3rd Annual Southern California Genitourinary Cancer Research Forum

Case-Based Trial Discussion: Localized Renal Cell Carcinoma (RCC), Front-line RCC, Salvage RCC, Non-Clear Cell RCC

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Speakers:

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Nataliya Mar, MD

Brian Shuch, MD

Hyung Kim, MD

Wesley Yip, MD

Disclosures

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This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Disclosures

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- *Consultant for Merck, Veracyte, and Telix. On the Speakers Bureau for Histosonic.*

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- *Consultant for Dendrion. Other Financial Relationship – License through Crown Bioscience.*

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- *Consultant for Telix. Grant/Research Support from Merck and Pfizer.*

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

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Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *How to enroll minority populations to trials.*
- *What issues do minority populations face with trial enrollment.*
- *Barriers to cross cultural inclusion in clinical trials.*
- *Disparities in care of under-represented patients.*
- *Gender differences in bladder cancer.*
- *Address tertiary care practice and how that may differ from a community practice setting.*

Kidney Cancer – Localized Disease

Non-Operative Management for Localized RCC

UCLA Health

Inclusion

- cT1/T2a, N0M0
- 1-2 lesions
- >80% solid
- not eligible for resection
- Not eligible for ablation
- No bilateral masses
- eGFR >45

Screening Cone Beam Angiogram

Y90 glass microspheres (Therasphere) planned dose 400 Gy

Primary Objective:

- To assess safety and toxicity

Secondary Objectives:

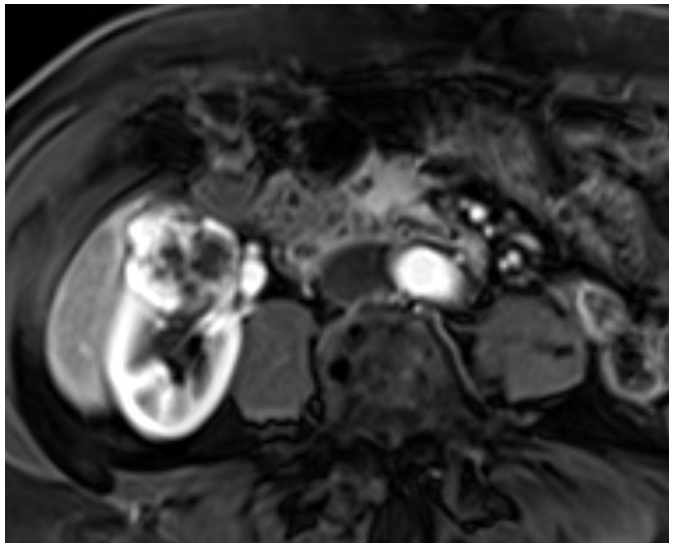
- response (Choi, RECIST, and modified RECIST criteria)
- time to disease progression
- RFS and OS
- renal functional changes
- QoL metrics

- SBRT delivers ~42 Gy that is moderately effective but has *renal toxicity*
  -FASTRACKII dropped eGFR 60→43 at 1 year
- y90 microspheres in the liver delivers high radiation doses with *low toxicity*
- UCLA Trial RENEGADE assesses 400 Gy treatment in localized RCC

NCT06432036

Contact: PI: Sid Padia, Co-PI Brian Shuch

Case Example



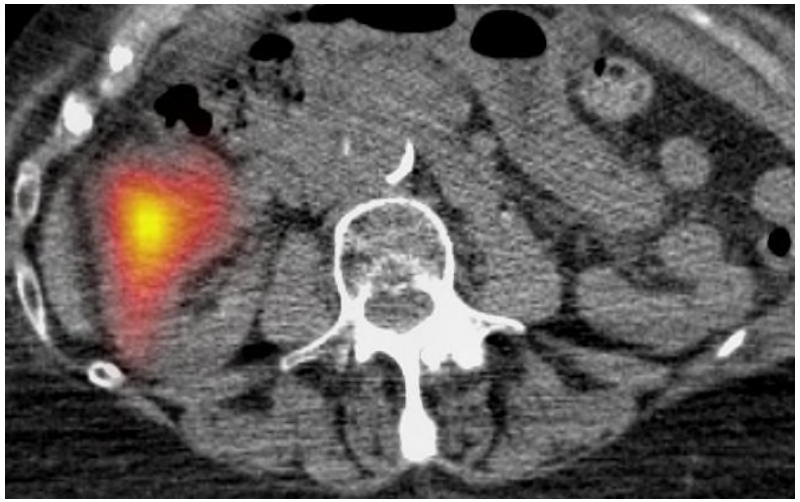
87-year-old woman
Clear cell RCC
Not interested in surgery

3.9 cm RCC
T1aN0M0

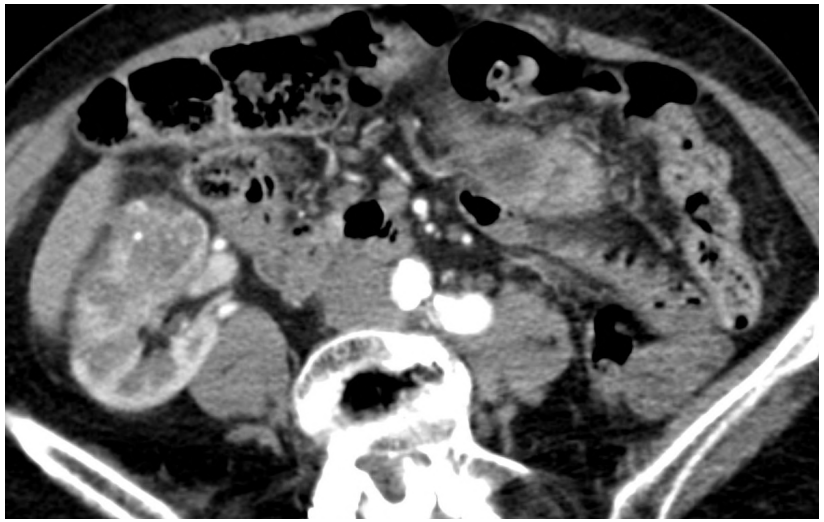
eGFR baseline 75→ 3 months 78

Angiogram

Y90 SPECT



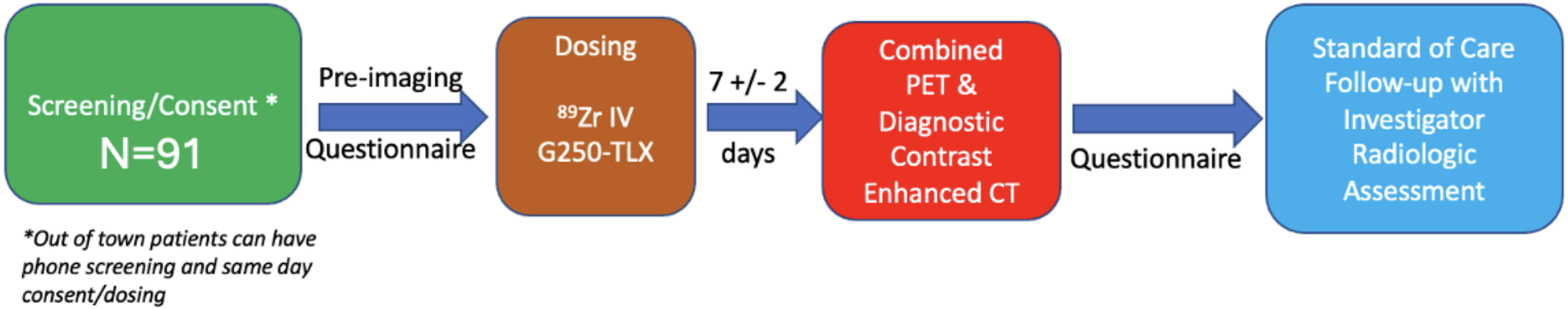
3 months



CA-NINE Trial @ UCLA

89-Zr-TLX250 PET/CT vs Contrast-Enhanced CT for Detection of Recurrent Clear Cell Renal Cell Carcinoma After Surgery

UCLA Health



**Out of town patients can have phone screening and same day consent/dosing*

- Patients will have first post-op imaging 4-16 weeks after surgery
- Adjuvant therapy plan does not impact participation

- 1˚ Endpoint: lesion detection (+/patient) (PET CT vs CT)
- 2˚ Endpoint: PPV for those with lesion validation, RFS, impact on management

Opened 9/2024, Enrollment 30/91
Soon to Pause for First Look At Data

NCT06447103

CA NINE Patient Example

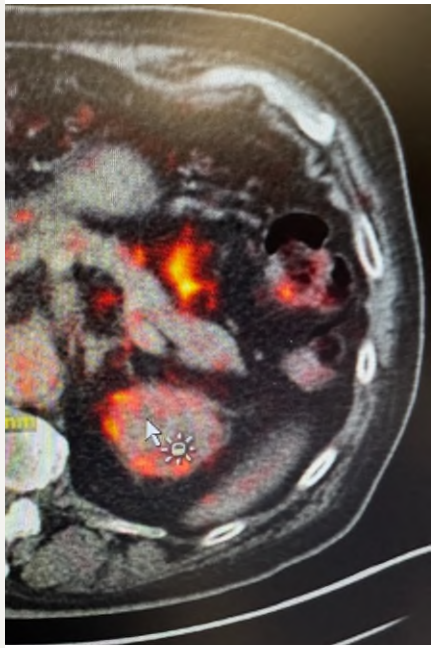
UCLA Health

Keck School of Medicine of USC

Special Thanks!

SARMAD SADEGHI, MD, PHD

Associate Professor of Clinical Medicine and Urology



31 x 25 mm SUV max 58.6
Not clearly seen on CT w/IV contrast

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Kidney Cancer – Perioperative Therapy

Kidney Cancer – Neoadjuvant Therapy

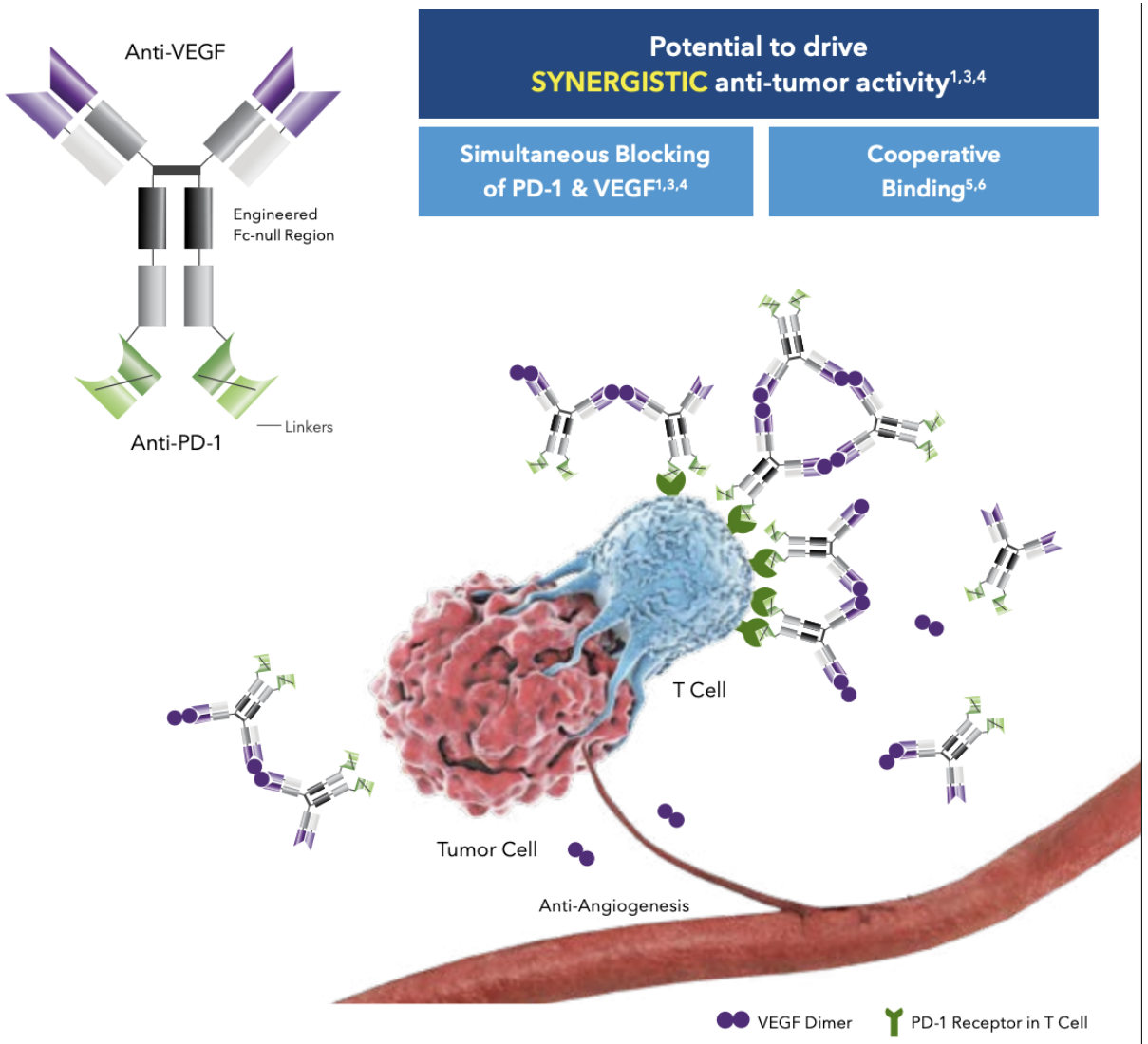
Case Presentation

- A 60-year-old man presents with a 9.5 cm right renal mass identified on CT urogram during evaluation for flank pain. Further staging reveals no evidence of lymphadenopathy or distant metastasis (cT3aN0M0). Percutaneous biopsy confirms clear cell renal cell carcinoma, Fuhrman grade 3. He is otherwise healthy (ECOG 0), with no relevant comorbidities.

➡️ **High-risk localized clear cell RCC (cT3aN0M0, Fuhrman grade 3)**

a) Radical nephrectomy alone
b) Neoadjuvant immunotherapy as part of a clinical trial
c) Deferred surgery with active surveillance
d) Systemic therapy with ICI+TKI

A Phase II Trial of Neoadjuvant Ivonescimab in Patients with High-Risk, Localized RCC



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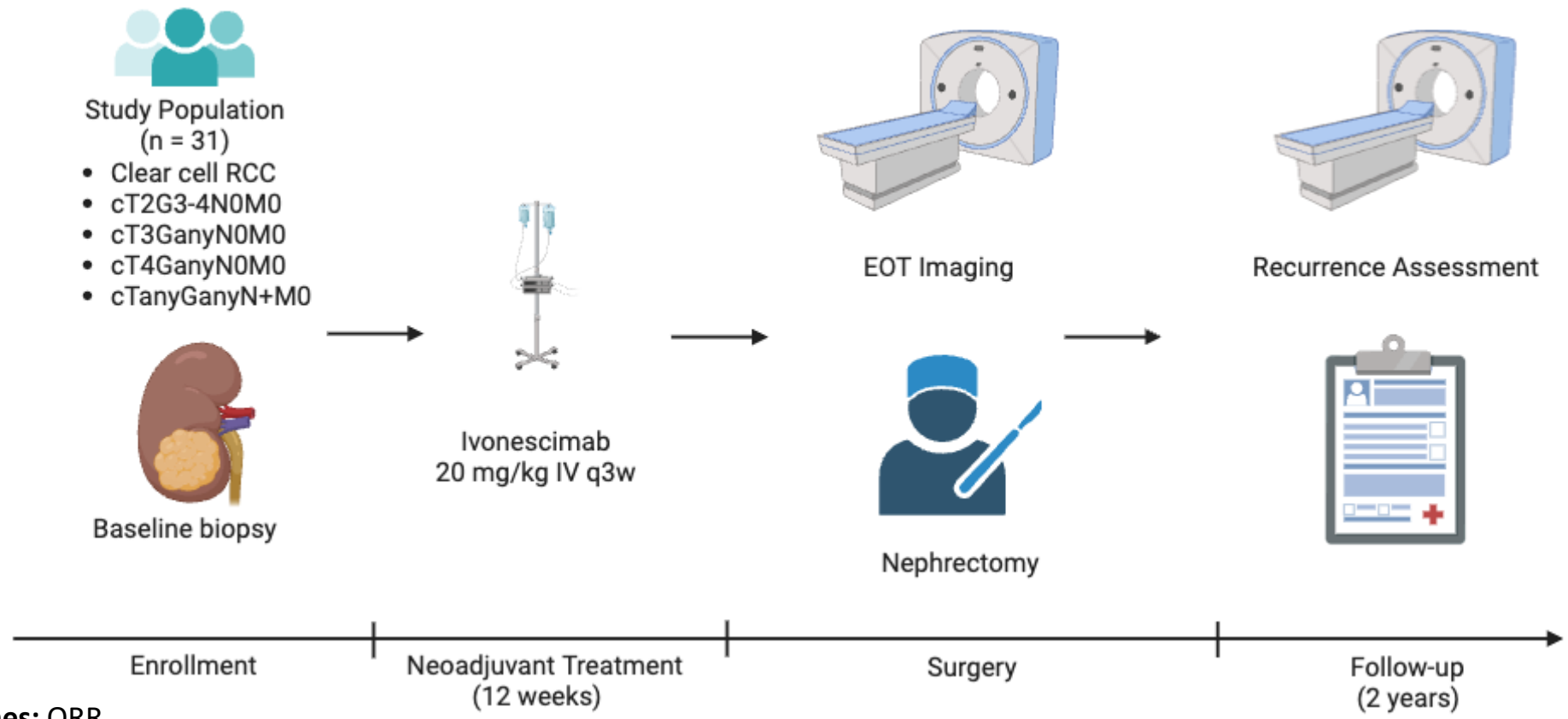
A Phase II Trial of Neoadjuvant Ivonescimab in Patients with High-Risk, Localized RCC



Primary Outcomes: ORR
Secondary Outcome: Toxicity, surgery feasibility, pathologic response, KIM-1, RFS, OS
Exploratory Outcomes: QOL

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Kidney Cancer – Adjuvant Therapy

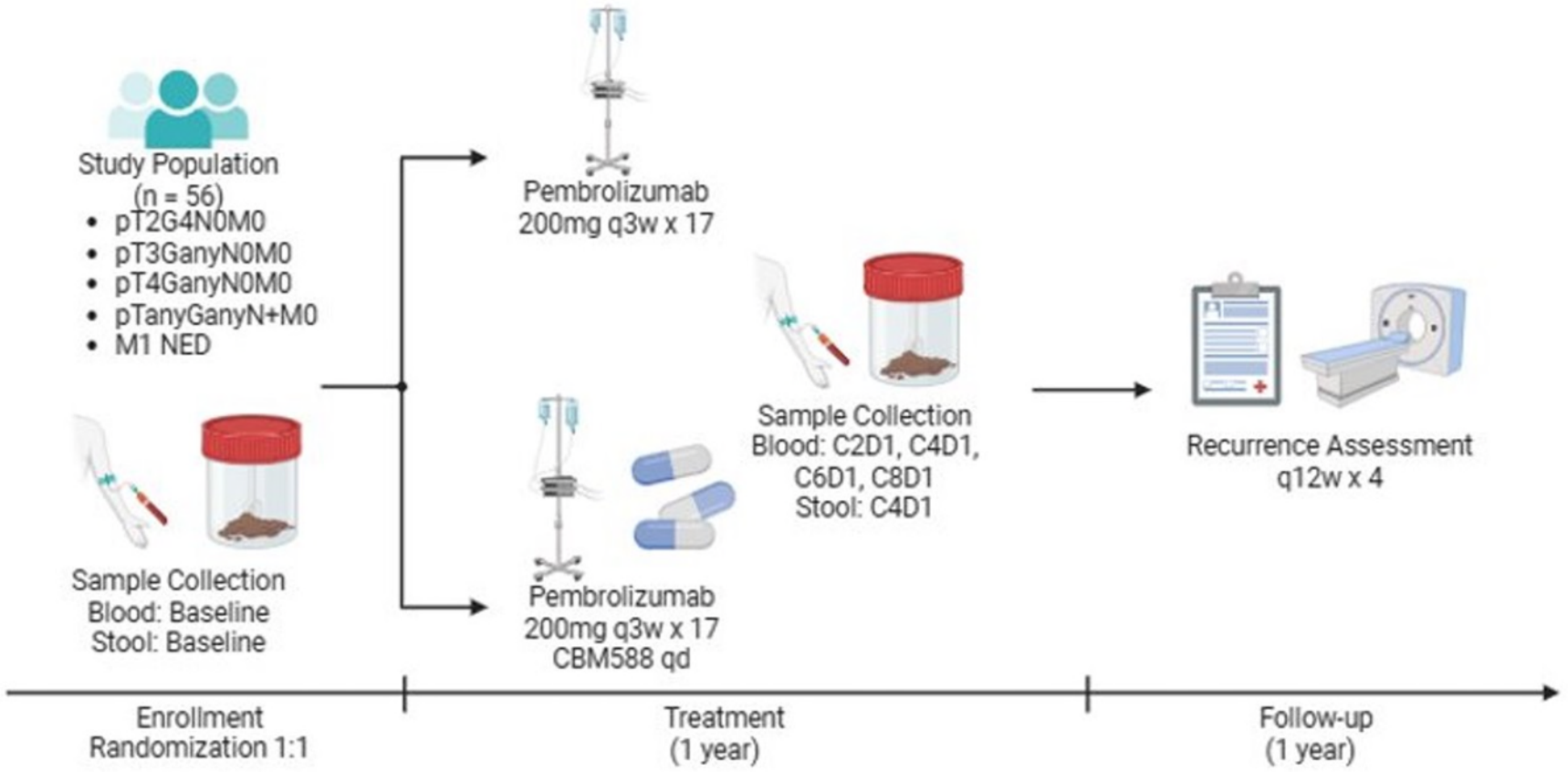
Case Presentation

- A 62-year-old man underwent radical nephrectomy for a 7.5 cm left renal mass. Final pathology revealed clear cell RCC, Fuhrman grade 4, with pT3a extension into perinephric fat, negative margins, and no lymph node involvement. No evidence of metastatic disease on staging CT scans. He is now 6 weeks post-surgery, recovering well, and is being evaluated for adjuvant therapy due to high risk of recurrence.

➡️ **High-risk localized clear cell RCC (pT3aN0M0, Grade 4) post-nephrectomy**

a) Observation with imaging surveillance
b) Adjuvant pembrolizumab
c) Adjuvant pembrolizumab + CBM588 (clinical trial)
d) Adjuvant pembrolizumab + tivozanib (clinical trial)

Impact of microbiome modulation with CBM588 in combination with pembrolizumab for adjuvant therapy of high-risk, resected renal cell carcinoma (RCC)



Primary Outcomes: Change in IL-12
Secondary Outcome: RFS, OS, stool microbiome, circulating cytokines
Exploratory Outcomes: QOL

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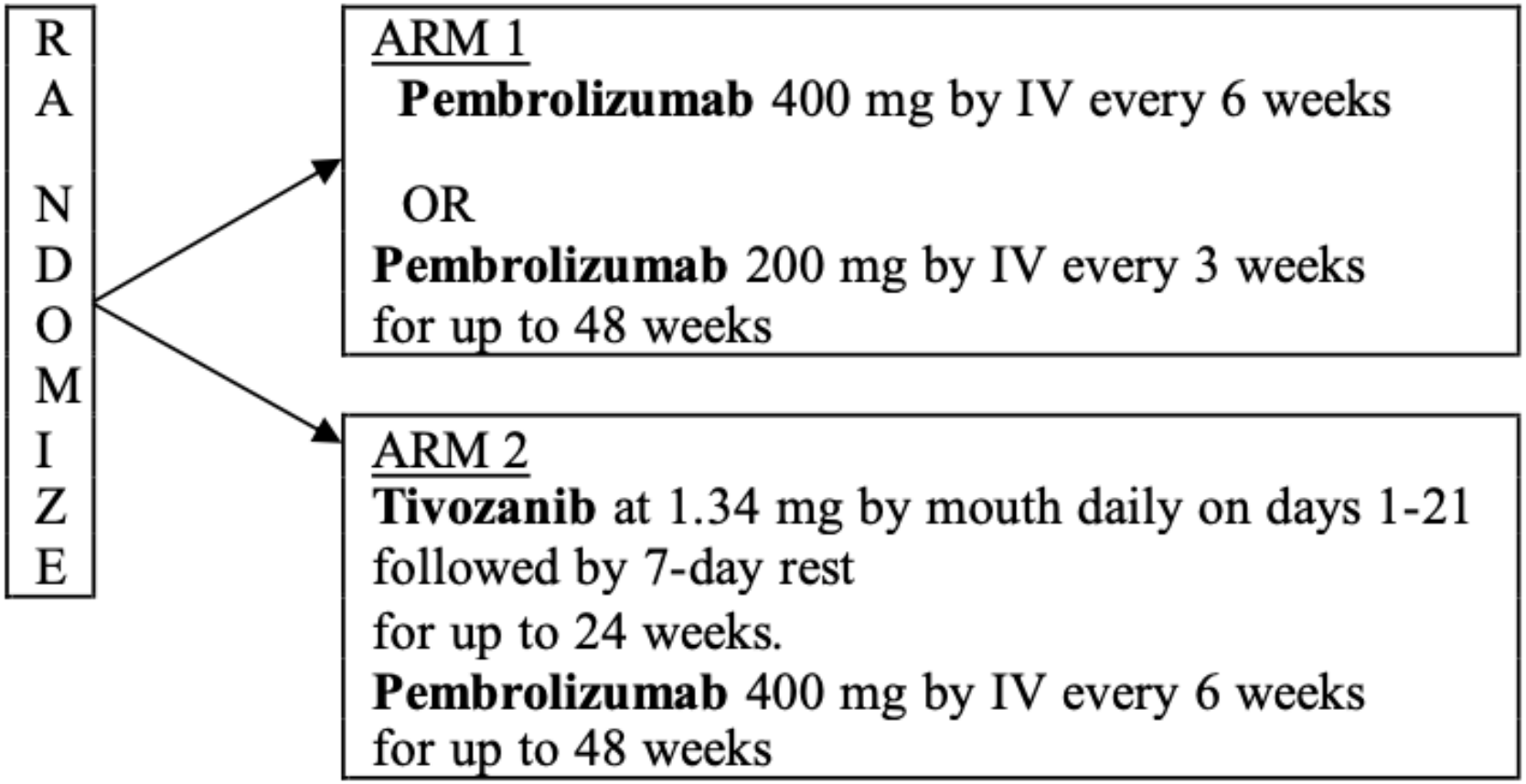
Short TeRm Intensified Pembrolizumab (KEytruda) and Tivozanib for High-Risk Renal Cell Carcinoma - STRIKE

Schema

1 Cycle = 12 weeks



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Kidney Cancer – Consolidation Therapy

Kidney Cancer – Consolidation Therapy

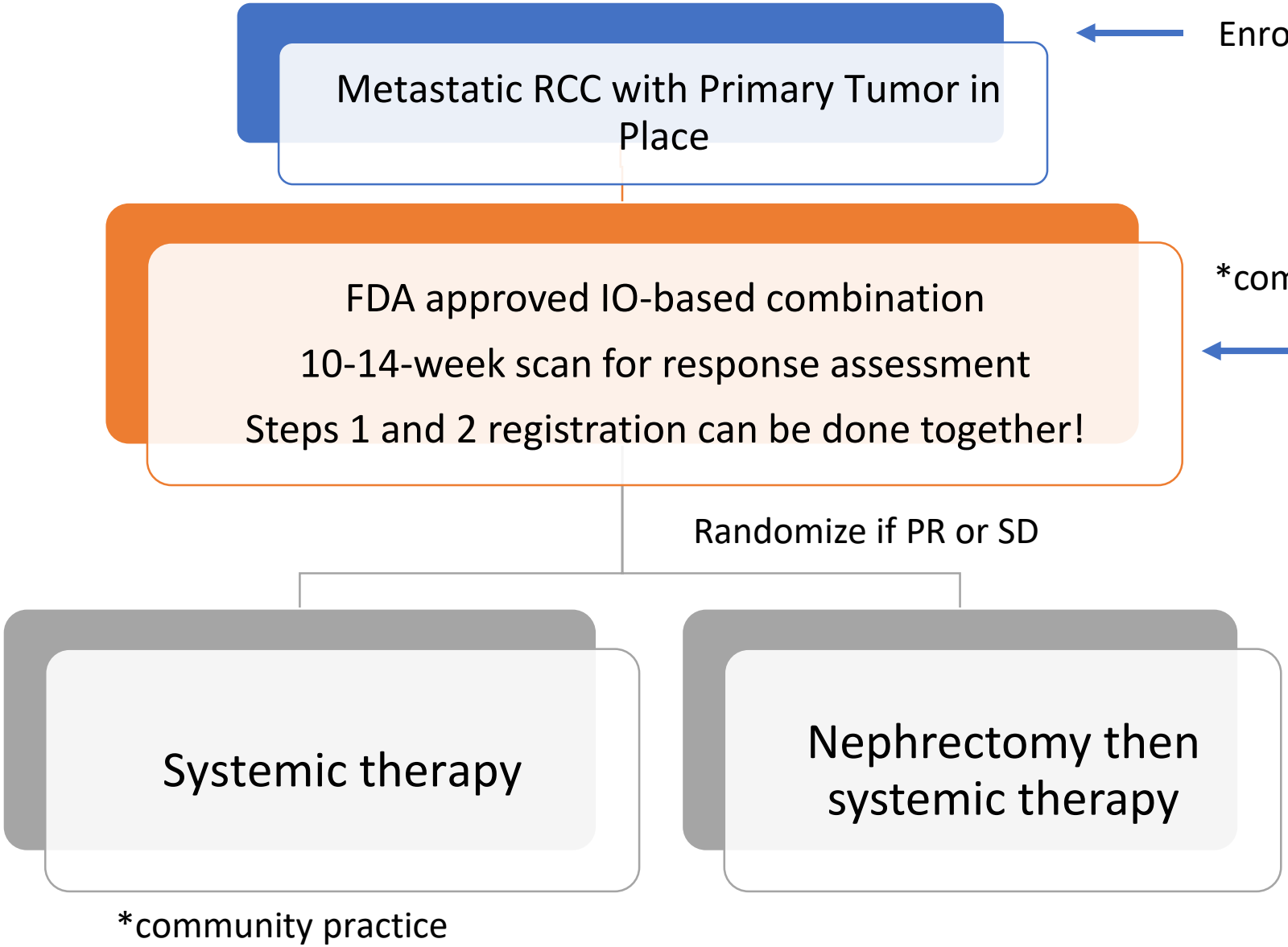
Case Presentation

- A 65-year-old man is diagnosed with metastatic clear cell renal cell carcinoma (ccRCC). Imaging reveals an 8 cm right renal mass and bilateral pulmonary metastases, with no liver, brain, or bone involvement. Biopsy confirms ISUP grade 2 ccRCC. He initiates nivolumab + cabozantinib per standard of care. A 12-week CT scan shows a partial response in lung metastases, and the primary tumor remains stable. He is ECOG 0, with good performance status and preserved renal function.

➡️ **Metastatic ccRCC with intact primary tumor**
➡️ **Initial response to immune checkpoint inhibitor-based therapy**

a) Cytoreductive nephrectomy
b) Continuation of systemic therapy without nephrectomy
c) Local therapy with radiation (e.g. SBRT to lung lesions)

SWOG 1931/PROBE Trial



Primary Endpoint:
Overall Survival

(Powered for 12 month improvement)

NCT04510597

Kidney Cancer – Post-Adjuvant Recurrence Therapy

Kidney Cancer – Post-Adjuvant Therapy

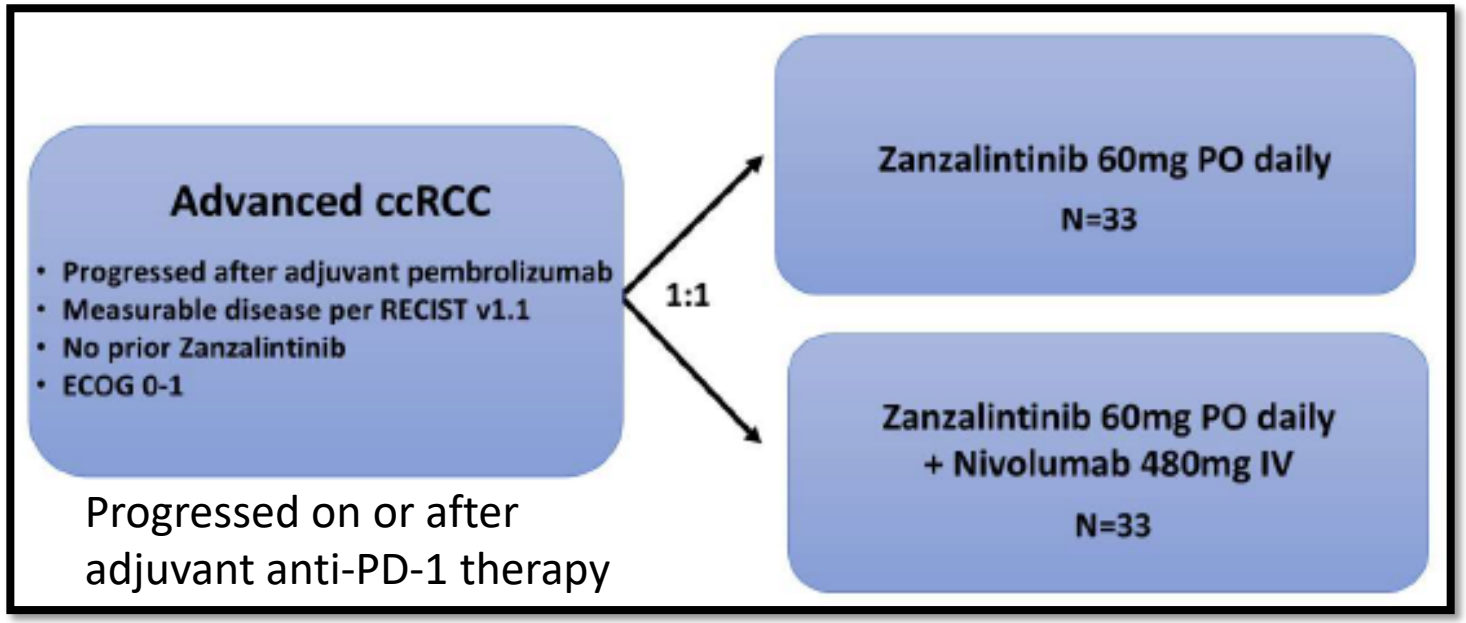
Case Presentation

- A 66-year-old man underwent nephrectomy for clear cell renal cell carcinoma (ccRCC) and completed one year of adjuvant pembrolizumab. Three months after completing therapy, routine imaging revealed new bilateral pulmonary nodules consistent with metastatic recurrence. ECOG performance status is 0, and he has no prior VEGFR-TKI exposure. Molecular profiling is unremarkable.

➡️ **Recurrent ccRCC after adjuvant PD-1 inhibitor**

a) Nivolumab + Ipilimumab
b) Cabozantinib
c) Lenvatinib + Everolimus
d) Zanzalintinib ± Nivolumab (Clinical trial)

EXACT: Randomized phase II trial of Zanzalintinib (XL092) in combination with immunotherapy in patients who progress on Adjuvant therapy in Clear Cell RCC



Primary Endpoint: ORR by 6 months
Secondary endpoints: PFS/OS/AE

PI: Karie Runcie, MD

hoosier SM CANCER RESEARCH NETWORK

NCT06863311

Kidney Cancer – First-Line Metastatic

Kidney Cancer – First-Line Metastatic

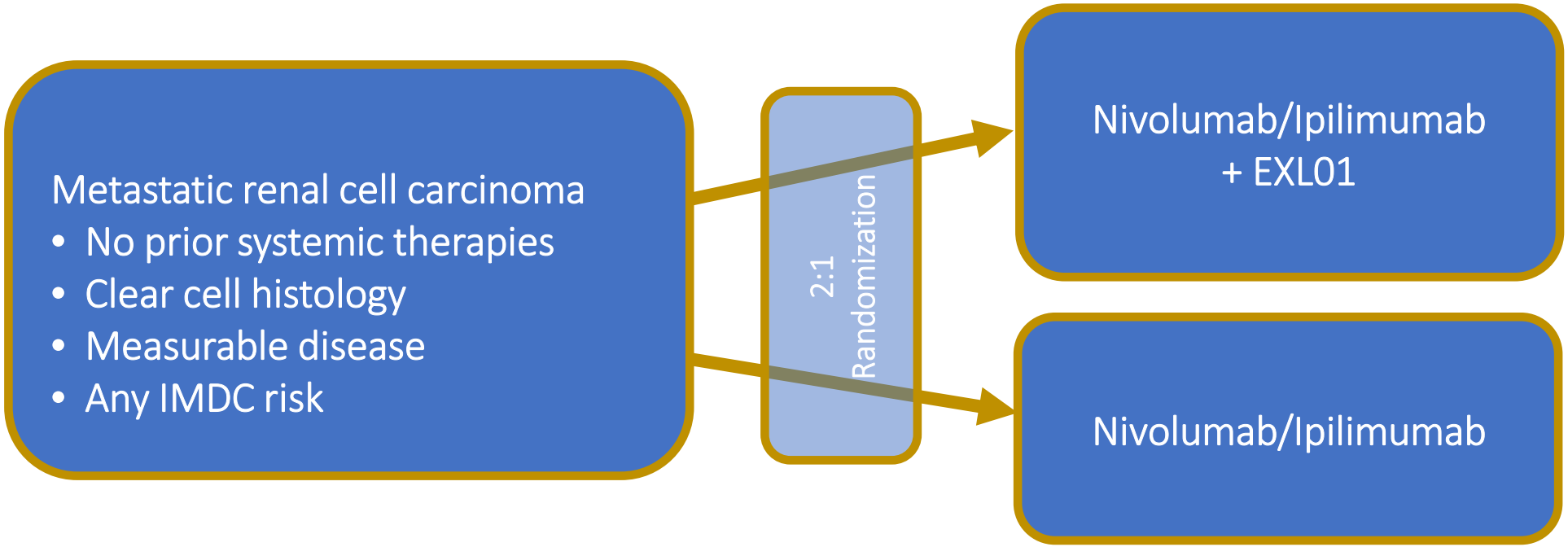
Case Presentation

- 66-year-old man presents with fatigue. Imaging reveals a 10 cm left renal mass with multiple bilateral pulmonary metastases. Biopsy confirms clear cell renal cell carcinoma, ISUP grade 2. He has ECOG performance status 0 and laboratory evaluation shows no abnormalities, consistent with IMDC intermediate-risk disease. He has received no prior systemic therapy.

➡️ **Treatment-naïve metastatic clear cell RCC**
➡️ **IMDC intermediate risk**

a) Nivolumab + Ipilimumab
b) Nivolumab + Cabozantinib
c) Pembrolizumb + Lenvantinib
d) Nivolumab + Ipilimumab ± EXL01 (Clinical trial)

A randomized study of nivolumab and ipilimumab with and without EXL01 in first-line treatment of metastatic renal cell carcinoma (mRCC)



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Kidney Cancer – Refractory Disease

Kidney Cancer – Refractory Disease

Case Presentation

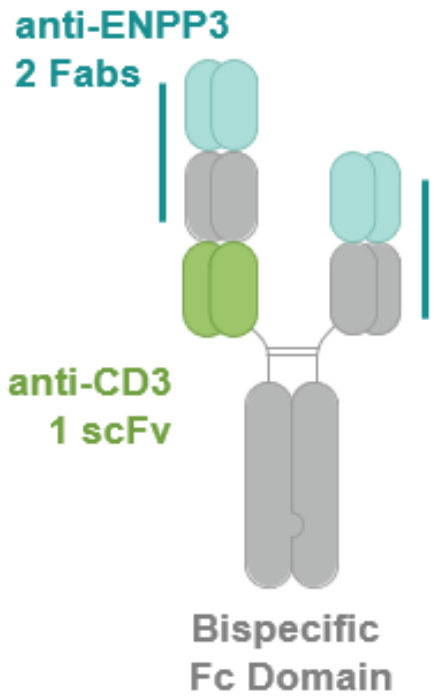
- A 68-year-old man with metastatic clear cell renal cell carcinoma initially underwent nephrectomy and subsequently received multiple lines of systemic therapy, including immune checkpoint inhibition, VEGFR TKI therapy, and a HIF-2α inhibitor. He experienced transient disease control with each regimen but ultimately developed progressive disease with enlarging pulmonary and retroperitoneal metastases. He remains ECOG performance status 1, with preserved organ function and no active autoimmune conditions.

➡️ **Heavily pretreated metastatic clear cell RCC**
➡️ **Refractory to IO, VEGFR TKIs, and HIF-2α inhibition**

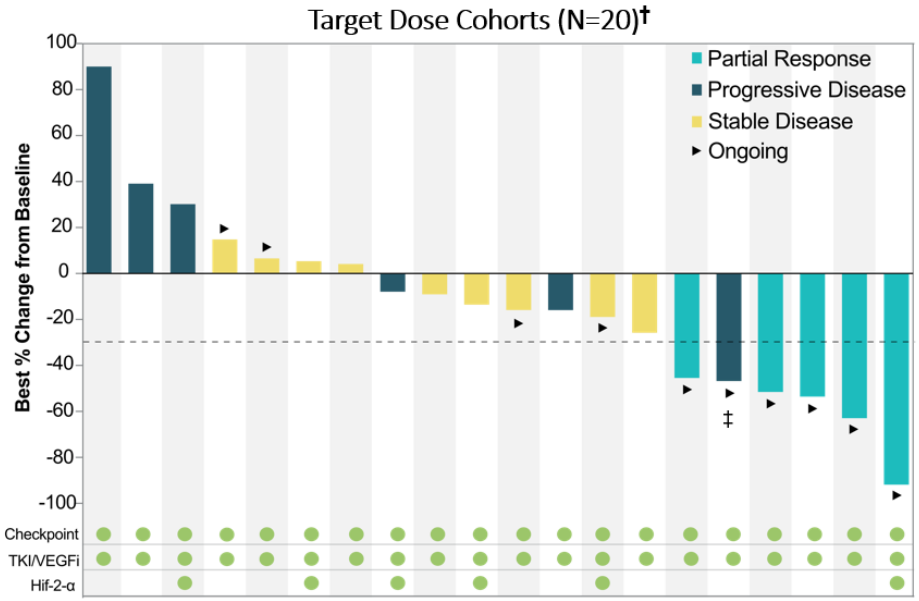
a) Best supportive care
b) Everolimus
c) Tivozanib
d) Clinical trial (ENPP3/CD3 bispecific - XMab0819)

XMab0819: ENPP3/CD3 bispecific

NOVEL THERAPIES: ENPP3



Prior Therapy	
N	69
# Prior regimens, Median (Min, Max)	4 (1, 8)
1, n (%)	5 (7)
2	16 (23)
3	13 (19)
4	9 (13)
≥5	26 (38)
Prior treatments, n (%)	
Checkpoint inhibitor	69 (100)
VEGF TKI	69 (100)
2 or more TKI	42 (61)
HIF2α inhibitor	25 (36)
Prior Nephrectomy, n (%)	47 (68)



† Excludes 3 patients without post-baseline scans and 1 patient with non-evaluable post-baseline measurements

‡ PD at first scan (D48) prior to receiving target dose on D50. Continued treatment post-progression resulted in 47% tumor reduction. Continues on study at week 30.

NCT05433142

Pal *et al* ASCO 2025

Kidney Cancer – Non-Clear Cell

Kidney Cancer – Non-Clear Cell

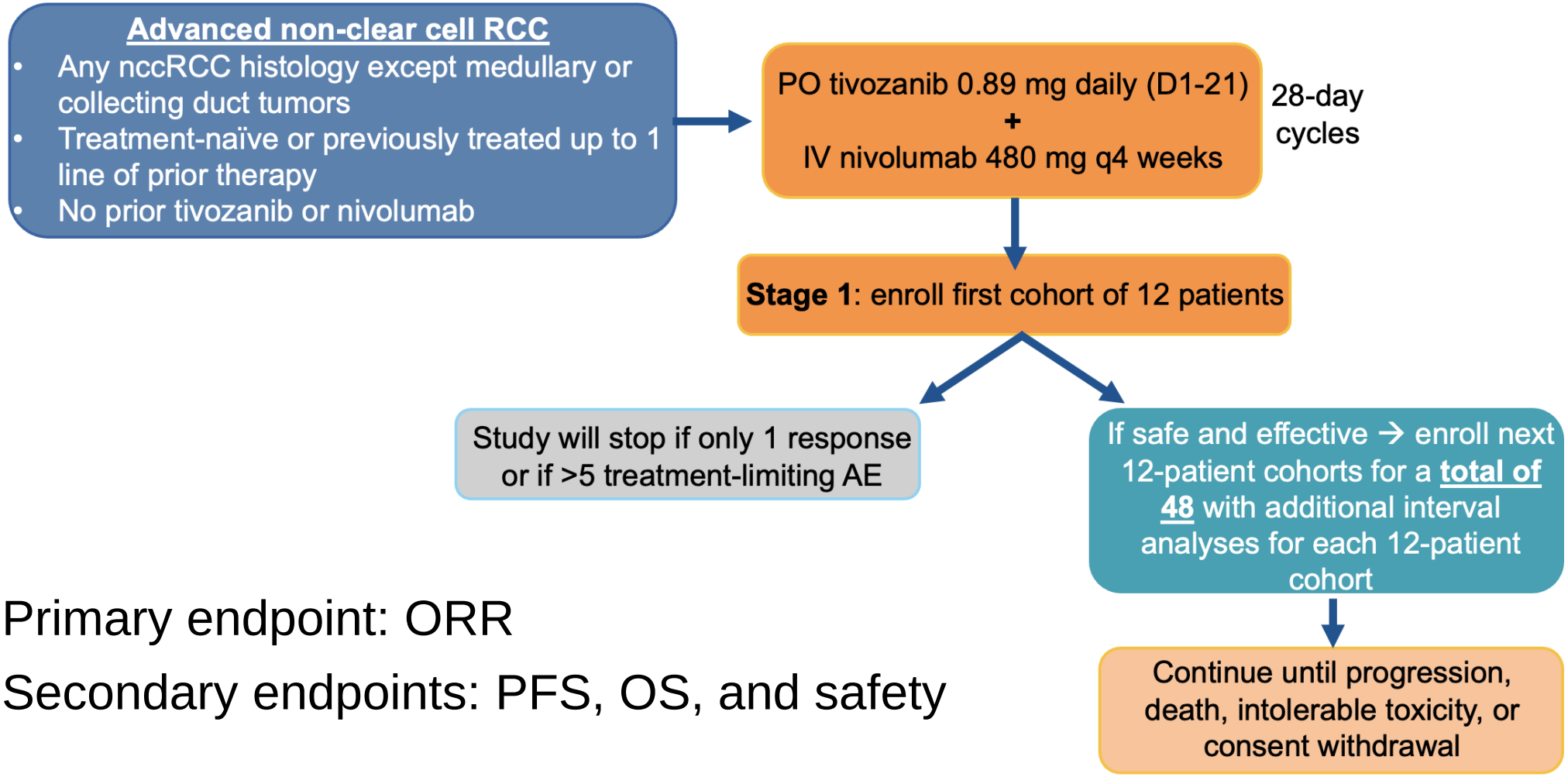
Case Presentation

- A 65-year-old woman with metastatic papillary renal cell carcinoma (type 2) was initially treated with cabozantinib, achieving stable disease for approximately 8 months before radiographic progression in the lungs and retroperitoneal lymph nodes. Biopsy confirms papillary RCC, ISUP grade 3. She is ECOG performance status 1, has no autoimmune disease, and has not received prior nivolumab or tivozanib.

➡️ **Advanced non–clear cell RCC (papillary RCC)**
➡️ **Progression after one prior line of systemic therapy**

a) Best supportive care
b) Erlotinib + Bevacizumab
c) Sunitinib
d) Tivozanib + Nivolumab (Clinical Trial)

FORTUNE trial schema



- Primary endpoint: ORR
- Secondary endpoints: PFS, OS, and safety

NCT06053658

FORTUNE trial

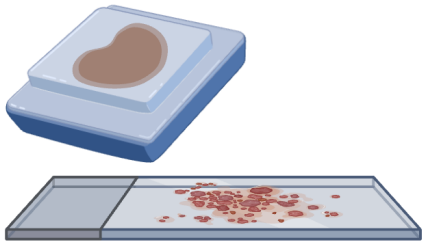
- Participating sites through the Kidney Cancer Research Consortium (KCRC)
  - University of Michigan
  - MD Anderson Cancer Center
  - UT Southwestern
  - Dana Farber Cancer Institute
  - City of Hope

KCRC Kidney Cancer RESEARCH CONSORTIUM

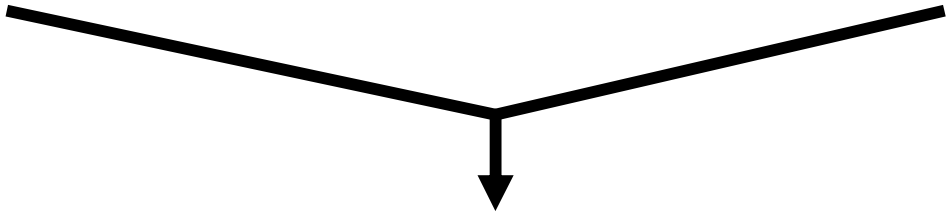
NCT06053658

FORTUNE trial correlatives

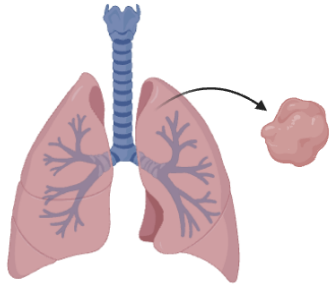
ctDNA analysis



Submitted archived tissue (baseline)



Analysis for genomic alterations, PD-L1, and TILs



On-treatment biopsy

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Kidney Cancer – Non-Clear Cell

Case Presentation

- A 62-year-old man with metastatic papillary renal cell carcinoma was initially treated with lenvatinib plus pembrolizumab in the first-line setting, achieving a partial response, but eventually developed disease progression. Somatic tumor sequencing performed on a repeat biopsy identified a pathogenic VHL alteration. He is ECOG performance status 1, with preserved organ function.

➡️ **Advanced papillary RCC, progressive disease after IO/TKI**
➡️ **Tumor harbors a somatic VHL alteration**

a) Cabozantinib
b) Erlotinib + Bevacizumab
c) Sunitinib
d) Belzutifan (Clinical Trial)

A Phase II open label, single-arm study of belzutifan in advanced non-clear cell renal cell carcinoma (nccRCC) with Von-Hippel-Lindau (VHL) alterations

UNIVERSITY of CALIFORNIA SAN DIEGO MEDICAL CENTER
MOORES CANCER CENTER

Eligibility

- Histologically confirmed nccRCC (medullary or collecting duct not eligible) with VHL alterations detected using a CLIA-certified standard-of-care panel
- Fumarate hydratase (*FH*)-deficient RCC or Succinate dehydrogenase (*SDH*)-deficient RCC with/without VHL alterations
- Previous treated with IO agents and anti-VEGF TKI (in combination or sequentially)
- At least one measurable disease per RECIST 1.1 criteria
- ECOG ≤ 2
- Hb ≥ 10.0

Simon's MiniMax Two-Stage Design

N=23

H_0: ORR ≤ 5% vs H_1: ORR ≥ 20%

(Power: 80%, one-sided α=0.05)

Belzutifan: 120 mg daily

- If 0 responses are observed in the first 12 patients, the trial stops after stage 1.
- If ≥1 response occurs, the trial proceeds to stage 2 with 9 additional patients (total evaluable patients N=21)
- If there are ≥3 responses overall, the treatment is deemed successful and the null hypothesis is rejected.
- The trial will accrue 23 patients to account for a 5% of early drop-out rate

Primary Endpoint:

- Overall response rate

Secondary Endpoints:

- Radiographic progression-free survival
- Disease control rate
- Overall survival

Exploratory endpoint:

- To evaluate molecular predictors of response and resistance to belzutifan