Phase II Randomized Trial of Radiotherapy With or Without Cisplatin for Surgically Resected Squamous Cell Carcinoma of the Head and Neck (SCCHN) With TP53 Sequencing

Overall Study Goal

To examine whether the addition of cisplatin to postoperative radiotherapy (PORT) will provide a survival benefit to patients with p53 mutated, surgically resected, stage III-IV squamous cell carcinoma of the head and neck (SCCHN).

Study Schema

Accrual goal = 345 patients.
Treatment must begin within 5 working days after registration and randomization to adjuvant treatment arm. IMRT is mandatory; IGRT is optional (margin reduction not permitted even when IGRT used). Patient is registered to screening (step 0) and tissue submitted to Foundation Medicine as soon as possible after surgery to meet this deadline.

*Submission to Foundation Medicine for Foundation One™ Assay + p53 mutation status.
†Registration to treatment (step 1) must occur within 8 weeks of resection surgery.
‡Cisplatin 40 mg/m² weekly × 6 during concurrent radiation (60 Gy) standard fractionation at 2 Gy/d.
IGRT = image-guided radiation therapy; IMRT = intensity-modulated radiation therapy; p53 = tumor protein 53.

Objectives

Primary Objective
- Evaluate the disease-free survival (DFS) of patients with stage III-IV SCCHN and disruptive p53 mutations after primary surgical resection followed by PORT alone or PORT with concurrent cisplatin.

Secondary Objectives
- Evaluate DFS of patients with stage III-IV SCCHN and nondisruptive p53 mutations.
- Evaluate DFS of patients with stage III-IV SCCHN and p53 wildtype.
- Evaluate toxicities.
- Evaluate p53 mutation as a predictive biomarker of survival benefit given postoperative concurrent radiation and cisplatin.
- Identify potential genomic alterations, in addition to TP53 mutations, that may be developed to a novel treatment approach.

Why This Trial Is Unique and Important

Advances in genomics have led this trial to ask whether tumors that appear to be intermediate risk by standard pathologic features are actually high risk, due to a subset of p53 mutations (that confer worse prognosis). We want to test whether these “disruptive p53 mutations” are a molecular high-risk feature that would benefit from treatment intensification using chemoradiation.
How Your Site Can Participate

- Before recruitment, investigators must be registered members of a NCTN network group.

- Investigators must have an NCI investigator number and maintain “active” investigator registration status by annually submitting a registration packet (current CV and signed FDA Form 1572, Supplemental Investigator Data Form, and Financial Disclosure Form) to the FDA and NCI. Please refer to the Cancer Therapy Evaluation Program (CTEP) Web site for information and forms.

- Requirements for EA3132 site registration:
  - CTSU IRB Certification (for sites not participating via the NCI CIRB)
  - CTSU IRB/Regulatory Approval Transmittal Sheet (for sites not participating via the NCI CIRB)
  - CTSU RT Facilities Inventory Form
    - NCI policy states that all institutions that participate on protocols with a radiation therapy component must also participate in the Radiological Physics Center (RPC) monitoring program
    - If this form has been previously submitted to CTSU it does not need to be resubmitted unless updates have occurred at the RT facility.
  - Sites participating on the NCI CIRB initiative and accepting CIRB approval need not submit separate IRB approval documentation to CTSU for initial, continuing, or amendment review. For these sites, IRB data automatically load to RSS. Other site registration requirements (eg, lab or protocol-specific training certifications, modality credentialing) must be submitted to the CTSU Regulatory Office, or compliance communicated per protocol instructions.

- Submit all required regulatory documents to:
  - CTSU Regulatory Office
    - 1818 Market Street, Suite 3000
    - Philadelphia, PA 19103
    - Fax: (215) 569-0206
    - E-mail: CTSURegulatory@ctsu.coccg.org

- Required regulatory documentation:
  - CTSU Regulatory Transmittal Form
  - Copy of IRB Informed Consent Document
  - CTSU IRB Certification Form or signed HHS OMB No. 0990-0263 (replaced Form 310) or IRB Approval Letter

  Note: Submission includes 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.

- Check registration status at https://www.ctsu.org

- Once documentation has been submitted and approved:
  - Patients must not start protocol treatment before randomization to step 1
  - 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 the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com
  - Surgical tumor tissue samples are submitted to Foundation Medicine Inc. (Associated Study #RAP-CLT-16-023) for FoundationOne™ assessment and determination of p53 mutation status per protocol (Section 10 and Appendix 1). If optimal tissue is submitted, FoundationOne™ assay turnaround is 14-21 days from specimen receipt. Central reviewers will evaluate results and enter p53 mutation status in the ECOG-ACRIN registration system within 72 hours of receiving FoundationOne™ results. Failure to appropriately complete the requisition form or specimens of suboptimal size, cellularity, or tumor content will delay assessment and may require submission of additional materials. Within 72 hours of notification of FoundationOne™ test completion, central reviewers will determine p53 disruptive mutation status and enter that information into ECOG-ACRIN registration system. Patients cannot be randomized to step 1 until central reviewers enter p53 mutation status. Result reporting is outlined in Section 11.1.1 and Appendix III.