2nd 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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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.

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- *No relevant financial relationships.*

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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.

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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:

- *Underrepresentation of minority populations in RCC clinical trials limits the generalizability of findings and may perpetuate disparities.*
- *Implicit biases may lead providers to overlook.*
- *Diversity in clinical trials.*
- *Bias in trial enrollment.*

Case 1:

- Mr. T.K., a 58-year-old male, presents with gross hematuria and left flank pain for six weeks. A CT scan reveals a 7.2 cm enhancing left renal mass without evidence of metastatic disease on staging scans. He undergoes a left radical nephrectomy. Final pathology was consistent with clear cell RCC, grade 4, negative surgical margins, pT3aN0M0.

- What would you offer as the best next option for this patient?

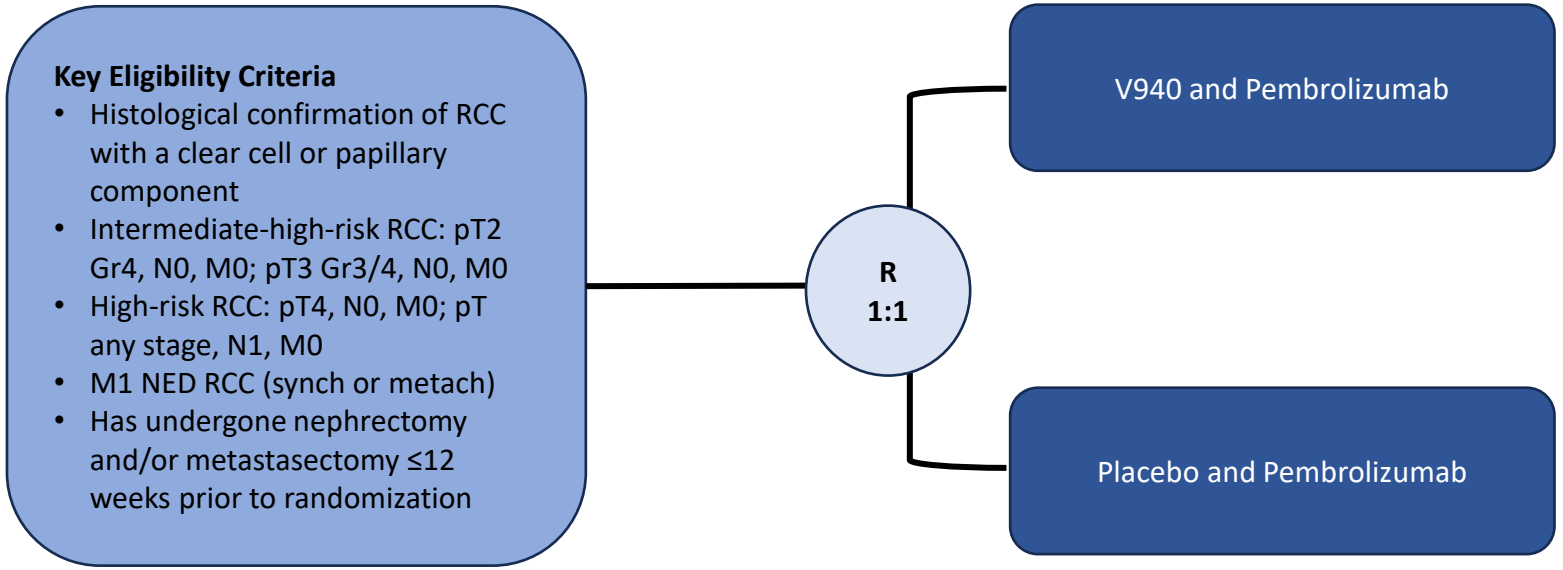
1) Surveillance

2) Adjuvant pembrolizumab

3) Trial: INTerpath-004

INTerpath-004: A Phase 2, Randomized, Double-blind, Clinical Study of V940 (mRNA-4157) Plus Pembrolizumab (MK-3475) Versus Placebo Plus Pembrolizumab in the Adjuvant Treatment of Participants With Renal Cell Carcinoma

NCT06307431



- **Primary endpoint**: disease-free survival
- **Key secondary endpoints**: OS, DMFS, AEs

Case 2:

- Mr. J.R., a 63-year-old male, presents with right-sided flank pain and gross hematuria for two months. A CT scan shows a 6.8 cm right renal mass, multiple bilateral pulmonary nodules, and enlarged retroperitoneal lymph nodes. A CT-guided biopsy of a lung nodule confirms clear cell renal cell carcinoma.

- What would you offer as the best next option for this patient?

1) IO+IO

2) IO+TKI

3) TKI monotherapy

4) Trial: NRG-GU012

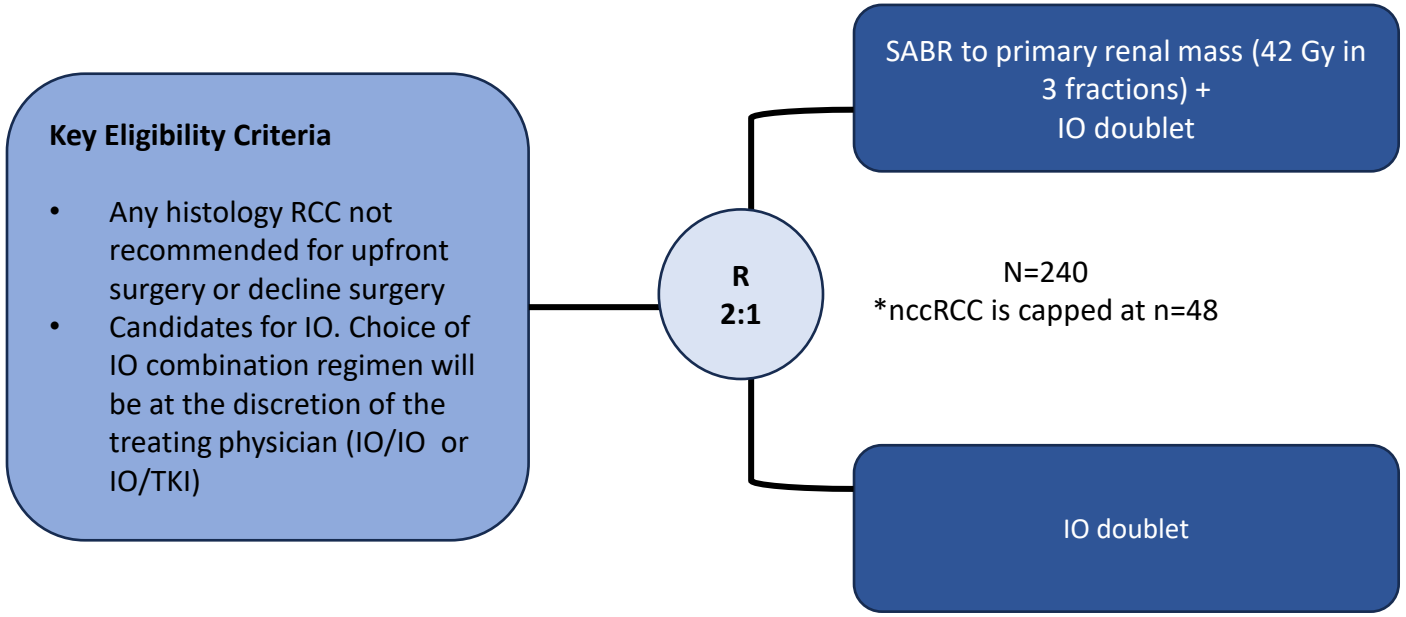
5) Trial: PROBE

6) Trial: ARCHITECT

7) Trial: OPTIC

NRG-GU012: Randomized Phase II Stereotactic Ablative Radiation Therapy (SABR) for Metastatic Unresected Renal Cell Carcinoma Receiving Immunotherapy (SAMURAI)

NCT05327686



Stratification factors

- IMDC intermediate vs poor risk
- IO regimen (IO/IO vs IO/TKI)
- Histology (ccRCC vs nccRCC)

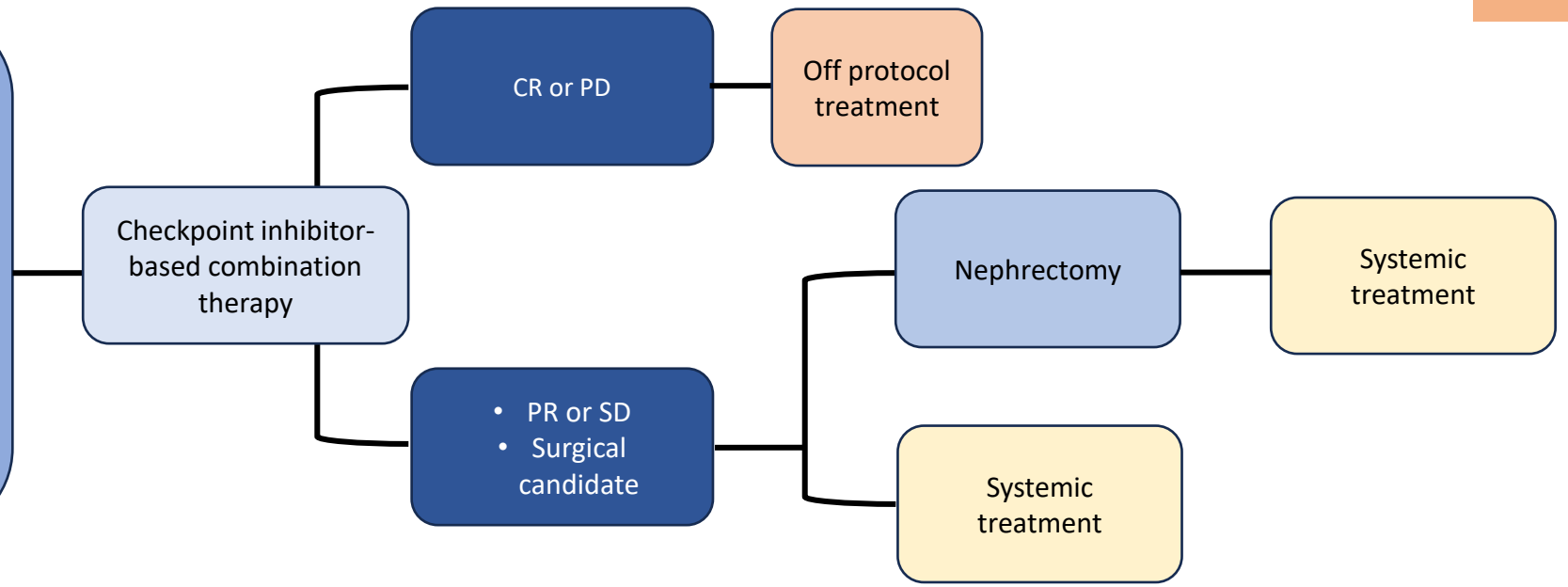
- **Primary endpoint**: nephrectomy or radiographic progression-free survival (nrPFS)
- **Key secondary endpoints**: ORR by iRECIST and RECIST; rPFS by iRECIST and RECIST; OS; treatment free survival.

PROBE Trial: Phase III Trial of Immunotherapy-Based Combination Therapy With or Without Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma

NCT04510597

Key Eligibility Criteria

- Histological confirmation of RCC with a clear cell or non-clear cell component
- Collecting duct carcinoma histology is not eligible
- Must have primary tumor in place
- Evidence of measurable or non-measurable metastatic disease
- No clear contraindications to nephrectomy



- **Primary endpoint**: OS
- **Key secondary endpoints**: OS between arms, Complication of surgery

ARCHITECT: Advanced Renal Cell Carcinoma Combination Immunotherapy Clinical Trial

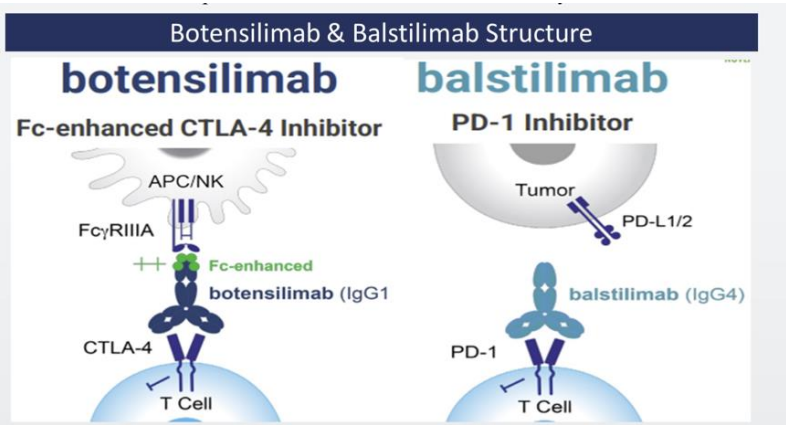
NCT05928806

Key Eligibility Criteria

- ECOG ≤2
- Histologically confirmed metastatic or unresectable ccRCC
- All IMDC Risk Group
- No prior adjuvant or systemic therapy
- Measurable disease per RECISI 1.1

R
2:1

- Botensilimab/balstilimab (n=80)
- Ipilimumab/Nivolumab (n=40)

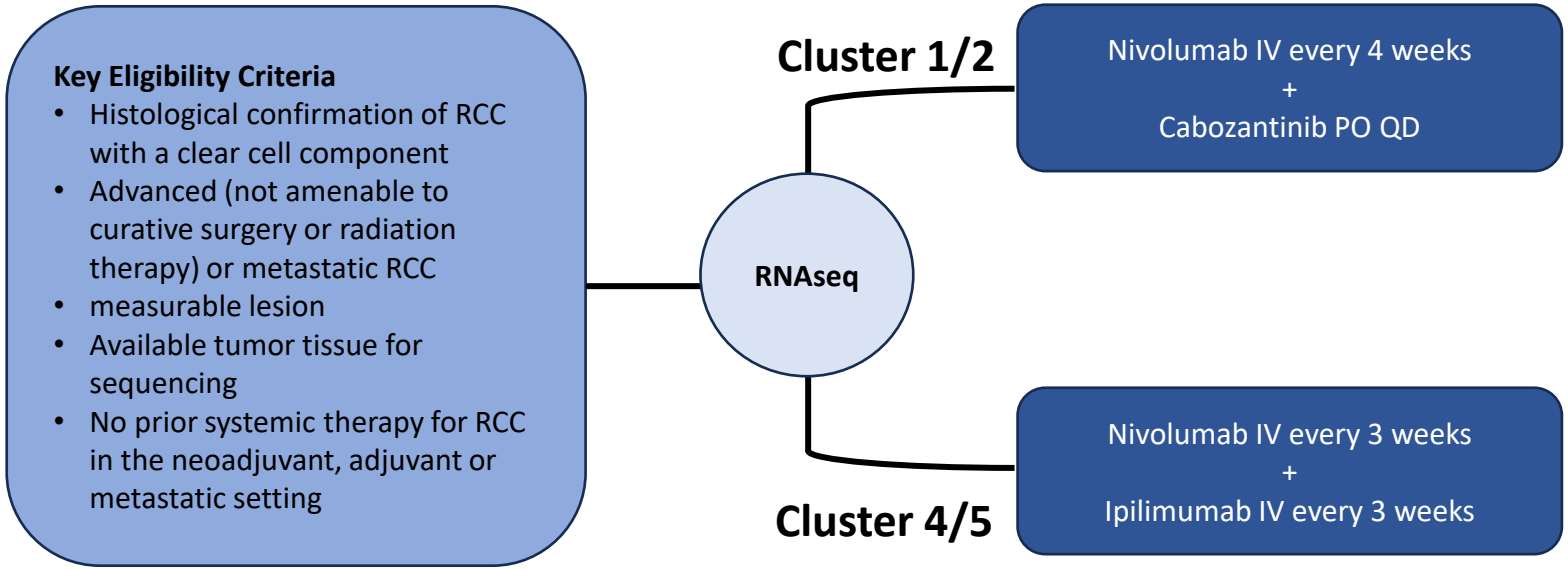


- Botensilimab (Bot) leverages novel FcγR-associated mechanisms of action:
  - Enhance T cell priming
  - Enhance Treg depletion
  - Enhance myeloid activation
  - reduce complement mediated toxicity

- **Primary endpoint**: to determine the objective response rate (ORR) per RECIST 1.1
- **Key secondary endpoints**: duration of response (DOR) per RECIST 1.1; 12- & 24-month landmark progression free survival (PFS); treatment free survival (TFS); safety and tolerability
- **Exploratory:** to evaluate the relationship between percentage of regulatory T cell (Treg) and efficacy outcomes (ORR, landmark PFS, TFS)

OPTIC: Genetic Testing to Select Therapy for the Treatment of Advanced or Metastatic Kidney Cancer

NCT05361720



- Stratification factors
  - Ribonucleic acid sequence (RNAseq)-defines biologic cluster

- **Primary endpoint**: ORR per RECIST
- **Key secondary endpoints**: PFS, Depth of response>80% at 6 months

Case 3:

- Mr. D.L., a 65-year-old male, initially presented with right flank pain. Imaging revealed a 9 cm right renal mass with multiple pulmonary nodules and retroperitoneal lymphadenopathy. A lung biopsy confirmed clear cell RCC, grade 3. He was started on first-line nivolumab + cabozantinib but experienced disease progression after 10 months with increasing lung nodules and new liver metastases. He was then switched to second-line lenvatinib + everolimus, achieving partial response for 8 months before progressing again with new bone metastases.

- What would you offer as the best next option for this patient?

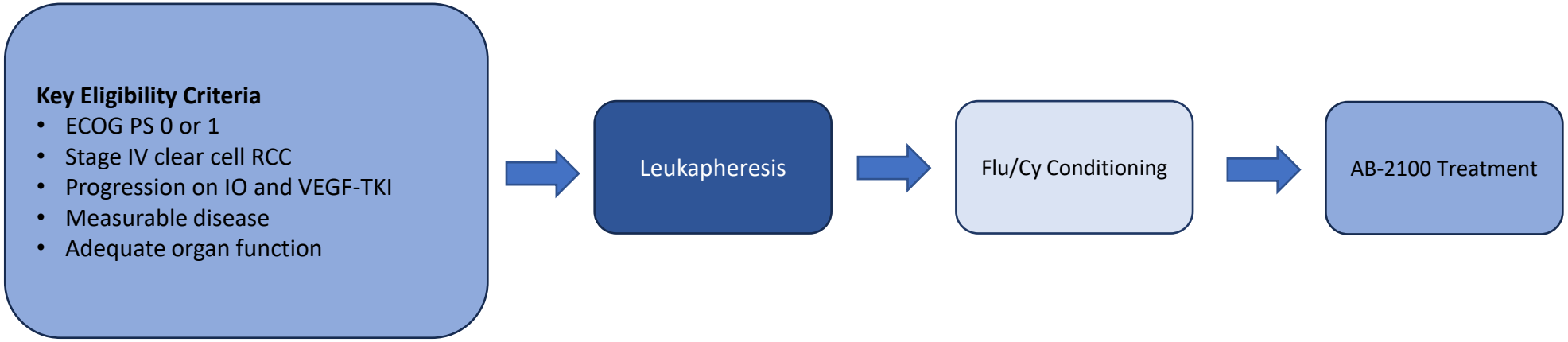
1) IO rechallenge

2) TKI monotherapy

3) Trial: AB-2100

An Open-label, Multicenter Phase 1/2 Study to Evaluate the Safety and Efficacy of AB-2100 in Patients with Recurrent Advanced or Metastatic Clear-cell Renal Cell Carcinoma

NCT06245915

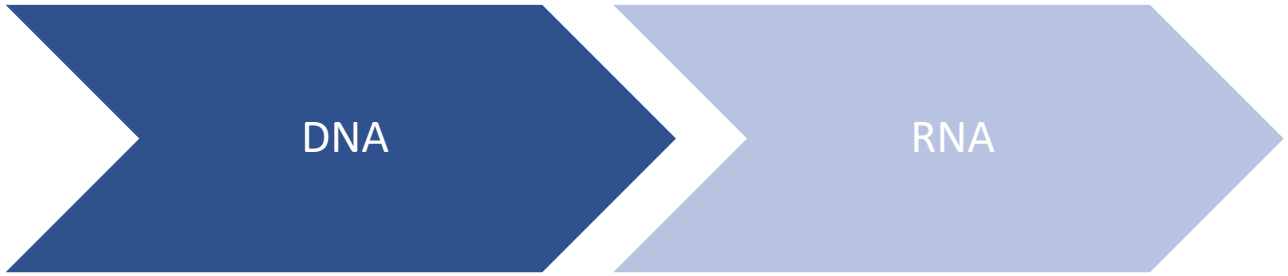


- AB-2100 manufacturing time is +/- 28 days
  - Retreatment is possible

- **Primary endpoint**: PFS
- **Key secondary endpoints**: OS, ORR, Safety

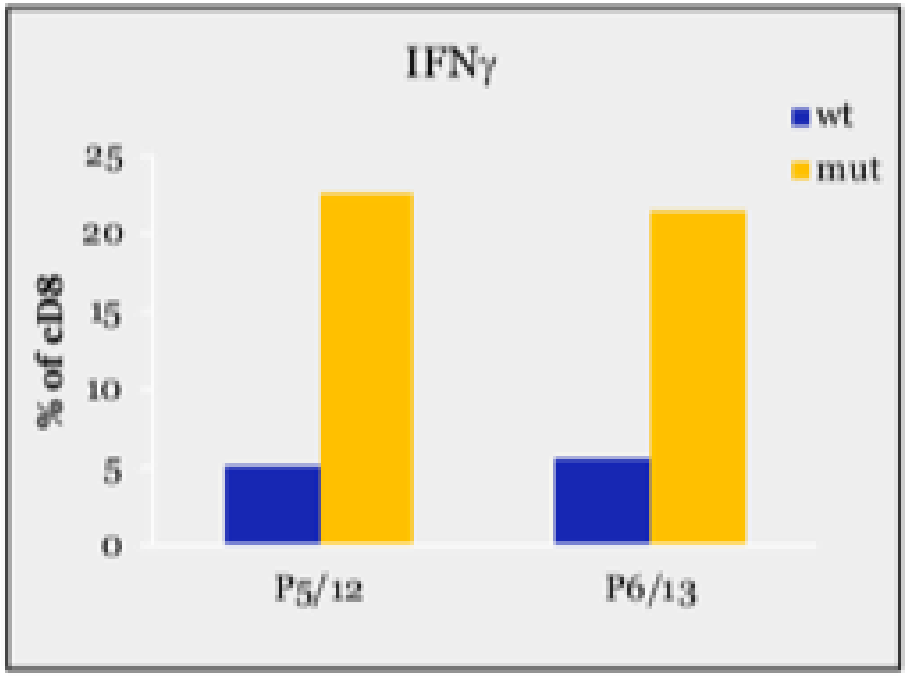
Tumor stimulates Immune Response Against Neoantigens

Using patient samples:



- Sequence whole exome from tumor and normal tissue
- Identify patient-specific mutation

- Sequence all mRNA to find transcribed mutations
- HLA type and synthesize peptide



Peptide stimulation

Case 4:

- Mr. R.S., a 61-year-old male, initially underwent a left radical nephrectomy three years ago and diagnosed with papillary RCC, pT1bN0M0. He was under active surveillance until now. Recent imaging reveals multiple bilateral lung nodules. A biopsy of a lung lesion confirms metastatic papillary RCC.

- What would you offer as the best next option for this patient?

1) TKI monotherapy

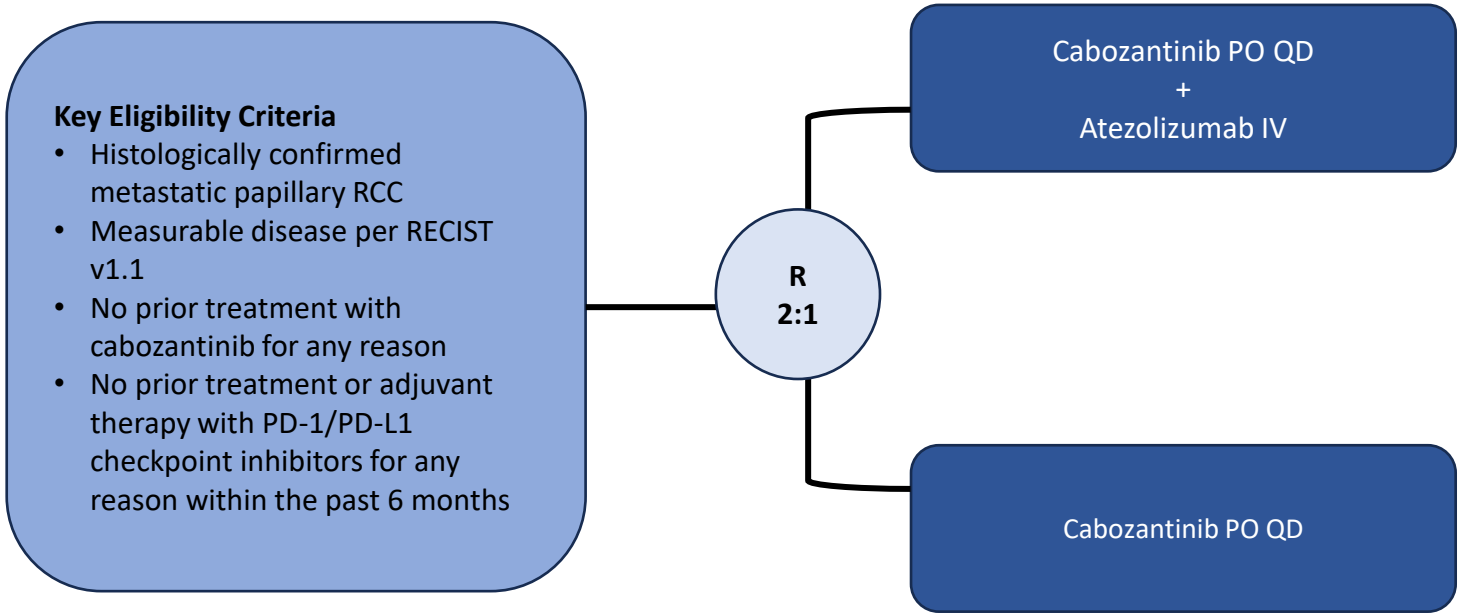
2) IO+TKI

3) IO+IO

4) Trial: PAPMET2

PAPMET2: A Phase II Randomized Trial of Cabozantinib With or Without Atezolizumab in Patients With Advanced Papillary Renal Cell Carcinoma

NCT05411081



- **Primary endpoint**: PFS
- **Key secondary endpoints**: OS, ORR, Safety