For Patients with Anal Cancer

EA2165 Available Through ECOG-ACRIN Cancer Research Group
A Randomized Phase II Study of Nivolumab After Combined Modality Therapy (CMT) in High Risk Anal Cancer

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Registration to Step 1 Eligibility Criteria:</strong></td>
<td><strong>Arm S- Step 1 Registration Following Standard Chemoradiotherapy:</strong></td>
</tr>
<tr>
<td>- Age ≥ 18 years, ECOG PS 0-2, adequate lab values</td>
<td>- Patients who have received chemotherapy as per suggested guidelines and registered to Step 2 will be randomized 1:1 to:</td>
</tr>
<tr>
<td>- Must have histologically proven stage IIB (T3N0M0), IIIB (T2N1M0), IIIC (T3N1M0, T4N1M0) invasive squamous cell carcinoma of the anus/anorectum (may include tumors of non-keratinizing histology, eg, basoloid, transitional cell, or cloacogenic); squamous cell carcinoma of the anal margin permitted per protocol</td>
<td>◦ Nivolumab 480 mg IV every 4 wks for 6 cycles/mos (Arm A), or</td>
</tr>
<tr>
<td>- Arm T: No prior chemoradiotherapy for anal cancer</td>
<td>◦ Observation: followed serially with CT imaging (Arm B); LTFU at 6 months</td>
</tr>
<tr>
<td>- HIV+ patients are permitted per protocol</td>
<td><strong>Arm T- Standard Chemoradiotherapy:</strong></td>
</tr>
<tr>
<td>- For patients registering prior to start of chemoradiotherapy, baseline scans must have been completed within 4 weeks prior to registration</td>
<td>- Any of 3 chemotherapy regimens per protocol:</td>
</tr>
<tr>
<td>- Patients with allogenic bone marrow/stem cell or solid organ transplant are excluded</td>
<td>◦ 5FU/mitomycin</td>
</tr>
<tr>
<td>- No prior potentially curative surgery for carcinoma of the anus; any surgery must have been completed ≥ 4 weeks prior to starting study treatment</td>
<td>◦ Capecitabine/mitomycin</td>
</tr>
<tr>
<td>- If history of other malignancy, must be disease-free for at least 2 years/deemed low risk for recurrence</td>
<td>◦ 5FU/cisplatin</td>
</tr>
<tr>
<td>- No active autoimmune disease in the past 2 years (exception per protocol)</td>
<td>- Radiation therapy (see protocol for details):</td>
</tr>
<tr>
<td>- No prior treatment with an immune checkpoint inhibitor</td>
<td>◦ IMRT or 3D conformal techniques; although not recommended, patients can also be treated using AP-PA fields</td>
</tr>
<tr>
<td>- No patients with immunodeficiency or receiving nivolumab equivalent to &gt; 10 mg prednisone per day</td>
<td>◦ PET-CT scans are recommended for target volume delineation</td>
</tr>
<tr>
<td>- No live vaccines within 30 days prior to registration</td>
<td>◦ High energy photons (≥ 6MV); minimum dose of 45 Gy to elective nodal region and 54 Gy to the primary</td>
</tr>
<tr>
<td>- No known interstitial lung disease that is symptomatic may interfere with the detection/management of suspected drug-related pulmonary toxicity</td>
<td>◦ Delivered once daily, 5 days per wk (all targets treated simultaneously for IMRT)</td>
</tr>
</tbody>
</table>

**Notes:**
- It is preferable that patients register to Step 1 prior to standard chemoradiation (Arm T) followed by Step 2 registration (following standard chemoradiotherapy); if a patient has already completed chemoradiation, the patient will register to Step 1 and immediately register to Step 2
- For patients on treatment at the time of Add#1 activation, the current full 4 wk cycle at 240 mg IV q2 wks should be completed; the next cycle will be 480mg IV q4 wks
- All doses are based on actual body weight

**Registration to Step 2 Eligibility Criteria:**
- Must have received at least 54 Gy of radiation to the PTVp and 45 Gy to PTVn for the treatment of anal cancer
- Adequate lab values; no history of allergic reactions attributed to nivolumab (or similar compositions)

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

**Protocol Information**

Please Enroll Your Eligible Patients!
EA2165 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase II Study of Nivolumab After Combined Modality Therapy (CMT) in High Risk Anal Cancer

Schema

Step 1
- Registration
  - Arm A: 5FU+mitomycin/XRT
  - Arm B: Capecitabine+mitomycin/XRT
  - Arm C: 5FU+cisplatin/XRT

Step 2
- Randomization
  - Stratification Factors
    - HIV Status (positive vs. negative)
    - Clinical Nodal Status (positive vs. negative)
    - Registration status (before vs. after chemo/RT)

LONG TERM FOLLOW UP
- Arm A: Nivolumab 480mg IV q4 weeks for 6 cycles
- Arm B: Observation

Cyde = 4 weeks (28 days)
Accrual Goal = 200 patients

1. High Risk Anal Cancer: Stage II B (T3N0M0 only), IIIA (T2N1M0), IIIB (T4N0M0), or IIIC (T3N1M0, T4N1M0) invasive squamous cell carcinoma of the anus or anorectum, according to the AJCC 8th edition. This may include tumors of non-keratinizing histology such as basooid, transitional cell, or cloacogenic histology. Individuals with squamous cell carcinoma of the anal margin are eligible if there is evidence of extension of the primary tumor into the anal canal. Patients can be registered prior to standard chemo/XRT or after completion of standard chemo/XRT.

2. Per treating physician.
3. Patients are eligible if completed standard chemo/XRT per Section 5.1.1.
5. Patients will be followed for up to 5 years from date of registration.
6. The total duration of observation should not exceed 6 months, at which point the patient will go into Long-term Follow-up.