**For Patients with Penile Cancer**

### EA8134 Available Through ECOG-ACRIN Cancer Research Group

**InPACT**: International Penile Advanced Cancer Trial  
(*International Rare Cancers Initiative Study*)

### Patient Population

**Inclusion Criteria:**
- Male, aged 18 years or older, PS 0-2
- Histologically-proven squamous cell carcinoma of the penis; Stage any T, N1-3, M0
- InPACT-neoadjuvant only: measurable disease (RECIST v1.1)
- Fit to receive the randomization options for which he is being considered (i.e., hematology, liver/renal function)
- Patients who are sexually active must be surgically sterile or must agree to use effective contraception

**Exclusion Criteria:**
- Pure verrucous carcinoma/non-squamous malignancy of the penis; squamous carcinoma of the urethra
- Stage M1; or regionally advanced (N1-3, M0) penile cancer with disease burden that is considered unresectable
- Previous chemotherapy/chemoradiotherapy outside of the InPACT trial
- Any absolute contraindication to chemotherapy (if eligible for that randomization)
- Concurrent malignancy (other than SCC or basal cell carcinoma of non-penile skin) that has required surgical/non-surgical treatment in the last 3 years
- Radiological evidence of macroscopic pelvic lymph node disease on post-ILND cross-sectional imaging

**Additional Neoadjuvant Criteria (see section 5.5):**
- Low disease burden: not eligible for the randomized component (entered directly/treated on Arm A); intermediate/high disease burden: suitable to receive neoadjuvant therapy (if no contraindication to chemotherapy)
- A GFR of ≥ 50 ml/min is acceptable for Arm B/C; will also accept 45-50 ml/min per protocol
- Patients with radiological evidence of macroscopic pelvic node involvement are eligible for randomization

**Additional Pelvis Criteria (see section 5.6):**
- Must be at high risk of relapse following ILND

### Treatment Plan

**Neoadjuvant chemotherapy**:
- Paclitaxel 175 mg/m² IV over 3 hours
- Ifosfamide 900 mg/m² IV over 1 hour outpatient; or 1200 mg/m² IV over 2 hours inpatient
- Cisplatin 15 mg/m² IV (outpatient) or 25 mg/m² IV (inpatient) over 1-2 hours

Patients will receive up to 4 cycles (1 cycle= 21 days). Then, they will proceed to therapeutic ILND (to occur 6-12 weeks after day 1 of the last chemotherapy cycle)

Synchronous chemoradiotherapy with cisplatin may be delivered in the neoadjuvant and the adjuvant setting, subject to patient’s treatment allocation, disease burden and GFR status:
- IMRT per protocol; for neoadjuvant treatment, the radiotherapy dose is 45 Gy in 25 fractions over 5 weeks; for adjuvant treatment, see the planning guidance document
- Cisplatin 40 mg/m² weekly

PLND will be performed as a separate procedure after inguinal lymphadenectomy in the majority of patients. It can be performed via infra-umbilical incision, extraperitoneal dissection, or by a minimally-invasive technique (robotic or laparoscopic)

### 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!
**TRIAL SCHEMA**

**InPACT-neoadjuvant**

Penis cancer patient with clinical OR radiological evidence of inguinal node metastases

Randomisation 1

Arm A

Therapeutic inguinal lymph node dissection

Pathological LOW risk

Pathological HIGH risk

InPACT-pelvis Randomisation*

Arm B

Neo-adjuvant Chemotherapy

RESTAGE

Therapeutic inguinal lymph node dissection

Pathological LOW risk

Pathological HIGH risk

InPACT-pelvis Randomisation*

Arm C

Neo-adjuvant Chemo-Radiotherapy

RESTAGE

Therapeutic inguinal lymph node dissection

Pathological LOW risk

Pathological HIGH risk

InPACT-pelvis Randomisation*

*Consent for InPACT-pelvis randomisation needed

**InPACT-pelvis**

Pathological HIGH risk patient

Have they already received neoadjuvant chemoradiotherapy?

No

Randomisation 2

Adjuvant Chemo-Radiotherapy*

Prophylactic Pelvic lymph node dissection

Arm Q

Arm P

Yes

Randomisation 2

Surveillance

Prophylactic Pelvic lymph node dissection

Arm Q

Arm P

*RT to groin & pelvis

*RT to groin alone or groin and pelvis