**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 anti-viral 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/metabolic foreign bodies, weight compatible with MRI scanner table)
- Women must not be pregnant/breast-feeding

**Eligibility (Step 2):**

- Postoperative ECOG PS 0-2 and adequate lab values
- Must be disease free following esophagectomy, demonstrated by having no evidence of disease on a post-surgical CT scan

### 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):
  - 3D-CRT and IMRT (credentialing required) is allowed; CT-based treatment planning is required; (4DCT based planning is allowed/preferred); Megavoltage equipment with effective photon energies ≥ 6MV is required; ICRU-50/ICRU-62 prescription and nomenclature shall be utilized
  - Total prescription dose will be 50.4 Gy in 28 fractions (1.8 Gy per fraction)
- 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:

- Doses are based on actual body weight except for nivolumab, which is given as a flat dose; the Calvert formula will be used for carboplatin dosing
- Premedications are not required prior to nivolumab
- Monitor patients per protocol prior to drug administration
- A missed dose of nivolumab should not be replaced; dose modifications for nivolumab are not permitted

---

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

**Schema**

**Step 1:**
- Arm A
  - Carboplatin IV weekly
  - Paclitaxel IV weekly
  - Radiation Therapy (RT)
  - Optional DWI-MRI; Baseline and 2-3 weeks after start of RT

- Arm B
  - Carboplatin IV weekly
  - Paclitaxel IV weekly
  - Radiation Therapy (RT)
  - Nivolumab IV d1, d15 of RT
  - Optional DWI-MRI; Baseline and 2-3 weeks after start of RT

- Esophagectomy

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

<table>
<thead>
<tr>
<th>Arm C</th>
<th>Arm D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab IV q2 weeks x12</td>
<td>Nivolumab IV q2 weeks x12</td>
</tr>
<tr>
<td>Ipilimumab IV q6 weeks x4</td>
<td>Ipilimumab IV q6 weeks x4</td>
</tr>
</tbody>
</table>

**Stratify**
- Lymph node status: Positive vs. Negative
- Path CR: Yes vs. No
- Step 1 arm: Arm A vs. Arm B

**N=278**

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.