Protocol Title: Multicenter, Open-label, Randomized, Phase 3 Trial to Compare the Efficacy and Safety of Lenvatinib in Combination with Everolimus or Pembrolizumab Versus Sunitinib Alone in First-Line Treatment of Subjects with Advanced Renal Cell Carcinoma

Target Population: Renal Cell Carcinoma (RCC)

Summary: This is a multicenter, randomized, open-label, Phase 3 study to compare the efficacy and safety of Lenvatinib in combination with Everolimus (Arm A) or Pembrolizumab (Arm B) versus Sunitinib (Arm C) as first-line treatment in participants with advanced Renal Cell Carcinoma.

Key Inclusion Criteria:
- Histological or cytological confirmation of Renal Cell Carcinoma (RCC) with a clear-cell component.
- At least 1 measurable target lesion according to RECIST 1.1.
- Karnofsky Performance Status (KPS) of ≥ 70.
- Adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as BP ≤ 150/90 mmHg at screening and no change in medications within 1 Week prior to Cycle 1/Day 1.
- Adequate organ function per blood work.

Key Exclusion Criteria:
- Participants who have received any systemic anticancer therapy for RCC, including anti-vascular endothelial growth factor (VEGF) therapy, or any systemic investigational anticancer agent.
- Subjects with CNS metastases are not eligible, unless they have completed local therapy and have discontinued the use of corticosteroids for this indication for at least 4 Weeks before starting treatment in this study.
- Active malignancy (except for RCC, definitively treated basal or squamous cell carcinoma of the skin, and carcinoma in-situ of the cervix or bladder) within the past 24 Months.
- Prior radiation therapy within 21 Days prior to start of study treatment with the exception of palliative radiotherapy to bone lesions, which is allowed if completed 2 Weeks prior to study treatment start.
- Received a live vaccine within 30 Days of planned start of study treatment.
- Participants with urine protein ≥ 1 gram/24 hour.
- Fasting total cholesterol > 300 milligram per deciliter (mg/dL) and/or fasting triglycerides level > 2.5 x ULN.
- Uncontrolled diabetes as defined by fasting glucose > 1.5 times the ULN.
- Prolongation of corrected QT (QTc) interval to > 480 milliseconds (ms).
- Bleeding or thrombotic disorders or subjects at risk for severe hemorrhage.
- Clinically significant hemoptysis or tumor bleeding within 2 Weeks prior to the first dose of study drug.
- Significant cardiovascular impairment within 6 Months of the first dose of study drug.
- Known history of, or any evidence of, interstitial lung disease or history of (non-infectious) pneumonitis that required steroids, or current pneumonitis.
- Active autoimmune disease (with the exception of psoriasis) that has required systemic treatment in the past 2 Years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs).

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02811861