# EA2176
For Patients with Metastatic Anal Cancer

**EA2176 Available Through ECOG-ACRIN Cancer Research Group**

A Randomized Phase III Study of Immune Checkpoint Inhibition with Chemotherapy in Treatment-Naïve Metastatic Anal Cancer Patients

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>See Section 3 for Complete Eligibility Details</strong></td>
<td><strong>See Section 5 for Complete Treatment Details</strong></td>
</tr>
</tbody>
</table>

**Cycle = 28 days**

**Arm A (Control Arm):**
- First, paclitaxel (80 mg/m²) IV Day 1, 8, and 15
- Followed by carboplatin (AUC= 5) IV Day 1
- Repeat cycles every 4 weeks, up to 6 cycles

**Arm B (Investigational Arm):**
- First, nivolumab 240 mg for the first cycle (cycle 1, day 1 and 15) followed by 480 mg IV q4 weeks (cycles ≥ 2 day 1)
- Then, paclitaxel (80 mg/m²) IV Day 1, 8, and 15
- Followed by carboplatin (AUC= 5) IV Day 1
- Repeat cycles every 4 weeks, up to 6 cycles (carboplatin and paclitaxel will be given for 6 cycles, however, nivolumab may continue as single agent therapy until disease progression or intolerance [max of 2 years])

**Notes:**
- Carboplatin doing is based on Calvert formula, using actual body weight for each cycle
- Paclitaxel doing is based on body surface area, using actual body weight
- Nivolumab is a flat dose
- See protocol 5.1.3 for suggested antiemetic therapy

**Patient Population**
- Age ≥ 18 years, ECOG PS ≤ 0-1, adequate lab values
- Must have inoperable, recurrent, or metastatic disease not amenable to curative therapy
- Must have histological/cytological confirmation of anal squamous cell carcinoma (includes basaloid and cloacogenic lesions) from the primary tumor or a newly diagnosed recurrent/metastatic lesion
- Must have measurable disease (RECIST 1.1); based on radiologic assessment < 4 weeks prior to randomization
- Palliative (limited-field) radiation therapy is allowed, as long as the lesion is not a target lesion and the patient is > 7 days from completion from palliative radiation
- Patients with brain metastasis are eligible per protocol
- HIV, HBV, HCV patients are permitted per protocol
- Patients with known history/current symptoms of cardiac disease should be NYHA class 2B or better
- Must not have had previous use of systemic chemotherapy or other investigational drugs for the treatment of inoperable recurrent/metastatic anal cancer (see protocol for exceptions)
- Must not have current/recent (within 30 days) treatment with another investigational drug/participation in another investigational study
- Must not have had prior immunotherapy
- Must not have a history of known hypersensitivity reaction to any platinum or taxane-based chemotherapy or monoclonal antibody
- Must not have active/history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment including chronic prolonged systemic corticosteroids
- No history/evidence of interstitial lung disease
- No known peripheral neuropathy > grade 1 at the time of randomization
- No live vaccines while on the study

**Study Chair:**
Cathy Eng, MD, FACP

**Co-Chairs:**
Kristen Ciombor, MD
Al B. Benson III, 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!
1. Randomization

1.2 (A-B)

Repeat cycle every 4 weeks up to 2 years

Cycl ode 1:
Nivolumab is given every 2 weeks during 4 cycles (cycles 2-7) at Day 1 (cycle 1) followed by 460 mg IV q4w for the first 4 cycles (cycle 1 and 2) or by 240 mg IV q4w for the first cycle (cycle 1) and 160 mg IV q4w for cycles 2-4.

Cycles only
Caudal or Pedalact were given up to 6

Pedalact (80 mg/m²) IV on Days 1, 8, 15
Caudal (AUC=5) IV on Day 1
1 q3d = 4 weeks (28 days)

A m A

Follow-Up?

Randomization

1.2

1. Randomization

1.2 (A-B)

Repeat cycle every 4 weeks up to 6 cycles

Pedalact (80 mg/m²) IV on Days 1, 8, 15
Caudal (AUC=5) IV on Day 1
1 q3d = 4 weeks (28 days)

A m A

Follow-Up?

either metastatic squamous cell or head/neck, unresectable, recurrent patients with surgically resectable disease.

Key Eligibility Criteria:

- HIV status (positive vs. negative/unknown)
- The primary tumor (yes/no)
- Prior history of chemoradiation with current intent to

Schema