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 T1-2N2-3 or T3-4N0-3 or < 10 pack-years, stage T4N0-3 or T3-4N2-3
• 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/m² 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/m² 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

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

Protocol Information

Please Enroll Your Eligible Patients!