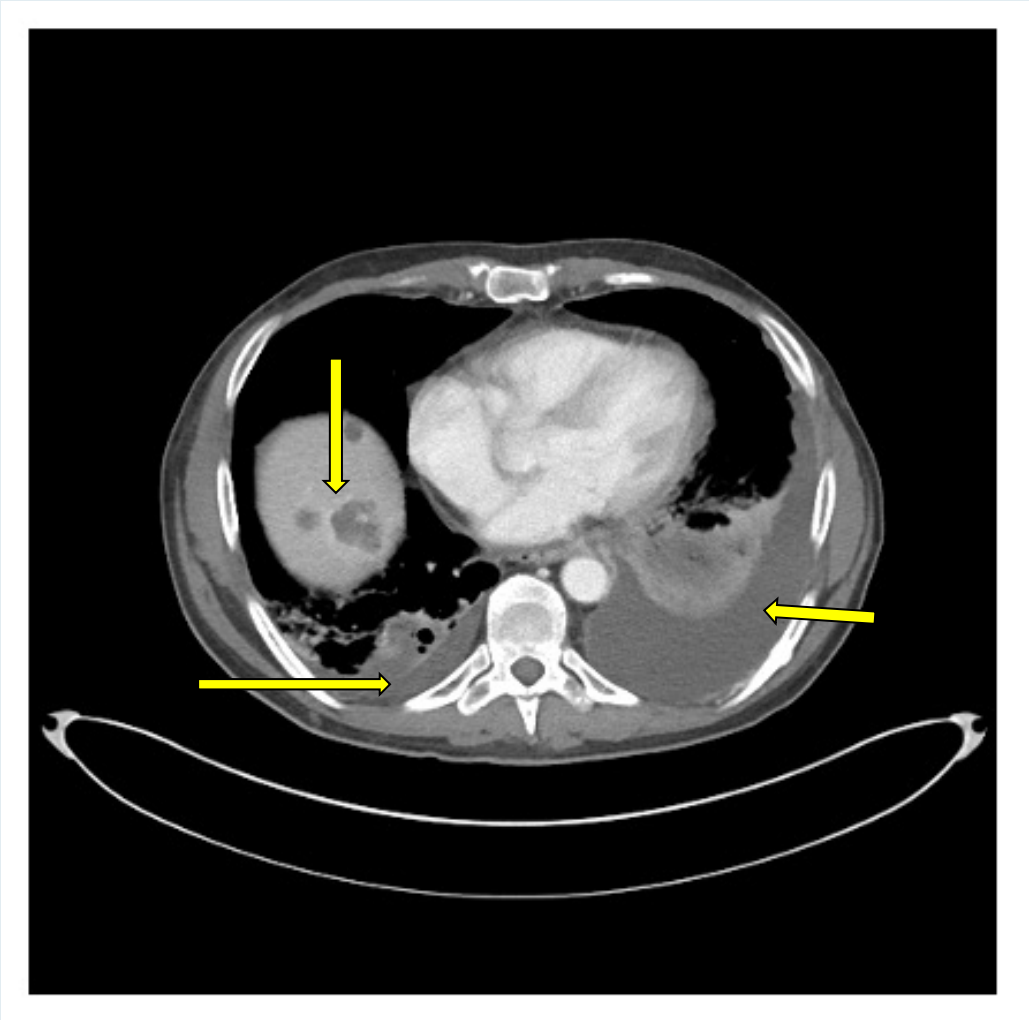
Case Presentation – Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis

Dr Eric Jonasch

- PMH: polymyositis requiring treatment with rituximab
- Extensive metastases in the lung, pancreas, bone, lymph nodes, and liver detected 2 years post-nephrectomy of primary RCC

Case Presentation – Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis (continued)

Dr Eric Jonasch



Case Presentation – Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis (continued)

Dr Eric Jonasch

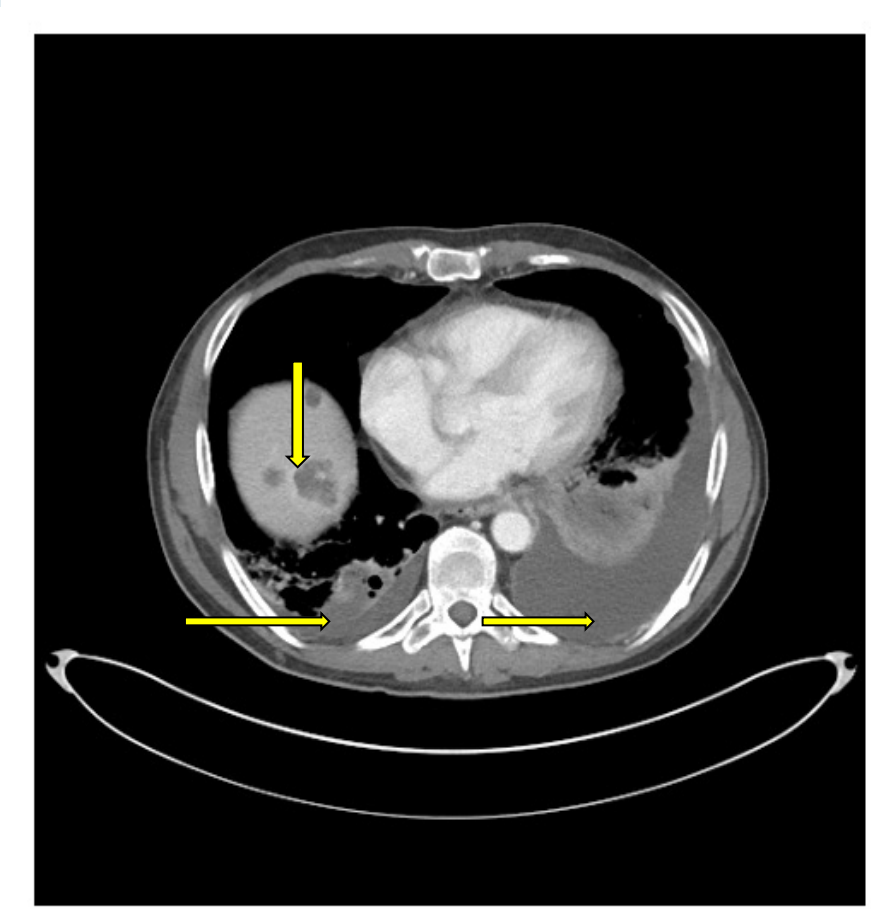
- PMH: polymyositis requiring treatment with rituximab
- Extensive metastases in the lung, pancreas, bone, lymph nodes, and liver detected 2 years post-nephrectomy of primary RCC
- ***Disease progression on axitinib, cabozantinib and lenvatinib/everolimus***
- ***Discontinued lenvatinib and pembrolizumab added***
- ***Colitis developed → pembrolizumab discontinued and restarted when colitis under control with treatment***

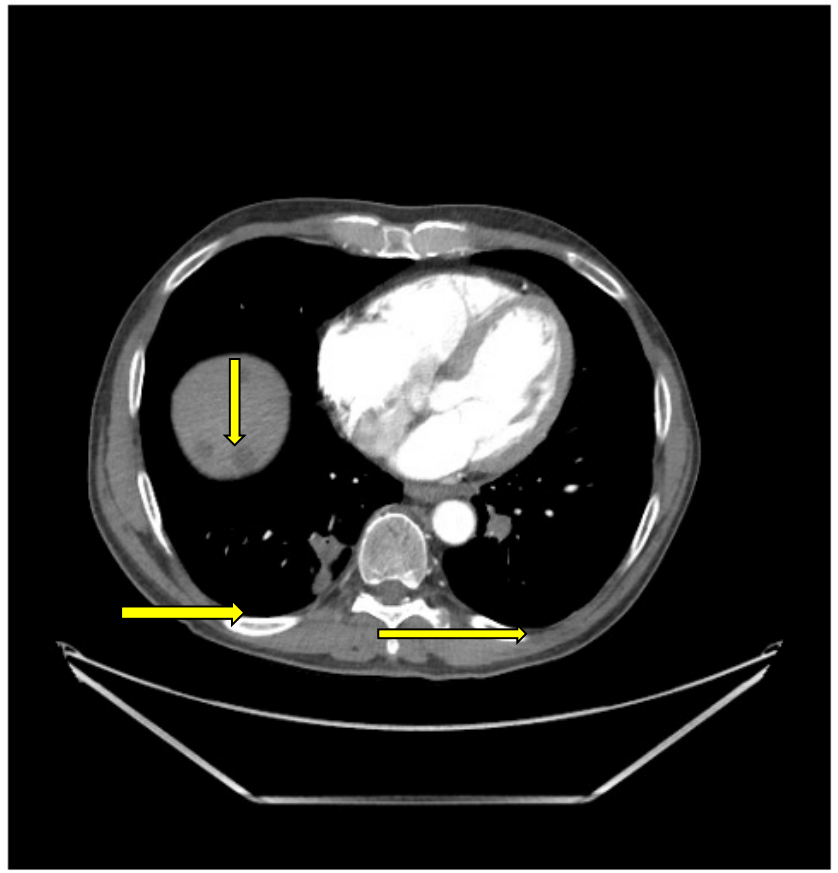
Questions

- ***What type of autoimmune past history would rise to the level that you would not consider using an IO agent, whether it be ipilimumab/nivolumab or pembrolizumab and initiate treatment with cabozantinib?***
- ***Would it be a past history of mild psoriasis? Would it be active lupus? Would it be a touch of RA at some point in the past? And how do you approach this? And how do you discuss this with your patients?***

Case Presentation – Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis (continued)

Dr Eric Jonasch





Case Presentation – Dr Gupta: A 61-year-old woman with metastatic papillary RCC

Dr Ranju Gupta

- Diagnosed with papillary RCC, with liver, bone and adrenal metastases and tumor emboli in the left renal vein
- Ipilimumab/nivolumab, discontinued after 10 weeks due to PD
- 7/2019: Cabozantinib
- 12/2019: Added nivolumab to cabozantinib
- 9/2020: Switched to lenvatinib (14 mg) and everolimus (5 mg)

Questions

- What are your preferred first-line, second-line and later-line therapies for non-clear cell RCC?
- Do you have a preferred second-line treatment after ipilimumab/nivolumab?
- How do you manage tumor emboli in RCC? Should the patient have been started on anticoagulation?

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Case Presentation – Dr Jonasch: A 67-year-old man with metastatic RCC

Dr Eric Jonasch

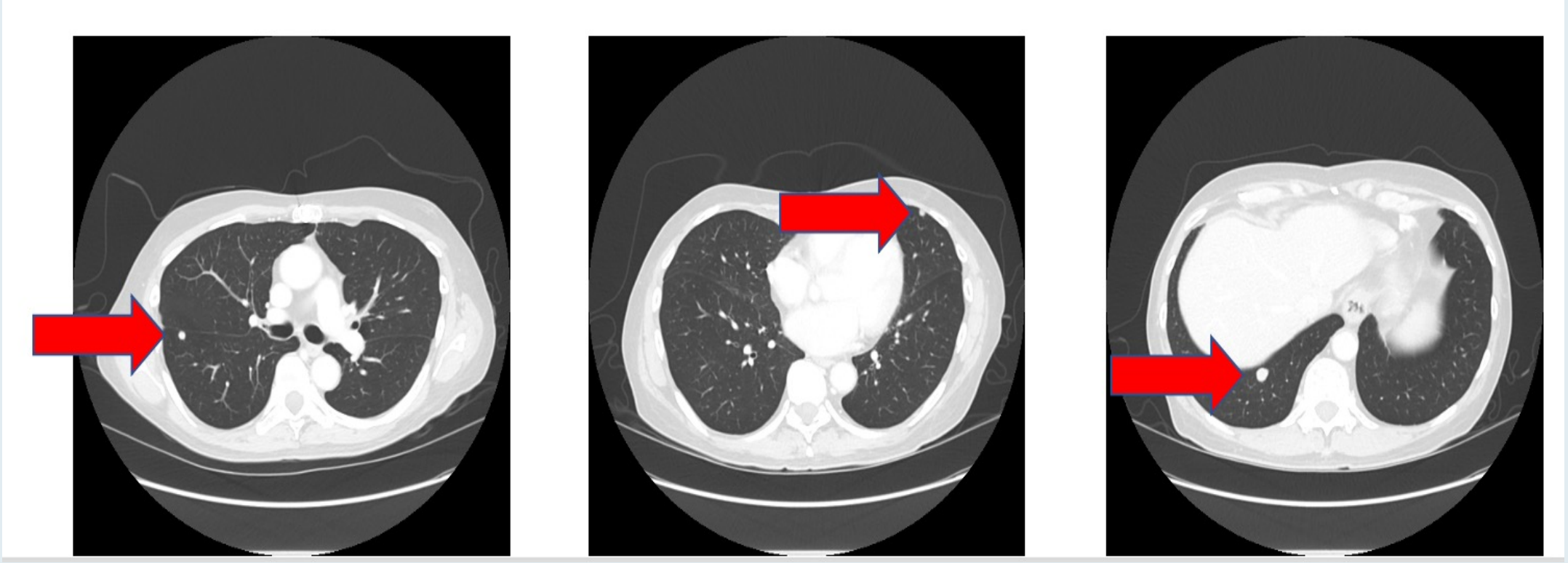
- PMH: Coronary artery bypass graft
- Develops sudden onset hematuria and imaging reveals large right renal mass
- Nephrectomy → postoperative imaging reveals multifocal bilateral pulmonary lesions
  - Asymptomatic

Questions

- What would you recommend for this patient? Would you recommend cytoreductive nephrectomy or initiation of systemic therapy?
- Does this patient need to start treatment immediately?

Case Presentation – Dr Jonasch: A 67-year-old man with metastatic RCC (continued)

Dr Eric Jonasch



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

Dr Regina Flores

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

Question

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

Case Presentation – Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein

Dr Eric Jonasch

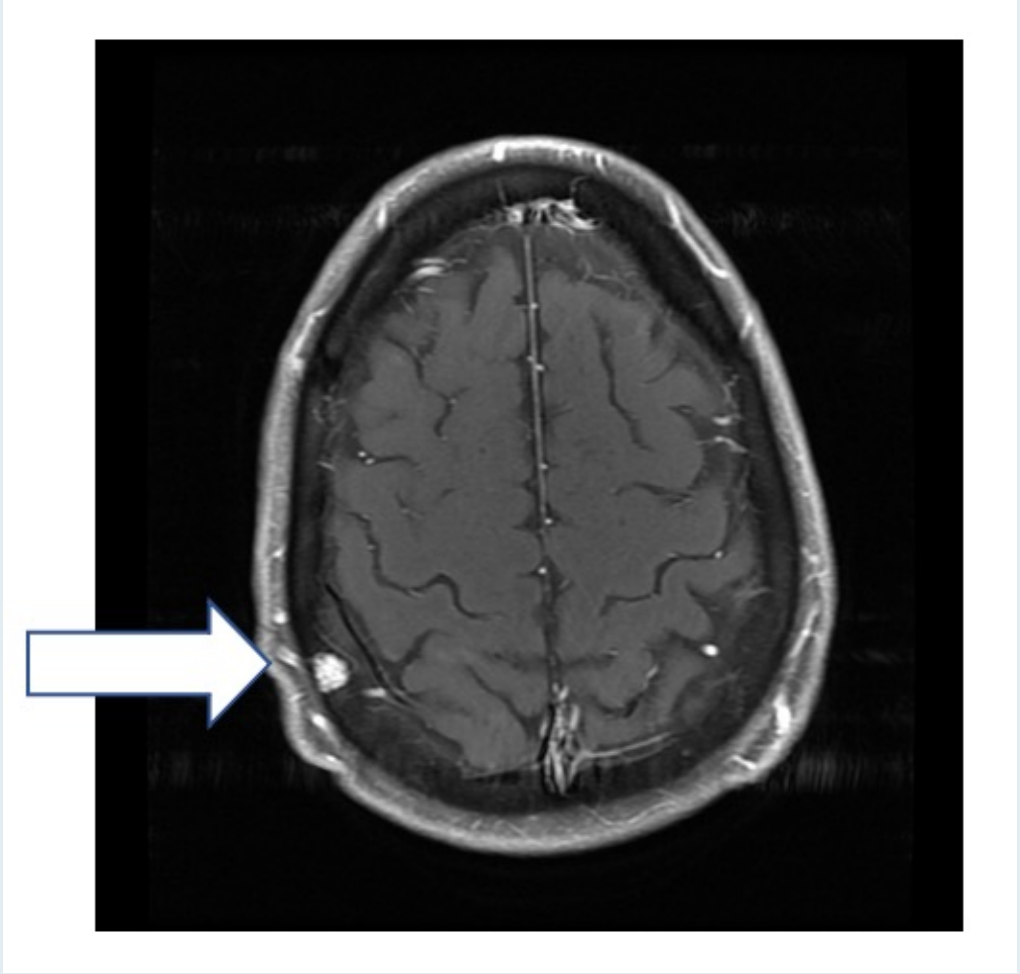
- Right renal mass found incidentally after presenting with abdominal pain and fever and diagnosis of diverticulitis
- Nephrectomy → Grade 3 clear cell RCC with renal vein invasion
- Post-operative imaging detects right parietal bone lesion

Questions

- What would you do next for this patient?

Case Presentation – Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein (continued)

Dr Eric Jonasch



Case Presentation – Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein (continued)

Dr Eric Jonasch

- Right renal mass found incidentally after presenting with abdominal pain and fever and diagnosis of diverticulitis
- Nephrectomy → Grade 3 clear cell RCC with renal vein invasion
- ***Benign parietal bone lesion***
- ***Adjuvant therapy not recommended***
- ***Observation x 2 years and ongoing***

Case Presentation – Dr Brooks: A 61-year-old man with metastatic clear cell RCC

Dr Philip Brooks

- 2013: Hematuria but no follow up until 2/2018
- Right radical nephrectomy, removal of part of the IVC and thrombectomy
  - T3bN0 clear cell RCC
- Mid-2019 follow up CT: Multiple pulmonary nodules (largest 16 x 13 mm) and a soft tissue mass to the right of the IVC measuring 3 cm
  - Asymptomatic
- Followed x 3 months but clear progression of pulmonary nodules
- 10/2019: Ipilimumab/nivolumab
  - Tolerated it very well but by the 4th dose of ipilimumab he developed hypothyroidism
  - Currently, receiving replacement thyroid and cortisol

Questions

- What are the treatment options for this asymptomatic patient?
- What are your thoughts about the use of nephrectomy in patients with metastatic disease?
- Would you delay treatment in order to get a patient vaccinated against COVID-19?

RTP RESEARCH TO PRACTICE

Meet The Professor with Prof Powles

MODULE 1: Case Presentations

- Dr Lamar: A 64-year-old woman with metastatic clear cell RCC
- Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis
- Dr Gupta: A 61-year-old woman with metastatic papillary RCC
- Dr Jonasch: A 67-year-old man with metastatic RCC
- Dr Flores: An obese 61-year-old man with metastatic RCC
- Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein
- Dr Brooks: A 61-year-old man with metastatic clear cell RCC

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Prof Powles

MODULE 4: Key Data Sets

RTP
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TO PRACTICE

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

RTP
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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 Prof Powles

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MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Prof Powles

MODULE 4: Key Data Sets

RTP
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Journal Club with Prof Powles

- Immunotherapy as curative therapy in advanced kidney and bladder cancer: Fantasy or reality?
- Molecular determinants of response to PD-L1 blockade across tumor types
- MK-6482, a HIF-2α inhibitor, versus everolimus in heavily pretreated, ICI-resistant, advanced ccRCC
- Learning from crisis: A multicentre study of oncology telemedicine clinics introduced during COVID-19
- 2021 Updated European Association of Urology Guidelines on RCC: ICI-based combination therapies
- CLEAR: Depth of response and efficacy for selected subgroups receiving lenvatinib and pembrolizumab
- Differences between PD-1 and PD-L1 inhibitors in metastatic RCC: A systematic review and meta-analysis
- KEYNOTE-052: First-line pembrolizumab in cisplatin-ineligible patients with advanced urothelial cancer
- KEYNOTE-426: Hepatic toxicity in patients with advanced RCC receiving first-line pembrolizumab plus axitinib
- KEYNOTE-426: Pembrolizumab plus axitinib versus sunitinib as first-line therapy for advanced ccRCC

Immunotherapy As Curative Therapy in Advanced Kidney and Bladder Cancer: Fantasy or Reality?

Thomas Powles

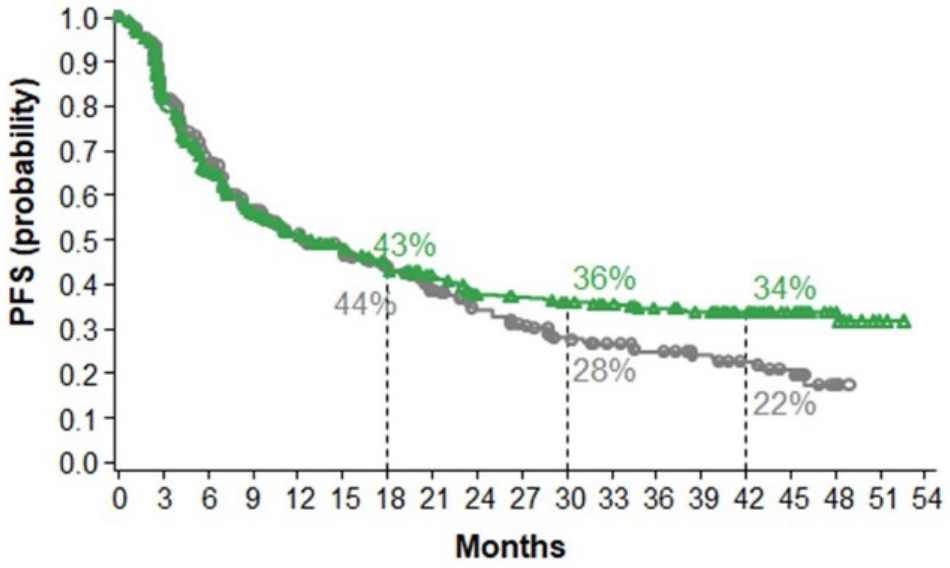
Director of Barts Cancer Center.
Professor of Urology Cancer, Barts Cancer Institute.

ASCO 2021 Education Session

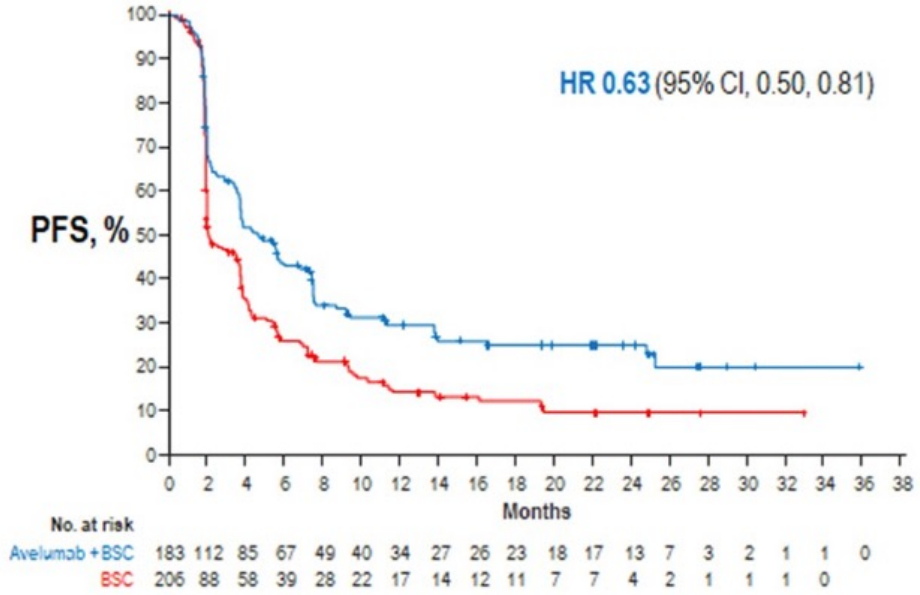
@tompowles1 @uromigos

How many patients are we actually curing?
Many of these are living with measurable disease

Ipilimumab and nivolumab
in advanced renal cancer (IMDC int/poor)



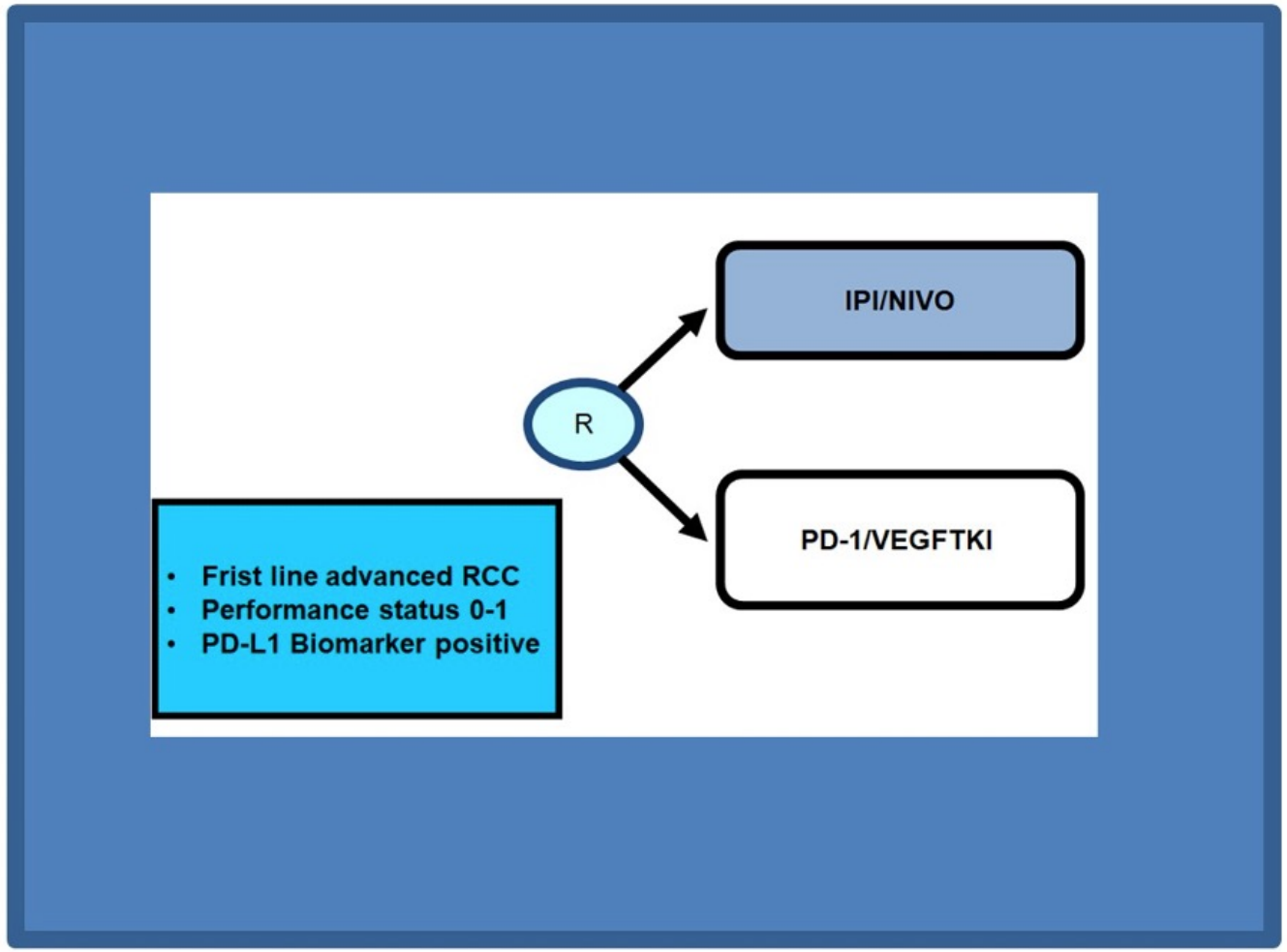
Maintenance avelumab
in UC patients not progressing on chemo.



Albigues et al 2021, Powles et al 2020

Powles T. ASCO 2021 Education Session

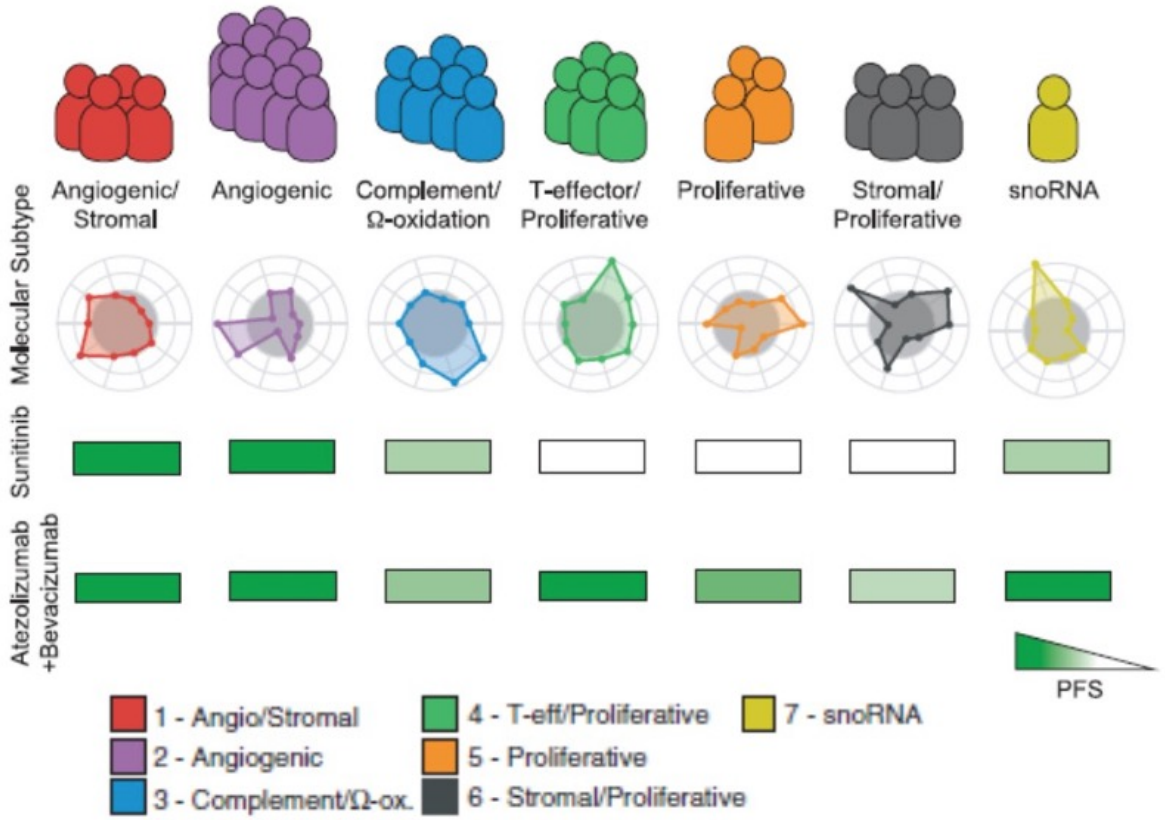
Biomarker trial designs for kidney cancer: Who will do it?

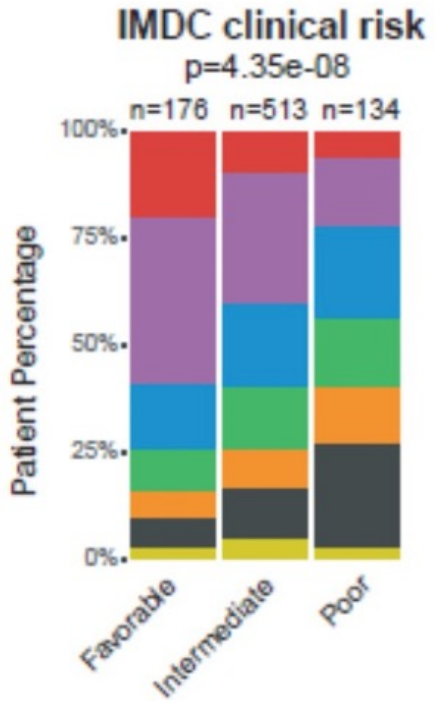


Powles T. ASCO 2021 Education Session

Cancer Cell

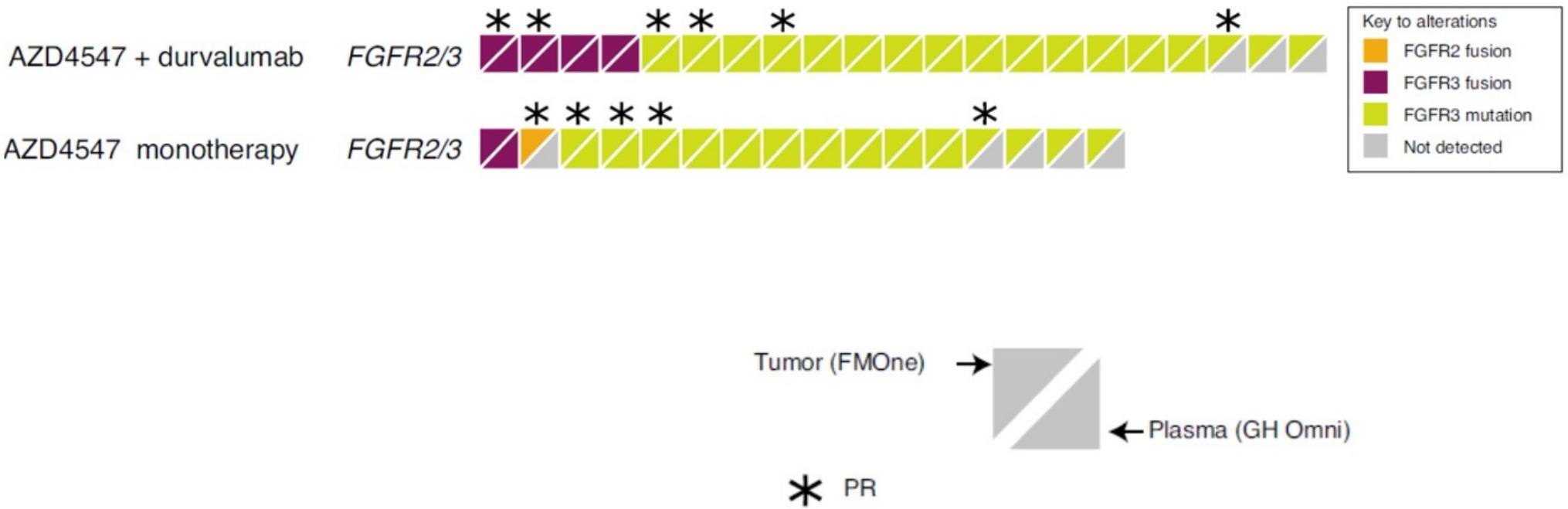
Molecular Subsets in Renal Cancer Determine Outcome to Checkpoint and Angiogenesis Blockade





Motzer Rini 2020

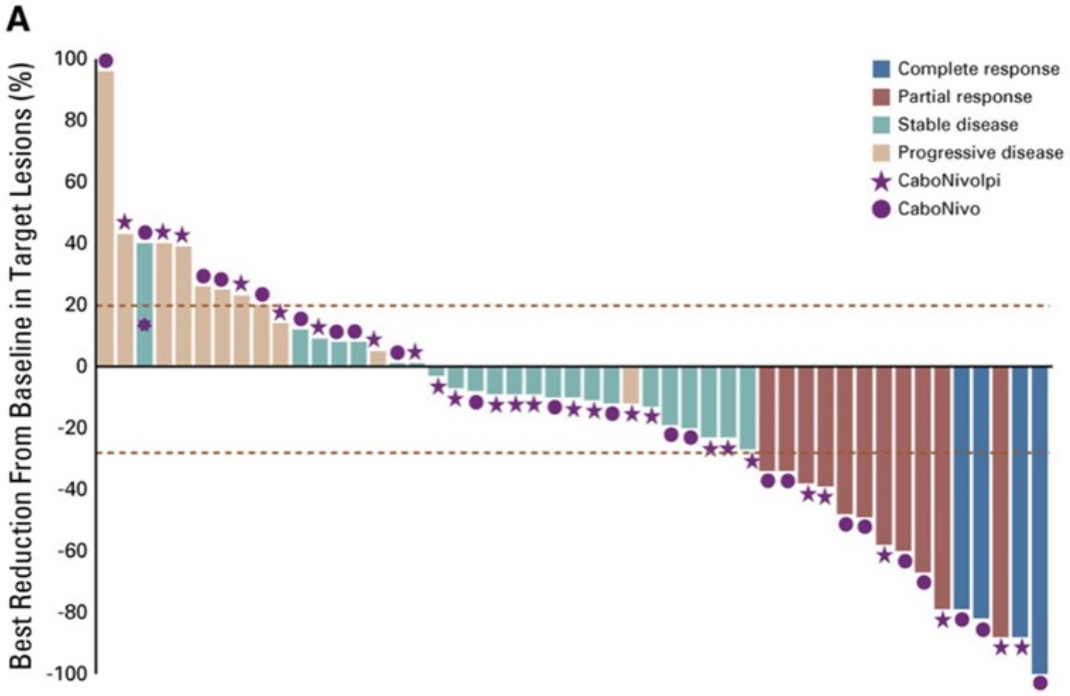
Circulating biomarker in urothelial cancer: FGFR DNA alterations from tissue and ctDNA strongly correlate



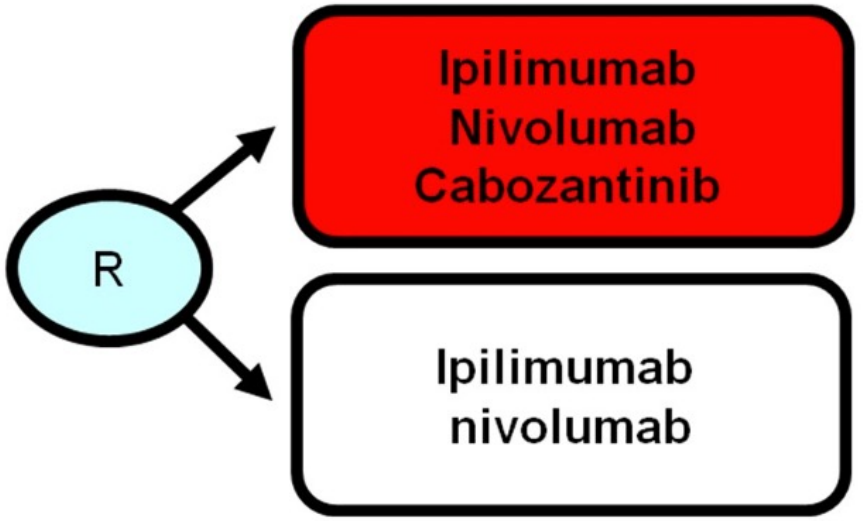
Carroll D ASCO 2019

Triplet therapy in clear cell renal cancer: will it improve cure?

Cabozantinib, ipilimumab and nivolumab in genito-urinary cancers.



COSMIC-313 trial



Apolo A JCO 2019

Powles T. ASCO 2021 Education Session

nature COMMUNICATIONS

Nat Commun 2021;12(1):3969

ARTICLE

https://doi.org/10.1038/s41467-021-24112-w OPEN

Molecular determinants of response to PD-L1 blockade across tumor types

Romain Banchereau[1]✉, Ning Leng[1], Oliver Zill[1], Ethan Sokol[2], Gengbo Liu[1], Dean Pavlick[2], Sophia Maund[1], Li-Fen Liu[1], Edward Kadel III[1], Nicole Baldwin[3], Suchit Jhunjhunwala[1], Dorothee Nickles[1], Zoe June Assaf[1], Daniel Bower[1], Namrata Patil[1], Mark McCleland[1], David Shames[1], Luciana Molinero[1], Mahrukh Huseni[1], Shomyseh Sanjabi[1], Craig Cummings[1], Ira Mellman[1], Sanjeev Mariathasan[1], Priti Hegde[4] & Thomas Powles[5]✉

MK-6482, a Hypoxia-Inducible Factor 2α Inhibitor (HIF-2α), versus Everolimus in Heavily Pretreated, Immune Checkpoint–Inhibitor-Resistant, Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Phase III Study

Choueiri TK et al.

ASCO 2021;Abstract TPS368.

J Cancer Educ 2021:1-9

Learning from Crisis: a Multicentre Study of Oncology Telemedicine Clinics Introduced During COVID-19

Michael Grant[1,2,3] · Helen Hockings[2] · Maria Lapuente[1,2] · Philip Adeniran[1,2] · Rabiah Abbas Saud[1,2] · Anjali Sivajothi[1,2] · Jubel Amin[1,2] · Shanthini M. Crusz[2] · Sukaina Rashid[2] · Bernadette Szabados[1,2] · Paula Wells[2] · Ekaterini Boleti[3] · Thomas B. Powles[1,2]

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

European Association of Urology

Eur Urol 2021:S0302-2838(21)00322-5

Platinum Opinion

The 2021 Updated European Association of Urology Guidelines on Renal Cell Carcinoma: Immune Checkpoint Inhibitor–based Combination Therapies for Treatment-naive Metastatic Clear-cell Renal Cell Carcinoma Are Standard of Care

Jens Bedke [a,b], Laurence Albiges [c], Umberto Capitanio [d,e], Rachel H. Giles [f], Milan Hora [g], Thomas B. Lam [h,i], Börje Ljungberg [j], Lorenzo Marconi [k], Tobias Klatte [l,m], Alessandro Volpe [n], Yasmin Abu-Ghanem [o], Saeed Dabestani [p], Sergio Fernández Pello [q], Fabian Hofmann [r], Teele Kuusk [s], Rana Tahbaz [t], Thomas Powles [u], Axel Bex [v,w,x,]*

Four ICI Combinations with Proven OS Benefit Form the New Standard First-Line Therapy for Metastatic ccRCC

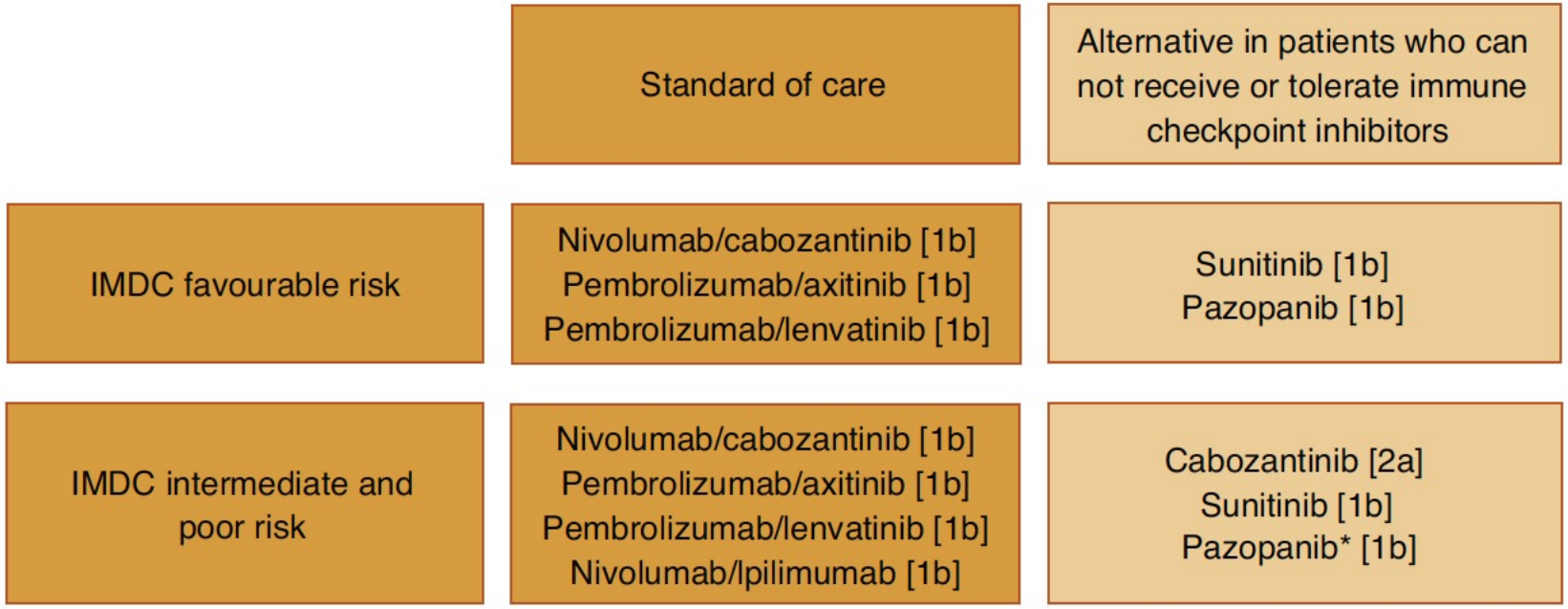


Fig. 1 – Updated European Association of Urology guidelines recommendations for the first-line treatment of metastatic clear-cell renal cancer.
IMDC = The International Metastatic Renal Cell Carcinoma Database Consortium.
***pazopanib for intermediate-risk disease only.**
[1b] = based on a randomised controlled phase III trial.
[2a] = based on a well-designed study without randomisation, or a subgroup analysis of a randomised controlled trial.

Bedke J et al. Eur Urol 2021;S0302-2838.

RTP RESEARCH TO PRACTICE

2021 ASCO ANNUAL MEETING

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

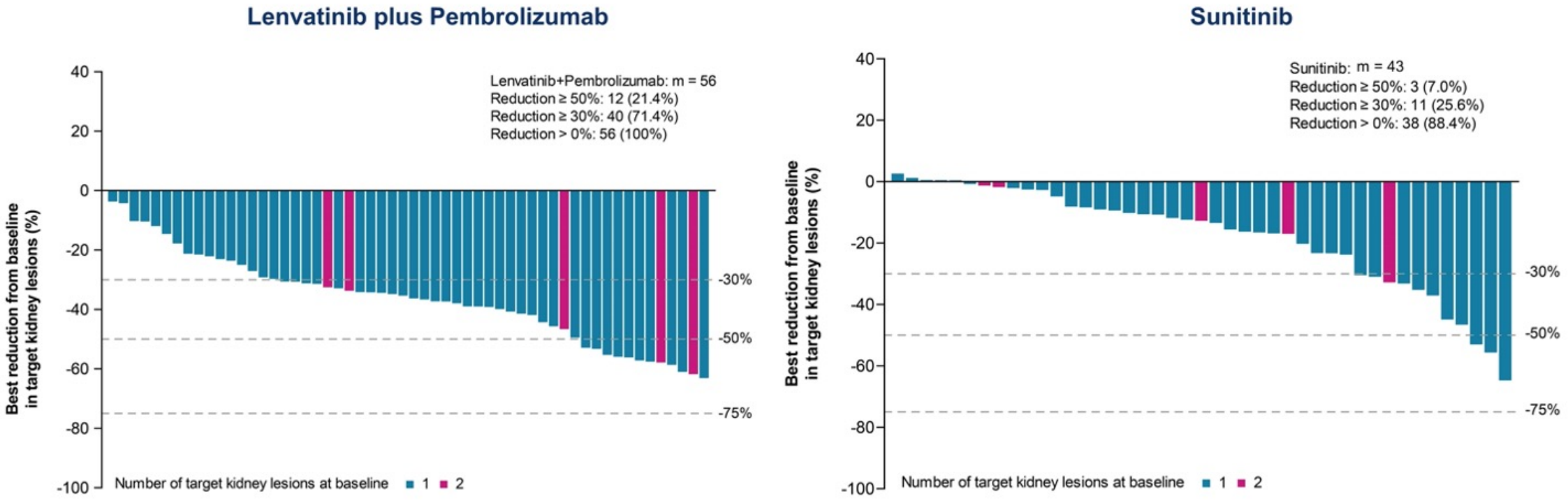
Viktor Grünwald[1], Thomas Powles[2], Evgeny Kopyltsov[3], Vadim Kozlov[4], Teresa Alonso Gordoa[5], Masatoshi Eto[6], Thomas Hutson[7], Robert Motzer[8], Eric Winquist[9], Pablo Maroto[10], Bhumsuk Keam[11], Giuseppe Procopio[12], Shirley Wong[13], Bohuslav Melichar[14], Frederic Rolland[15], Mototsugu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

June 4–8, 2021

Abstract No. 4560

Depth of Response in Target Kidney Lesions



Conclusion: Overall, these results show that lenvatinib plus pembrolizumab improved efficacy outcomes versus sunitinib across evaluable subgroups. Notably, all patients with a complete response to lenvatinib plus pembrolizumab at 6 months were alive at 2 years.

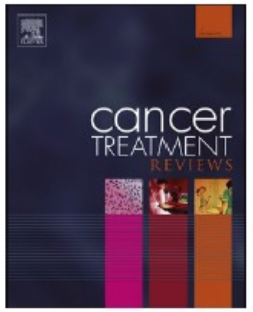
Maximum Tumor Shrinkage From Baseline in Target Kidney Lesions; tumors assessed by Independent Review Committee per RECIST v1.1

Cancer Treatment Reviews 99 (2021) 102242

Contents lists available at ScienceDirect

Cancer Treatment Reviews

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



Systematic or Meta-analysis Studies

Differences in oncological and toxicity outcomes between programmed cell death-1 and programmed cell death ligand-1 inhibitors in metastatic renal cell carcinoma: A systematic review and meta-analysis

Keiichiro Mori [a,b,1], Benjamin Pradere [a,1], Fahad Quhal [a,c], Satoshi Katayama [a,d], Hadi Mostafaei [a,e], Ekaterina Laukhtina [a,f], Victor M. Schuettfort [a,g], David D'Andrea [a], Shin Egawa [b], Karim Bensalah [h], Manuela Schmidinger [i], Thomas Powles [j], Shahrokh F. Shariat [a,f,k,l,m,n,o,*]

First-Line Pembrolizumab in Cisplatin-Ineligible Patients With Advanced Urothelial Cancer: Response and Survival Results Up to 5 Years From the KEYNOTE-052 Phase 2 Study

P. H. O'Donnell[1]; A. V. Balar[2]; J. Vuky[3]; D. E. Castellano[4]; J. Bellmunt[5]; T. Powles[6]; D. F. Bajorin[7]; P. Grivas[8]; N. M. Hahn[9]; E. R. Plimack[10]; J. Z. Xu[11]; J. L. Godwin[11]; B. Homet Moreno[11]; R. de Wit[12]

[1]The University of Chicago, Chicago, IL, USA; [2]Perlmutter Cancer Center, NYU Langone Health, New York, NY, USA; [3]Oregon Health & Science University, Portland, OR, USA; [4]Hospital Universitario 12 de Octubre, Madrid, Spain; [5]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [6]Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [8]University of Washington, Seattle, WA, USA; [9]The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medicine, Baltimore, MD, USA; [10]Fox Chase Cancer Center, Philadelphia, PA, USA; [11]Merck & Co., Inc., Kenilworth, NJ, USA; [12]Erasmus MC Cancer Institute, Rotterdam, Netherlands

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

Eur Urol Oncol 2021:S2588-9311(21)00113-9

European Association of Urology

Characterization and Management of Treatment-emergent Hepatic Toxicity in Patients with Advanced Renal Cell Carcinoma Receiving First-line Pembrolizumab plus Axitinib. Results from the KEYNOTE-426 Trial

Brian I. Rini[a,*], *Michael B. Atkins*[b], *Elizabeth R. Plimack*[c], *Denis Soulières*[d], *Raymond S. McDermott*[e], *Jens Bedke*[f], *Sophie Tartas*[g], *Boris Alekseev*[h], *Bohuslav Melichar*[i], *Yaroslav Shparyk*[j], *Chihiro Kondoh*[k], *Przemyslaw Langiewicz*[l], *Lori A. Wood*[m], *Hans Hammers*[n], *Cynthia G. Silber*[o], *Barbara Haber*[o], *Erin Jensen*[o], *Mei Chen*[o], *Thomas Powles*[p]

JC JOURNAL CLUB RTP RESEARCH TO PRACTICE

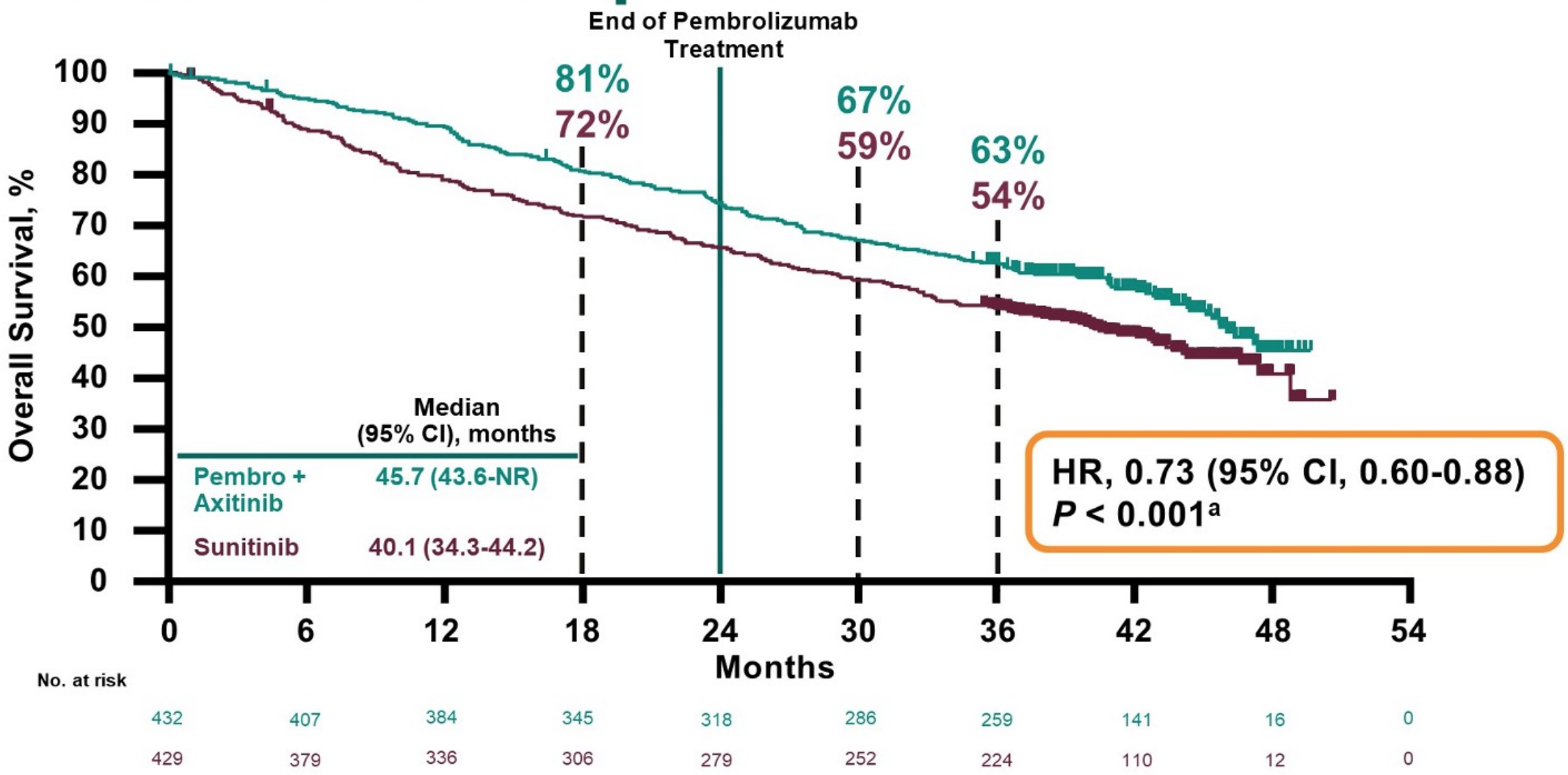
Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

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]

ASCO 2021;Abstract 4500

[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

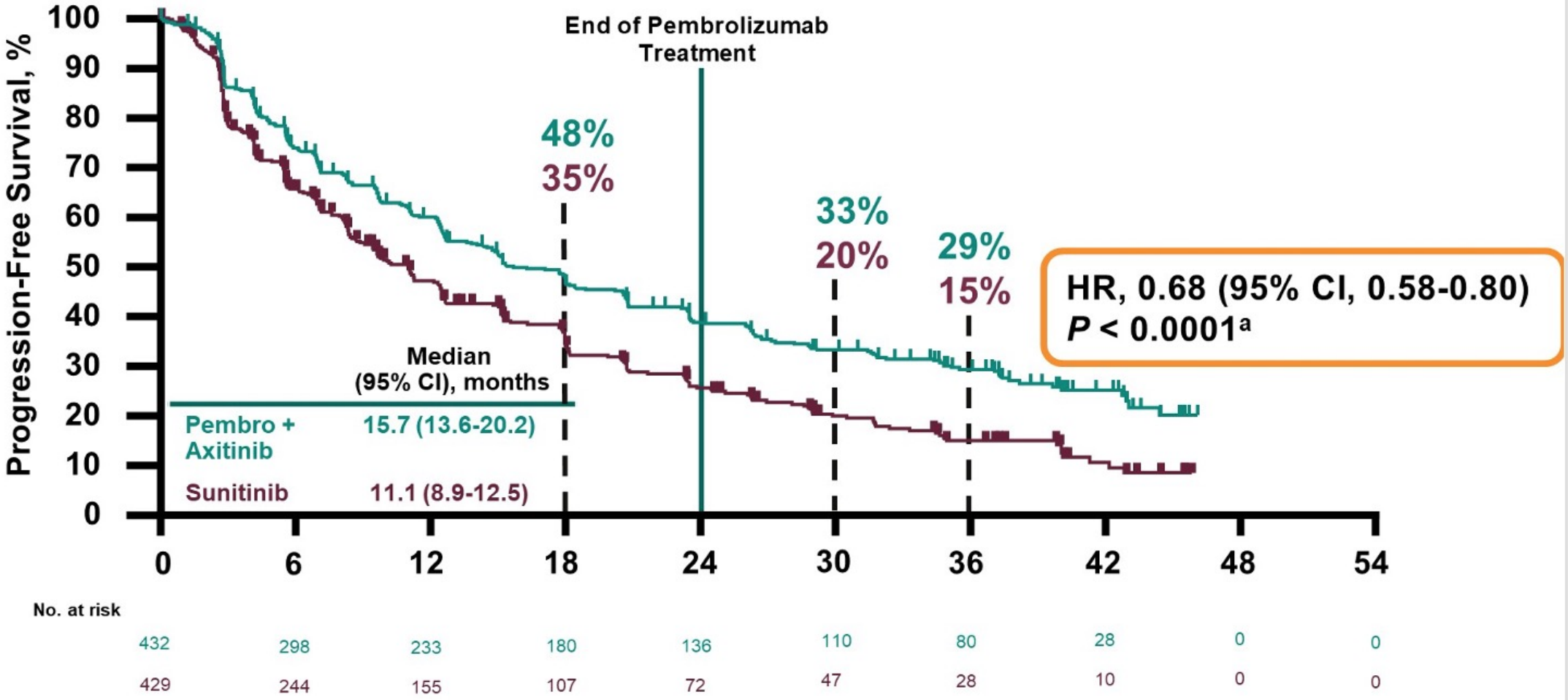
OS in the ITT Population



[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 a. 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 a. ASCO 2021;Abstract 4500.

Meet The Professor with Prof Powles

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- Dr Jonasch: A 58-year-old man with metastatic RCC and a history of polymyositis
- Dr Gupta: A 61-year-old woman with metastatic papillary RCC
- Dr Jonasch: A 67-year-old man with metastatic RCC
- Dr Flores: An obese 61-year-old man with metastatic RCC
- Dr Jonasch: A 64-year-old man with clear cell RCC invasive into the renal vein
- Dr Brooks: A 61-year-old man with metastatic clear cell RCC

MODULE 2: Beyond the Guidelines

MODULE 3: Journal Club with Prof Powles

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]

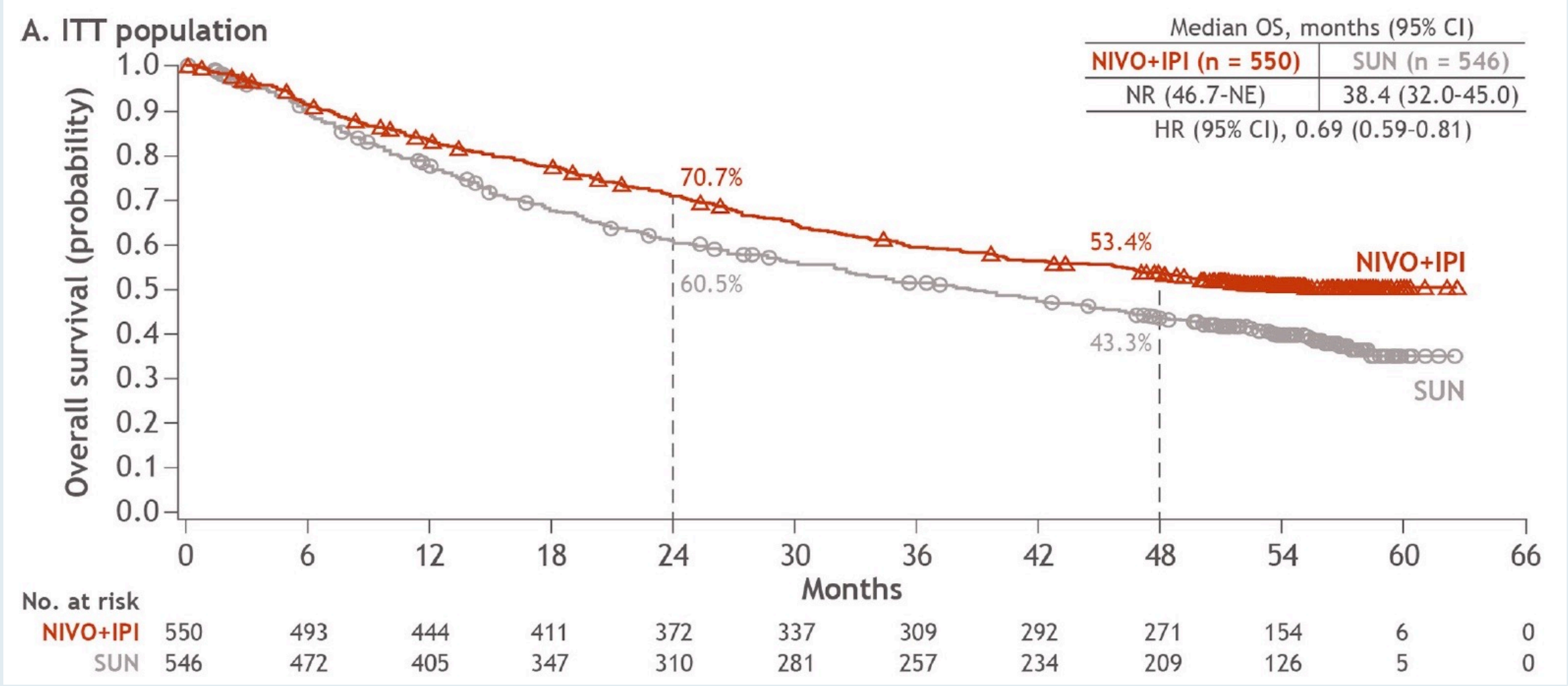
ESMO Open 2020;5(6):e001079.

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%

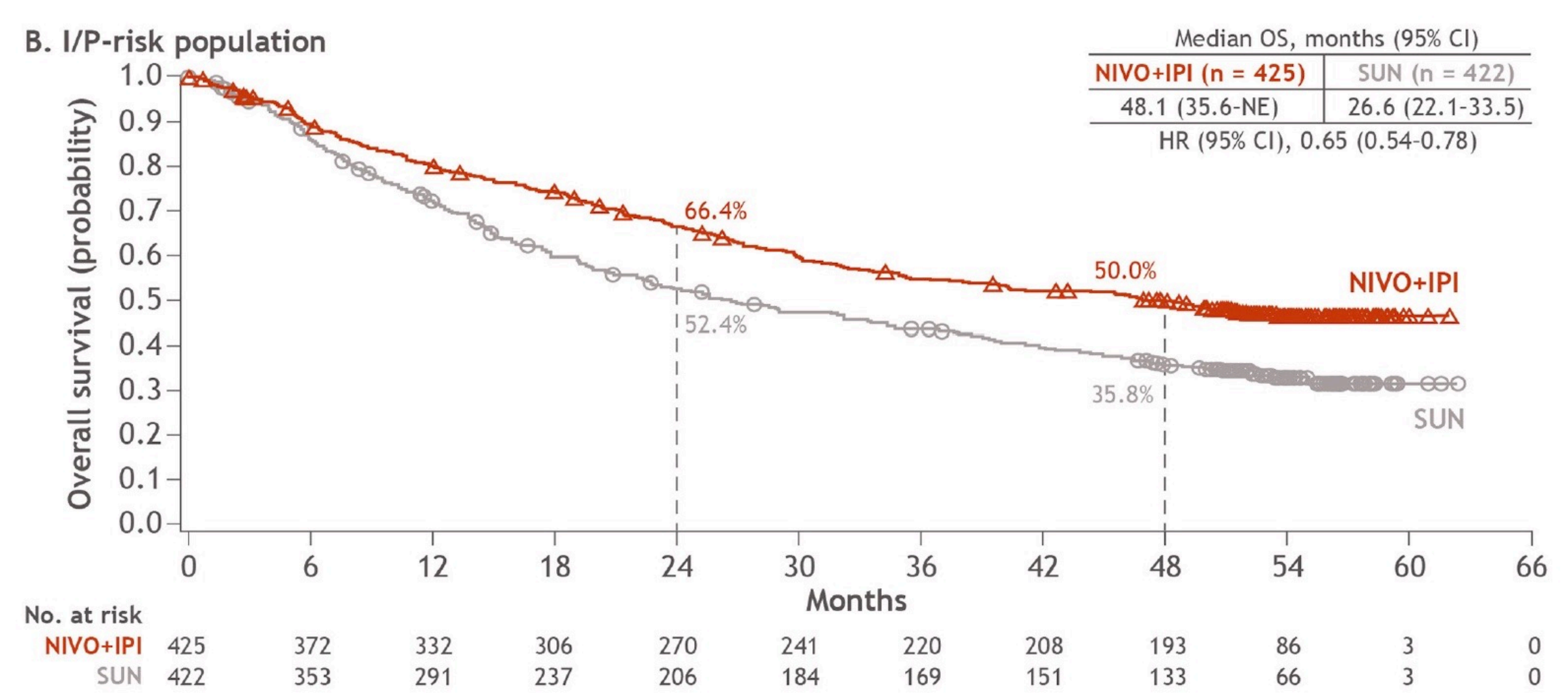
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

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.

ORIGINAL ARTICLE

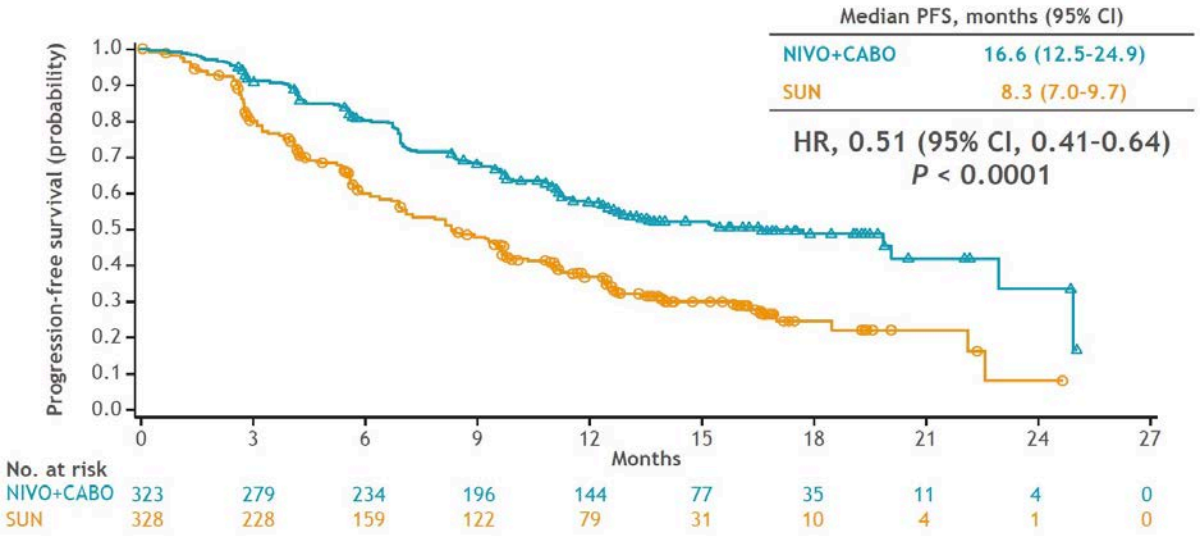
Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

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*

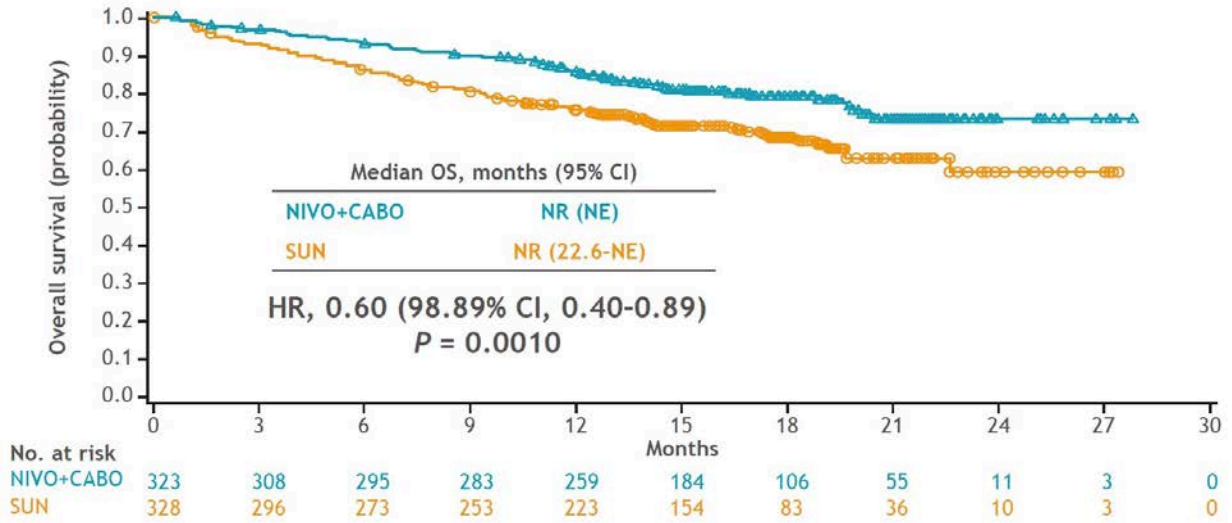
N Engl J Med 2021;384(9):829-41.

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

Memorial Sloan Kettering Cancer Center™

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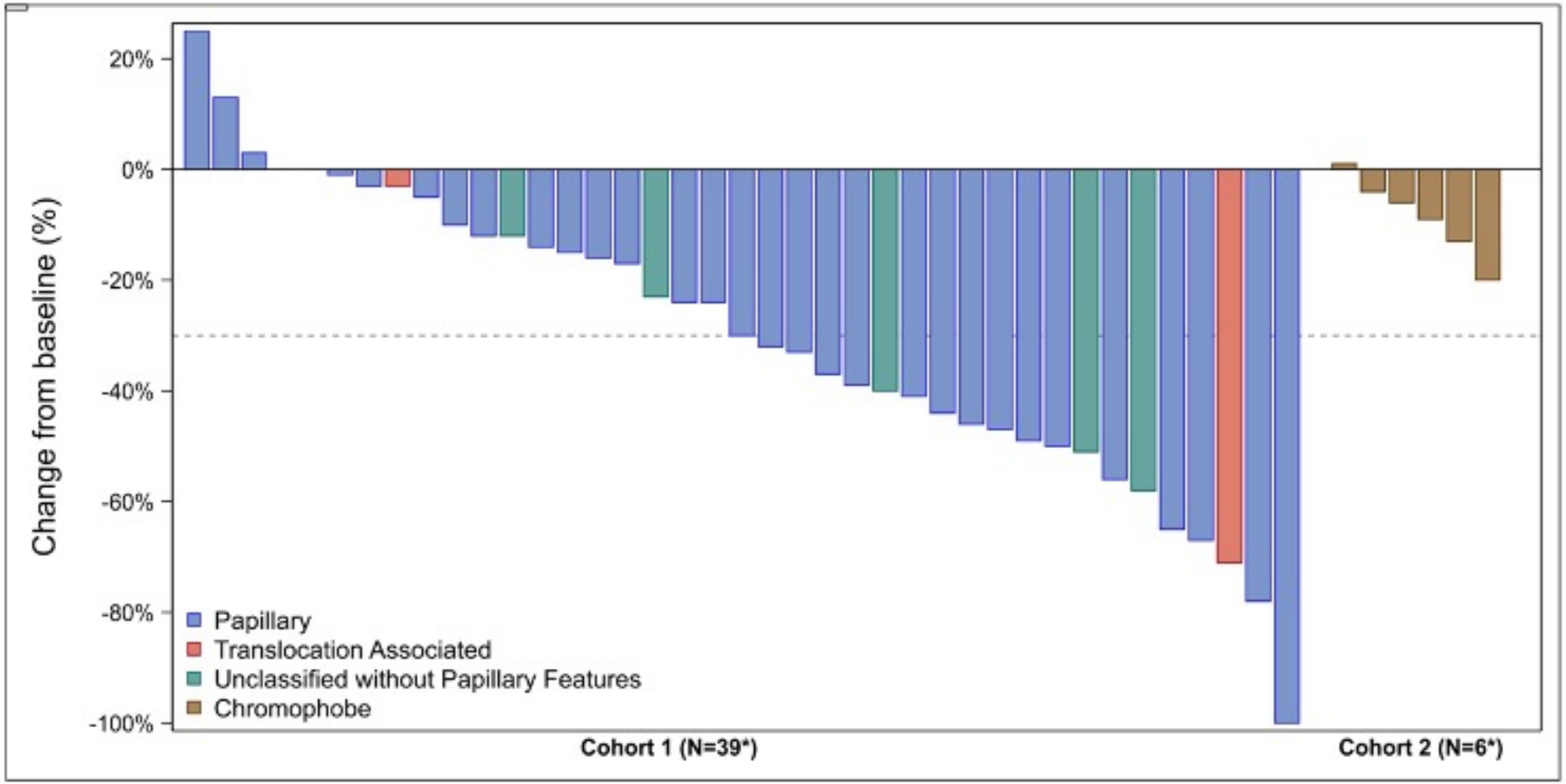
Lee CH et al. ASCO 2021;Abstract 4509.

RTP RESEARCH TO PRACTICE

Maximum Change in Target Lesions by Histology



Lee CH et al. ASCO 2021;Abstract 4509.

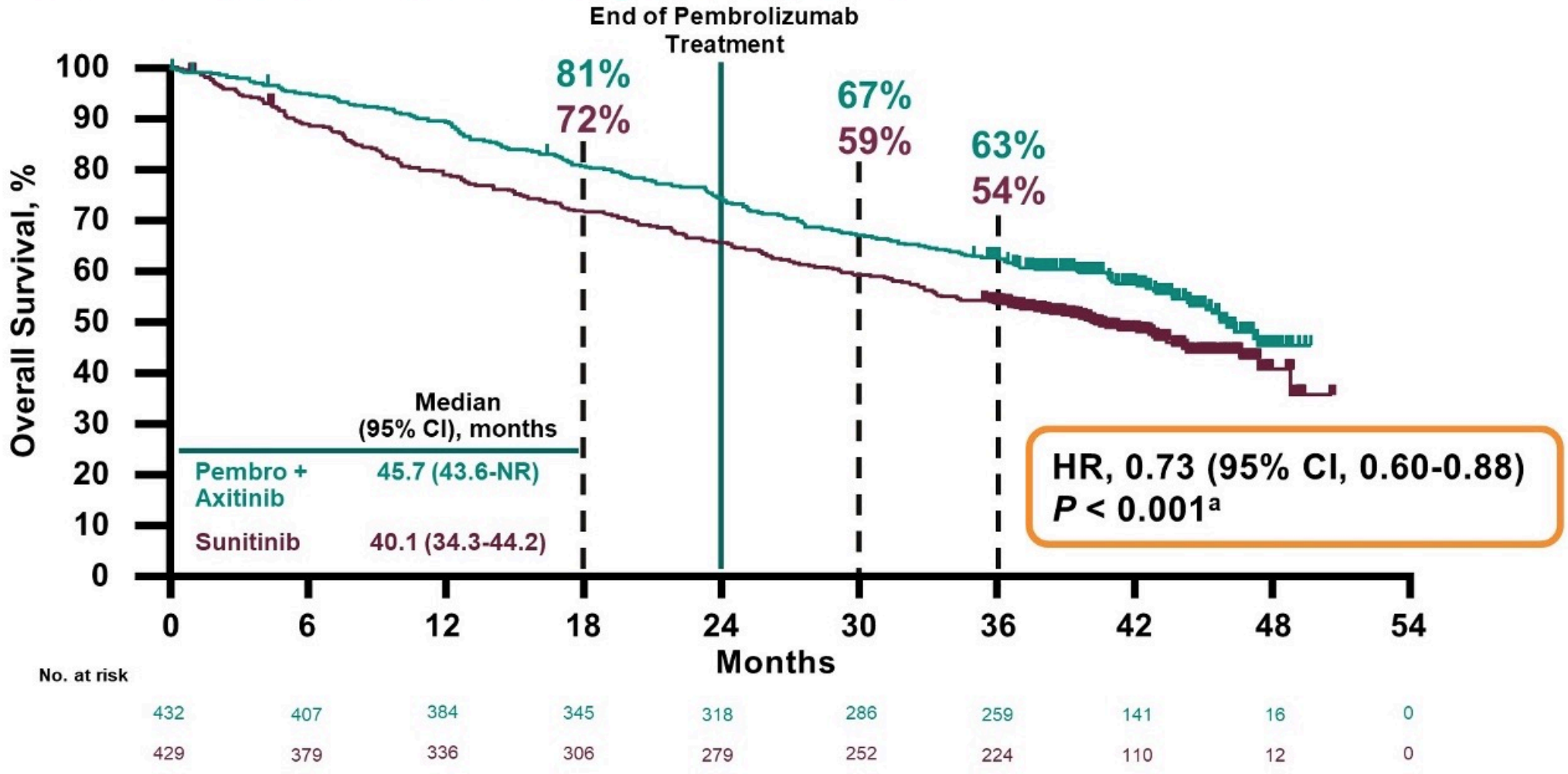
Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

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

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

Rini BI et al. ASCO 2021;Abstract 4500.

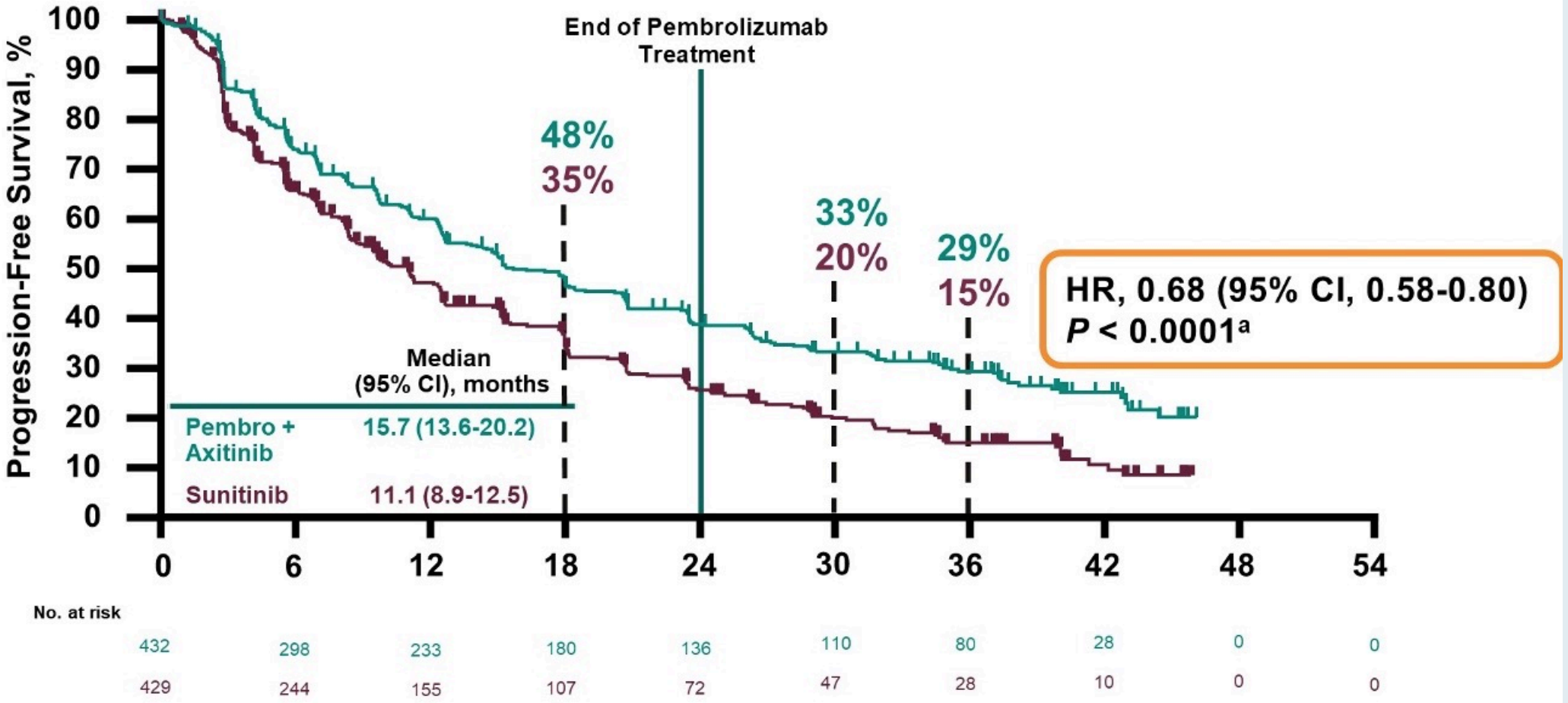
OS in the ITT Population



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

Rini BI et al. ASCO 2021;Abstract 4500.

PFS in the ITT Population



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

Rini BI et al. ASCO 2021;Abstract 4500.

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

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

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

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

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

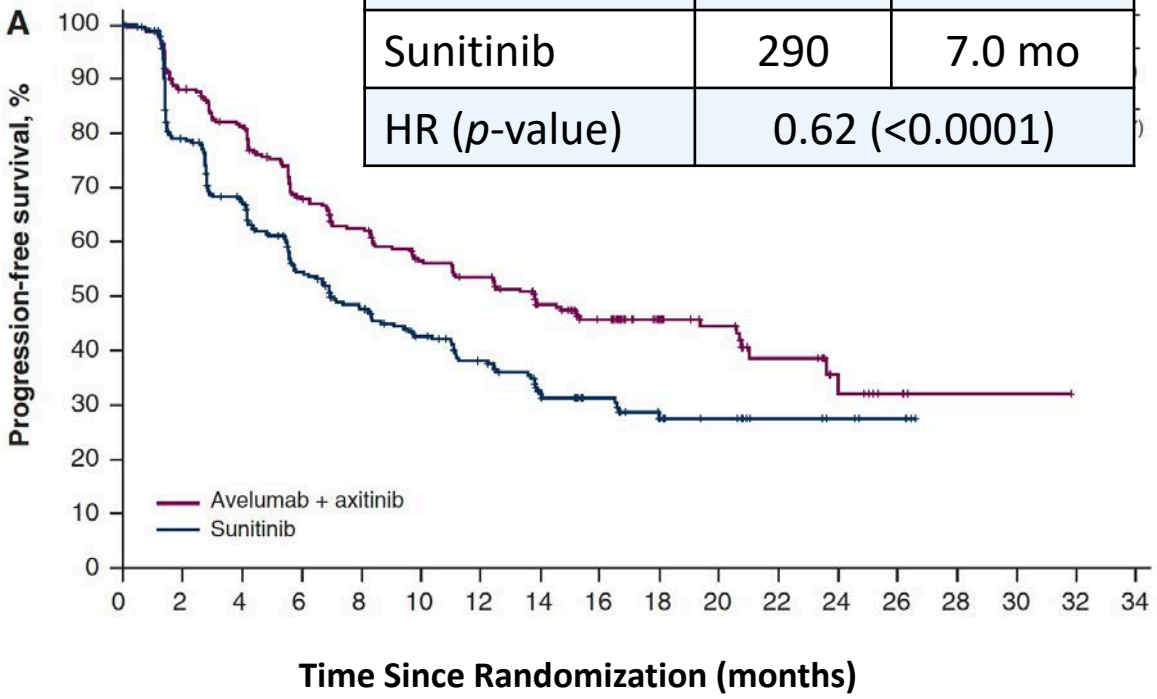
	PD-L1-positive		Overall	
	Avelumab + axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing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

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

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

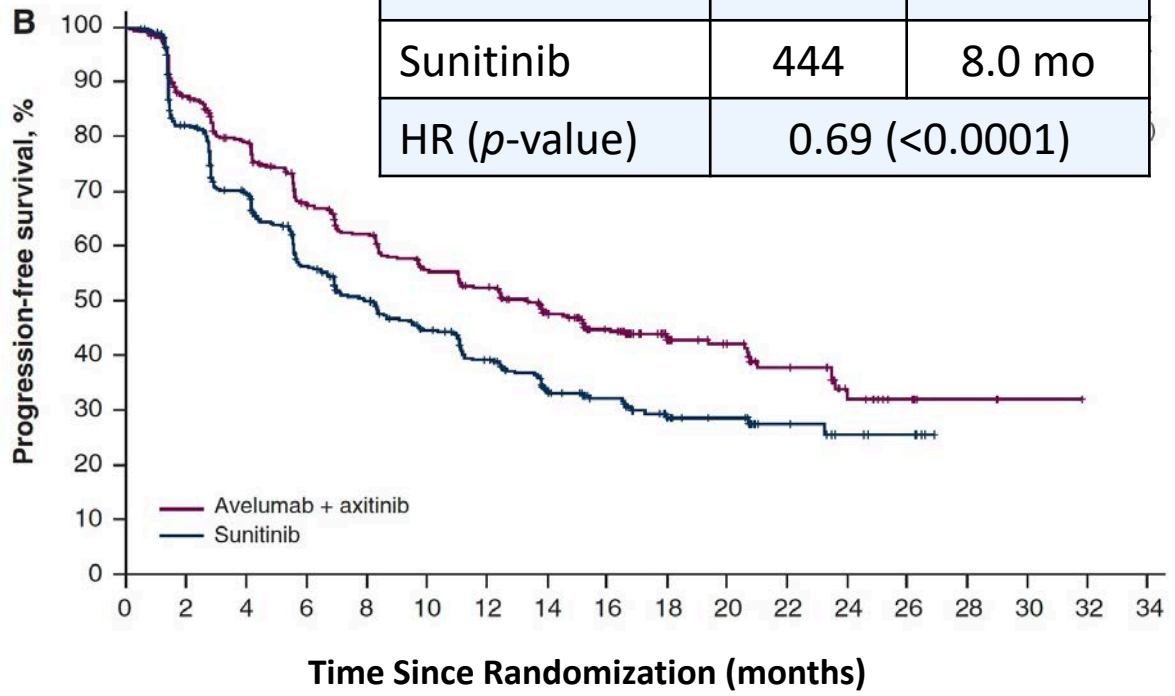
PD-L1 ≥ 1% Population

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



Overall Population

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



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

RTP RESEARCH TO PRACTICE

The NEW ENGLAND JOURNAL of MEDICINE

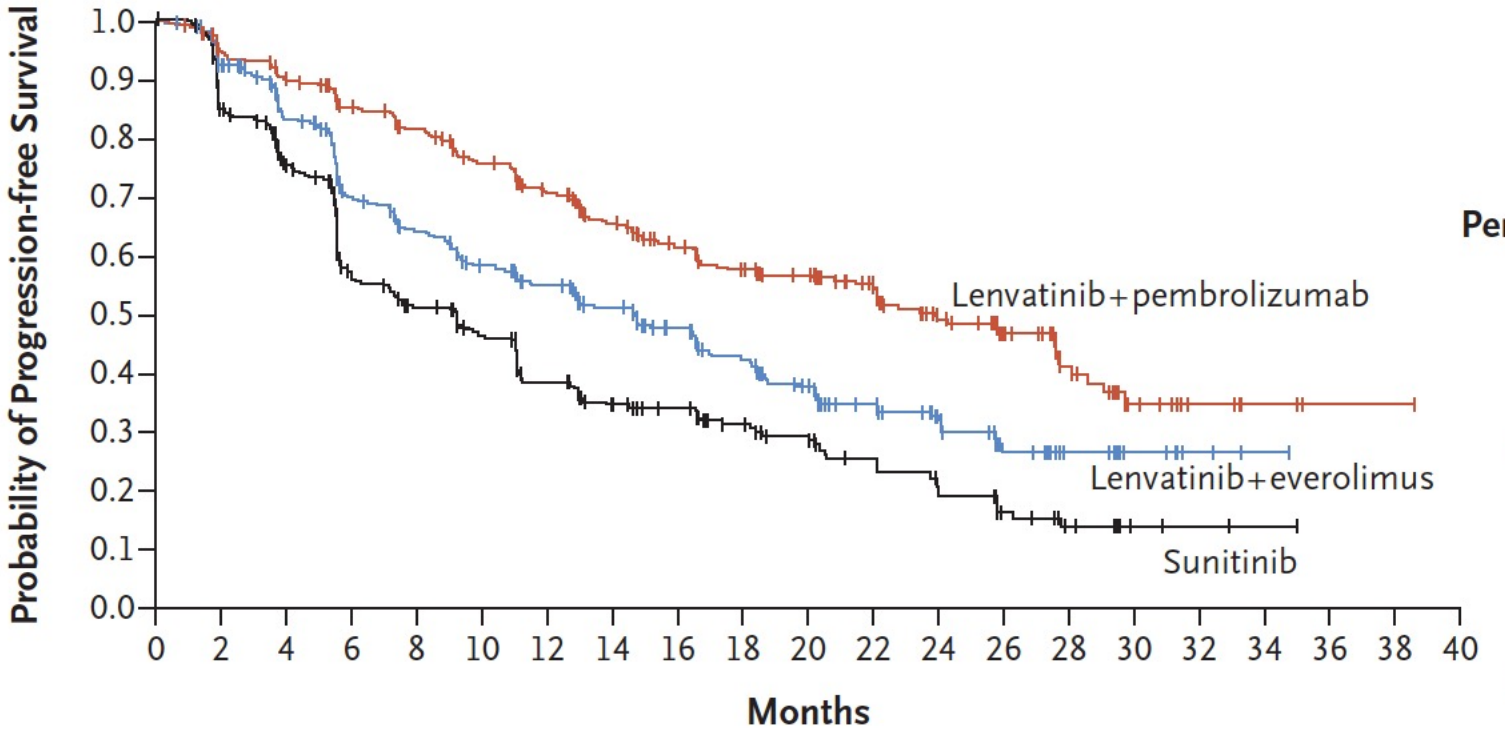
ORIGINAL ARTICLE

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)

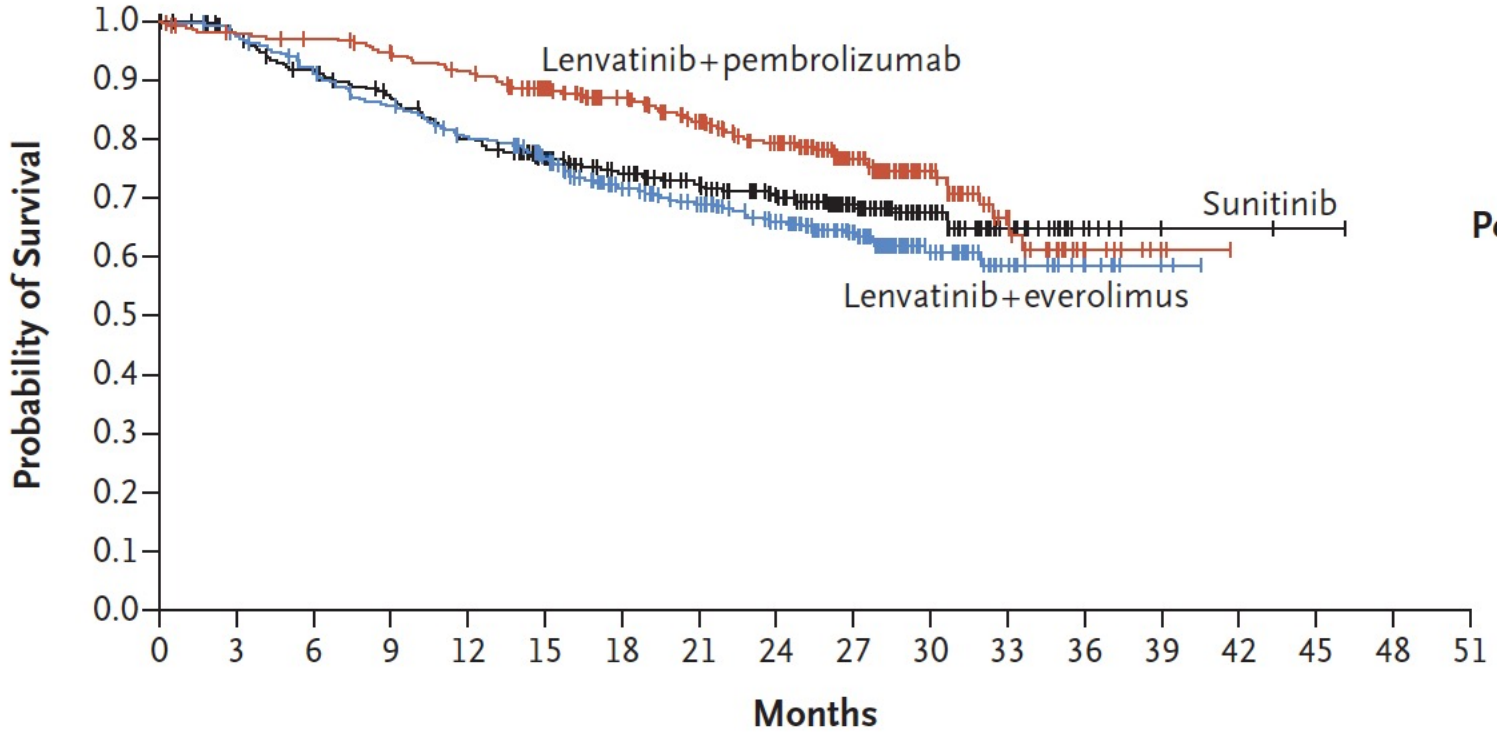
Hazard ratio for disease progression or death (lenvatinib+ pembrolizumab vs. sunitinib), 0.39 (95% CI, 0.32–0.49); P<0.001

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

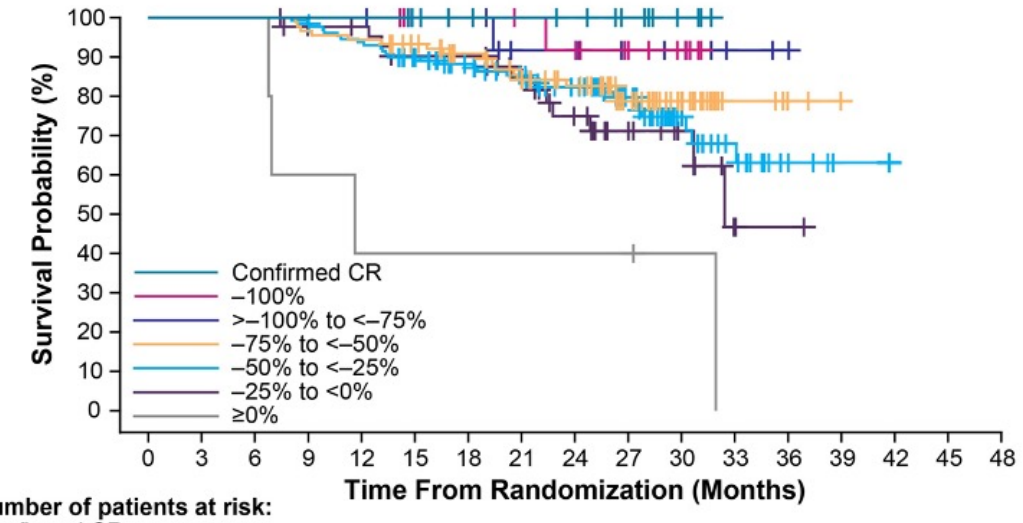
Viktor Grünwald[1], Thomas Powles[2], Evgeny Kopyltsov[3], Vadim Kozlov[4], Teresa Alonso Gordoa[5], Masatoshi Eto[6], Thomas Hutson[7], Robert Motzer[8], Eric Winquist[9], Pablo Maroto[10], Bhumsuk Keam[11], Giuseppe Procopio[12], Shirley Wong[13], Bohuslav Melichar[14], Frederic Rolland[15], Mototsugu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

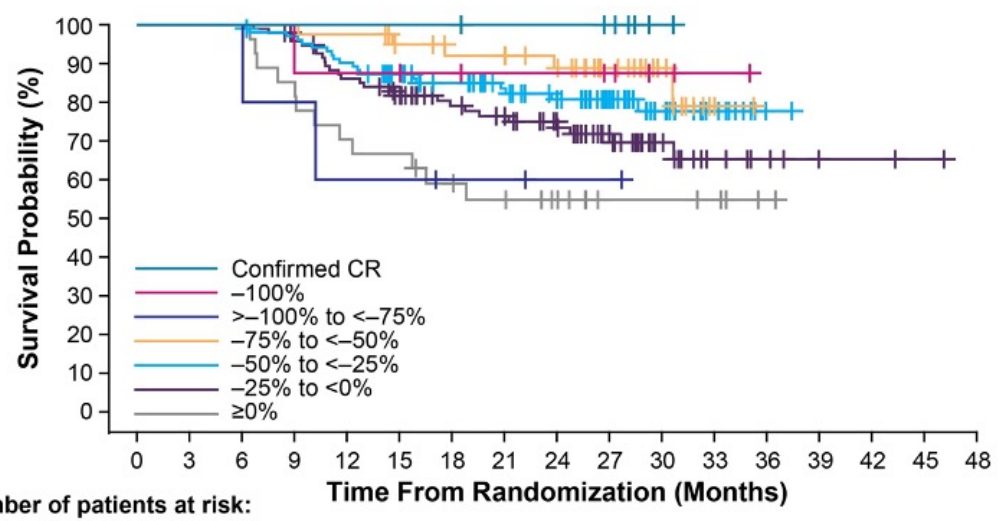
Lenvatinib plus Pembrolizumab



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

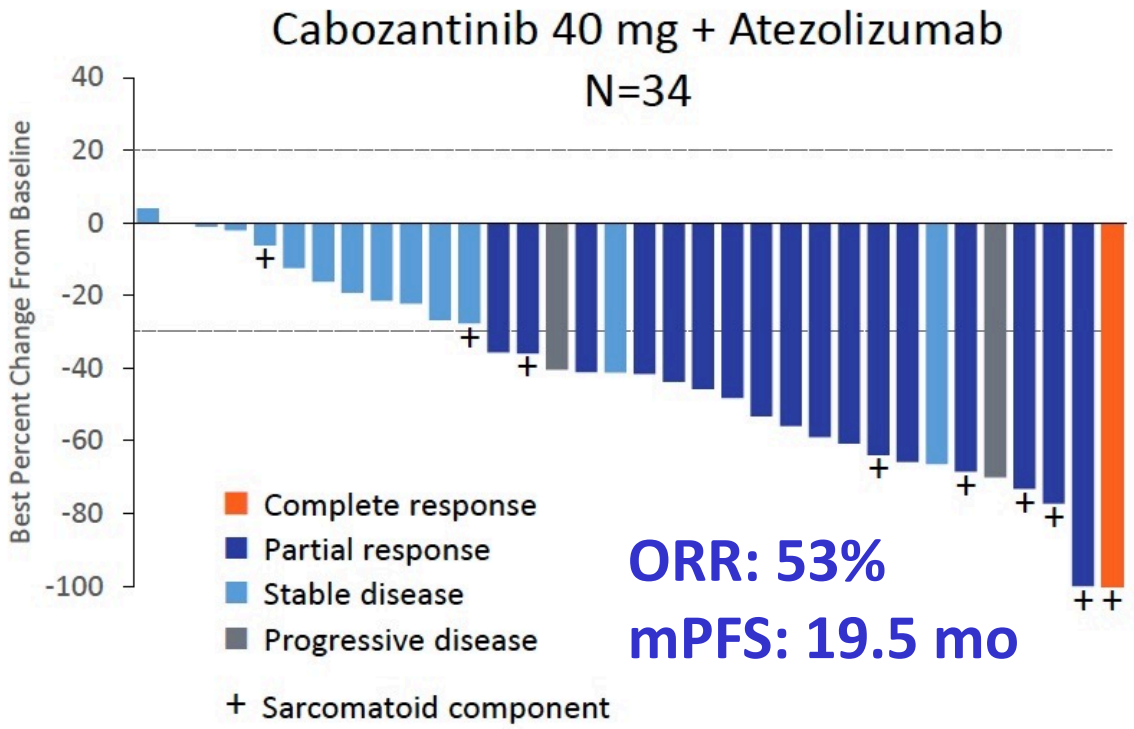
Grunwald V et al. ASCO 2021;Abstract 4560.

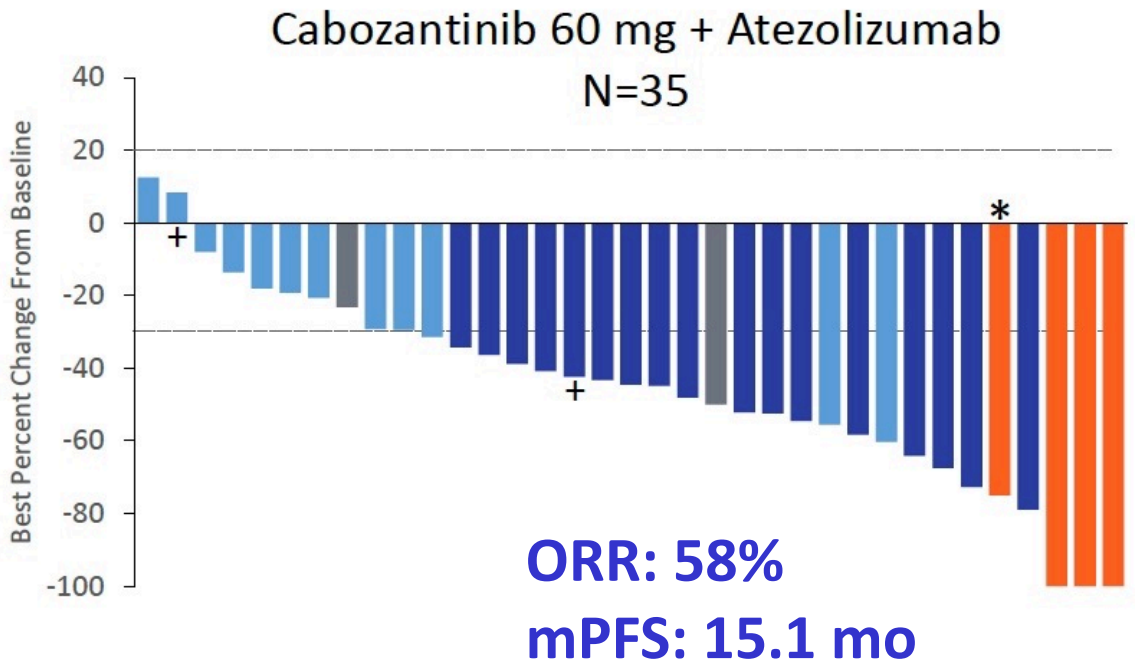
Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

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 • Placebo + nivolumab + ipilimumab (4 doses) → placebo + nivolumab	PFS	Nov 2021
PDIGREE	1,046	After induction nivolumab/ipilimumab • Pts with CR → Nivolumab • Pts with non-CR or non-PD, *randomized* → Nivolumab → Nivolumab + cabozantinib • Pts with PD → Cabozantinib	OS	Sept 2021

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

FDA Approves Tivozanib for Relapsed or Refractory Advanced RCC

Press Release: March 10, 2021

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

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

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

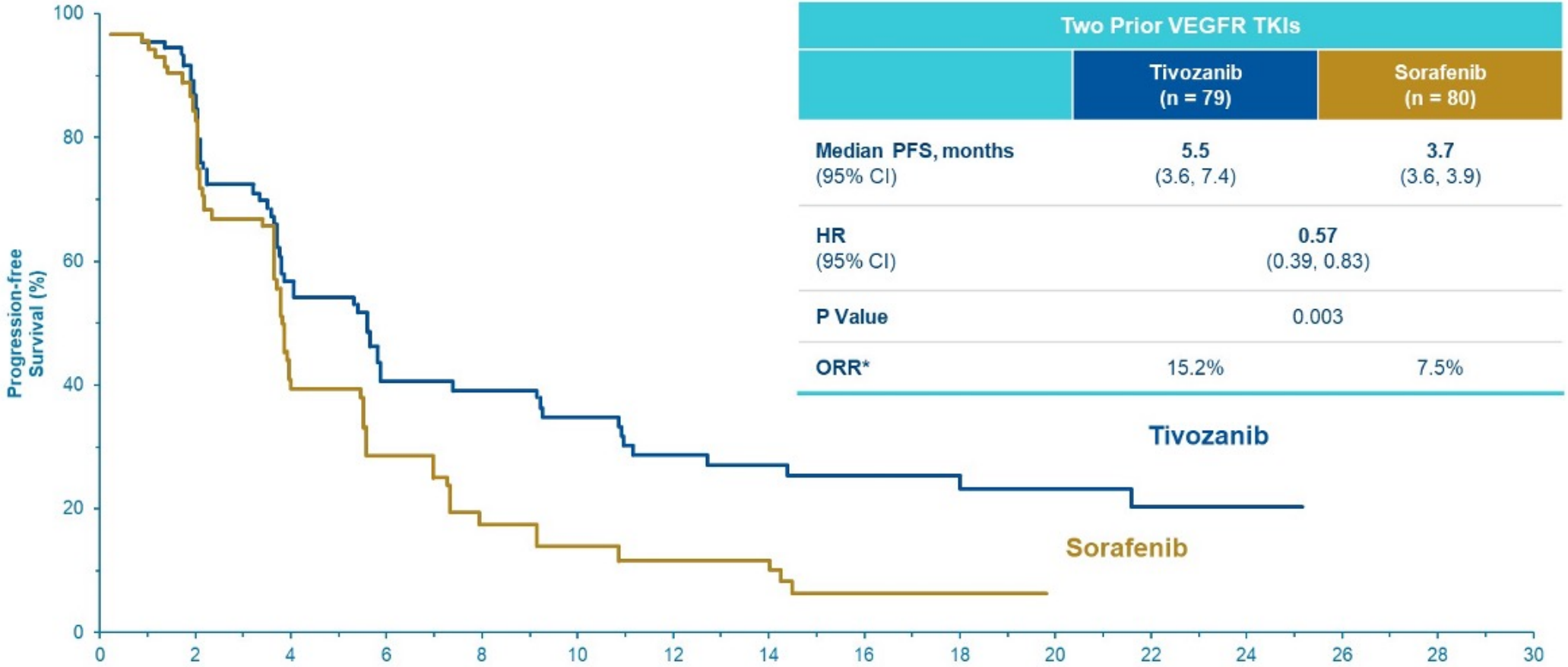
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

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

Rini BI et al.

Genitourinary Cancers Symposium 2021;Abstract 278.

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



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

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

TIVO-3: Tivozanib After Axitinib

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

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

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

Verzoni et al.
ASCO 2021;Abstract 4546.

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

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

FDA 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."

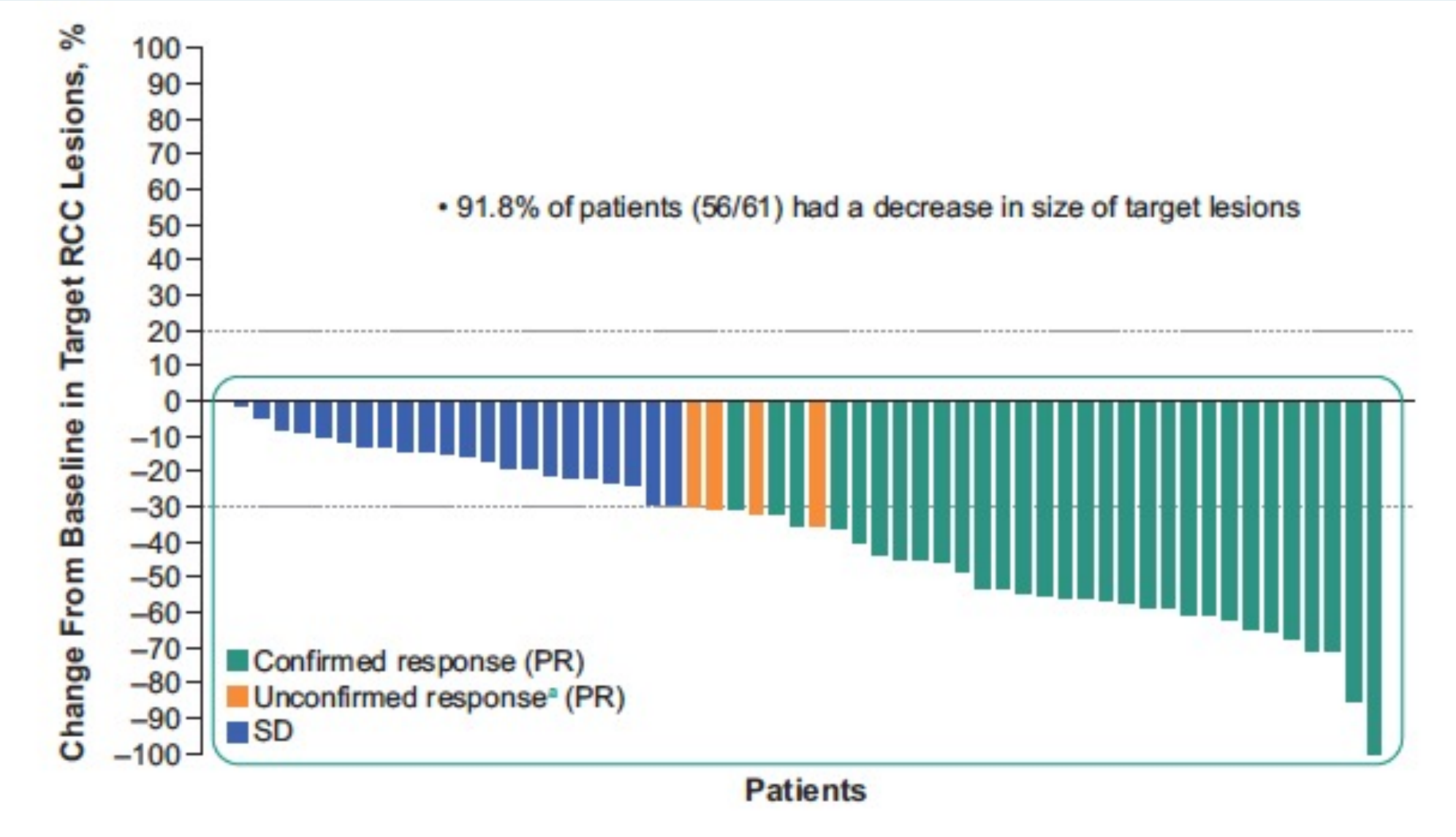
https://www.cancernetwork.com/view/fda-grants-priority-review-to-belzutifan-for-von-hippel-lindau-disease-associated-rcc

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.

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Genitourinary Cancers Symposium 2021;Abstract 272.

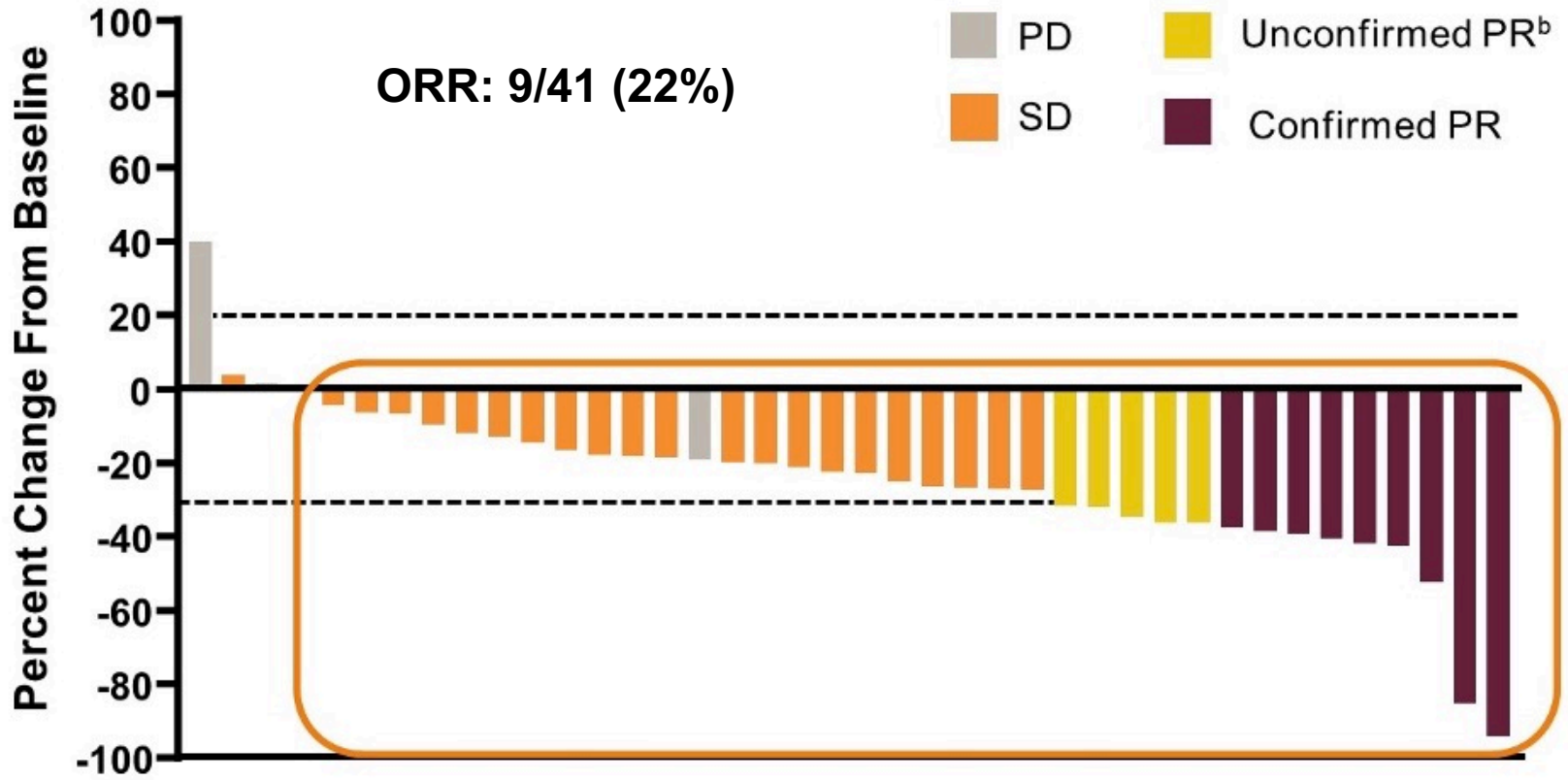
Phase 2 Study of the Oral Hypoxia-Inducible Factor 2α Inhibitor Belzutifan (MK-6482) in Combination With Cabozantinib in Patients With Advanced Clear Cell Renal Cell Carcinoma

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.

Expert Second Opinion — Investigators Discuss How They and Their Colleagues Navigate Emerging Clinical Research and Challenging Patients with Acute Myeloid Leukemia and Myelodysplastic Syndromes

Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

Monday, August 9, 2021
7:00 PM – 8:30 PM ET

Faculty

Krishna Gundabolu, MD
Richard M Stone, MD
Eunice S Wang, MD

Moderator

Harry Paul Erba, MD, PhD

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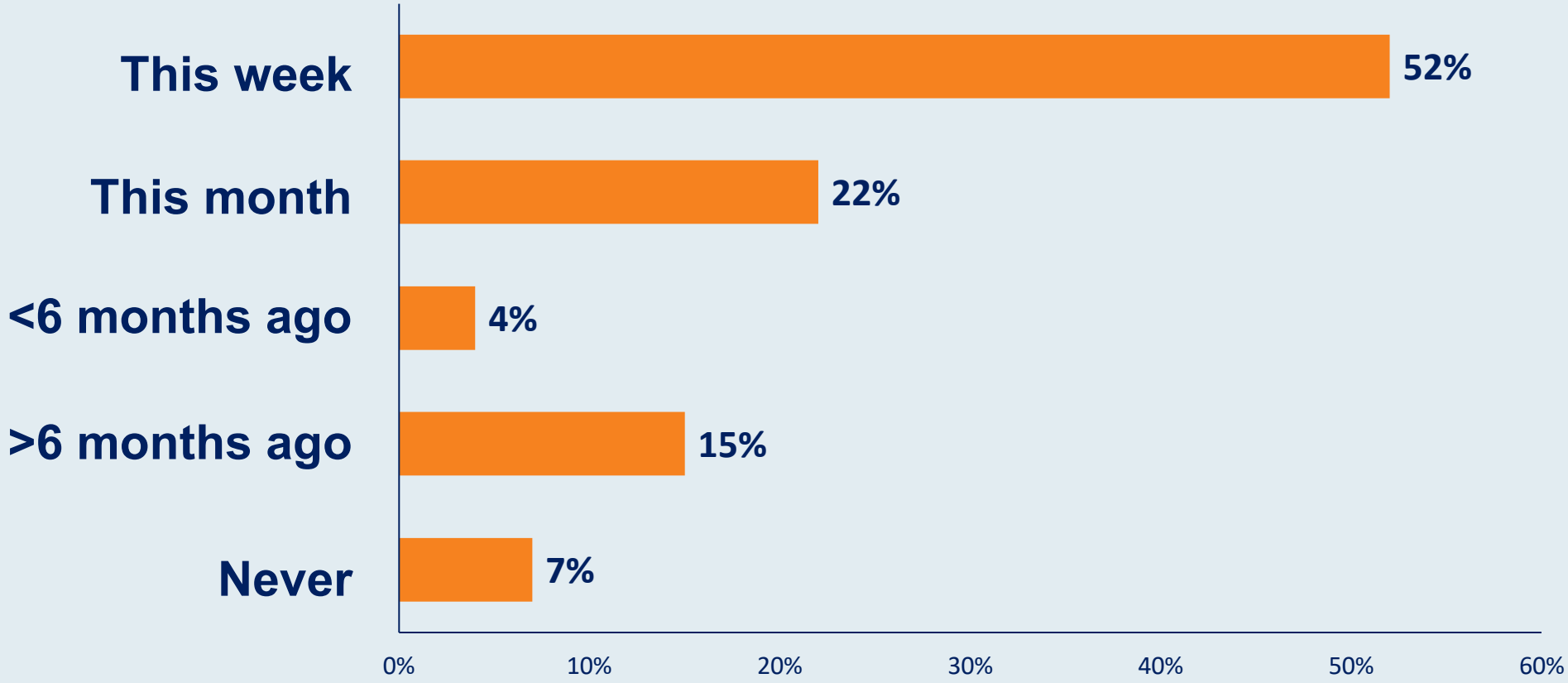
When was the last time that you presented, or had a case presented for you, at a local tumor board meeting?



Premeeting survey: July 2021

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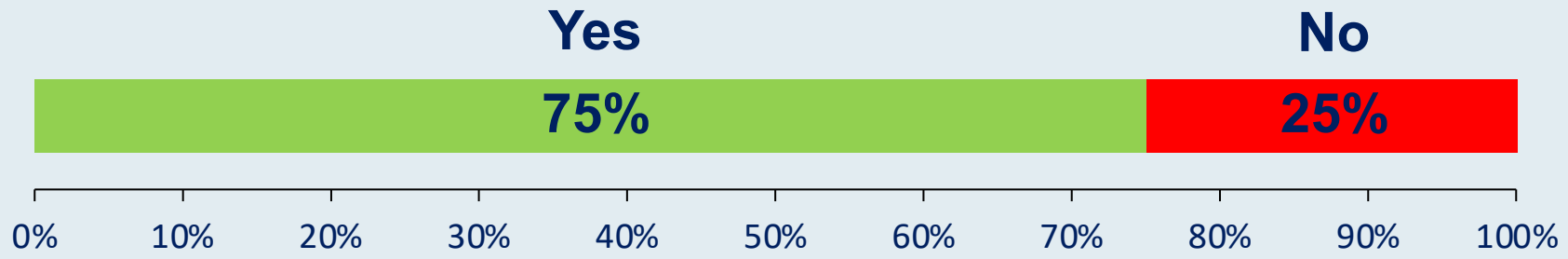
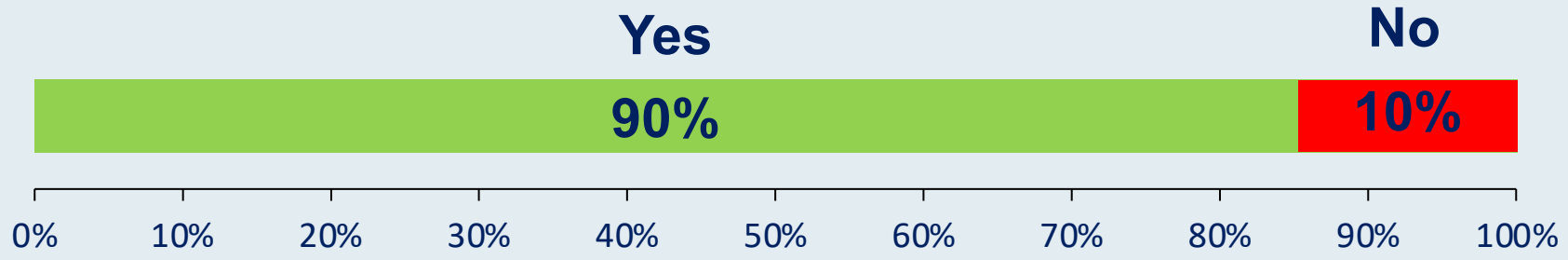
In the past month have you listened to audio podcasts not related to medicine?



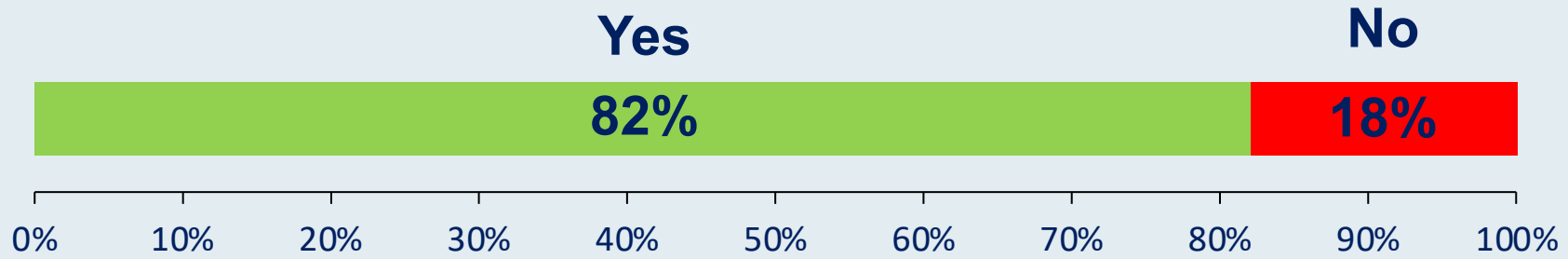
Median: 5 hours
Range: 1-60

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

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