

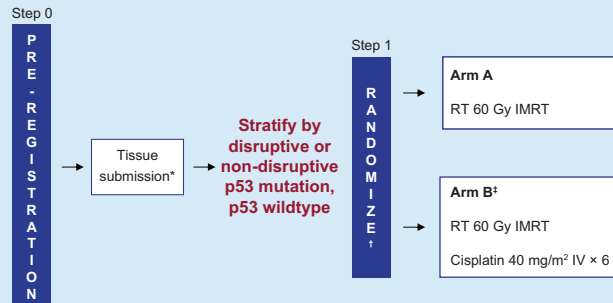
Phase II Randomized Trial of Radiotherapy with or without Cisplatin for Surgically Resected Squamous Cell Carcinoma of the Head and Neck (SCCHN) With TP53 Sequencing



Overall EA3132 Study Objective

To examine whether the addition of cisplatin to post-operative 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 = 189 (Step 1)

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).

*Submission to Foundation Medicine for Foundation One™ Assay + p53 mutation status.

†Registration to treatment (step 1) must occur within 8 weeks of resection surgery. Patient is registered to screening (step 0) and tissue submitted to Foundation Medicine as soon as possible after surgery to meet this deadline.

‡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.

Study 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 post-operative concurrent radiation and cisplatin
- Identify potential genomic alterations, in addition to *TP53* mutations, that may be developed to a novel treatment approach

Financial Toxicity Objectives

- Primary: Assess delays in definitive diagnosis for Black patients
- Secondary: Assess levels of financial toxicity of Black patients

Eligibility Criteria*

Main Inclusion Criteria

- ≥ 18 years of age, ECOG PS 0-1
- Pathologically proven diagnosis of squamous cell carcinoma (including variants such as verrucous carcinoma, spindle cell carcinoma, carcinoma not otherwise specified) of the head or neck (oral cavity, oropharynx, hypopharynx, or larynx); pathologic stage III or IVA (AJCC 8): T3–T4a, N0–3, M0 or T1–T2, N1–3, M0

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.

- Total resection of the primary tumor with curative intent
Note: Patient is to be pre-registered to screening (step 0) and tissue submitted to Foundation Medicine as soon as possible after surgery, to meet the 8-week deadline to register to step 1 after surgery. Full assay minimum turnaround time is 17–24 days
- For oropharynx primary tumors, must have negative HPV status of tumor based on p16 protein expression using immunohistochemistry
- If history of curatively treated malignancy, disease-free for ≥ 2 years *except* for carcinoma in situ of cervix and/or non-melanomatous skin cancer

- Per the operative report, gross total resection of the primary tumor with curative intent completed within 8 weeks prior to randomization
- Assessments completed ≤ 8 weeks prior to randomization: examination by a head and neck surgeon, and chest x-ray (or chest CT scan or CT/PET of chest or MRI) to rule out distant metastatic disease
- Adequate renal and hepatic function within 4 weeks prior to randomization
- Use of effective contraception or abstinence

Main Exclusion Criteria

- Positive margin(s) not superseded by additional margin of tumor-negative tissue, nodal extracapsular extension, and/or gross residual disease after surgery
- Received chemotherapy or investigational therapy within 2 years of surgical resection of the primary tumor
- Previous irradiation to head and neck that would result in overlap in radiation fields for current disease
- Recurrent disease or multiple primaries
- Intercurrent illness likely to interfere with protocol therapy

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.

