Protocol Title: Randomized, Phase II Efficacy Assessment of Multiple MET Kinase Inhibitors (Cabozantinib [NSC #761968], Crizotinib [NSC #749005], Savolitinib [NSC #785348], and Sunitinib [NSC #736511]) in Metastatic Papillary Renal Carcinoma (PAPMET)

Target Population: Recurrent, Stage III or IV Renal Cell Carcinoma
- Type 1 or 2 Papillary Renal Cell Carcinoma

Summary: To compare Progression-Free Survival (PFS) in patients with Metastatic Papillary Renal Cell Carcinoma (mPRCC) treated with Sunitinib Malate (Sunitinib) to PFS in patients with mPRCC treated with MET Kinase Inhibitors.

Key Inclusion Criteria:
- Patients must have histologically or cytologically confirmed Papillary Histology Renal Cell Carcinoma, which is metastatic or locally advanced disease not amenable to surgical resection.
  - Mixed histologies containing type I or type II will be allowed provided that they contain ≥ 50% of the papillary component.
- Patients must also have measurable disease.
- Patients with a history of treated brain metastases who are asymptomatic and have not received steroid therapy in the 14 Days prior to registration are eligible.
  - Anti-seizure medications are allowed provided they are non-enzyme inducing (e.g. Topiramate, Levetiracetam, Gabapentin).
- Patients must not have Cavitating Pulmonary Lesions.
  - Patients must not have tumor invading the Gastrointestinal Tract or evidence of Endotracheal or Endobronchial Tumor within 28 Days prior to registration.
- Patients may have received prior surgery.
  - At least 28 Days must have elapsed since surgery and patient must have recovered from any adverse effects of surgery.
- Patients may have received up to 1 prior systemic therapy for advanced or metastatic Renal Cell Carcinoma.
  - If a patient develops metastatic disease within 6 Months of discontinuation of adjuvant therapy, this will constitute one prior systemic therapy for advanced or metastatic Renal Cell Carcinoma (RCC).
  - If a patient develops metastatic disease and more than 6 Months has elapsed since discontinuation of adjuvant therapy, this will not constitute prior systemic therapy for advanced or metastatic RCC.
  - Patients must not have received a MET / Hepatocyte Growth Factor (HGF) Inhibitor or Sunitinib as prior therapy.
  - At least 14 Days must have elapsed since completion of prior systemic therapy.
  - Patients must have recovered from all associated toxicities at the time of registration.
- Patients may have received prior radiation therapy, but must have measurable disease outside the radiation port.
  - At least 14 Days must have elapsed since completion of prior radiation therapy.
  - Patients must have recovered from all associated toxicities at the time of registration.
- Patients must not be taking, nor plan to take while on protocol treatment, Strong CYP3A4 Inhibitors and / or Strong CYP3A4 Inducers within 14 Days prior to randomization.
- Patients must have a complete physical examination and medical history within 28 Days prior to registration.
- Baseline urinalysis should show urine protein < 3+ and must be obtained within 28 Days prior to registration.
  - If urine protein is ≥ 3+, then 24 hour urine collection must show less than 3 grams of protein.
- Patients must have tissue available and be willing to submit for central pathologic review in order to classify Type I versus Type II Papillary Renal Cell Carcinoma.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02761057