Objective

- **SAMETA** (NCT05043090) is a Phase III, open-label, randomized, controlled, multicenter study assessing the efficacy and safety of savolitinib in combination with durvalumab compared with sunitinib and durvalumab monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic PRCC (Table 1).

Summary

- Genomic abnormalities resulting in the dysregulation of MET signaling are common in PRCC, providing a potential target in these MET-driven cases.
- As the MET pathway may play a role in immunomodulation, data suggests combining MET inhibition (e.g., savolitinib) with a checkpoint inhibitor (e.g., durvalumab) may provide a synergistic anti-tumor effect.
- Based on results from the SAVOIR and CALYPSO studies, the Phase III SAMETA study (NCT05043090) will analyze treatment with savolitinib and durvalumab in patients with MET-driven PRCC.
- SAMETA is currently enrolling patients.

Plain language summary

**Why are we performing this research?**

Kidney cancer is one of the top 10 most common cancers in the world. Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer. The second most common type of renal cell carcinoma, papillary renal cell carcinoma (PRCC), is associated with advanced disease and poor outcomes.

**How are we performing this research?**

The SAMETA study will investigate patients with MET-driven PRCC. In the SAMETA study, patients will receive either:

- savolitinib with durvalumab
- sunitinib (current global standard treatment option)
- durvalumab on its own

The study aims to see how effective the treatment is against MET-driven PRCC, as well as any side effects to the treatments.

**Where can I access more information?**

- For more information about the SAMETA trial, please visit [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/NCT05043090).
- To learn more about prilocitinib, visit [prilocitinib.com](http://prilocitinib.com).

**Key inclusion criteria**

- ≥18 years of age
- Histologically confirmed unresectable or locally advanced or metastatic PRCC
- PRCC must be centrally confirmed as MET-driven by a sponsor-designated, validated, NGS assay
- No prior systemic anti-cancer treatment in the metastatic setting; no prior exposure to MET inhibitors, durvalumab, or sunitinib in any setting

**Key exclusion criteria**

- History of liver cirrhosis or other serious liver disease
- Spinal cord compression or brain metastases
- Active or prior cardiac disease or clinically significant ECG abnormalities
- Active infection (including COVID-19)
- Active interstitial lung disease / pneumonitis
- Active or prior documented autoimmune and inflammatory disorders
- Receipt of active immunotherapy within 30 days prior to the first dose of study intervention
- PRCC is associated with poor clinical outcomes and a high incidence of metastases. At present, there are no therapies approved specifically for PRCC.
- Many PRCC cases are MET-driven, a result of genomic abnormalities resulting in dysregulation of the MET signaling pathway, making these abnormalities a potential target for treatment.
- In a Phase II study with advanced PRCC (NCT01277710), approximately 40% of tumors were found to be MET-driven.

**Rationale**

- Savolitinib is an oral, potent, and highly selective MET (tyrosine kinase inhibitor) (TKI) with high affinity for MET, a protein that is overexpressed in many types of cancer and is a known driver of PRCC.
- In the Phase III SAMETA study (NCT03091192), savolitinib demonstrated encouraging antitumor activity compared with standard-of-care sunitinib in patients with MET-driven, advanced/metastatic ccRCC. Cross-study, intention-to-treat survival (PFS), overall survival (OS), and response rate (RR) were all numerically greater with savolitinib vs sunitinib.
- While sample size and follow-up were limited in SAVOIR due to premature termination of the study, median PFS was 7.0 months (95% confidence interval [CI] 2.8-11.2, not calculated [NC]) vs 5.6 months (95% CI 4.1, 6.9, respectively) [hazard ratio (HR) = 0.71; 95% CI 0.37, 1.36; p = 0.31], median OS was NC (95% CI 11.9, NC) vs 13.2 months (95% CI 7.6, NC) [HR = 0.51; 95% CI 0.21, 1.17; p = 0.07], and DCR was 27% (95% CI 13.3, 45.6) vs 7% (95% CI 0.9, 24.3) [p = 0.07].
- The study is recruiting across 25 countries at 165 centers globally, with an estimated 200 patients to be randomized (Figure 1).

**Trial design**

- Study design is shown in Figure 2.
- Prior to randomization, participants will undergo a two-part screening process:
  - Part 1: screening involves prospective testing of tumor specimens to determine MET-driven status without co-occurring FH mutations and PD-L1 biomarker status. If a participant has confirmed MET-driven PRCC, they proceed to part 2 screening.
  - Part 2: screening involves determining whether the participant meets the rest of the eligibility criteria.
- Participants will be randomized in a 2:1:1 ratio into one of three treatment arms (A-C) with stratification for metastatic status and PD-L1 expression status.
- Study treatment continues until Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 progression or another discontinuation criterion is met.
- Participants will undergo imaging assessments (every 4 weeks relative to first dose) of MET-driven disease and PRCC, as assessed by BICR, per RECIST 1.1.
- The primary objective of the study is to demonstrate the effectiveness of savolitinib plus durvalumab relative to sunitinib by assessing PFS in patients with MET-driven, unresectable and locally advanced or metastatic PRCC (Table 1).
- An additional follow-up scan was performed 7 days relative to first dose.

**SAMETA**

- **SAMETA** is a Phase III, open-label, randomized, controlled, global, multicenter study assessing the efficacy and safety of savolitinib in combination with durvalumab vs sunitinib vs durvalumab monotherapy in patients with MET-driven, unresectable and locally advanced or metastatic PRCC (Table 1).
- **SAMETA** (NCT05043090) can be accessed at: [clinicaltrials.gov/ct2/show/NCT05043090](https://clinicaltrials.gov/ct2/show/NCT05043090).
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