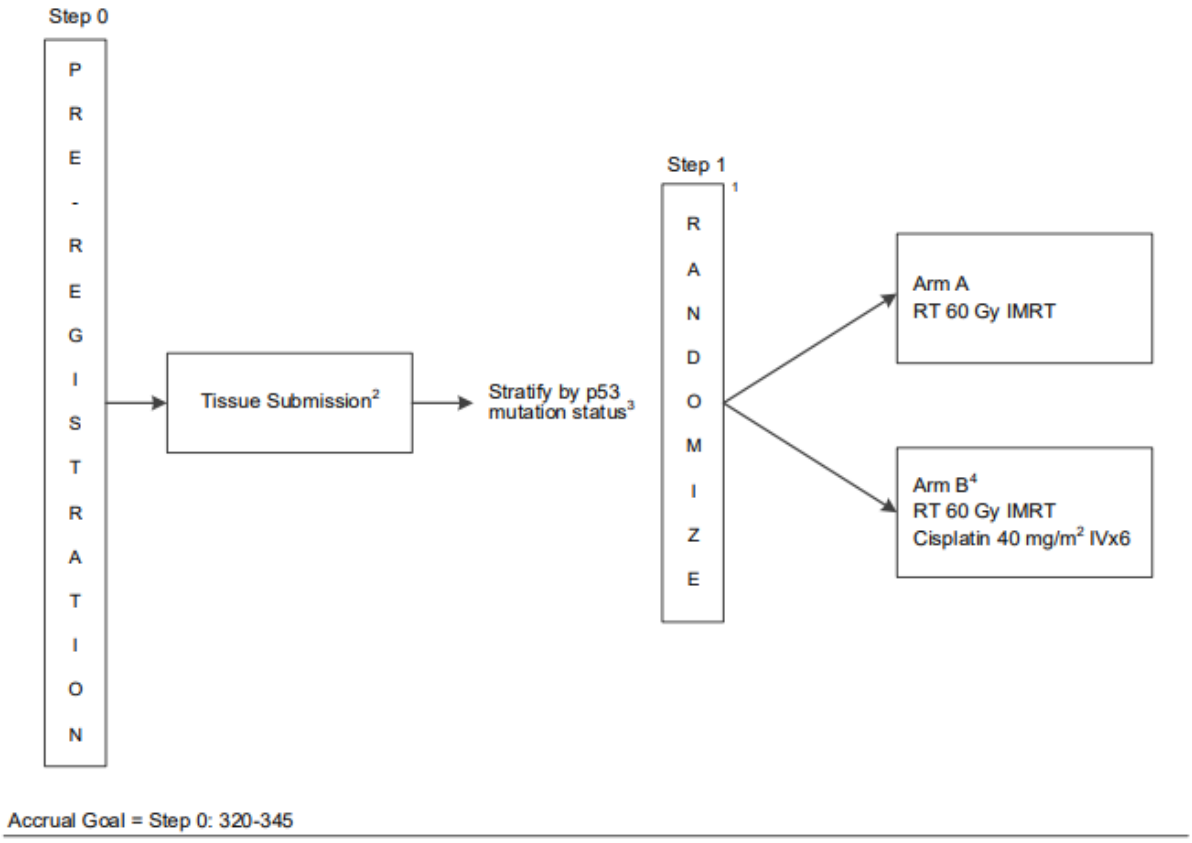
FAST FACTS

EA3132: 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

Schema



Pre-Registration (Step 0)

1. Age ≥ 18 years.
2. Pathologically proven diagnosis of squamous cell carcinoma (including variants such as verrucous carcinoma, spindle cell carcinoma, carcinoma NOS) of the head/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.
3. Patient has undergone 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 (per Appendix I) as soon as possible after surgery in order to meet the 8 week deadline to register the patient to Step 1 after surgery. Full assay minimum turn-around time is 14 days.
4. For oropharynx primary tumors, the patient must have negative HPV status of the tumor as determined by p16 protein expression using immunohistochemistry (IHC).

5. Patients with, per the operative and/or pathology report, positive margin(s) [tumor present at the cut or inked edge of the tumor] which is not superceded by an additional margin of tumor-negative tissue, nodal extracapsular extension, and/or gross residual disease after surgery are not eligible.
6. A paraffin-embedded surgical tumor tissue specimen has been located is available for shipment to Foundation Medicine, Inc. following pre-registration as indicated in Section 10 and Appendix I.
   NOTE: Complete the EA3132-specific FoundationOne CDx requisition form as outlined in Section 10.1.2 and Appendix I.
7. Patients with a history of a curatively treated malignancy must be disease-free for at least two years except for carcinoma in situ of cervix and/or non-melanomatous skin cancer. Patients must not have received chemotherapy or investigational therapy within two years of surgical resection of the primary tumor.
8. Patient must not have had previous irradiation to the head and neck that would result in overlap in radiation fields for the current disease.
9. Patients with recurrent disease or multiple primaries are ineligible.

Randomization (Step 1)

NOTE: Patient must meet all eligibility criteria outlined in Section 3.1. Patient may not be randomized until site has been notified that the central determination of p53 mutation status of the surgical tumor tissue has been completed and site has been notified of assay completion (see Sections 4.2 and 10).

1. Per the operative report, the gross total resection of the primary tumor with curative intent was completed within 8weeks prior to randomization.
2. The patient must have the following assessments done ≤ 8 weeks prior to randomization:
   - Examination by a Head & Neck Surgeon, but the treating medical or radiation oncologist is permissible.
   - Chest x-ray (or chest CT scan or CT/PET of the chest or MRI) to rule out distant metastatic disease.
3. Patient has ECOG Performance Status 0-1 within 2 weeks prior to randomization
4. Women must not be pregnant or breast-feeding due to exposure to cisplatin chemo-and/or radiotherapy. Females of childbearing potential must have a blood or urine study within 2 weeks prior to randomization to rule out pregnancy.
   A female of childbearing potential is any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).
5. Women of childbearing potential and sexually active males must be strongly advised to use an accepted and effective method of contraception or to abstain from sexual intercourse for the duration of their participation in the study and until 60 days from the last study treatment.
6. Patients must have acceptable renal and hepatic function within 4 weeks prior to randomization as defined below:
   - Absolute neutrophil count ≥1,500/mm3

- Platelets ≥ 100,000/mm3
- Total bilirubin ≤ the upper limit of normal (ULN)
- Calculated creatinine clearance must be > 60 ml/min using the Cockcroft-Gault formula: (140-age)*wt(kg)/([Cr]*72). For women the calculation may be multiplied by 0.85

7. Patient must not have an intercurrent illness likely to interfere with protocol therapy.