NCI National Clinical Trials Network

EA3161

ECOG-ACRIN cancer research group

For Patients with Oropharyngeal Squamous Cell Carcinoma

EA3161 Available Through ECOG-ACRIN Cancer Research Group

A Phase III Randomized Study of Maintenance Nivolumab versus Observation in Patients with Locally Advanced, Intermediate Risk HPV Positive OPSCC

Patient Population

See Section 3 or Complete Eligibility Details

Eligibility Criteria for Step 1 Randomization:

- Age ≥ 18 years, ECOG PS 0-1, adequate lab values
- Must have oropharynx cancer (AJCC 8) that is p16-positive by immunohistochemistry ***or*** p16 equivocal by IHC and HPV positive by in situ hybridization, with: ≥ 10 pack-years, stage T1-2N2-N3 or T3-4N0-3 ***or*** < 10 pack-years, stage T4N0-N3 or T1-3N2-3
- Must not have known hypersensitivity to nivolumab/ compounds of similar chemical/biological composition; no history of allergic reactions attributed to platinum-based chemotherapy agents
- Must not have had prior systemic therapy, radiation treatment or surgery for p16 positive OPSCC (see protocol for details)
- Must not have received previous radiation for head and neck tumor, skull base, or brain tumors
- Patients with evidence of distant metastases/ leptomeningeal disease are excluded
- No patients with uncontrolled inter-current illness that would interfere with the ability to undergo therapy
- Patients with a history of prior/2nd malignancy are excluded (see protocol for exceptions)
- Must have measurable disease per protocol
- Must have tumor measurements with CT of neck and CT of chest (or CT of neck and FDG PET/CT if standard of care) within 4 wks prior to step 1 randomization
- Must not have autoimmune disease(s) per protocol
- Must not have baseline clinically significant hearing loss

Eligibility Criteria for Step 2 Registration:

- Must have progression (RECIST) and tissue-proven progression on Arm B treatment within 12 mos after completion of radiation therapy
- Must not have received non-protocol anti-cancer therapy after completion of radiation and chemotherapy
- ECOG PS 0-1 and adequate lab values
- Tumor measurements with CT of neck and CT of chest (or CT of neck and FDG PET/CT if standard of care) within 4 wks prior to step 2 registration

Treatment Plan

See Section 5 for Complete Treatment Details

Arm A:

- Cisplatin 40 mg/m^2 weekly (+/- 2 days) during a 5 days/wk radiation schedule with 70 Gy of radiation administered once daily; 7 weeks
- Maintenance therapy with nivolumab will initiate within 4-8 weeks after completion of concurrent therapy of cisplatin/RT
  - ◊ Nivolumab administered at 480 mg IV q4 wks for 12 cycles (thus completing 1 yr maintenance therapy provided there is no evidence of disease progression/other reason for discontinuation, i.e., toxicity)

Arm B:

- Cisplatin 40 mg/m^2 weekly during a 5 days/wk radiation schedule with 70 Gy of radiation administered once daily; 7 weeks
- Following the completion of the 7 weeks of concurrent therapy of cisplatin/RT, the patient will go on to observation

Arm C:

- Patients who were randomized to observation will be offered the option to cross over if they have clearly documented progression per protocol
- After progression and registration to Step 2, nivolumab will be administered at 480 mg IV q4 wks for 12 cycles starting within 2 wks of Step 2 registration
- Patients will complete a total of 1 yr of therapy provided there is no evidence of disease progression/ other reason for discontinuation

Notes:

- *See protocol for hydration and antiemetic details*
- *See protocol for salvage surgery details (Arms A and B)*
- *See protocol for RT credentialing requirements*
  - ◊ *IMRT and IGRT are required; proton therapy is not permitted; at least 4 MV shall be used; cyberknife treatment is not allowed*
- *CT simulation is required for all patients*

Study Chair:
Nabil F. Saba, MD

Patient Enrollment

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

Protocol Information

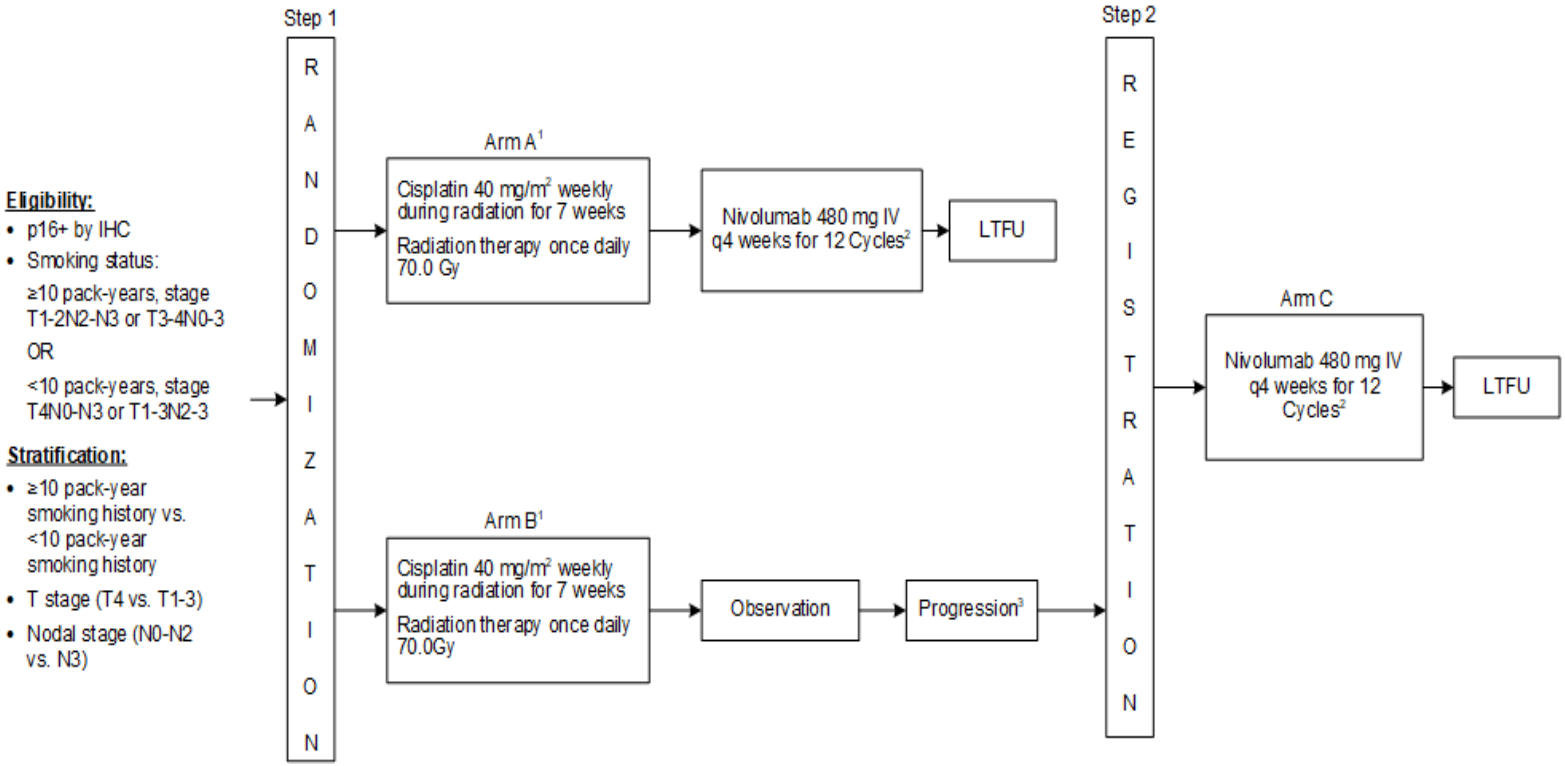
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

Version 08/18/23 (Add. #5)

EA3161

Schema



Accrual Goal: 636

1. Submit tissue for PD-L1 testing.
2. Cycle length = 28 days
3. Patients who were randomized to observation will be offered the option to cross over if they have clearly documented progression by the RECIST criteria and tissue-proven progression within 12 months from the end of cisplatin/radiation therapy.