# For Patients with Locoregional Esophageal and Gastroesophageal Junction Adenocarcinoma

## EA2174 Available Through ECOG-ACRIN Cancer Research Group

A Phase II/III Study of Peri-operative Nivolumab and Ipilimumab in Patients with Locoregional Esophageal and Gastroesophageal Junction Adenocarcinoma

### Patient Population

**See Section 3.0 for Complete Eligibility Details**

- Age ≥ 18 years, ECOG PS 0-1 and adequate lab values
- Must have histologically confirmed T1N1-3M0 or T2-3N0-2M0 esophageal or gastroesophageal junctional adenocarcinoma (Siewert I and II)
- Must be deemed a surgical candidate by a thoracic surgeon, surgical oncologist, or surgeon qualified to perform an esophagectomy
- No prior chemotherapy/radiation therapy for management of this malignancy; no prior immunotherapy for management of this malignancy/any other past malignancy
- No contraindication to receiving carboplatin/paclitaxel chemotherapy/radiation therapy (RT)
- No active autoimmune disease/history of autoimmune disease that might recur, which may affect vital organ function/require immune suppressive treatment (see protocol)
- No condition requiring systemic treatment with corticosteroids/other immunosuppressive medications within 14 days of study drug administration (see protocol)
- Adequate cardiac function per protocol
- Must not test positive for HepB/C per protocol; HIV/AIDS patients must have no detectable viral load on a stable antiviral regimen
- No patients with uncontrolled intercurrent illness (see protocol)
- Patients must be able to tolerate MRI scans if they answer ‘Yes’ to taking part in the imaging portion (no claustrophobia, no MR incompatible implants/devices/metallic foreign bodies, weight compatible with MRI scanner table)
- Women must not be pregnant/breast-feeding

### Treatment Plan

**See Section 5.0 for Complete Treatment Details**

**Step 1:** day 1 will begin on the first day of RT +/- 2 days

- **Arm A:** Weeks 1-5: Carboplatin AUC of 2 once weekly AND, Paclitaxel 50 mg/m² IV once weekly
- **Arm B:** Weeks 1-5: Carboplatin AUC of 2 once weekly AND, Paclitaxel 50 mg/m² IV once weekly AND, Nivolumab 240 mg IV days 1 and 15

**Radiation Therapy** (to begin within 10 days after Step 1 registration):

- Photon (3D-CRT and IMRT) or proton therapy (passive-scattering and scanning beam; requires credentialing) are allowed
- Total prescription dose: 50.4 Gy in 28 fractions (1.8 Gy per fraction); 41.4 Gy to 50.4 Gy is permitted per treating radiation oncologist discretion

- **Surgical resection** to occur 4-8 weeks after treatment completion, although surgery may be performed up to 12 weeks post therapy completion; surgical approach is at the treating surgeons discretion (see protocol)

**Step 2:** 1 cycle = 2 weeks

- **Arm C:** 6 month course of therapy; nivolumab 240 mg IV day 1 cycles 1-12
- **Arm D:** 6 month course of therapy; nivolumab 240 mg IV day 1 cycles 1-12 AND, ipilimumab 1 mg/kg IV once every 6 weeks day 1 cycles 1, 4, 7, 10

### Notes:

- All doses are based on actual body weight except for nivolumab, which is given as a flat dose (see protocol for details); Calvert formula will be used for carboplatin dosing
- Monitor patients per protocol prior to drug administration
- Nivolumab: a missed dose should not be replaced; dose modifications are not permitted/dose delays are allowed
- If a week of carboplatin and paclitaxel is missed, it may be made up during week 6 as long as there is RT still to be administered (max = 5 doses)

### Patient Enrollment

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

### Protocol Information

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

Please Enroll Your Eligible Patients!
1. Please reference Section 5.1 for treatment dosing specifics.

2. Optional diffusion weighted imaging-MRI (DWI-MRI) should be obtained at step 1, baseline and 2-3 weeks after initiation of protocol treatment.

Schema

- \( E \rightarrow \text{Baseline DWI-MRI} \rightarrow \text{Optional DWI-MRI} \)
- \( \text{Am A} \rightarrow \text{Am B} \)
- \( \text{RT} \) and 2-3 weeks after start of RT
- \( \text{PET/CT} \)
- \( \text{Am A} \rightarrow \text{Am B} \)
- \( \text{Enrollment Therapy} \) (RT)
- \( \text{Radiation Therapy} \) (RT)
- \( \text{Clinical vs. Negative} \)
- \( \text{Am A} \rightarrow \text{Am B} \)
- \( \text{Enrollment Therapy} \) (RT)
- \( \text{Radiation Therapy} \) (RT)
- \( \text{PET/CT} \)
- \( \text{Am A} \rightarrow \text{Am B} \)
- \( \text{Enrollment Therapy} \) (RT)
- \( \text{Radiation Therapy} \) (RT)
- \( \text{PET/CT} \)
- \( \text{Am A} \rightarrow \text{Am B} \)
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- \( \text{Am A} \rightarrow \text{Am B} \)