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

Hans Hammers, MD, PhD

Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
Division of Hematology and Oncology
UT Southwestern Medical Center
Dallas, Texas



Commercial Support

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



Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.



Research To Practice CME Planning Committee Members, Staff and Reviewers

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

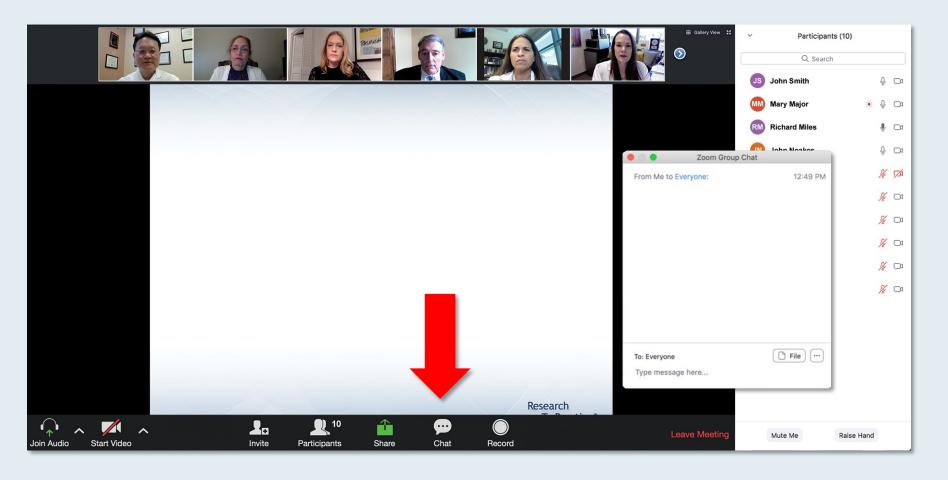


Dr Hammers — Disclosures

Advisory Committee	ARMO BioSciences, a wholly owned subsidiary of Eli Lilly and Company, Bristol-Myers Squibb Company, Corvus Pharmaceuticals, Exelixis Inc, Merck, Novartis, Pfizer Inc, Surface Oncology
Contracted Research	Bristol-Myers Squibb Company, Merck



We Encourage Clinicians in Practice to Submit Questions

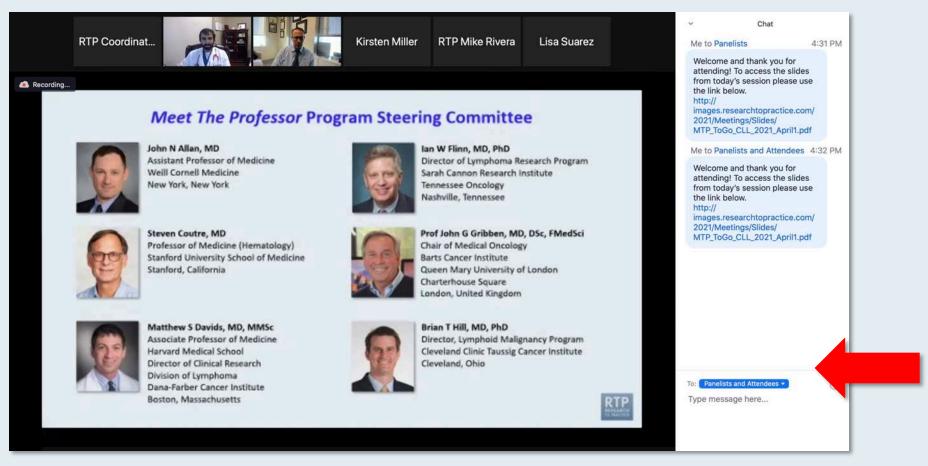


Feel free to submit questions now before the program begins and throughout the program.



Familiarizing Yourself with the Zoom Interface

Expand chat submission box

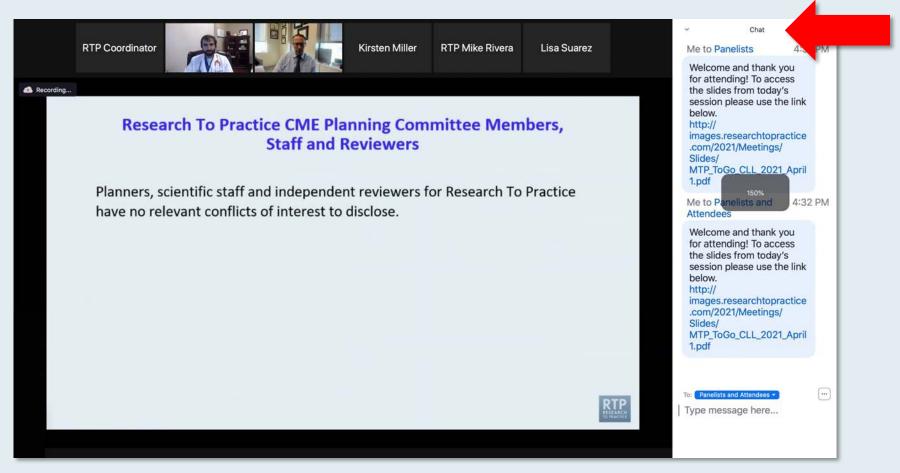


Drag the white line above the submission box up to create more space for your message.



Familiarizing Yourself with the Zoom Interface

Increase chat font size



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



ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Genitourinary Cancers from the 2021 ASCO Annual Meeting



DR ARJUN BALAR
NYU PERLMUTTER CANCER CENTER









Identifying, Managing and Mitigating Therapy-Related Adverse Events in Patients with Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Monday, October 4, 2021 5:00 PM – 6:00 PM ET

Faculty
Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist Daniel J Lenihan, MD



Meet The Professor

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

Wednesday, October 6, 2021 5:00 PM - 6:00 PM ET

Faculty
Virginia Kaklamani, MD, DSc



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

Friday, October 8, 2021 12:00 PM - 1:00 PM ET

Faculty
Eileen M O'Reilly, MD



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

Monday, October 11, 2021 5:00 PM - 6:00 PM ET

Faculty
Elizabeth R Plimack, MD, MS



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

A CME-MOC/NCPD Accredited Virtual Event

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

Faculty

Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD

Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH

Additional faculty to be announced.



Thank you for joining us!

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



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

Hans Hammers, MD, PhD

Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
Division of Hematology and Oncology
UT Southwestern Medical Center
Dallas, Texas



Meet The Professor Program Participating Faculty



Neeraj Agarwal, MD
Professor of Medicine
Senior Director for Clinical Research Innovation
Huntsman Cancer Institute Presidential Endowed Chair of Cancer Research
Director, Center of Investigational Therapeutics
Director, Genitourinary Oncology Program
Huntsman Cancer Institute, University of Utah
Salt Lake City, Utah



Hans Hammers, MD, PhD

Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
Division of Hematology and Oncology
UT Southwestern Medical Center
Dallas, Texas



Toni K Choueiri, MD

Director, Lank Center for Genitourinary Oncology

Department of Medical Oncology

Dana-Farber Cancer Institute

The Jerome and Nancy Kohlberg Professor of Medicine

Harvard Medical School

Boston, Massachusetts



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



Meet The Professor Program Participating Faculty



Eric Jonasch, MD
Professor of Medicine
Department of Genitourinary Medical Oncology
The University of Texas
MD Anderson Cancer Center
Houston, Texas



Robert J Motzer, MD
Attending Physician, Department of Medicine
Jack and Dorothy Byrne Chair in Clinical Oncology
Memorial Sloan Kettering Cancer Center
New York, New York



David F McDermott, MD
Chief, Medical Oncology
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
The Tisch Cancer Institute
Mount Sinai Health System
New York, New York



Meet The Professor Program Participating Faculty



Elizabeth R Plimack, MD, MS

Chief, Division of Genitourinary Medical Oncology
Director, Genitourinary Clinical Research
Professor, Department of Hematology/Oncology
Fox Chase Cancer Center, Temple Health
Philadelphia, Pennsylvania



Brian I Rini, MD
Chief of Clinical Trials
Vanderbilt-Ingram Cancer Center
Ingram Professor of Medicine
Division of Hematology/Oncology
Vanderbilt University Medical Center
Nashville, Tennessee



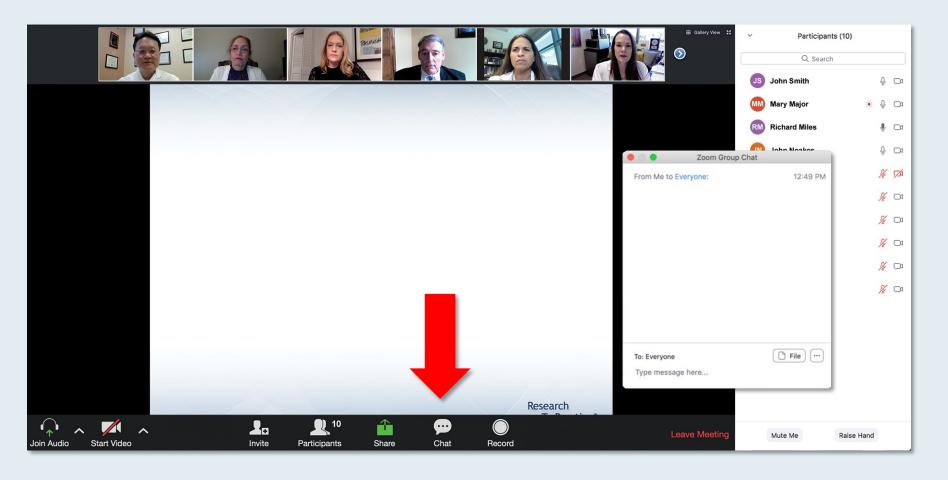
Thomas Powles, MBBS, MRCP, MD
Professor of Genitourinary Oncology
Barts Cancer Institute
Director of Barts Cancer Centre
Queen Mary University of London
London, United Kingdom



Moderator
Neil Love, MD
Research To Practice
Miami, Florida



We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.



Identifying, Managing and Mitigating Therapy-Related Adverse Events in Patients with Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Monday, October 4, 2021 5:00 PM – 6:00 PM ET

Faculty
Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist Daniel J Lenihan, MD



Meet The Professor

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

Wednesday, October 6, 2021 5:00 PM - 6:00 PM ET

Faculty
Virginia Kaklamani, MD, DSc



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

Friday, October 8, 2021 12:00 PM - 1:00 PM ET

Faculty
Eileen M O'Reilly, MD



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

Monday, October 11, 2021 5:00 PM - 6:00 PM ET

Faculty
Elizabeth R Plimack, MD, MS



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

A CME-MOC/NCPD Accredited Virtual Event

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

Faculty

Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD

Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH

Additional faculty to be announced.



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

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

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

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

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

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

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

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



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

Hans Hammers, MD, PhD

Eugene P Frenkel, MD Scholar in Clinical Medicine
Co-Leader, Kidney Cancer Program
Co-Leader, Experimental Therapeutics
Associate Professor, Internal Medicine
Division of Hematology and Oncology
UT Southwestern Medical Center
Dallas, Texas





Eric Jonasch, MD
Professor of Medicine
Department of Genitourinary
Medical Oncology
The University of Texas
MD Anderson Cancer Center
Houston, Texas



Kapisthalam (KS) Kumar, MD
Physician Partner
Florida Cancer Specialists and
Research Institute
New Port Richey, Florida



Philip Glynn, MD
Director, Medical Oncology
Mercy Medical Center
Springfield, Massachusetts



Elizabeth R Plimack, MD, MS
Chief, Division of Genitourinary
Medical Oncology
Director, Genitourinary Clinical
Research
Professor, Department of
Hematology/Oncology
Fox Chase Cancer Center
Temple Health
Philadelphia, Pennsylvania



Dhatri Kodali, MD
Medical Oncologist
Texas Oncology
Houston, Texas



Meet The Professor with Dr Hammers

MODULE 1: Case Presentations

- Dr Plimack: A 69-year-old man with metastatic clear cell RCC
- Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features
- Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease
- Dr Glynn: An 81-year-old man with metastatic RCC

MODULE 2: ESMO 2021 Review and Journal Club with Dr Hammers

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets



Meet The Professor with Dr Hammers

MODULE 1: Case Presentations

- Dr Plimack: A 69-year-old man with metastatic clear cell RCC
- Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features
- Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease
- Dr Glynn: An 81-year-old man with metastatic RCC

MODULE 2: ESMO 2021 Review and Journal Club with Dr Hammers

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets



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



Dr Elizabeth Plimack

- Age 58: S/p bilateral partial nephrectomies for Stage I ccRCC
- Ten years later: Small lung metastases biopsy-confirmed ccRCC Slow growth trajectory
- Pazopanib x 1 year
 - Dose holds/adjustments for diarrhea
 - Discontinued for fatigue while responding
- Cabozantinib x 6 months
 - Dose reduced, then discontinued due to poor tolerance in the setting of PD due to subtherapeutic dosing
- Ipilimumab/nivolumab
 - LFT abnormalities, hepatitis → Hospitalization and steroids

Question

• In this patient who had initially an excellent response to ipilimumab and nivolumab, had immunemediated hepatitis as an adverse effect of that treatment, now with progression having been off that treatment, would anyone rechallenge this patient with nivolumab versus switching to alternate therapy?



Case Presentation – Dr Plimack: A 69-year-old man with metastatic clear cell RCC (continued)



Dr Elizabeth Plimack

- Age 58: S/p bilateral partial nephrectomies for Stage I ccRCC
- Ten years later: Small lung metastases biopsy-confirmed ccRCC Slow growth trajectory
- Pazopanib x 1 year
 - Dose holds/adjustments for diarrhea
 - Discontinued for fatigue while responding
- Cabozantinib x 6 months
 - Dose reduced, then discontinued due to poor tolerance in the setting of PD due to subtherapeutic dosing
- Ipilimumab/nivolumab
 - LFT abnormalities, hepatitis → Hospitalization and steroids
- Re-challenged with nivolumab but PD after 6 months
 - No recurrent hepatitis



Case Presentation – Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features



Dr KS Kumar

- PMH: Hailey-Hailey skin disorder (benign pemphigus)
- Left clear cell RCC, with 3-4 small, bilateral pulmonary nodules
- Radical nephrectomy, clear cell RCC with 10-15% rhabdoid features
- Double IO therapy planned

Questions

- In light of the rhabdoid differentiation, would you administer double IO therapy, or would you go with a TKI/IO combination regimen?
- Would you treat the pulmonary nodules or observe those for now since they are quite small?
- Is there a contraindication to IO therapy in patients with non-autoimmune pemphigus?
- Am I making a mistake by not treating her immediately, or should I treat her right away?



Case Presentation – Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC



Dr Dhatri Kodali

- Father and sister RCC at a young age
- S/p radical nephrectomy and periaortic dissection for T3aN0 clear cell RCC
- Surveillance → Recurrent ascites, with negative cytology
- Laparoscopy: Widespread peritoneal carcinomatosis, papillary RCC
- Awaiting germline genetic testing results

Questions

- Do you see a role for combination therapy for this patient?
- Is there a difference between hereditary and sporadic RCC, especially when there is doubt between clear cell or papillary, or mixed kind in terms of first-line therapy?



Case Presentation – Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC (continued)

- Father and sister RCC at a young age
- S/p radical nephrectomy and periaortic dissection for T3aNO clear cell RCC
- Surveillance → Recurrent ascites, with negative cytology
- Laparoscopy: Widespread peritoneal carcinomatosis, papillary RCC
- Awaiting germline genetic testing results
- Nivolumab/cabozantinib



Dr Dhatri Kodali



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

- Began surveillance in his early 20s
- PMH: hemangioblastoma, small renal cell mass



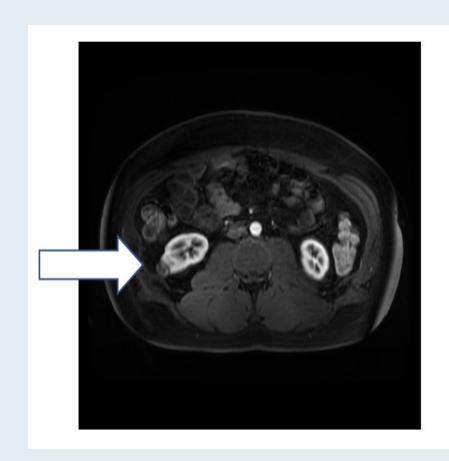
Dr Eric Jonasch

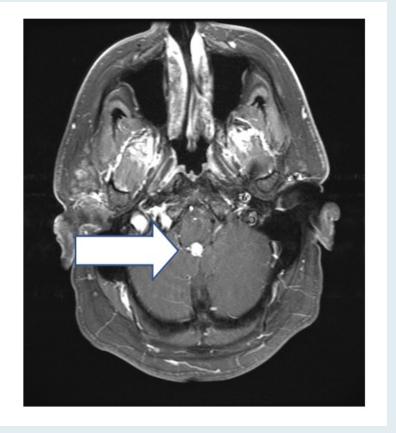


Case Presentation – Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease (continued)



Dr Eric Jonasch







Case Presentation – Dr Glynn: An 81-year-old man with metastatic RCC



Dr Philip Glynn

- 8/2019: Progressive weight loss, anemia
- CT: Left renal lesion, with involvement of renal vein \rightarrow surgical resection, T3N0
- 8/2020 radiographic assessment: Pulmonary nodularity → biopsy-proven mRCC
- Pembrolizumab/axitinib
- 2/2021 radiographic assessment: Mild-to-moderate improvement in pulmonary nodules

Question

• In 2021, with the availability of the cabozantinib/nivolumab regimen, would you have made a different selection for initial treatment, or would you have gone with pembrolizumab/axitinib?



Meet The Professor with Dr Hammers

MODULE 1: Case Presentations

- Dr Plimack: A 69-year-old man with metastatic clear cell RCC
- Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features
- Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease
- Dr Glynn: An 81-year-old man with metastatic RCC

MODULE 2: ESMO 2021 Review and Journal Club with Dr Hammers

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets



ESMO 2021 Review

- Choueiri TK et al. Pembrolizumab (pembro) vs placebo as adjuvant therapy for patients (pts) with renal cell carcinoma (RCC): Patient-reported outcomes (PRO) in KEYNOTE-564. ESMO 2021; Abstract 6530.
- Derosa L et al. Antibiotic (ATB) therapy and outcome from nivolumab (N) in metastatic renal cell carcinoma (mRCC) patients (pts): Results of the GETUG-AFU 26 NIVOREN multicentric phase II study. ESMO 2021; Abstract 657MO.
- Rini BI et al. Randomized, open-label, 3-arm phase III study comparing MK-1308A +
 lenvatinib and pembrolizumab (pembro) + belzutifan + lenvatinib versus pembro +
 lenvatinib as first-line (1L) treatment for advanced clear cell renal cell carcinoma (ccRCC).
 ESMO 2021;Abstract 717TiP.
- McDermott DF et al. Phase II study of belzutifan (MK-6482), an oral hypoxia-inducible factor 2α (HIF-2α) inhibitor, plus cabozantinib for treatment of advanced clear cell renal cell carcinoma (ccRCC). ESMO 2021;Abstract 656MO.



ESMO 2021 Review

- Vasudev NS et al. Nivolumab in combination with alternatively scheduled ipilimumab in first-line treatment of patients with advanced renal cell carcinoma: A randomized phase II trial (PRISM). ESMO 2021;Abstract LBA29.
- Choueiri TK et al. **Phase III CLEAR trial in advanced renal cell carcinoma (aRCC): Outcomes in subgroups and toxicity update.** ESMO 2021; Abstract 660P.
- Motzer RJ et al. Conditional survival and 5-year follow-up in CheckMate 214: First-line nivolumab + ipilimumab (N + I) versus sunitinib (S) in advanced renal cell carcinoma (aRCC). ESMO 2021; Abstract 661P.
- Procopio G et al. A phase II prospective trial of frontline cabozantinib in metastatic collecting ducts renal cell carcinoma: The BONSAI trial (Meeturo 2). ESMO 2021;Abstract 654MO.



Journal Club with Dr Hammers

- Choueiri TK et al; KEYNOTE-564 Investigators. **Adjuvant pembrolizumab after nephrectomy** in renal-cell carcinoma. *N Engl J Med* 2021;385(8):683-94.
- Patel V et al. Acute interstitial nephritis, a potential predictor of response to immune checkpoint inhibitors in renal cell carcinoma. *J Immunother Cancer* 2020;8(2):e001198.
- Singla N et al. Improved survival after cytoreductive nephrectomy for metastatic renal cell carcinoma in the contemporary immunotherapy era: An analysis of the National Cancer Database. *Urol Oncol* 2020;38(6):604.e9-17.
- Rini Bl et al. Characterization and management of treatment-emergent hepatic toxicity in
 patients with advanced renal cell carcinoma receiving first-line pembrolizumab plus axitinib.
 Results from the KEYNOTE-426 trial. Eur Urol Oncol 2021; [Online ahead of print].



Journal Club with Dr Hammers

- Gorin MA et al. Neoadjuvant nivolumab in patients with high-risk nonmetastatic renal cell carcinoma. Eur Urol Oncol 2021;[Online ahead of print].
- Harrison MR et al. Active surveillance of metastatic renal cell carcinoma: Results from a prospective observational study (MaRCC). Cancer 2021;127(13):2204-12.
- Gul A et al. Salvage ipilimumab and nivolumab in patients with metastatic renal cell carcinoma after prior immune checkpoint inhibitors. *J Clin Oncol* 2020;38(27):3088-94.
- Hannan R et al. Phase II trial of stereotactic ablative radiation (SAbR) for oligoprogressive kidney cancer. ASCO 2021;Abstract 4564.
- McGregor BA et al. Cabozantinib (C) in combination with nivolumab (N) and ipilimumab (I)
 (CaNI) for advanced renal cell carcinoma with variant histology (aRCCVH). ASCO 2021;
 Abstract TPS4592.
- Plimack ER et al. A phase 1b/2 umbrella study of investigational immune and targeted combination therapies as first-line therapy for patients with advanced renal cell carcinoma (RCC). ASCO 2021; Abstract TPS4594.



Meet The Professor with Dr Hammers

MODULE 1: Case Presentations

- Dr Plimack: A 69-year-old man with metastatic clear cell RCC
- Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features
- Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease
- Dr Glynn: An 81-year-old man with metastatic RCC

MODULE 2: ESMO 2021 Review and Journal Club with Dr Hammers

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets



Optimizing Front-Line Decision-Making for Advanced RCC

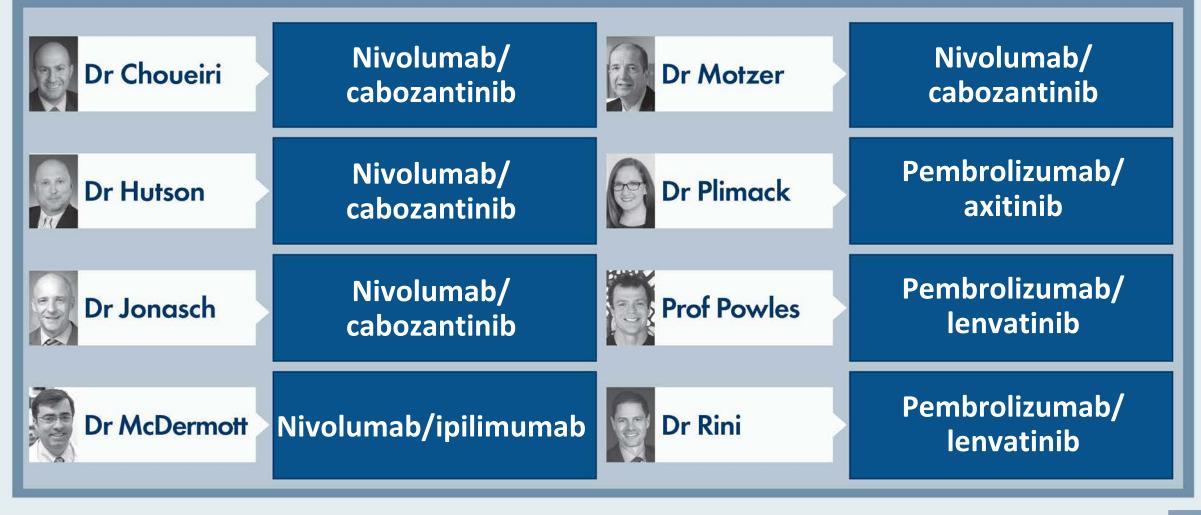


Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a 65-year-old patient with a history of nephrectomy for clear cell renal cell carcinoma (RCC) who on routine follow-up 3 years later is found to have asymptomatic bone metastases (PS 0)?

- 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 <u>65-year-old</u> 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)?



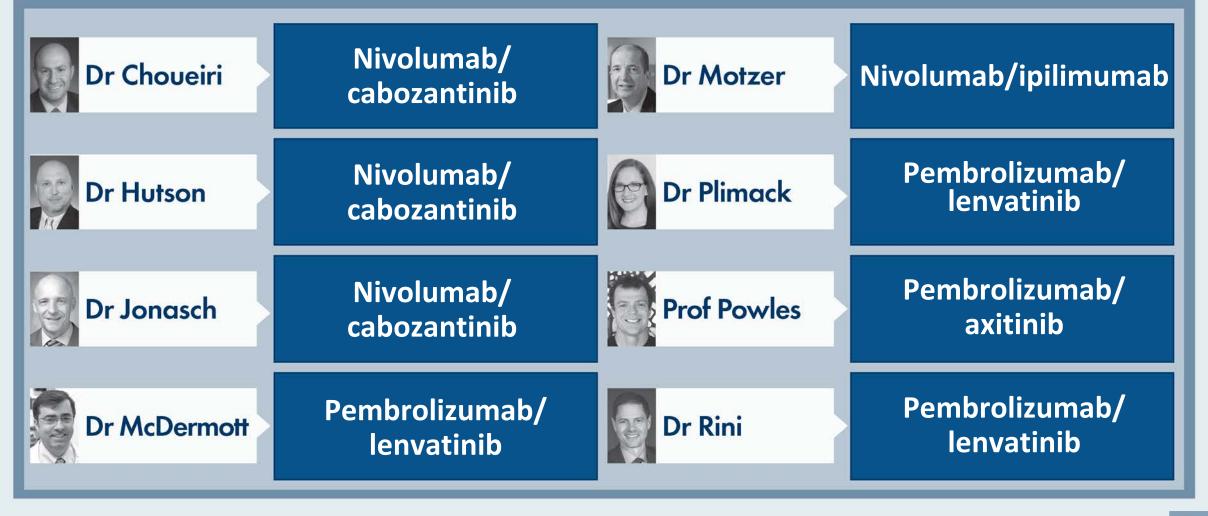


Regulatory and reimbursement issues aside, which first-line therapy would you recommend for a <u>65-year-old</u> patient who presents with clear cell RCC with multiple painful bone metastases and hemoglobin (Hb) of 11.4 g/dL (PS 1)?

- 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 <u>65-year-old</u> patient who presents with clear cell RCC with multiple painful bone metastases and hemoglobin (Hb) of 11.4 g/dL (PS = 1)?



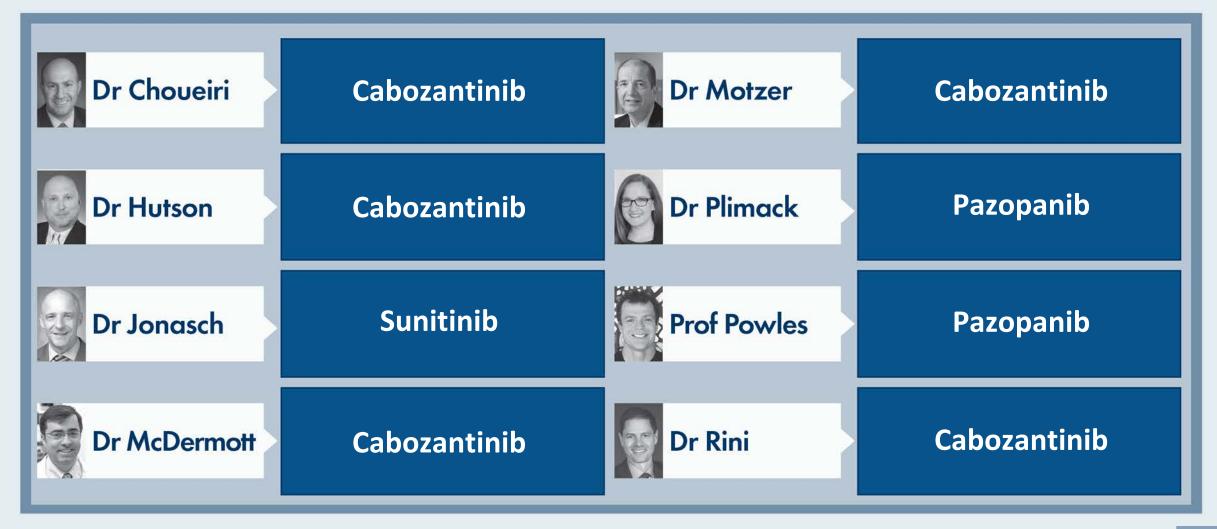


In general, which first-line therapy would you recommend for a 65-year-old patient who presents with metastatic clear cell RCC and for whom the use of immune checkpoint inhibitors is contraindicated?

- 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?





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?





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?





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

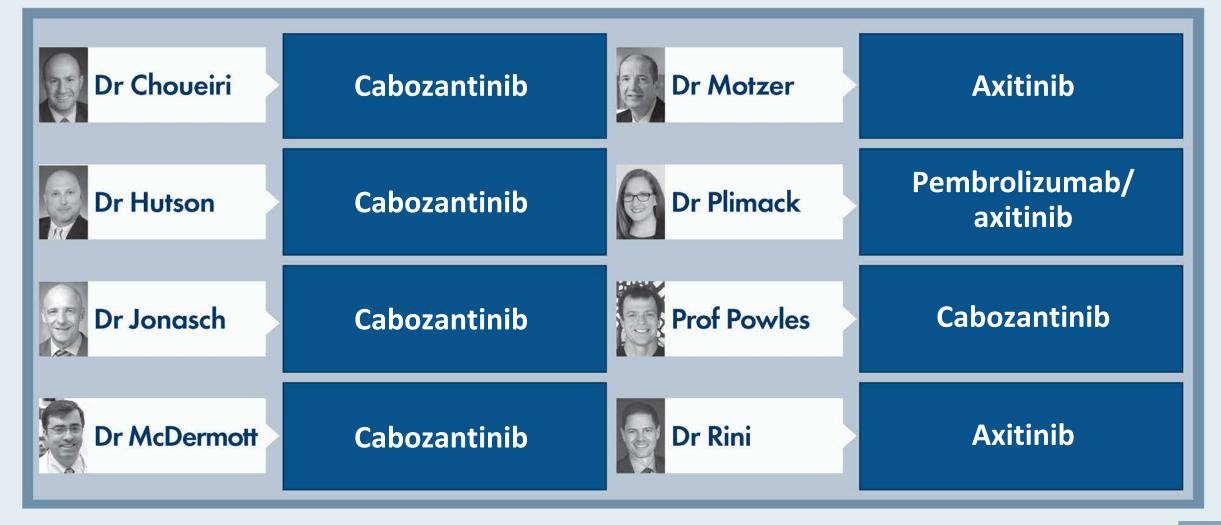


In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear-cell RCC who receives first-line <u>ipilimumab/nivolumab</u> and experiences disease progression after 12 months?

- 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?





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

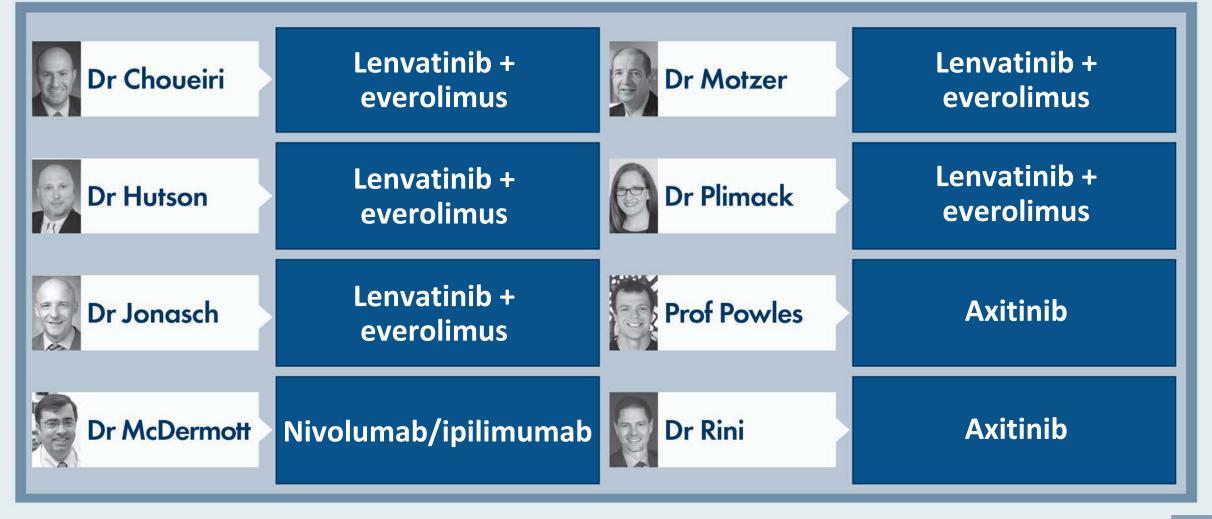


In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear cell RCC who receives first-line pembrolizumab/axitinib and experiences disease progression after 12 months?





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?





Meet The Professor with Dr Hammers

MODULE 1: Case Presentations

- Dr Plimack: A 69-year-old man with metastatic clear cell RCC
- Dr Kumar: A 53-year-old woman with metastatic RCC with rhabdoid features
- Dr Kodali: A 34-year-old man with widespread peritoneal carcinomatosis and papillary RCC
- Dr Jonasch: A 30-year-old man with von Hippel-Lindau disease
- Dr Glynn: An 81-year-old man with metastatic RCC

MODULE 2: ESMO 2021 Review and Journal Club with Dr Hammers

MODULE 3: Beyond the Guidelines

MODULE 4: Key Data Sets



Open access



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, Mauricio Burotto, David McDermott, ^{4,5} Elizabeth R Plimack,⁶ Philippe Barthélémy,^{7,8} Camillo Porta ⁽¹⁾, 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 Motzer²⁴

ESMO Open 2020;5(6):e001079.

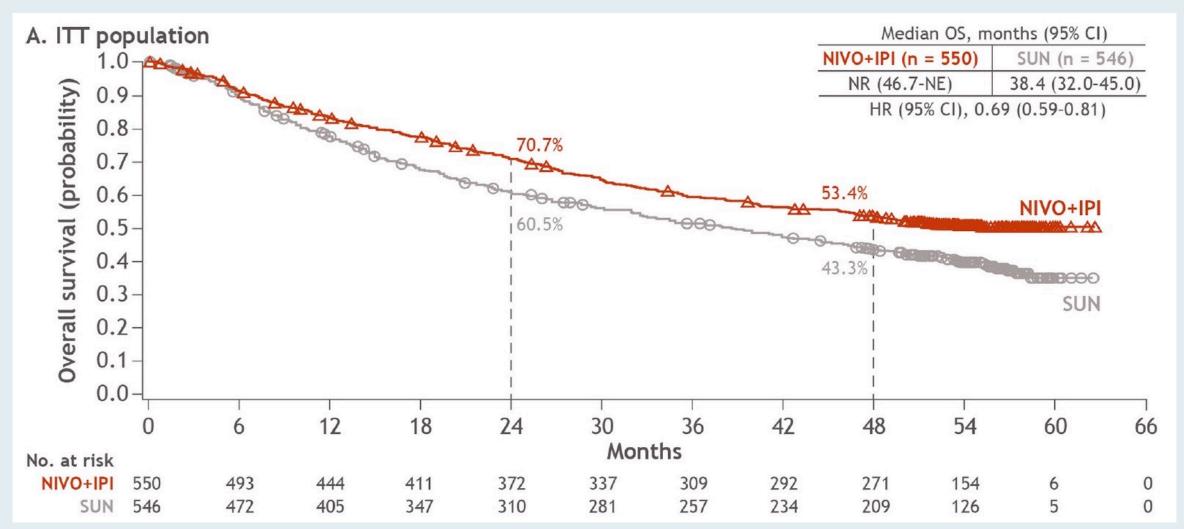


CheckMate 214: Overall Response and Best Response Rate per IRRC at 4 Years Minimum Follow-Up in ITT Population

	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%

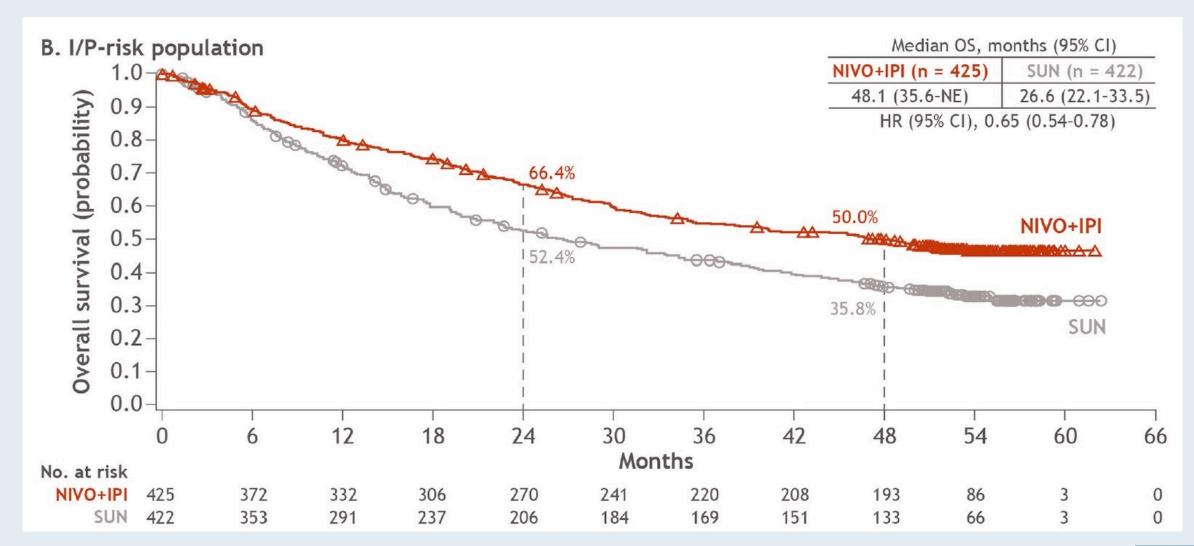


CheckMate 214: Overall Survival (ITT)





CheckMate 214: Overall Survival (Intermediate/Poor Risk)





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

The NEW ENGLAND JOURNAL of MEDICINE

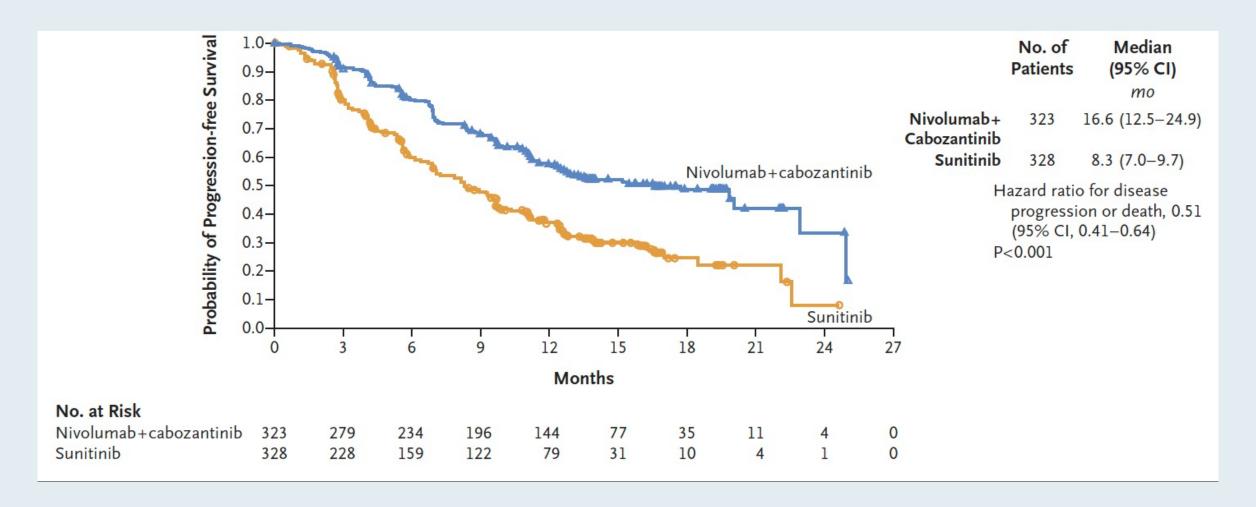
ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

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

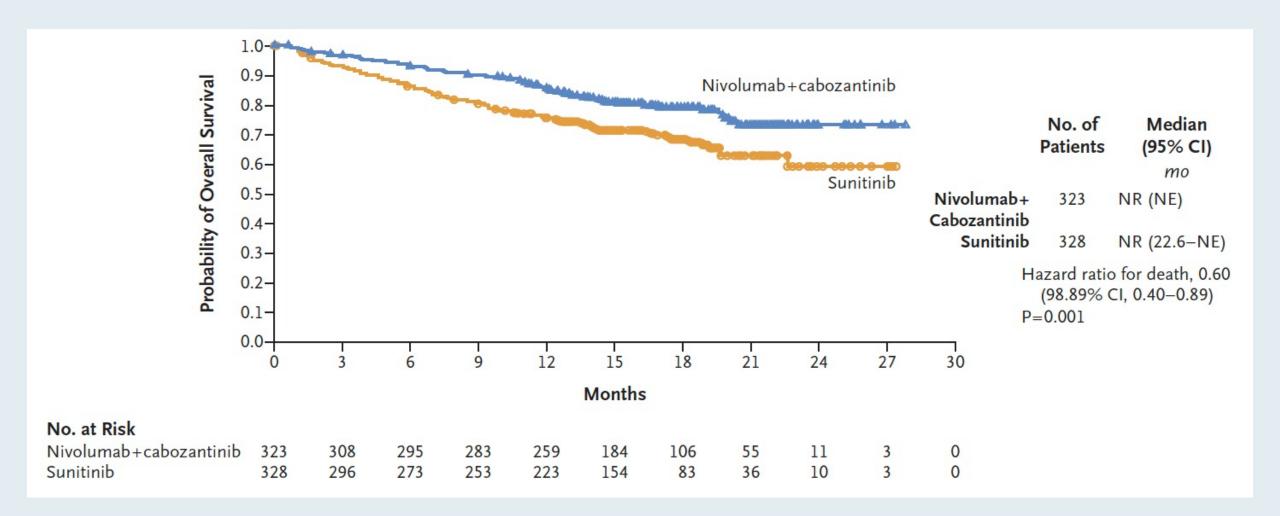


CheckMate 9ER: Progression-Free Survival





CheckMate 9ER: Overall Survival





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

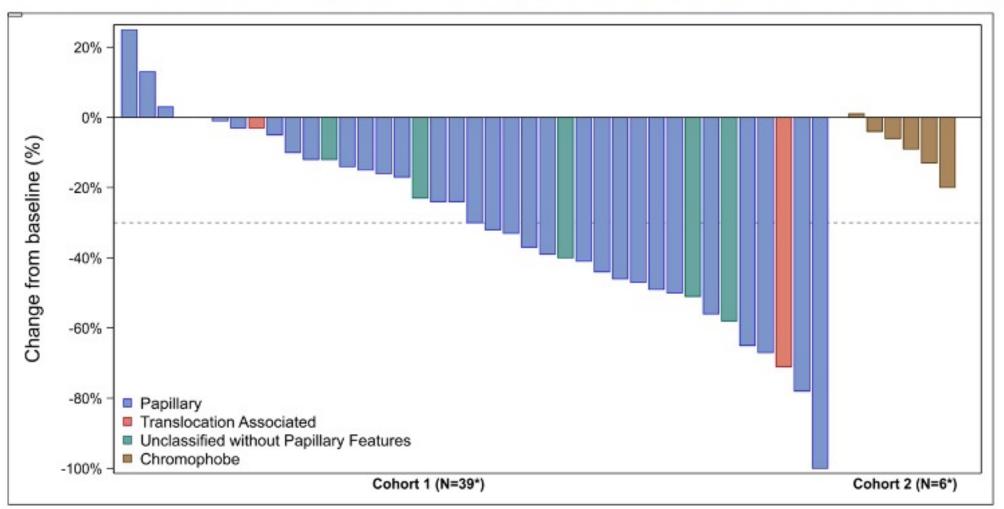
Chung-Han Lee, Martin H Voss, Maria Isabel Carlo, Ying-Bei Chen, Ed Reznik, Andrea Knezevic, Robert A Lefkowitz, Natalie Shapnik, Diana Tassone, Chloe Dadoun, Mark Zucker, Neil J. Shah, Colette Ngozi Owens, Deaglan Joseph McHugh, David Henry Aggen, Andrew Leonard Laccetti, Ritesh Kotecha, Darren R. Feldman, Robert J. Motzer June 6, 2021



Corresponding Author Contact: Dr. Chung-Han Lee leec4@mskcc.org



Maximum Change in Target Lesions by Histology





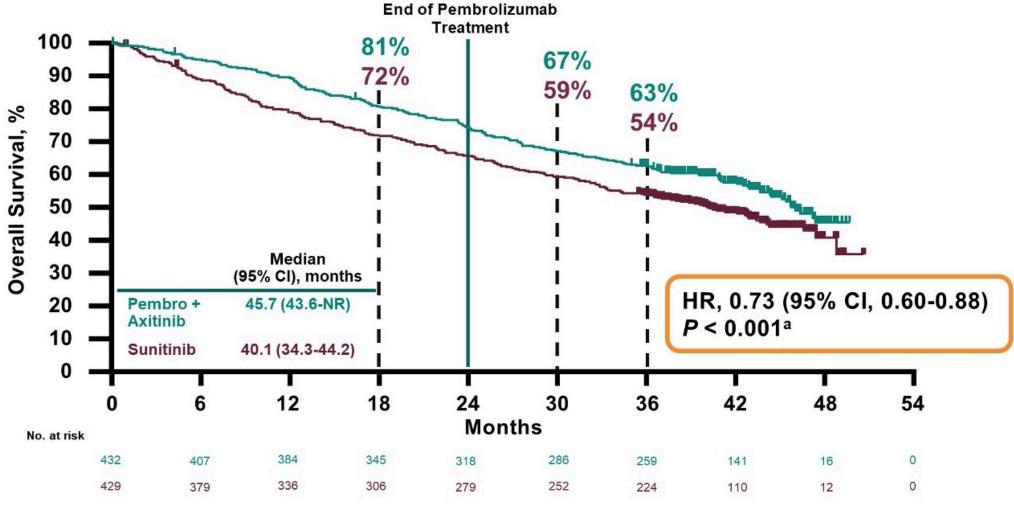
Pembrolizumab Plus Axitinib Versus Sunitinib as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma: Results From 42-Month Follow-Up of KEYNOTE-426

- B. I. Rini¹; E. R. Plimack²; V. Stus³; T. Waddell⁴; R. Gafanov⁵; F. Pouliot⁶; D. Nosov⁷;
- B. Melichar⁸; D. Soulieres⁹; D. Borchiellini¹⁰; I. Vynnychenko¹¹; R. S. McDermott¹²;
- S. J. Azevedo¹³; S. Tamada¹⁴; A. Kryzhanivska¹⁵; C. Li¹⁶; J. E. Burgents¹⁶;
- L. R. Molife¹⁷; J. Bedke¹⁸; T. Powles¹⁹

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



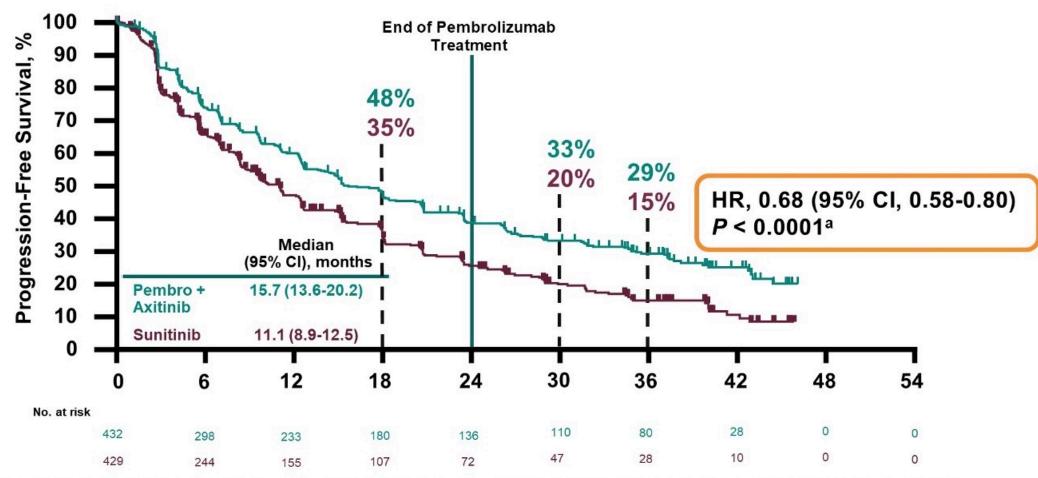
OS in the ITT Population



^aBecause 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.



PFS in the ITT Population



^aBecause 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.



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





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

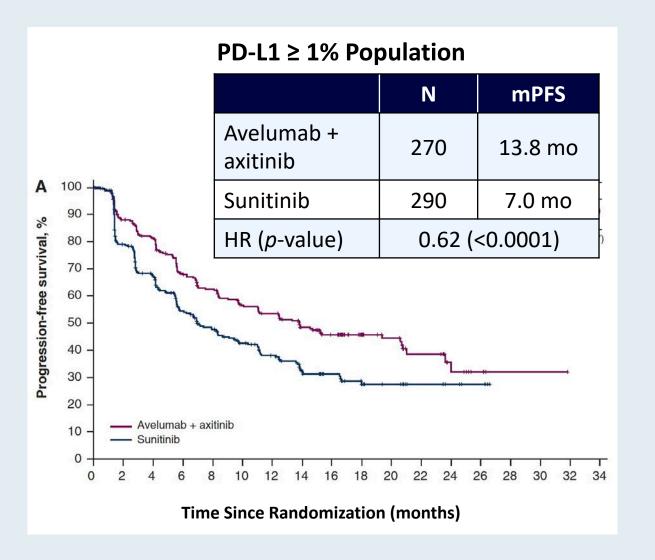


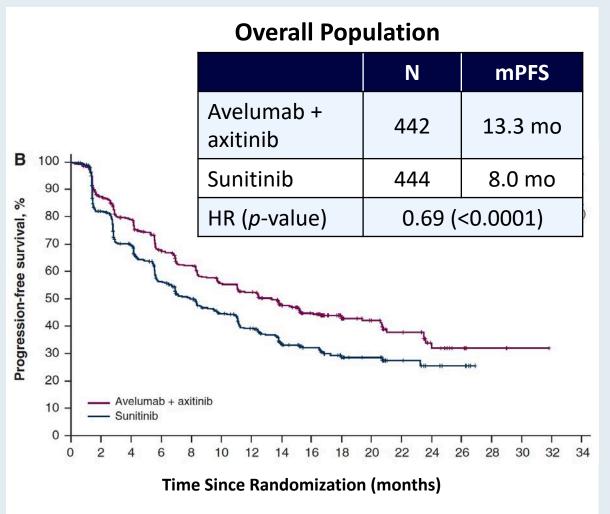
JAVELIN Renal 101: Overall Response and Best Response Rate in the PD-L1-Positive and Overall Populations

	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%	



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







FDA Approves Lenvatinib with Pembrolizumab for Advanced RCC

Press Release – August 10, 2021

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

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

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



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

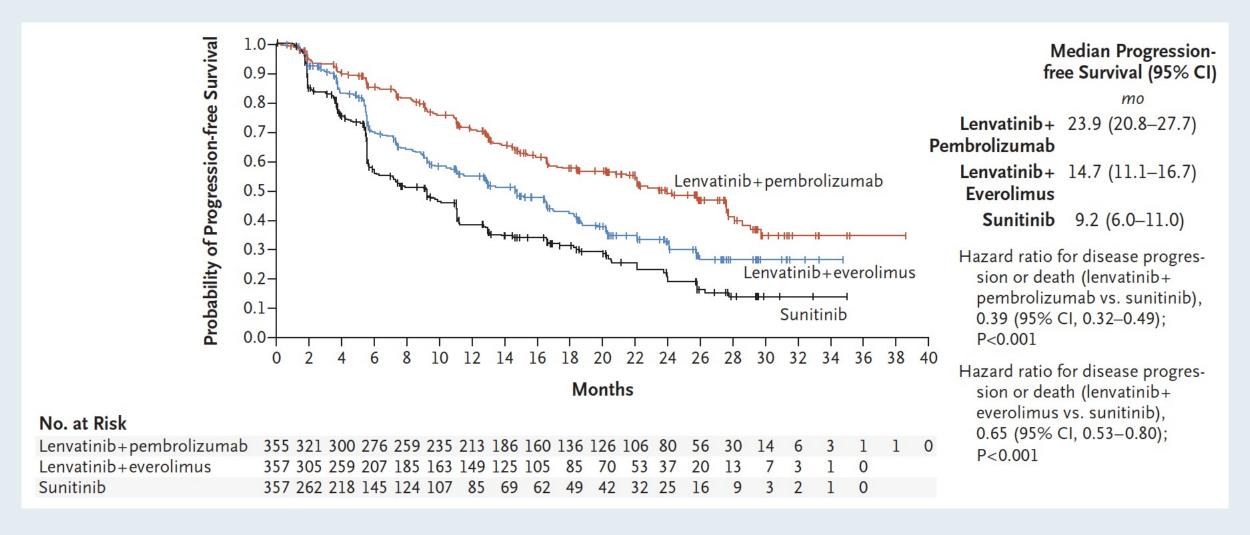
Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma

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].

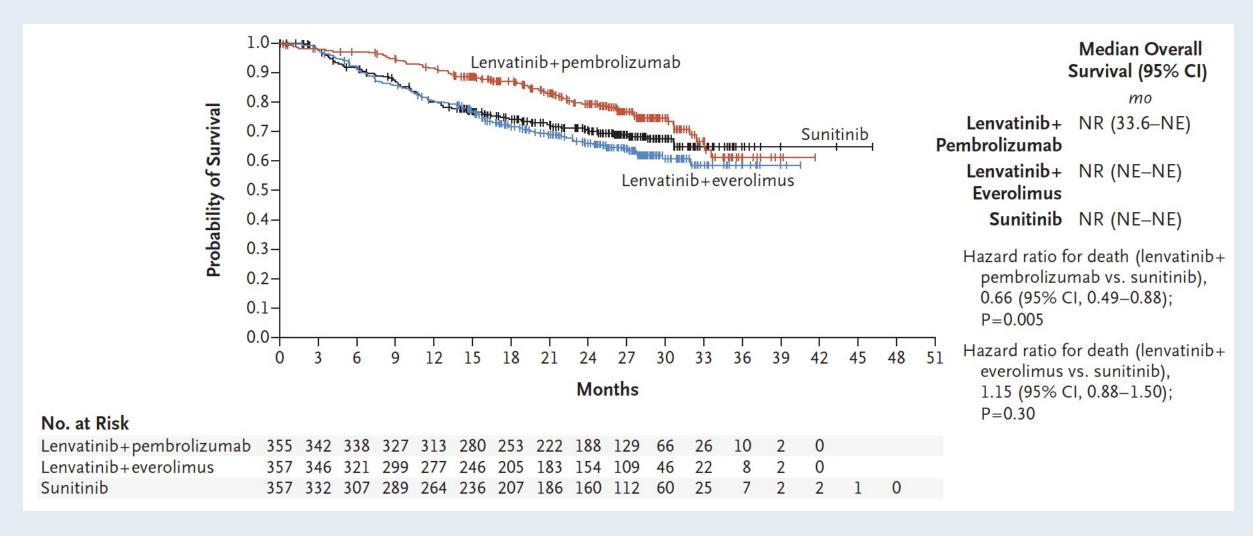


CLEAR: Progression-Free Survival





CLEAR: Overall Survival





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

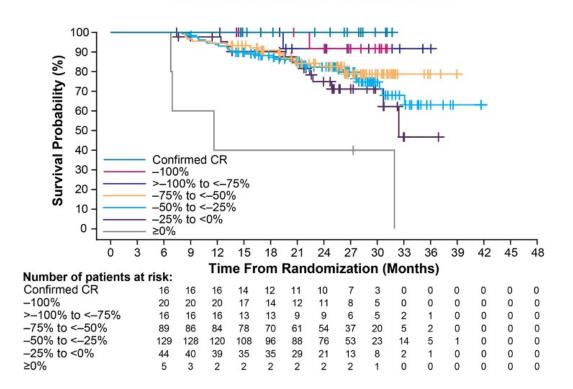
Viktor Grünwald¹, Thomas Powles², Evgeny Kopyltsov³, Vadim Kozlov⁴, Teresa Alonso Gordoa⁵, Masatoshi Eto⁶, Thomas Hutsonժ, Robert Motzer⁶, Eric Winquist⁶, Pablo Maroto¹⁰, Bhumsuk Keam¹¹, Giuseppe Procopio¹², Shirley Wong¹³, Bohuslav Melichar¹⁴, Frederic Rolland¹⁵, Mototsugu Oya¹⁶, Karla Rodriguez-Lopez¹ժ, Kenichi Saito¹⁶, Alan Smith¹⁶, Camillo Porta²⁰

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

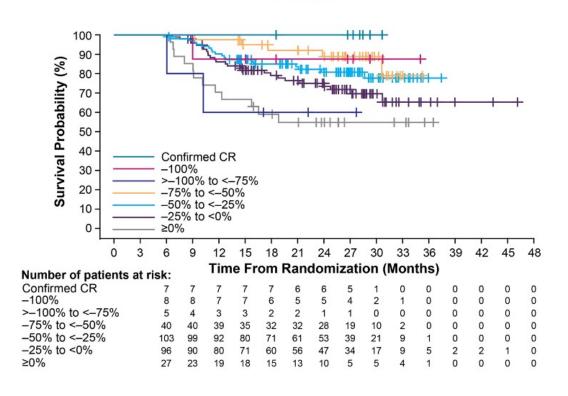


CLEAR: 6-Month OS Analysis by Depth of Response

Lenvatinib plus Pembrolizumab



Sunitinib



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



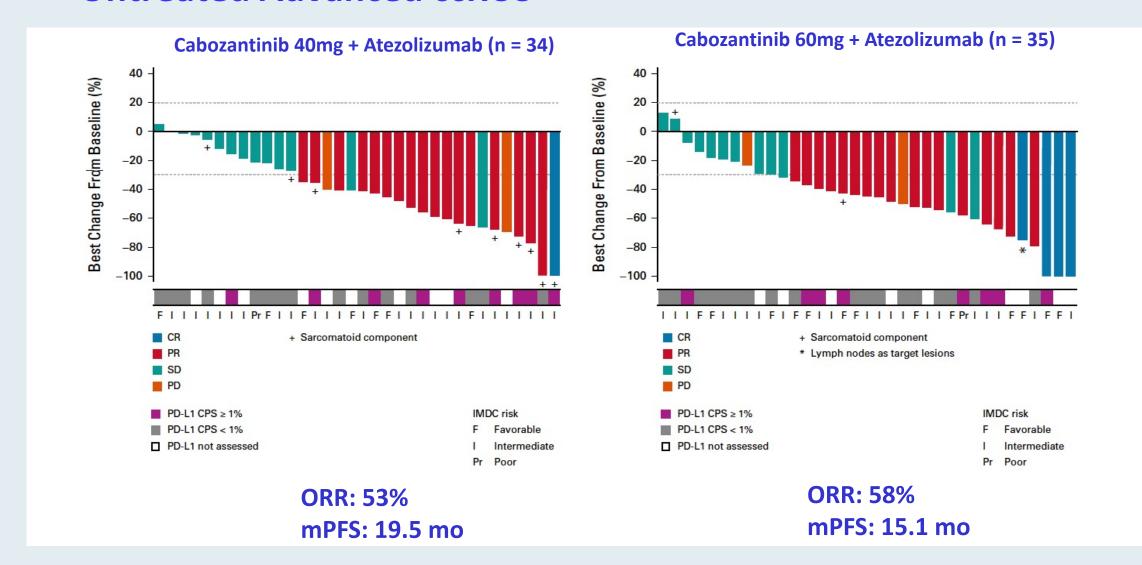
Cabozantinib in Combination With Atezolizumab for Advanced Renal Cell Carcinoma: Results From the COSMIC-021 Study

Sumanta K. Pal, MD¹; Bradley McGregor, MD²; Cristina Suárez, MD³; Che-Kai Tsao, MD⁴; William Kelly, DO⁵; Ulka Vaishampayan, MD⁶,⁷; Lance Pagliaro, MD³; Benjamin L. Maughan, MD⁰; Yohann Loriot, MD¹⁰; Daniel Castellano, MD¹¹; Sandy Srinivas, MD¹²; Rana R. McKay, MD¹³; Robert Dreicer, MD¹⁴; Thomas Hutson, DO¹⁵; Sarita Dubey, MD¹⁶; Scott Werneke, PhD¹⁷; Ashok Panneerselvam, PhD¹⁷; Dominic Curran, MBChB¹⁷; Christian Scheffold, MD¹⁷; Toni K. Choueiri, MD²; and Neeraj Agarwal, MD⁰

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



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





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, <u>randomized</u> → 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."



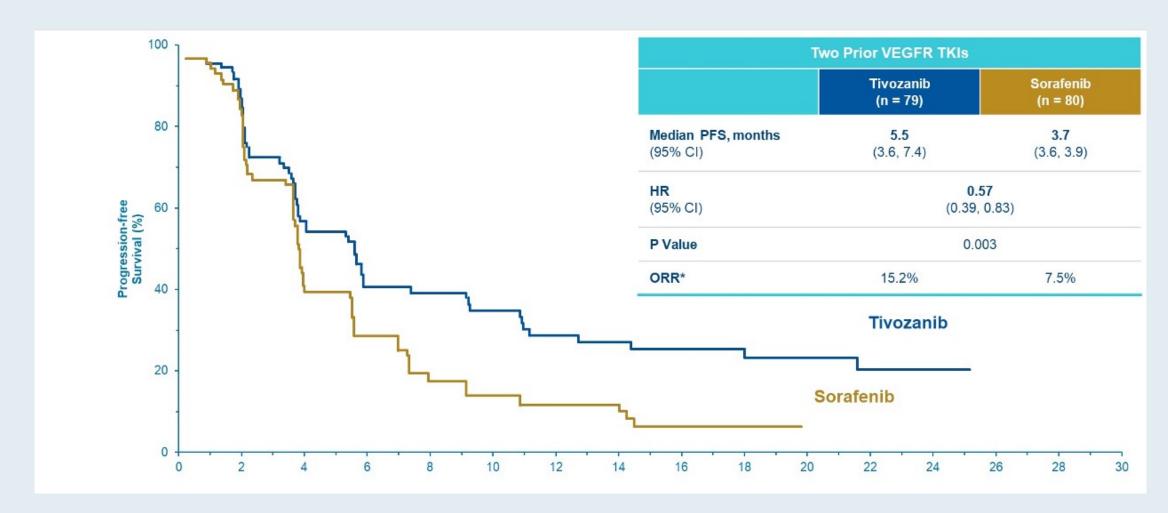
Tivozanib in Patients with Advanced Renal Cell Carcinoma (aRCC) Who Have Progressed After Prior Treatment of Axitinib: Results from TIVO-3

Rini BI et al.

Genitourinary Cancers Symposium 2021; Abstract 278.



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





TIVO-3: Tivozanib After Axitinib

RCC Population	N (sub	jects)	mPFS (m	nonths)	HR	OF	RR
	<u>Tivo</u>	<u>Sor</u>	<u>Tivo</u>	<u>Sor</u>		<u>Tivo</u>	<u>Sor</u>
ITT	175	175	5.6	3.9	0.73	18%	8%
3 rd Line Any Prior Axitinib	47	46	5.5	3.9	0.71	16%	6%
4 th Line Any Prior Axitinib	36	43	5.5	3.6	0.64	11%	10%
3 rd and 4 th Line Any Prior Axitinib	83	89	5.5	3.7	0.68	13%	8%



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

Verzoni et al.

ASCO 2021; Abstract 4546.

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

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



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

Press Release – August 13, 2021

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

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



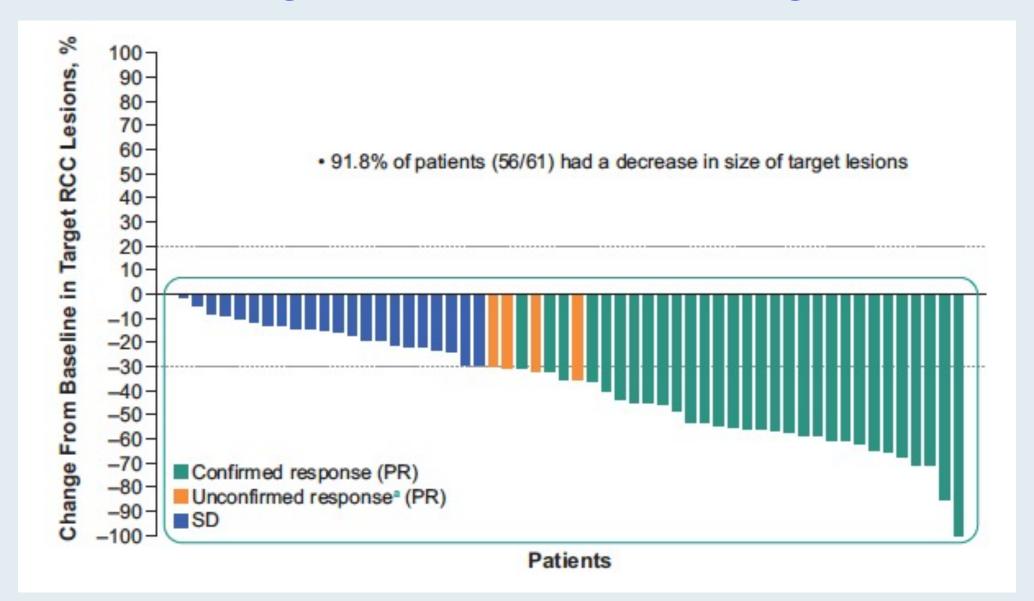
Phase 2 Study of Belzutifan (MK-6482), an Oral Hypoxia-Inducible Factor 2α (HIF-2α) Inhibitor, for Von Hippel-Lindau (VHL) Disease-Associated Clear Cell Renal Cell Carcinoma (ccRCC)

Srinivasan R et al.

ASCO 2021; Abstract 4555.



Maximum Change from Baseline in Sum of Target RCC Lesions





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

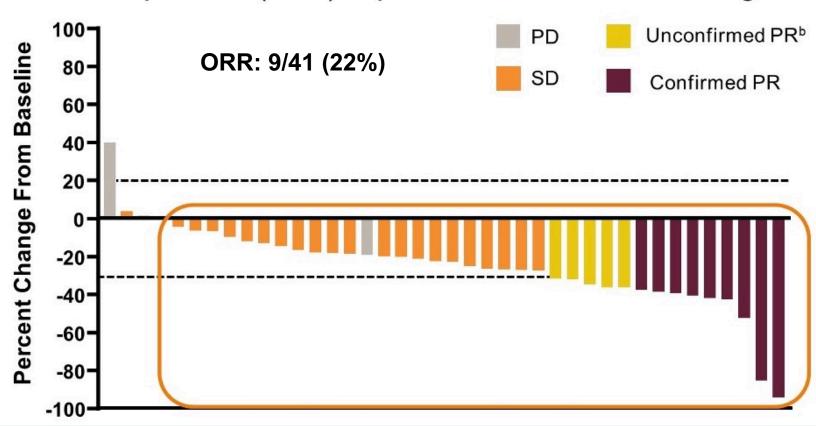
<u>Toni K. Choueiri</u>¹; Todd M. Bauer²; David F. McDermott³; Edward Arrowsmith⁴; Ananya Roy⁵; Rodolfo Perini⁵; Donna Vickery⁵; Scott S. Tykodi⁶

¹Dana-Farber Cancer Institute, Boston, MA, USA; ²Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; ³Beth Israel Deaconess Medical Center, Boston, MA, USA; ⁴Tennessee Oncology, Chattanooga, TN, USA; ⁵Merck & Co., Inc., Kenilworth, NJ, USA; ⁶University 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 sizea





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)°
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 belzutifanf	6 (12)
Discontinued cabozantinibg	8 (15)



Treatment-Related Adverse Events

Treatment-Related	Safety Analysis Set N = 52				
AEs in ≥15% of	Α	ny Grade	Grad	Grade 3	
Patients	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)	

- 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)



^aAll patients who received ≥1 dose of treatment. Data cutoff: October 15, 2020.

Identifying, Managing and Mitigating Therapy-Related Adverse Events in Patients with Chronic Lymphocytic Leukemia and Mantle Cell Lymphoma

A CME/MOC-Accredited Virtual Event

Monday, October 4, 2021 5:00 PM – 6:00 PM ET

Faculty
Richard R Furman, MD
Lindsey Roeker, MD

Consulting Cardiologist Daniel J Lenihan, MD

Moderator Neil Love, MD



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

A CME-MOC/NCPD Accredited Virtual Event

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

Faculty

Tanios Bekaii-Saab, MD
Kristen K Ciombor, MD, MSCI
Brad S Kahl, MD
Mark Levis, MD, PhD
Mark D Pegram, MD

Daniel P Petrylak, MD
Noopur Raje, MD
David Sallman, MD
Lecia V Sequist, MD, MPH

Additional faculty to be announced.

Moderator Neil Love, MD



ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Presentations on Genitourinary Cancers from the 2021 ASCO Annual Meeting



DR ARJUN BALAR
NYU PERLMUTTER CANCER CENTER









Thank you for joining us!

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

