NCI National Clinical Trials Network

EA3211

ECOG-ACRIN cancer research group

For Patients with Oligometastatic HNSCC

Please Enroll Your Eligible Patients!

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 protocol Section 3 for complete eligibility criteria

Step 1 Registration:

- ≥ 18 years of age, ECOG PS 0-1, adequate lab values, measurable disease defined per protocol
- Biopsy-proven metastatic squamous cell carcinoma, originating in the oral cavity, larynx, oropharynx or hypopharynx, with either 1) synchronous disease defined as active disease present in both the head and neck (H&N) and distant sites (Cohort S) or 2) metachronous disease defined as active disease only in distant sites with no evidence of locoregional recurrence with the primary H&N therapy completed at least 6 months prior to registration (Cohort M)
  - ◊ Note: 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
- Cohort S: Can have prior surgical resection of a primary cancer in the H&N at any previous time; but, residual/recurrent disease in the H&N must be present on baseline imaging. Cohort S: No prior H&N radiotherapy
- Must have ≤ 4 metastatic sites (defined by number of isocenters required to treat the metastatic disease) prior to starting any treatment, with thoracic nodal disease considered a single site if encompassable in a tolerable RT hypofractionated field (i.e., ≤ 15 fractions; see protocol)
- Arm S: must have received chemoimmunotherapy consistent with Section 5.1
- No active autoimmune disease that has required systemic treatment in the past 2 years, per criterion 3.1.16

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
- No signs of progression on restaging imaging (neck, chest, and abdomen CT), done after Step 1/initial systemic chemotherapy and ≤ 7 days prior to Step 2 randomization

Treatment Plan

See protocol Section 5 for complete treatment details

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

- Cycle = 21 days +/- 3 days; continue same regimen for 3 cycles (note: dose mods permitted per Section 5.5; if mods not sufficient, may switch regimens)
- **Option 1**: Pembro 200 mg IV Day 1 or 400 mg IV every 6 weeks; Carboplatin AUC 5 on Day 1 or AUC 2 on Days 1 and 8; Paclitaxel 175 mg/m² IV on Day 1 or 80 mg/m² or 100 mg/m² on Days 1 and 8
- **Option 2**: Pembro 200 mg IV Day 1 or 400 mg IV every 6 weeks; Cisplatin 100 mg/m² IV on Day 1; 5-FU 1000 mg/m² IV/day on continuous infusion Days 1-4
- **Option 3**: Pembro 200 mg IV Day 1 or 400 mg IV every 6 weeks; Carboplatin AUC 5 on Day 1; 5-FU 1000 mg/m² IV/day on continuous infusion Days 1-4
- After 3 cycles, restaging imaging; patients without progression will be randomized to Arm A or B

Step 2 – Arm A (consolidative RT + pembro):

- All patients will receive a 4th cycle of initial systemic therapy before consolidation (see Section 5.1.2)
- Patients in Cohort S- RT per Section 5.2: 66 Gy total over 30 daily fractions (6 weeks); begin ≤ 3 weeks after completion of Cycle 4
- Pembro 200 mg or 400 mg IV until progression or 2 years from start of chemo-immunotherapy

Step 2 – Arm B (pembro monotherapy):

- All patients will receive a 4th cycle of initial systemic therapy before consolidation (see Section 5.1.3)
- Pembro 200 mg or 400 mg IV until progression or 2 years from the start of chemoimmunotherapy

Note: post-progression therapy is at the discretion of the treating oncologist. If all progression is within sites of disease present at Step 1 registration, treating oncologists are encouraged to treat per Arm A while continuing pembro

Study Chair:
David J. Sher, MD, MPH

Study Co-Chair:
Jessica Bauman, MD

NCTN Study Champions:
•Alliance:
Ari Rosenberg, MD
•NRG:
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Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

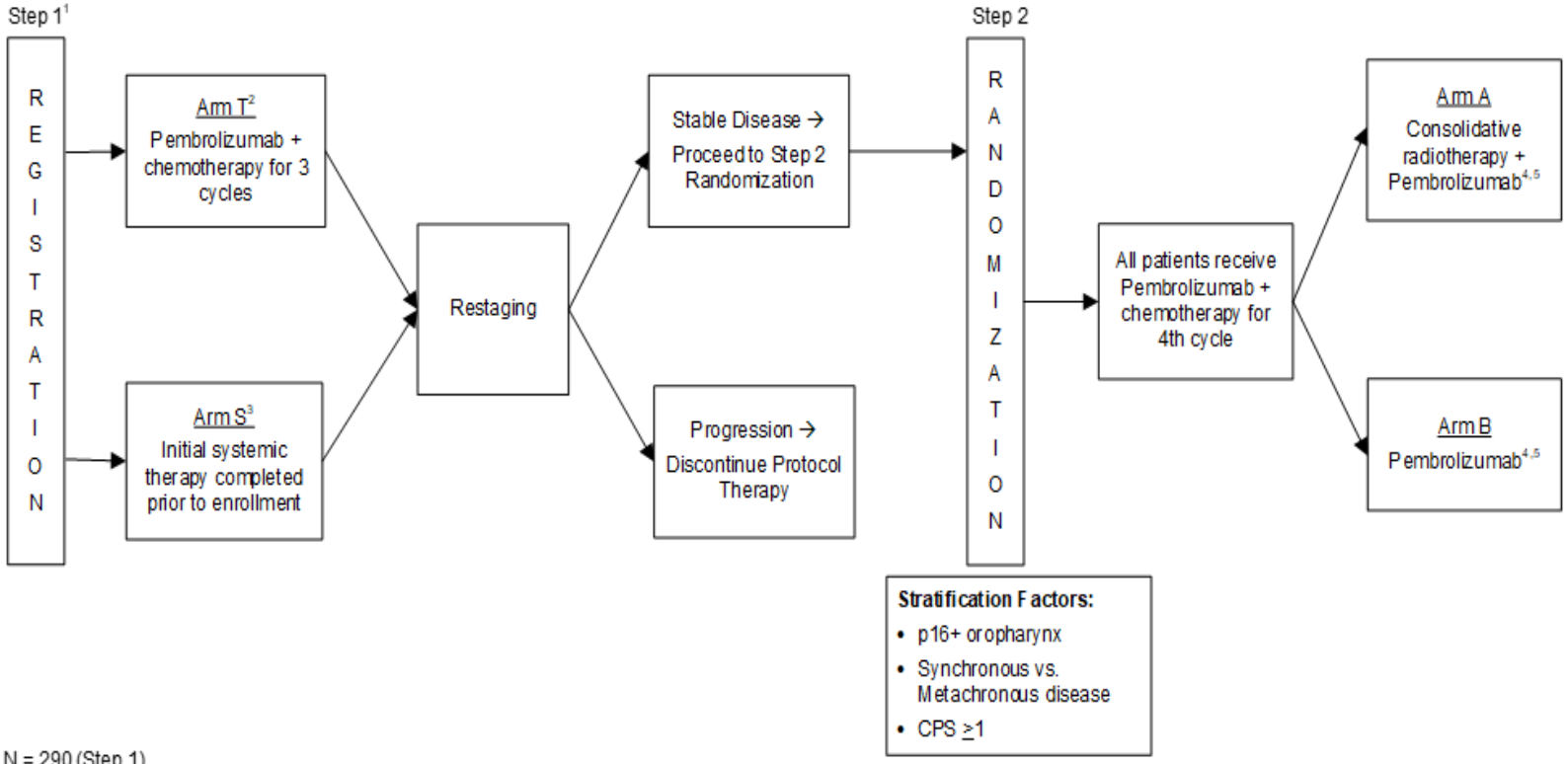
Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

v.04/22/25 (Add. #6)

EA3211

Schema



N = 290 (Step 1)

1. PET-CT imaging is strongly recommended at baseline and 12-14 weeks from the conclusion of radiotherapy (Arm A) or 21-23 weeks after randomization (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 treat per Arm A, any future treatment will be at the investigator's discretion.