Cancer Research Consortium of West Michigan
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FAST FACTS

EA2182 - A Randomized Phase II Study of De-Intensified ChemoRadiation for Early- Stage Anal Squamous Cell Carcinoma (DECREASE)

Eligibility Criteria

1. Patient must be ≥ 18 years of age.
2. Patient must have histologically proven T1-2N0M0 invasive anal canal or anal margin squamous cell carcinoma with tumors measuring ≤ 4cm within 4 weeks prior to randomization. This may include tumors of non-keratinizing histology such as basaloid, transitional cell or cloacogenic histology. Measurable disease is as defined in Section 6.1.2.
   Patients with T1N0M0 anal margin squamous cell carcinoma who underwent surgical excision with negative margins are not eligible.
3. Patient must have histologically proven T1-2N0M0 invasive anal canal or anal margin squamous cell carcinoma with tumors measuring ≤ 4cm within 4 weeks prior to registration. This may include tumors of non-keratinizing histology such as basaloid, transitional cell or cloacogenic histology.
   Measurable disease is not required.
   Patients with T1N0M0 anal margin squamous cell carcinoma who underwent surgical excision with negative margins are not eligible.
4. Patient must have HIV status documented at baseline. For patients without a history of HIV infection, it is recommended (but not required) that updated HIV testing be performed within one year of study enrollment.
5. Patients who are HIV-negative must not have lymph nodes that are radiographically-concerning for cancer involvement using CT and FDG-PET/CT-based criteria (see table and bullet list below).

Anatomic Location	CT/MRI-based Size **OR**	CT/MRI-based Morphology **OR**	PET-based FDG uptake
Mesorectal, Presacral	Short axis > 5mm	Irregular Border **OR** Central necrosis (only for LN > 3mm on MRI)	> Blood pool (Deauville 3-5)
Internal Iliac, Obturator	Short axis > 7mm	Irregular Border **OR** Central necrosis	> Blood pool (Deauville 3-5)
Common Iliac and External Iliac	Short axis > 10mm	Irregular Border **OR** Central necrosis	> Blood pool (Deauville 3-5)
Inguinal	No size criteria	Irregular Border **OR** Central necrosis	> Liver (Deauville 4-5)

   a. Patients will be considered to be lymph node (LN) positive and thereby not eligible in this study if the lymph nodes meet any of the following criteria:
      i. Mesorectal, Presacral, internal iliac or obturator LN with:
         1. Short axis measuring > 5mm based on CT / MRI
            OR

2. Morphologic features of irregular border or central necrosis if assessed on MRI and LN measures > 3 mm
   OR
3. FDG uptake > blood pool (Deauville 3-5) based on FDG-PET/CT or PET/MRI.

ii. Internal Iliac or Obturator LN with:
1. Short-axis measuring > 7mm based on CT / MRI
   OR
2. Morphologic features of irregular border or central necrosis based on CT / MRI
   OR
3. FDG uptake > blood pool (Deauville 3-5) based on FDG-PET/CT or PET/MRI

iii. External Iliac and Common Iliac:
1. Short-axis measuring > 10mm based on CT / MRI
   OR
2. Morphologic features of irregular border or central necrosis based on CT / MRI
   OR
3. FDG uptake > blood pool (Deauville 3-5) based on FDG-PET/CT or PET/MRI.

b. Inguinal LN (superficial and deep) meeting any of the following criteria will be ineligible unless an FNA is performed and resulting cytology is negative.
   i. Morphologic features of irregular border or central necrosis based on CT / MRI
   ii. FDG uptake > liver (Deauville 4) based on FDG-PET/CT.
   iii. Patients who are HIV-negative and have inguinal lymph nodes that do not meet the above criteria must undergo fine needle aspiration and have negative histology to be eligible.

6. Patients who are HIV-positive must have:
   a. A CD4 count ≥ 200.
   b. Confirmation of no lymph node involvement by central real-time review of imaging per Section 10.
      NOTE: Patients will be pre-registered to Arm S. Upon central confirmation of no lymph node involvement, eligible patients may proceed to randomization on Step 1.
   c. No history of AIDS-related complications within past year other than a history of low CD4+ T-cell count (>200/mm3) prior to initiation of combination antiretroviral therapy
   d. Patient must be healthy on the basis of HIV disease with high likelihood of near normal life span were it not for the anal cancer
   e. Patient MUST receive appropriate care and treatment for HIV infection, including antiretroviral medications when clinically indicated, and should be under the care of a physician experienced in HIV management. Participants will be eligible regardless of antiretroviral medication provided the regimen has been stable for at least 4 weeks.

7. Patient must have ECOG-ACRIN performance status of 0-2.
8. Patient must have no history of prior radiation or chemotherapy for this malignancy.
9. Patient must not have had prior potentially curative surgery (i.e. abdominal-perineal resection) for carcinoma of the anus.
10. Patients with excisional biopsy procedure are eligible provided there was tumor involvement of the anal canal and/or anal verge prior to resection, or if the stage is T2N0 based on tumor size before the procedure.
11. Patient must not be receiving any other standard anti-cancer therapy or experimental agent concurrently with the study drugs.
12. Patient must not have intercurrent illness including, but not limited to, ongoing or active infection or psychiatric/social situations that, in the judgement of the investigator, would limit compliance with study requirements.
13. Patient must not have had significant cardiovascular disease including myocardial infarction, unstable angina, stroke, transient ischemic attack, symptomatic coronary artery disease, symptomatic congestive heart failure, or uncontrolled cardiac arrhythmia within 6 months of randomization.
14. Patient must not have a history of a different malignancy unless they have been disease-free for at least 2 years and are deemed by the investigator to be at low risk of recurrence. Individuals with the following cancers are eligible if diagnosed and treated within the past 5 years: cervical cancer in situ and basal cell or squamous cell carcinoma of the skin.
15. Patient must not have active autoimmune or connective tissue disease.
16. Patients who are on anti-coagulation with warfarin within 2 weeks prior to registration and are considering the use of capecitabine, must use an alternative anti-coagulant.
    NOTE: Low molecular weight heparin is permitted provided the patient's PT/INR is < 1.5.
17. Patients who will receive capecitabine and are on Dilantin for a seizure disorder must have Dilantin levels checked weekly.
18. Within 2 weeks prior to registration, patient must have
    a. Evidence of adequate hematologic function by:
        i. Hemoglobin > 10g/dL
        ii. Platelets ≥ 100,000/mm3
        iii. Absolute Neutrophil Count ≥ 1500/mm3
    b. Serum creatinine must be <1.5 X ULN, or calculated creatinine clearance must be > 50 ml/min.
       Serum creatinine _____Date of Test:_____
       or
       Creatinine clearance:_____ Date of Test:_____
    c. Evidence of adequate hepatic function by:
        i. Total bilirubin must be < 2X ULN.
        ii. AST/ALT ≤ 2.5 X institutional ULN.
    d. Albumin ≥ 3.0 g/dL.
19. Women must not be pregnant or breast-feeding because the study treatment administered may cause harm to an unborn fetus or breastfeeding child. All females of childbearing potential must have a blood test or urine study within 2 weeks prior to registration to rule out pregnancy. A female of childbearing potential is any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal (amenorrhea

following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).
Female of child bearing potential? _____ (Yes or No)
Date of blood test or urine study: _____

20. Women of childbearing potential and sexually active males must be strongly advised to use accepted and effective method(s) of contraception or to abstain from sexual intercourse for the duration of their participation in the study and for at least 6 months after the completion of treatment.

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