

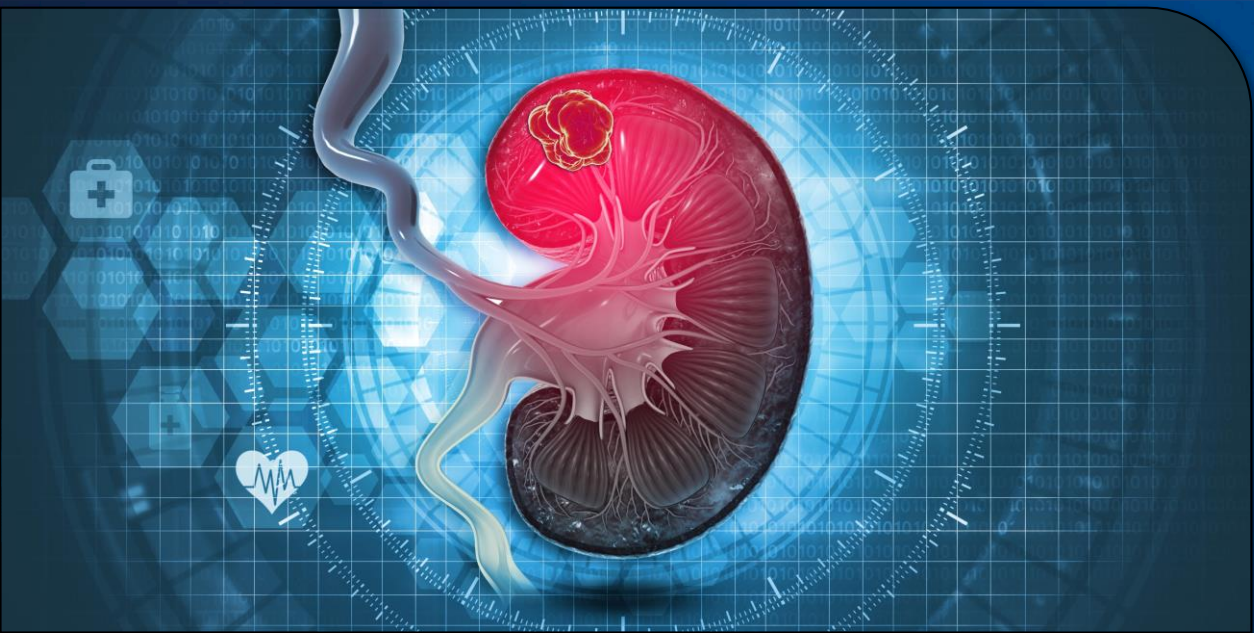
Unlocking the Potential of Modern RCC Therapies

*Expert Approaches to Tailoring Care
and Optimizing Outcomes*

PeerView
Live



KidneyCancerAssociation
Unstoppable Together.



*Not an official event of the 2026
ASCO® Genitourinary Cancers
Symposium. Not sponsored,
endorsed, or accredited by
ASCO®, Association for Clinical
Oncology, or Conquer Cancer®,
the ASCO Foundation.*

- Tonight's panelists: Sumanta Kumar Pal, MD, FASCO; Pedro C. Barata, MD, MSc, FACP; and Cristina Suárez, MD, PhD
- Thank you to PeerView and Kidney Cancer Association for providing this session and AVEO, Eisai, Exelixis, and Merck for providing the educational grants for this symposium
- If you haven't already, please complete the pre-event survey
- Reminder: Look out for additional polling during the presentation
- Submit your questions, and we will answer them during the Q&A session
 - **In-room learners**, use your personal device to scan the QR code on the following slides to respond to polls and ask the faculty questions
 - **Virtual learners**, please respond to polls on your screen and enter questions in the chat window

Goals for Today

During this session, we will learn that...

- Clinical evidence supports the use of numerous approved and investigational therapies for the management of RCC
- Individualized treatment plans that incorporate novel strategies can maximize patient outcomes
- Team-based approaches that include proactive management of TRAEs and patient education support effective treatment

Kidney Cancer Association (KCA): Our Patient Advocacy Partner

Download the
Practice Aid!



KidneyCancerAssociation

Unstoppable Together.

For more than 30 years, the KCA has stood for **excellence in research and education** as well as the thoughtful, **patient-driven services** they extend to the patients and care partners who have placed their trust in them

The KCA is committed to being a **global community** dedicated to **supporting and empowering** patients and care partners and leading change through **education, research, and advocacy**



SUPPORT AND EMPOWER

The KCA is dedicated to patients and care partners, providing information, guidance, and supportive resources to all communities.



EDUCATE

As the first and largest kidney cancer advocacy group, the KCA is the only organization to promote scientific advances and education globally.



RESEARCH

The KCA's annual grant program funds innovative investigators pursuing high-impact research with the potential to improve kidney cancer treatment and care.

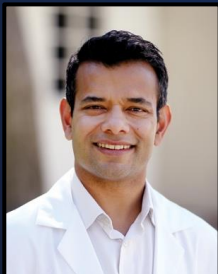


ADVOCATE

The KCA is active in legislative advocacy efforts, specifically by encouraging individuals to contact their congressional leaders through our letter-writing campaigns to advocate for more government-funded research.

PeerView

Advanced in Treatment of RCC in the Adjuvant/Perioperative Setting



Sumanta Kumar Pal, MD, FASCO

Professor & Vice Chair of Academic Affairs

Department of Medical Oncology & Therapeutics Research

Co-Director, Kidney Cancer Program

City of Hope Comprehensive Cancer Center

Duarte, California

Traditionally Limited Options for Patients With Localized RCC^{1,2}

Need for perioperative systemic therapy

While perioperative systemic treatments have been successful in several other solid tumors (eg, cancers of the bladder, breast, colon, and lung), effective strategies for perioperative systemic therapy have traditionally lagged in RCC

Need to reduce recurrence

Nephrectomy can potentially offer patients a cure in early localized disease; however, in stage II and III RCC, the risk of recurrence is significant, with 20% to 40% of patients experiencing a local or distant recurrence

Need for effective therapies in earlier stages

RCTs Investigating the Role of Adjuvant TKIs in RCC¹

Trial	Experimental Therapy	Therapy Duration, y	Completion	Histology	Enrollment	Endpoint	Statistically Significant?
ASSURE	Sunitinib ^a or sorafenib	1	2010	Any	1,943	DFS	No ^b
SORCE	Sorafenib ^a	3	2012	Any	1,656	DFS	No
S-TRAC	Sunitinib ^c	1	2016	Clear cell	674	DFS	Yes
PROTECT	Pazopanib ^a	1	2016	Clear cell	1,538	DFS	No ^d
ATLAS	Axitinib	3	2017	Clear cell	592	DFS	No
EVEREST	Everolimus	1	2023	Clear cell or non-clear cell	1545	RFS	No

FDA
Approved
2017

^a Trial required amendments for dose reduction of starting dose. ^b Subset analysis of high-risk clear cell RCC patients similar to S-TRAC failed to show DFS difference. ^c FDA approved use of sunitinib in the adjuvant setting for up to 1 year; however, because of limited benefit and the toxicities/inconvenience of treatment, real-world use has been limited. ^d Subset analysis of patients receiving 800-mg dose showed a significant DFS benefit.

1. Cosso F et al. *Int J Mol Sci.* 2023;24:4243.

KEYNOTE-564: Adjuvant Pembrolizumab^{1,2,a}

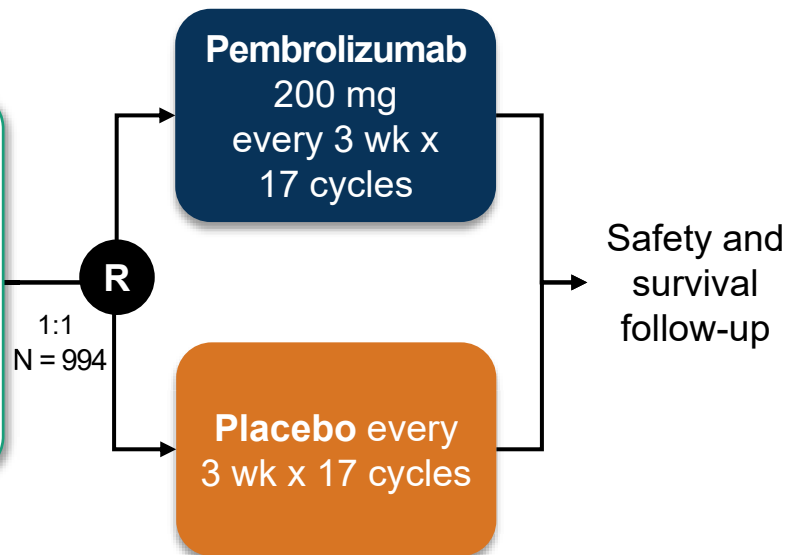
FDA Approved
2021

Key Eligibility Criteria

- RCC with clear cell component
- Post nephrectomy (total/partial) with intermediate/high risk for recurrence
 - pT2: grade 4 or sarcomatoid, N0M0
 - pT3: any grade N0M0
 - pT4: any grade N0M0
 - pT any stage: any grade, N+M0
- Post nephrectomy (total/partial) plus complete resection of metastasis
 - M1 NED
- Nephrectomy ≤12 wk prior to randomization
- No prior systemic therapy
- ECOG PS 0 or 1

Stratification

- M0 vs M1 NED
- Within M0
 - ECOG PS: 0 vs 1
 - US: yes vs no



Endpoints

- **Primary:** DFS per investigator
- **Key secondary:** OS
- **Other secondary:** safety

^a Data cutoff date: June 14, 2021; 30 months follow-up.

1. Choueiri TK et al. *N Engl J Med*. 2021;385:683-694. 2. Powles T et al. *Lancet Oncol*. 2022;23:1133-1144.

Adjuvant Pembrolizumab Continued to Improve DFS Versus Placebo in the Adjuvant Setting After 5 Years of Follow-Up¹⁻⁴

Phase 3 KEYNOTE-564

DFS^a

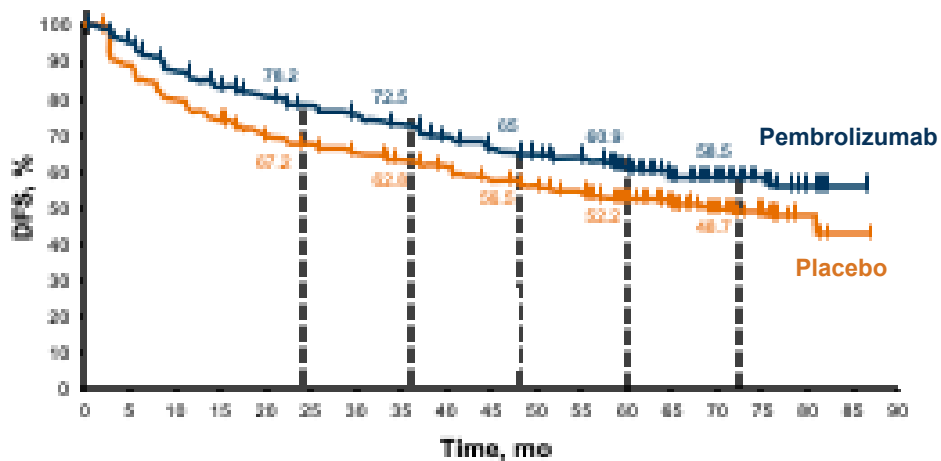
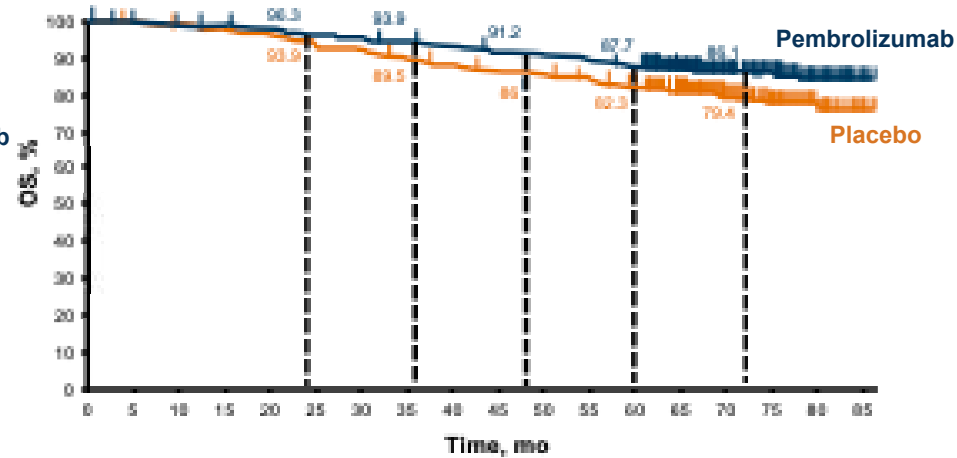
	Events, n	Median, mo (95% CI)
Pembro (n = 496)	188	NR (NR-NR)
Placebo (n = 498)	241	68.3 (51.7-NR)

Median follow-up was 69.5 mo (range, 60.2-86.9)
HR = 0.71 (95% CI, 0.59-0.86)

OS^b

	Events, n	Median, mo (95% CI)
Pembro (n = 496)	68	NR (NR-NR)
Placebo (n = 498)	99	NR (NR-NR)

Median follow-up was 69.5 mo (range, 60.2-86.9)
HR = 0.66 (95% CI, 0.48-0.90)



^a Primary DFS endpoint was met at IA1 and was not formally statistically tested thereafter. Data cutoff date: September 25, 2024.

^b Primary OS endpoint was met at IA3 and was not formally statistically tested thereafter. Data cutoff date: September 25, 2024.

1. Choueiri TK et al. *N Engl J Med*. 2021;385:683-694. 2. Powles T et al. *Lancet Oncol*. 2022;23:1133-1144.

3. Choueiri TK et al. *N Engl J Med* 2024;390:1359-13714. 4. Haas NB et al. ASCO 2025. Abstract 4514.

Combination Approaches in the Adjuvant Setting?

RAMPART: Durvalumab Combined With Tremelimumab¹

Confirmed RCC and high or intermediate risk of relapse (Leibovich risk score) or with fully resected synchronous ipsilateral adrenal metastases or with a single fully resected soft tissue metastasis

R

3:2:2

Arm A

Active monitoring

Arm B

Durvalumab
1,500 mg Q4W for 1y

Arm C

Durvalumab
1,500 mg Q4W for 1y
+
tremelimumab
75 mg at d 1 and wk 4

Adjuvant therapy with durvalumab + tremelimumab after resection of RCC improved DFS, particularly among those at highest risk of relapse

Arm	n	3-Year DFS, %
Durvalumab + tremelimumab	225	81
Active monitoring	340	73
Median follow-up: 3 y		

ITT: HR = 0.65 (95% CI, 0.45-0.93)

Arm	n	3-Year DFS, %
Durvalumab + tremelimumab	122	78
Active monitoring	189	61
Median follow-up: 3 y		

Higher-Risk ITT: HR = 0.52 (95% CI, 0.34-0.80)

Arm	n	3-Year DFS, %
Durvalumab + tremelimumab	103	86
Active monitoring	151	87
Median follow-up: 3.1 y		

Intermediate-Risk ITT: HR = 1.19 (95% CI, 0.61-2.32)

Combination Approaches in the Adjuvant Setting?

LITESPARK-022: Pembrolizumab Plus Belzutifan^{1,2}

Key Eligibility Criteria

- Histologically confirmed diagnosis of clear cell RCC
 - Intermediate/high risk: pT2, grade 4 or sarcomatoid, N0M0; pT3, any grade, N0M0
 - High risk: pT4, any grade, N0M0; any pT, any grade, N+M0
 - M1 NED after surgery (≤ 2 y from nephrectomy)
- Complete resection of primary tumor (partial or radical nephrectomy) and metastatic lesions (for M1 NED)
- Randomized ≤ 12 wk after surgery
- ECOG PS 0-1
- No pre-existing brain or bone metastatic lesions
- No prior systemic therapy or radiotherapy for RCC

1:1
(blinded)
N = 1,600

R

**Belzutifan 120 mg QD x ~54 wk +
pembrolizumab 400 mg Q6W
x 9 cycles**

**Placebo QD x 54 wk +
pembrolizumab 400 mg Q6W
x 9 cycles**

- **Primary endpoint:** DFS
- **Secondary endpoints:** OS, safety, disease recurrence-specific survival, and PROs

1. <https://clinicaltrials.gov/study/NCT05239728>.

Combination Approaches in the Adjuvant Setting?¹

2026
ASCO GU
SYMPOSIUM

Abstract LBA418

**Title: Adjuvant Pembrolizumab Plus Belzutifan Versus Pembrolizumab for ccRCC:
The Randomized Phase 3 LITESPARK-022 Study**

Oral Abstract Session C

Saturday, February 28, 2026, at 8:25 AM PST

Presenter: Toni K. Choueiri

PRESS RELEASE¹

October 2025

- **The combination of pembrolizumab plus belzutifan demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of DFS compared with pembrolizumab in combination with placebo**
- **The trial will continue to evaluate OS, a key secondary endpoint**

1. <https://www.merck.com/news/merck-announces-keytruda-pembrolizumab-plus-welireg-belzutifan-met-primary-endpoint-of-disease-free-survival-dfs-in-certain-patients-with-clear-cell-renal-cell-carcinoma-rcc-follow/>.

Combination Approaches in the Adjuvant Setting?

2026
ASCO GU
SYMPOSIUM

Abstract TPS577/Poster J6

Title: Short Term Intensified Pembrolizumab and Tivozanib for High-Risk RCC: STRIKE! (Alliance A032201)

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

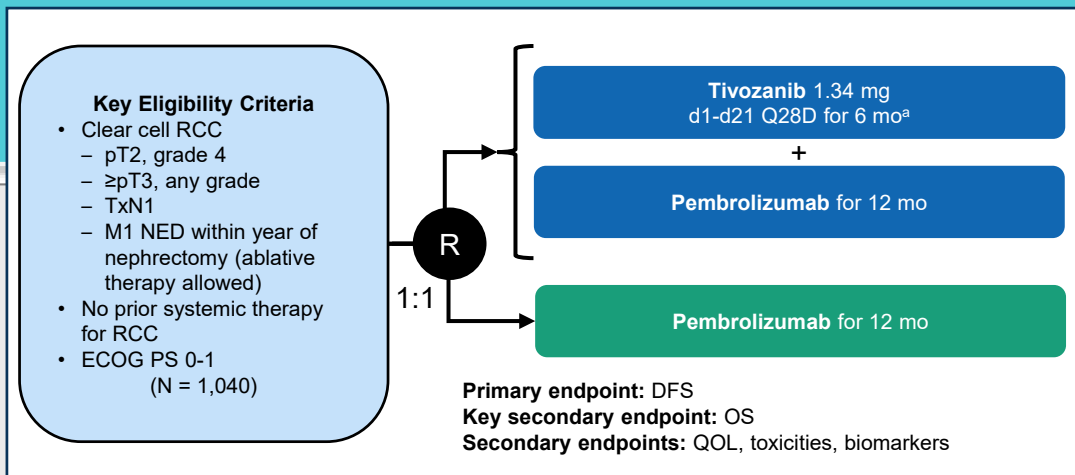
Presenter: Bradley A McGregor

Abstract Summary

Despite improvement in RFS and OS with adjuvant pembrolizumab, 20% of patients still experienced a relapse within 2 years, with no biomarker yet identified to predict who will respond or require adjuvant therapy.

Addition of TKI to IO in the adjuvant setting?

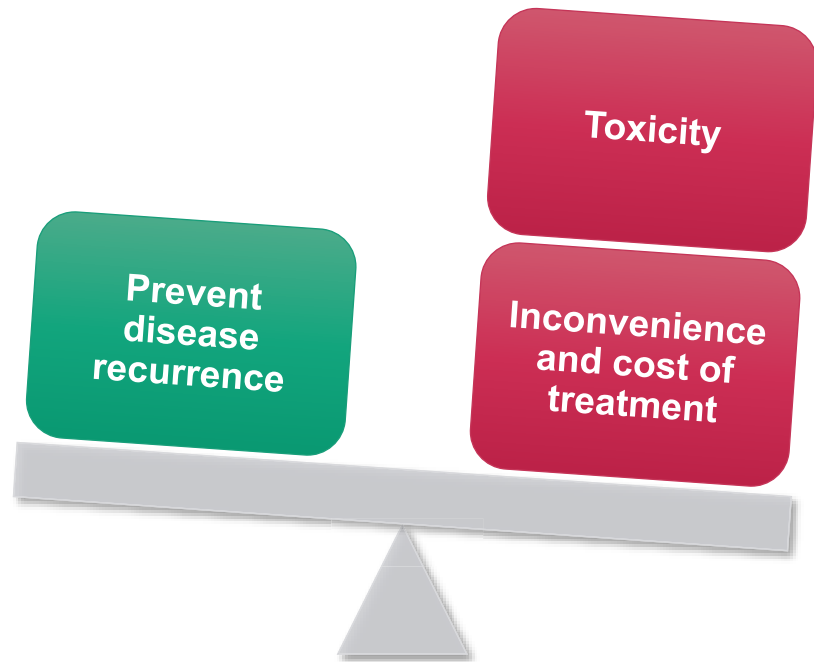
Phase 3 STRIKE was developed to explore the benefit of 6 months of **tivozanib** added to **pembrolizumab** vs pembrolizumab alone in the adjuvant setting for patients with resected high-risk clear cell RCC. It opened to accrual in April 2025 and, at this time, has enrolled 106 patients.



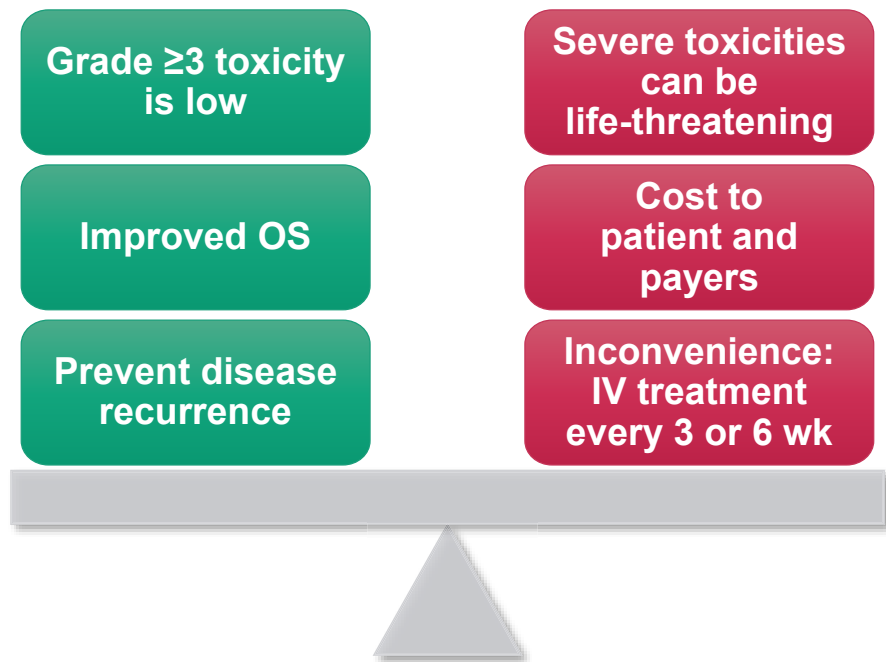
^a Reductions to 0.89 mg d5-d21, 0.89 mg every other day; no limit on dose interruptions.

Balancing Benefit/Risk: Heightened in the Adjuvant Setting

- Patients undergoing surgery for nonmetastatic kidney cancer have varying degrees of risk for recurrent disease post surgery
- The ultimate goal of “adjuvant therapy” is to reduce the incidence of recurrent disease and to cure more patients



Balancing Benefit/Risk in the RCC Adjuvant Setting



- The choice to use adjuvant therapy depends on patient preferences/priorities, tolerance for toxicity, and goals for treatment (shared decision-making)
- Additional data and outcomes from ongoing trials will be important

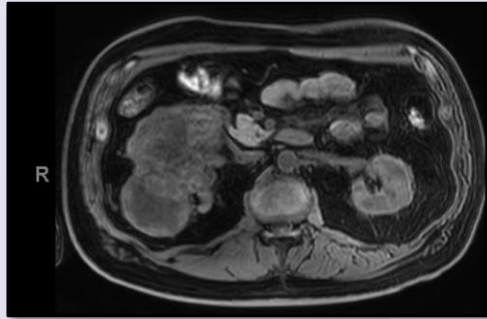
Let's Discuss a Patient Case

**Alan, a 60-year-old patient,
presents with gross hematuria**

Abdominal CT shows a 13-cm right renal mass with hemorrhage into the ureter and bladder

Undergoes a radical right nephrectomy

- 12.5-cm tumor at resection, with distal renal vein involvement
 - Invading perinephric fat, negative margins
 - Grade 3 with clear cell histology
 - Rhabdoid and focal sarcomatoid differentiation
 - Multifocal tumor necrosis; margins negative pT3aNxMx



**What would you discuss
with Alan?**

- Assessing risk of recurrence?
- Surveillance
- Pembrolizumab
- Pembrolizumab + belzutifan
- Clinical trial
- How might recent data change future considerations?
- How does treatment choice at this point of care impact later options, depending on when progression occurs?

Alan recovers well, and post-surgical imaging is clear

KCA Resources: Virtual Support Groups for Patients and Caregivers

Download the
Practice Aid!

- Peer-led meetings for those affected by kidney cancer
- Separate groups for patients and care partners
- Held online monthly
- Help patients and care partners form meaningful connections and learn from others through conversation, shared experiences, guest speakers, and resource sharing



Caregiver Connections

This support group is open to: kidney cancer caregivers, family members, and friends. Meetings are held on the last Tuesday of each month at 6:00 pm CT/7:00 pm ET. Register to receive the Zoom link.

[Sign up for Caregiver Connections](#)



Moderated by: Salima Witt
Kidney Cancer Patient & Advocate

Patient Perspectives

This support group is open to: kidney cancer patients and survivors. Meetings are held on the last Wednesday of each month at 7:00 pm CT/8:00 pm ET. Register to receive the Zoom link.

[Sign up for Patient Perspectives](#)



Moderated by: Peggy Zuckerman
Kidney Cancer Patient & Advocate

Optimizing First-Line Therapy in mRCC



Pedro C. Barata, MD, MSc, FACP

Miggo Family Chair in Cancer Research

Co-Leader Genitourinary (GU) Disease Team

Director of GU Medical Oncology Research Program

University Hospitals Seidman Cancer Center

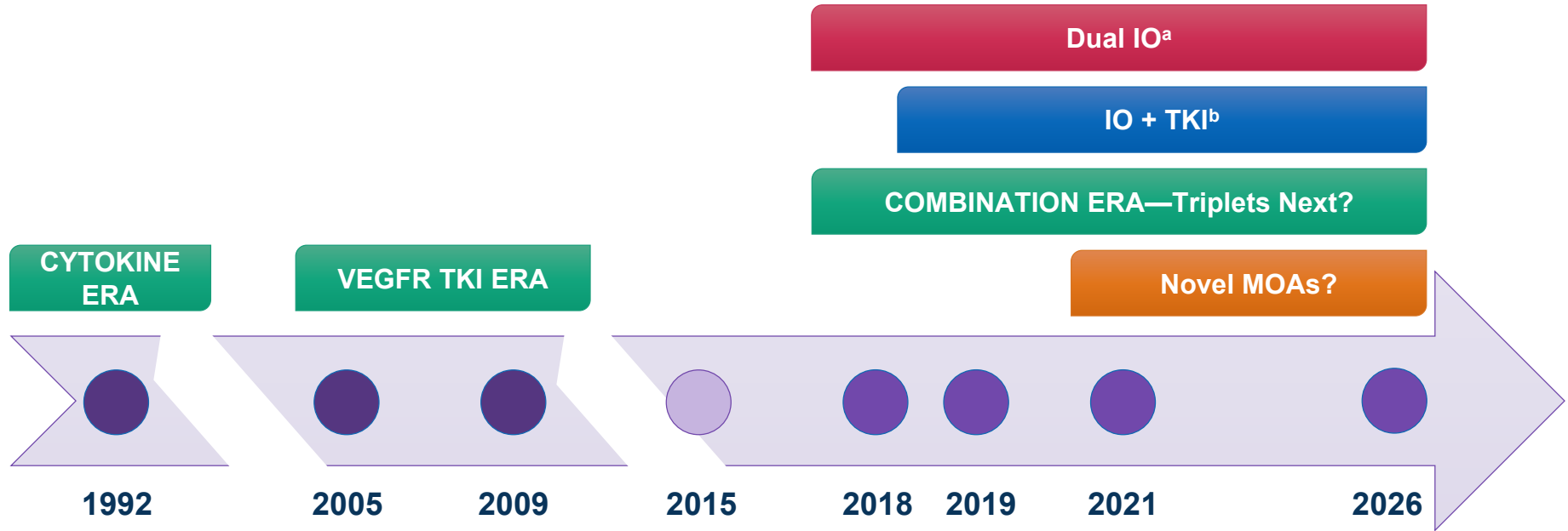
Associate Professor of Medicine

Case Western Reserve University

Case Comprehensive Cancer Center

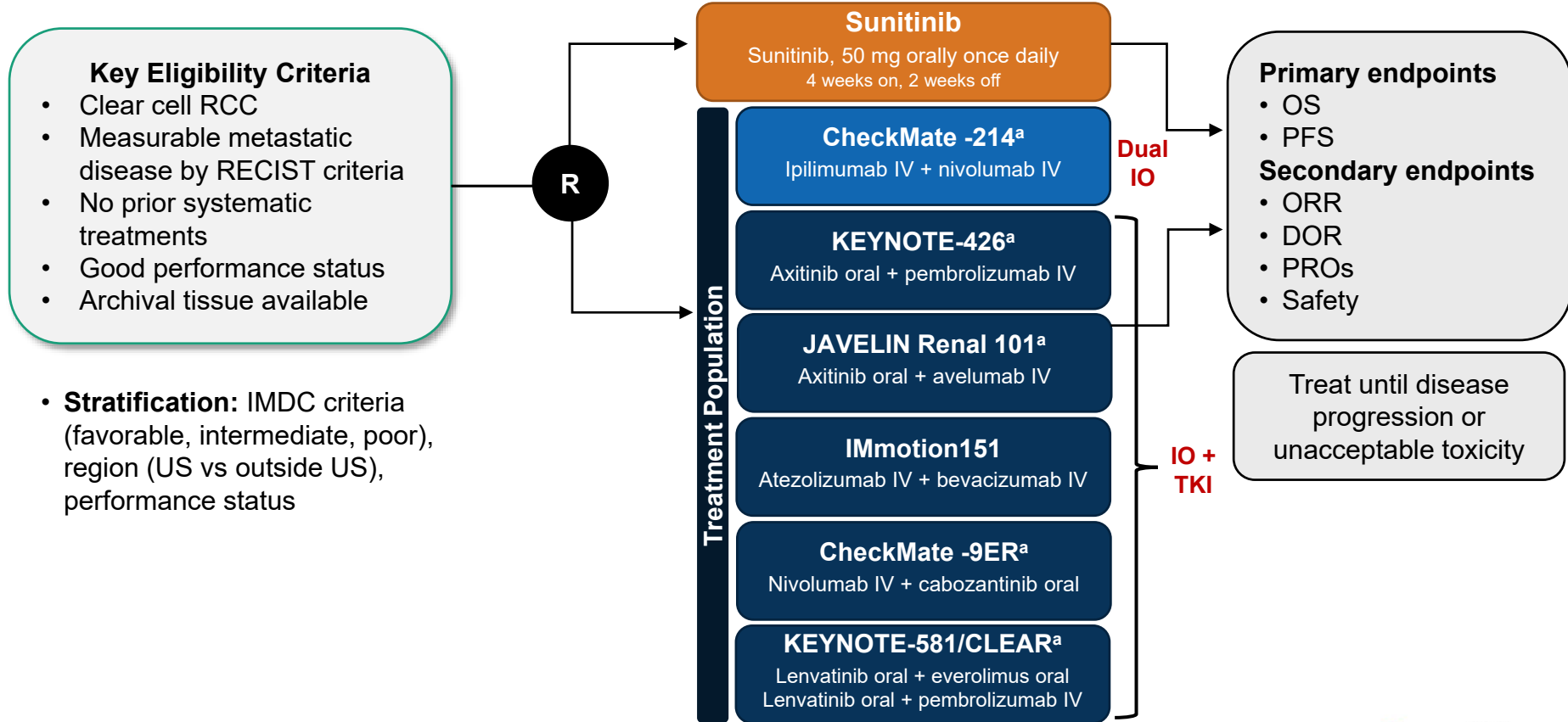
Cleveland, Ohio

Timeline of FDA-Approved Regimens for Metastatic Clear-Cell RCC in the 1L Setting



^a Nivolumab + ipilimumab. ^b Avelumab + axitinib, pembrolizumab + axitinib, pivolumab + cabozantinib, and pembrolizumab + lenvatinib.

Numerous Regimens for Metastatic Clear-Cell RCC in the 1L Setting



^a FDA approved.

Final Analysis Update: 9-Year Follow-Up for Phase 3 CheckMate -214¹

ITT

9-y/Final HR = 0.71

HR at the primary analysis = 0.68

Intermediate/Poor Risk

9-y/Final HR = 0.69

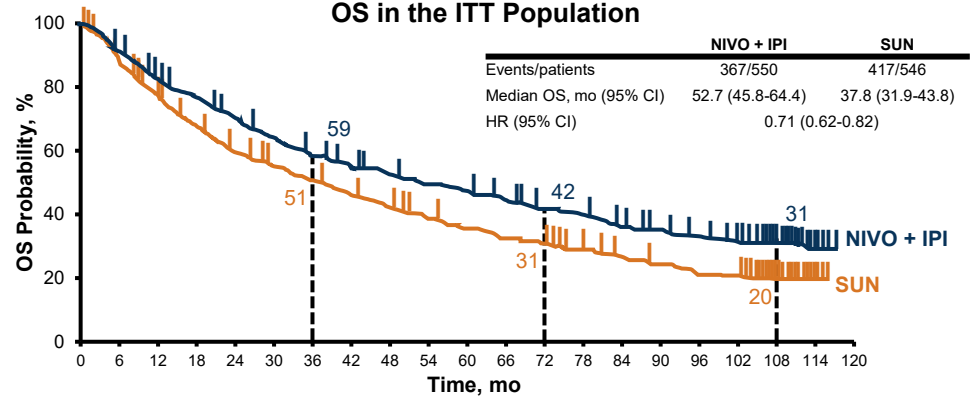
HR at the primary analysis = 0.63

Favorable

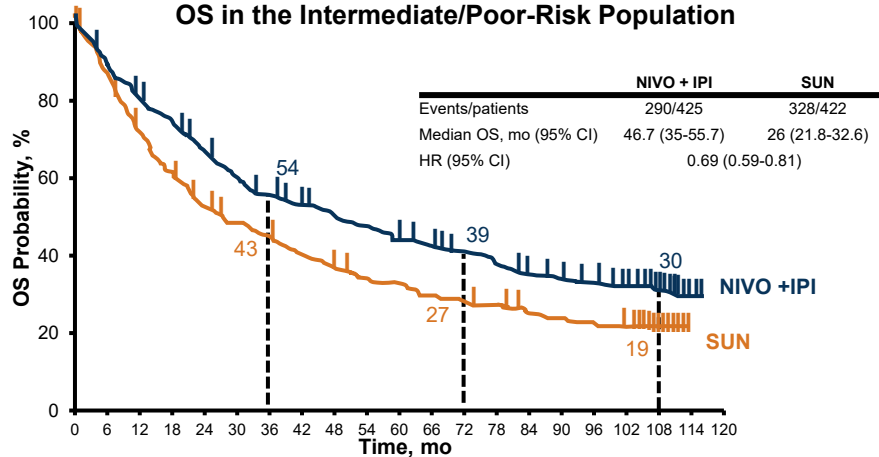
9-y/Final HR = 0.80

HR at the primary analysis = 1.45

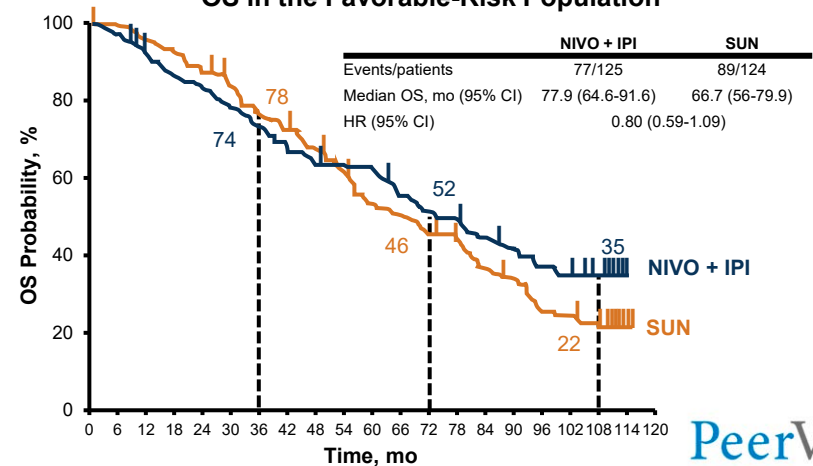
OS in the ITT Population



OS in the Intermediate/Poor-Risk Population



OS in the Favorable-Risk Population



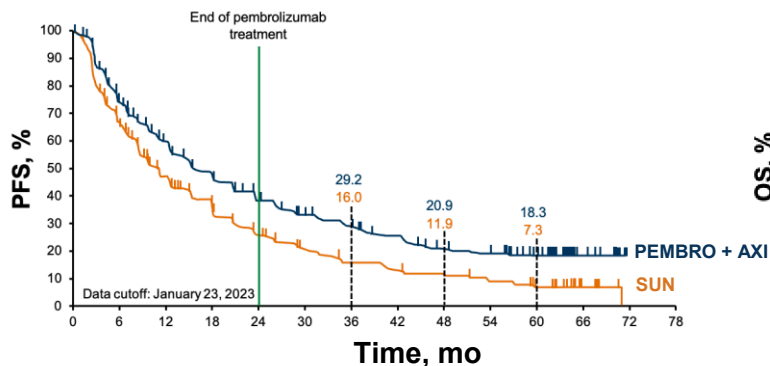
Phase 3 KEYNOTE-426: Sustained Benefit With Pembrolizumab Plus Axitinib¹

Median follow-up: 67.2 mo

PFS

	Events, n	Median PFS (95% CI), mo
PEMBRO + AXI	306	15.7 (13.6-20.2)
SUN	311	11.1 (8.9-12.5)

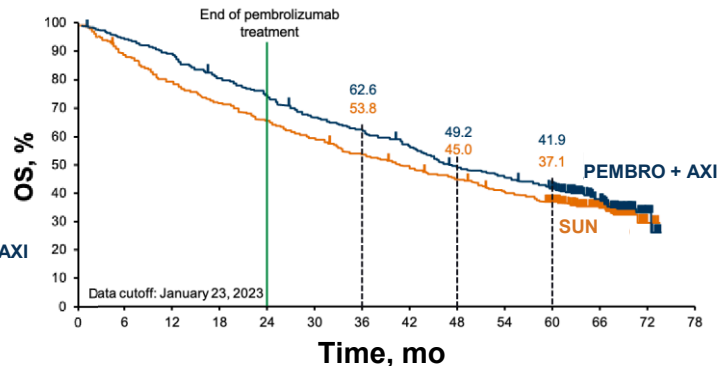
HR = 0.69 (95% CI, 0.59-0.81)



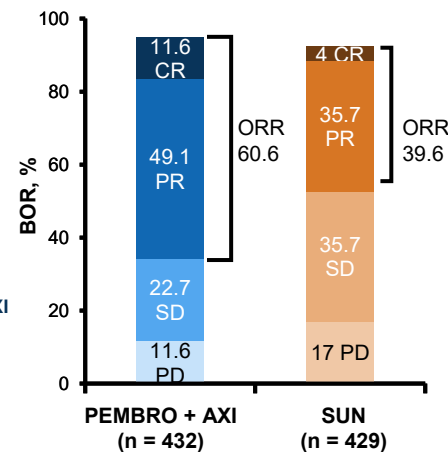
OS

	Events, n (%)	Median OS (95% CI), mo
PEMBRO + AXI	270 (62.5)	47.2 (43.6-54.8)
SUN	280 (65.3)	40.8 (34.3-47.5)

HR = 0.84 (95% CI, 0.71-0.99)



ORR in the ITT Population



Phase 3 CLEAR: Sustained Benefit With Pembrolizumab Plus Lenvatinib¹

Median follow-up: 50 mo

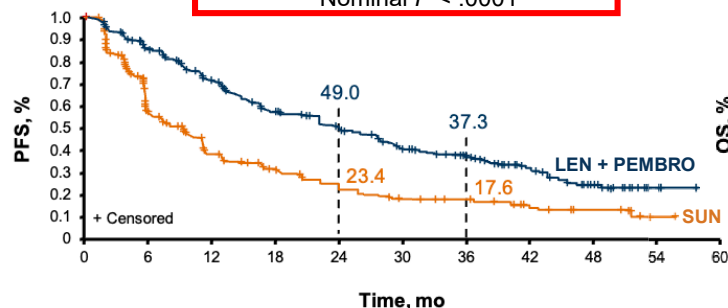
PFS

Median PFS, mo (95% CI)

LEN + PEMBRO	23.9 (20.8-27.7)
SUN	9.2 (6.0-11.0)

HR = 0.47 (95% CI, 0.38-0.57)

Nominal $P < .0001$



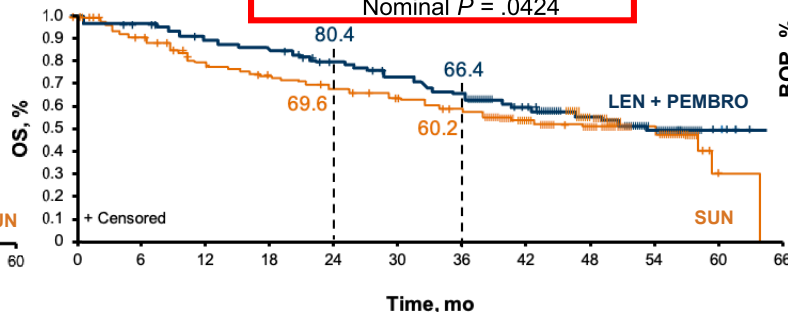
Final OS Analysis

Median OS, mo (95% CI)

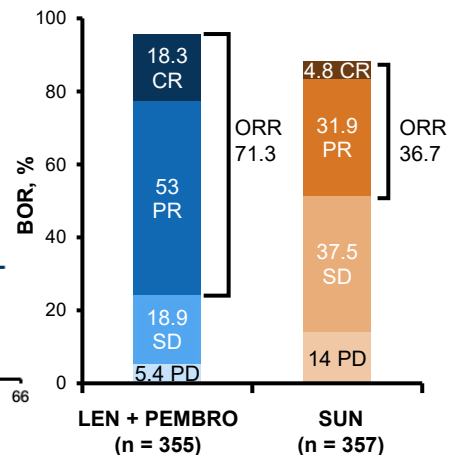
LEN + PEMBRO	53.7 (48.7-NE)
SUN	54.3 (40.9-NE)

HR = 0.79 (95% CI, 0.63-0.99)

Nominal $P = .0424$



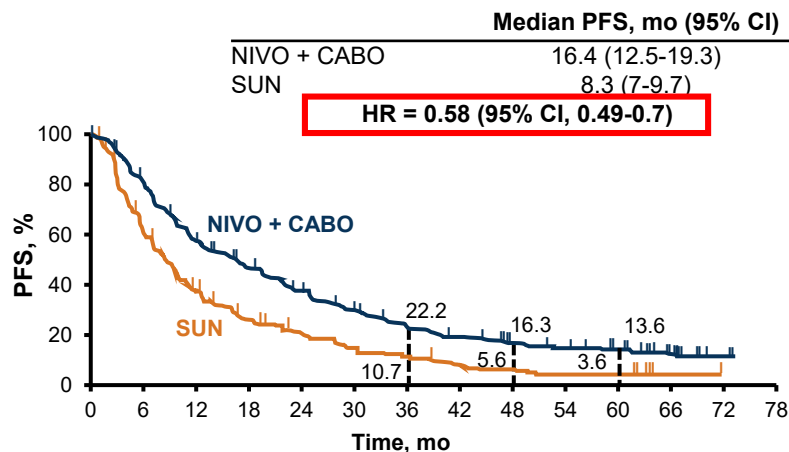
ORR



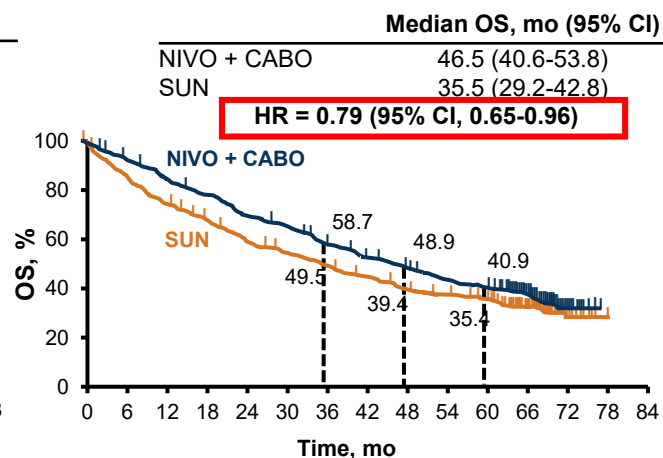
Phase 3 CheckMate -9ER: Sustained Benefit With Nivolumab Plus Cabozantinib^{1-3,a}

Median follow-up: 68 mo

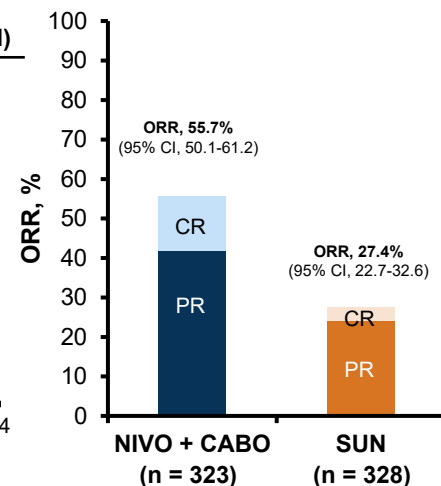
PFS per BCR



OS



ORR per BICR



^a Median follow-up, 67.6 (range, 60.2-80.2) months (ITT population).

1. Motzer RJ et al. *Ann Oncol*. 2026;37:33-43.

CheckMate -9ER: Long-Term Follow-Up Showed Durable Responses

2026
ASCO GU
SYMPOSIUM

Abstract 508/Poster D18

Title: Characterization of Depth and Durability of Response in Patients with Previously Untreated Advanced Renal Cell Carcinoma Who Received Cabozantinib Plus Nivolumab: Long-term Follow-up and Exploratory Analysis of CheckMate -9ER

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Cristina Suárez

Abstract Summary: Exploratory, post hoc analysis that characterized the depth and durability of responses with long-term follow-up (based on the final analysis of CheckMate -9ER) in patients receiving cabo + nivo

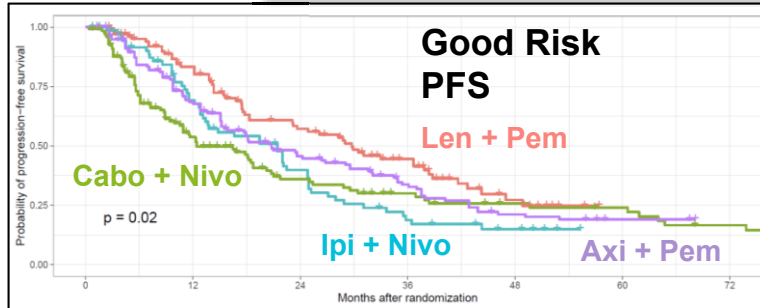
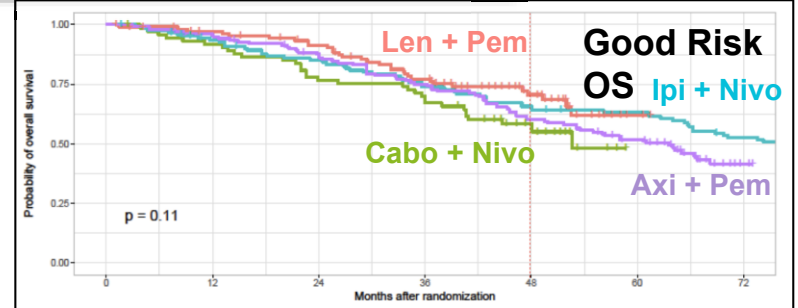
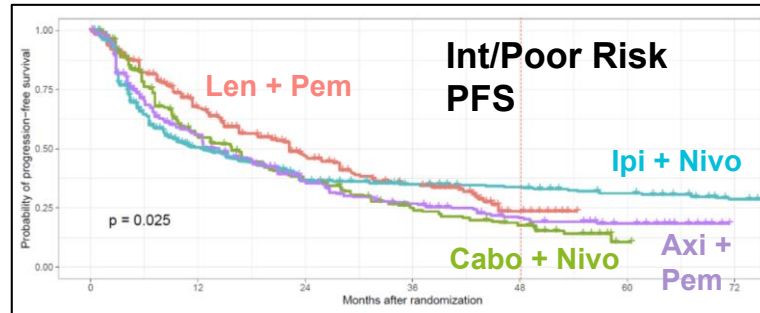
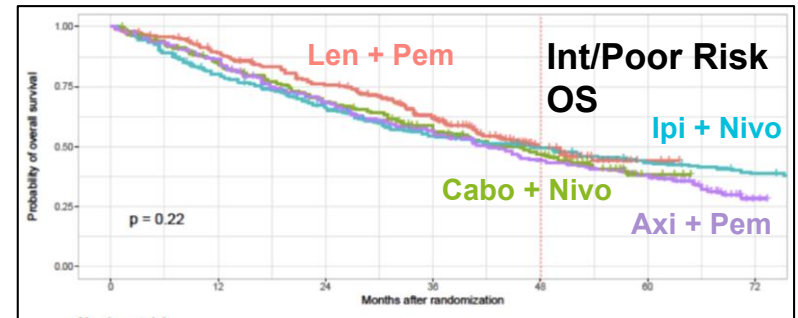
- Of 323 patients randomized to cabo + nivo, 243 were alive, and 234 were alive and progression-free at the 6-mo LM
 - These were categorized by BOR subgroup
- With a median follow-up of 67.6 mo, patients with a CR exhibited a durable response and improved benefit in OS, PFS, and ORR (all $P < .05$) compared with other response categories (PR1-PR3)

Conclusion

- This exploratory analysis revealed durable responses in patients who experienced a CR
- Patients who responded to treatment (CR or any PR) included those with poor prognostic characteristics

Durable Responses to ICI-Based Regimens for Metastatic Clear Cell RCC Stratified by IMDC Risk Groups¹

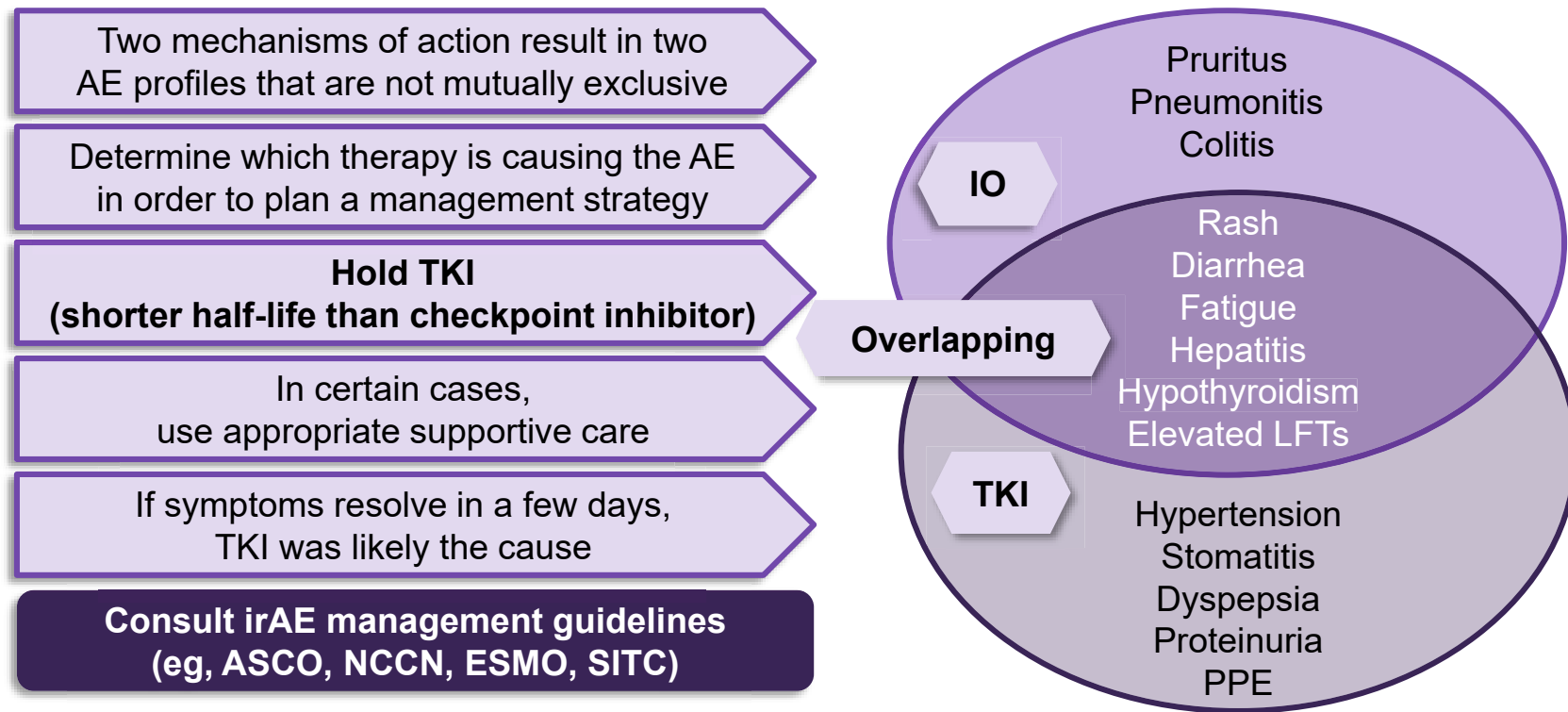
A pooled analysis of four randomized phase 3 trials



TKI + ICI was overall associated with higher durable response and extreme durable response, regardless of risk status compared with dual IO, but long-term OS rates were similar between these four regimens when stratified by risk

Management of AEs in IO Plus TKI Therapy¹⁻⁵

Download the
Practice Aid!

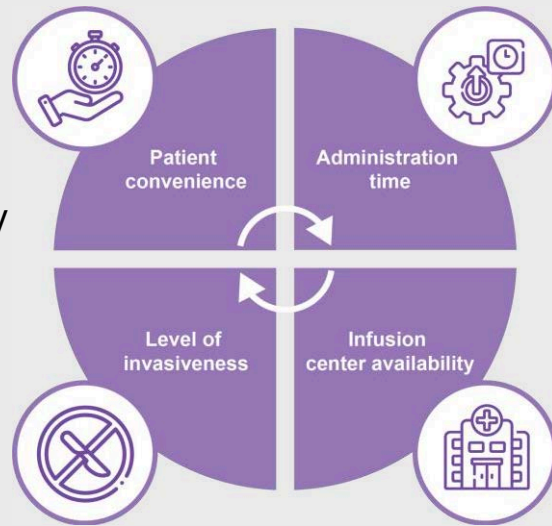


1. Martins F et al. *Nat Rev Clin Oncol*. 2019;16:563-580. 2. Postow MA et al. *N Engl J Med*. 2018;378:158-168. 3. Schneider BJ et al. *J Clin Oncol*. 2021;39:4073-4126. 4. NCCN Clinical Practice Guidelines in Oncology. Management of Immune Checkpoint Inhibitor–Related Toxicities. Version 1.2026. https://www.nccn.org/professionals/physician_gls/pdf/ici_tox.pdf. 5. Haanen J et al. *Ann Oncol*. 2022;33:1217-1238.

Potential for Improving Daily Management: Subcutaneous IO

SC administration provides an alternative with potential benefits for both patients and providers

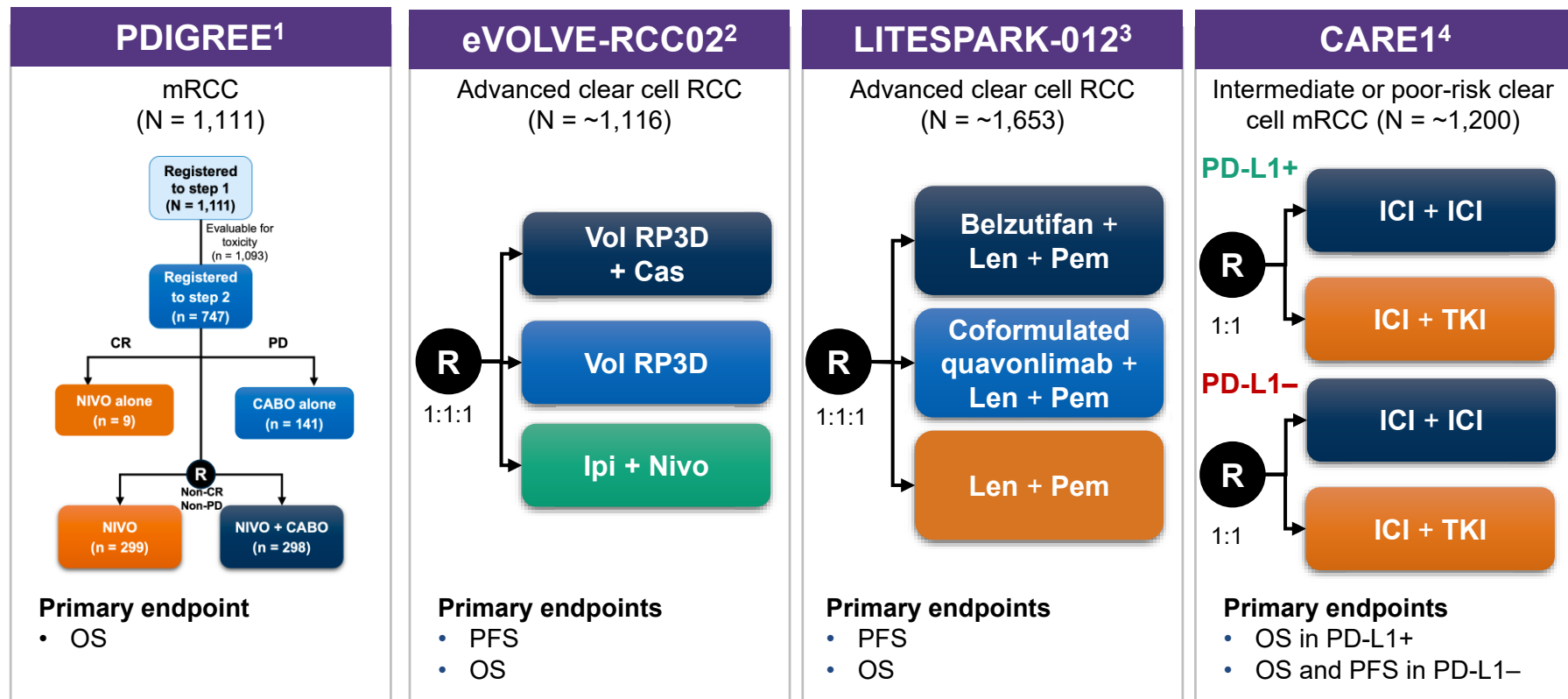
- Alleviates the need for IV vein ports
- Allows more patient flexibility
- Reduces dose preparation and administration times
- Optimizes occupancy in infusion centers



Subcutaneous formulations of **nivolumab** and **pembrolizumab** are now FDA- and EMA-approved for all indications, including mRCC¹⁻⁷

1. Albiges L et al. *Ann Oncol.* 2025;36:99-107. 2. Opdivo Qvantig (nivolumab and hyaluronidase-nvhy) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761381s005lbl.pdf. 3. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-and-hyaluronidase-nvhy-subcutaneous-injection>. 4. Felip E et al. *Ann Oncol.* 2025;7:775-785. 5. Keytruda Qlex (pembrolizumab and berahyaluronidase alfa-pmph) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761467Orig1s002lbl.pdf. 6. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pembrolizumab-and-berahyaluronidase-alfa-pmph-subcutaneous-injection>. 7. https://www.ema.europa.eu/en/documents/product-information/keytruda-epar-product-information_en.pdf.

Ongoing Phase 3 Trials in 1L mRCC

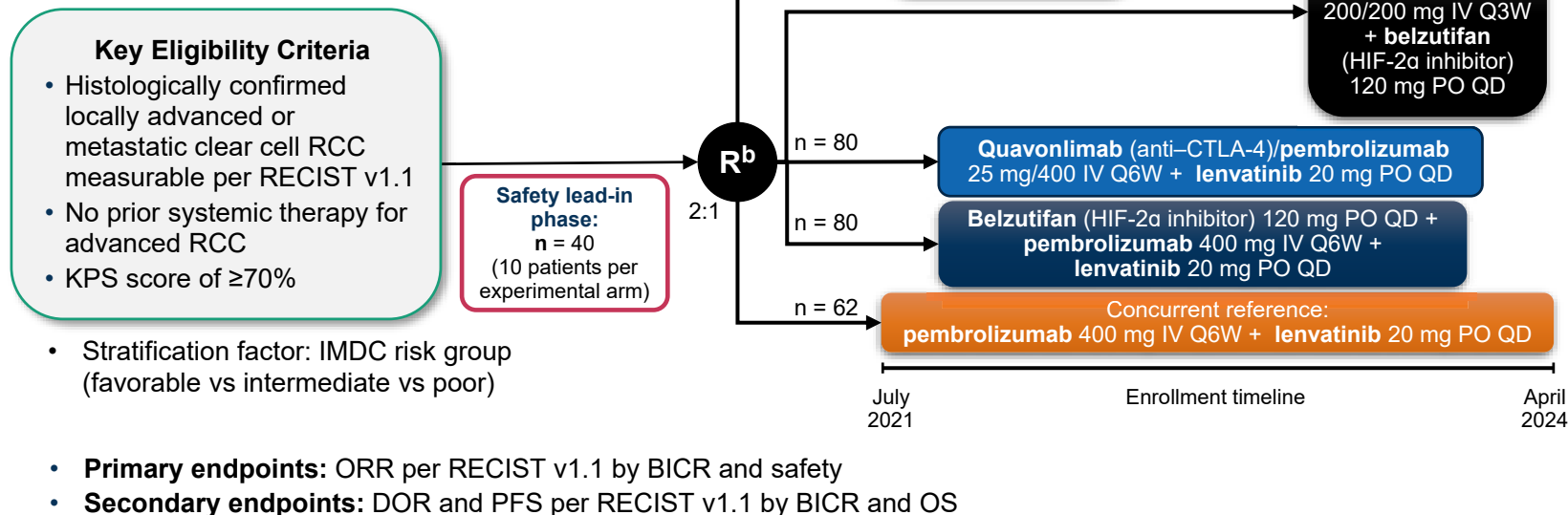


1. Zhang T et al. ASCO 2025. Abstract 4516. 2. <https://clinicaltrials.gov/study/NCT07000149>. 3. Choueiri TK et al. *Future Oncol.* 2023;19:2631-2640.
4. Albiges L et al. ESMO 2024. Abstract 1717.

What About Triplet Regimens?

What is the impact of adding a novel MOA as the third agent?

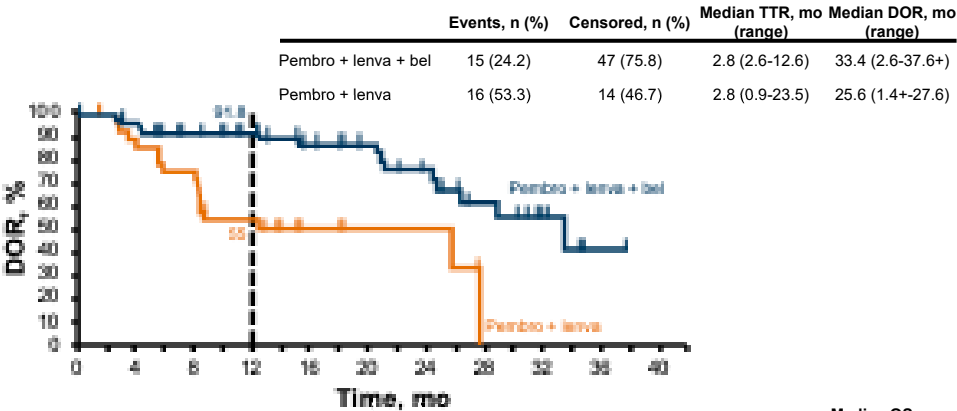
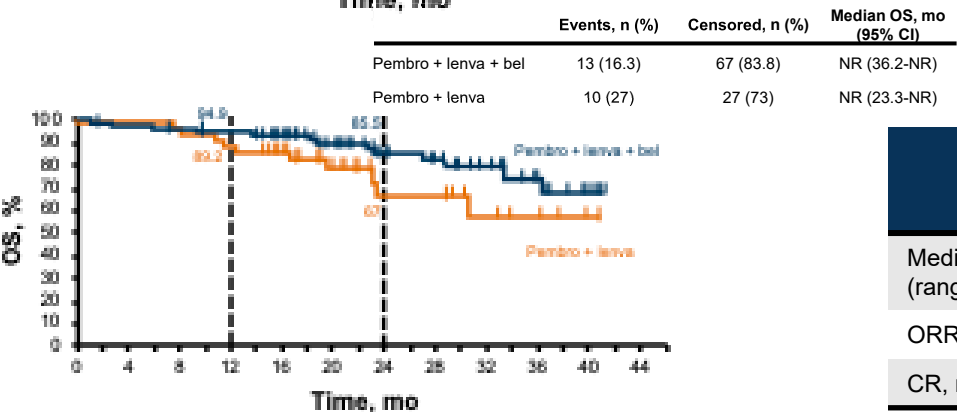
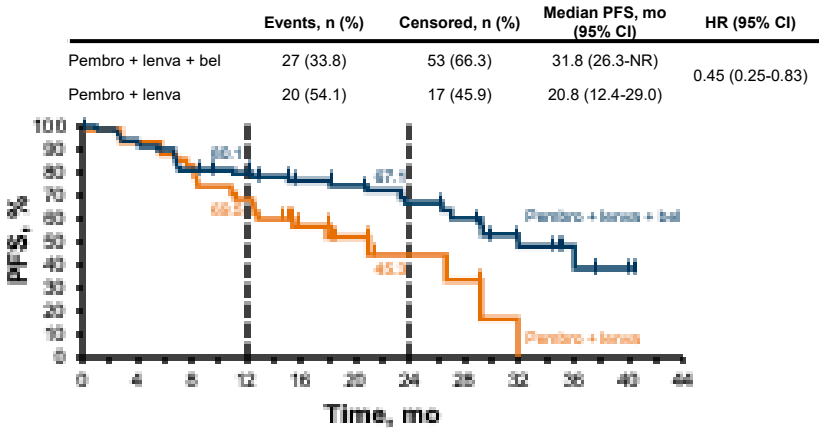
- **KEYMAKER-U03 Substudy 03A** of the umbrella phase 1/2 KEYMAKER-U03 trial evaluates novel pembrolizumab-based regimens in the first line for patients with advanced ccRCC¹



^a Enrollment ended early in January 2023 per data monitoring committee recommendation. ^b For each new investigational arm, additional patients were enrolled to the reference arm as needed to maintain the 2:1 randomization ratio.

1. Suárez C et al. *Ann Oncol.* 2026;37:229-240.

Pembrolizumab Plus Lenvatinib Plus Belzutifan Improved DOR, PFS, and OS in 1L mRCC^{1,a}



	Pembrolizumab + Lenvatinib + Belzutifan (n = 80)	Pembrolizumab + Lenvatinib (n = 62)
Median follow-up, mo (range)	23.4 (14.1-41)	21.2 (11.9-44.4)
ORR, % (95% CI)	77.5 (66.8-86.1)	80.6 (68.6-89.6)
CR, n, %	10 (12.5)	4 (6.5)

^a Data cut-off: March 31, 2025.
¹ Suárez C. et al. *Ann Oncol.* 2026;37:229-240.

Triplet Therapy?

Phase 3 LITESPARK-012

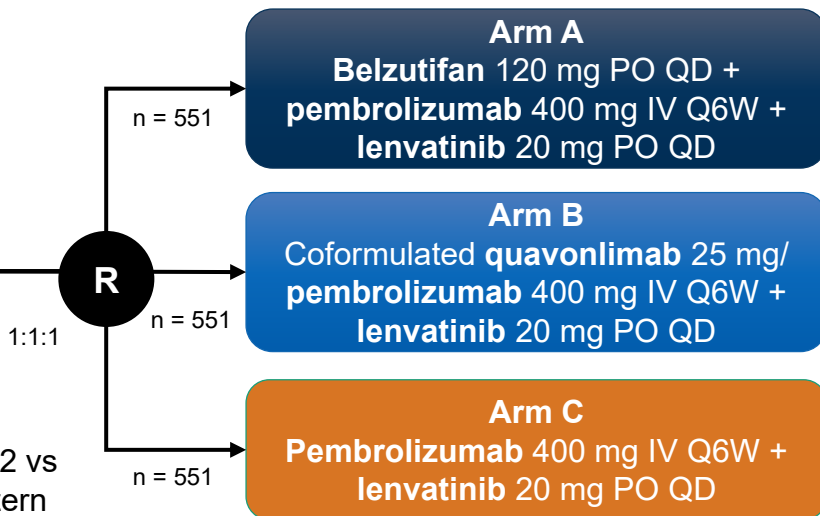
Key Eligibility Criteria

- Advanced or metastatic clear cell RCC
- No prior systemic therapy
- Measurable disease per RECIST v1.1
- KPS score $\geq 70\%$
(N ~ 1,653)

- **Stratification:** IMDC prognostic scores (0 vs 1-2 vs 3-6), geographic region (North America vs Western Europe vs ROW), sarcomatoid features (yes vs no)

- Treatment with pembrolizumab or pembrolizumab/quavonlimab will be limited to 18 infusions (approximately 2 years)
- Treatment with belzutifan and lenvatinib may continue until treatment discontinuation event

- **Primary endpoints:** PFS per RECIST v1.1 by BICR and OS
- **Secondary endpoints:** ORR per RECIST v1.1 by BICR, DOR per RECIST v1.1 by BICR, safety, and tolerability



Tumor imaging at week 12, then Q6W up to week 78, and then Q12W thereafter

Zanzalintinib Targets Pathways Associated With Tumor Immunosuppression

TAM Kinase (AXL, MER) Inhibition

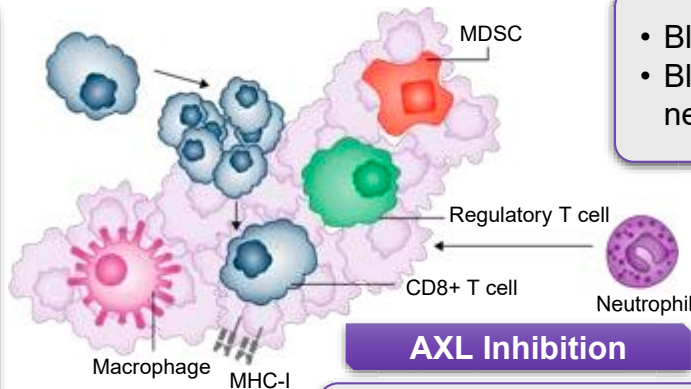
- Increases numbers of circulating and tumor-infiltrating CD8⁺ T cells
- Promotes macrophage phenotype transition from M2 (immunosuppressive) to M1 (immune stimulating)

VEGFR2 Inhibition

- Decreases number/function of regulatory T cells and MDSCs

MET Inhibition

- Blocks MET-induced tumor expression of PD-L1
- Blocks mobilization of immunosuppressive neutrophils



AXL Inhibition

- Increases tumor MHC class I expression

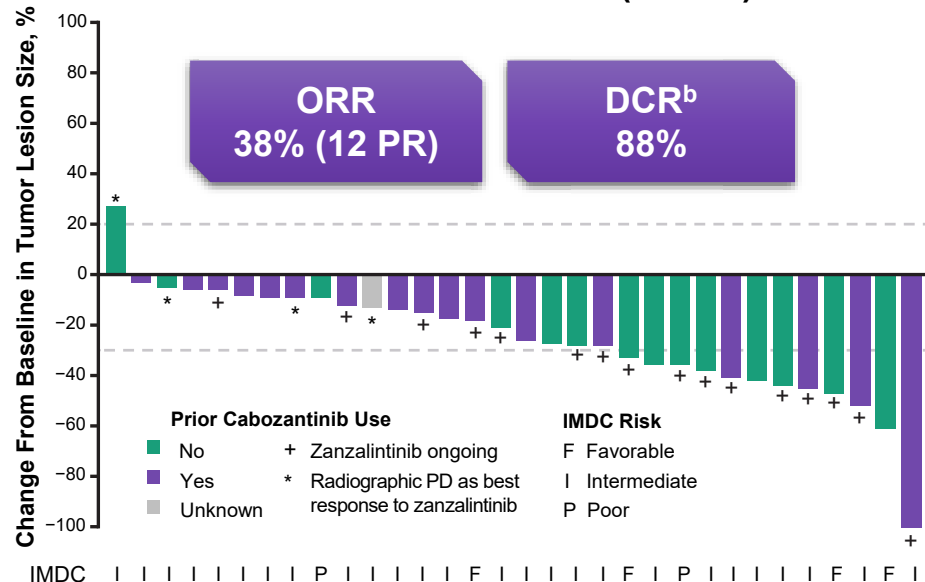
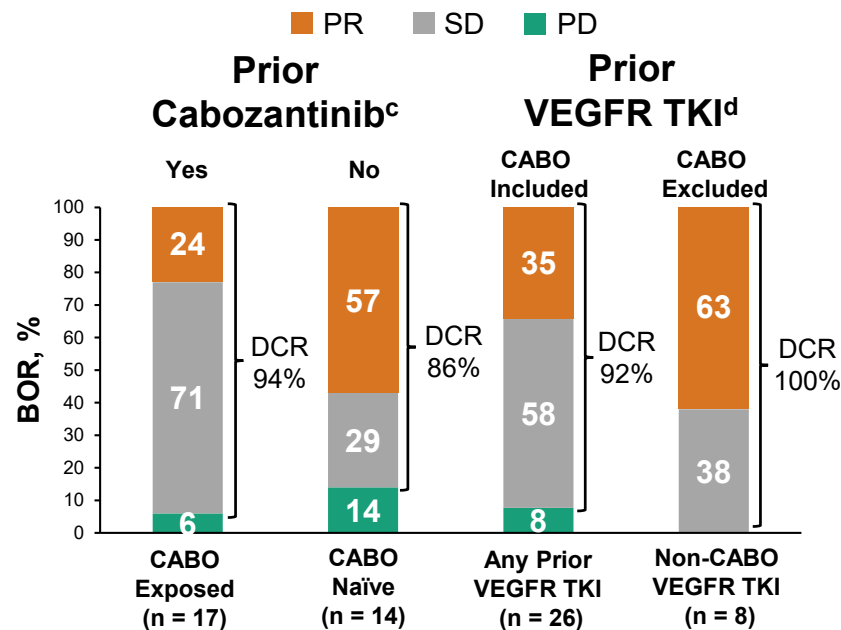
- TKI of VEGFR2, MET, AXL, and MER
- Similar target profile to cabozantinib
 - Shorter clinical half-life (16-22 hours)
 - PK properties for once-daily oral dosing

Phase 1b/2 STELLAR-001: Best Response to Zanzalintinib^{1,a}

Clear Cell RCC Cohort (N = 32)

ORR
38% (12 PR)

DCR^b
88%



Three of the four cabozantinib-exposed patients who responded to zanzalintinib had discontinued prior cabozantinib due to disease progression

^a Data cutoff: June 10, 2023. ^b DCR is defined as proportion of patients with a BOR of confirmed CR/PR or any single best response of SD.

^c Cabozantinib exposure was unknown for one patient. ^d These subgroups are not mutually exclusive.

1. Pal SK et al. IKCS 2023.

Phase 1b STELLAR-002 Study Design^{1,2,a}

Cohort 1 1L Clear Cell RCC

- Clear cell RCC (sarcomatoid features allowed)
- No prior systemic therapy^a

ZANZA +
NIVO

ZANZA +
NIVO +
IPI

ZANZA +
NIVO +
RELA

Cohort 2 2L Clear Cell RCC

- Clear cell RCC (sarcomatoid features allowed)
- Progressed on 1 prior systemic ICI-based combination therapy^b

ZANZA

ZANZA +
NIVO

ZANZA +
NIVO +
RELA

Cohort 6 1L Non-Clear Cell RCC

- Non-clear cell RCC (sarcomatoid features allowed)^c
 - Papillary, unclassified, or translocation-associated histologies
- No prior systemic therapy

ZANZA

ZANZA +
NIVO

Primary Objectives

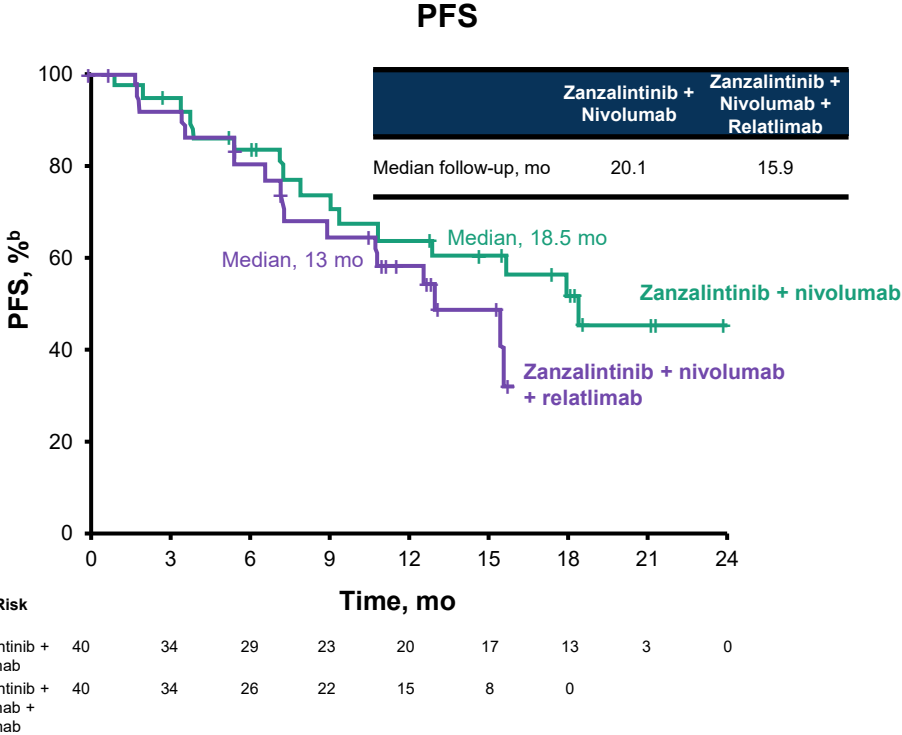
- **Dose escalation:** safety and RDs of combination therapies
- **Expansion:** ORR per RECIST v1.1 by investigator; safety (AEs/SAEs/AESIs)

^a Dose-escalation stage will determine the recommended doses for the expansion stage. ^b Combination therapy consisting of a PD-1/PD-L1 inhibitor + VEGFR TKI or a PD-1 + CTLA-4 inhibitor. Prior triplets, including VEGFR TKI, PD-1, and CTLA-4 inhibitors, are not allowed. ^c Chromophobe, renal medullary carcinoma, and pure collecting duct non-clear cell RCC are excluded.

1. <https://clinicaltrials.gov/study/NCT05176483>. 2. Motzer RJ et al. KCRS 2023. Abstract TIP 63.

STELLAR-002 Cohort 1 Update: Antitumor Activity of Zanzalintinib + Nivolumab ± Relatlimab in 1L Clear Cell RCC^{1,a}

	Zanzalintinib + Nivolumab (n = 40)	Zanzalintinib + Nivolumab/Relatlimab (n = 40)
ORR, % (95% CI)	63 (46-77)	40 (25-57)
Confirmed CR, n (%)	3 (8)	1 (3)
Confirmed PR, n (%)	22 (55)	15 (38)
SD, n (%)	11 (28)	20 (50)
PD, n (%)	2 (5)	3 (8)
DCR, % (95% CI)	90 (76-97)	90 (76-97)
Median DOR, mo (95% CI)	NE (11.1-NE)	NE (4-NE)
12-month DOR, % (95% CI)	73.4 (50-87.1)	74.1 (39.1-90.9)
Median TTR, mo (range)	2.1 (1.7-11)	3.6 (1.7-12.8)
Median PFS, mo (95% CI)	18.5 (9.5-NE)	13 (7.4-NE)
6-month PFS, % (95% CI)	83.4 (66.8-92.2)	80.4 (63.1-90.2)
12-month PFS, % (95% CI)	64.4 (45.7-78.1)	58.4 (39.9-73)

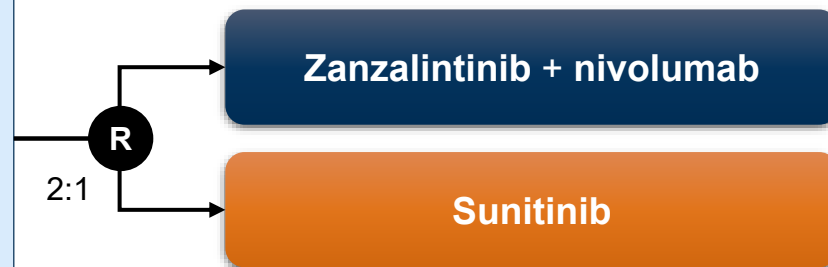


^a Per RECIST v1.1. ^b Kaplan-Meier estimate.
1. Chahoud J et al. ASCO 2025. Abstract 4515.

Phase 3 STELLAR-304: Combination Approach for 1L Non–Clear Cell RCC¹⁻³

Key Eligibility Criteria

- Histologically confirmed non–clear cell RCC that is unresectable, advanced, or metastatic
 - Papillary, unclassified, and translocation-associated non–clear cell RCC histologic subtypes, with or without sarcomatoid features
 - Measurable disease per RECIST v1.1 by investigator
 - KPS $\geq 70\%$
 - Archival tumor tissue available
 - No prior systemic therapy
- (N = ~291)

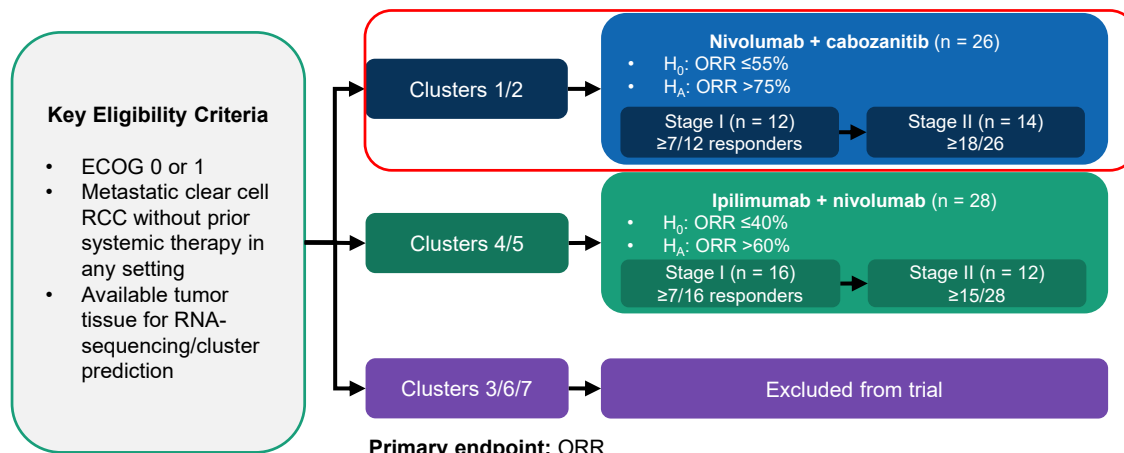


- **Dual primary endpoints:** PFS and ORR per RECIST v1.1 by BICR
- **Secondary endpoint:** OS
- **Other endpoints:** safety, including incidence and severity of AEs

Biomarker Approach?

OPTimal Treatment by Invoking Biologic Clusters in Renal Cell Carcinoma (OPTIC RCC)¹

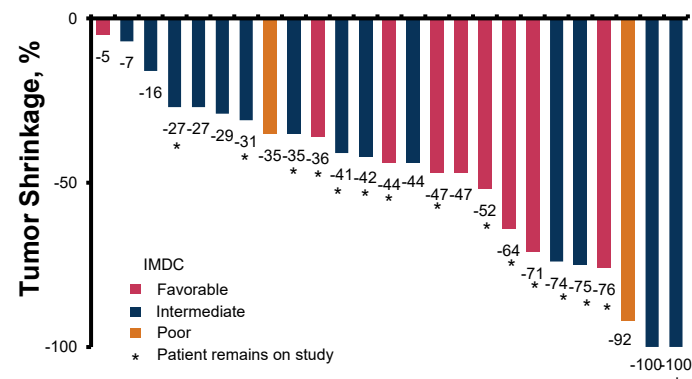
Simon's Minimax Two-Stage Design



Primary endpoint: ORR

Secondary endpoints: PFS, depth of response $> 80\%$ at 6 mo, and irAEs

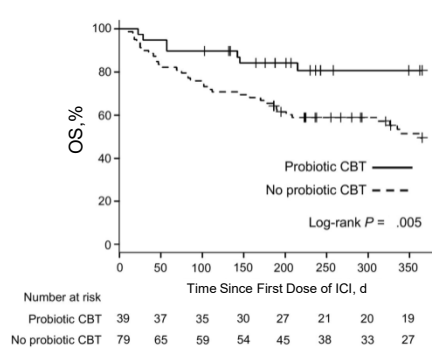
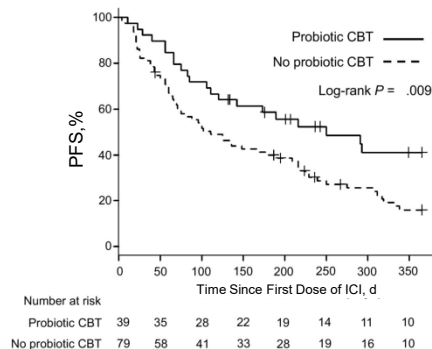
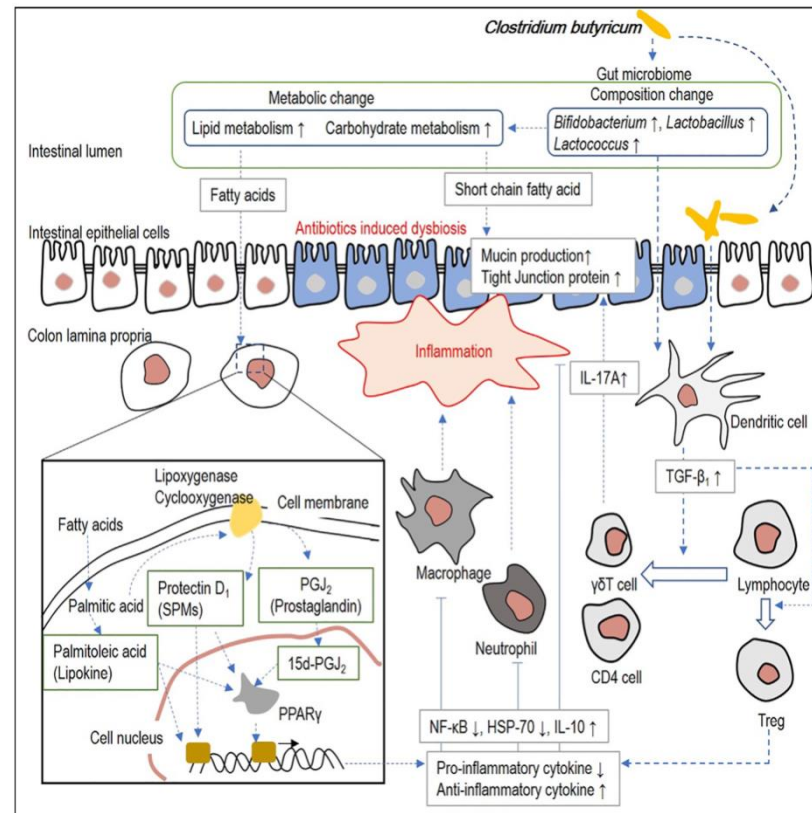
Depth of Response



- Prospective investigation of tissue-based RNAseq biomarkers to guide therapy in a 1L mccRCC population
- Primary and metastatic tumors exhibit different gene expression signatures, requiring metastatic tumor biopsies for a biomarker-driven study
- Selection of patients exhibiting an angiogenic gene expression signature enriches for clinical outcome to cabozantinib + nivolumab
- A high objective response rate, reduction of tumor burden in all patients, and lack of primary progressive disease were observed

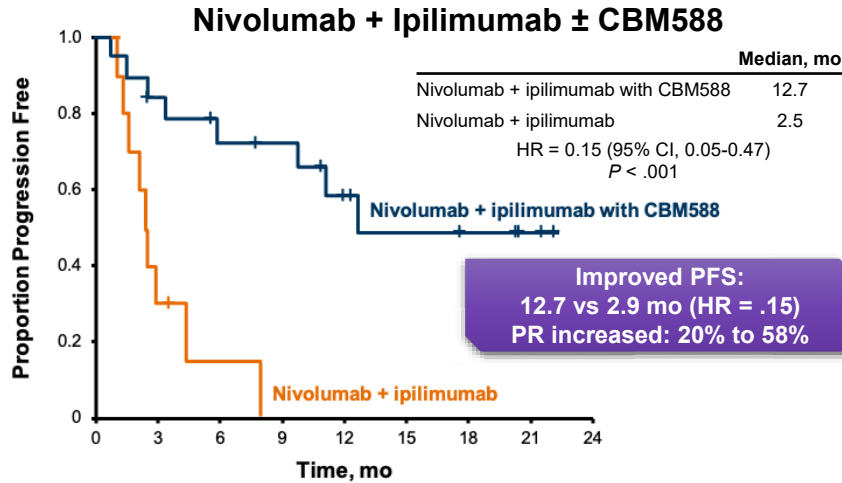
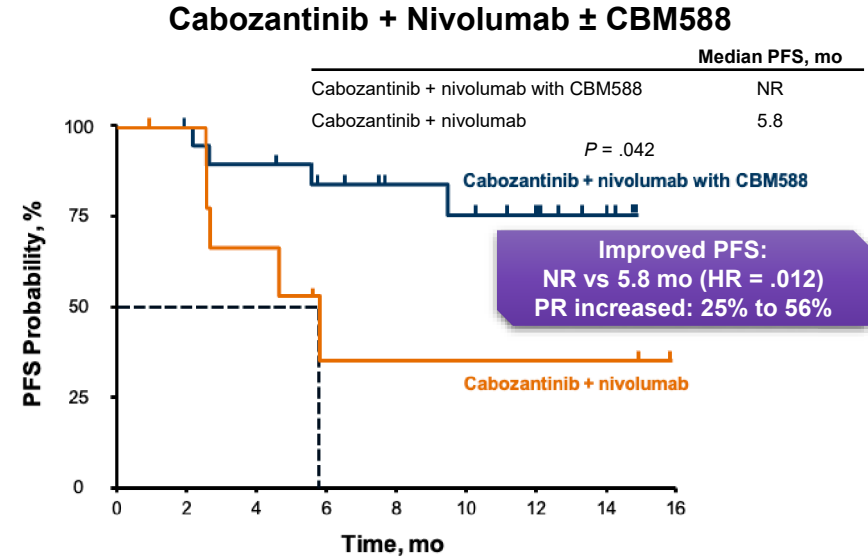
Novel Approaches: Predictive Capacity of the Microbiome¹

- Recent data suggests that the gut microbiome may predict outcome with checkpoint inhibitors²
- Retrospective data suggest that CBM-588, a live bacterial product containing *Clostridium butyricum*, can augment the activity of checkpoint inhibitors in NSCLC³
- This may occur via immunomodulation of the gut and/or alteration of gut microbiome composition⁴

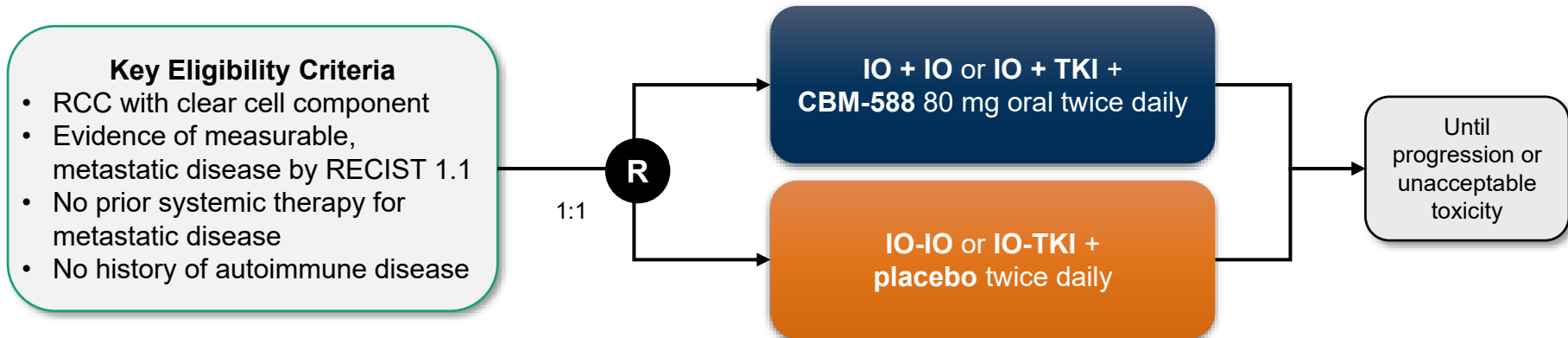


The Gut Microbiome May Predict Outcome With Immune Checkpoint Inhibitors¹⁻³

CBM588, a live bacterial product containing *Clostridium butyricum*



Phase 3 BioFront: A Definitive Study Assessing CBM588¹



- **Stratification:** IMDC risk group (good vs int vs poor), sarcomatoid/rhabdoid features (yes/no), IO-IO vs IO-TKI

- **Primary endpoints**
 - Phase 2: DCR at 6 months
 - Phase 3: PFS

1. <https://clinicaltrials.gov/study/NCT07383441>.

Panel Discussion: Treatment Decisions for 1L mRCC

Janice, a 68-year-old woman

- Aggressive disease
- Multiple hepatic metastases, with early onset following nephrectomy
- **Goal: disease control**

Discussion



Depending on tumor burden/histologic subtype/patient goals:

- When would you choose dual IO?
- When would you choose IO + TKI?

How does recurrence after adjuvant immunotherapy impact care plans?

How do you counsel patients (and their care partners) about AE expectations and proper management?

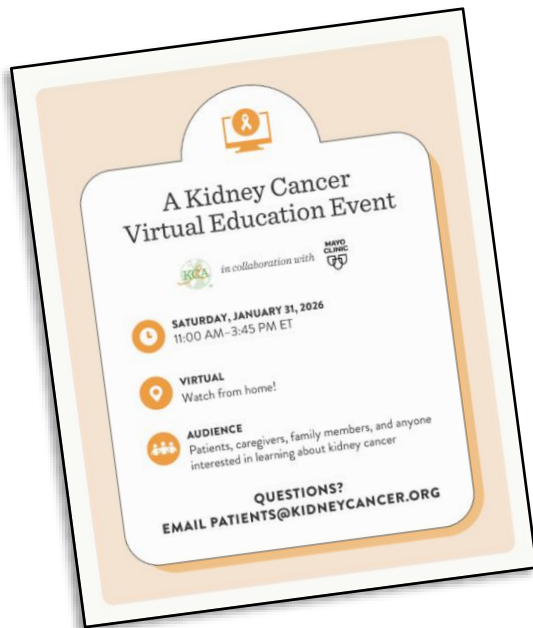
What new approaches would you consider?

When do you discuss clinical trials?

What if she has non-clear cell RCC?

KCA Provides Numerous Tools for Patient Education

Download the
Practice Aid!



Educational Events

In-person and online educational events for patients and care partners throughout the year cover topics such as innovative treatment options, support services, and more.

FAQ Videos

Hear from kidney cancer experts as they provide answers and insights to commonly asked questions. Topics include kidney cancer basics, diagnosis, treatment, clinical trials, side effect management and more.

Educational Materials

Patients and care partners can request printed and downloadable educational materials and care packs.



KidneyCancerAssociation
Unstoppable Together.

Individualized Treatment Selection in Refractory mRCC



Cristina Suárez, MD, PhD

Head of Genitourinary, CNS, Sarcomas, AYAs
and Cancers of Unknown Primary Site Unit
Medical Oncology Department
Vall d'Hebron University Hospital
Barcelona, Spain

Therapeutic Selection in Refractory Disease: Patient-Specific Considerations¹

Factors to Consider When Selecting 2L Therapy and Beyond for Patients With mRCC

Biological Factors

- What was the mechanism of 1L therapy?
- How deep and durable was the response to 1L therapy?
- How rapid was progression, and what is the tumor?

Patient Factors

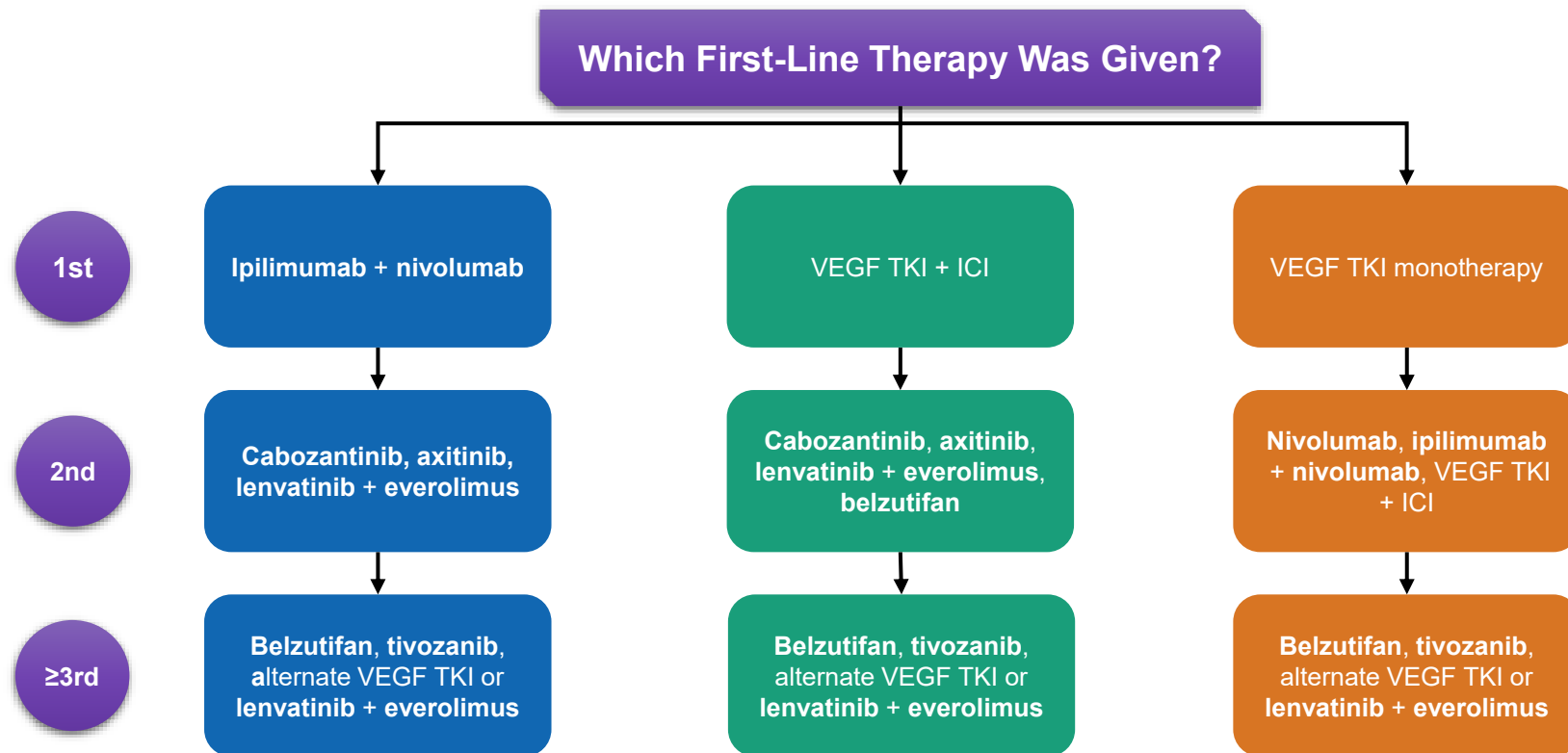
- What is the patient's age and performance status?
- How symptomatic is the disease?
- Did the patient experience significant toxicity in the 1L?
- How did the patient manage toxicity from 1L therapy?
- What comorbid conditions are present?

Shared Decisions

- What are the patient's goals for therapy?
- What is the prognosis and the patient's understanding of the prognosis?
- What is the patient's tolerance for risk and toxicity?
- What support system is available to the patient?
- How prepared are they to assist with potential challenges?

1. <https://dailynews.ascopubs.org/doi/challenges-remain-rcc-treatment-beyond-contemporary-first-line-io-therapy-second-line>.

Therapeutic Selection in Refractory Disease¹



Phase 2 CaboPoint: Pure 2L Cabozantinib^{1,2}

Key Eligibility Criteria

- Histologically confirmed, advanced, or metastatic RCC with a clear cell component
- Radiographic disease progression following ICI + ICI therapy or ICI + VEGF-targeted therapy
- No previous use of cabozantinib or untreated brain or leptomeningeal metastases

Cohort A
Patients with disease progression after dual IO (IPI + NIVO)

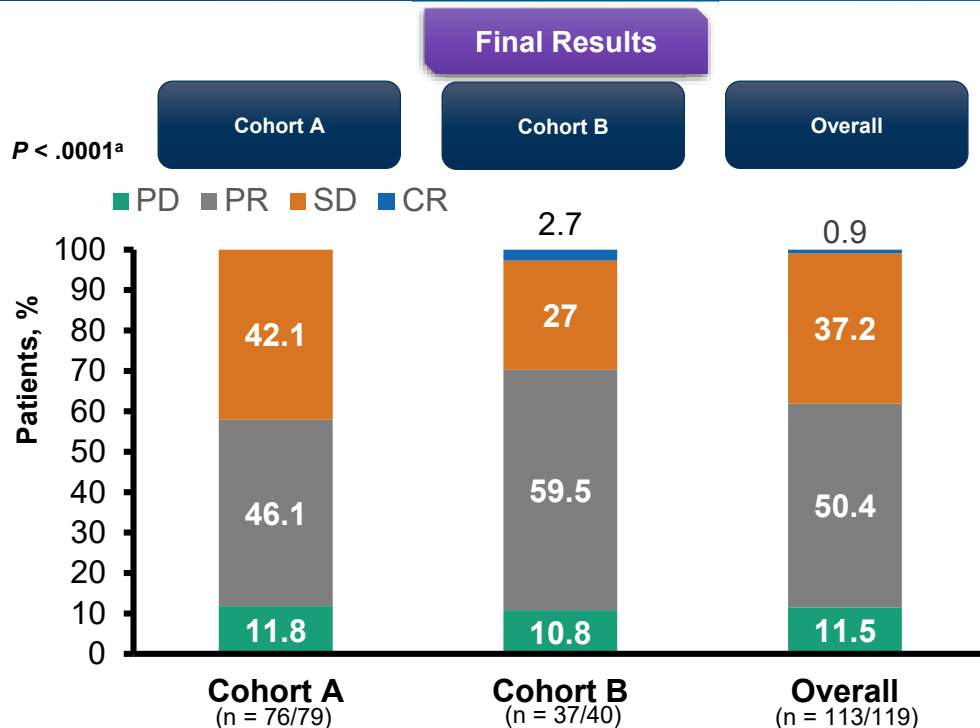
Cohort B
Patients with disease progression after IO + TKI

Cabozantinib 60 mg/day

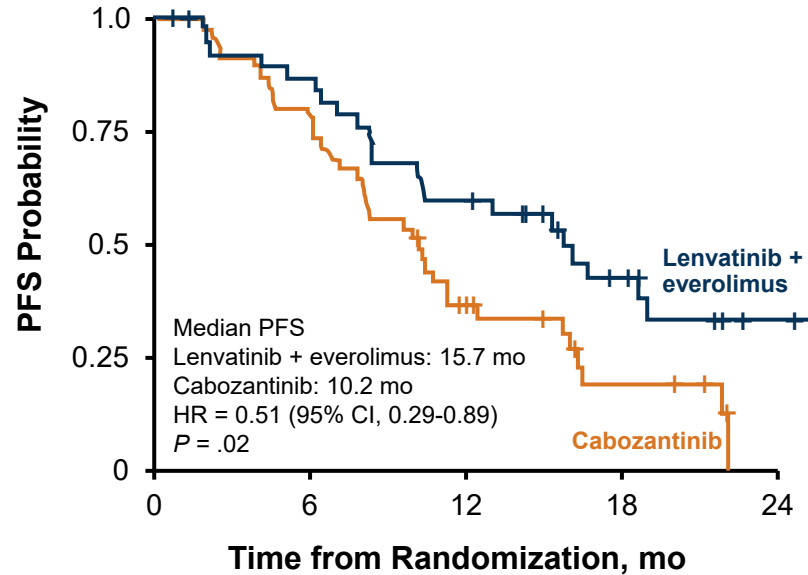
- **Primary endpoint:** ORR per RECIST v1.1 in cohort A by independent central review
- **Secondary endpoints:** ORR in cohort B by independent central review, ORR for both cohorts by local investigator review, TTR, DOR, DCR, PFS, OS, and change in disease-related symptoms, safety, and tolerability

^a Eight patients (6 in cohort A and 2 in cohort B) were excluded from the primary analysis efficacy population because they lacked baseline target lesions for central tumor assessment.

1. Albiges L et al. *Future Oncol.* 2022;18:915-926. 2. Albiges L et al. *Eur Urol.* 2026;89:210-219.



Phase 2 LEN-CABO: Lenvatinib Plus Everolimus Versus Cabozantinib After Disease Progression ¹



n (%)	Lenvatinib + Everolimus (n = 40)	Cabozantinib (n = 46)
ORR	20 (52.6)	17 (38.6)
CR	0 (0)	0 (0)
PR	20 (52.6)	17 (38.6)
SD	15 (39.5)	24 (54.5)
PD	3 (7.9)	3 (6.8)
NE	2	2

LEN-CABO: Toxicity Profile

Treatment-Related Safety Summary

n (%)	Lenvatinib + Everolimus (n = 40)	Cabozantinib (n = 46)	Odds ratio (95% CI)
Serious AEs	11 (27.5)	9 (19.6)	1.56 (0.57-4.24)
Grade $\geq$ 4 AEs	27 (67.5)	23 (50)	2.08 (0.86-5.02)
Dose interruptions	28 (70)	36 (78.3)	0.65 (0.24-1.73)
Dose reductions	23 (57)	28 (60.9)	0.80 (0.33-1.93)
Treatment discontinuation	8 (20)	5 (10.9)	2.05 (0.61-6.91)

Higher toxicity rate with combination

Any Grade TRAEs of Interest

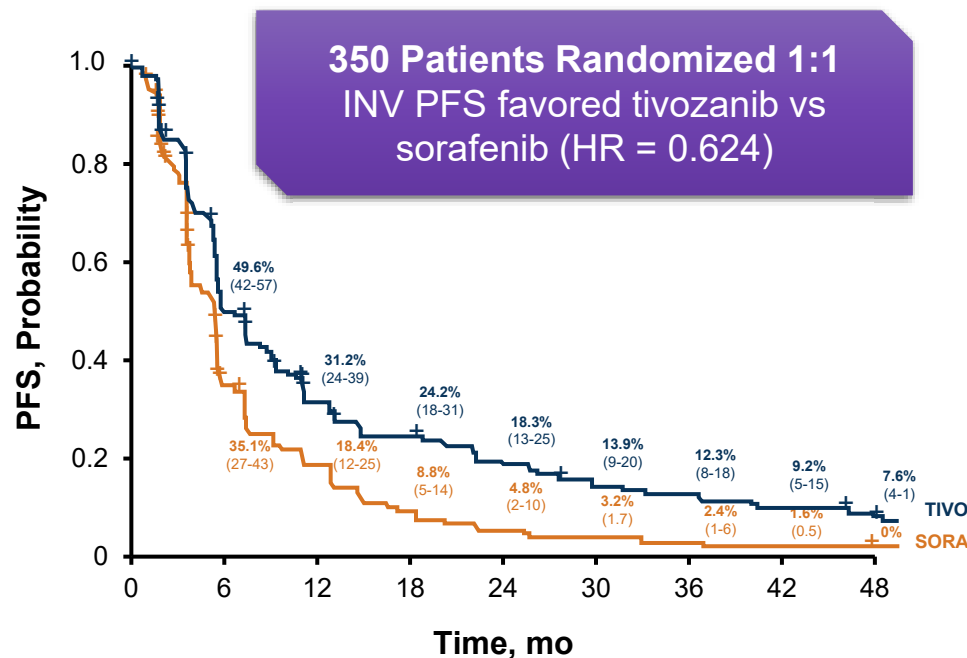
AE, n (%)	Lenvatinib + Everolimus (n = 40)	Cabozantinib (n = 46)
Diarrhea	28 (70)	34 (73.9)
Fatigue	29 (72.5)	28 (60.9)
Proteinuria	26 (65)	17 (37)
Hypertension	23 (57.5)	18 (39.1)
Nausea	16 (40)	18 (39.1)
Palmar-plantar erythrodysesthesia syndrome	8 (20)	24 (52.2)
Vomiting	13 (32.5)	16 (34.8)
Oral mucositis	6 (15)	20 (43.5)

Will this combination change practice from SOC cabozantinib?

Phase 3 TIVO-3: Tivozanib in RCC^{1,a}

FDA Approved
March 2021

Tivozanib: a selective and potent VEGFR TKI that inhibits VEGFR 1, 2, and 3 and has a long half-life



- Long-term follow-up in TIVO-3 suggests that early and consistent PFS benefit with tivozanib vs sorafenib may be associated with an improvement in OS HR over time as more events accumulate
- Tivozanib demonstrated favorable tolerability and, compared with sorafenib, was associated with fewer:
 - All-grade and grade ≥ 3 TEAEs
 - Dose reductions, interruptions, and discontinuations, despite a longer time on therapy
- Tivozanib was better tolerated than sorafenib, regardless of age or prior immune checkpoint inhibitor treatment^b

^a Data cutoff: May 24, 2021.

^b 26% received prior immunooncology therapy and a VEGFR TKI sequentially or in combination.

1. Beckerman KE et al. *Oncologist*. 2024;29:254-262.

Abstract 477/Poster C13

Title: Real-world Efficacy and Safety of Tivozanib in mRCC in a Diverse Cohort: A Multicenter Study from the City of Hope Enterprise

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Jaden C Fann

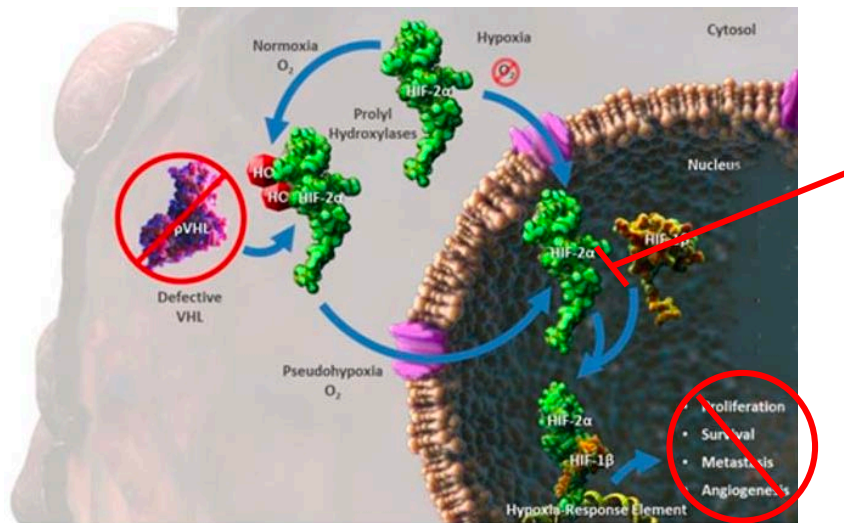
Abstract summary: multi-center, retrospective study of tivozanib-treated patients with mRCC

- Among 128 patients with mRCC treated with tivozanib, 83 had adequate follow-up data and were included in the analysis
 - Among this cohort, 72% were male and **18% were Hispanic**
 - Median of 3 lines of therapy in metastatic setting prior to tivozanib
 - At the start of therapy, the **most common metastatic sites: lungs, lymph nodes, liver, and bone**
 - **DCR: >80%; mOS was >13 months; mPFS was >6 months**

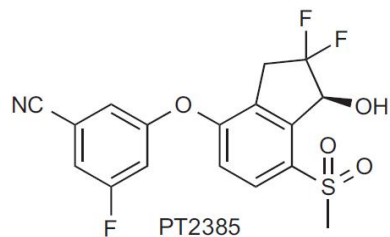
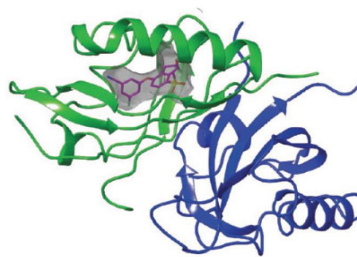
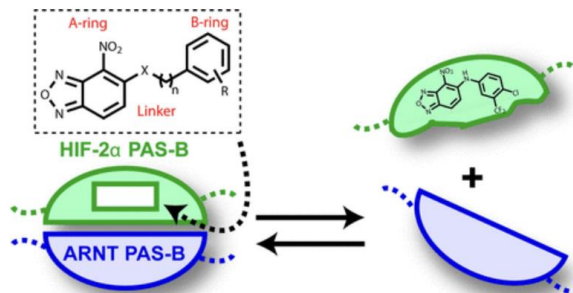
Conclusion:

- In this ethnically diverse cohort of heavily pretreated patients with mRCC and frequent rates of visceral disease, tivozanib demonstrated clinical efficacy
- The toxicity profile remained largely consistent with prior experiences

Modern Mode of Action: HIF-2 α Inhibition in RCC¹⁻³



- The HIF pathway is central to the pathophysiology of clear cell RCC and von Hippel-Lindau (VHL) disease
- **Belzutifan** is a first-in-class oral HIF-2 α inhibitor that blocks heterodimerization with HIF-1 β and downstream oncogenic pathways



1 Jonasch E et al. *New Engl J Med.* 2021;385:2036-2046. 2. Choueiri TK et al. *Nat Med.* 2021;27:802-805.

3. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-belzutifan-advanced-renal-cell-carcinoma>.

Modern Mode of Action: HIF-2 α Inhibition With Belzutifan in RCC^{1-3a}

FDA Approved
December 2023

Phase 3 Study: LITESPARK-005

Key Eligibility Criteria

- Unresectable, locally advanced, or metastatic clear cell RCC
- Previously received ≤ 3 prior systemic regimens

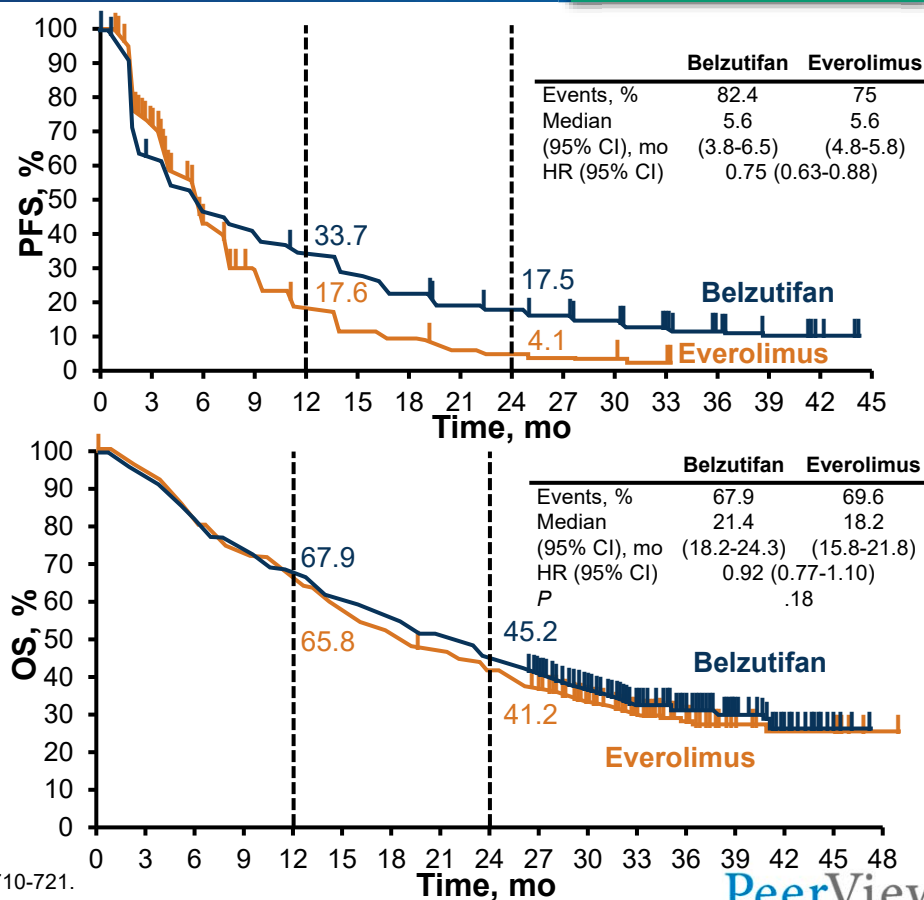
- **Primary endpoints:** PFS, OS

ORR

22.7% with belzutifan vs
3.5% with everolimus

mDOR

19.3 mo with belzutifan vs
13.7 mo with everolimus



Data cutoff date: April 15, 2024. Median follow-up: 35.8 months.

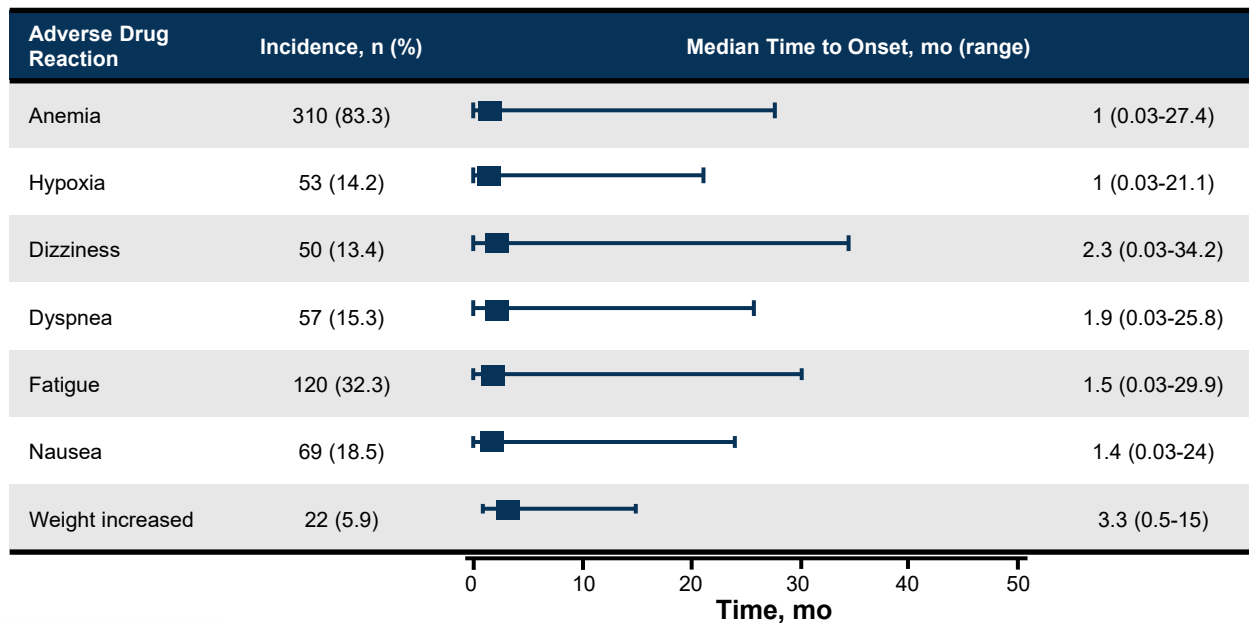
1. <https://clinicaltrials.gov/study/NCT04195750>. 2. Choueiri TK et al. *N Engl J Med*. 2024;391:710-721.

3. Rini BI et al. ESMO 2024. Abstract LBA74.

Most Common Any-Grade Adverse Drug Reactions Had a Median Time to Onset of Less Than 2 Months¹

- Fewer patients discontinued belzutifan (6.2%) vs everolimus (15.3%) due to any-cause AEs
- Median duration of therapy was longer with belzutifan (7.6 months vs 3.9 months)
- Rate of grade ≥ 3 treatment-related AEs (39.5% vs 40%) was similar between arms

Time to the First Onset of Common Any-Grade AEs Attributed to Belzutifan (Adverse Drug Reactions)

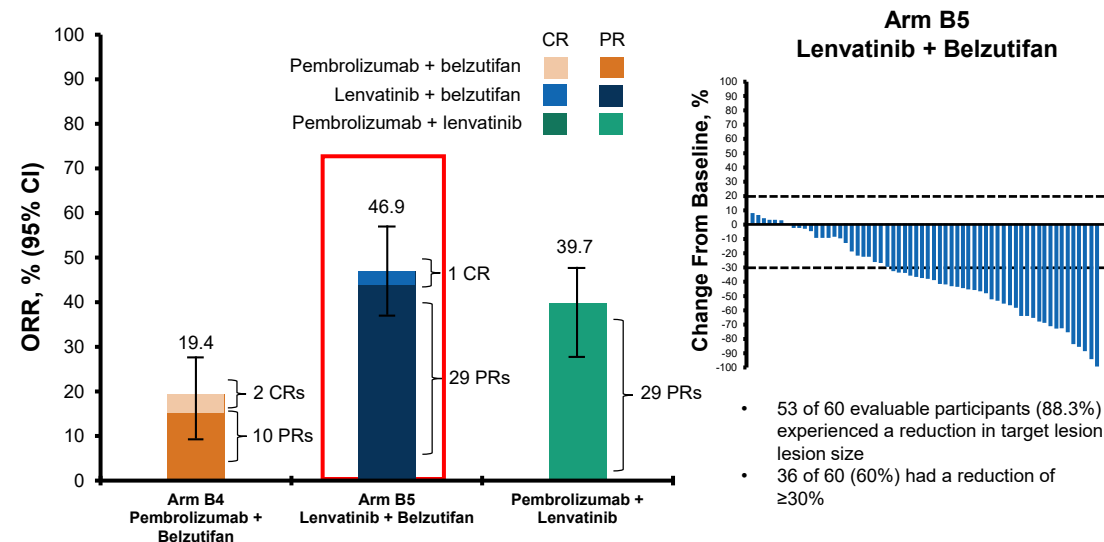


PRO results indicated better disease-specific symptoms and QOL with belzutifan compared with everolimus in patients with advanced clear cell RCC²

What About a Combination Approach? Belzutifan Plus TKI

2026
ASCO GU
SYMPOSIUM

Phase 1/2 KEYMAKER-U03B: Belzutifan + Lenvatinib (Arm B5)^{1,2a}



^a mPFS of 12.5 months.

1. Albiges L et al. ASCO 2023. Abstract 4553. 2. Beckermann K et al. ASCO GU 2025. Abstract 440.

Abstract 505/Poster D15

Title: KEYMAKER-U03 Substudy 03B:
Novel Investigative Regimens for Previously
Treated Advanced ccRCC

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Laurence Albiges

Abstract Summary

ORR: bel + len: 50%; pembro + len: 44%

mOS: bel + len: >36 mo; pembro + len: >35 mo

Conclusions

- Bel + len continued to demonstrate high antitumor activity followed by pembro + len
- Pembro + bel activity was similar to historical bel monotherapy
- The HIF/VEGF axis continues to represent a key therapeutic target in previously treated clear cell RCC and warrants further investigation

What About a Combination Approach? Belzutifan Plus TKI

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Phase 3 LITESPARK-011: Belzutifan + Lenvatinib vs Cabozantinib¹

Key Eligibility Criteria

- Unresectable, locally advanced, or metastatic clear cell RCC
- Disease progression after first- or second line anti-PD-1/PD-L1 therapy or as neoadjuvant/adjuvant treatment with progression on or within 6 mo of last dose
- Therapy immediately preceding must be anti-PD-1/PD-L1
- Received ≤2 prior systemic regimens
- Measurable disease per RECIST v1.1
- KPS score ≥70%
(N = 708)

R

1:1

Belzutifan
120 mg/d orally
+ **lenvatinib**
20 mg/d orally
(n = 354)

Cabozantinib
60 mg/d orally
(n = 354)

- **Stratification:** IMDC (0 vs 1-2 vs 3-6), line of anti-PD-1/PD-L1 treatment (adj or 1L vs 2L), geographic region (NA vs W Eur vs ROW)
- **Primary endpoints:** PFS and OS
- **Secondary endpoints:** ORR, DOR, and safety

^a OS will be tested at a subsequent analysis per the clinical protocol.

1. <https://clinicaltrials.gov/study/NCT04586231>. 2. <https://www.eisai.com/news/2025/news202575.html>. 3. <https://www.merck.com/news/merck-and-eisai-announce-welireg-belzutifan-plus-lenvima-lenvatinib-met-primary-endpoint-of-progression-free-survival-pfs-in-certain-previously-treated-patients-with-advanced-renal-c/>

LBA 417

Title: Belzutifan Plus Lenvatinib vs Cabozantinib for Advanced RCC After PD-(L)1 Therapy: Open-label Phase 2 LITESPARK-011 Study

Oral Abstract Session C

Saturday, February 28, 2026, at 8:15 AM PST

Presenter: Robert J. Motzer

Press Release (October 2025)²

- LITESPARK-011 met primary endpoint of PFS
 - Statistically significant and clinically meaningful improvement in PFS compared with cabozantinib
- Statistically significant improvement in key secondary endpoint of ORR compared to cabozantinib
- A trend toward improvement in OS was observed; however, this result did not reach statistical significance at the time of this interim analysis^a

What About a Combination Approach? Belzutifan Plus Zanzalintinib

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~30% of patients experience a recurrence within 3 years of initiating adjuvant pembrolizumab

~80 % of eligible adjuvant RCC patients in the United States currently receive pembrolizumab

Phase 3 LITESPARK-033¹ Belzutifan + Zanzalintinib in mRCC Post-Adjuvant IO

Key Eligibility Criteria

- Clear cell RCC
- No prior treatment for mRCC (except adjuvant for M1 NED)
- Disease recurrence during adjuvant IO or post-adjuvant IO (≤ 24 mo) (N = 904)



- **Primary endpoints:** PFS and OS
- **Key secondary endpoints:** ORR, DOR, and QOL

Abstract TPS579/Poster J8

**Title: Phase 1b/2 KEYMAKER-03
Substudy 03C of Belzutifan Plus Zanzalintinib or
Belzutifan Monotherapy for Recurrent ccRCC
During or After Anti-PD-(L)1 Therapy**

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Robert J. Motzer

Abstract summary: safety and efficacy of bel + zanza (Arm C1) or bel monotherapy (Arm C2)

Safety Lead-In Phase

- Arm C1a: bel 120 mg I + zanza 60 mg
- Arm C1b: bel 120 mg + zanza 100 mg
- Primary endpoint: RP2D

Efficacy Phase

- N = ~120; R2:1 bel+ zanza (RP2D) vs bel 120 mg
- Primary endpoint: safety, ORR
- Currently enrolling

1. <https://clinicaltrials.gov/study/NCT07227402>.

Rapid Oral Abstract 423

Title: Ascending Dose Escalation of Belzutifan Plus Palbociclib for Previously Treated Advanced ccRCC: Phase 1/2 LITESPARK-024 Study Part 1

Rapid Oral Abstract Session C

Saturday, February 28, 2026, at 1:00 PM PST

Presenter: David F. McDermott

Abstract Summary

- Novel MOAs remain an unmet need for patients with advanced clear cell RCC with PD after multiple therapies
- **Combination of HIF-2 α and CDK4/6 inhibitors** showed synthetic lethality in preclinical clear cell RCC models
- Phase 1/2 LITESPARK-024 study evaluates safety and efficacy of **belzutifan** + the CDK4/6 inhibitor **palbociclib** in patients with advanced clear cell RCC with PD after ≥ 2 systemic regimens, including both IO and VEGFR-TKI therapy, and no prior HIF-2 α and CDK4/6 inhibitors

Conclusion:

- Bel + palbo had a manageable safety profile
- No TRAEs grade ≥ 3 were frequent; no new safety signals occurred

Abstract 545/Poster F3

Title: Biomarker Analysis from the Phase 2 LITESPARK-013 Study of 2 Different Belzutifan Doses in Participants with Advanced ccRCC

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Neeraj Agarwal

Abstract Summary

Exploratory biomarker analysis (including HIF-2 α IHC, RNAseq, and WES)

- HIF-2 α TPS and H-score potentially associated with PFS
- *BAP1* mutation was potentially predictive of improved ORR
- Molecular subtypes, other RCC-related signatures, and *VHL* mutation showed no association with ORR, PFS, or OS

Abstract 528/Poster E12

Title: Genomic and Clinical Correlates of Belzutifan Treatment in RCC: A Retrospective Analysis of 240 RCC Patients

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Yu-Wei Chen

Abstract Summary

- DNA and RNA sequencing carried out on 240 samples from patients treated with belzutifan and stratified into responders and nonresponders
- Responders exhibited enrichment for alterations in the PI3K/AKT/mTOR pathway and DNA damage response alterations
- Nonresponders showed higher frequencies in chromatin remodeling mutations
- Warrants further investigation

HIF-2 α Inhibition With Casdatifan in RCC

Phase 1 ARC-20 Dose-Escalation and Dose-Expansion Study of Casdatifan in 2L+ Clear Cell RCC¹

- Promising clinical activity across doses (N = 93)
 - 50 mg BID, 25% ORR
 - 50 mg QD, 29% ORR
 - 100 mg QD, 33% ORR
- Well tolerated, with a comparable safety profile across doses

Preliminary Confirmed Tumor Response Rate With Casdatifan + Cabozantinib

	(n = 24) ^a
Median follow-up, mo (range)	5.3 (2.8-9.1)
Confirmed ORR^b, % (n)	46 (11)
(95% CI)	(25.6-67.2)
BOR, n (%)	
CR	1 (4)
PR ^b	10 (42)
SD	12 (50)
PD	1 (4)

Data cutoff date: March 14, 2025.

^a All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.

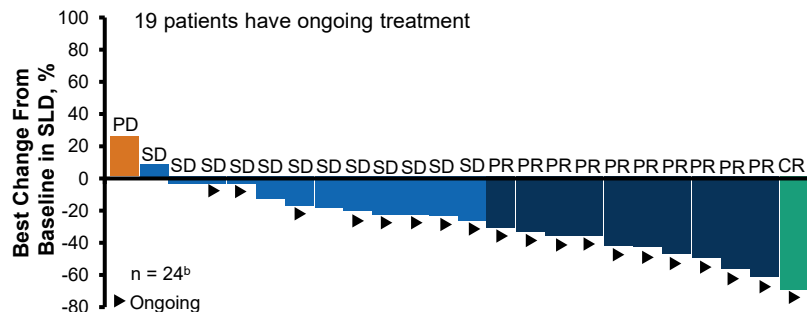
^b Inclusive of one patient who had confirmed PR after March 14, 2025.

1. Choueiri TK et al. ASCO GU 2025. Abstract 441. 2. Choueiri TK et al. ASCO 2025. Abstract 4506.

Phase 1 ARC-20 Casdatifan + Cabozantinib Expansion Cohort²

- N = 27 previously treated clear cell RCC
 - Most common all grade AEs: anemia and fatigue
 - Most common grade ≥ 3 AEs: anemia and hypoxia
 - No cardiac events
 - ORR = 46%
 - Activity was seen across all IMDC risk groups

Preliminary^a Change in Measurable Disease With Casdatifan + Cabozantinib



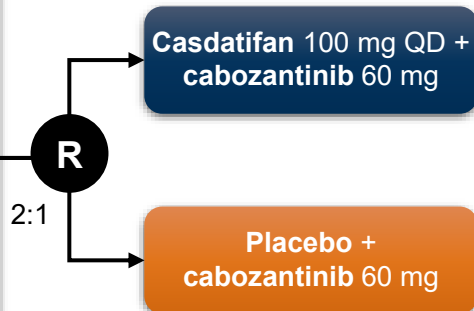
HIF-2 α Inhibition With Casdatifan in RCC

2026
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Phase 3 PEAK-1¹ Casdatifan + Cabozantinib in mRCC Following Prior PD-1 Therapy

Key Eligibility Criteria

- Unresectable, locally advanced or metastatic clear cell RCC
- Measurable disease per RECIST v1.1
- Have had prior anti-PD-1/PD-L1 therapy
- Have not received cabozantinib
- HIF-2 α -inhibitor naïve (N = ~700)



- **Primary endpoint:** PFS
- **Key secondary endpoint:** OS

Abstract 493/Poster D3

Title: Activity and Biomarker Analyses with Casdatifan, a Next-Generation HIF-2 α Inhibitor, in Refractory ccRCC: Results from ARC-20

Poster Session C

Saturday, February 28, 2026, at 7:00 AM PST

Presenter: Toni K. Choueiri

Abstract Summary

- Cas elicits reductions in serum erythropoietin (sEPO)
- Data are reported from cas monotherapy expansion cohorts from phase 1 ARC-20 assessing change in sEPO and correlated with efficacy
- Deep sEPO reduction was observed by study week 2 and sustained through week 52
- Deeper sEPO reduction was associated with higher rates of CR/PR and lower rates of PD

1. <https://clinicaltrials.gov/study/NCT07011719>.

Panel Discussion: Treatment Decisions for Refractory mRCC

**Jose,
a 72-year-old man**

- Dual IO in 1L
- **Progresses...**
- IO + TKI in 1L
- **Progresses...**

Discussion



How do you approach 2L and beyond...

What would you discuss with Jose?

- Treatment sequencing?
- Monotherapy?
 - Cabozantinib?
 - Belzutifan?
 - Tivozanib?
- Combinations? / Enroll on a clinical trial?
 - Len + ev
 - Zanza + belzutifan
 - Len + belzutifan
 - Cas + cabo
- Tolerability and AE impact?
- Impact of DOR?

Tool to Support Patients Searching for Clinical Trials in RCC

Download the Practice Aid!

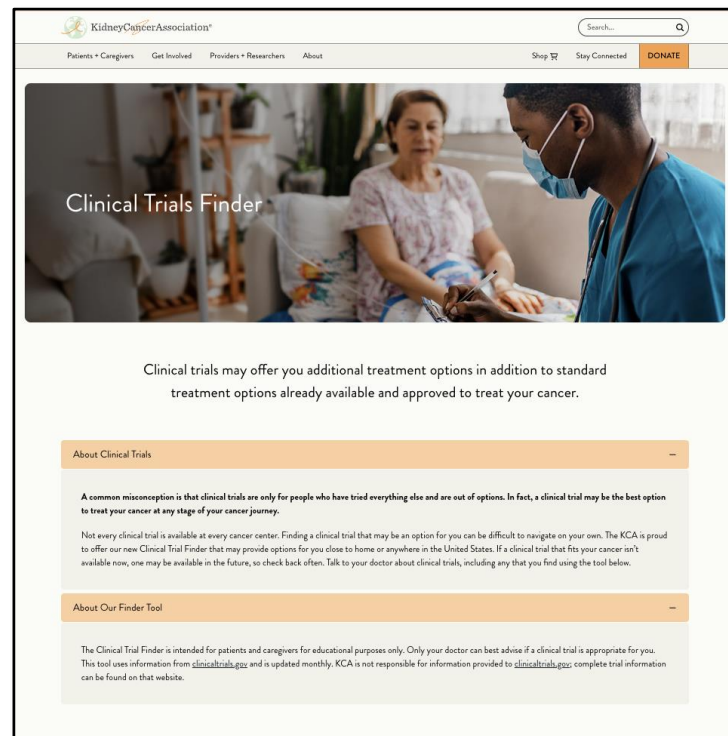
The KCA **Clinical Trial Finder** enables patients and their caregivers to search for clinical trials based on their condition and geographic location (ie, state).

Find a Clinical Trial

Filter by Condition Filter by State

Select a Condition ▼ Select a State ▼ [Reset Filters](#)

- Uses information from clinicaltrials.gov
- Updated monthly



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Abbreviations

1L: first line	IO: immuno-oncology	PRO: patient-reported outcome
2L: second line	irAE: immune-related adverse event	Q12W: every 12 weeks
AES: adverse events of special interest	ITIM: immunoreceptor tyrosine-based inhibitory motif	Q3W: every 3 weeks
ASCO GU: American Society of Clinical Oncology Genitourinary	KCA: Kidney Cancer Association	Q6W: every 6 weeks
ASCO: American Society of Clinical Oncology	KPS: Karnofsky performance status	QD: once daily
BCR: B-cell receptor	MDSC: myeloid-derived suppressor cell	RCC: renal cell carcinoma
BICR: blinded independent central review	MHC: major histocompatibility complex	RECIST: Response Evaluation Criteria in Solid Tumours
BID: twice daily	mOS: median overall survival	ROW: rest of world
CBT: cognitive-behavioral therapy	mPFS: median progression-free survival	RWD: real-world data
ccRCC: clear cell renal cell carcinoma	mRCC: metastatic renal cell carcinoma	SAE: severe/serious adverse event
CD: cluster of differentiation	NCCN: National Comprehensive Cancer Network	SC: subcutaneous
CR: complete response	NE: not evaluated	SD: stable disease
CTLA-4: cytotoxic T-lymphocyte associated protein 4	NED: no evidence of disease	SITC: Society for Immunotherapy of Cancer
DCR: disease control rate	NF- κ B: nuclear factor kappa-light-chain-enhancer of activated B cells	SPM: second primary malignancy
DFS: disease-free survival	NR: not reached	TGF- β : transforming growth factor-beta
DOR: duration of response	ORR: objective response rate	TIGIT: T cell immunoreceptor with Ig and ITIM domains
EMA: European Medicines Agency	PD-1: programmed cell death protein 1	TRAE: treatment-related adverse event
ESMO: European Society for Medical Oncology	PD-L1: programmed cell death-ligand 1	VEGFR: vascular endothelial growth factor receptor
HIF-2 α : hypoxia-inducible factor 2-alpha	PD: partial disease	VEGFR2: vascular endothelial growth factor receptor 2
ICI: immune checkpoint inhibitor	PGJ: prostaglandin	
IKCS: International Kidney Cancer Symposium	PO: orally	
IL: interleukin	PPAR: peroxisome proliferator-activated receptors	
IMDC: International Metastatic RCC Database Consortium	PPE: palmar-plantar erythrodysesthesia	
	PR: partial response	