Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Renal Cell Carcinoma (Part 2 of a 3-Part Series)

Monday, March 1, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas E Hutson, DO, PharmD
Thomas Powles, MBBS, MRCP, MD

Moderator

Neil Love, MD

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Faculty

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

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

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Commercial Support

This activity is supported by an educational grant from Exelixis Inc.

Dr Love — Disclosures

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Dr Hutson — Disclosures

No financial interests or affiliations to disclose

Prof Powles — Disclosures

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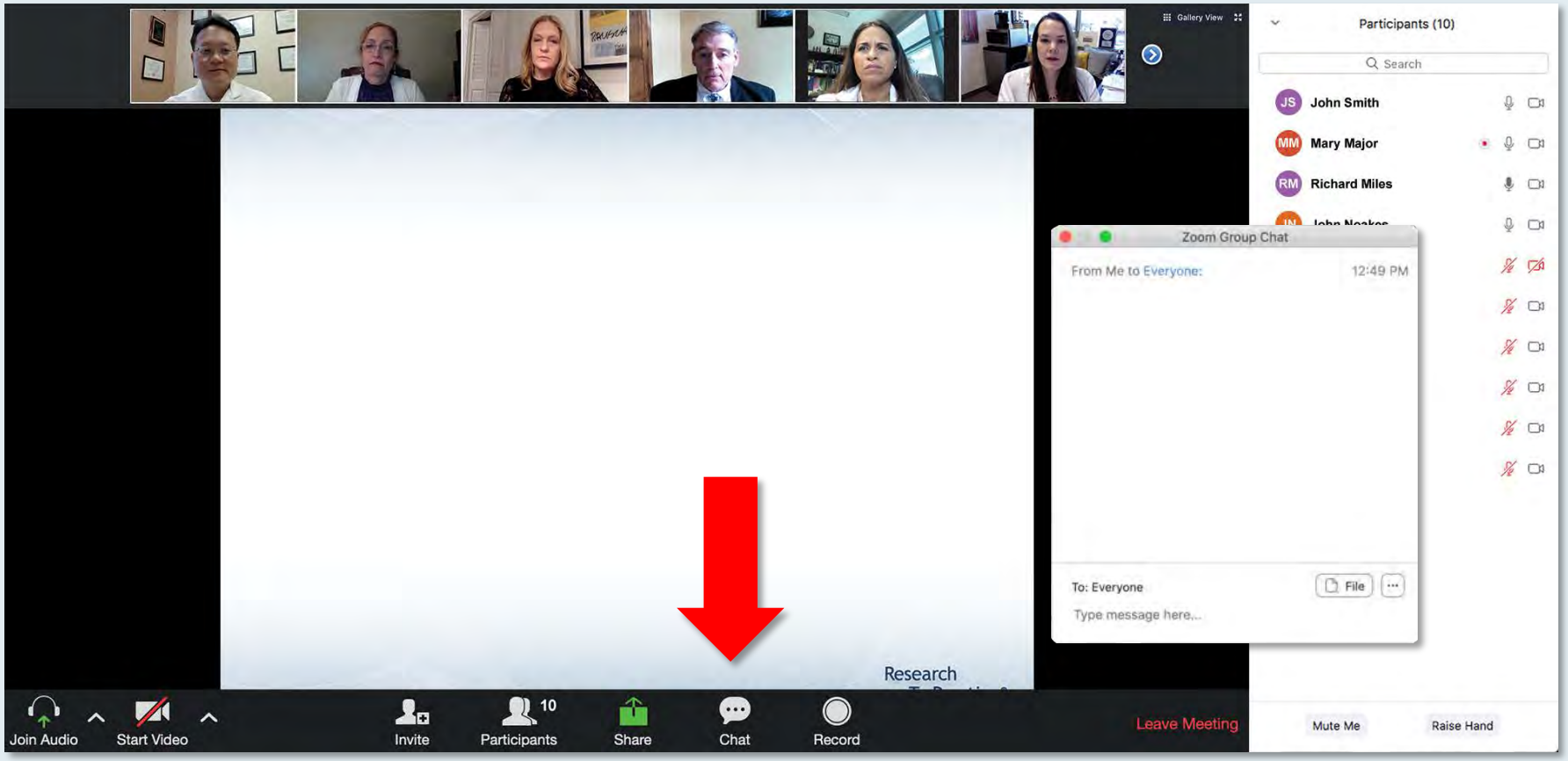
We Encourage Clinicians in Practice to Submit Questions



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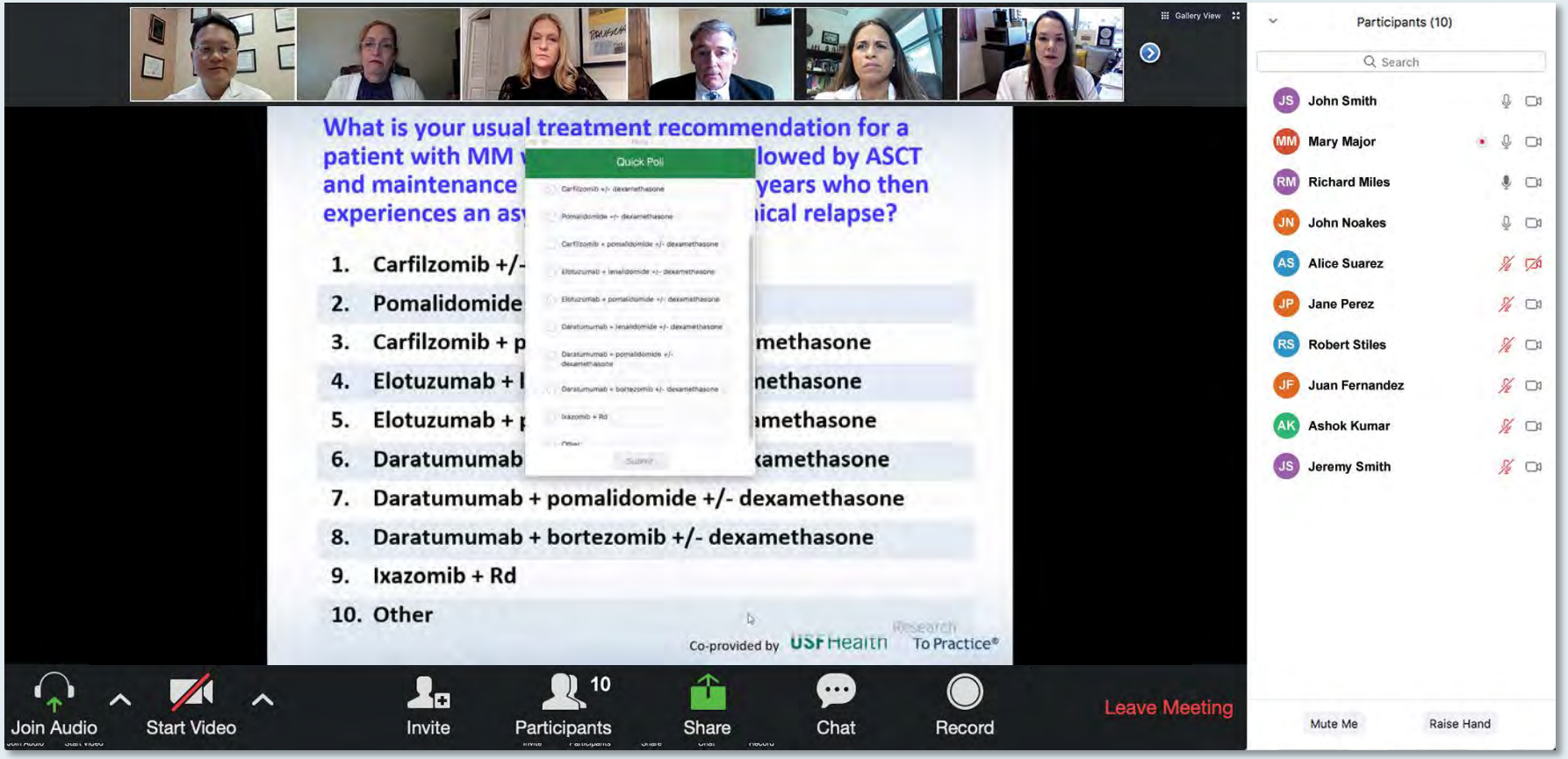

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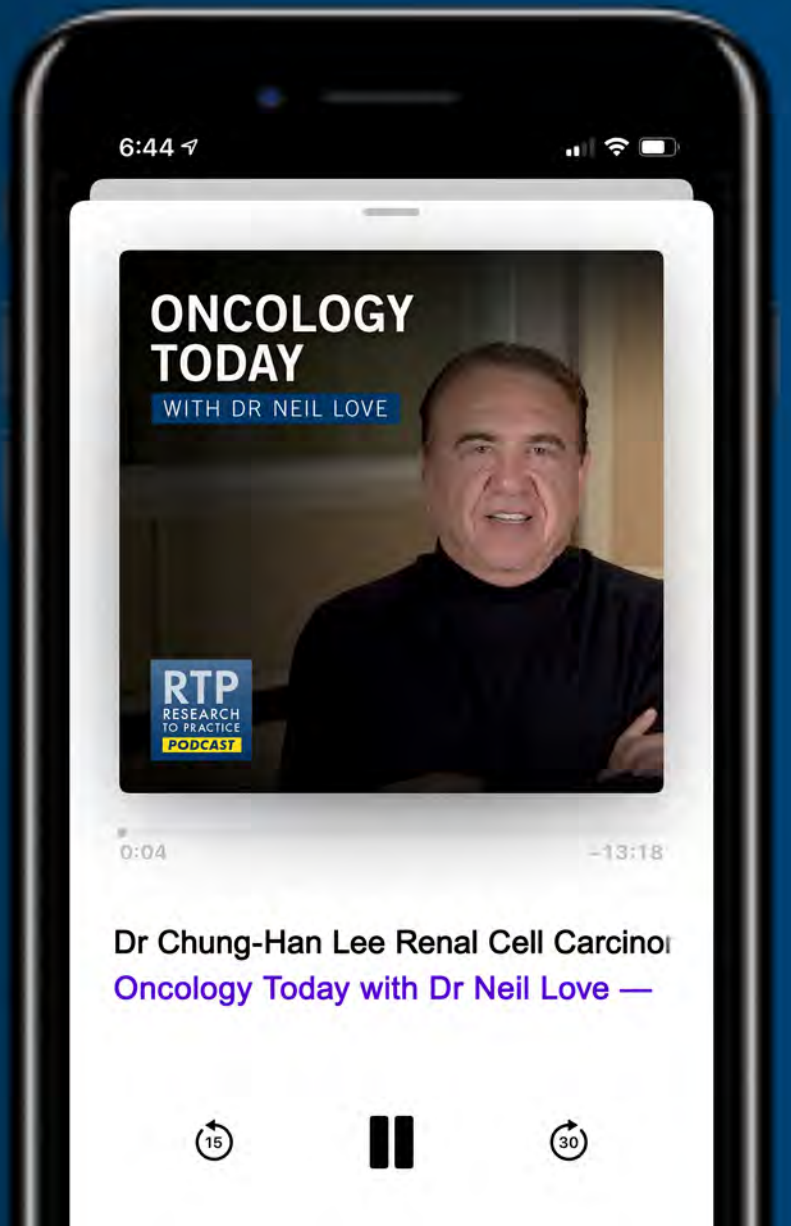
WITH DR NEIL LOVE

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 Ovarian Cancer

Tuesday, March 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD

Moderator

Neil Love, MD

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Meet The Professor
Management of Multiple Myeloma

Wednesday, March 3, 2021
5:00 PM – 6:00 PM ET

Faculty

Morie A Gertz, MD, MACP

Moderator

Neil Love, MD

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Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Urothelial Bladder Carcinoma (Part 3 of a 3-Part Series)

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Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Management of HER2-Positive Breast Cancer

Monday, March 8, 2021
5:00 PM – 6:00 PM ET

Faculty

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Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Data + Perspectives: Investigators Discuss the Effects of Emerging Research on the Care of Patients with Acute Myeloid Leukemia

Wednesday, March 10, 2021
7:00 PM – 8:00 PM ET

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Thursday, March 11, 2021
5:00 PM – 6:00 PM ET

Faculty

Steven Coutre, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.


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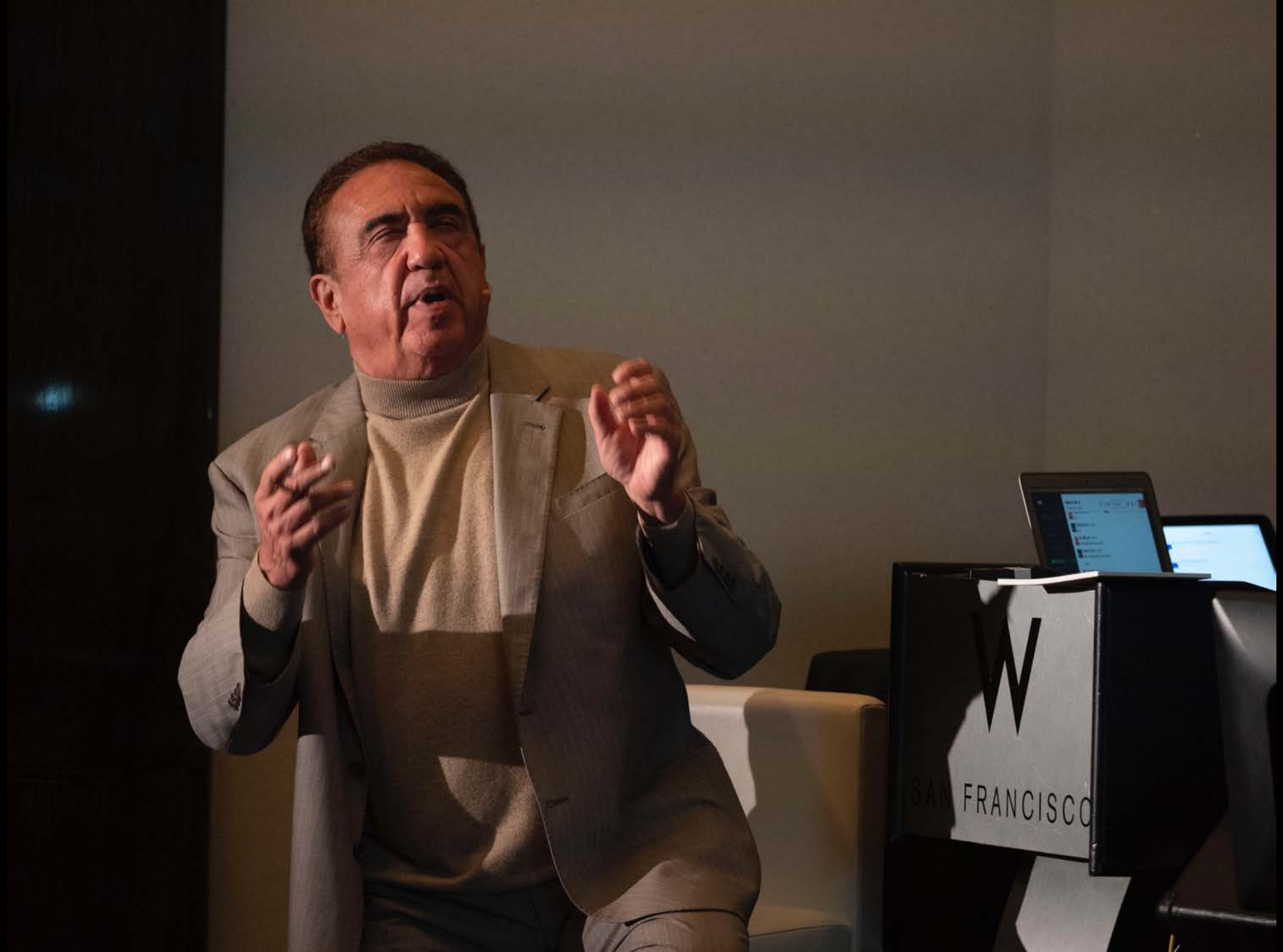
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EXIT


Email from Dr Ibrahim
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ViewSonic


MARRIOTT MARQUIS SAN FRANCISCO
Yes, along with absolute PSA level
No
Yes
Yes
No

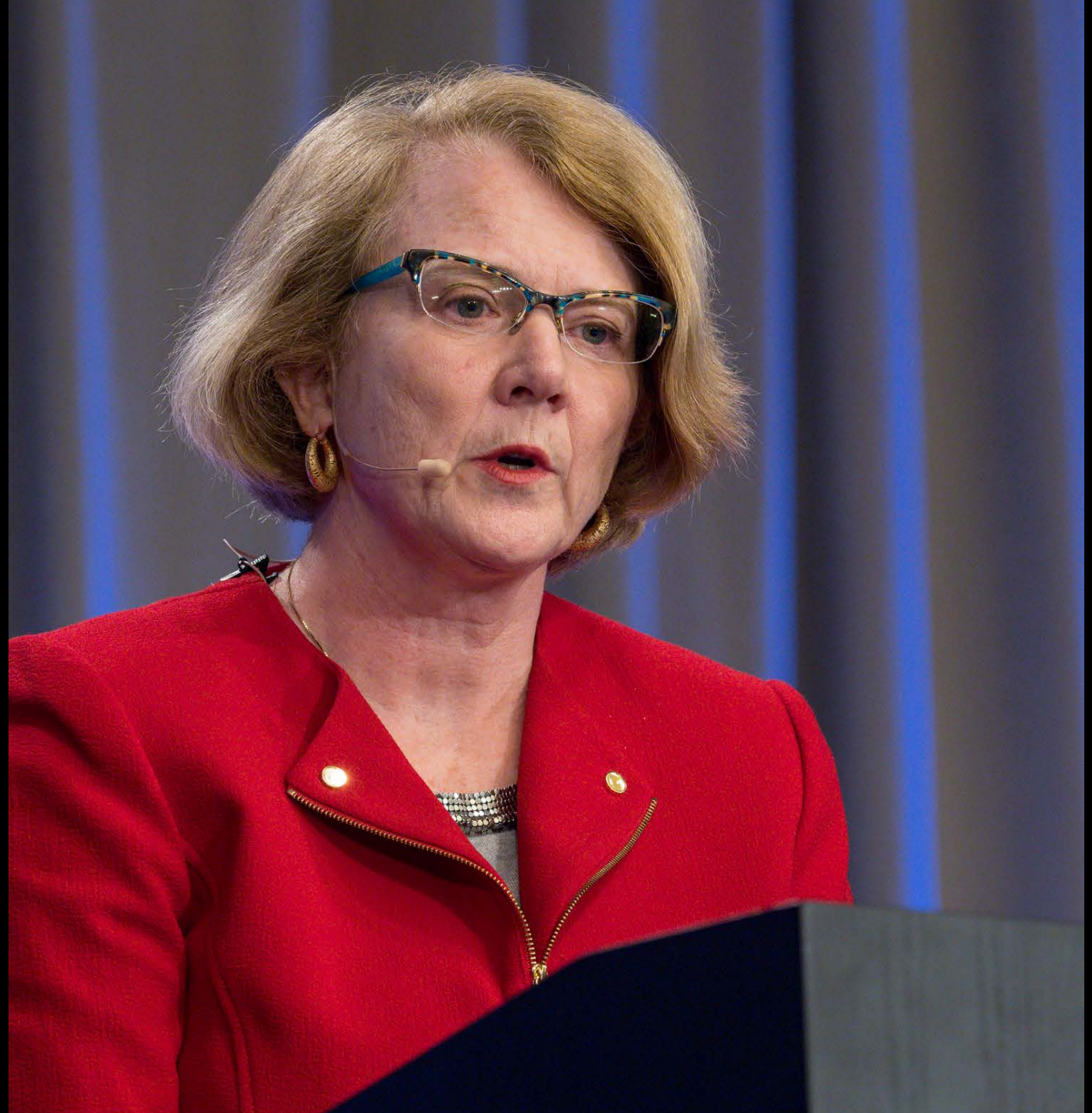

EXIT


Regulatory and reinbursement issues aside, what systemic therapy, if any, would you typically add to androgen deprivation for a 60-year-old patient presenting with Gleason 8 prostate cancer and 3 asymptomatic rib metastases?


MARRIOTT MARQUIS
SAN FRANCISCO
A 65-year-old man s/p radical prostatectomy follows
PSA-only recurrence (M0) receives an LHRH agonis
to a PSA level of 14 ng/dL with a doubling time of 3
imaging are negative. The patient has asked you to
diagnosed with metastatic disease in 3 years if he c
alone. How would you respond?
Less than 5%
5%–10%
11%–25%
26%–55%
56%–70%
Greater than 70%


A 65-year-old man s/p radical prostate
PSA-only recurrence (M0) receives an
to a PSA level of 14 ng/dL with a doub
imaging are negative. The patient has
reduction in the chance he will be dia
he continues the LHRH agonist in co
How would you respond?
Less than 2%
2%-10%
11%-30%
31%-40%
41%-50%
MARRIOTT MARQUIS
SAN FRANCISCO
MARRIOTT MARQUIS
SAN FRANCISCO


Consensus or Controversy?
Clinical Investigators Provide
Perspectives on the Current and Future
Management of Prostate Cancer




In addition to LHRH agonist/antagonist treatment, which of the following would you recommend for a 60-year-old man presenting with Gleason 9 prostate cancer and 6 mildly symptomatic bone metastases?
Docetaxel
6
Docetaxel + abiraterone
5
Abiraterone
11
Docetaxel or abiraterone "coin flip"
3
N = 25


A 68-year-old man underwent prostatectomy for Glea
cancer followed by radiation therapy for early PSA re
nadir at 0.9 ng/mL. Eighteen months later PSA rises t
the next 12 months continues to rise to 15 ng/mL with
of 6 months. Would you administer ADT?
Yes
No
4


Existing and Emerging Therapeutic
Strategies for the Management
of M0 Prostate Cancer

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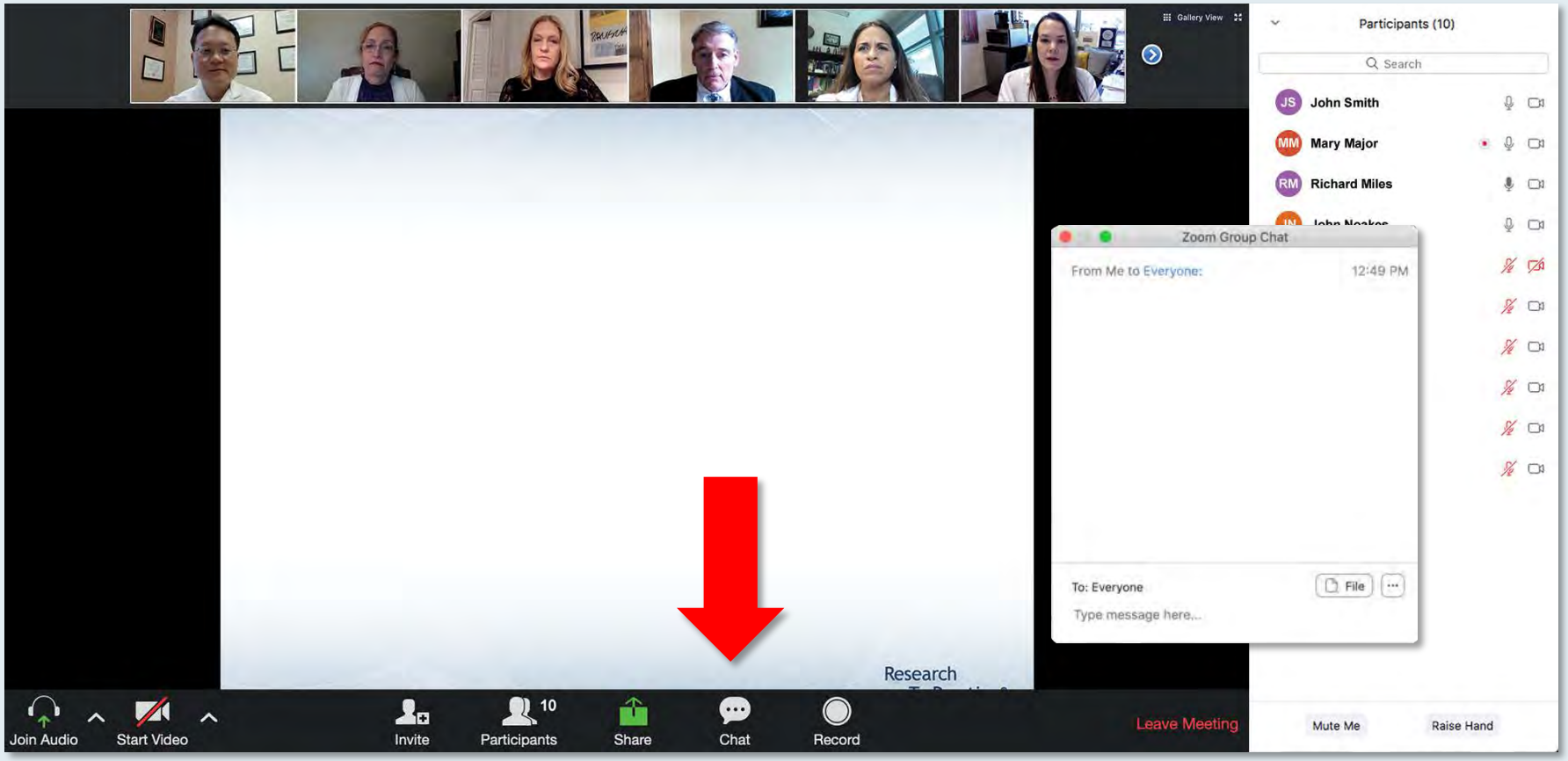

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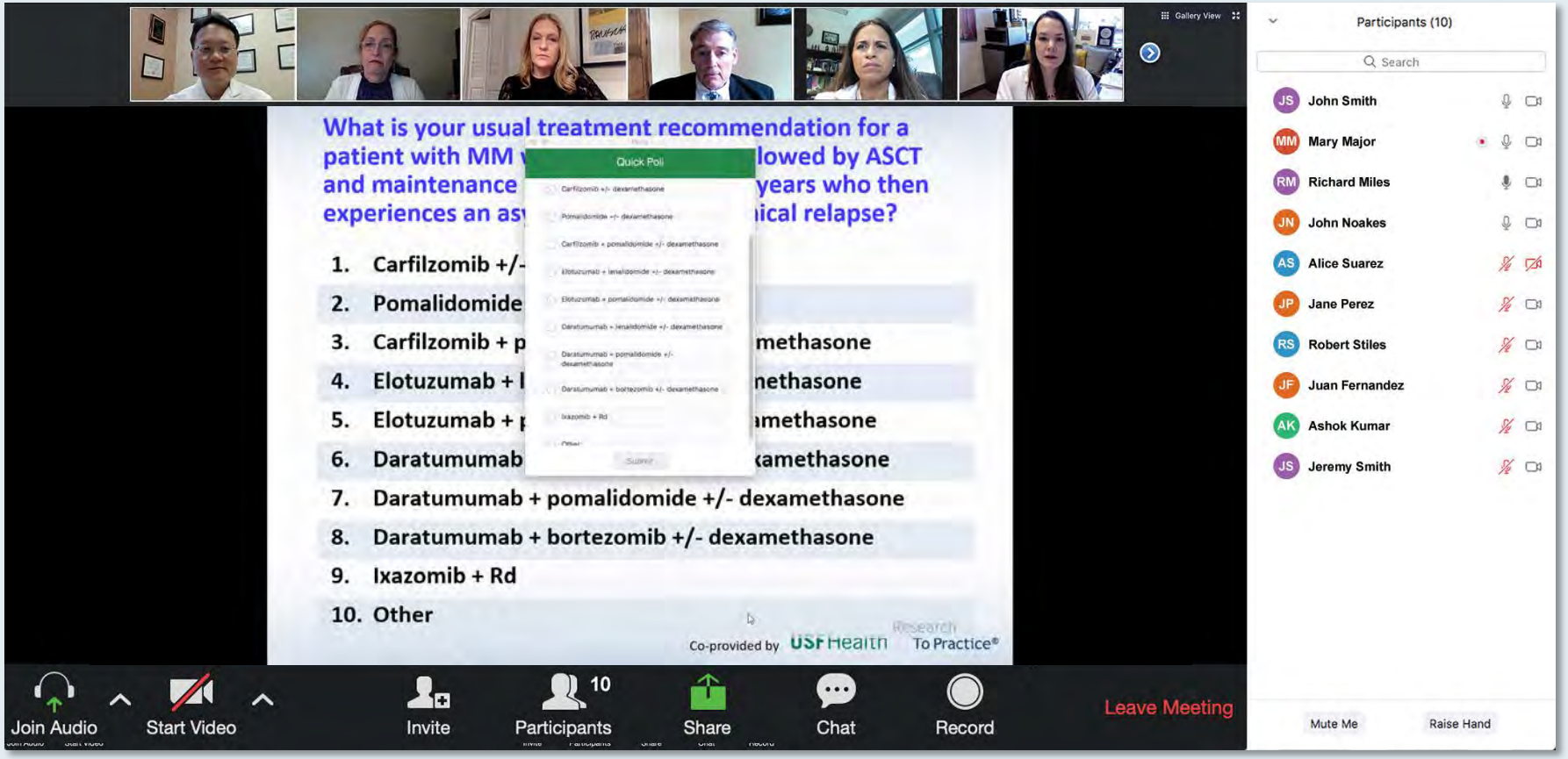

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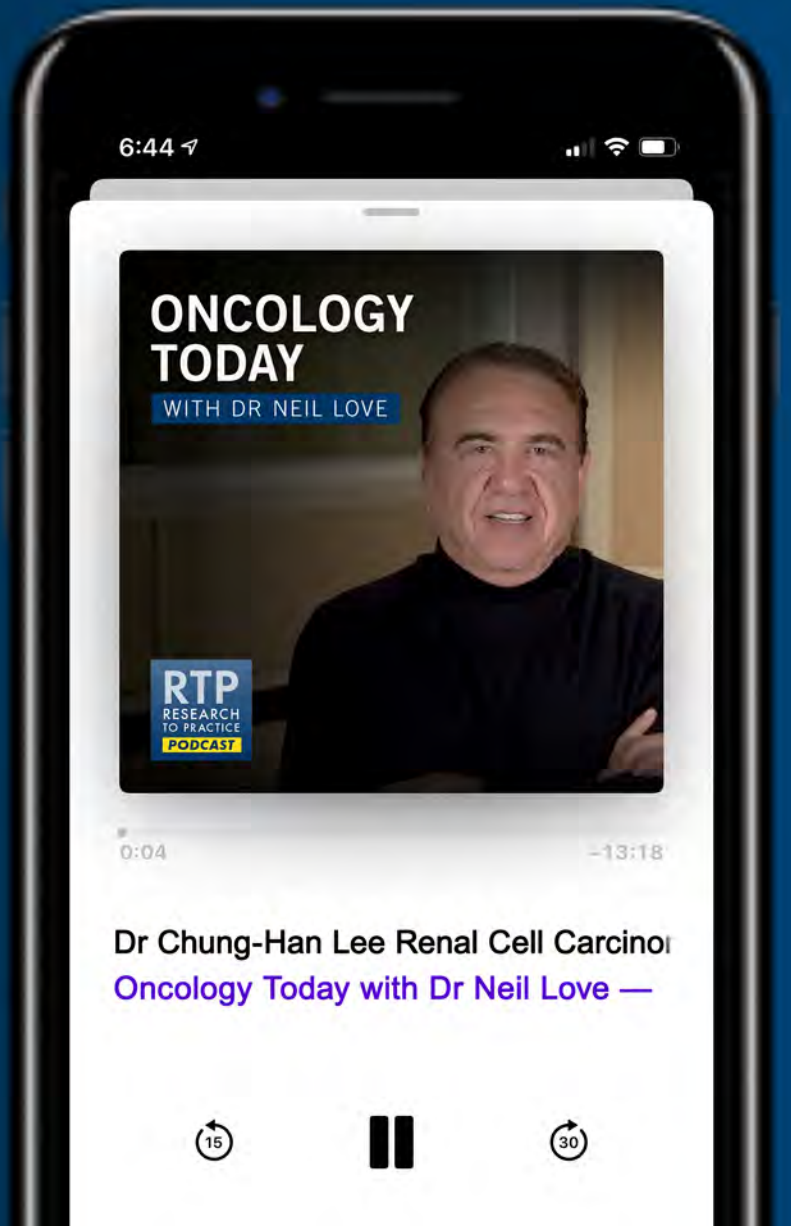

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Rahul Gosain, MD
Division of Hematology and Oncology
Guthrie Corning Cancer Center
Corning, New York

Kelly Yap, MD
Assistant Clinical Professor
City of Hope
Arcadia, California

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

Syed F Zafar, MD
Hematologist and Medical Oncologist
Florida Cancer Specialists and Research Institute
Chief, Division of Hematology and Oncology, Lee Health
Fort Myers, Florida

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Agenda

Module 1: Front-line treatment of advanced renal cell carcinoma (RCC)

- Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma
- Dr Gosain: A 67-year-old man with metastatic RCC
- Dr Yap: A 60-year-old man with Stage IV clear cell RCC
- Dr Zafar: An 85-year-old man with metastatic RCC

Module 2: Sequencing of therapies for relapsed/refractory RCC

- Dr Plimack: A 24-year-old woman with translocation clear cell RCC

Module 3: Novel approaches for advanced RCC

Module 4: Sarcomatoid RCC

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Newly approved front line regimens for metastatic RCC

Thomas Powles

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

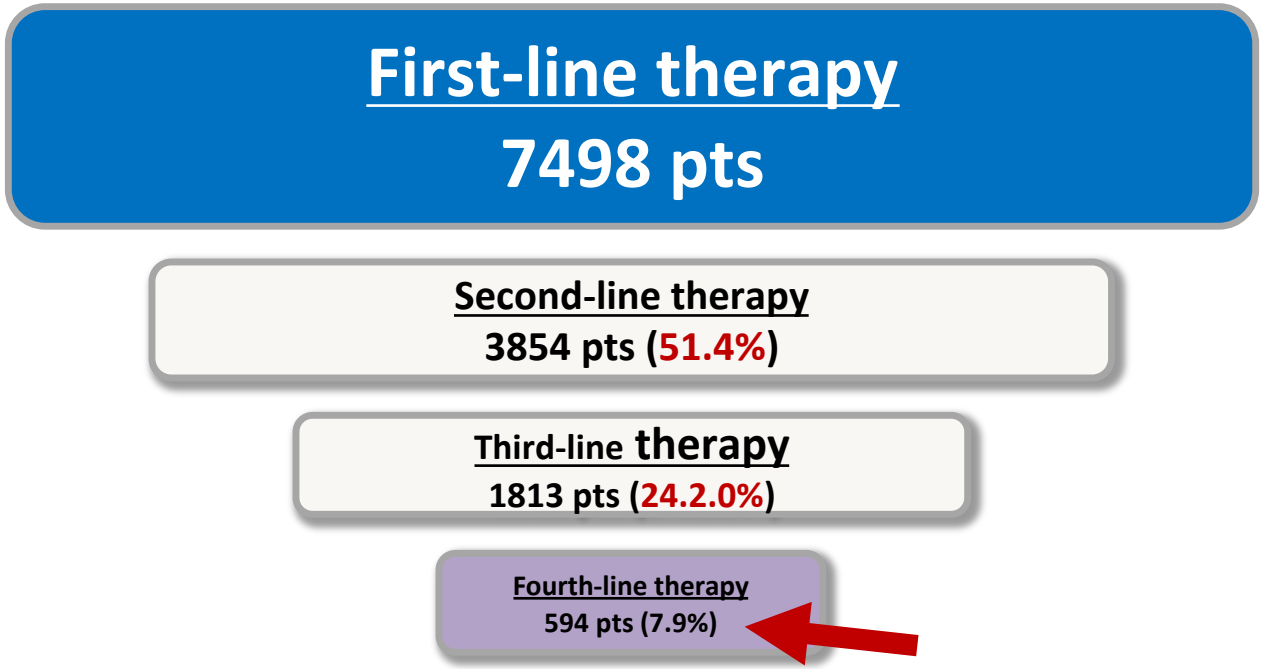
Management Issues For Patients with Advanced Renal Cell Carcinoma

Thomas E Hutson, DO, PharmD, FACP

Director, GU Oncology Program
Co-Director, Urologic Cancer Research and Treatment Center
Texas Oncology
Baylor Sammons Cancer Center
Dallas, Texas

Professor of Medicine
Texas A&M College of Medicine

Attrition Across Lines of Therapy (IMDC Data)

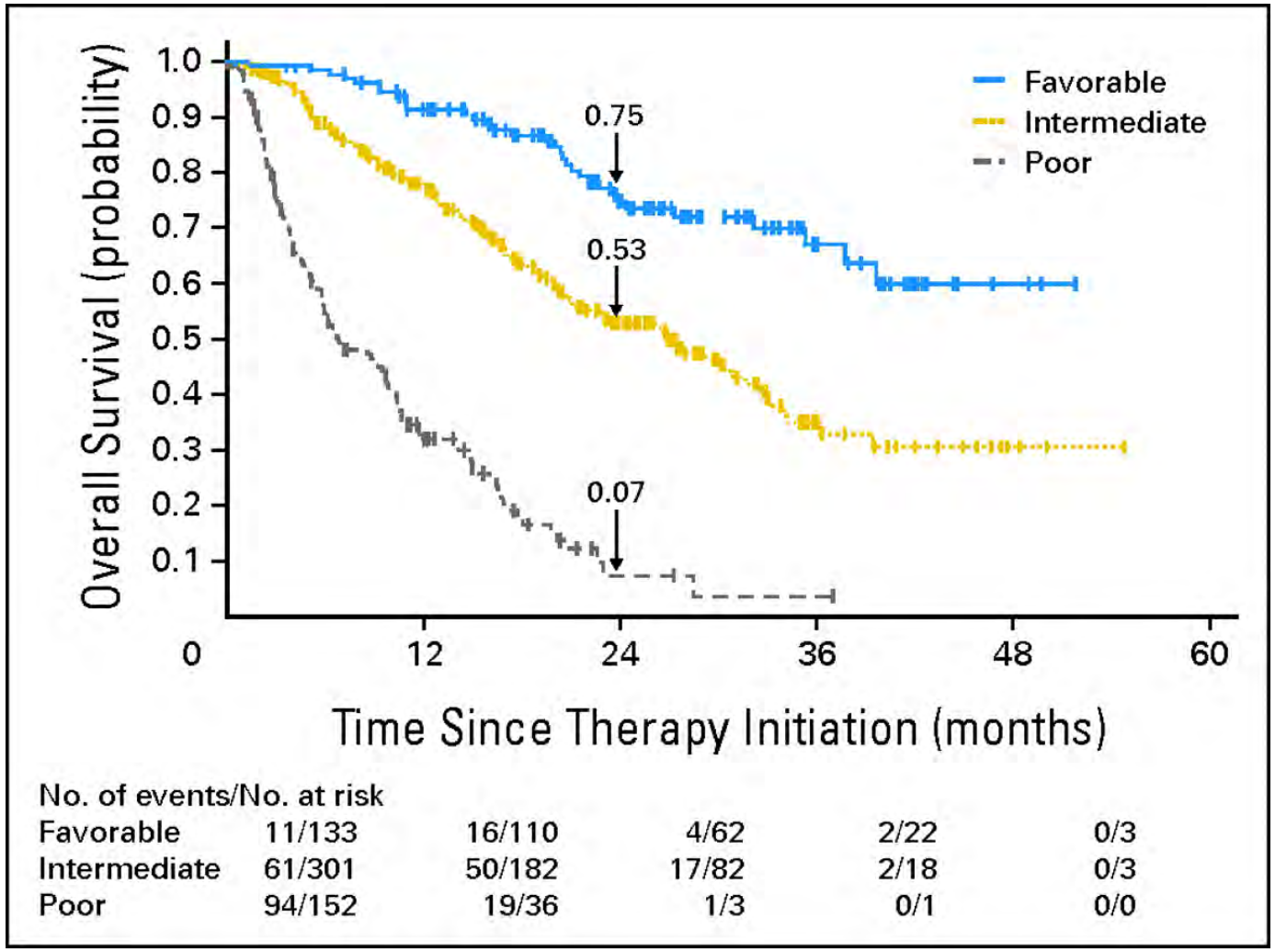


Stukalin et al, Kidney Cancer, 2018

Courtesy of Thomas E Hutson, DO, PharmD

Overall Survival Probability for Patients with mRCC Treated with VEGF-Targeted Agents

According to time after therapy initiation and risk group



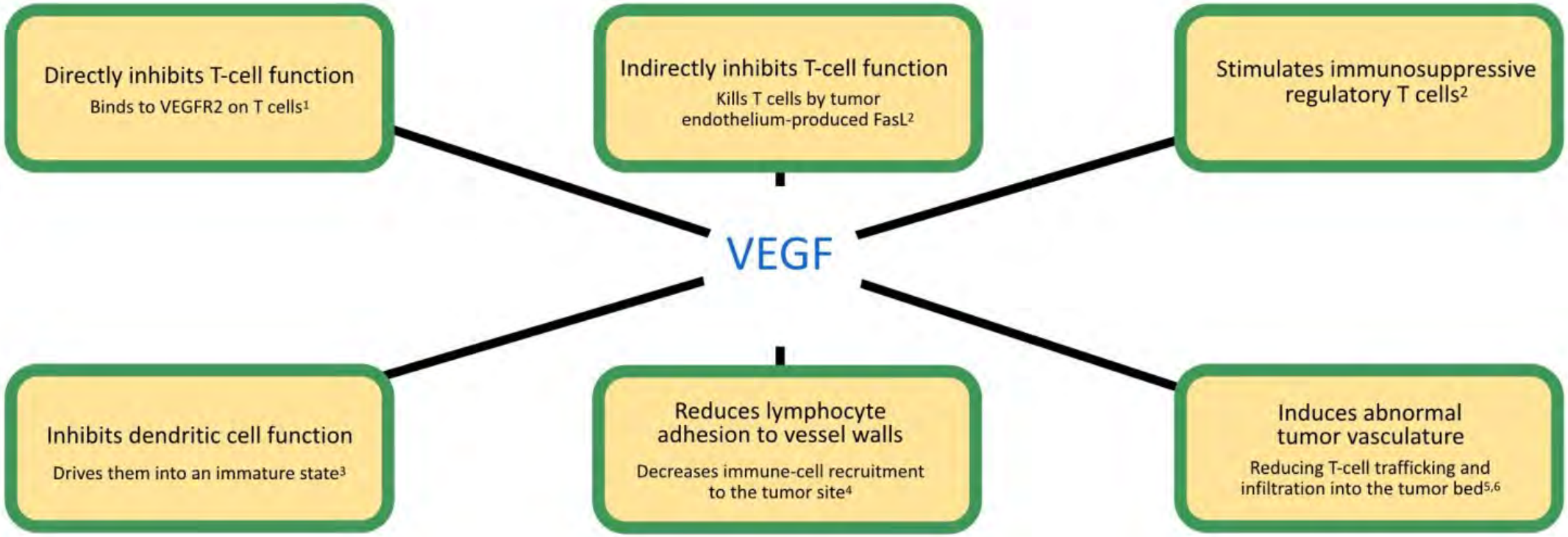
No. of events/No. at risk					
Favorable	11/133	16/110	4/62	2/22	0/3
Intermediate	61/301	50/182	17/82	2/18	0/3
Poor	94/152	19/36	1/3	0/1	0/0

Heng DYC et al. JCO 2009;27:5794-5799

Courtesy of Thomas E Hutson, DO, PharmD

RATIONALE FOR IO–TKI COMBINATIONS

EFFECTS OF VEGF ON THE TUMOR MICROENVIRONMENT



1. Gavalas NG et al. Br J Cancer 2012;107:1869–75; 2. Terme M et al. Cancer Res 2013;73:539–49; 3. Coukos G et al. Br J Cancer 2005;92:1182–7; 4. Bouzin C etal. J 5. Immunol 2007;178:1505–11; 5. Shrimali RK et al. Cancer Res 2010;70:6171–80; 6. Chen DS & Mellman I. Immunity 2013;39:1–10

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Module 3: Novel approaches for advanced RCC

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Case Presentation – Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma

Dr Syed Zafar

- Presented with a large neck lump on the right cervical area
  - 8 or 9 cm lymph node on a CT neck, initially characterized as a poorly differentiated carcinoma
- PET scan: hypermetabolic neck lesion
- Treated as head and neck primary of head and neck cancer with an unknown primary
  - Did not respond to chemoradiotherapy
- Conducted unknown primary assay testing
  - Results revealed high probability of a renal cell carcinoma
  - Repeated CT scan revealed a left-sided renal mass and probable adrenal mass
- Biopsy consistent with clear cell renal cell carcinoma

Questions

- What are the faculty's thoughts on the fact that PET scans can be notoriously negative in renal cell?
- In this case, what led me to look further was the unknown primary proteomic and genomic testing that told me that certainly it could be a probability as renal cell.

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Case Presentation – Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma

Dr Syed Zafar

MI GPSai™

The MI GPSai℠ (MI Genomic Prevalence Score - Artificial Intelligence) is a cancer-type similarity assessment which compares the characteristics of a patient's tumor against other tumors in the Caris database. MI GPSai analyzes a tumor's molecular signature and provides the prevalence of that signature in the Caris Life Sciences genomic and transcriptomic database across 21 distinct cancer categories.

Cancer Category	Prevalence
Renal Cell Carcinoma	98 %
Lung Adenocarcinoma	2 %
Breast Adenocarcinoma	0 %
Central Nervous System Cancer	0 %
Cervical Adenocarcinoma	0 %
Cholangiocarcinoma	0 %
Colon Adenocarcinoma	0 %
Gastroesophageal Adenocarcinoma	0 %
GIST	0 %
Hepatocellular carcinoma	0 %
Melanoma	0 %
Meningioma	0 %
Ovarian, Fallopian Tube Adenocarcinoma	0 %
Ovarian Granulosa Cell Tumor	0 %
Pancreas Adenocarcinoma	0 %
Prostate Adenocarcinoma	0 %
Squamous Cell Carcinoma	0 %
Thyroid Cancer	0 %
Urothelial Carcinoma	0 %
Uterine Endometrial Adenocarcinoma	0 %
Uterine Sarcoma	0 %

Methods

MI GPSai℠ is a machine learning platform that was trained on genomic data from 34,352 cases and transcriptomic data from over 11,000 cases. In a validation set of over 12,000 additional cases, MI GPSai accurately predicted the cancer category in the labeled data set with an accuracy of over 93%. The accuracy increased to 97% when the second highest ranking predicted cancer type was included. The profile has been validated to differentiate among 21 distinct cancer types. MI GPSai prevalence tables were produced at or above the required confidence level for 93% of samples in the validation set. Samples that do not generate a score at or above this confidence level will not receive a MI GPSai result.

Notes of Significance

SEE APPENDIX FOR DETAILS

Clinical Trials Connector ℠ opportunities based on biomarker expression: 13 Targeted Therapy Trials. See page 6 for details.

Specimen Information

Specimen ID: G-02506-20-A2

Specimen Collected: 04/07/2020

Specimen Received: 06/25/2020

Other Testing Initiated: 07/06/2020

Gross Description: 1 (A) Paraffin Block - Client ID(G-02506-20-A2) from Gulf Coast Medical Center, Fort Myers, FL, with the corresponding pathology report labeled "G-02506-20".

Pathologic Diagnosis: Right neck lymph node, needle core biopsies: Positive for malignancy, tissue involved by an invasive carcinoma composed of foamy/vacuolated-appearing cells.

Dissection Information: A laboratory technician harvested targeted tissues for extraction from the marked areas using a dissection microscope.

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Case Presentation – Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma

Dr Syed Zafar

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Cervical Adenocarcinoma	0 %

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Gosain: A 67-year-old man with metastatic clear cell RCC

Dr Rahul Gosain

- Sister with history of metastatic RCC and breast cancer
  - Germline mutation negative
- Presented with painless hematuria, bilateral renal masses and no distant metastases
- Underwent left-sided radical nephrectomy and right-sided partial nephrectomy
  - Pathology consistent with clear cell carcinoma
- Lost to follow-up → re-presented with metastatic disease (intermediate risk), psoriasis (controlled)
- NGS: MUTYH germline mutation | VHL somatic mutation
- **Treatment plan:** Pembrolizumab plus axitinib

Questions

- Would the faculty consider discontinuing pembrolizumab if his psoriasis was to get worse?
- What would be their second-line therapy if the patient experiences disease progression?
- What would be their recommendation for family screening in someone who has germline mutations such as MUTYH mutation?
- How do you dissect the differences between immunotherapy and TKI side effects, because there are times that they overlap?

RTP RESEARCH TO PRACTICE

FDA Approves Nivolumab with Cabozantinib for Advanced RCC

Press Release: January 22, 2021

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

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

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

RTP RESEARCH TO PRACTICE

Nivolumab plus cabozantinib versus sunitinib in first-line treatment for advanced renal cell carcinoma: first results from the randomized phase 3 CheckMate 9ER trial

Toni K. Choueiri,[1] Thomas Powles,[2] Mauricio Burotto,[3] Maria T. Bourlon,[4] Bogdan Zurawski,[5] Víctor Manuel Oyervides Juárez,[6] James J. Hsieh,[7] Umberto Basso,[8] Amishi Y. Shah,[9] Cristina Suarez,[10] Alketa Hamzaj,[11] Carlos Barrios,[12] Martin Richardet,[13] David Pook,[14] Yoshihiko Tomita,[15] Bernard Escudier,[16] Joshua Zhang,[17] Burcin Simsek,[17] Andrea B. Apolo,[18] Robert J. Motzer[19]

- [1]Dana-Farber Cancer Institute, The Lank Center for Genitourinary Oncology, Boston, MA, USA; [2]Barts Cancer Institute, Cancer Research UK Experimental Cancer Medicine Centre, Queen Mary University of London, Royal Free National Health Service Trust, London, UK; [3]Bradford Hill Clinical Research Center, Santiago, Chile; [4]Urologic Oncology Clinic, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; [5]Professor Franciszek Lukaszczyk Oncology Centre, Bydgoszcz, Poland; [6]Centro Universitario contra el Cáncer Hospital Universitario "Dr. José Eleuterio González" Universidad Autónoma de Nuevo León, Nuevo León, Mexico; [7]Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, USA; [8]Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; [9]MD Anderson Cancer Center, Houston, TX, USA; [10]Vall d'Hebron Institute of Oncology, Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [11]Ospedale San Donato, Istituto Toscano Tumori, Arezzo, Italy; [12]Oncology Research Center, Hospital São Lucas, PUCRS, Porto Alegre, Brazil; [13]Fundacion Richardet Longo, Instituto Oncologico de Cordoba, Cordoba, Argentina; [14]Cabrini Monash University Department of Medical Oncology, Cabrini Health, Malvern, VIC, Australia; [15]Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [16]Gustave Roussy, Villejuif, France; [17]Bristol-Myers Squibb Company, Princeton, NJ, USA; [18]Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA; [19]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Presentation Number 696O

Courtesy of Thomas Powles, MBBS, MRCP, MD

CheckMate 9ER: Study design

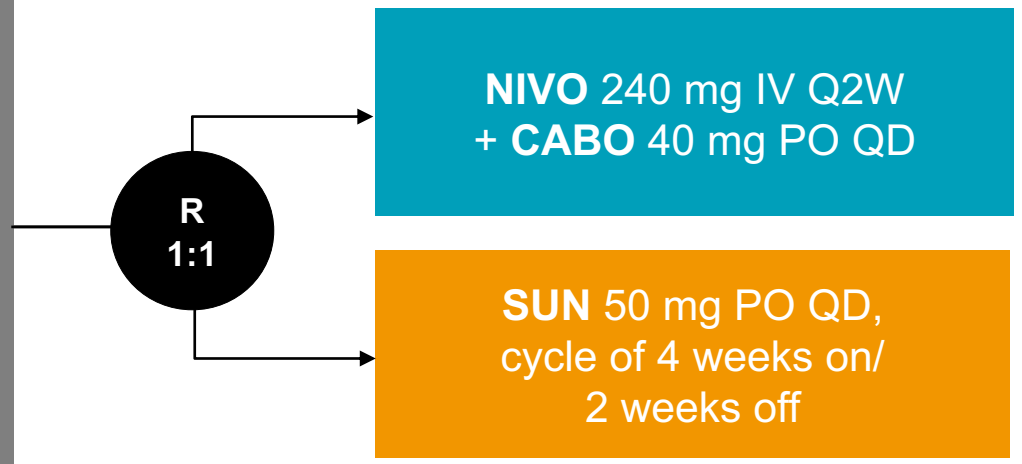
Stratification factors:

- IMDC risk score
- Tumor PD-L1 expression[a]
- Geographic region

N = 651

Key inclusion criteria[1,2]

- Previously untreated advanced or metastatic RCC with a clear cell component
- Any IMDC risk group
- No prior systemic therapy



Treat until RECIST v1.1–defined progression or unacceptable toxicity[b]

Median study follow-up, 18.1 months (range, 10.6–30.6 months)

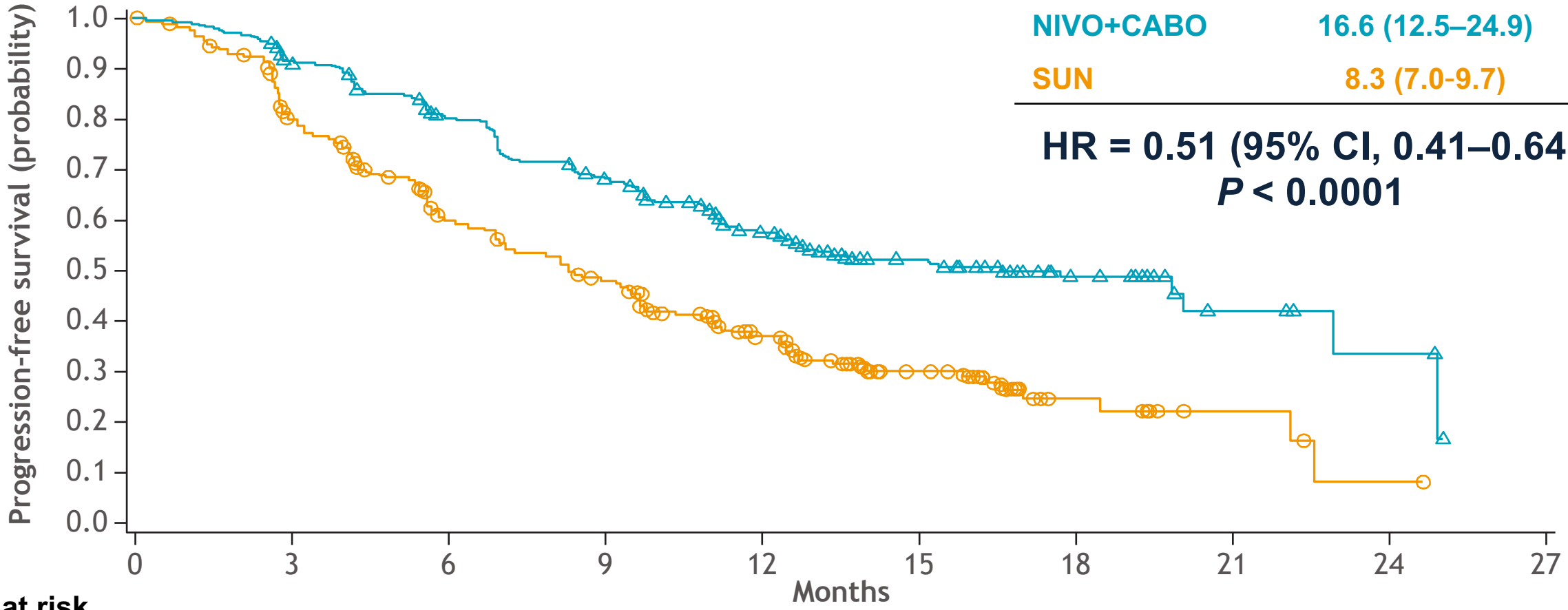
[a]Defined as the percent of positive tumor cell membrane staining in a minimum of 100 evaluable tumor cells per validated Dako PD-L1 immunohistochemistry assay.
[b]NIVO dosing may not exceed a total of 2 years (from cycle 1); CABO and SUN treatment may continue beyond 2 years in the absence of progression or unacceptable toxicity. Patients may be treated beyond progression.
IMDC, International Metastatic Renal Cell Carcinoma Database Consortium; IV, intravenously; PD-L1, programmed death ligand 1; PO, orally; Q2W, every 2 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors.
1. clinicaltrials.gov/ct2/show/NCT03141177. Accessed June 8, 2020; 2. Choueiri et al. Poster presented at the American Society of Clinical Oncology Annual Meeting 2018. TPS4598.

Courtesy of Thomas Powles, MBBS, MRCP, MD

CheckMate 9ER: Progression-free survival per BICR

Median PFS, months (95% CI)	
NIVO+CABO	16.6 (12.5–24.9)
SUN	8.3 (7.0-9.7)

HR = 0.51 (95% CI, 0.41–0.64)
***P* < 0.0001**



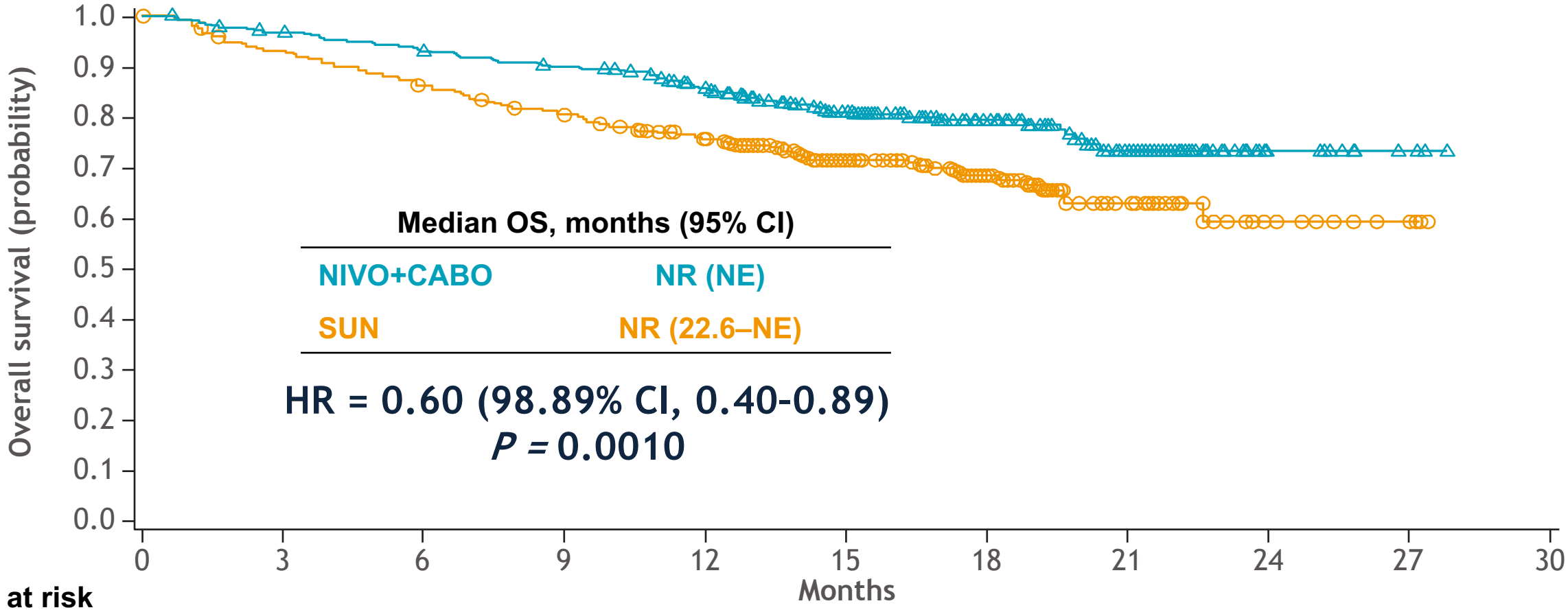
No. at risk

NIVO+CABO	323	279	234	196	144	77	35	11	4	0
SUN	328	228	159	122	79	31	10	4	1	0

Minimum study follow-up, 10.6 months.

Courtesy of Thomas Powles, MBBS, MRCP, MD

CheckMate 9ER: Overall survival



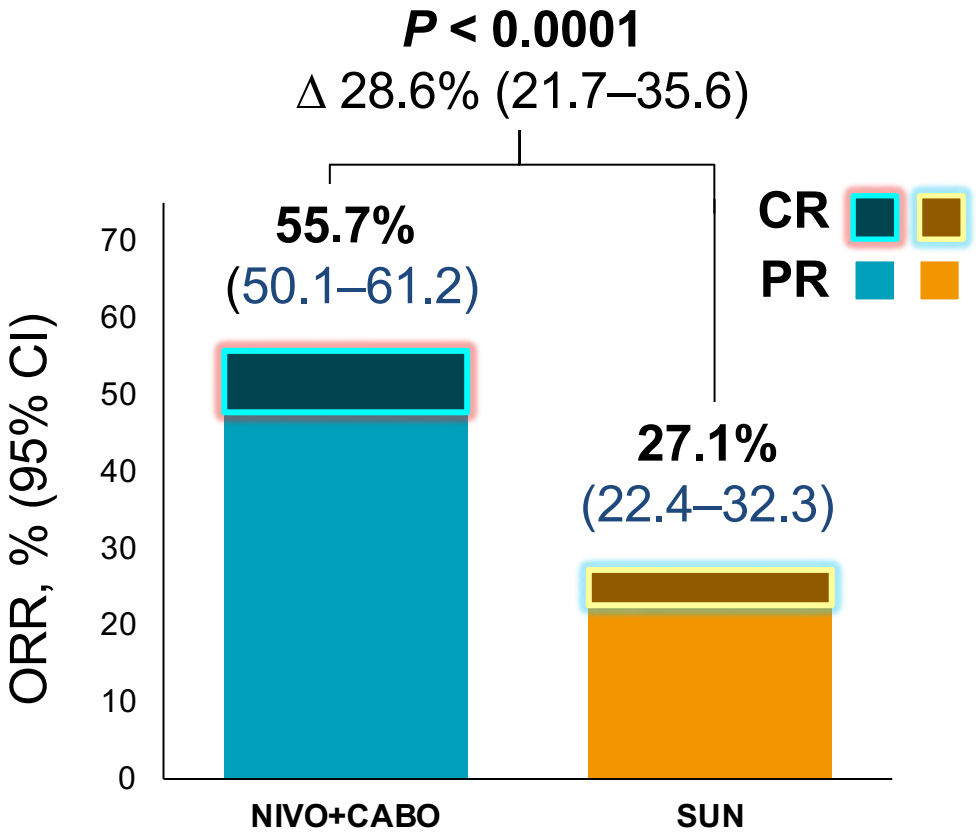
No. at risk

NIVO+CABO	323	308	295	283	259	184	106	55	11	3	0
SUN	328	296	273	253	223	154	83	36	10	3	0

Minimum study follow-up, 10.6 months.
NE, not estimable; NR, not reached.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Objective response and best overall response per BICR



Outcome, %	NIVO+CABO (N = 323)	SUN (N = 328)
Complete response	8.0	4.6
Partial response	47.7	22.6
Stable disease	32.2	42.1
Progressive disease	5.6	13.7
Not evaluable/not assessed[a]	6.5	17.1
Median time to response (range), months[b]	2.8 (1.0–19.4)	4.2 (1.7–12.3)
Median duration of response (95% CI), months[b]	20.2 (17.3–NE)	11.5 (8.3–18.4)

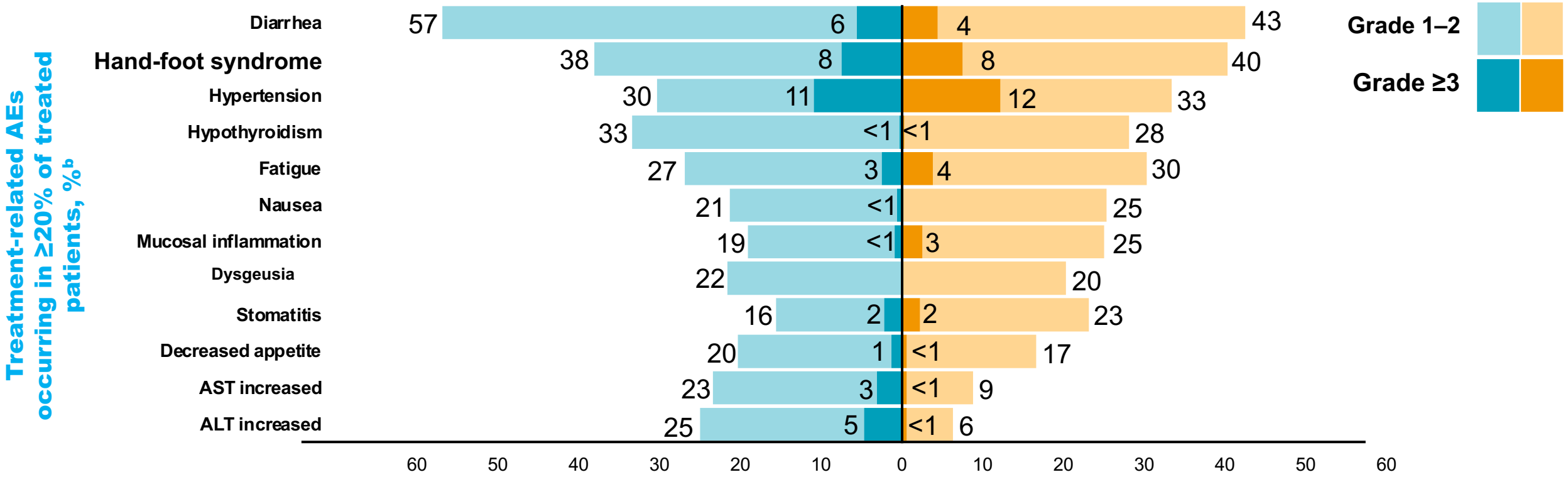
- ORR favored NIVO+CABO over SUN across subgroups including by IMDC risk status, tumor PD-L1 expression (≥ 1% vs < 1%), and bone metastases

BICR-assessed ORR and BOR by RECIST v1.1.
[a]Includes patients who were never treated, those who discontinued/died before disease assessment, those without measurable disease at baseline per BICR, or other reason not reported/specified; [b]Median time to and duration of response were calculated for patients who had a complete or partial response (n = 180 with NIVO+CABO, n = 89 patients with SUN).

Courtesy of Thomas Powles, MBBS, MRCP, MD

CheckMate 9ER: Safety Summary

Events, %[a]	NIVO+CABO, N = 320		SUN, N = 320	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
All-cause AEs	100	75	99	71
Treatment-related AEs	97	61	93	51



[a]Includes events that occurred on therapy or within 30 days after the end of the treatment period of all treated patients. Treatment-related deaths per investigator: NIVO+CABO n = 1 (small intestine perforation), SUN n = 2 (pneumonia, respiratory distress); [b]Total bar represents treatment-related AEs of any grade ≥ 20% in either treatment arm; of these events, none were grade 5.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Phase 3 trial of lenvatinib plus pembrolizumab or everolimus versus sunitinib monotherapy as a first-line treatment for patients with advanced renal cell carcinoma (CLEAR study)

Robert Motzer[1], Camillo Porta[2], Masatoshi Eto[3], Thomas Powles[4], Viktor Grünwald[5], Thomas E. Hutson[6], Boris Alekseev[7], Sun Young Rha[8], Evgeny Kopyltsov[9], María José Méndez-Vidal[10], Sung-Hoo Hong[11], Anil Kapoor[12], Teresa Alonso Gordoa[13], Jeffrey C. Goh[14], Jaime R. Merchan[15], Alan D. Smith[16], Kalgi Mody[17], Rodolfo F. Perini[18], Dongyuan Xing[17], and Toni K. Choueiri[19]

[1]Memorial Sloan Kettering Cancer Center; New York, NY, USA; [2]San Matteo University Hospital Foundation, Pavia, Italy; [3]Kyushu University, Fukuoka, Japan; [4]The Royal Free NHS Trust, London, England, UK; [5]University Hospital Essen, Essen, Germany; [6]Texas Oncology, Dallas, TX, USA; [7]P.A. Hertsen Moscow Cancer Research Institute, Moscow, Russia; [8]Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea; [9]State Institution of Healthcare "Regional Clinical Oncology Dispensary", Omsk, Russia; [10]Maimonides Institute for Biomedical research of Cordoba (IMIBIC) Hospital Universitario Reina Sofía, Medical Oncology Department, Córdoba, Spain; [11]Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, South Korea; [12]McMaster University Hamilton, Ontario, Canada; [13]Hospital Universitario Ramón y Cajal, Madrid, Spain; [14]ICON Research, South Brisbane & University of Queensland, St Lucia, Queensland, Australia; [15]University of Miami Sylvester Comprehensive Cancer Center, Miami, FL, USA; [16]Eisai Ltd., Hatfield, UK; [17]Eisai Inc., Woodcliff Lake, NJ, USA; [18]Merck & Co., Inc., Kenilworth, NJ, USA; [19]Dana-Farber Cancer Institute, Boston, MA, USA.

PRESENTED AT: Genitourinary Cancers Symposium

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Abstract #269

#GU21

Genitourinary Cancers Symposium 2021;Abstract 269.

RTP RESEARCH TO PRACTICE

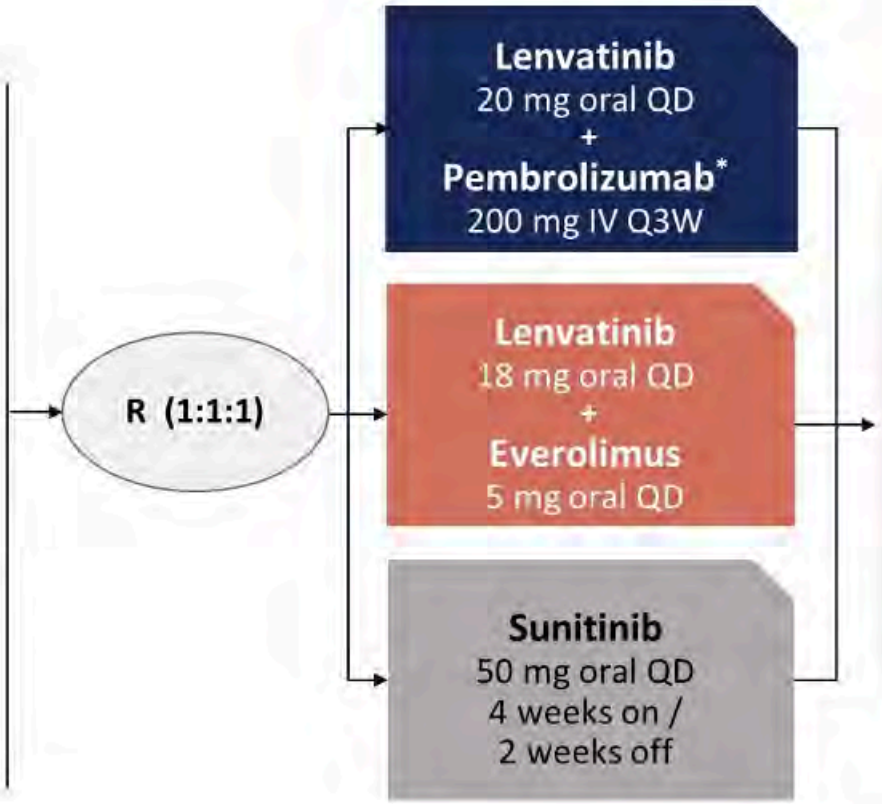
CLEAR: Phase III Trial Design

Key eligibility criteria

- Advanced clear-cell RCC
- Treatment-naïve
- Karnofsky performance status ≥70
- Measurable disease
- Adequate organ function

Stratification factors

- **Geographic region:** Western Europe and North America vs Rest of the World
- **MSKCC risk category:** Favorable, Intermediate, or Poor



Primary endpoint

- PFS by IRC per RECIST v1.1

Secondary endpoints

- OS
- ORR by IRC per RECIST v1.1
- Safety
- HRQoL

Key exploratory endpoints

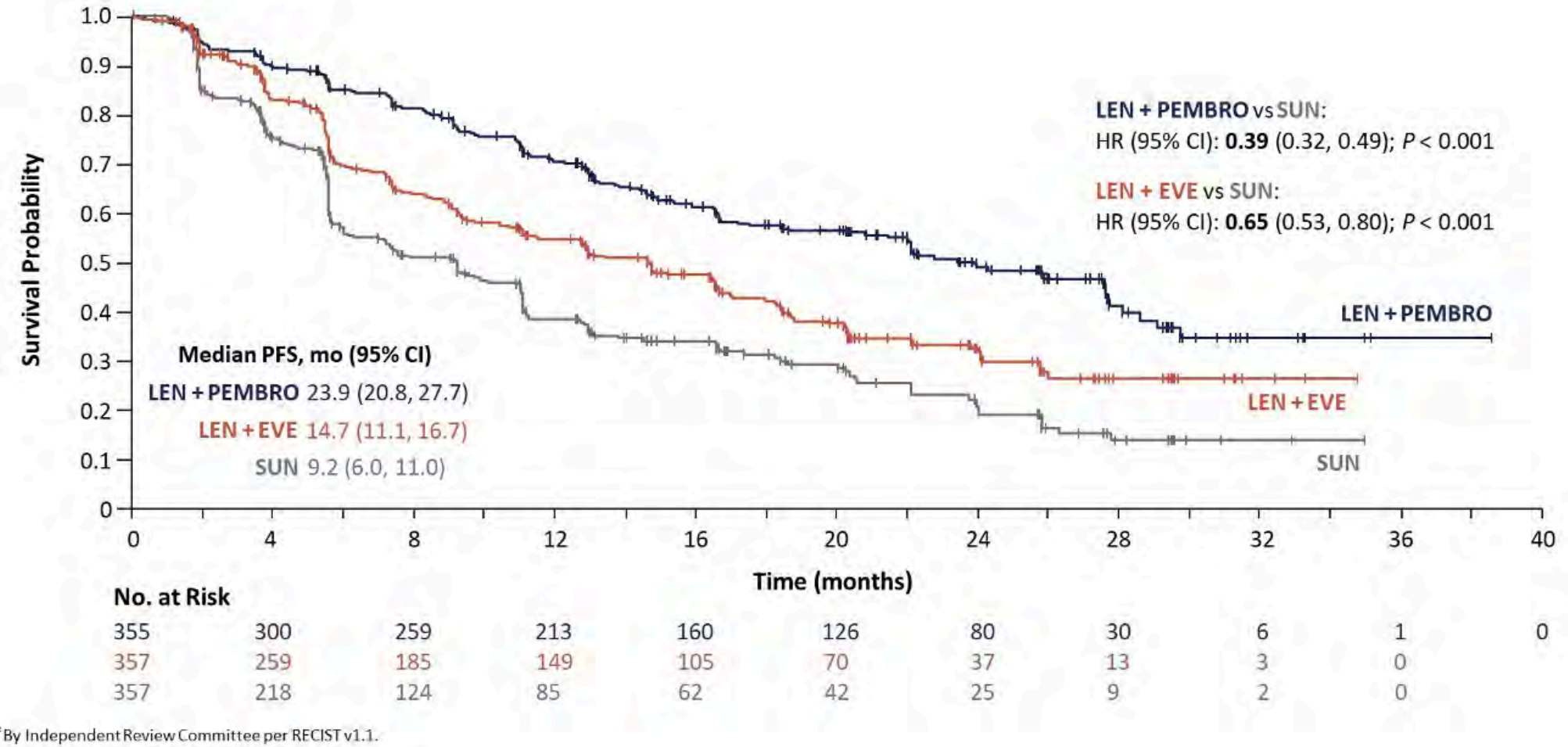
- DOR
- Biomarkers

*Patients could receive a maximum of 35 pembrolizumab treatments.
DOR, duration of response; HRQoL, Health-related quality of life; IRC, Independent Review Committee; MKSCC, Memorial Sloan Kettering Cancer Center; ORR, objective response rate; OS, overall survival; R, randomization.

Motzer R et al. Genitourinary Cancers Symposium 2021;Abstract 269.

RTP RESEARCH TO PRACTICE

CLEAR: Progression-Free Survival



*By Independent Review Committee per RECIST v1.1.

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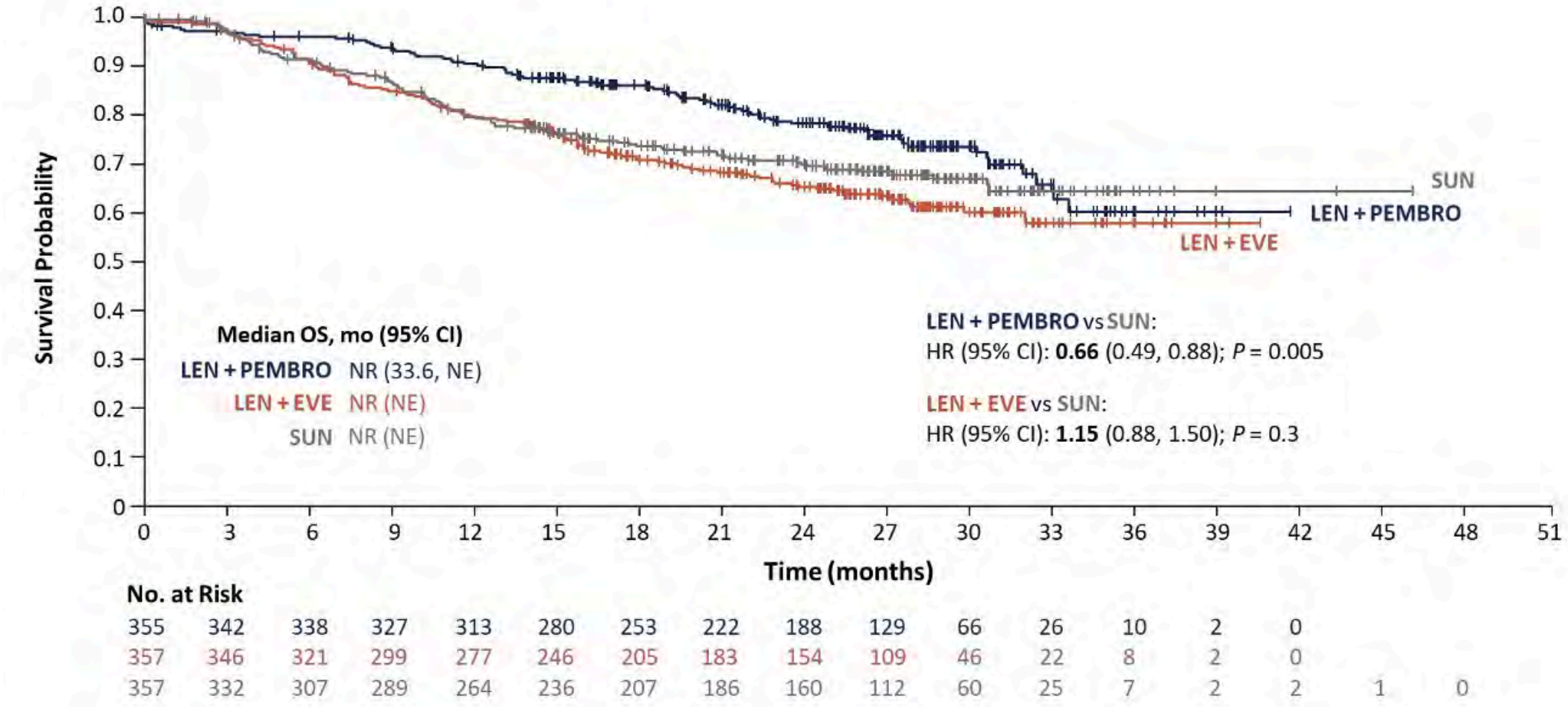
CLEAR: Overall Survival



NE, not estimable; NR, not reached.

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RTP RESEARCH TO PRACTICE

CLEAR: Response and Survival Analyses

	LEN + PEMBRO (n = 355)	LEN + EVE (n = 357)	SUNITINIB (n = 357)
Median PFS	24 mo	15 mo	9 mo
PFS HR vs SUN *p*-value	0.39 $p < 0.0001$	0.65 $p < 0.0001$	—
Median OS	NR	NR	NR
OS HR vs SUN *p*-value	0.66 $p = 0.0049$	1.15 $p = 0.2975$	—
24-month OS rate	79%	66%	70%
ORR	71%	54%	36%
ORR odds ratio vs SUN Descriptive *p*-value	4.35 $p < 0.0001$	2.15 $p < 0.0001$	—
Complete response	16%	10%	4%
Median DoR	26 mo	17 mo	15 mo

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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)
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Landmark OS 12 mo Landmark OS 24 mo	**83%** vs. 78% **71%** vs. 61%			
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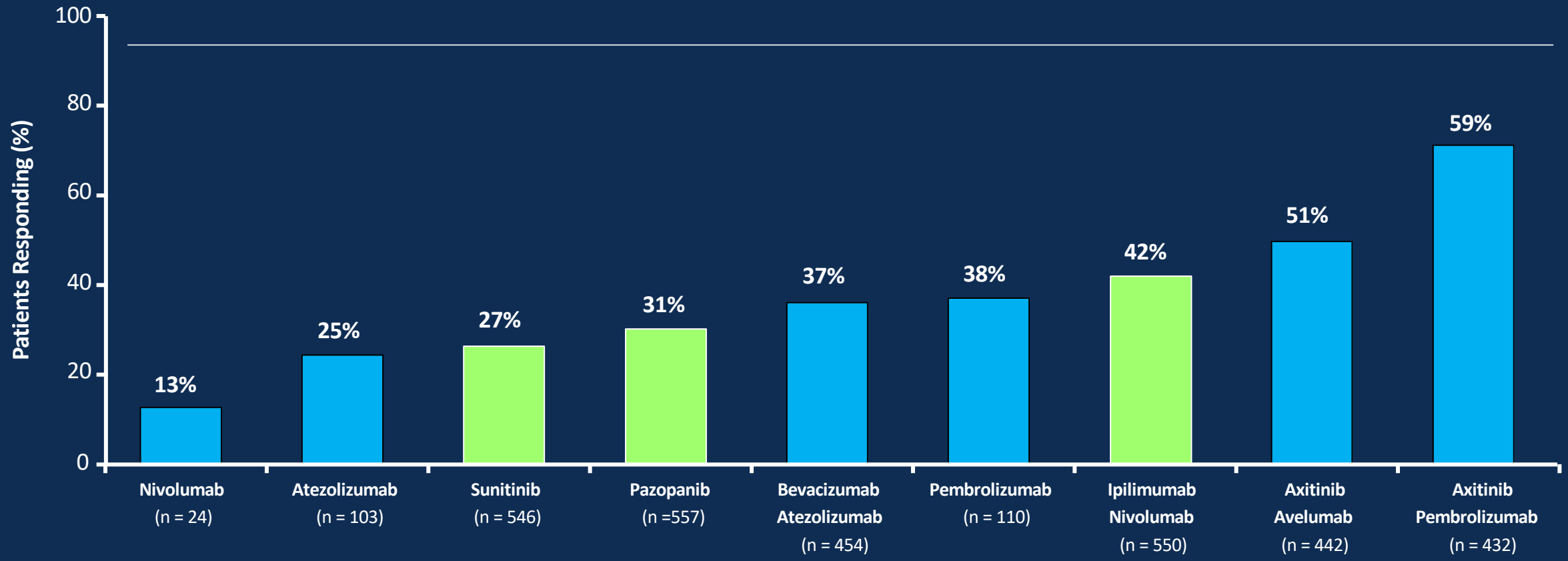
ORR, %	**39** vs 32			
CR, %	**11** vs 3			
Med f/u, months	**55**			
Prognostic risk, % Favorable Intermediate Poor	 23 61 17			
Prior nephrectomy	82%			
Subsequent systemic therapies for sunitinib arm, %	Overall (69%) IO (42%)			

Please handle with care….

Courtesy of Thomas Powles, MBBS, MRCP, MD

Response Rates in Frontline Metastatic ccRCC (ITT; All Risk Groups)



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Courtesy of Thomas E Hutson, DO, PharmD

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 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

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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

RTP RESEARCH TO PRACTICE

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

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Axitinib
5. Other

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Case Presentation – Dr Yap: A 60-year-old man presenting with weight loss and RCC metastatic to the lungs

Dr Kelly Yap

- Presented with significant weight loss, flank pain
- Diagnosed with Stage IV RCC with thoracic metastases
- Underwent cytoreductive nephrectomy
- Following surgery, decision was made for systemic therapy prior to metastasectomy
- Patient was treated with ipilimumab/nivolumab

Questions

- Is there still a role for cytoreductive nephrectomy in this era of immunotherapy and antiangiogenic TKIs?
- How do you choose between first-line ipilimumab and nivolumab versus axitinib with pembrolizumab in poor-risk disease? How about the combination of cabozantinib and nivolumab?
- How would you approach a case if the patient has an absolute contraindication to immune checkpoint inhibitors?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Zafar: An 85-year-old man with metastatic RCC

Dr Syed Zafar

- 2001: History of left nephrectomy
- History of remote adrenal insufficiency post abdominal surgery
  - Physiologic doses of steroids for 20+ years
- 2019: New onset pulmonary effusion
  - Pleural fluid thoracentesis reveals malignant cells
  - Further staging scans reveal pulmonary nodules, fulminant abdominal adenopathy, pleural based lung metastases
- Consistent with clear cell carcinoma
- Patient is quite symptomatic

Questions

- What would the faculty consider as a first-line treatment at this point in time, given the fact he's been on steroids?
- I would not consider ipi/nivo for this patient. So, the question would be a single agent versus a combination IO/axitinib?

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Front-line treatment of advanced renal cell carcinoma (RCC)

- Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma
- Dr Gosain: A 67-year-old man with metastatic RCC
- Dr Yap: A 60-year-old man with Stage IV clear cell RCC
- Dr Zafar: An 85-year-old man with metastatic RCC

Module 2: Sequencing of therapies for relapsed/refractory RCC

- Dr Plimack: A 24-year-old woman with translocation clear cell RCC

Module 3: Novel approaches for advanced RCC

Module 4: Sarcomatoid RCC

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Phase 2 trial of lenvatinib plus pembrolizumab for disease progression after PD-1/PD-L1 immune checkpoint inhibitor (ICI) in metastatic clear cell renal cell carcinoma

Chung-Han Lee[1], Amishi Y. Shah[2], James J. Hsieh[3], Arpit Rao[4], Alvaro Pinto[5], Mehmet Asim Bilen[6], Allen Lee Cohn[7], Christopher Di Simone[8], David R. Shaffer[9], Regina Girones Sarrio[10], Sara Gunnestad Ribe[11], Jane Wu[12], Emmett V. Schmidt[13], Rodolfo Perini[13], Peter Kubiak[12], Alan D. Smith[14], Robert J. Motzer[1]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]MD Anderson Cancer Center, University of Texas, Houston, TX, USA; [3]Washington University School of Medicine, St. Louis, MO, USA; [4]Masonic Cancer Center, University of Minnesota, Minneapolis, MN, USA; [5]Hospital Universitario La Paz, Madrid, Spain; [6]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [7]Rocky Mountain Cancer Center, Denver, CO, USA; [8]Arizona Oncology Associates, Tucson, AZ, USA; [9]New York Oncology Hematology, Albany, NY, USA; [10]Medical Oncology Service, Hospital Universitari i Politècnic La FE, Valencia, Spain; [11]Sorlandet Hospital Kristiansand, Kristiansand, Norway; [12]Eisai Inc., Woodcliff Lake, NJ, USA; [13]Merck & Co. Inc., Kenilworth, NJ, USA; [14]Eisai Ltd., Hatfield, UK.

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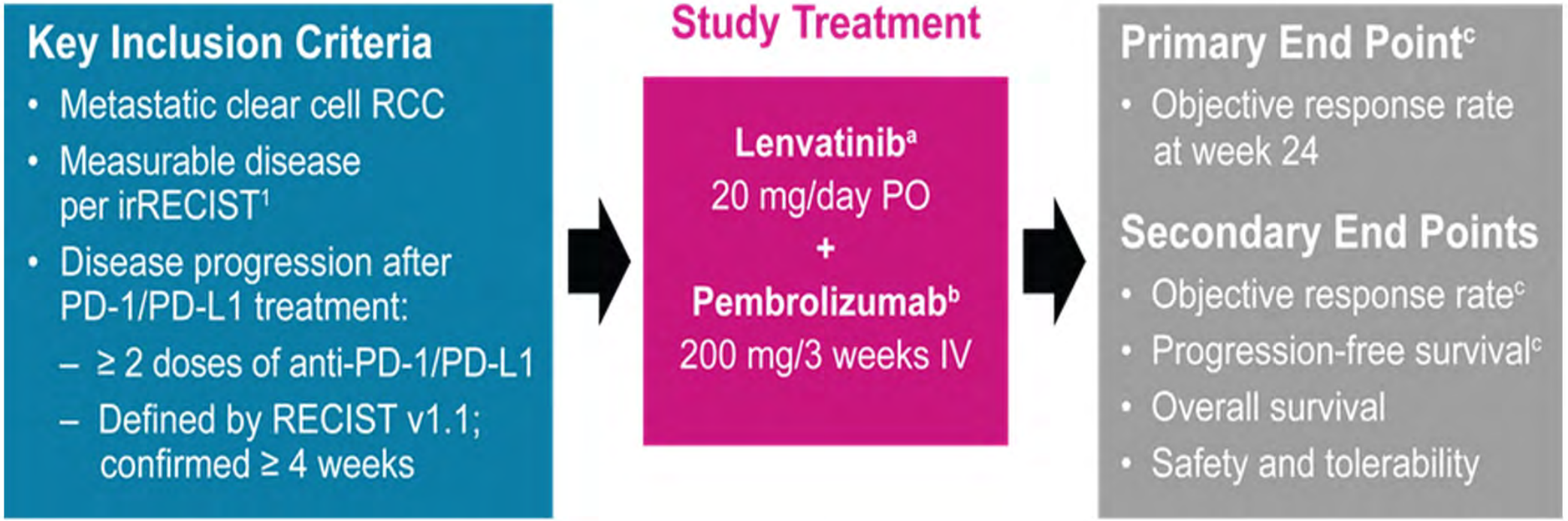
PRESENTED BY: Dr Chung-Han Lee

Presented By Chung-Han Lee

Courtesy of Thomas E Hutson, DO, PharmD

Study Design for the Phase 2 RCC Cohort



[a] Dose reductions to lenvatinib 14 mg/day, 10 mg/day, 8 mg/day and 4 mg/day were allowed to manage toxicities; dose reductions below 4 mg/day were discussed with the sponsor; [b] maximum of 35 treatments (approximately 2 years); [c] per irRECIST, by investigator assessment.

1. Perrone A. Immuno-Oncology 360° conference. New York, NY. 2016.

IV, intravenously; PO, by mouth; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1.

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Presented By Chung-Han Lee

Courtesy of Thomas E Hutson, DO, PharmD

Tumor Response by Investigator Assessment

Parameter	irRECIST N = 104	RECIST v1.1[a] N = 104
ORR at week 24, % (95% CI)	51 (41–61)	–
ORR, % (95% CI)	55 (45–65)	52 (42–62)
Best objective response, %		
Partial response	55	52
Stable disease	36	38
Progressive disease	5	6
Not evaluable	5	5
Median DOR, months (95% CI)	12 (9–18)	12 (9–18)

[a] Up to 10 target lesions could be selected (up to 5 per organ).

DOR, duration of response.

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Courtesy of Thomas E Hutson, DO, PharmD

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(27):3088-94.

Retrospective Analysis: Salvage Ipilimumab with Nivolumab for mRCC After Prior ICI Targeting PD-1

- Patients with mRCC included in the study (n = 45)
- All patients received prior ICI targeting the PD-1 pathway
- The median age was 62 years (range, 21-82 years)
- Median follow-up on Ipi/Nivo: 12 months
- Objective response rate: 20%
- Median PFS: 4 months (range, 0.8-19 months)
- irAEs with Ipi/Nivo:
  - Any Grade, 29 (64%)
  - Grade 3, 6 (13%)
- **Conclusion:** Ipi/Nivo demonstrated antitumor activity with acceptable toxicity in patients with mRCC who had received prior ICI therapy

Gul A et al. *J Clin Oncol* 2020;38(27):3088-94.

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

Brian I. Rini, Sumanta K. Pal, Bernard Escudier, Michael B. Atkins, Thomas E. Hutson, Camillo Porta, Elena Verzoni, Michael N. Needle, David F. McDermott

Vanderbilt-Ingram Cancer Center, Nashville, TN; Department of Medical Oncology & Therapeutics, City of Hope Comprehensive Cancer Center, Duarte, CA; Gustave Roussy, Villejuif, France; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; Texas A&M College of Medicine, Bryan, TX; University of Bari 'A. Moro', Bari, Italy; Department of Medical Oncology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Aveo Oncology, Boston, MA; Beth Israel Deaconess Medical Center, Dana-Farber/Harvard Cancer Center, Boston, MA

PRESENTED AT: Genitourinary Cancers Symposium

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PRESENTED BY: Brian I. Rini, MD, FASCO

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Genitourinary Cancers Symposium 2021;Abstract 278.

RTP RESEARCH TO PRACTICE

TIVO-3: Pivotal Trial in RCC

TIVO-3

Phase 3, Randomized, Controlled, Multi-Center, Open-Label Study to Compare Tivozanib to Sorafenib in Subjects With R/R RCC

Tivozanib is an orally bioavailable inhibitor of VEGFR-1/2/3.

N = 350

- Histologically / cytologically confirmed recurrent/metastatic RCC
- ECOG PS 0 or 1
- Failed at least two prior regimens including VEGFR-TKI
- Stratified by IMDC and prior regimen (TKI-TKI; TKI-CPI; TKI-Other)

Randomize 1:1

Tivozanib

Sorafenib

Treatment Until Progression*

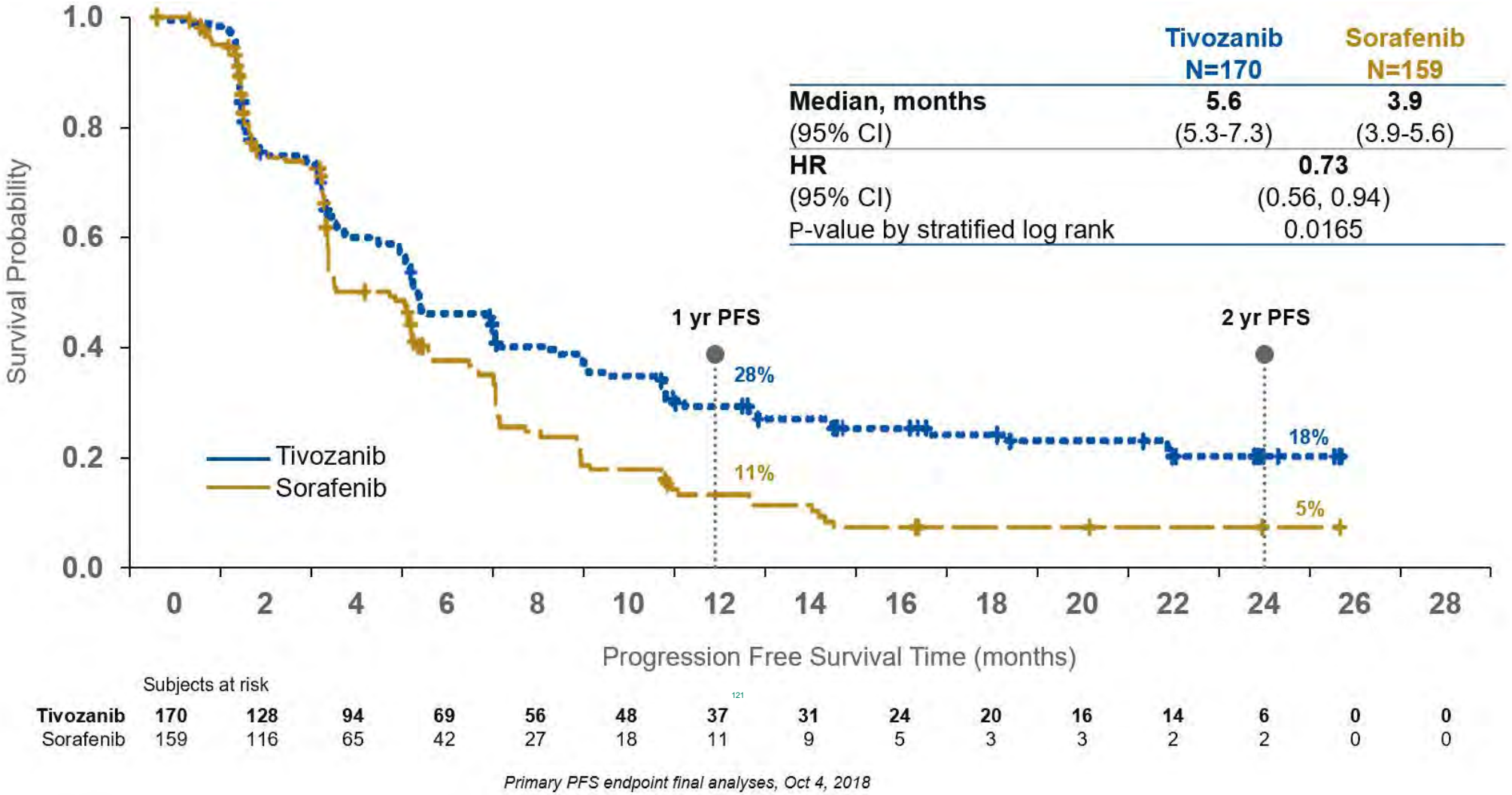
Endpoints

- Primary: PFS
- Secondary: OS, ORR, DoR, Safety and Tolerability

Results published in Lancet Oncology in December 2019

Courtesy of Thomas E Hutson, DO, PharmD

TIVO-3: Met Primary Endpoint of Superior PFS in aRCC Patients treated with 2 or 3 prior regimens



	Tivozanib N=170	Sorafenib N=159
Median, months	**5.6**	**3.9**
(95% CI)	(5.3-7.3)	(3.9-5.6)
HR	**0.73**	
(95% CI)	(0.56, 0.94)	
P-value by stratified log rank	0.0165	

Primary PFS endpoint final analyses, Oct 4, 2018

Courtesy of Thomas E Hutson, DO, PharmD

Tivozanib after Axitinib in the TIVO-3 Study

Clinical Outcome	No. of pts (n)	PFS HR	95% CI	Tivo ORR	Sora ORR
ITT	350	0.73	0.56, 0.94	18%	8%
Any prior axitinib	172	0.66	0.46, 0.93	13%	8%

Courtesy of Thomas E Hutson, DO, PharmD

Have you administered or would you administer nivolumab/ ipilimumab to a patient with metastatic RCC who had received a prior checkpoint inhibitor either alone or in combination with an anti-angiogenic agent?

1. I have
2. I have not but would for the right patient
3. I have not and would not

RTP RESEARCH TO PRACTICE

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

1. Sunitinib
2. Pazopanib
3. Cabozantinib
4. Sorafenib
5. Nivolumab/ipilimumab
6. Nivolumab/cabozantinib
7. Lenvatinib + everolimus
8. Other

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Case Presentation – Dr Plimack: A 24-year-old woman with translocation clear cell RCC – Part 1

Dr Elizabeth Plimack

- 2011: Right partial nephrectomy. T1aN0M0
- 2012: Local recurrence
- 2012 – 2014: Observation of slow growing metastatic disease x 2 years
- 2014: Ipilimumab + nivolumab on study → colitis
  - Resolved with steroid, taper is complete
  - Imaging revealed resolution of lung metastases but slight progression of abdominal metastases

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Case Presentation – Dr Plimack: A 24-year-old woman with translocation clear cell RCC – Part 2

Dr Elizabeth Plimack

- 2011: Right partial nephrectomy. T1aN0M0
- 2012: Local recurrence
- 2012 – 2014: Observation of slow growing metastatic disease x 2 years
- 2014: Ipilimumab + nivolumab on study → colitis
  - Resolved with steroid, taper is complete
  - Imaging revealed resolution of lung metastases but slight progression of abdominal metastases
- Re-challenged with single-agent nivolumab
  - Adrenal insufficiency, hypothyroidism, treated with replacement therapy
- Severe infusion reactions, mitigated with premeds
- Observed for a number of years without treatment
- Cabozantinib active with dose mitigation

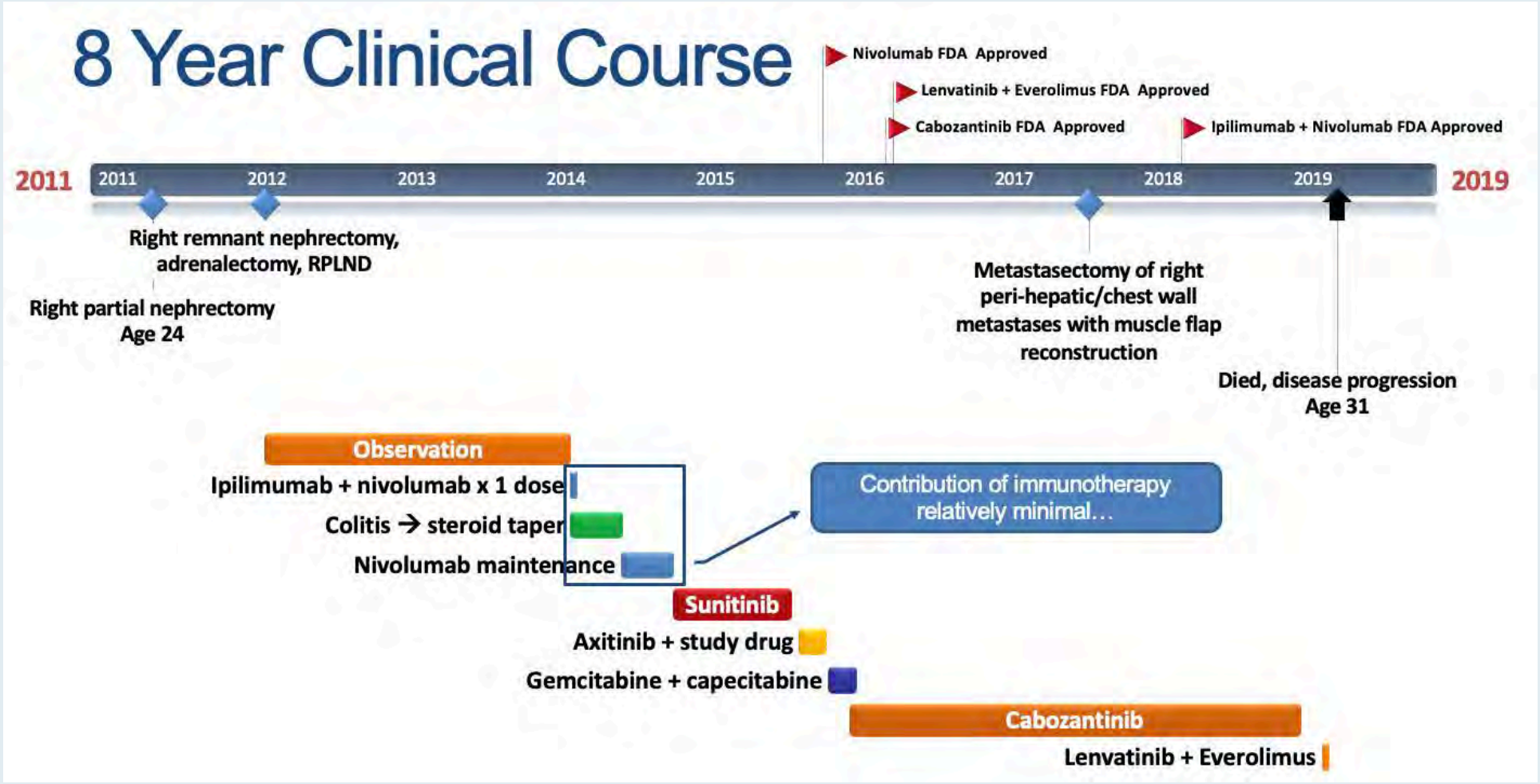
Question

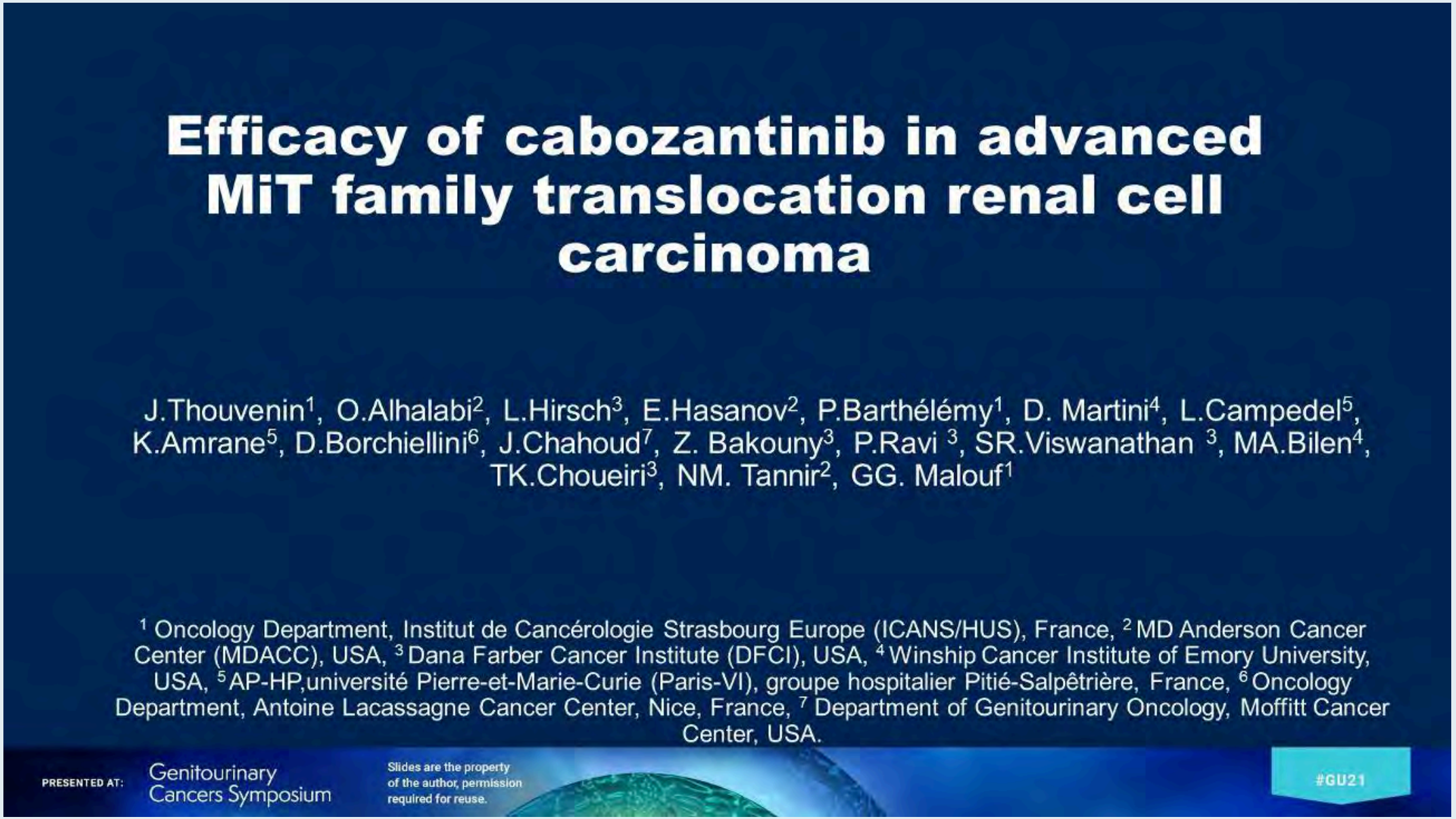
- How would the faculty treat a patient such as this today?

RTP RESEARCH TO PRACTICE

Case Presentation – Dr Plimack: A 24-year-old woman with translocation clear cell RCC

Dr Elizabeth Plimack





Genitourinary Cancers Symposium 2021;Abstract 274.

RTP RESEARCH TO PRACTICE

Retrospective Analysis of Cabozantinib for Advanced RCC with MiT Family Translocation: ORR and Safety

Outcome	Rate %, N = 24
Objective response rate, %	**4 (16.7%)**
Best overall response, %	
Complete response	1 (4.2%)
Partial response	3 (12.5%)
Stable disease	11 (45.8%)
Progressive disease	9 (37.5%)

	N = 24
Treatment-related grade 3-4 adverses events, %	9 (37.5%)
Treatment-related adverses events leading to discontinuation, %	5 (20.8%)
Treatment-related deaths, n	0

Thouvenin J et al. Genitourinary Cancers Symposium 2021;Abstract 274.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Front-line treatment of advanced renal cell carcinoma (RCC)

- Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma
- Dr Gosain: A 67-year-old man with metastatic RCC
- Dr Yap: A 60-year-old man with Stage IV clear cell RCC
- Dr Zafar: An 85-year-old man with metastatic RCC

Module 2: Sequencing of therapies for relapsed/refractory RCC

- Dr Plimack: A 24-year-old woman with translocation clear cell RCC

Module 3: Novel approaches for advanced RCC

Module 4: Sarcomatoid RCC

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

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

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

Genitourinary Cancers Symposium 2021;Abstract 273.

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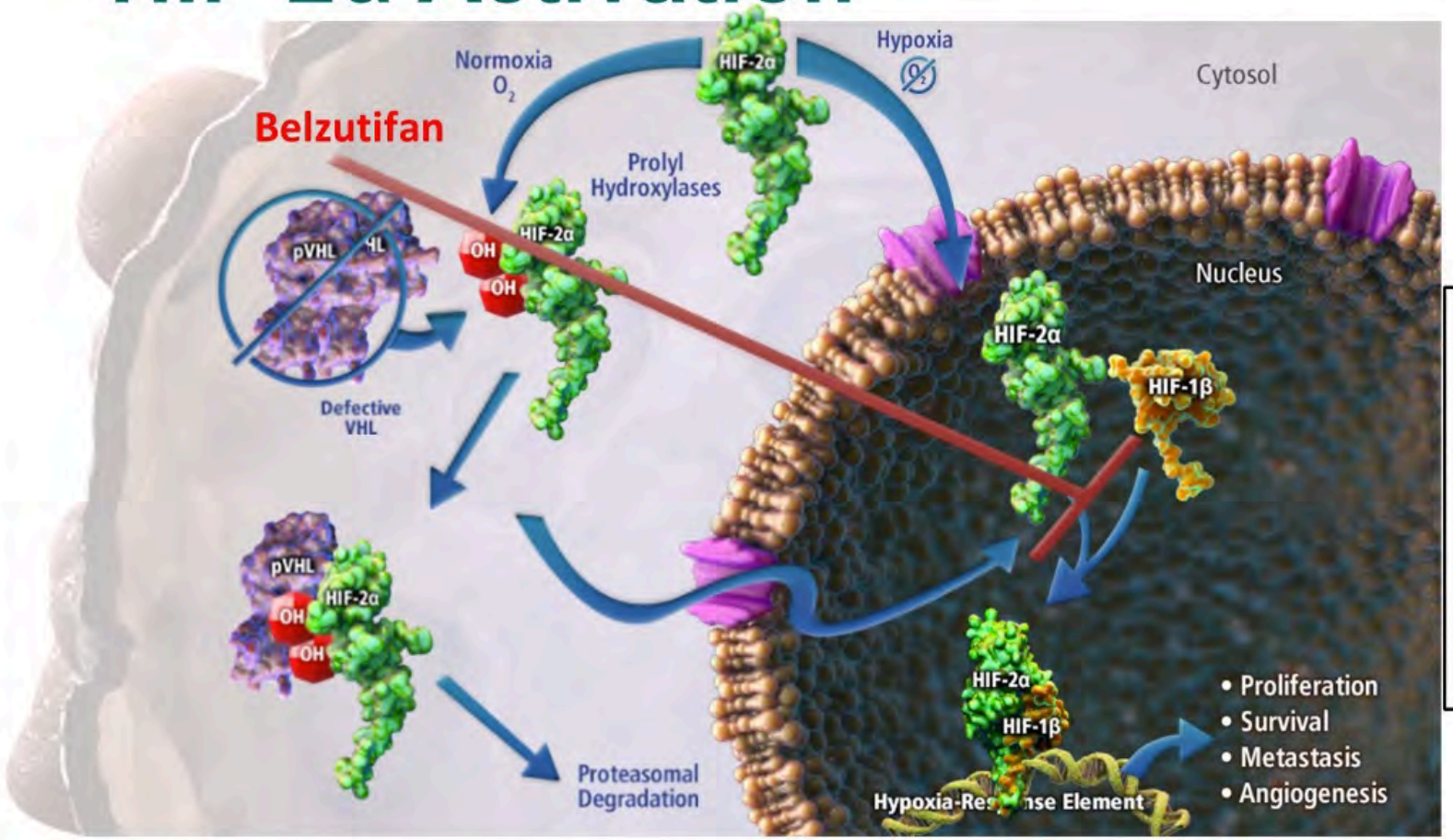
pVHL Deficiency Results in HIF-2α Activation



- 90% of patients with sporadic ccRCC have defective pVHL function[1]
- Loss of pVHL function results in constitutive activation of HIF-2α[2]
- Belzutifan is a potent, selective, small molecule HIF-2α inhibitor

1. Linehan WM, Rickets CJ. *Nat Rev Urol*. 2019;16:539-552. 2. Couvé S et al. *Cancer Res*. 2014;74:6554-6564.

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

RTP RESEARCH TO PRACTICE

Best Confirmed Objective Response by RECIST v1.1 per Investigator Assessment (dose-escalation cohorts)

Efficacy Parameter, n (%) [95%CI]	20 mg QD N = 6	40 mg QD N = 6	80 mg QD N = 6	120 mg QD N = 6	160 mg QD N = 6	240 mg QD N = 7	120 mg BID N = 6
Objective Response Rate	0	0	0	1 (17) [0.4-64]	2 (33) [4-78]	2 (29) [4-71]	1 (17) [0.4-64]
Complete Response (CR)	0	0	0	0	0	0	0
Partial Response (PR)	0	0	0	1 (17)[a]	2 (33)[b]	2 (29)[a]	1 (17)[a]
Stable Disease (SD)	2 (33)	2 (33)	2 (33)	3 (50)	3 (50)	1 (14)	2 (33)
Disease Control Rate (CR + PR + SD)	2 (33) [4-78]	2 (33) [4-78]	2 (33) [4-78]	4 (67) [22-96]	5 (83) [36-100]	3 (43) [10-82]	3 (50) [12-88]
Progressive Disease	3 (50)	2 (33)	3 (50)	2 (33)	1 (17)	2 (29)	3 (50)
Not Evaluable	1 (17)	2 (33)	1 (17)	0	0	2 (29)	0

[a]All responses in ccRCC; [b]Responses observed in ccRCC (n = 1) and anaplastic ependymoma (n=1). Data cutoff: June 1, 2020.

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

RTP RESEARCH TO PRACTICE

Summary of Adverse Events (ccRCC cohort)

n (%)	N = 55
Any grade AE	55 (100)
Grade 3-5 AE	39 (71)
Any grade treatment-related AEs	53 (96)
Grade 3-5 treatment-related AE	22 (40)
Discontinuation of treatment due to an AE[a]	5 (9)
Discontinuation of treatment due to a treatment-related AE[b]	2 (4)
Deaths due to an AE[c]	4 (7)
Death due to a treatment-related AE	0 (0)

- Fifty-three patients (96%) had a treatment-related AE
  - Twenty-two patients (40%) had a grade 3 treatment-related AE
  - There were no grade 4/5 treatment-related AEs
  - Two patients (4%) discontinued due to a treatment-related AE (both hypoxia)[b]

[a]5 patients experienced 7 adverse events (hypoxia [n = 2], abdominal pain [n = 1], cardiac arrest [n = 1], decreased appetite [n = 1], disease progression [n = 1], and fatigue [n = 1]). [b]One patient discontinued treatment due to grade 2 hypoxia and one patient discontinued due to grade 3 hypoxia. [c]Deaths were due to disease progression (n = 1), malignant neoplasm progression (n = 1), acute kidney injury (n = 1), and cardiac arrest (n = 1). Data cutoff: June 1, 2020.

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

RTP RESEARCH TO PRACTICE

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

Toni K. Choueiri[1]; Todd M. Bauer[2]; David F. McDermott[3]; Edward Arrowsmith[4]; Ananya Roy[5]; Rodolfo Perini[5]; Donna Vickery[5]; Scott S. Tykodi[6]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [3]Beth Israel Deaconess Medical Center, Boston, MA, USA; [4]Tennessee Oncology, Chattanooga, TN, USA; [5]Merck & Co., Inc., Kenilworth, NJ, USA; [6]University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Genitourinary Cancers Symposium 2021;Abstract 272.

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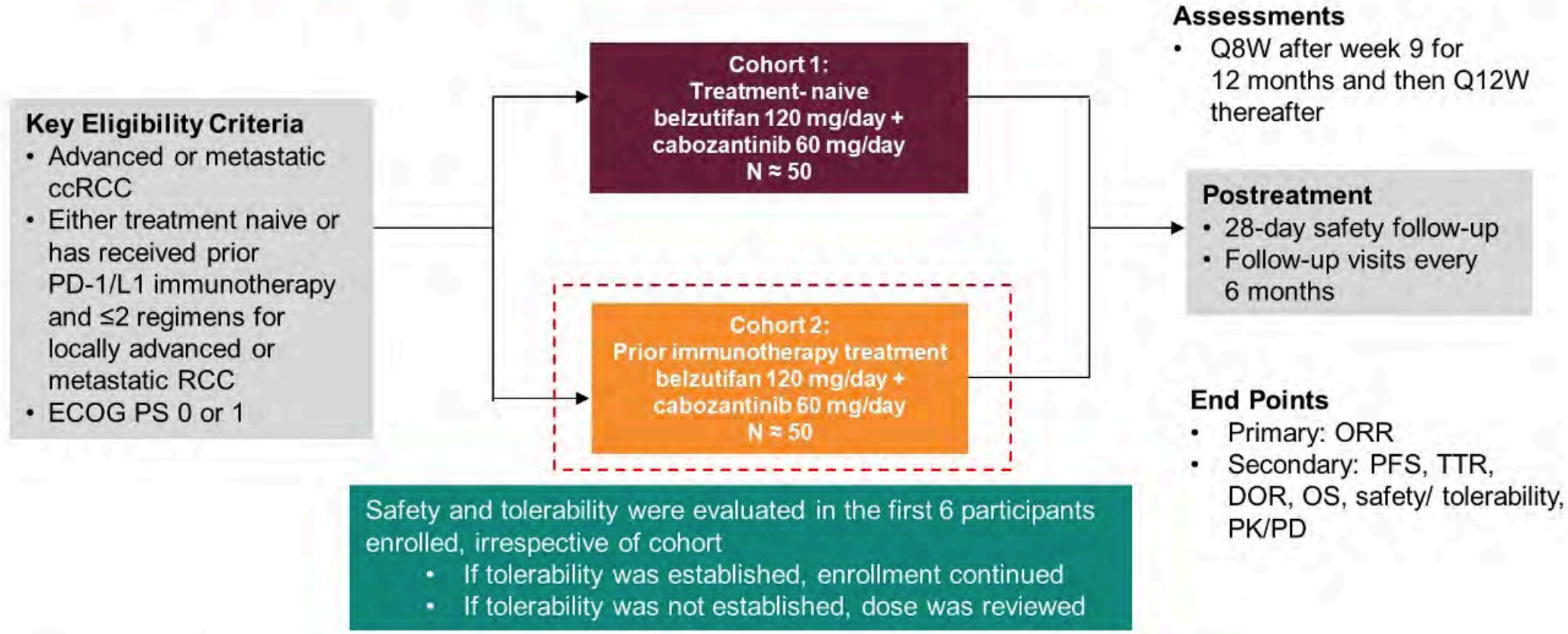
Study Design (NCT03634540)



Data cutoff: October 15, 2020.

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

Best Confirmed Objective Response: Efficacy Analysis Set

Efficacy Parameter, n (%) [95%CI]	Efficacy Analysis Set N = 41
Objective response rate (CR + PR)	9 (22) [11-38]
Disease control rate (CR + PR + SD)	37 (90) [77-97]
Best response	
Complete response	0 (0)
Partial response	9 (22)
Stable disease	28 (68)
Unconfirmed partial response[a]	5 (12)
Progressive disease	3 (7)
Not available	1 (2)

[a]Documented at one time point and to be confirmed at a subsequent time point.
Data cutoff: October 15, 2020.

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

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Best Tumor Change From Baseline: Efficacy Analysis Set

- 36 of 41 patients (88%) experienced a reduction in target lesion size[a]

[a]One patient had a response of "not available" and was recorded as having no change from baseline value. [b]Documented at one time point and to be confirmed at a subsequent time point. Data cutoff: October 15, 2020.

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

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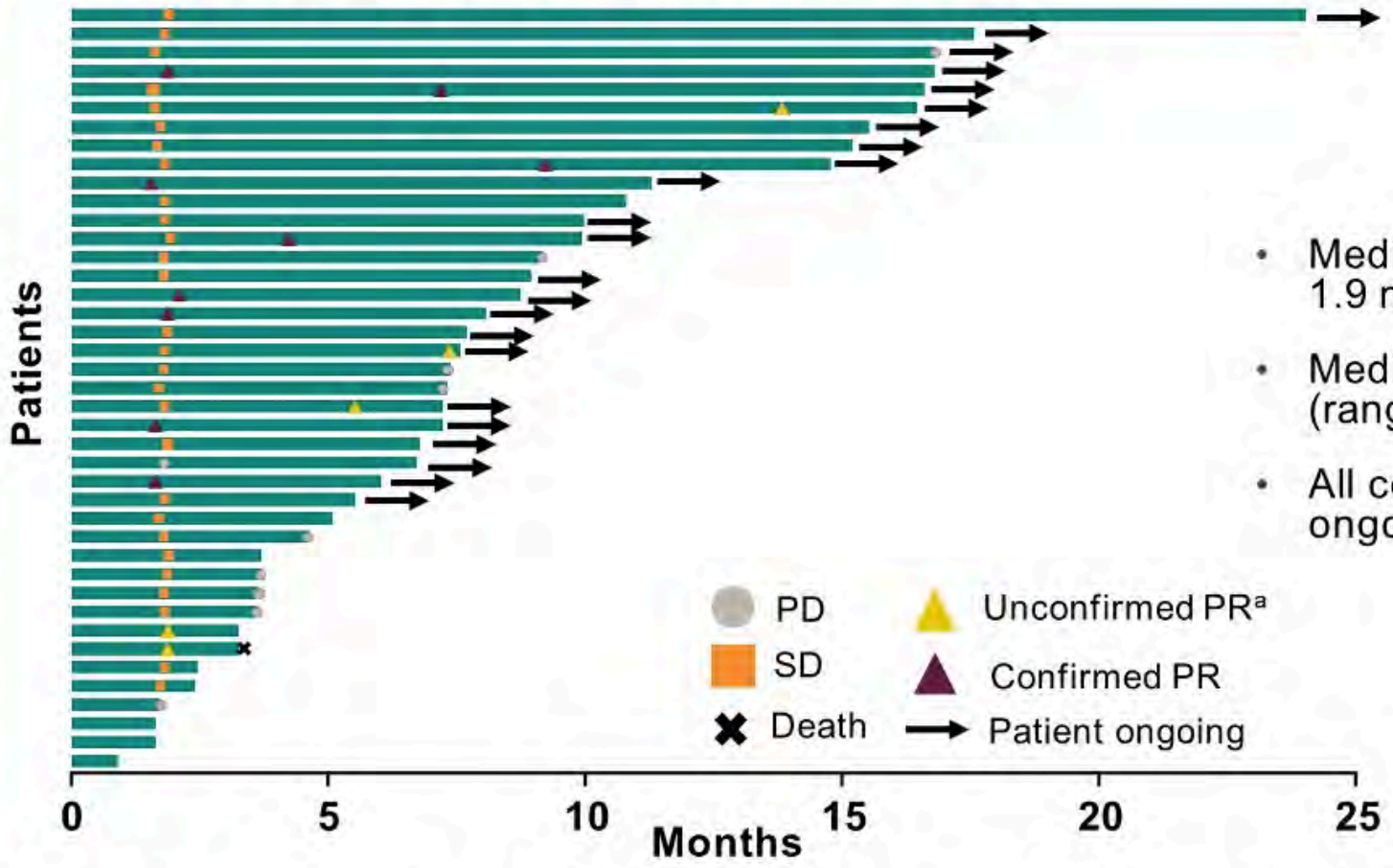
Time to Response and Response Duration: Efficacy Analysis Set



- Median time to response was 1.9 months (range, 1.5-9.2)
- Median DOR was not reached (range, 3.7+ to 14.8+ months)
- All confirmed responses were ongoing as of the data cutoff date

[a]Documented at one time point and to be confirmed at a subsequent time point. "+" indicates ongoing response. Data cutoff: October 15, 2020.

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

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Summary of Adverse Events: Safety Analysis Set[a]

n (%)	N = 52
Any grade treatment-emergent AE	52 (100)
Any grade treatment-related AE	51 (98)
Related to belzutifan	51 (98)
Related to cabozantinib	51 (98)
Grade 3-5 treatment-emergent AEs	35 (67)
Grade 3[b] treatment-related AEs	31 (60)
Related to belzutifan	17 (33)
Related to cabozantinib	28 (54)
Serious treatment-emergent AEs	16 (31)
Serious treatment-related AEs	7 (13)
Related to belzutifan	4 (8)
Related to cabozantinib	4 (8)

n (%)	N = 52
Deaths due to a treatment-emergent AE	1 (2)[c]
Deaths due to a treatment-related AE	0 (0)
Belzutifan dose reduced[d]	10 (19)
Cabozantinib dose reduced[e]	25 (48)
Discontinued any drug due to a treatment-emergent AE	8 (15)
Discontinued belzutifan[f]	6 (12)
Discontinued cabozantinib[g]	8 (15)

[a]All patients who received ≥1 dose of treatment. [b]There were no grade 4 or 5 treatment-related AEs. [c]Death due to disease progression. [d]Ten patients had 14 AEs (fatigue [n=5], ALT increased [n=2], decreased appetite [n=2], anemia [n=1], diarrhea [n=1], headache [n=1], hypoxia [n=1], oral pain [n=1]). [e]Twenty-five patients had 37 AEs (fatigue [n=7], hand-foot syndrome [n=7], ALT increased [n=2], decreased appetite [n=2], nausea [n=2], platelet count decreased [n=2], stomatitis [n=2], acute kidney injury [n=1], ageusia [n=1], anemia [n=1], *Clostridium difficile* colitis [n=1], diarrhea [n=1], dysgeusia [n=1], headache [n=1], oral pain [n=1], muscle spasms [n=1], muscular weakness [n=1], noncardiac chest pain [n=1], urinary retention [n=1], vomiting [n=1]). [f]Six patients had 6 AEs (fatigue [n =2], ALT increased [n=1], anemia [n=1], disease progression [n=1], mental status changes [n=1]). [g]Eight patients had 9 AEs [ALT increased [n=3], fatigue [n=2], disease progression [n=1], exertional dyspnea [n=1], mental status changes [n=1], and myocardial infarction [n=1]). Data cutoff: October 15, 2020.

Choueiri TK et al. Genitourinary Cancers Symposium 2021;Abstract 272.

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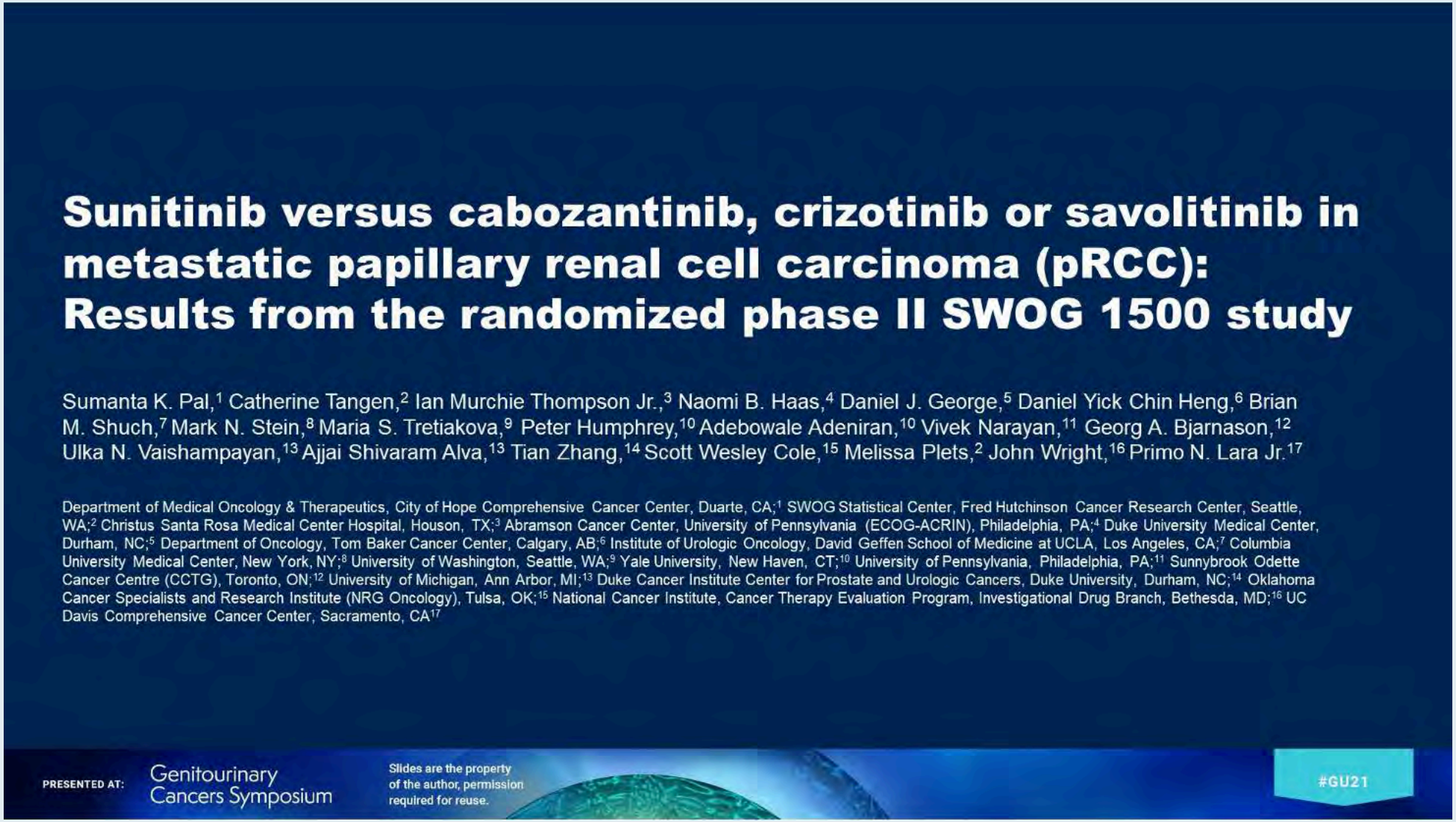
FDA Grants Breakthrough Therapy Designation, Orphan Drug Designation to MK-6482

Press Release: July 29, 2020

- The US Food and Drug Administration (FDA) has granted breakthrough therapy designation to the hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor MK-6482, a novel investigational candidate in the oncology pipeline, for the treatment of patients with von Hippel-Lindau (VHL) disease-associated renal cell carcinoma (RCC) with nonmetastatic RCC tumors less than 3 centimeters in size, unless immediate surgery is required.
- The FDA also granted orphan drug designation to MK-6482 for VHL disease.
- These designations are based on data from a Phase 2 trial evaluating MK-6482 in patients with VHL-associated clear cell RCC.

https://www.cancernetwork.com/view/fda-grants-breakthrough-therapy-designation-orphan-drug-designation-to-mk-6482



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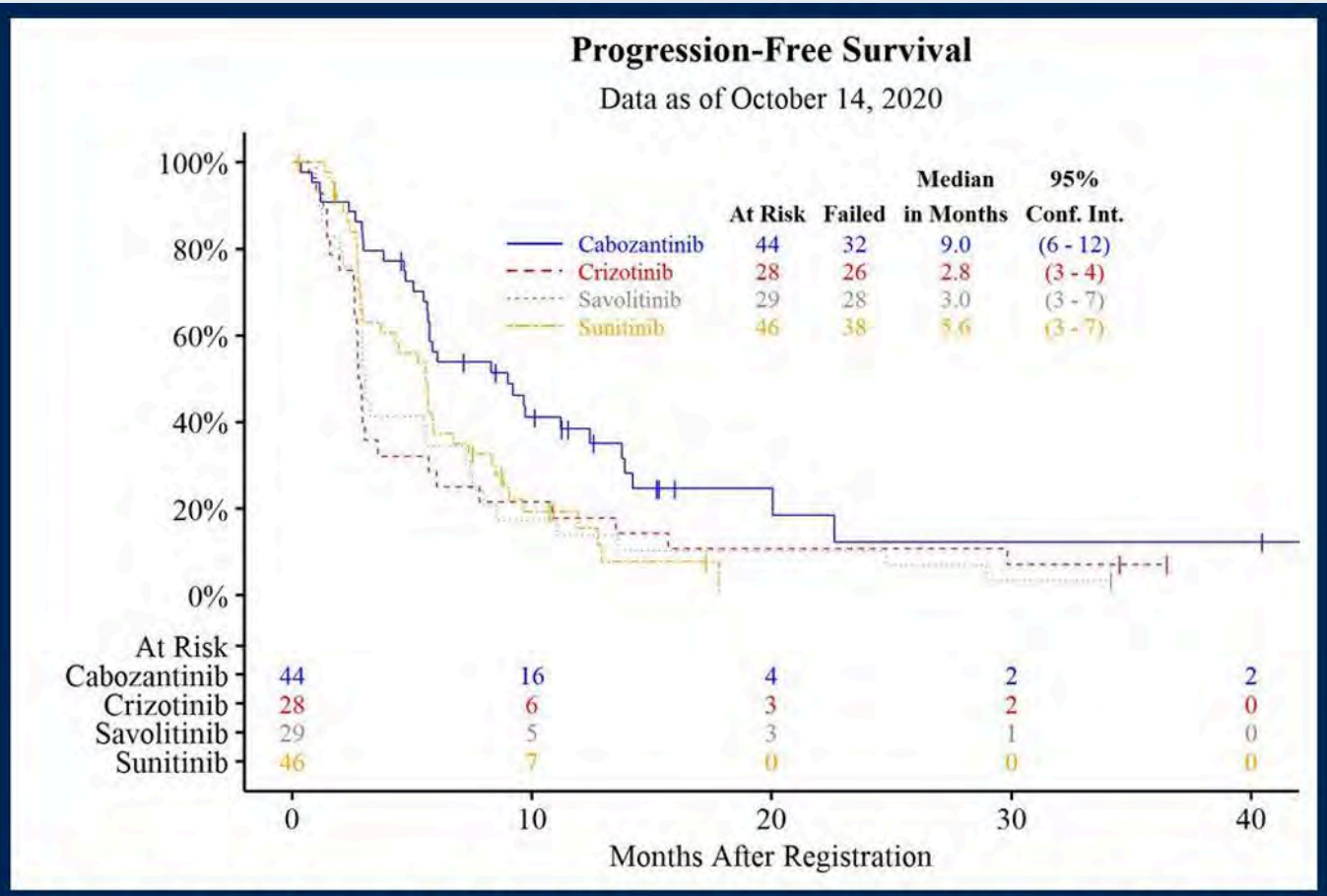
SWOG-1500: Progression-Free Survival



- Cabozantinib significantly prolonged PFS relative to sunitinib: HR 0.60 (95% CI 0.37-0.97 [1-sided *p*-value = 0.019])

Pal SK et al. Genitourinary Cancers Symposium 2021;Abstract 270.

RTP RESEARCH TO PRACTICE

Agenda

Module 1: Front-line treatment of advanced renal cell carcinoma (RCC)

- Dr Zafar: A 53-year-old man with RCC initially treated as head and neck carcinoma
- Dr Gosain: A 67-year-old man with metastatic RCC
- Dr Yap: A 60-year-old man with Stage IV clear cell RCC
- Dr Zafar: An 85-year-old man with metastatic RCC

Module 2: Sequencing of therapies for relapsed/refractory RCC

- Dr Plimack: A 24-year-old woman with translocation clear cell RCC

Module 3: Novel approaches for advanced RCC

Module 4: Sarcomatoid RCC

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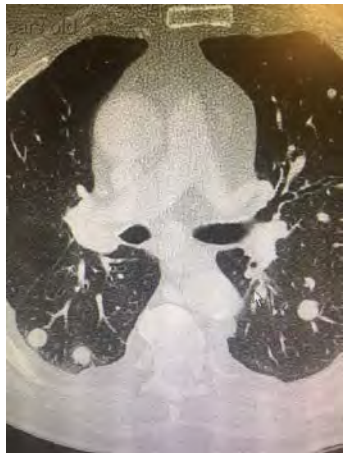
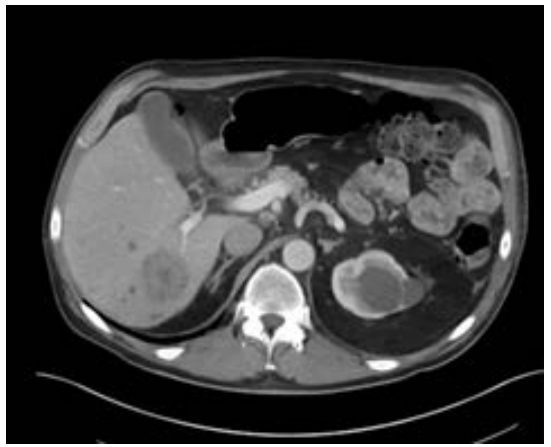
Case Presentation – Prof Powles: A 69-year-old man with advanced RCC

Patient characteristics	69 year old male Performance status 1 Past medical history of heavy smoking and airways disease.
Tumor characteristics	Liver and lung mets. Renal Mass Biopsy from lung mets: mainly sarcomatoid features suspected renal origin view of imaging. IMDC: poor risk disease.





Cabozantinib and nivolumab.

Courtesy of Thomas Powles, MBBS, MRCP, MD

Data on sarcomatoid RCC with cabozantinib/nivolumab from ASCO GU 2021

	With sRCC		Without sRCC	
	NIVO+CABO n = 34	SUN n = 41	NIVO+CABO n = 279	SUN n = 278
PFS HR (95% CI)	0.39 (0.22–0.70)		0.54 (0.43–0.69)	
Median PFS, months	10.9	4.2	17.7	9.4
OS HR (95% CI)	0.36 (0.16–0.82)		0.68 (0.48–0.95)	
Median OS, months	NR	19.7	NR	NR
ORR, % (95% CI)	55.9 (37.9–72.8)	22.0 (10.6–37.6)	56.6 (50.6–62.5)	28.4 (23.2–34.1)

The other combinations have good data in sarcomatoid RCC too.

ASCO GU FEB 21 - abstract 308 - NCT03141177

Courtesy of Thomas Powles, MBBS, MRCP, MD

Case Presentation – Prof Powles: A 69-year-old man with advanced RCC (cont)

Patient characteristics	69 year old male Performance status 1 Past medical history of heavy smoking and airways disease.
Tumor characteristics	Liver and lung mets. Renal Mass Biopsy from lung mets: mainly sarcomatoid features suspected renal origin view of imaging.

Week 4: Due C2 D1 (4 weekly nivolumab)
G2 Palmar Plantar Erythema
G1 diarrhea
G2 fatigue

Courtesy of Thomas Powles, MBBS, MRCP, MD

Case Presentation – Prof Powles: A 69-year-old man with advanced RCC (cont)

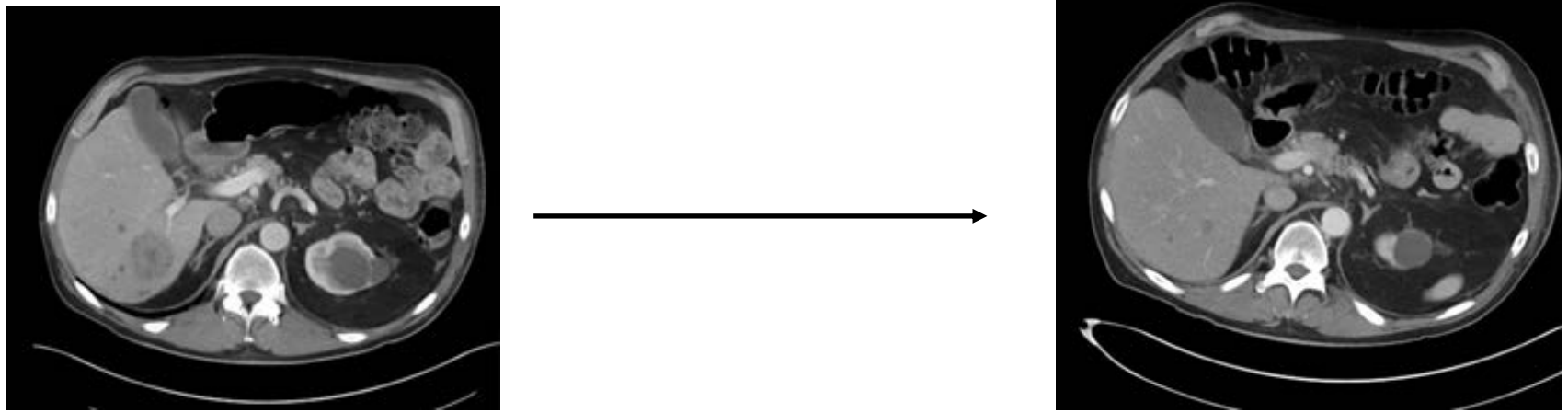
Patient characteristics	69 year old male Performance status 1 Past medical history of heavy smoking and airways disease.
Tumor characteristics	Liver and lung mets. Renal Mass Biopsy from lung mets: mainly sarcomatoid features suspected renal origin view of imaging.

Week 8: Due C3 D1:Improved adverse events.
G2 Palmar Plantar Erythema
G1 diarrhea
G2 fatigue
Dose reduce to 20mg

Courtesy of Thomas Powles, MBBS, MRCP, MD

Case Presentation – Prof Powles: A 69-year-old man with advanced RCC (cont)

Patient characteristics	69 year old male Performance status 1 Past medical history of heavy smoking and airways disease.
Tumor characteristics	Liver and lung mets. Renal Mass Biopsy from lung mets: mainly sarcomatoid features suspected renal origin view of imaging.



Courtesy of Thomas Powles, MBBS, MRCP, MD

Case Presentation – Prof Powles: A 69-year-old man with advanced RCC (cont)

Patient characteristics	69 year old male Performance status 1 Past medical history of heavy smoking and airways disease.
Tumor characteristics	Liver and lung mets. Renal Mass Biopsy from lung mets: mainly sarcomatoid features suspected renal origin view of imaging.

Is there ever a time to remove the kidney?

What is the best treatment option at progression?

Courtesy of Thomas Powles, MBBS, MRCP, MD

Meet The Professor
Management of Ovarian Cancer

Tuesday, March 2, 2021
5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.