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 3.0 for 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 5.0 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

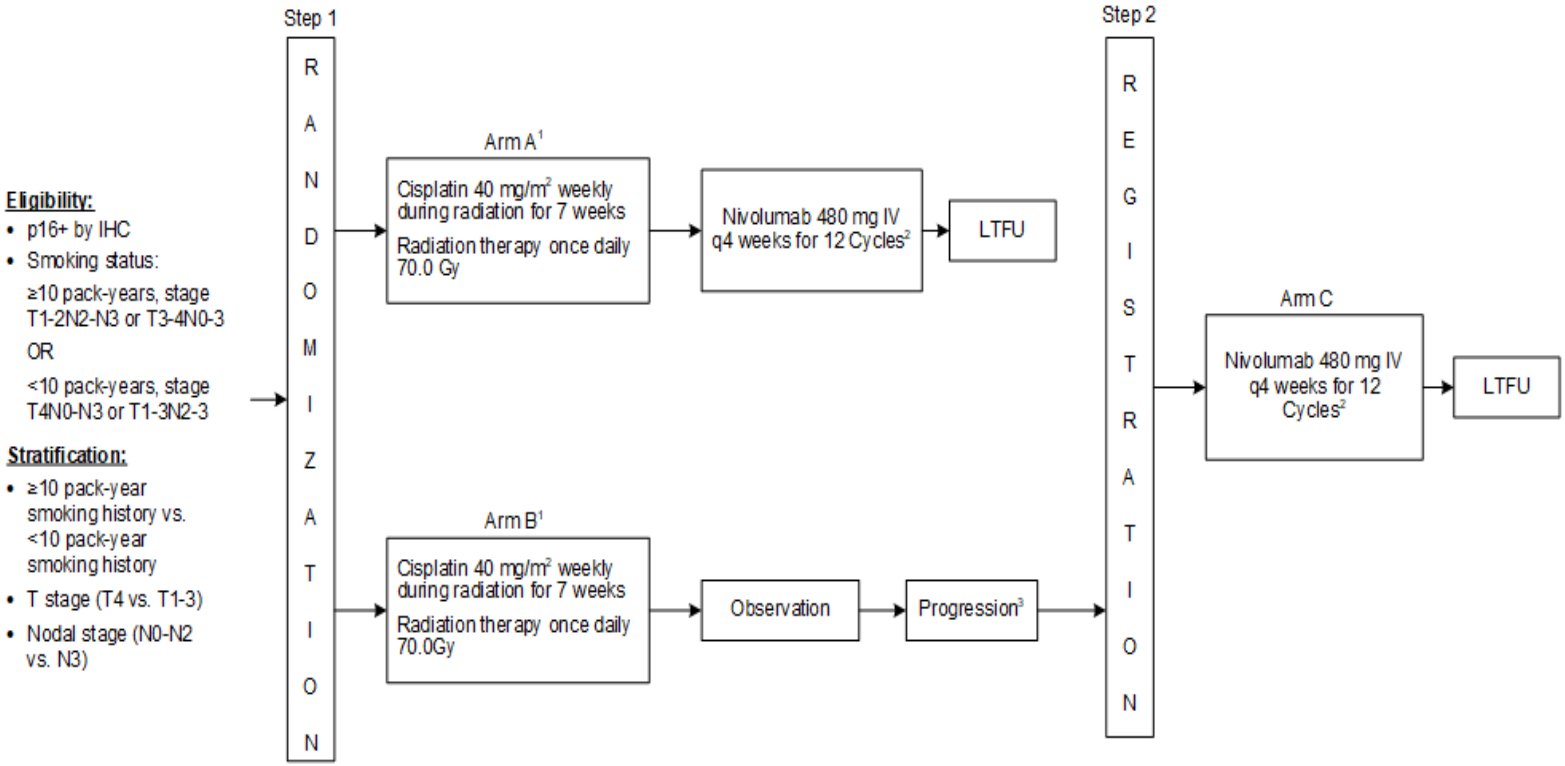
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

Version 12/02/21 (Add. #4)

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.