Meet The Professor

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

Thursday, March 25, 2021
5:00 PM – 6:00 PM ET

Faculty

Robert J Motzer, MD

Moderator

Neil Love, MD

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Commercial Support

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

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Dr Love — Disclosures

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Dr Motzer — Disclosures

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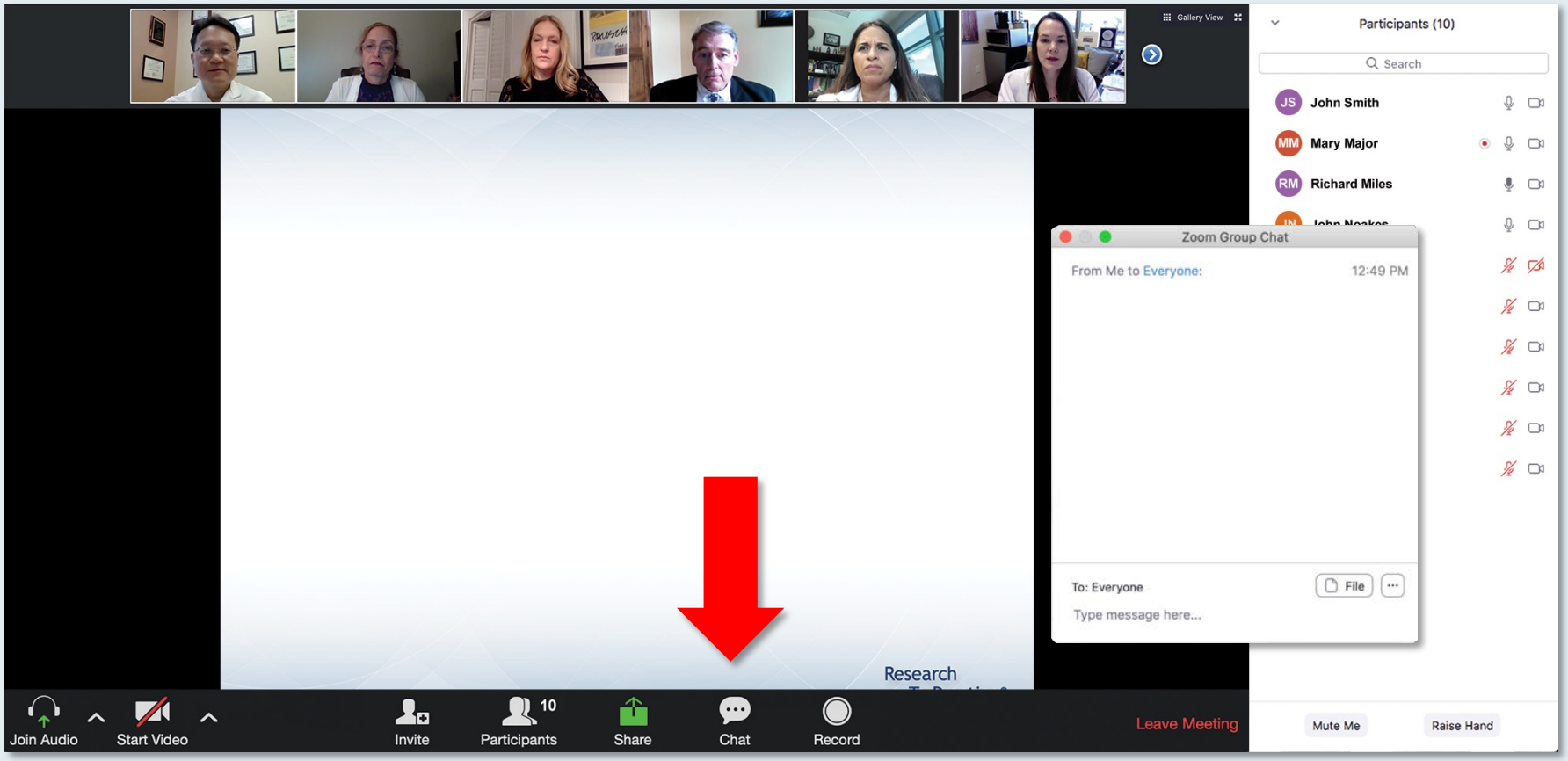
We Encourage Clinicians in Practice to Submit Questions



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Familiarizing Yourself with the Zoom Interface

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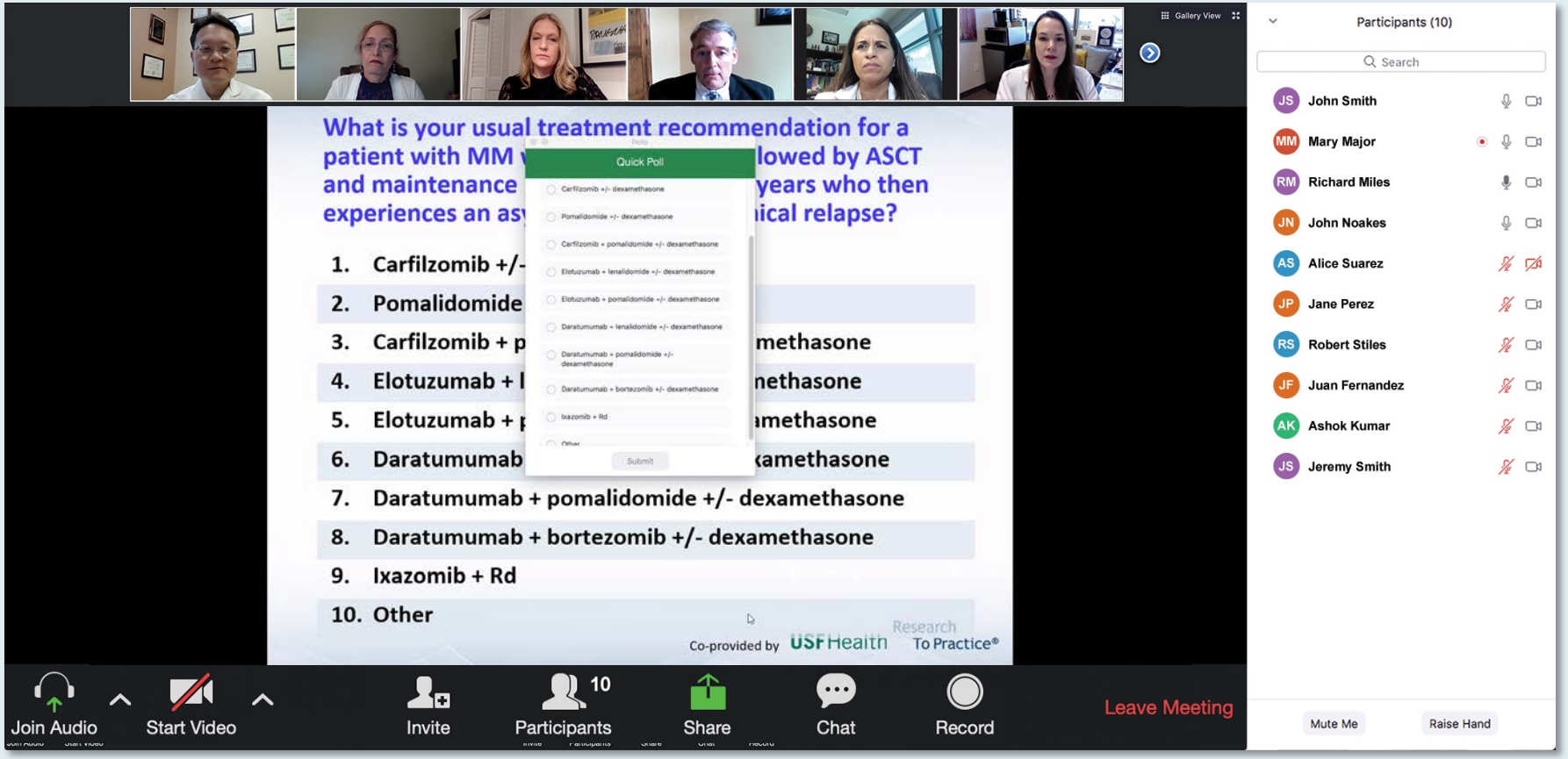

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ONCOLOGY TODAY

WITH DR NEIL LOVE

Renal Cell Carcinoma

DR CHUNG-HAN LEE

MEMORIAL SLOAN KETTERING CANCER CENTER

NEW YORK, NEW YORK

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Monday, March 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Philip A Thompson, MB, BS

Moderator

Neil Love, MD

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Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

Monday, April 5, 2021
5:00 PM – 6:00 PM ET

Faculty

Bradley J Monk, MD

Moderator

Neil Love, MD

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

Tuesday, April 6, 2021
12:00 PM – 1:00 PM ET

Faculty

Sumanta K Pal, MD

Moderator

Neil Love, MD

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Meet The Professor

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

Thursday, April 8, 2021
5:00 PM – 6:00 PM ET

Faculty

Dirk Arnold, MD, PhD

Moderator

Neil Love, MD

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Ask the Investigators: Applying Emerging Clinical Research to the Care of Patients with Gastroesophageal Cancers

Monday, April 12, 2021
6:30 PM – 7:30 PM ET

Faculty

Joseph Chao, MD
Yelena Y Janjigian, MD

Moderator

Neil Love, MD

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Meet The Professor

Management of Chronic Lymphocytic Leukemia

Thursday, April 15, 2021
5:00 PM – 6:00 PM ET

Faculty

John N Allan, MD

Moderator

Neil Love, MD

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Thank you for joining us!

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

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Meet The Professor Program Participating Faculty

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

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
Dallas, Texas

Eric Jonasch, MD
Professor of Medicine
Department of Genitourinary Medical Oncology
The University of Texas
MD Anderson Cancer Center
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Meet The Professor Program Participating Faculty

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

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

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

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Meet The Professor Program Participating Faculty

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

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

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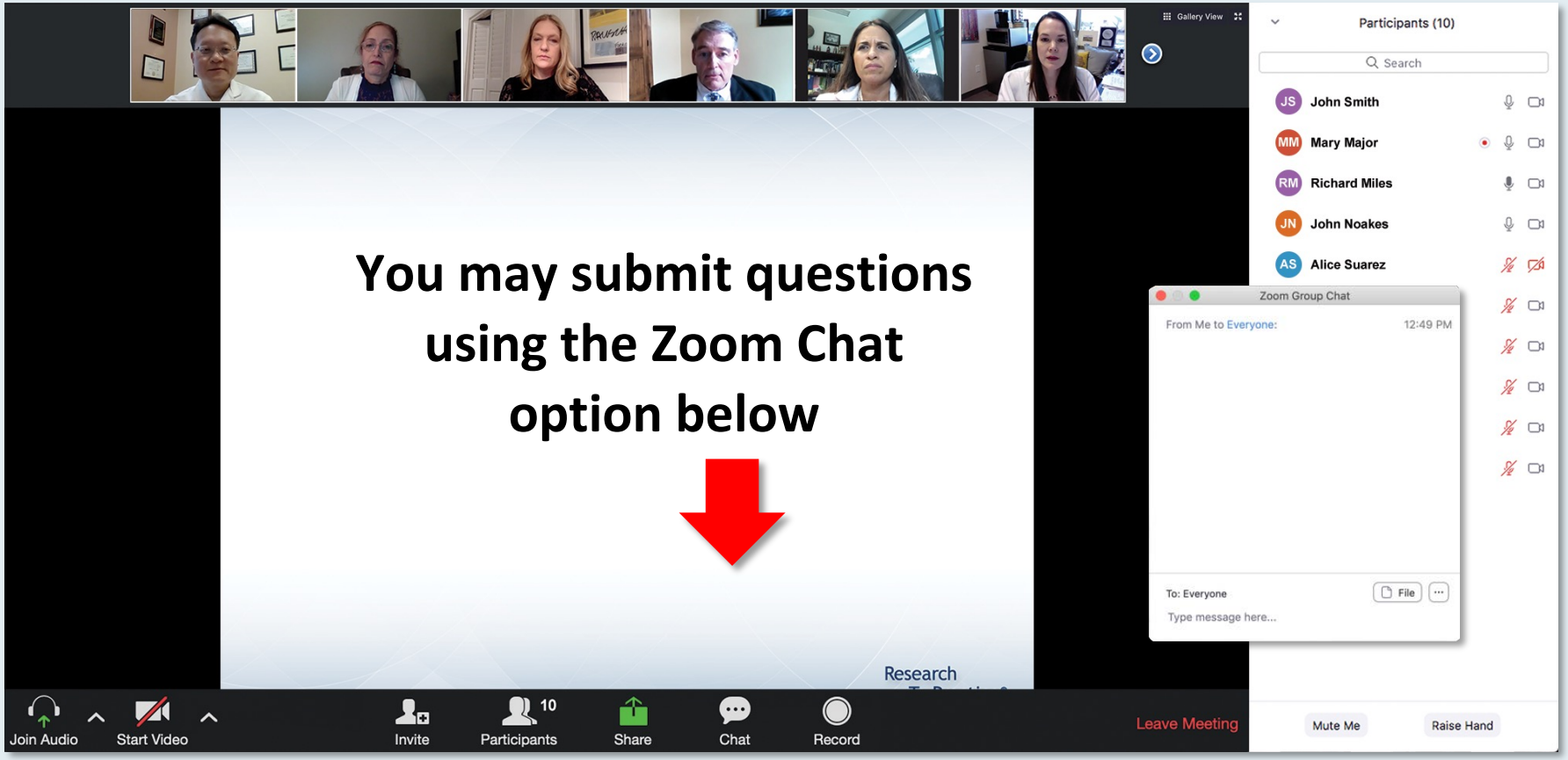

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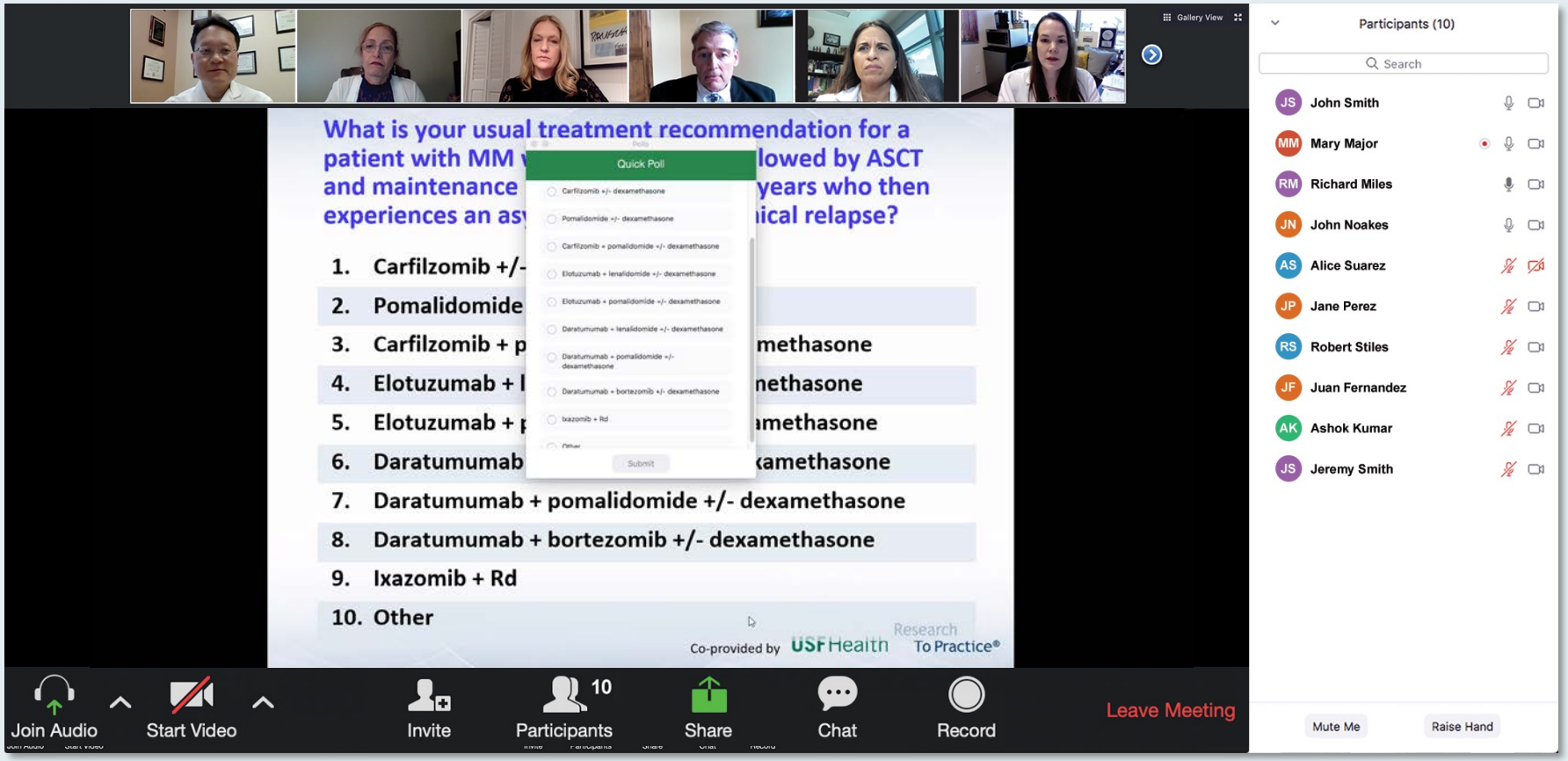

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Vikas Malhotra, MD
Staff Medical Oncologist-Hematologist
Florida Cancer Specialists and Research Institute
Spring Hill, Florida

Ina J Patel, DO
Assistant Professor of Internal Medicine
Division of Hematology/Oncology
Moncrief Cancer Institute
Fort Worth, Texas

John Yang, MD
Chief of Hematology/Oncology
Steward/St Anne's Hospital
Westwood, Massachusetts

Meet The Professor with Dr Motzer

MODULE 1: Cases from General Medical Oncology Practices

- Dr Patel: A 63-year-old man with metastatic clear cell renal cell carcinoma (ccRCC)
- Dr Yang: A 63-year-old woman with metastatic ccRCC
- Dr Malhotra: A 65-year-old woman with high-grade RCC and brain metastases
- Dr Patel: A 62-year-old man with bilateral renal masses
- Dr Yang: A 60-year-old man with metastatic RCC
- Dr Malhotra: A 69-year-old woman with metastatic RCC

MODULE 2: Beyond the Guidelines

MODULE 3: Key Data Sets

MODULE 4: Journal Club with Dr Motzer

MODULE 5: Other Recent Data Sets

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Case Presentation – Dr Patel: A 63-year-old man with metastatic ccRCC

Dr Ina Patel

- 2/2019: Clear cell RCC, with clinical lung metastases, s/p radical nephrectomy
  - Biopsy attempt x 3 of lung nodules unsuccessful
- 5/2020: Ipilimumab/nivolumab x 1, with severe hepatic immunoreaction 6 days later
  - Steroids initiated

Date	AST	ALT	Notes
5/13/2020	23	23	
6/11/2020	**1164**	**2075**	**Steroids initiated at 2 mg/kg twice daily**
6/15/2020	113	843	
6/22/2020	22	154	Steroids changed to 1 mg/kg daily
6/25/2020	74	1818	Steroids increased to 1.5 mg/kg daily
6/29/2020	978	2437	***Admitted ICU with atrial fibrillation with rapid ventricular response***
6/30/2020	**2095**	**2849**	**2 grams IV solumedrol x 1 → 2 mg/kg iv bid and mycophenolate 1 gram po bid added**
7/1/2020	439	1959	
7/2/2020	266	1395	

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Case Presentation – Dr Patel: A 63-year-old man with metastatic ccRCC

Dr Ina Patel

Questions

- What is your next line of treatment recommendation in a patient with metastatic renal cell carcinoma if they don't tolerate immunotherapy?
- Do you ever rechallenge with immunotherapy once there are adverse effects?

Case Presentation – Dr Yang: A 63-year-old woman with metastatic ccRCC

Dr John Yang

- 11/2018: Diagnosed with metastatic ccRCC
- Nephrectomy, with ECOG PS 2 afterwards
- Offered pazopanib but unable to afford insurance co-payment
- Nivolumab, with CR after 4 months
- Currently, she has completed 2 years of immunotherapy and is asking about risks/benefits of continued treatment

Questions

- What is the data supporting removal of the primary tumor in a patient with metastatic RCC?
- What are the risks and benefits of continuing immunotherapy beyond 2 years?

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Case Presentation – Dr Malhotra: A 65-year-old woman with high-grade RCC and brain metastases

Dr Vikas Malhotra

- Presents de novo with high-grade mRCC, with LDH approximately 900
- Lenvatinib/pembrolizumab, with a good response x 6 months
- Progressive disease with brain metastases

Question

- In a setting where a patient has developed brain metastases on a TKI and immunotherapy combination, is there data to support the use of cabozantinib, or would you use ipilimumab/nivolumab?

Case Presentation – Dr Patel: A 62-year-old man with bilateral renal masses

Dr Ina Patel

- Long smoking history, father died of RCC, possible ovarian cancer in maternal lineage
- Bilateral flank pain past 3-4 years, gross hematuria during past 2-3 months
- CT: Bilateral renal masses
- 10/2019 CT-guided core needle biopsy of right kidney: ccRCC
- Testing: No clinically significant mutation identified, no germline mutations
- 12/2019: Neoadjuvant axitinib/pembrolizumab
  - 6 months later CT c/a/p: Bilateral renal masses improved in appearance and size
- Robotic assisted partial right nephrectomy – (y)pT0NX, with no viable tumor seen
- Subsequently, left partial nephrectomy completed (pathology pending)

Questions

- Do you see future roles for clinical trials in the adjuvant or neoadjuvant setting?
- For patients who don't have clear cell RCC, how do you approach the other pathologies? What are the treatments or trials that you're looking into to approach those types of cancers?

Case Presentation – Dr Patel: A 62-year-old man with bilateral renal masses (follow-up)

Dr Ina Patel

March 24, 2021

Hello Dr. Love, Creatinine now is 0.89 and he is doing well!

Path from the left

Component
Final Diagnosis
A. Kidney, left, partial nephrectomy: - Multiloculated cyst wall with fibrosis, calcifications, chronic xanthomatous inflammation, stromal hyalinization, and hemosiderin laden macrophages (See comment) - No viable tumor is seen - Status post treatment - AJCC 8TH edition pathologic staging: (y) pT0 Nx

summary:

1. Clinical bilateral renal cell carcinoma presenting with pain and gross hematuria. He required neoadjuvant treatment in order to be able to have a partial nephrectomy on the right. We used pembrolizumab and Axitinib.

A. **Right kidney** 10/28/2020–status post **right** partial nephrectomy
   -No viable tumor present, treatment effect present

B. The left kidney was then partially resected Jan 2021. See path above

Kind Regards,

Ina J. Patel, DO

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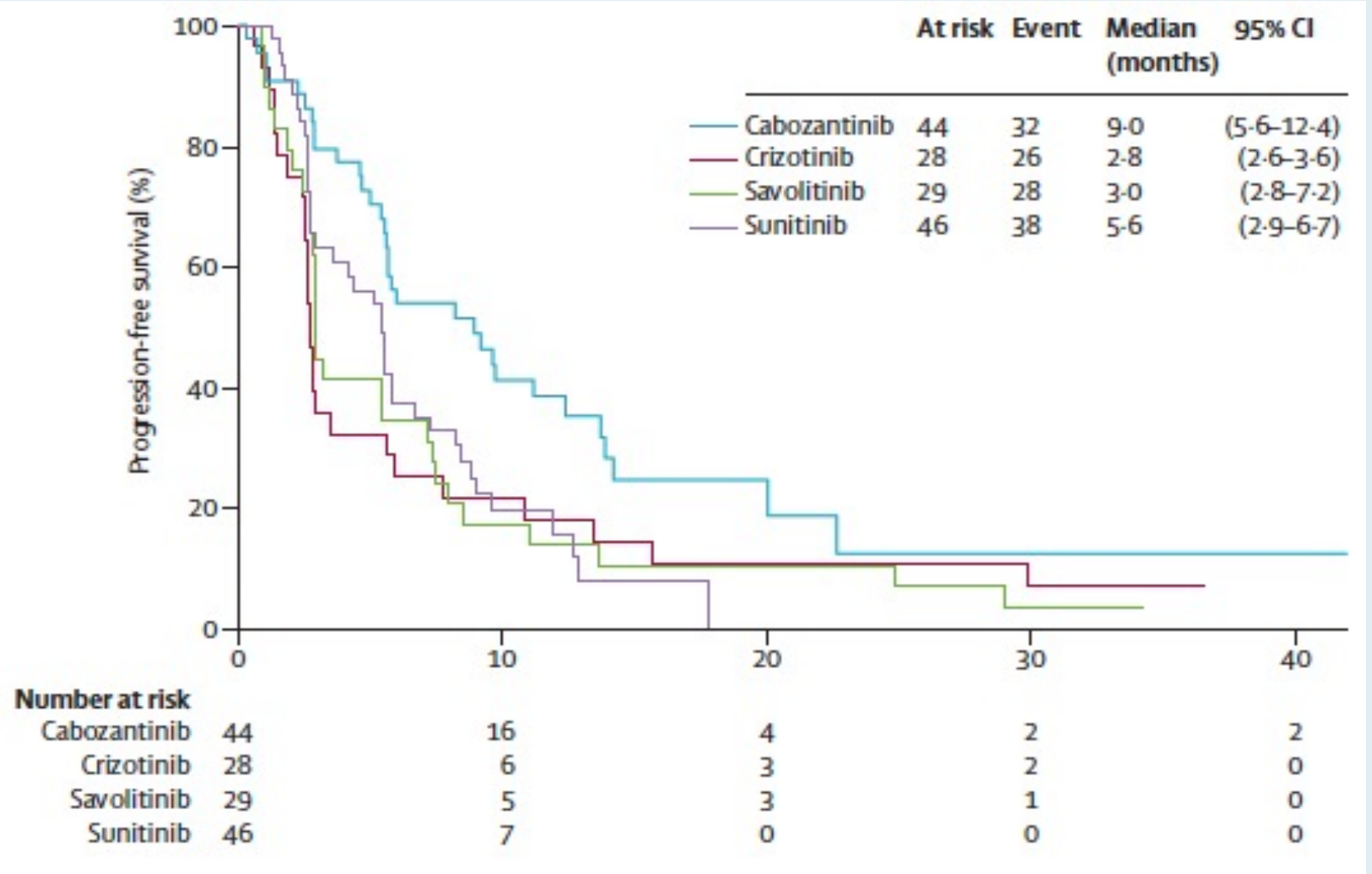
Lancet 2021;397:695-703

A comparison of sunitinib with cabozantinib, crizotinib, and savolitinib for treatment of advanced papillary renal cell carcinoma: a randomised, open-label, phase 2 trial

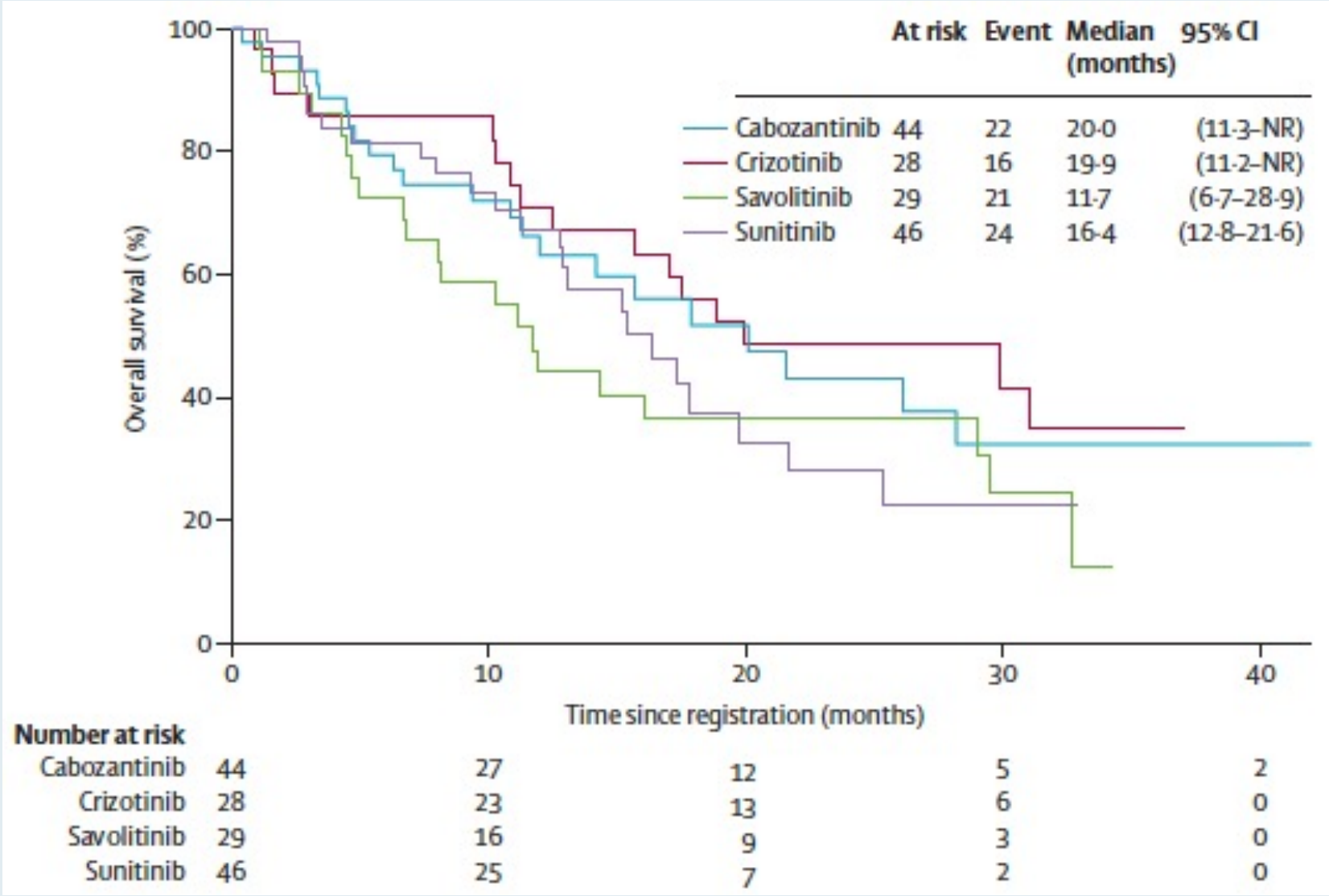
Sumanta K Pal, Catherine Tangen, Ian M Thompson Jr, Naomi Balzer-Haas, Daniel J George, Daniel Y C Heng, Brian Shuch, Mark Stein, Maria Tretiakova, Peter Humphrey, Adebowale Adeniran, Vivek Narayan, Georg A Bjarnason, Ulka Vaishampayan, Ajjai Alva, Tian Zhang, Scott Cole, Melissa Plets, John Wright, Primo N Lara Jr

Kaplan-Meier Analysis of Progression-Free Survival



Pal SK et al. *Lancet* 2021;397:695-703.

Kaplan-Meier Analysis of Overall Survival



Pal SK et al. *Lancet* 2021;397:695-703.

Case Presentation – Dr Yang: A 60-year-old man with metastatic RCC

Dr John Yang

- Incidental finding of left kidney mass at age 52
- PET: Mass in pancreatic head, biopsy-proven metastatic RCC
- Temsirolimus x 1 year → Whipple surgery
- No evidence of disease until age 59, when he presented with widespread metastatic disease
- Pembrolizumab/axitinib, with recurrent episodes of fatigue and hyperkalemia → PD after a few months
  - Axitinib held at times due to toxicity
- Recently initiates lenvatinib/everolimus

Questions

- What treatment would you consider if he does not respond to lenvatinib/everolimus?

Case Presentation – Dr Malhotra: A 69-year-old woman with mRCC

Dr Vikas Malhotra

- 2015: Stage III, 10-cm right RCC s/p right radical nephrectomy at Moffitt Cancer Center
- Two months post-surgery: Biopsy-confirmed liver metastases
- Enrolled on a clinical trial and received atezolizumab/bevacizumab, with CR
- Currently, on atezolizumab/bevacizumab off study (5 years in CR)

Questions

- In the future if she develops disease progression, how would they sequence the TKIs?
- Would you combine a TKI with any of the other immunotherapies, or would you use the TKIs as a single agent?
- Do you have any insights about why this patient had such an amazing and durable response to the atezolizumab/bevacizumab?
- After what amount of time would you be comfortable stopping treatment and monitoring her?

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Meet The Professor with Dr Motzer

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MODULE 2: Beyond the Guidelines

MODULE 3: Key Data Sets

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

1. Nivolumab/ipilimumab
2. Avelumab/axitinib
3. Pembrolizumab/axitinib
4. Pembrolizumab/lenvatinib
5. Nivolumab/cabozantinib
6. Tyrosine kinase inhibitor (TKI) monotherapy
7. Anti-PD-1/PD-L1 monotherapy
8. Other

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

 Dr Choueiri	Cabozantinib or Cabo/nivo	 Dr Motzer	Nivolumab/ cabozantinib
 Dr Hutson	Nivolumab/ cabozantinib	 Dr Plimack	Pembrolizumab/ axitinib
 Dr Jonasch	Nivolumab/ cabozantinib	 Prof Powles	Pembrolizumab/ axitinib
 Dr McDermott	Nivolumab/ipilimumab	 Dr Rini	Pembrolizumab/ axitinib

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Regulatory and reimbursement issues aside, which first-line therapy would you recommend for an 80-year-old patient with a history of nephrectomy for clear cell 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/ axitinib
 Dr McDermott	Nivolumab	 Dr Rini	Pembrolizumab/ axitinib

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/ axitinib and radiation therapy
 Dr Jonasch	Nivolumab/ cabozantinib	 Prof Powles	Pembrolizumab/ axitinib
 Dr McDermott	Nivolumab/ipilimumab	 Dr Rini	Pembrolizumab/ axitinib

RTP RESEARCH TO PRACTICE

Regulatory and reimbursement issues aside, which first-line therapy would you recommend for an 80-year-old patient who presents with clear cell RCC with multiple painful bone metastases and Hb of 11.4 g/dL (PS 1)?

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

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For a patient with metastatic RCC who experiences a complete response to checkpoint inhibitor-based therapy and is tolerating it well, for how long would you continue treatment?

 Dr Choueiri	2 years	 Dr Motzer	2 years
 Dr Hutson	About 1 year	 Dr Plimack	2 years
 Dr Jonasch	1 year	 Prof Powles	At least 1 year
 Dr McDermott	3 months	 Dr Rini	Usually 1 year

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For a patient with metastatic RCC who experiences a partial response to checkpoint inhibitor-based therapy and is tolerating it well, how long would you continue treatment?

 Dr Choueiri	2 years	 Dr Motzer	Continue nivolumab as long as responding/tolerating, stop pembro after 2 years
 Dr Hutson	About 1 year	 Dr Plimack	2 years
 Dr Jonasch	Indefinitely	 Prof Powles	At least 2 years
 Dr McDermott	2 years	 Dr Rini	Usually 1 year

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

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

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

 Dr Choueiri	Axitinib	 Dr Motzer	Cabozantinib
 Dr Hutson	Cabozantinib	 Dr Plimack	Cabozantinib
 Dr Jonasch	Cabozantinib	 Prof Powles	Axitinib
 Dr McDermott	Cabozantinib	 Dr Rini	Pembrolizumab/ axitinib

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In general, what would you recommend as second-line treatment for a 65-year-old patient (PS 0) with metastatic clear cell RCC who receives first-line 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

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What would be your most likely third-line systemic therapy recommendation for a 65-year-old patient with metastatic RCC who experienced disease progression on first-line pembrolizumab/axitinib and second-line cabozantinib (PS 0)?

 Dr Choueiri	Lenvatinib + everolimus	 Dr Motzer	Lenvatinib + everolimus
 Dr Hutson	Lenvatinib + everolimus	 Dr Plimack	Lenvatinib + everolimus
 Dr Jonasch	Lenvatinib + everolimus	 Prof Powles	Lenvatinib + everolimus
 Dr McDermott	Clinical trial of HIF-2a	 Dr Rini	Axitinib

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In general, how would you compare the efficacy of tivozanib to that of other commercially approved tyrosine kinase inhibitors (TKIs; eg, axitinib, cabozantinib, lenvatinib) in patients with relapsed metastatic RCC?

 Dr Choueiri	I don't know	 Dr Motzer	Efficacy is about the same
 Dr Hutson	Efficacy is about the same	 Dr Plimack	I don't know (likely same as axitinib)
 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 other commercially available TKIs (eg, axitinib, cabozantinib, lenvatinib) in patients with relapsed metastatic RCC?

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

RTP RESEARCH TO PRACTICE

Meet The Professor with Dr Motzer

MODULE 1: Cases from General Medical Oncology Practices

- Dr Patel: A 63-year-old man with metastatic clear cell renal cell carcinoma (ccRCC)
- Dr Yang: A 63-year-old woman with metastatic ccRCC
- Dr Malhotra: A 65-year-old woman with high-grade RCC and brain metastases
- Dr Patel: A 62-year-old man with bilateral renal masses
- Dr Yang: A 60-year-old man with metastatic RCC
- Dr Malhotra: A 69-year-old woman with metastatic RCC

MODULE 2: Beyond the Guidelines

MODULE 3: Key Data Sets

MODULE 4: Journal Club with Dr Motzer

MODULE 5: Other Recent Data Sets

RTP RESEARCH TO PRACTICE

Indirect comparison of the 4 regimens available.

	CheckMate 214 (Ipi/Nivo) [1] (n=550 vs n=546)	KEYNOTE-426 (Axi/Pembro)[2] (n=432 vs n=429)	CheckMate 9ER (Cabo/Nivo)[3] (n=323 vs n=328)	CLEAR (Len/Pembro)[4] (N=355 vs n=357)
mOS, months HR (CI);	NR vs 38.4 **0.69** (0.59–0.81);	NR vs 35.7 **0.68** (0.55-0.85);	NR vs NR **0.60** (0.40–0.89);	NR vs NR **0.66** (0.49-0.88)
Landmark OS 12 mo Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%	**90%** vs. 79% **74%** vs. 66%	**87%** vs. 78% (est) **74%** vs 60% (est)	**90%** vs 79% (est.) **79%** vs. 70%
mPFS, months HR (CI)	**12.2** vs 12.3 0.89 (0.76–1.05)	**15.4** vs 11.1 0.71 (0.60–0.84)	**16.6** vs 8.3 0.51 (0.41–0.64)	**23.9** vs 9.2 0.39 (0.32-0.49)
ORR, %	**39** vs 32	**60** vs 40	**56** vs 27	**71** vs 36
CR, %	**11** vs 3	**9** vs 3	**8** vs 5	**16** vs 4
Med f/u, months	**55**	**30.6**	**18.1**	**27**
Prognostic risk, % Favorable Intermediate Poor	 23 61 17	 32 55 13	 23 58 19	 31 59 9
Prior nephrectomy	82%	83%	69%	74%
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)	Overall (69%) IO (48%)	Overall (40%) IO (29%)	NR

Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

Indirect comparison of the 4 regimens available.

	CheckMate 214 (Ipi/Nivo)[1] (n=550 vs n=546)	KEYNOTE-426 (Axi/Pembro)[2] (n=432 vs n=429)	CheckMate 9ER (Cabo/Nivo)[3] (n=323 vs n=328)	CLEAR (Len/Pembro)[4] (N=355 vs n=357)
mOS, months HR (CI);	NR vs 38.4 **0.69** (0.59–0.81);			
Landmark OS 12 mo Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%			
mPFS, months HR (CI)	**12.2** vs 12.3 0.89 (0.76–1.05)			
ORR, %	**39** vs 32			
CR, %	**11** vs 3			
Med f/u, months	**55**			
Prognostic risk, % Favorable Intermediate Poor	 23 61 17			
Prior nephrectomy	82%			
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)			

Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

Open access Original research

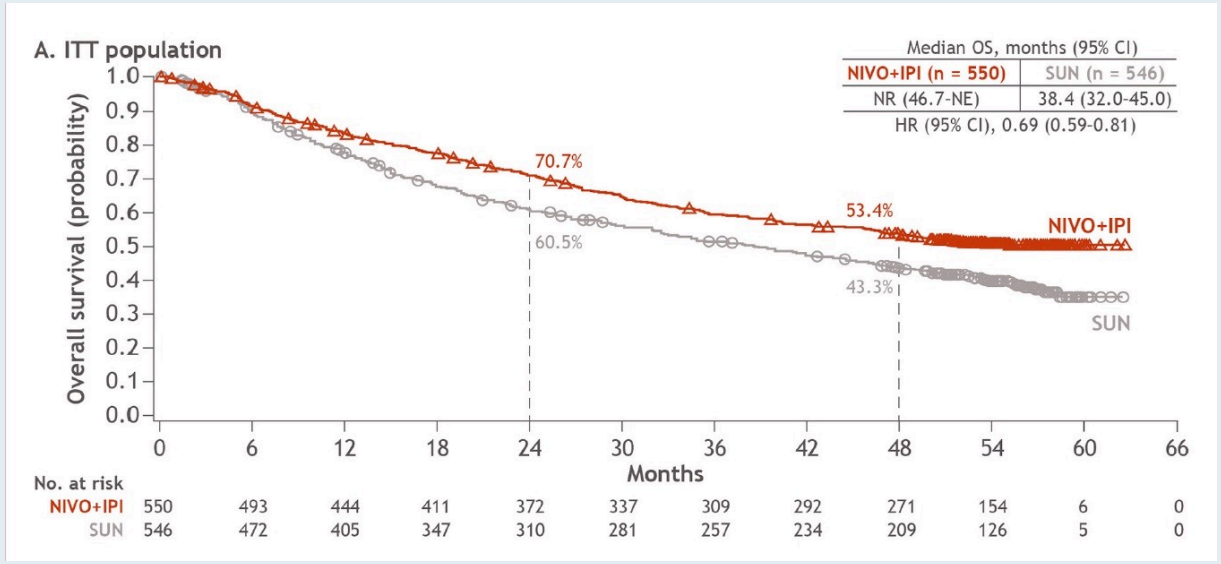
ESMO Open
Cancer Horizons

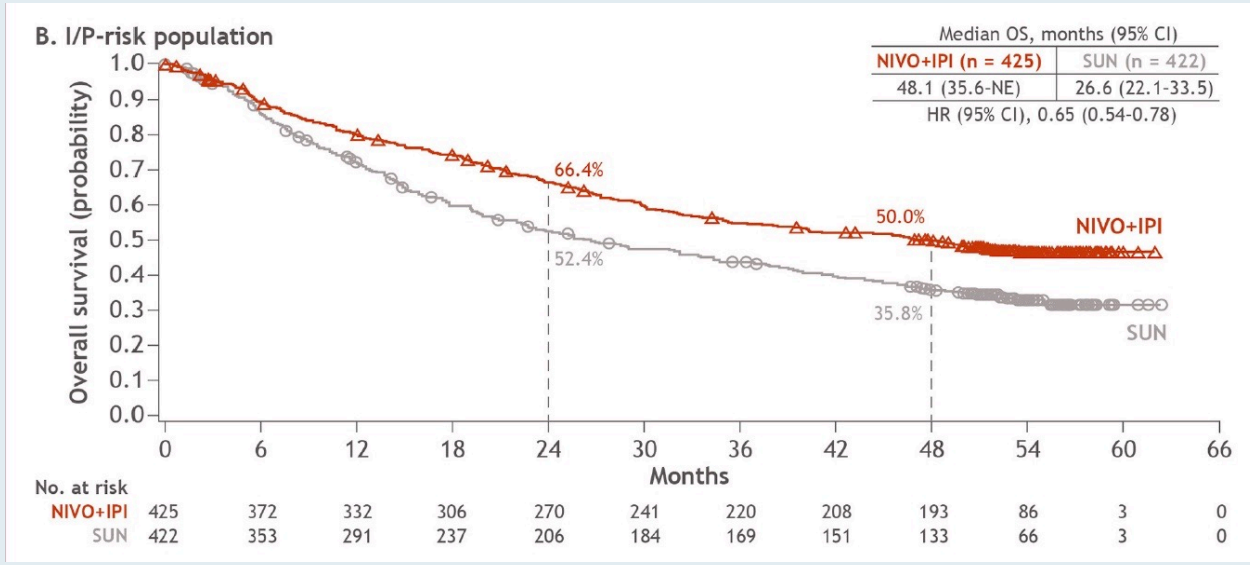
Nivolumab plus ipilimumab versus sunitinib for first-line treatment of advanced renal cell carcinoma: extended 4-year follow-up of the phase III CheckMate 214 trial

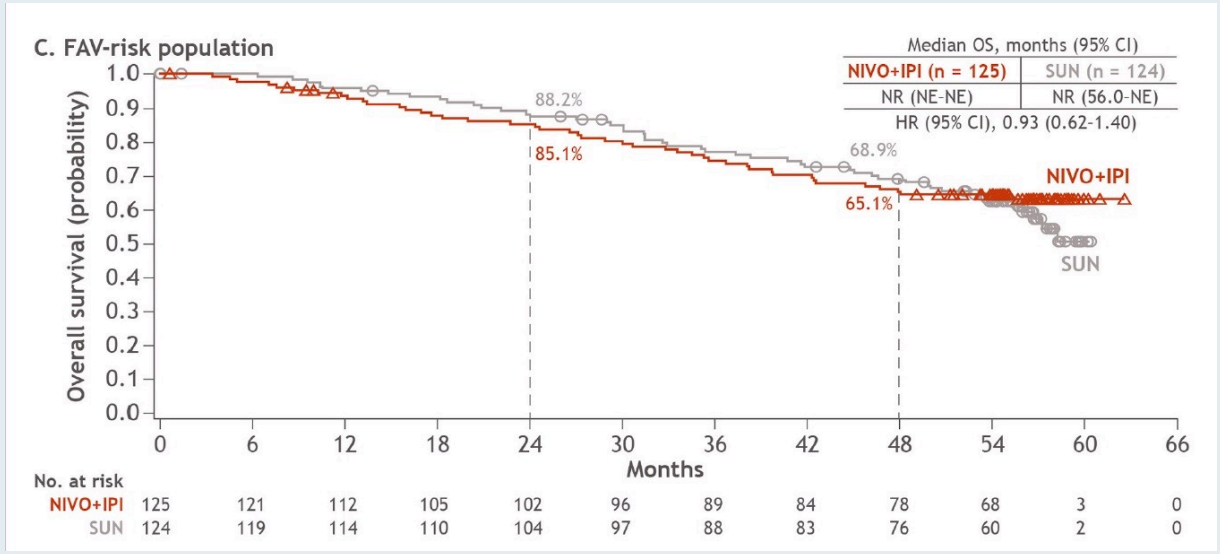
Laurence Albiges ,[1] Nizar M Tannir,[2] Mauricio Burotto,[3] David McDermott,[4,5] Elizabeth R Plimack,[6] Philippe Barthélémy,[7,8] Camillo Porta ,[9] Thomas Powles,[10,11] Frede Donskov,[12] Saby George,[13] Christian K Kollmannsberger,[14] Howard Gurney,[15,16] Marc-Oliver Grimm,[17] Yoshihiko Tomita,[18] 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: OS in ITT, Intermediate/Poor-Risk and Favorable-Risk Populations



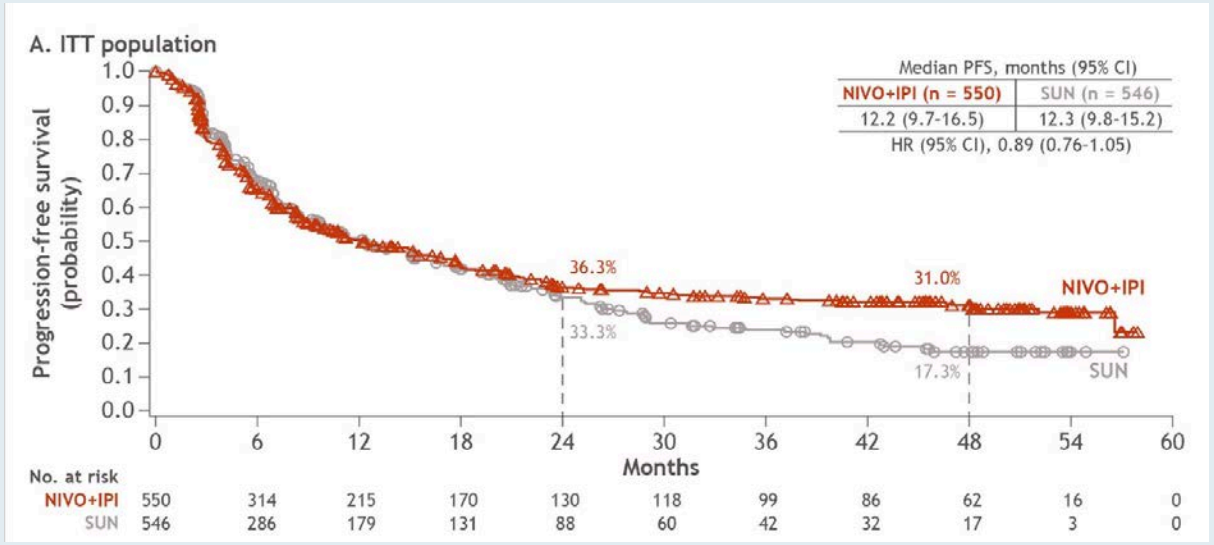


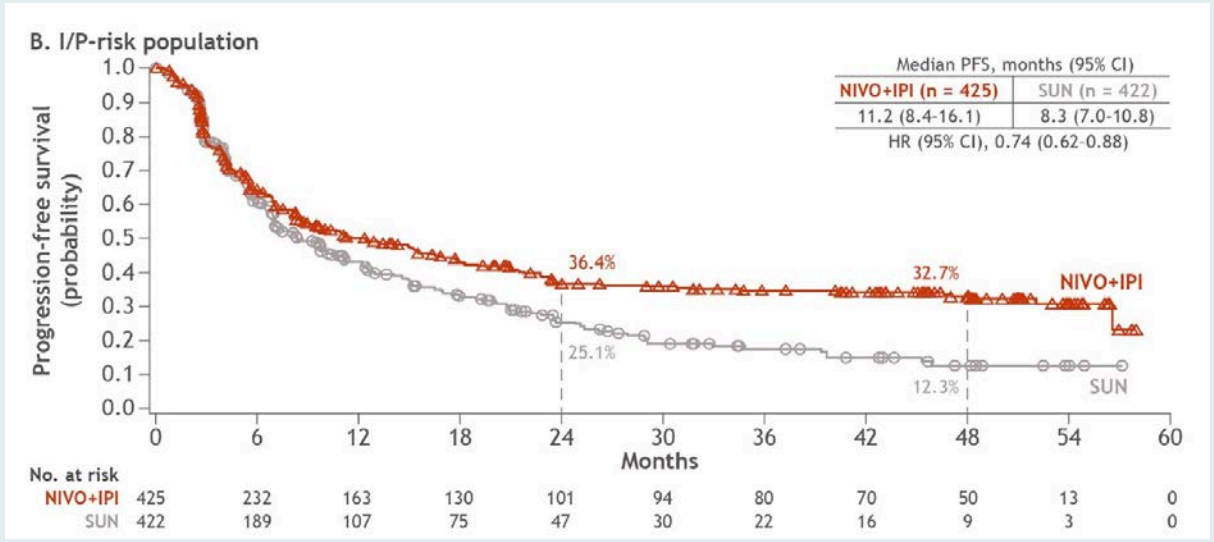


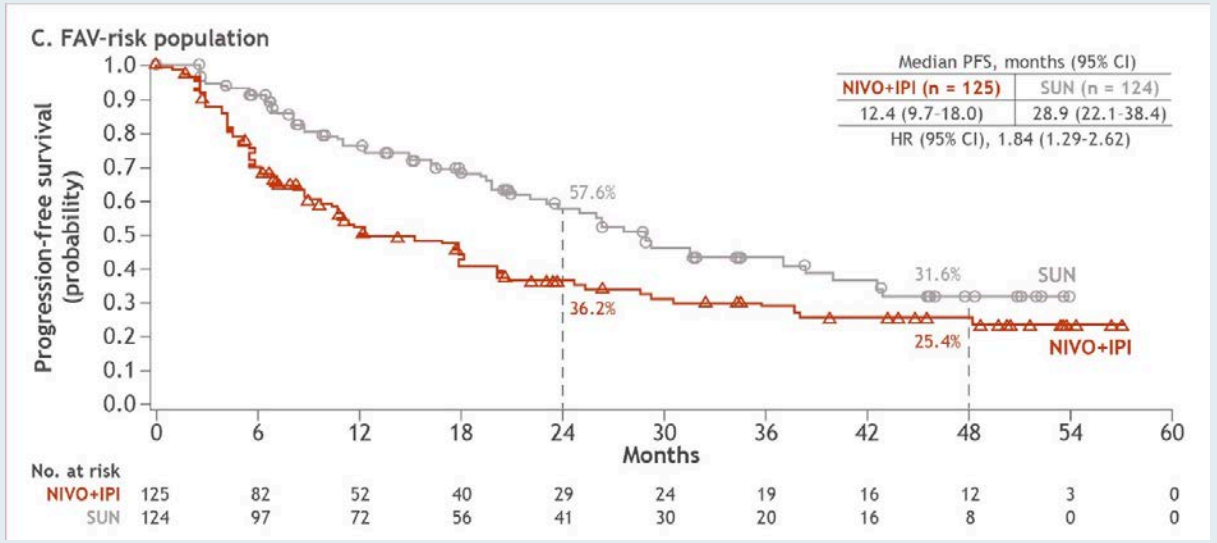
Albiges L et al. *ESMO Open* 2020;5(6):e001079.

RTP RESEARCH TO PRACTICE

CheckMate 214: PFS in ITT, Intermediate/Poor-Risk and Favorable-Risk Populations







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

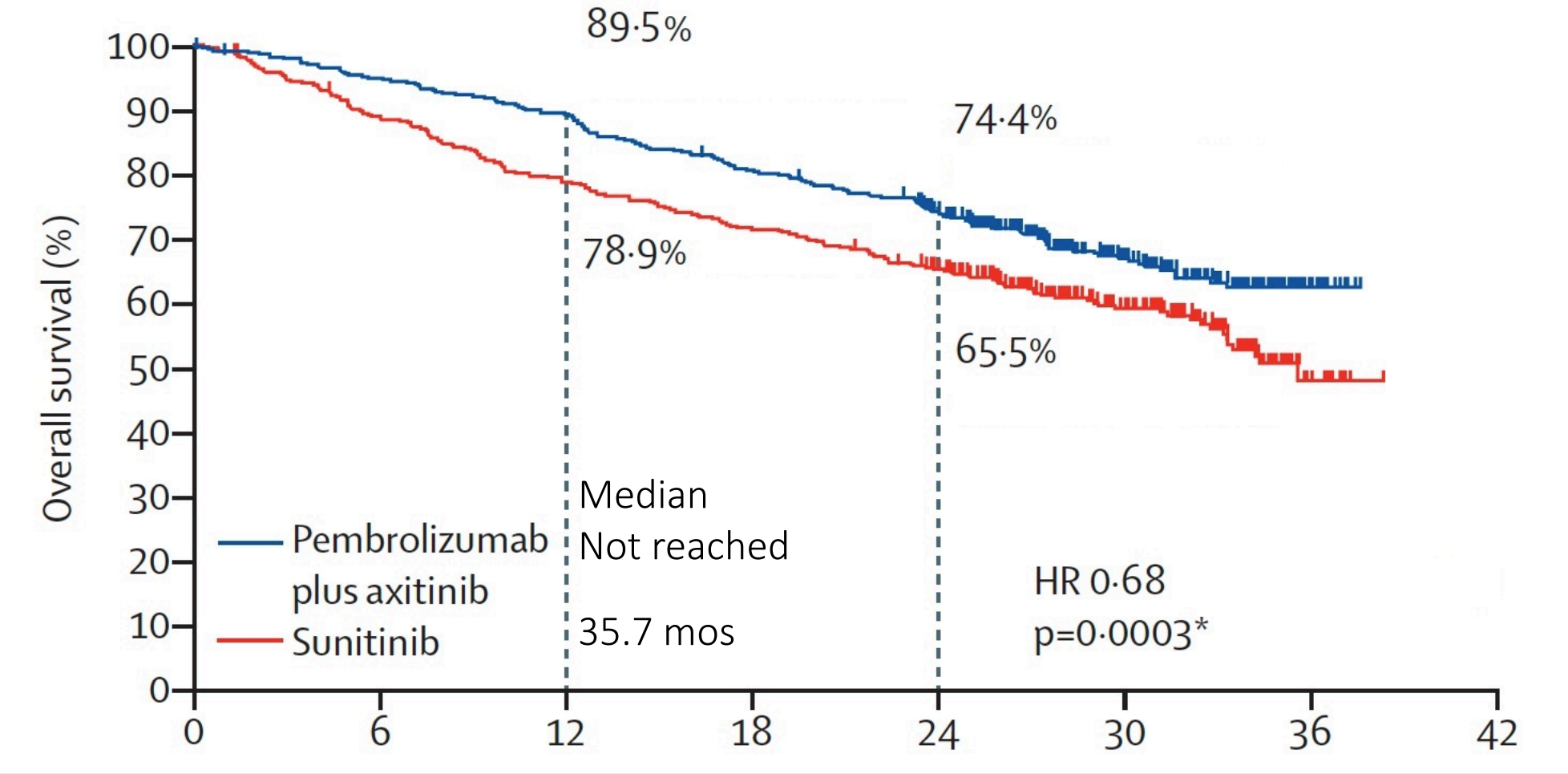
RTP RESEARCH TO PRACTICE

Lancet Oncol 2020;21:1563-73

Pembrolizumab plus axitinib versus sunitinib monotherapy as first-line treatment of advanced renal cell carcinoma (KEYNOTE-426): extended follow-up from a randomised, open-label, phase 3 trial

Thomas Powles, Elizabeth R Plimack, Denis Soulières, Tom Waddell, Viktor Stus, Rustem Gafanov, Dmitry Nosov, Frédéric Pouliot, Bohuslav Melichar, Ihor Vynnychenko, Sergio J Azevedo, Delphine Borchiellini, Raymond S McDermott, Jens Bedke, Satoshi Tamada, Lina Yin, Mei Chen, L Rhoda Molife, Michael B Atkins, Brian I Rini

KEYNOTE-426: Overall Survival with Extended Follow-Up



Powles T et al. *Lancet Oncol* 2020;21:1563-73.

RTP RESEARCH TO PRACTICE

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

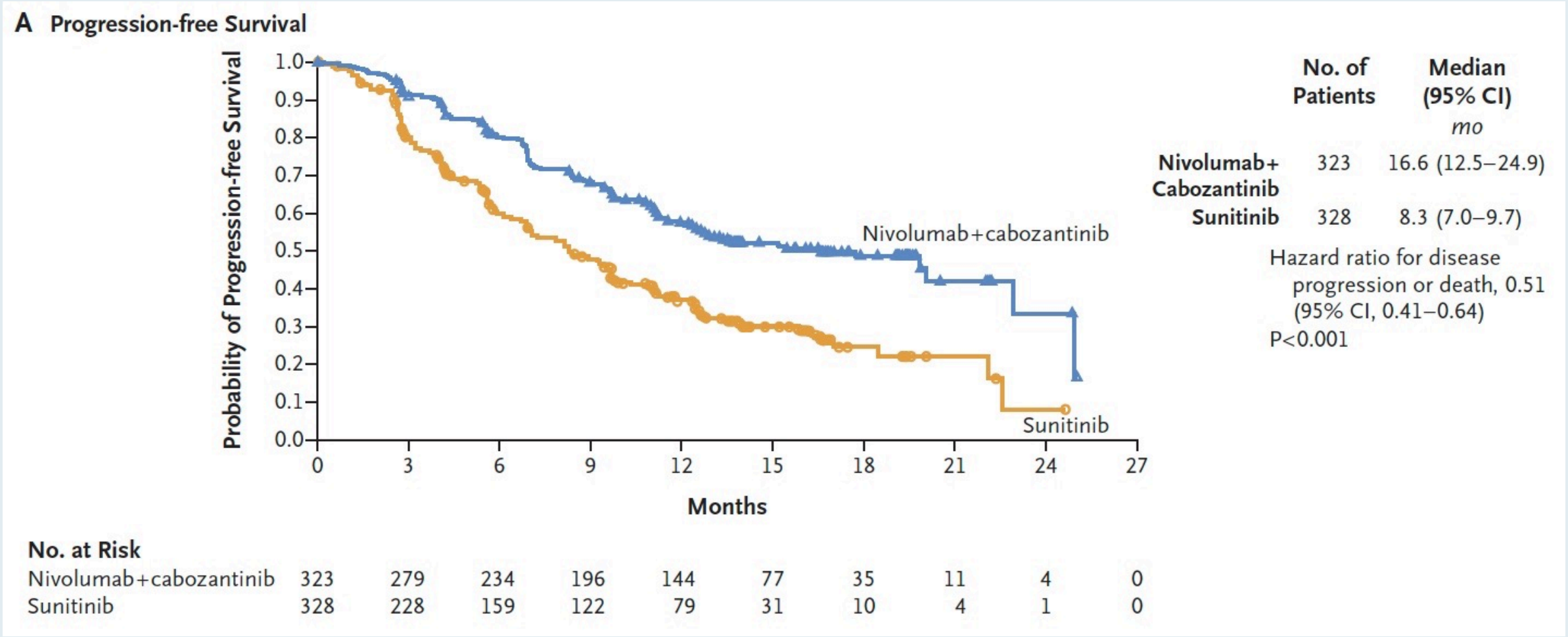
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma

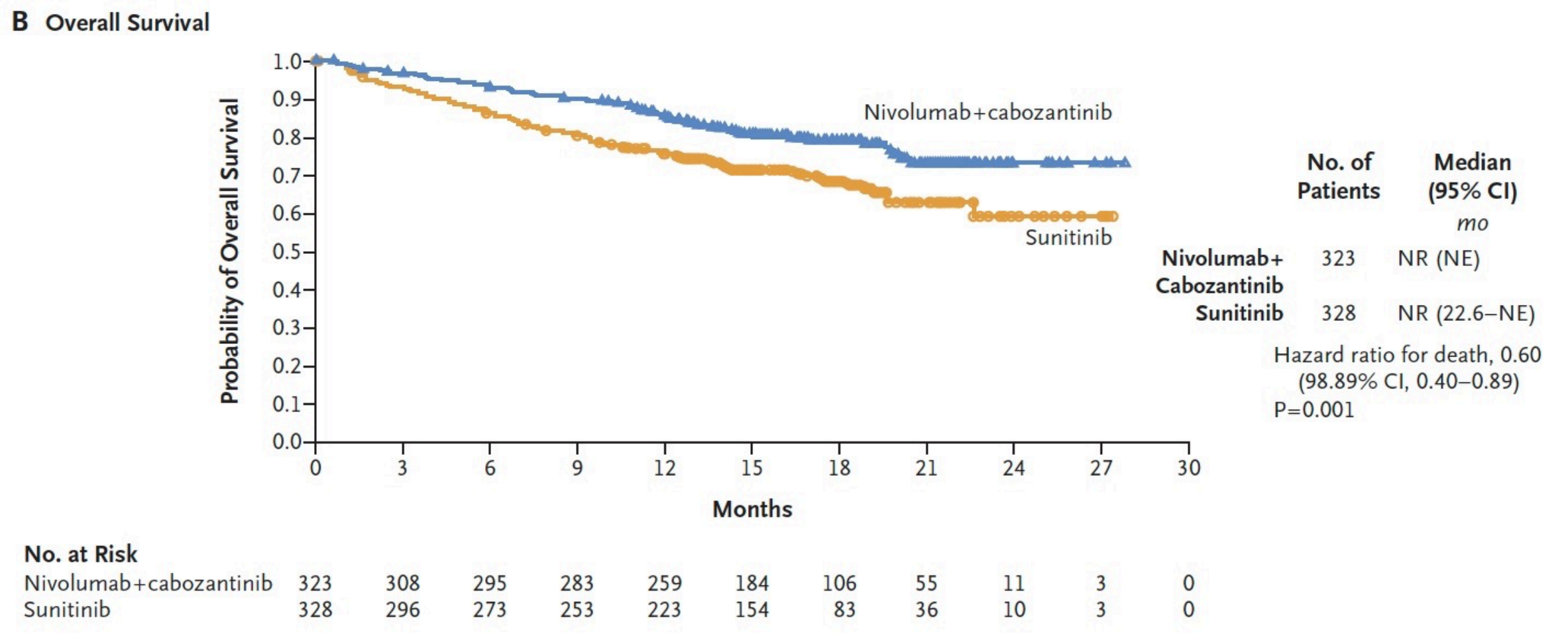
T.K. Choueiri, T. Powles, M. Burotto, B. Escudier, M.T. Bourlon, B. Zurawski, V.M. Oyervides Juárez, J.J. Hsieh, U. Basso, A.Y. Shah, C. Suárez, A. Hamzaj, J.C. Goh, C. Barrios, M. Richardet, C. Porta, R. Kowalyszyn, J.P. Feregrino, J. Żołnierek, D. Pook, E.R. Kessler, Y. Tomita, R. Mizuno, J. Bedke,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

Progression-Free Survival in the Intention-to-Treat Population



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

Overall Survival in the Intention-to-Treat Population



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

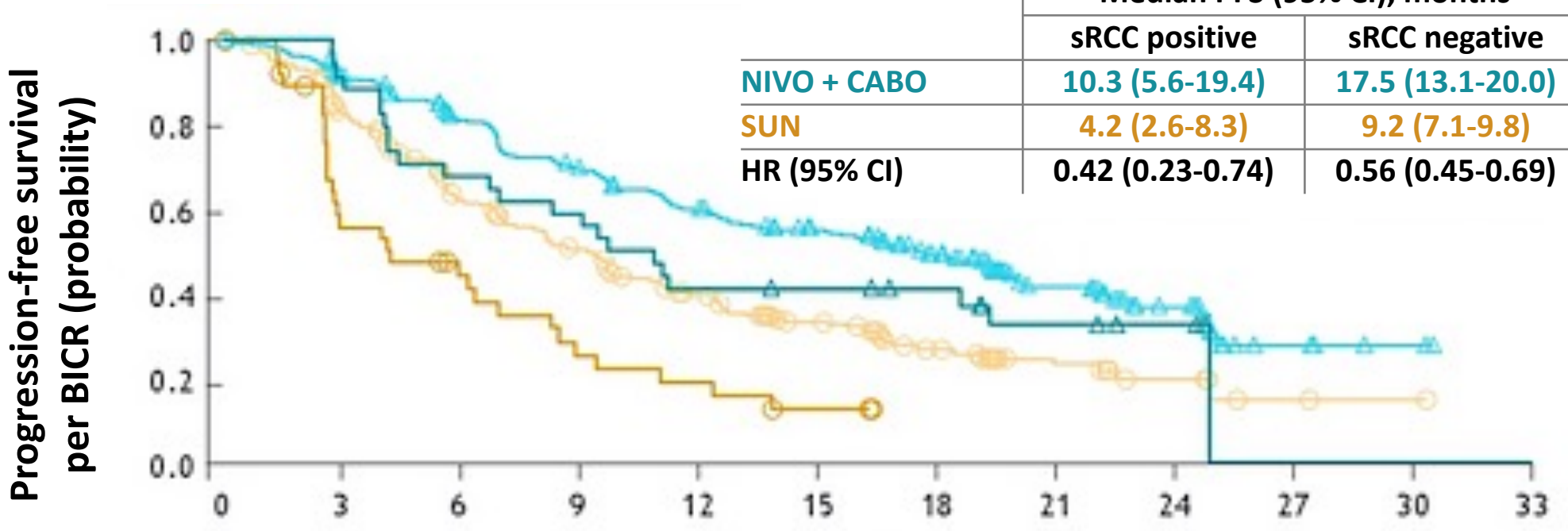
Nivolumab + Cabozantinib (NIVO + CABO) versus Sunitinib (SUN) for Advanced Renal Cell Carcinoma (aRCC): Outcomes by Sarcomatoid Histology and Updated Trial Results with Extended Follow-Up of CheckMate 9ER

Motzer RJ et al.

Genitourinary Cancers Symposium 2021;Abstract 308.

Progression-Free Survival per BICR by Sarcomatoid Histology

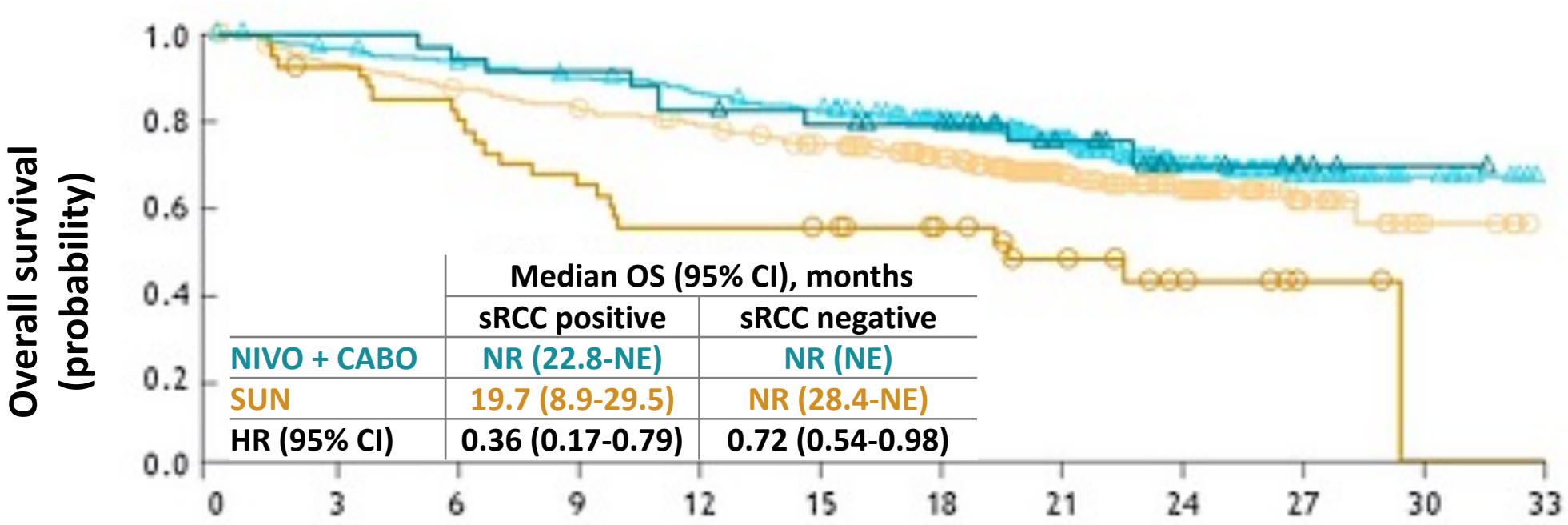
	Median PFS (95% CI), months	
	sRCC positive	sRCC negative
NIVO + CABO	10.3 (5.6-19.4)	17.5 (13.1-20.0)
SUN	4.2 (2.6-8.3)	9.2 (7.1-9.8)
HR (95% CI)	0.42 (0.23-0.74)	0.56 (0.45-0.69)



No. at risk												
NIVO + CABO sRCC positive	34	31	23	20	14	13	11	7	4	0	0	0
SUN sRCC positive	41	20	14	8	6	2	0	0	0	0	0	0
NIVO + CABO sRCC negative	289	249	213	181	152	132	91	49	22	5	2	0
SUN sRCC negative	287	210	146	114	81	59	37	17	7	2	1	0

Motzer RJ et al. Genitourinary Cancers Symposium 2021;Abstract 308.

Overall Survival by Sarcomatoid Histology



	Median OS (95% CI), months	
	sRCC positive	sRCC negative
NIVO + CABO	NR (22.8-NE)	NR (NE)
SUN	19.7 (8.9-29.5)	NR (28.4-NE)
HR (95% CI)	0.36 (0.17-0.79)	0.72 (0.54-0.98)

No. at risk												
NIVO + CABO sRCC positive	34	34	32	31	28	26	24	16	7	3	1	0
SUN sRCC positive	41	37	32	26	22	21	17	12	6	2	0	0
NIVO + CABO sRCC negative	289	274	263	252	241	229	196	131	77	37	9	0
SUN sRCC negative	287	258	240	228	214	196	172	106	56	20	4	0

Motzer RJ et al. Genitourinary Cancers Symposium 2021;Abstract 308.

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

The NEW ENGLAND JOURNAL of MEDICINE

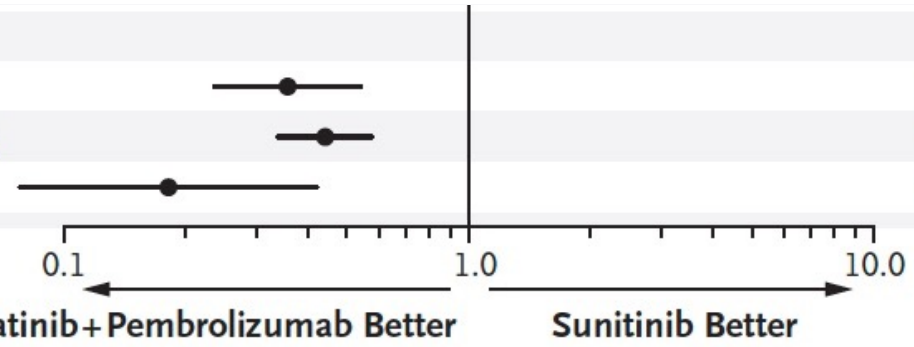
ORIGINAL ARTICLE

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*

Subgroup Analysis of Progression-Free Survival: MSKCC Risk Group

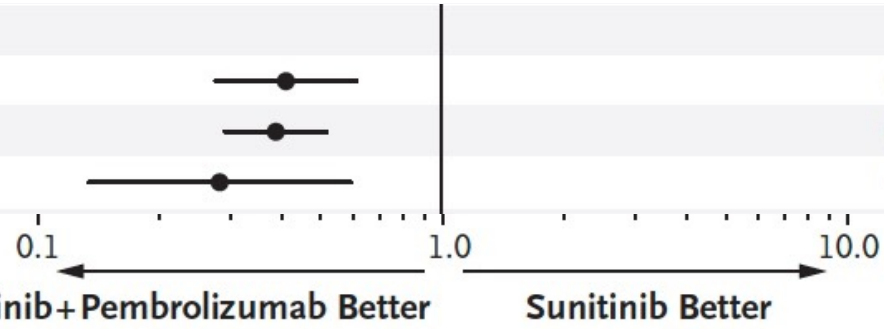
Subgroup	Lenvatinib+ Pembrolizumab	Sunitinib	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/no. of patients		
MSKCC risk group			
Favorable	39/96	60/97	0.36 (0.23–0.54)
Intermediate	101/227	126/228	0.44 (0.34–0.58)
Poor	20/32	19/32	0.18 (0.08–0.42)



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

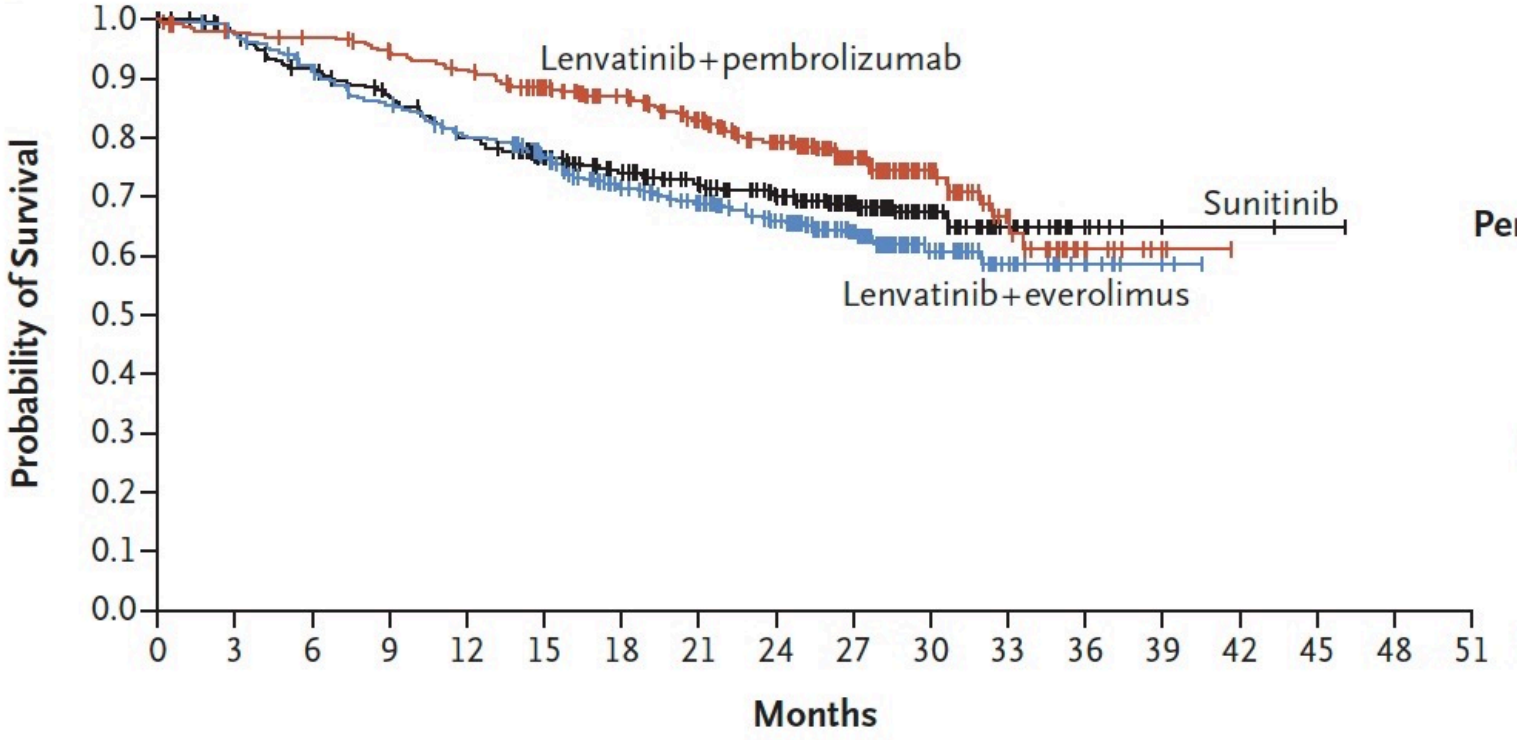
Subgroup Analysis of Progression-Free Survival: IMDC Risk Group

Subgroup	Lenvatinib+ Pembrolizumab	Sunitinib	Hazard Ratio for Disease Progression or Death (95% CI)
	no. of events/no. of patients		
IMDC risk group			
Favorable	43/110	67/124	0.41 (0.28–0.62)
Intermediate	97/210	110/192	0.39 (0.29–0.52)
Poor	18/33	26/37	0.28 (0.13–0.60)



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

Kaplan-Meier Analysis of 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

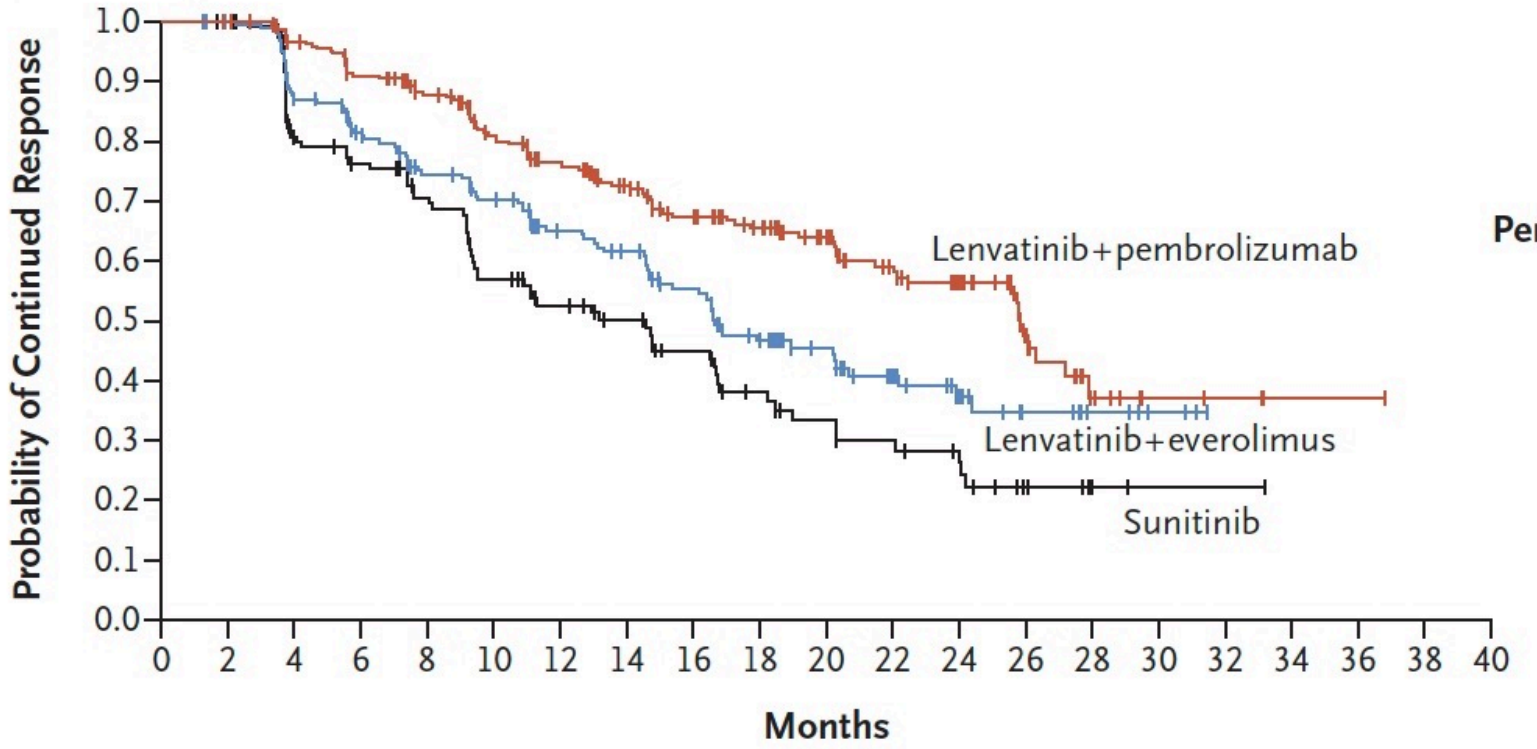
Hazard ratio for death (lenvatinib+ everolimus vs. sunitinib), 1.15 (95% CI, 0.88–1.50); P=0.30

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].

Kaplan-Meier Analysis of Response Duration



Median Duration of Response (95% CI)	*mo*
Lenvatinib+ Pembrolizumab	25.8 (22.1–27.9)
Lenvatinib+ Everolimus	16.6 (14.6–20.6)
Sunitinib	14.6 (9.4–16.7)

No. at Risk

Lenvatinib+pembrolizumab	252	250	234	215	197	172	153	131	112	101	83	63	45	23	9	4	3	1	1	0
Lenvatinib+everolimus	191	186	159	142	125	113	93	83	65	50	39	27	18	11	6	3	0			
Sunitinib	129	125	91	82	73	57	47	40	33	25	20	17	13	7	2	1	1	0		

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

Confirmed Tumor Responses

Measure	Lenvatinib plus Pembrolizumab (N = 355)	Lenvatinib plus Everolimus (N = 357)	Sunitinib (N = 357)
Objective response (95% CI) — %†	71.0 (66.3–75.7)	53.5 (48.3–58.7)	36.1 (31.2–41.1)
Relative risk vs. sunitinib (95% CI)	1.97 (1.69–2.29)	1.48 (1.26–1.74)	Reference
Best overall response — no. (%)			
Complete response	57 (16.1)	35 (9.8)	15 (4.2)
Partial response	195 (54.9)	156 (43.7)	114 (31.9)
Stable disease	68 (19.2)	120 (33.6)	136 (38.1)
Progressive disease	19 (5.4)	26 (7.3)	50 (14.0)
Unknown or could not be evaluated‡	16 (4.5)	20 (5.6)	42 (11.8)
Median time to response (range) — mo	1.94 (1.41–18.50)	1.91 (1.41–14.36)	1.94 (1.61–16.62)
Median duration of response (95% CI) — mo	25.8 (22.1–27.9)	16.6 (14.6–20.6)	14.6 (9.4–16.7)

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

RTP RESEARCH TO PRACTICE

Selected Adverse Events of Any Cause That Emerged or Worsened During Treatment in at Least 25% of the Patients in Any Treatment Group

Event	Lenvatinib plus Pembrolizumab (N = 352)		Lenvatinib plus Everolimus (N = 355)		Sunitinib (N = 340)	
	Any Grade	Grade ≥3†	Any Grade	Grade ≥3†	Any Grade	Grade ≥3†
	number of patients (percent)					
Any event	351 (99.7)	290 (82.4)	354 (99.7)	295 (83.1)	335 (98.5)	244 (71.8)
Diarrhea	216 (61.4)	34 (9.7)	236 (66.5)	41 (11.5)	168 (49.4)	18 (5.3)
Hypertension	195 (55.4)	97 (27.6)	162 (45.6)	80 (22.5)	141 (41.5)	64 (18.8)
Hypothyroidism‡	166 (47.2)	5 (1.4)	95 (26.8)	2 (0.6)	90 (26.5)	0
Decreased appetite	142 (40.3)	14 (4.0)	144 (40.6)	22 (6.2)	105 (30.9)	5 (1.5)
Fatigue	141 (40.1)	15 (4.3)	149 (42.0)	27 (7.6)	125 (36.8)	15 (4.4)

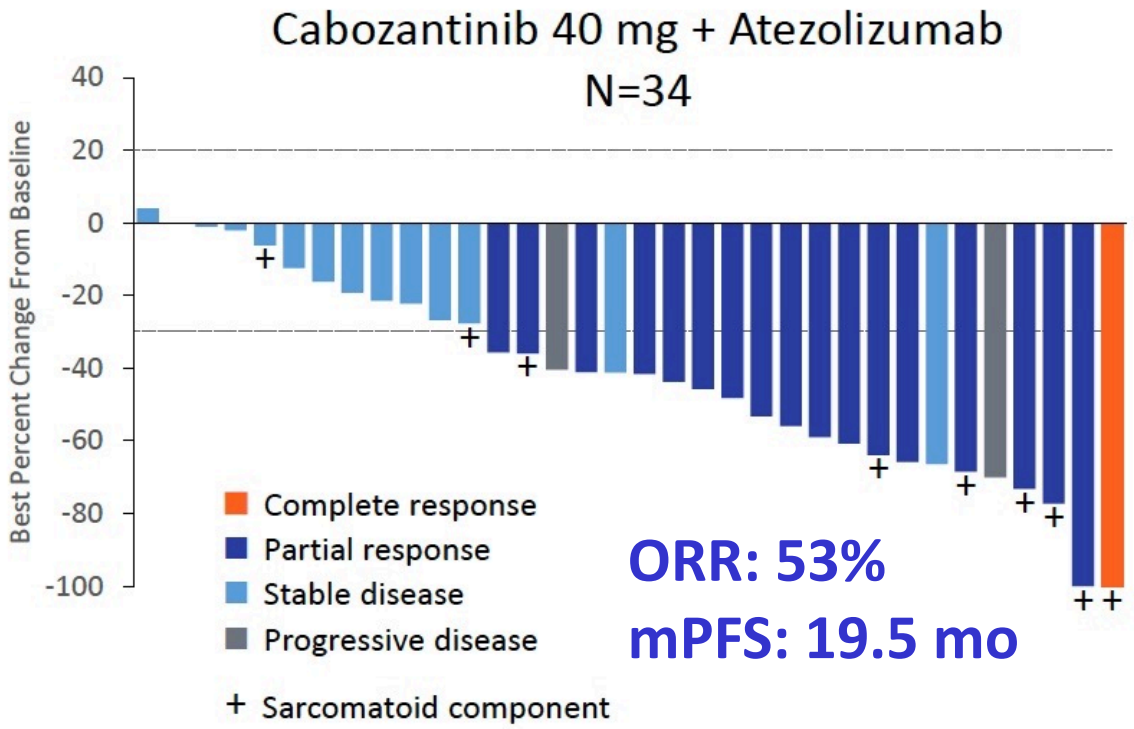
Motzer R et al. *N Engl J Med* 2021;[Online ahead of print].

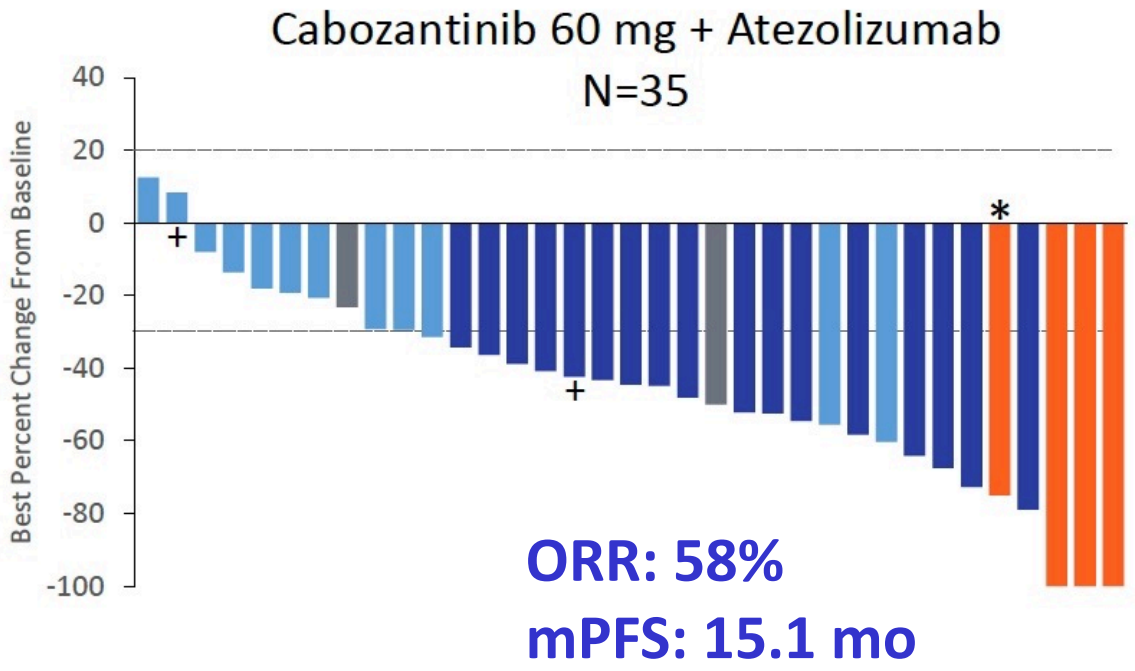
Cabozantinib (C) in Combination with Atezolizumab (A) as First-Line Therapy for Advanced Clear Cell Renal Cell Carcinoma (ccRCC): Results from the COSMIC-021 Study

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 Renal Cell Carcinoma

Study acronym	Target accrual	Randomization	Primary endpoint(s)	Estimated primary completion
COSMIC-313	840	• Cabozantinib + nivolumab + ipilimumab (4 doses) → cabozantinib + nivolumab • Placebo + nivolumab + ipilimumab (4 doses) → placebo + nivolumab	PFS	Nov 2021
PDIGREE	1,046	After Induction nivolumab/ipilimumab • Pts with CR → Nivolumab • Pts with non-CR or non-PD, *randomized* → Nivolumab → Nivolumab + Cabozantinib • Pts with PD → Cabozantinib	OS	Sept 2021

RTP RESEARCH TO PRACTICE

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."

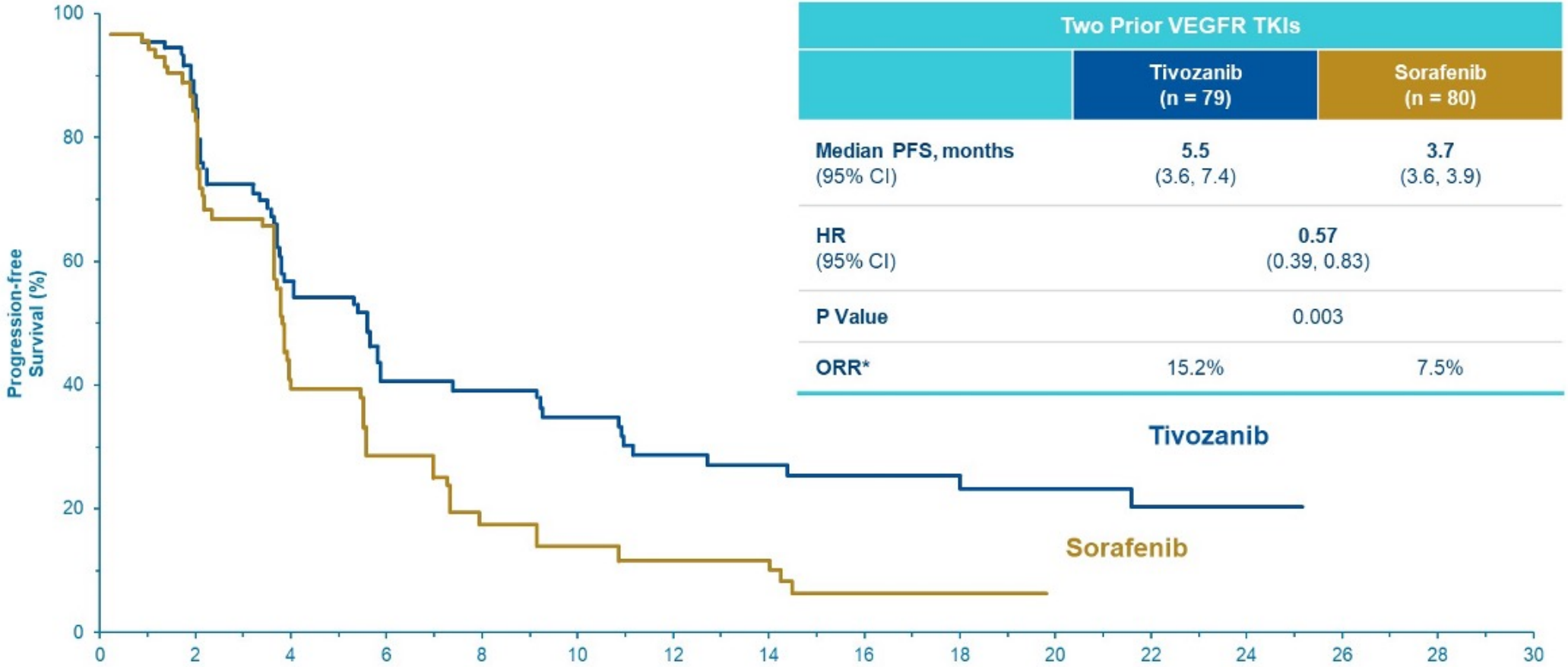
https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-tivozanib-relapsed-or-refractory-advanced-renal-cell-carcinoma

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.

Meet The Professor with Dr Motzer

MODULE 1: Cases from General Medical Oncology Practices

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MODULE 3: Key Data Sets

MODULE 4: Journal Club with Dr Motzer

- Sarcomatoid RCC: Biology, natural history and management
- Phase II trial of everolimus with bevacizumab as first-line treatment for advanced papillary-variant RCC
- Prognosis of incidental brain metastases in advanced RCC
- IMmotion150 trial: Atezolizumab/bevacizumab after disease progression on atezolizumab or sunitinib for metastatic RCC
- IMmotion151 trial: Atezolizumab/bevacizumab versus sunitinib for untreated metastatic RCC with sarcomatoid features
- Evaluation of the role of tumor load in cytoreductive nephrectomy

MODULE 5: Other Recent Data Sets

RTP
RESEARCH
TO PRACTICE

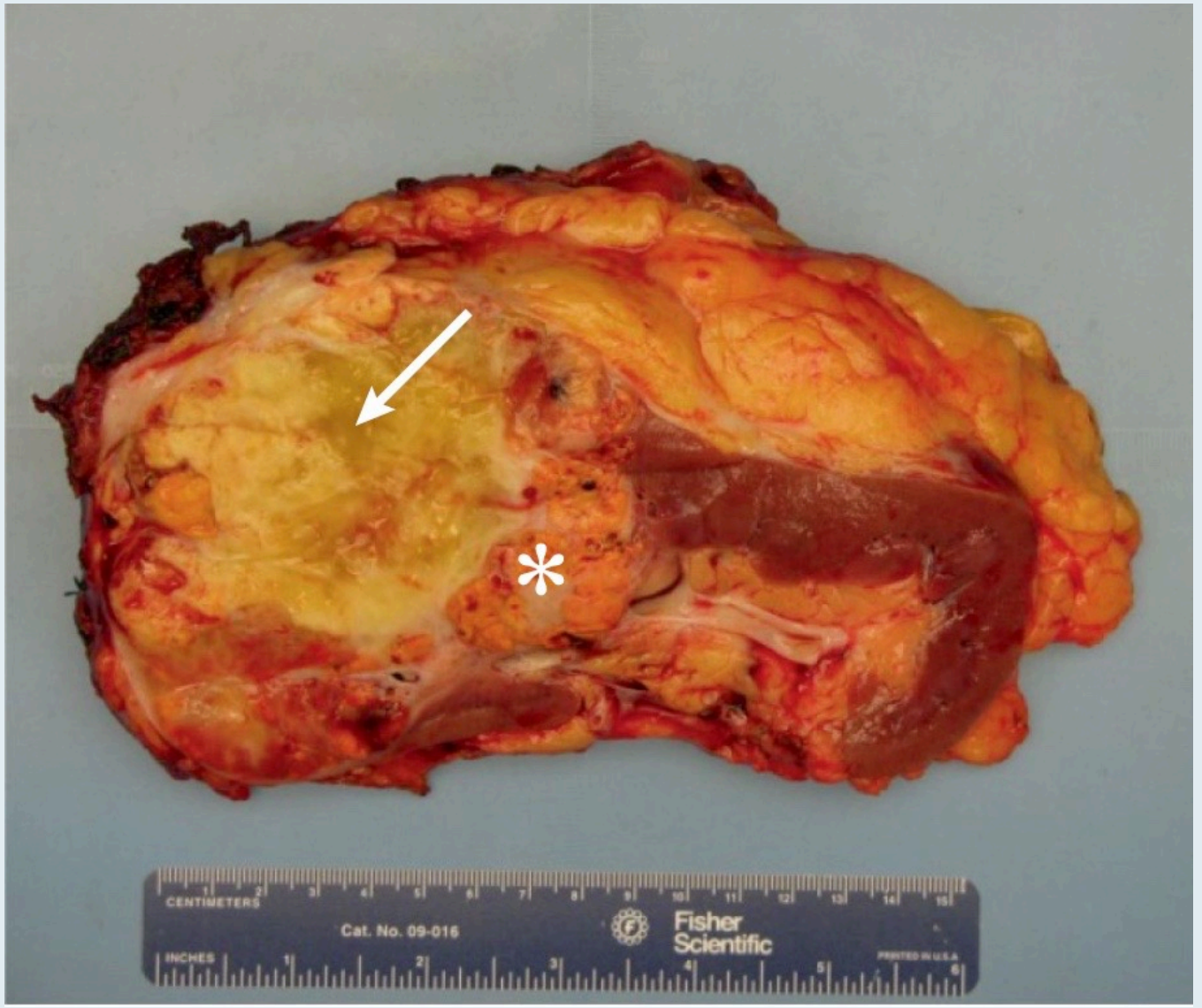
Nat Rev Urol 2020;17(12):659-78

REVIEWS

Sarcomatoid renal cell carcinoma: biology, natural history and management

Kyle A. Blum[1], Sounak Gupta[2], Satish K. Tickoo[2], Timothy A. Chan[3], Paul Russo[1], Robert J. Motzer[4], Jose A. Karam[5,6] and A. Ari Hakimi[1,6]✉

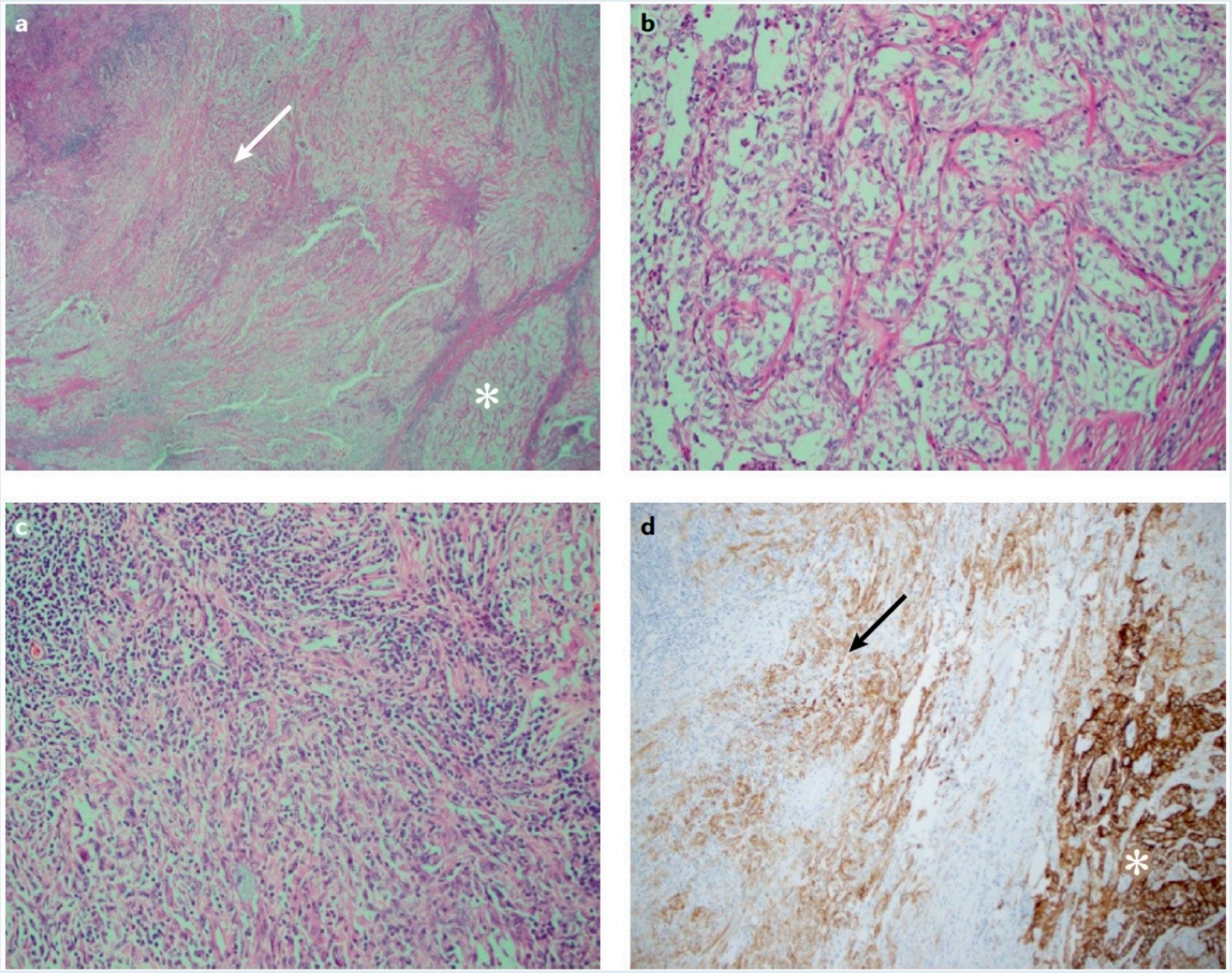
Gross Sections of a Sarcomatoid RCC After Radical Nephrectomy



Blum KA et al. *Nat Rev Urol* 2020;17(12):659-78.

RTP RESEARCH TO PRACTICE

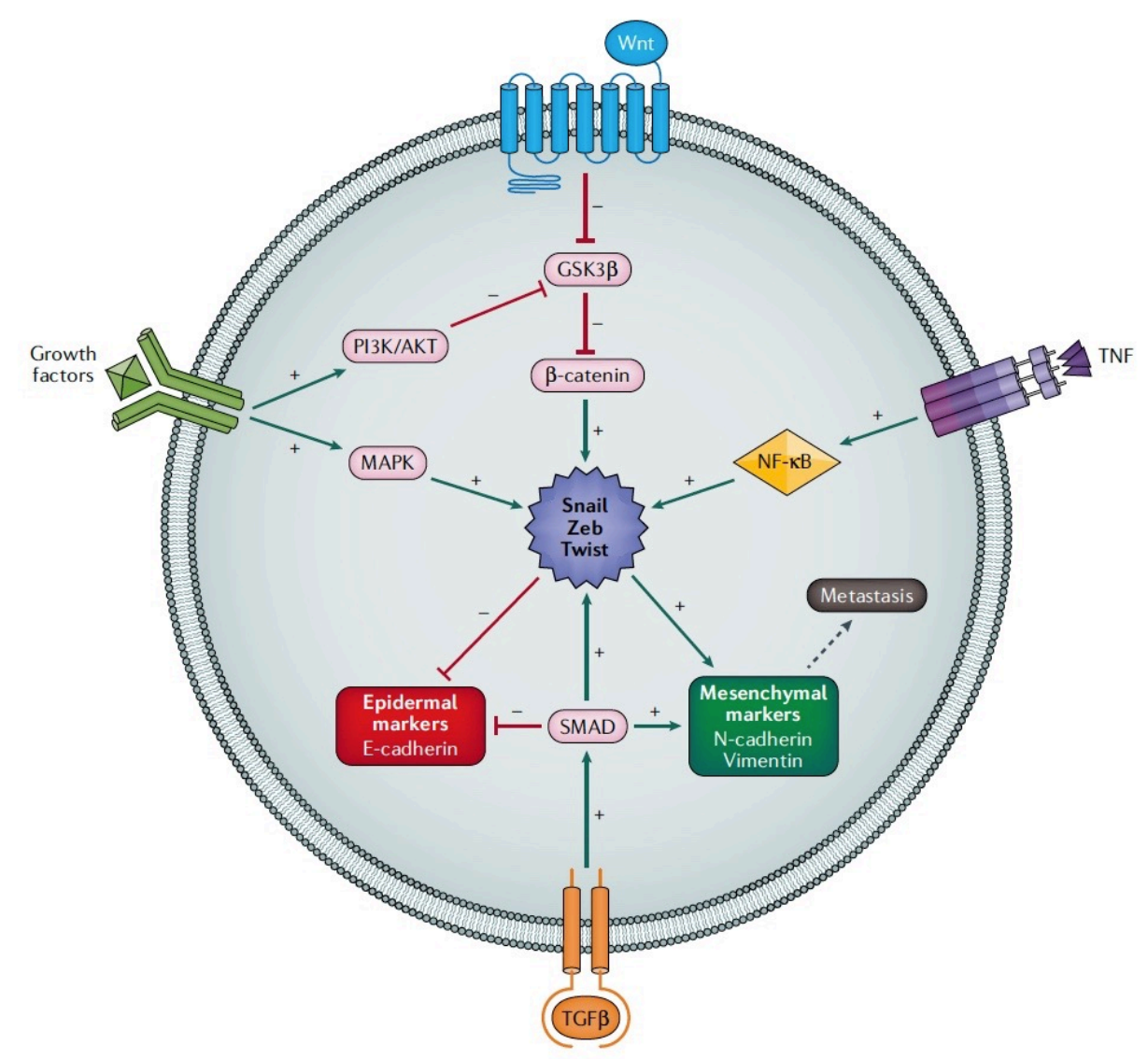
Histopathology of Sarcomatoid RCC



Blum KA et al. *Nat Rev Urol* 2020;17(12):659-78.

RTP RESEARCH TO PRACTICE

Signaling Pathways Involved in EMT Reported in Sarcomatoid RCC



EMT = epithelial to mesenchymal transition

Blum KA et al. *Nat Rev Urol* 2020;17(12):659-78.

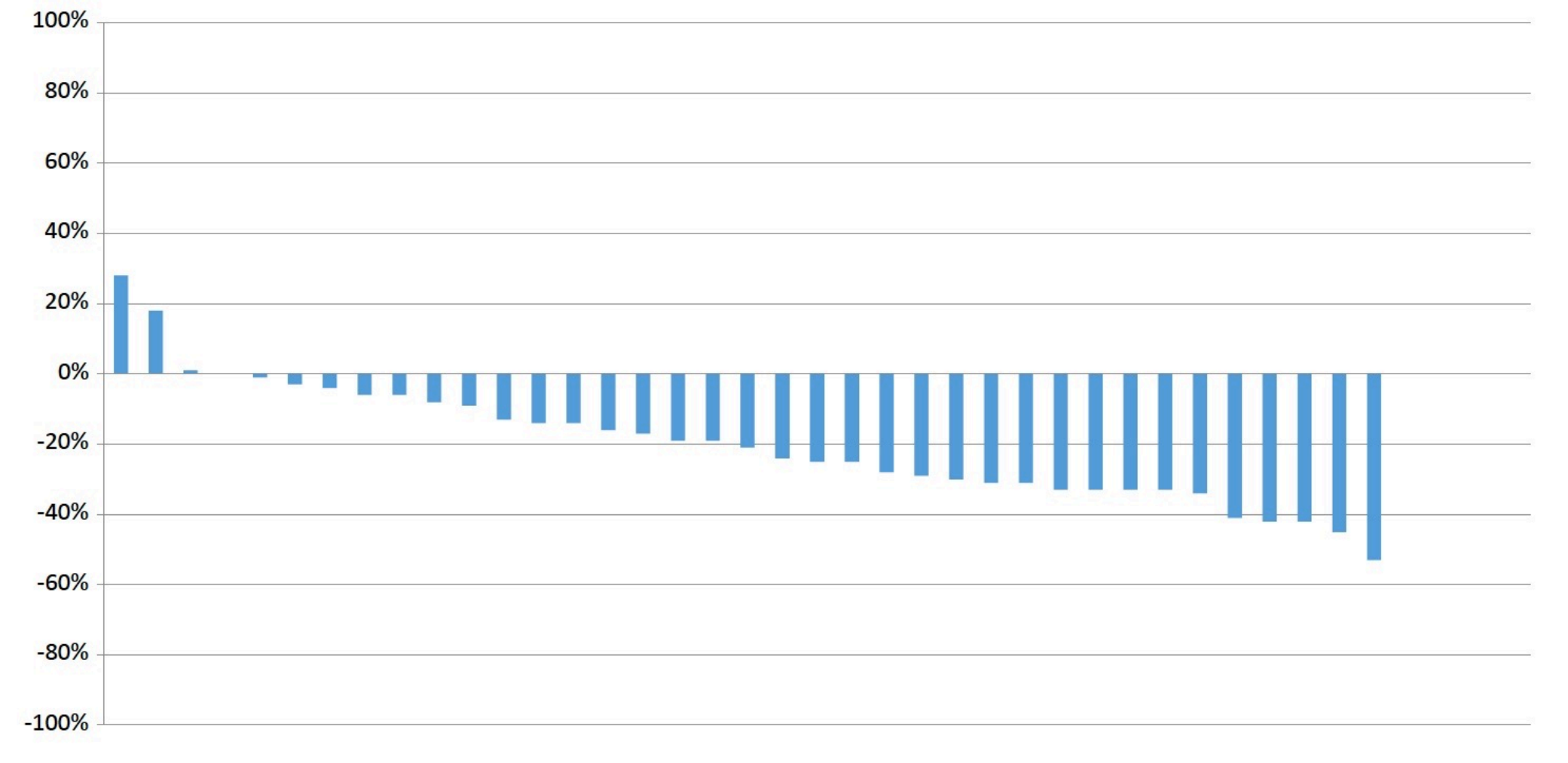
Cancer 2020;126(24):5247-55

Original Article

Everolimus Plus Bevacizumab Is an Effective First-Line Treatment for Patients With Advanced Papillary Variant Renal Cell Carcinoma: Final Results From a Phase II Trial

Darren R. Feldman, MD [1,2]; Yasser Ged, MBBS [1]; Chung-Han Lee, PhD[1,2]; Andrea Knezevic, MS[3]; Ana M. Molina, MD[2]; Ying-Bei Chen, PhD[4]; Joshua Chaim, DO[5]; Devyn T. Coskey, MS[1]; Samuel Murray, MS[1]; Satish K. Tickoo, MD[4]; Victor E. Reuter, MD[4]; Sujata Patil, PhD[3]; Han Xiao, MD[6]; Jahan Aghalar, MD[7]; Arlyn J. Apollo, MD[8]; Maria I. Carlo, MD[1,2]; Robert J. Motzer, MD [1,2]; and Martin H. Voss, MD [1,2]

Waterfall Plot of Efficacy Depicting the Greatest Degree of Change in Tumor Burden by RECIST



Feldman DR et al. *Cancer* 2020;126(24):5247-55.

RTP RESEARCH TO PRACTICE

ORIGINAL RESEARCH

Prognosis of Incidental Brain Metastases in Patients With Advanced Renal Cell Carcinoma

Ritesh R. Kotecha, MD[1]; Ronan Flippot, MD, MSc[2]; Taylor Nortman, BS[1]; Annalisa Guida, MD[2,3]; Sujata Patil, PhD[4]; Bernard Escudier, MD[2]; Robert J. Motzer, MD[1]; Laurence Albiges, MD[2]; and Martin H. Voss, MD[1]

J Natl Compr Canc Netw 2021 Feb 12:1-7

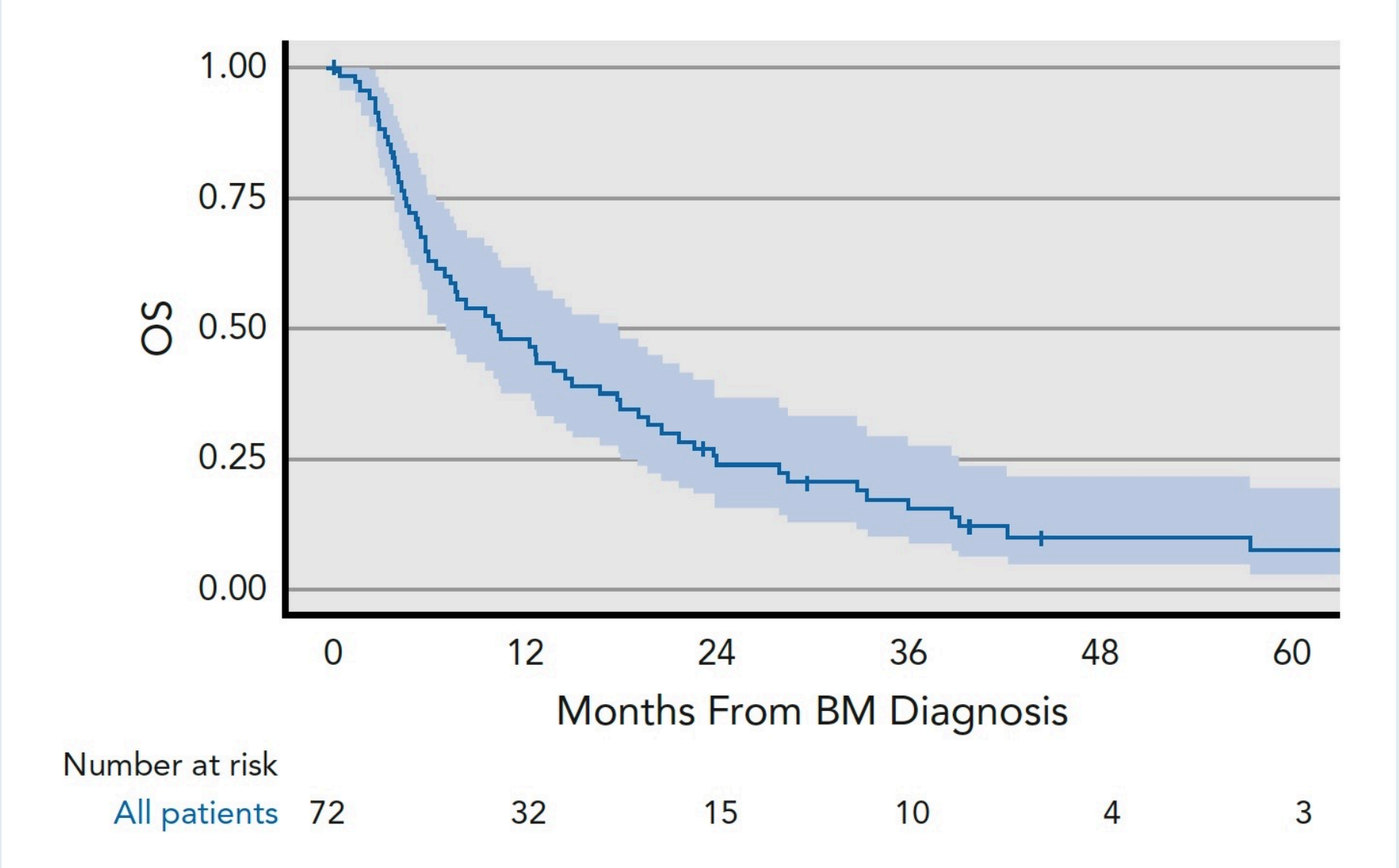
Brain Metastasis Characteristics

Characteristic	n (%)
Patients, N	72
Solitary lesion	45 (63)
Multifocal	27 (38)
2 lesions	10 (14)
≥3 lesions	17 (24)
Associated edema present	57 (79)
Size of brain metastases (longest axis, largest lesion)	
≤1 cm	40 (56)
>1 cm	27 (38)
Unknown	5
If >1 cm, median size of CNS metastasis (range), cm	1.75 (1.1–5.1)

Kotecha RR et al. *J Natl Compr Canc Netw* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Overall Survival from Diagnosis of Brain Metastasis in RCC



Kotecha RR et al. *J Natl Compr Canc Netw* 2021;[Online ahead of print].

RTP RESEARCH TO PRACTICE

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

European Association of Urology

Platinum Priority – Kidney Cancer

Editorial by XXX on pp. x–y of this issue

Efficacy and Safety of Atezolizumab Plus Bevacizumab Following Disease Progression on Atezolizumab or Sunitinib Monotherapy in Patients with Metastatic Renal Cell Carcinoma in IMmotion150: A Randomized Phase 2 Clinical Trial

Thomas Powles[a,], Michael B. Atkins[b], Bernard Escudier[c], Robert J. Motzer[d], Brian I. Rini[e], Lawrence Fong[f], Richard W. Joseph[g], Sumanta K. Pal[h], Mario Sznol[i], John Hainsworth[j], Walter M. Stadler[k], Thomas E. Hutson[l], Alain Ravaud[m], Sergio Bracarda[n], Cristina Suarez[o], Toni K. Choueiri[p], James Reeves[q], Allen Cohn[r], Beiying Ding[s], Ning Leng[s], Kenji Hashimoto[t], Mahrukh Huseni[s], Christina Schiff[s], David F. McDermott[u]*

***Eur Urol* 2021;[Online ahead of print].**

RTP RESEARCH TO PRACTICE

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

European Association of Urology

Platinum Priority Brief Correspondence

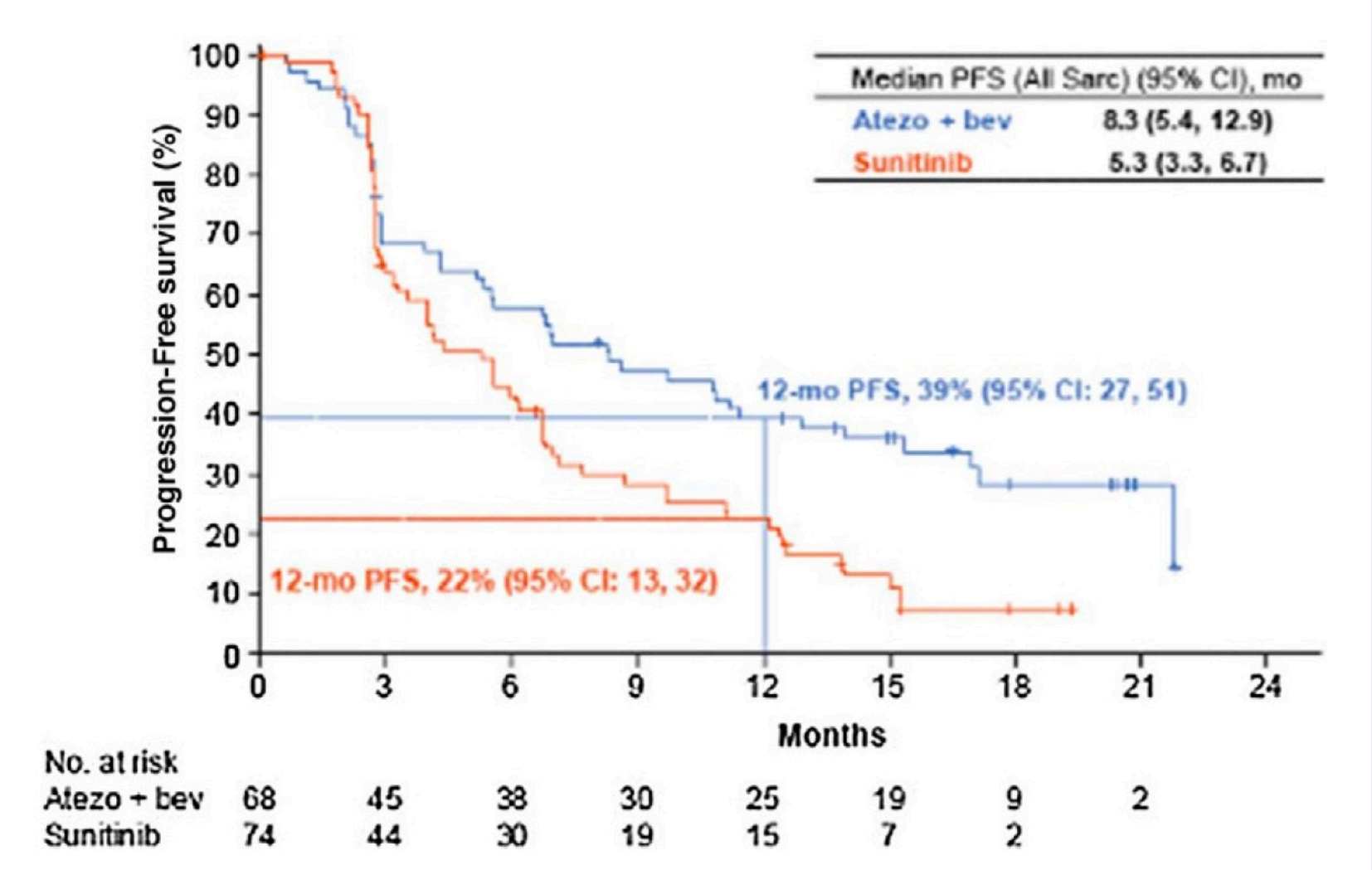
Editorial by XXX on pp. x-y of this issue.

Atezolizumab plus Bevacizumab Versus Sunitinib for Patients with Untreated Metastatic Renal Cell Carcinoma and Sarcomatoid Features: A Prespecified Subgroup Analysis of the IMmotion151 Clinical Trial

Brian I. Rini[a,], Robert J. Motzer[b], Thomas Powles[c], David F. McDermott[d], Bernard Escudier[e], Frede Donskov[f], Robert Hawkins[g], Sergio Bracarda[h], Jens Bedke[i], Ugo De Giorgi[j], Camillo Porta[k], Alain Ravaud[l], Francis Parnis[m], Enrique Grande[n], Wei Zhang[o], Mahrukh Huseni[o], Susheela Carroll[o,†], Roxana Sufan[o], Christina Schiff[o], Michael B. Atkins[p]*

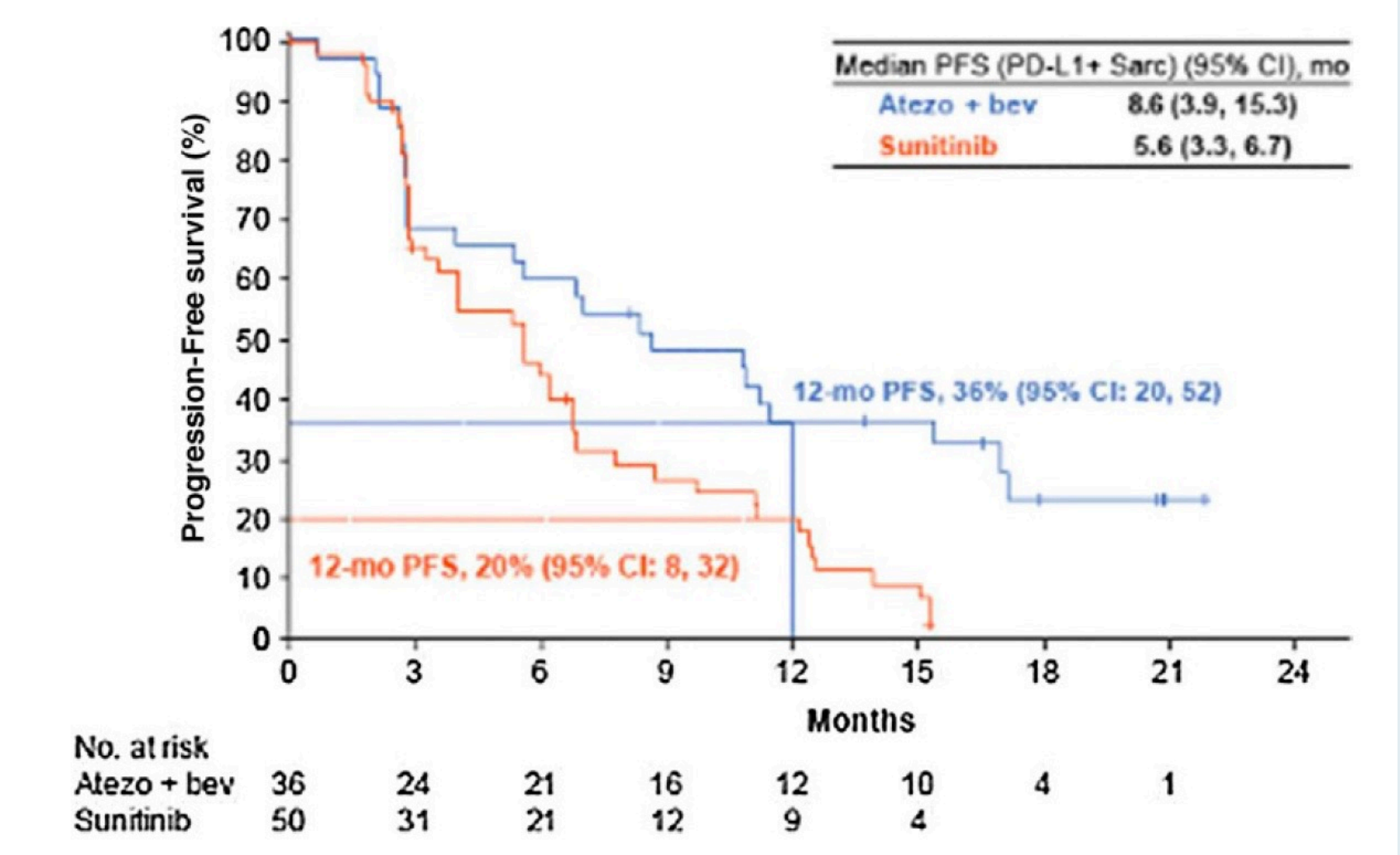
Eur Urol 2020;[Online ahead of print]

IMmotion151: PFS in the Overall Sarcomatoid Population



Rini BI et al. *Eur Urol* 2020;[Online ahead of print].

IMmotion151: PFS in the PD-L1+ Sarcomatoid Histology Group



Rini BI et al. *Eur Urol* 2020;[Online ahead of print].

RTP RESEARCH TO PRACTICE

Can Urol Assoc J 2020;14(12):E625-30

ORIGINAL RESEARCH

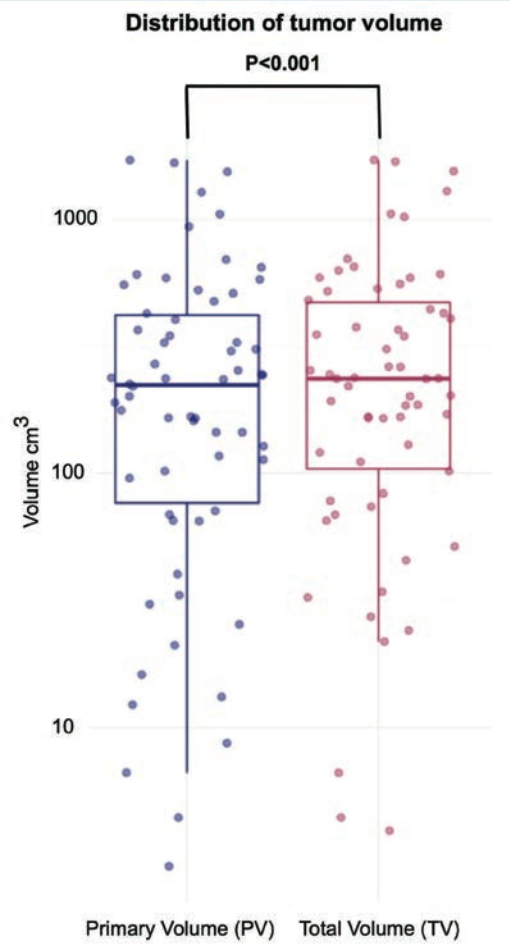
An evaluation of the role of tumor load in cytoreductive nephrectomy

Andrew W. Silagy, MD[1,2]; Cihan Duzgol, MD[3]; Julian Marcon, MD[1]; Renzo G. DiNatale, MD[1]; Roy Mano, MD[1]; Kyle A. Blum, MD[1]; Ed Reznik, MD[4]; Martin H. Voss, MD[5]; Robert J. Motzer, MD[5]; Jonathan A. Coleman, MD[1]; Paul Russo, MD[1]; Oguz Akin, MD[3]; A. Ari Hakimi, MD[1]

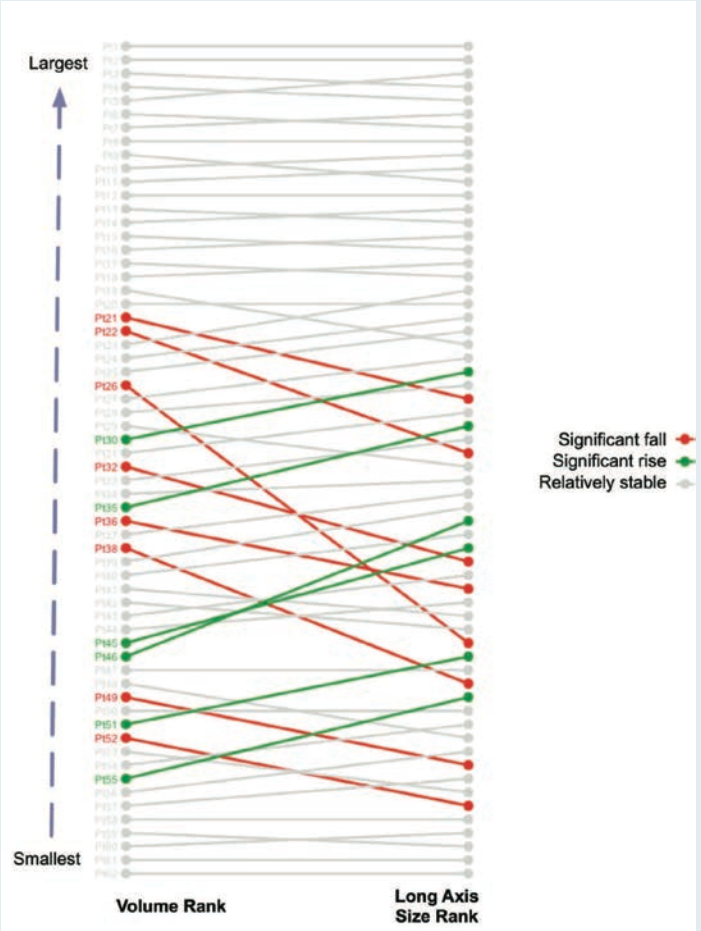
[1]Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, United States; [2]Department of Surgery, University of Melbourne, Austin Hospital, Melbourne, Australia; [3]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, United States; [4]Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, United States; [5]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, United States

Tumor Load in Cytoreductive Nephrectomy

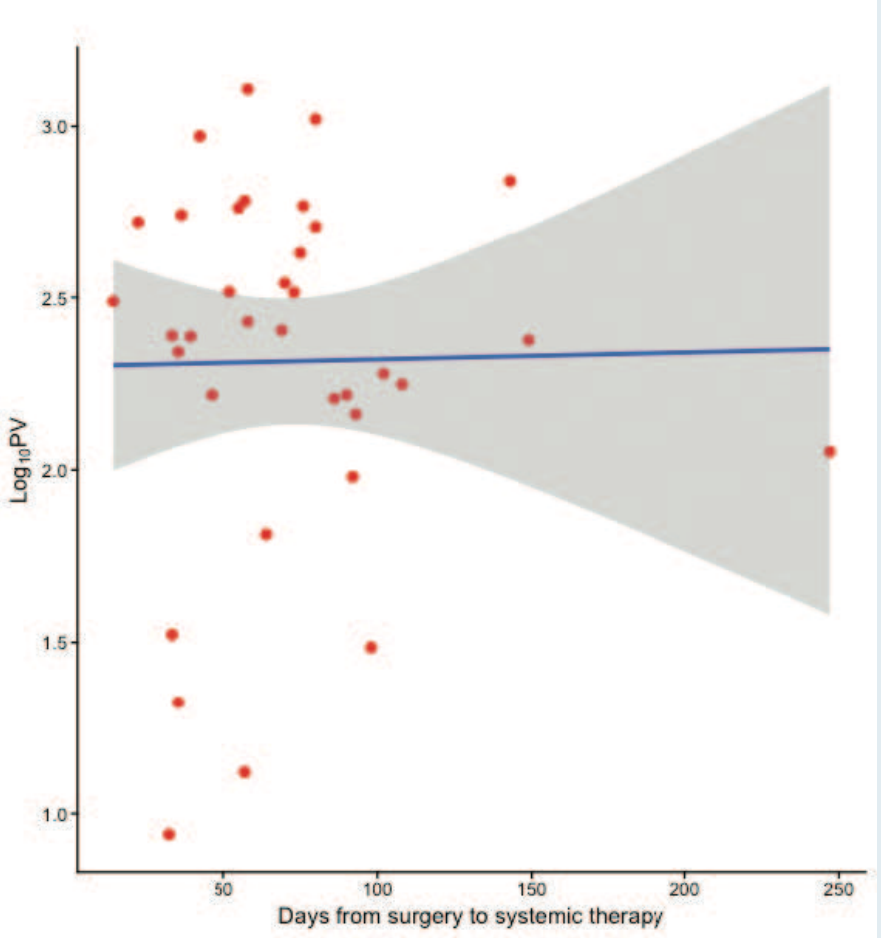
Distribution of tumor volume



Order of patients by tumor size



Primary volume and time to treatment



Silagy AW et al. *Can Urol Assoc J* 2020;14(12):E625-30.

Meet The Professor with Dr Motzer

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- Evaluation of the role of tumor load in cytoreductive nephrectomy

MODULE 5: Other Recent Data Sets

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

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

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

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

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

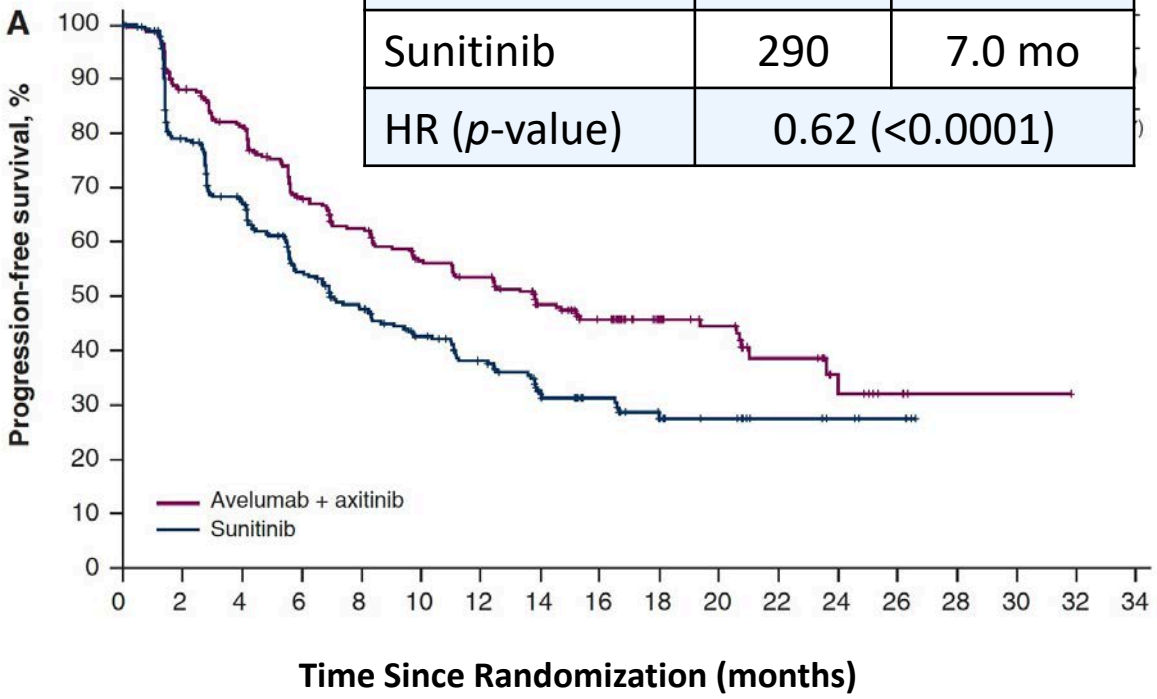
	PD-L1-positive		Overall	
	Avelumab + axitinib (n = 270)	Sunitinib (n = 290)	Avelumab + axitinib (n = 442)	Sunitinib (n = 444)
Confirmed ORR	55.9%	27.2%	52.5%	27.3%
CR	5.6%	2.4%	3.8%	2.0%
PR	50.4%	24.8%	48.6%	25.2%
Stable disease	27.0%	41.4%	28.3%	43.7%
Progressive disease	11.5%	22.4%	12.4%	19.4%
Ongoing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

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

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

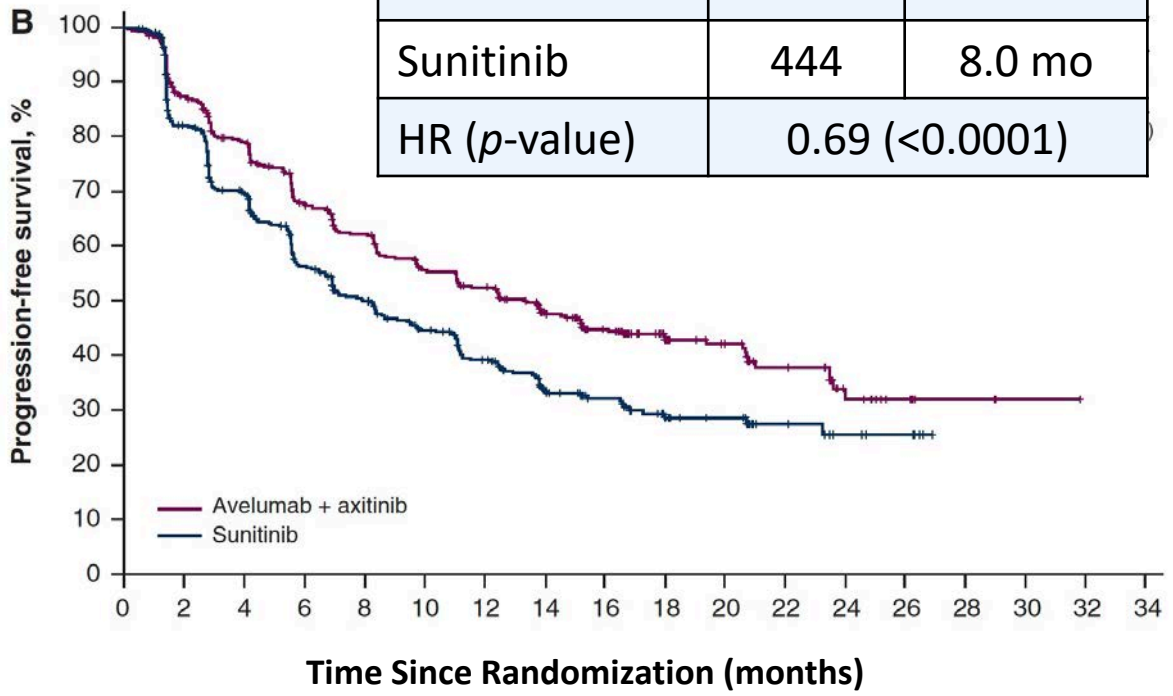
PD-L1 ≥ 1% Population

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



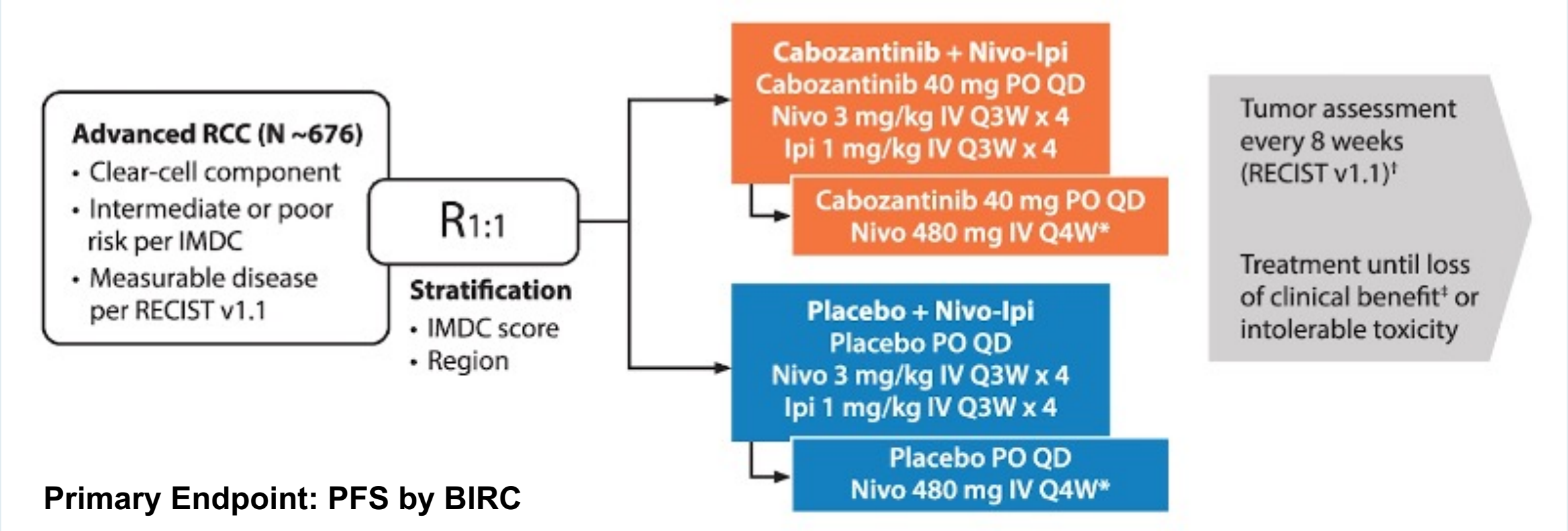
Overall Population

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



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

COSMIC-313 Phase III Schema



Primary Endpoint: PFS by BIRC

https://www.urotoday.com/conference-highlights/asco-2020/asco-2020-kidney-cancer/121877-asco-2020-cosmic-313-phase-iii-study-of-cabozantinib-in-combination-with-nivolumab-and-ipilimumab-in-patients-with-previously-untreated-advanced-renal-cell-carcinoma-of-intermediate-or-poor-risk.html

RTP RESEARCH TO PRACTICE

Sequencing of Therapy for Patients with Relapsed/Refractory (R/R) RCC; Novel Approaches Under Investigation

rapid communications

Salvage Ipilimumab and Nivolumab in Patients With Metastatic Renal Cell Carcinoma After Prior Immune Checkpoint Inhibitors

Anita Gul, MD[1]; Tyler F. Stewart, MD[2,3]; Charlene M. Mantia, MD[4]; Neil J. Shah, MD[5]; Emily Stern Gatof, MD[4]; Ying Long, PharmD[2]; Kimberly D. Allman, MSN, CNP[1]; Moshe C. Ornstein, MD, MA[1]; Hans J. Hammers, MD, PhD[6]; David F. McDermott, MD[4]; Michael B. Atkins, MD[5]; Michael Hurwitz, MD, PhD[2]; and Brian I. Rini, MD[1]

J Clin Oncol 2020;38:3088-94.

Salvage Ipilimumab/Nivolumab for mRCC After Prior ICI Therapy

Variable	No. (%)
No. of prior lines of systemic therapy	
1	9 (20)
2	12 (27)
3	8 (18)
4	6 (13)
> 4	10 (22)
Prior VEGF receptor inhibitor[a]	27 (60)
Prior immunotherapy	
Anti–PD-1[b]	34 (76)
Anti–PD-L1[b]	11 (24)
IL-2[c]	14 (31)
Best response to prior ICI	
PR	24 (53)
SD	12 (27)
PD	9 (20)

BOR to Prior ICI	No. (%)	BOR to Salvage Ipilimumab and Nivolumab	No. (%)
PR	24 (53)	PR	4 (17)
		SD	2 (8)
		PD	17 (71)
		NE	1 (4)
SD	12 (27)	PR	3 (25)
		SD	5 (42)
		PD	4 (33)
PD	9 (20)	PR	2 (22)
		PD	7 (78)

Abbreviations: BOR, best objective response; ICI, immune checkpoint inhibitor; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Gul A et al. *J Clin Oncol* 2020;38:3088-94.

A Pooled Analysis of the Efficacy and Safety of Cabozantinib Post Immunotherapy in Patients with Advanced Renal Cell Carcinoma

Oya M et al.

ASCO 2020;Abstract 5089.

Efficacy of Cabozantinib with or without Prior Immunotherapy

	Prior IO (N = 33)	No Prior IO (N = 332)
Objective response rate	21.2%	17.2%
Clinical benefit rate	75.8%	83.7%
Median PFS	Not reached	7.4 mo
6-months PFS	65.5%	58.3%
Median PFS	19.5 mo	21.9 mo
6-months OS	90.8%	90.6%

Oya M et al. ASCO 2020;Abstract 5089.

Phase II Trial of Lenvatinib (LEN) plus Pembrolizumab (PEMBRO) for Disease Progression After PD-1/PD-L1 Immune Checkpoint Inhibitor (ICI) in Metastatic Clear Cell Renal Cell Carcinoma (mccRCC)

Lee C-H et al.

ASCO 2020;Abstract 5008.

Efficacy of Lenvatinib/Pembrolizumab in Patients Previously Treated with Immunotherapy

	Anti-PD-1/PD-L1 (N = 104)	Anti-PD-1/PD-L1 and anti-VEGF (n = 68)	Nivolumab + ipilimumab (n = 38)
ORR	55%	59%	47%
Median DOR	12 mo	9 mo	Not reached
Median PFS (irRECIST)	11.7 mo	Not reported	Not reported
OS at 12 months	77%	Not reported	Not reported

Lee C-H et al. ASCO 2020;Abstract 5008.

Meet The Professor

Management of Chronic Lymphocytic Leukemia

Monday, March 29, 2021
5:00 PM – 6:00 PM ET

Faculty

Philip A Thompson, MB, BS

Moderator

Neil Love, MD

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Thank you for joining us!

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

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