Key Inclusion Criteria

- Age ≥18 years
- Histologically confirmed diagnosis of nccRCC
- Locally advanced/metastatic disease
- No prior systemic therapy for advanced nccRCC
- Measurable disease per RECIST v1.1 by BICR
- KPS score ≥70%
- Imaging of chest/abdomen/pelvis and response assessment

Key Exclusion Criteria

- Collecting duct histology
- Left ventricular ejection fraction below the institutional (or local laboratory) normal range, as determined by multigated acquisition scan or echocardiography
- Urine protein level ≥1 g/24 hours
- Preexisting gastrointestinal fistula grade ≥3
- Radiographic encasement or invasion of a major blood vessel, or intratumoral cavitation
- Clinically significant cardiovascular disease within 12 months from the first dose of study drug, including class III or IV congestive heart failure per New York Heart Association criteria, unstable angina, myocardial infarction, cerebral vascular accident, or cardiogenic shock associated with hemodynamic instability
- Gastrointestinal malabsorption, gastrointestinal anastomosis, or any condition that might affect the absorption of lenvatinib
- Participants may be discontinued, lenvatinib cannot be continued without PD
- Participants who were enrolled in another study of lenvatinib or pembrolizumab until 90 days before
- Participants with a history of radiosurgery, radiation therapy, or any radiation for an active malignancy within 12 months prior to the study
- Participants with a history of or active untreated or unstable intracranial neoplasms

End Points

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

References