# EA3191

## For Patients with Head and Neck Squamous Cell Carcinoma

**EA3191 Available Through ECOG-ACRIN Cancer Research Group**

A Phase II Randomized Trial of Adjuvant Therapy with Pembrolizumab after Resection of Recurrent/Second Primary Head and Neck Squamous Cell Carcinoma with High Risk Features

### Patient Population
See Section 3 for Complete Eligibility Details

- 18-79 years of age, ECOG PS 0-1, and adequate lab values
- Must have locoregionally recurrent or second primary HNSCC (oral cavity, oropharynx, larynx, hypopharynx) in a previously radiated field
- Must have undergone surgery with gross total resection and must be randomized within 8 weeks of surgery
- Must have high risk disease defined per protocol
- Must have a PD-L1 CPS ≥ 1 (in a CLIA laboratory)
- Must have had prior radiation to the area of recurrent/second primary tumor (defined per protocol); completed a minimum of 6 months prior to randomization
- Must not have any evidence of distant disease based on baseline imaging done within 28 days prior to randomization
- Must not have received anti-PD-1/PD-L1 therapy for recurrent disease (see protocol for details)
- HIV-infected patients are eligible per protocol
- Must have no known history of Hepatitis B or active Hepatitis C infection
- Must not have a current active infection that requires systemic treatment within 30 days prior to randomization
- No history of non-infectious pneumonitis requiring steroids within 3 years prior to randomization
- No history of solid organ/stem cell transplant
- Must not be on immunosuppressive medication within 7 days of randomization (exceptions per protocol)
- Patients with known history/current symptoms of cardiac disease/history of treatment with cardiotoxic agents: NYHA Class III/IV heart failure is not eligible
- Must not have received a live vaccine within 30 days prior to first dose of study drug
- Must not have ≥ Grade 3 hypersensitivity to pembrolizumab and/or any of its excipients
- Must not have an active autoimmune disease that required systemic treatment in the past 2 years (see protocol for details)

### Treatment Plan
See Section 5 for Complete Treatment Details

**Arm B (re-irradiation plus platinum chemo):**
- Re-irradiation (IMRT or Proton) 2 Gy once daily x 30 fractions for a total of 60 Gy
- Cisplatin 40 mg/m² IV (infused over 1 hour) weekly x 6 cycles OR carboplatin AUC 2 IV (infused over 1 hour) weekly x 6 cycles; see protocol for criteria of when to give carboplatin

**Arm C (pembrolizumab monotherapy):**
- Pembrolizumab 400 mg IV over 30 minutes q 6 weeks x 9 cycles (~12 months of therapy)

Notes:
- A patient must be randomized within 8 weeks of surgery and treatment started within 10 weeks of surgery
- Doses of chemotherapy can be given before or after radiation
- All cycles of pembrolizumab have a +/- 3 day window for administration
- Radiation must start on a Monday, Tuesday, or Wednesday

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**Study Chair:**
Dan P. Zandberg, MD

**Study Co-chairs:**
Zain Husain, MD
Mihir Patel, MD

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

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

Please Enroll Your Eligible Patients!
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Schema (Post-Addendum #7)

Actively enrolling upon activation of Addendum #7

Arm B
- Reirradiation 2 Gy once daily x 30 fractions for a total of 60 Gy
- Cisplatin 40mg/m² IV weekly x 6 cycles OR Carboplatin AUC 2 IV weekly x 6 cycles

Arm C
- Pembrolizumab 400mg IV q 6 weeks X 9 cycles

Stratification Factors:
- HPV status oropharynx only (p16 positive vs. negative by local testing)
- PD-L1 by Combined Positive Score (1-19 vs. ≥20)
- Received prior anti-PD-1/PD-L1 as part of curative intent therapy. Yes vs. No

Accrual Goal: 188

1. High risk features include Positive Margins and/or Extranodal Extension.
2. Randomization is 1:1 across all arms.
3. Carboplatin will be given for patients who are ineligible for cisplatin.