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

Overall Study Goal

To examine whether the addition of perioperative nivolumab to radical or partial nephrectomy can improve clinical outcomes in patients with renal cell carcinoma (RCC)

Study Schema

Objectives

Primary Objective

- Compare recurrence-free survival (RFS) between patients with RCC randomly assigned to perioperative nivolumab in conjunction with radical or partial nephrectomy with patients randomized to surgery alone

Secondary Objectives

- Evaluate RFS in a subset of patients with clear cell histology
- Compare overall survival (OS)
- Evaluate safety and tolerability

Correlative Objectives

- Correlate the primary tumor’s expression of programmed death–ligand 1 (PD-L1) with outcome
- Correlate the expression of immune cells and PD-L1 on tumor tissue at nephrectomy and recurrence with outcome

- Archive images for potential central confirmation of recurrence and for future correlative work with ACRIN, including markers predicting outcome or response
- Prospectively collect tumor and biologic specimens (eg, serum, peripheral blood mononuclear cells [PBMCs])
- Characterize pharmacokinetics of nivolumab and explore exposure response relationships with respect to safety and efficacy
- Characterize immunogenicity of nivolumab

Quality of Life Objective

- Evaluate differences in change from baseline in patient-reported symptoms and toxicities among patients randomized to treatment with nivolumab compared with surgery alone

Exploratory Objectives

- Explore descriptively the efficacy of nivolumab treatment in patients with non-clear cell (including unclassified) histologies
- Characterize the effects of nivolumab on bone metabolism and bone density
How Your Site Can Participate

- Before recruitment, investigators must be registered members of an NCTN network group.
- All individuals contributing to NCI-sponsored trials must register and renew annually.
- Investigator (IVR), Non-physician Investigator (NPIVR), or Associate Plus (AP) must complete annual registration using CTEP’s Web-based Registration and Credential Repository (RCR) (https://ctepcore.nci.nih.gov/rrcr).
- Required documentation for IVR, NPIVR, and AP includes FDA Form 1572, Financial Disclosure Form, NCI Biosketch, HSP/GCP training, Agent Shipment Form (if applicable), and CV (optional).
- IVRs and NPIVRs must list clinical practice sites and IRBs covering their practice sites on FDA Form 1572 in RCR to allow the following: added to a site roster; assigned treating, credit, consenting, or drug shipment (IVR only) tasks in OPEN; acting as site-protocol Principal Investigator (PI) on IRB approval; assigned Clinical Investigator role on Delegation of Tasks Log (DTL).
- For questions, please contact RCR Help Desk via e-mail: RCRHelpDesk@nih.gov.

Requirements for EA8143 site registration:
- IRB approval.
- For sites not participating via the NCI Central Institutional Review Board (CIRB), the following are accepted: local IRB documentation, IRB-signed Cancer Trials Support Unit (CTSU) IRB Certification Form, Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form, or combination.
- EA8143 Protocol Training.

Submit all required regulatory documents to:
- CTSU Regulatory Office via the Regulatory Submission Portal, to be entered and tracked in the CTSU RSS.
- When applicable, mail original documents to: CTSU Regulatory Office 1818 Market Street, Suite 3000 Philadelphia, PA 19103.
- Each site must complete a protocol-specific DTL, reviewed and signed by the Clinical Investigator (CI) prior to the site receiving an approved registration status and enrolling patients.

Required regulatory documentation (see protocol Section 4):
- Copy of IRB Informed Consent Document.
- CTSU IRB Certification Form or Signed HHS OMB No. 0990-0263 (replaced Form 310) or IRB Approval Letter.
- Copies of the EA8143-specific regulatory documents required for site registration.

Note: Above submissions include all sites approved for the protocol under an assurance number; OHRP assurance number of reviewing IRB; full protocol title and number; version date; type of review (full board vs expedited); date of review; signature of IRB official.
- CV for PI and sub-investigators; submit at study start-up, labeled EA8143.
- FDA Form 1572; submit at study start-up and when information changes.
- Financial Disclosure Form; submit at study start-up, any time there is a financial status change, any time a new investigator is added.
- EA8143 Institutional Review Board Chairman Collection Form; submit at study start-up and at any change in Chair oversight or IRB of record (not required if NCI CIRB is the IRB of record for EA8143).
- Check registration status at https://www.ctsu.org.

Once documentation has been submitted and approved:
- Patients must not start protocol treatment before registration.
- Patient enrollment is via OPEN, accessed at https://open.ctsu.org. Data collection is exclusively through Medidata Rave. Address OPEN and Medidata Rave questions to CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.
- Pathologic samples must be submitted for central diagnostic review and classification (mandatory) and future research (per patient consent), biologic samples submitted (per patient consent), and serum samples submitted for pharmacokinetic and immunogenicity studies for arm A only, per protocol (Section 10).
- Copies of all imaging studies are submitted via TRIAD; send questions to TRIAD-Support@acr.org.
- Prior to the first patient enrollment at a participating site, one investigator must review and complete the EA8143 training course, by accessing https://coecg813.mindflash.com/PublicCoursePage.aspx?c=1710661420. OPEN will block enrollment until this training is completed. Direct questions to EAClinEd@ecog-acrin.org.
- ECOG-ACRIN is automatically e-mailed a copy of the certificate and provides the information electronically to CTSU Regulatory Office.

Contact Information

General Contacts
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For Further Information
- For more information about the EA8143 study, please visit the following:
  - Clinicaltrials.gov; search NCT03055013.
- For more information about ECOG-ACRIN, visit ecog-acrin.org.