NCI National Clinical Trials Network

EA3211

ECOG-ACRIN cancer research group

For Patients with Oligometastatic HNSCC

EA3211 Available Through ECOG-ACRIN Cancer Research Group

Phase III Randomized Trial of Immunotherapy with or without Consolidative Radiotherapy for Oligometastatic Head and Neck Squamous Cell Carcinoma

Patient Population

See Section 3.0 for Complete Eligibility Details

Step 1 Registration:

- ≥ 18 years of age, ECOG PS 0-1, adequate lab values
- Must have biopsy-proven metastatic squamous cell carcinoma, originating in the oral cavity, larynx, oropharynx or hypopharynx, with active disease present in both the head and neck (H&N) and distant sites
  - ◊ Note: the tumor from an oropharynx primary site must have known p16 status; p16 positive cancer of unknown primary is allowed provided the disease presentation is consistent with a H&N primary
- Can have prior surgical resection of a primary cancer in the H&N at any previous time; however, residual/recurrent disease in the H&N must be present on baseline imaging; no prior H&N radiotherapy
- Must have 4 or fewer metastatic sites prior to starting any treatment, with thoracic nodal disease considered a single site if encompassable in a tolerable radiotherapy hypofractionated field (i.e., 15 fractions or less; see protocol)
- Must have measurable disease defined per protocol
- HIV, HBV, and HCV patients are permitted per protocol
- Arm S: must have received chemoimmunotherapy consistent with protocol section 5.1
- Patients with a prior/concurrent malignancy whose natural history/treatment does not have the potential to interfere with safety/efficacy are eligible
- No active autoimmune disease that has required systemic treatment in the past 2 years (see protocol)

Step 2 Randomization:

- ECOG PS 0-2; must have completed 3 cycles of initial systemic chemotherapy
- Arm S: must have at least stable disease after completing 3 cycles of pembrolizumab + chemotherapy (defined per protocol section 5.1)
- Must have no signs of progression (CR/PR/SD) on restaging imaging (consisting of neck, chest, and abdomen CT), done after initial Step 1 therapy and within 7 days prior to Step 2 randomization

Treatment Plan

See Section 5.0 for Complete Treatment Details

Step 1– Arms S and T (pembro + chemotherapy):

- Cycle = 21 days; patients to continue with the same regimen until 3 cycles are completed (note: if dose modifications are not sufficient, patients may switch regimens per the investigator's discretion)
- **Option 1**: pembro 200 mg IV day 1 of each cycle; carboplatin AUG 5 day 1; paclitaxel per protocol
- **Option 2**: pembro 200 mg IV day 1 of each cycle; cisplatin 100 mg/m² IV day 1 of each cycle; 5-FU 1000 mg/m² IV per day on continuous infusion days 1-4 of each cycle
- **Option 3**: pembro 200 mg IV day 1 of each cycle; carboplatin AUG 5 day 1; 5-FU 1000 mg/m² IV per day on days 1-4 of each cycle
- Restaging imaging; patients without progression will be randomized to Arms A or B

Step 2– Arm A (consolidative radiotherapy with pembrolizumab):

- All patients will receive a 4th cycle of initial systemic therapy before consolidation
  - ◊ Radiation therapy per protocol Section 5.2 (once daily x 30 fractions for a total of 66 Gy)
  - ◊ Pembro 200 mg IV day 1 of each cycle until progression or a total of 2 years from the start of chemoimmunotherapy (note: pembro 400 mg IV every 6 weeks may be used after radiation ends)

Step 2– Arm B (pembro monotherapy):

- All patients will receive a 4th cycle of initial systemic therapy before consolidation
  - ◊ Pembro 200 mg IV day 1 of each 21-day cycle for 6 cycles followed by pembro 400 mg IV day 1 of each 42-day cycle until progression or a total of 2 years from the start of chemoimmunotherapy

Note: post-progression therapy is at the discretion of the treating oncologist

Study Chair:
David J. Sher, MD, MPH

Patient Enrollment

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

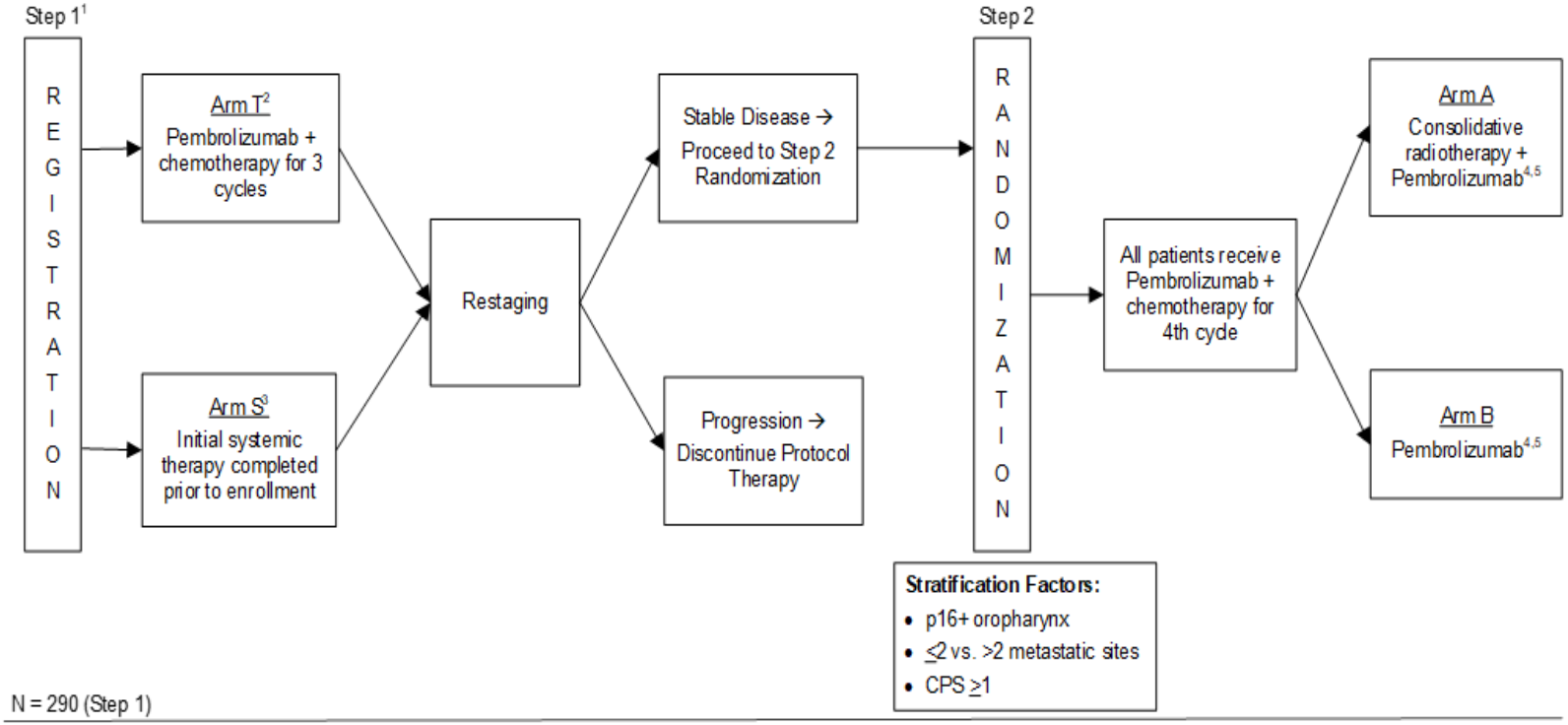
Protocol Information

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

Please Enroll Your Eligible Patients!

EA3211

Schema



1. PET-CT imaging is strongly recommended at baseline and 12-14 weeks from the conclusion of radiotherapy (Arm A) or from the start of cycle 7 (Arm B).
2. Patients who have not started any initial systemic therapy or who have started but not completed their initial systemic therapy will be enrolled on Arm T to complete their 3 cycles of initial systemic therapy. See Section 5.1 for details regarding the systemic therapy options.
3. Patients who have completed 3 cycles of initial systemic therapy as defined in Section 5.1 prior to enrollment on Step 1 will be enrolled on Arm S and proceed directly to Step 2 randomization (after verifying eligibility).
4. Patients will receive maintenance treatment on Step 2 until progression or a total of 2 years. Thereafter, patients will be followed for survival.
5. Patients on Arm A: At the time of progression, any future treatment will be at the investigator's discretion. Patients on Arm B: At the time of progression, if all progression is within sites of disease present at registration, treating oncologists are encouraged but not required to treat progressing disease per Arm A (See Sections 5.1.2 and 5.2) while continuing Pembrolizumab. If the decision is not to treatment per Arm A, any future treatment will be at the investigator's discretion.