For Patients with Renal Cell Carcinoma

EA8143 Available Through ECOG-ACRIN Cancer Research Group

A Phase 3 Randomized Study Comparing PERioperative Nivolumab vs. Observation in Patients with Renal Cell Carcinoma Undergoing Nephrectomy (PROSPER RCC)

Patient Population
See Section 3.0 for Complete Eligibility Details

Eligibility Criteria for Step 0:
- Renal mass consistent with clinical stage ≥ T2Nx/TanyN+ RCC for which radical/partial nephrectomy is planned
- No clinical/radiological evidence of distant metastases unless the presumed M1 disease is planned to be resected/definitely treated per protocol
- If histological confirmation of RCC has not been done within 12 months prior to Step 0, patient must be willing to undergo a core biopsy if randomized to Arm H
- No prior systemic/local anti-cancer therapy for the current RCC (see protocol for examples/exceptions)
- Age ≥ 18 years and ECOG PS 0-1
- No prior history of RCC that was resected with curative intent within the past 5 years; no concurrent malignancies; no active/known or suspected autoimmune disease (see protocol for all exceptions)
- No ongoing condition requiring systemic treatment with corticosteroids (>10 mg daily prednisone equivalent) or other immunosuppressive medications (see protocol for details/exceptions)
- No uncontrolled adrenal insufficiency
- No known chronic active liver disease or evidence of acute/chronic HBV/HCV; no known evidence of HIV
- No serious intercurrent illness, including ongoing/active infection requiring parental antibiotics
- No known medical condition that increases the risk of study participation/interpretation of safety results
- No major surgery within 28 days prior to randomization
- No history of severe hypersensitivity to a monoclonal antibody

Eligibility Criteria for Randomization, Step 1:
- Arm H—core tumor biopsy must demonstrate RCC of any histology (see protocol)
- Not pregnant/breast feeding; adequate lab values

Treatment Plan
See Section 5.0 for Complete Treatment Details

See Protocol for the Dose and Schedule for Patients Enrolled PRIOR to the Activation of Add#4

Arm A—Perioperative Nivolumab:
- Nivolumab 480mg IV:
  - After registration to Step 1, neoadjuvant dose must be given ≤ 28 days of registration and prior to partial/radical nephrectomy
  - Adjuvant dosing: 9 doses; 1 dose every 4 weeks for 9 months (1 dose of neoadjuvant nivolumab is required unless the patient meets Section 5.6.1)
  - Nephrectomy should be at a minimum 7 days from the neoadjuvant dose and no more than 28 days; 1st dose of adjuvant nivolumab should be within 4-10 weeks post-nephrectomy/last local treatment

Arm B—Observation:
- Partial/radical nephrectomy followed by observation
  - Nephrectomy should be within 8 weeks after registration to Arm B

Notes:
- Bilateral RCC/metastectomy cases: timeframes are clarified per protocol
- Nephrectomy can be done at any qualified hospital
- See protocol for prohibited/restricted treatments: Immunosuppressive agents/doses of systemic corticosteroids (except stated per protocol); concurrent anti-neoplastic therapy that would affect the primary endpoint
- See protocol for permitted therapy: certain corticosteroids (with minimal systemic absorption); physiologic replacement doses of systemic corticosteroids; brief course of corticosteroids for prophylaxis/treatment of non-autoimmune conditions; VEGF inhibitors if used according to approved ocular indication; resection/other definitive local treatments

Patient Enrollment
All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

Please Enroll Your Eligible Patients!
2. Patients randomized to Arm A are encouraged but not required to have a biopsy prior to other randomization.

Notes: After randomization to Arm A, all patients continue to follow-up in the standard fashion at 6 months.

Eligibility:
- Age: 18-80 years
- ECOG performance status: 0-2
- Histological diagnosis: adenocarcinoma
- No prior chemotherapy
- No prior hormonal therapy
- No prior immunotherapy
- No prior targeted therapy

In Arm A:
- Observation for 6 months
- No intervention

In Arm B:
- Patients undergo surgical specimen orientation
- Histology
- Randomization
- Arm D
- Arm E
- Arm F
- Arm G
- Arm H

Step 1: Randomization to Arm D or Arm E
- Arm D: 4-weeks x 9 doses
- Arm E: 1 dose x 7 doses

Step 2: Randomization to Arm F or Arm G
- Arm F: 3 doses x 4 doses
- Arm G: 2 doses x 4 doses

Step 3: Randomization to Arm H
- Arm H: 1 dose x 3 doses

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