Version 08/15/23 (Add. #3)

NCI National Clinical Trials Network

# EA2176

ECOG-ACRIN cancer research group

## 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

### Patient Population

See Section 3 for Complete Eligibility Details

- 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

### Treatment Plan

See Section 5 for Complete Treatment Details

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*

**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

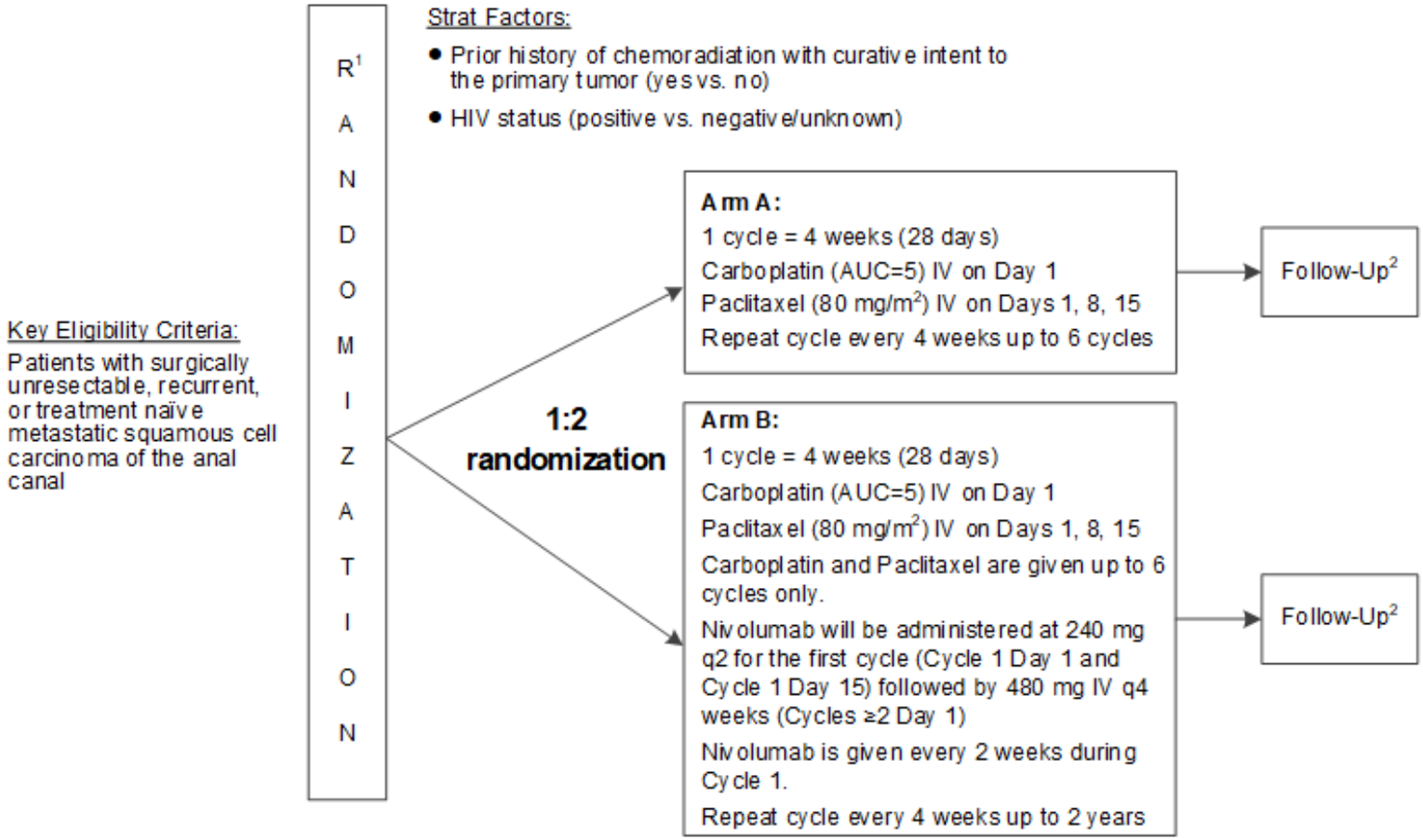
**Protocol Information**

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

## Please Enroll Your Eligible Patients!

EA2176

## Schema




1. Randomization is 1:2 (A:B).
2. For this protocol, all patients, including those who discontinue protocol therapy early, will be followed for response until disease progression, even if non-protocol therapy is initiated, and for survival every 3 months for two years from the date of randomization. All patients must also be followed through completion of all protocol therapy.