Cancer Research Consortium of West Michigan
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FAST FACTS

NRG-GU015, The Phase III Adaptive Radiation and Chemotherapy for Muscle Invasive Bladder Cancer Trial "ARCHER"

On Study Guidelines

Physicians should consider the following when evaluating if the patient is appropriate for this protocol:

- Patients must have adequate health that permits completion of the study requirements and required follow up.
- For patients with known HIV, HBV, and/or HCV:
    - HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.
    - For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.
    - Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.
- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
- Patients must be planning to receive one of the protocol-specified chemotherapy regimens.
- Participants of childbearing potential (participants who may become pregnant or who may impregnate a partner) must be willing to use highly effective contraceptives during therapy and for up to 14 months after completing study therapy because the treatment in this study may be significantly teratogenic (See protocol section 9 for definition of highly effective contraception).

Eligibility Criteria

3.2.1 Documentation of Disease

- Histologically proven, cT2-T3,N0M0 urothelial carcinoma of the bladder prior to randomization.
- *Note: Patients with mixed urothelial carcinoma will be eligible for the trial, but the presence of small cell carcinoma will make a patient ineligible.*

3.2.2 Definition of Disease

- Must undergo a TURBT prior to randomization. Patients may have either completely or partially resected tumors as long as the treating urologist attempted maximal resection.

- Must undergo radiological staging prior to randomization. Imaging of chest, abdomen, and pelvis must be performed using CT or MRI (with or without contrast is acceptable). Patients must not have evidence of T4 or node positive disease. FDG PET Imaging is acceptable for radiological staging.

- If any lymph nodes ≥ 1.0 cm in shortest cross-sectional diameter are noted on imaging (CT / MRI of abdomen and pelvis), then the patient must have had a biopsy of the enlarged lymph node showing no tumor involvement prior to randomization.

- No diffuse CIS based on cystoscopy and biopsy.

- No definitive clinical or radiologic evidence of metastatic disease.

- Must not have had urothelial carcinoma or histological variant at any site outside of the urinary bladder within 24 months prior to registration except Ta/T1/Carcinoma in situ (CIS) of the upper urinary tract including renal pelvis and ureter if the patient had undergone complete nephroureterectomy.

3.2.3 Age ≥ 18

3.2.4 Zubrod Performance Status of ≤ 2

3.2.5 Not Pregnant and Not Nursing

- Negative urine or serum pregnancy test (in persons of childbearing potential) within 14 days prior to registration. Childbearing potential is defined as any person who has experienced menarche and who has not undergone surgical sterilization (hysterectomy or bilateral oophorectomy) or who is not postmenopausal.

3.2.6 Required Initial Laboratory Values

- Adequate hematologic function defined as follows:
    - Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3
    - Platelets ≥ 100,000 cells/mm3
    - Hemoglobin ≥ 8.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8.0 g/dl is acceptable).
- Adequate renal function defined as follows:
    - Creatinine clearance (CrCL) of ≥30 mL/min by the Cockcroft-Gault formula below

$$\text{CrCl (mL/min)} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{creatinine (mg / dL)}} \quad \{\times 0.85 \text{ for female patients}\}$$

- Adequate hepatic function defined as follows:
    - Total bilirubin ≤ 2 x institutional upper limit of normal (ULN)
    - AST (SGOT) and ALT (SGPT) ≤3 x institutional ULN

3.2.7 Prior Treatment

- All adverse events associated with any prior therapy must have resolved to CTCAE Grade ≤ 3 prior to randomization.
- For patients who have completed neoadjuvant therapy, they are eligible if the pre-neoadjuvant therapy diagnosis (TURBT path) is within 180 days before randomization.
- Must not have had prior pelvic radiation.

3.2.8 Comorbid Conditions

- New York Heart Association Functional Classification II or better (NYHA Functional Classification III/IV are not eligible) (Note: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification.)
- No active infection requiring IV antibiotics
- Patients with hydronephrosis are eligible if they have unilateral hydronephrosis and kidney function meet criteria specified in section 3.2.6.

NRG-GU015
SCHEMA

cT2-cT3 Muscle invasive bladder cancer (MIBC) that is clinically node negative (cN0)

STRATIFY

- Clinical Stage (T2 vs. T3)
- Type of Radiosensitizing Chemotherapy planned**
- Neoadjuvant therapy (yes vs. no)

RANDOMIZE*

Arm 1	**Arm 2**
4 weeks Radiosensitizing Chemotherapy + Hypofractionation (55 Gy/20 Fractions)	4 weeks Radiosensitizing Chemotherapy + SBRT (Ultra-hypofractionation) (32.5 Gy/ 5 Fractions)

*Randomization is 1:1.
**Types of chemotherapy regimens are:

- Cisplatin
- Gemcitabine
- Mitomycin-C/5-Fluorouracil