Cancer Research Consortium of West Michigan
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FAST FACTS

NRG GU002
PHASE II-III TRIAL OF ADJUVANT RADIOTHERAPY AND ANDROGEN DEPRIVATION FOLLOWING RADICAL PROSTATECTOMY WITH OR WITHOUT ADJUVANT DOCETAXEL

Eligibility Criteria

All eligibility criteria below must be met prior to Step 1 Registration

1. Patients post-prostatectomy with baseline Gleason ≥ 7 (per prostatectomy pathology)
2. Baseline PSA prior to start of androgen deprivation therapy nadir ≥ 0.2 ng/ml (post-operative value is never undetectable) obtained prior to Step 1 registration
3. Baseline testosterone level obtained post-prostatectomy prior to start of androgen deprivation therapy and prior to Step 1 registration
4. Pathologically (histologically) proven diagnosis of adenocarcinoma of the prostate as confirmed at time of prostatectomy. Prostatectomy must have been performed within 365 days (1 year) prior to Step 1 registration and any type of radical prostatectomy is permitted, including retropubic, perineal, laparoscopic or robotically assisted. (Please note: Prior ablative treatment for benign prostatic hypertrophy or focal HIFU prior to prostatectomy is allowed).
5. Surgical FFPE specimen must be available for submission to GenomeDx for genomic analysis on DECIPHER GRID platform (See Section 10.1.1 for details).

Please note:

– If a patient already has a Decipher risk score and meets all of the other eligibility criteria, the patient is eligible to be registered; however, the Decipher risk report will need to be submitted to GenomeDx for validation.

6. Prior androgen deprivation therapy (LHRH agonist and/or non-steroidal anti-androgen) is allowed if:
   • Androgen deprivation therapy was initiated within 30 days prior to study enrollment.
   • Androgen deprivation therapy was given for ≤ 90 days duration prior to radical prostatectomy.
   Please note: Finasteride or dutasteride must be stopped before registration but prior usage will not affect eligibility.

7. Pathologically lymph node negative by pelvic lymphadenectomy (pN0) or lymph node status pathologically unknown (undissected pelvic lymph nodes [pNx]).
8. Any pT-stage based on American Joint Committee on Cancer 7th edition is eligible. Study entry will be based on the following diagnostic workup:
   • History/physical examination within 60 days prior to Step 1 registration.
   • Negative distant metastatic workups:
   o A CT scan of the abdomen and/or pelvis (with contrast [CT without contrast is permitted if the patient is not a candidate for contrast, i.e., renal function or allergy]), or MRI of the abdomen and/or pelvis with contrast within 120 days prior to Step 1 registration.
   (Please note: Lymph nodes will be considered negative (N0) if they are < 1.5 cm short axis);
   o Bone scan within 120 days prior to Step 1 registration.

[Please note: a NaF PET/CT is an acceptable substitute and if the bone scan is suspicious, a plain x-ray, CT scan, NaF PET/CT and/or MRI must be obtained to rule out metastasis. Axumin scans are not allowed for determination of eligibility (e.g. a positive Axumin can in the setting of negative bonescan and CT does not exclude a patient from being eligible for enrollment)].

9. Age ≥ 18
10. ECOG Performance Status of ≤ 1 within 60 days prior to Step 1 registration
11. Adequate hematologic function within 60 days prior to Step 1 registration defined as follows and based upon a CBC
    • Platelets ≥ 100,000 cell/mm3;
    • Hemoglobin ≥ 10.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 10.0 g/dl is NOT allowed);
    • Absolute neutrophil count ≥ 1500 cells/mm3.

12. Adequate hepatic function within 60 days prior to Step 1 registration defined as follows:
• AST or ALT < 1.5 x the upper limit of institutional normal
• Total bilirubin (≤ 1.5 mg/dl) unless history of Gilbert's syndrome

13. The patient or a legally authorized representative must provide study-specific informed consent prior to Step 1 registration.

Ineligibility criteria

All criteria must be evaluated prior to Step 1 Registration

1. Definitive clinical or radiologic evidence of metastatic disease
2. Prior invasive malignancy (except non-melanomatous skin cancer or other in-situ malignancies, or stage Ta bladder cancer) unless disease free for a minimum of 2 years
3. Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields
4. Prior systemic chemotherapy for the study cancer; note that prior chemotherapy for a different cancer is allowable if completed more than two years prior to Step 1 registration. Prior androgen deprivation is allowed as defined in Section 3.2.6.
5. Prior whole gland ablative therapy [i.e. cryoablation or high intensity focused ultrasound (HIFU)] for prostate cancer is not allowed
6. Prostatectomy performed greater than 365 days (1 year) prior to Step 1 registration.
7. Severe and/or active co-morbidity defined as follows:
    • History of inflammatory bowel disease
    • History of active hepatitis B or C; blood tests are not required to determine if the patient has had hepatitis B or C, unless the patient reports a history of hepatitis.
    • Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
    • Transmural myocardial infarction within the last 6 months
    • Acute bacterial or fungal infection requiring intravenous antibiotics at the time of Step 1 registration
    • Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization within 15 days of Step 1 registration or precluding study therapy at the time of Step 1 registration
    • Uncontrolled severe illness or medical condition (including uncontrolled diabetes), which in the judgment of the treating physician would make the administration of chemotherapy inadvisable

    8 HIV positive with CD4 count < 200 cells/microliter. Note that patients who are HIV positive are eligible, provided they are under treatment with highly active antiretroviral therapy (HAART) and have a CD4 count ≥ 200 cells/microliter within 30 days prior to Step 1 registration. Note also that HIV testing is not required for eligibility for this protocol. This exclusion criterion is necessary because the treatments involved in this protocol may be significantly immunosuppressive.

SCHEMA (26-AUG-2019)

STEP 1 REGISTRATION

Submission of tissue for DECIPHER Radical Prostatectomy analysis
NOTE: Decipher analysis results must be completed before STEP 2 randomization can occur***

Androgen deprivation therapy*

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STEP 2 RANDOMIZATION

STRATIFY

Gleason score	PSA	Decipher risk category
1. 7	1. ≥ 0.2 - < 1.0 ng/ml	1. Low/Average
2. 8-10	2. ≥ 1.0 ng/ml	2. High

RANDOMIZE 1:1

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Arm 1

External Beam Radiation:
Starting 8 weeks after initiation of ADT
68.4 Gy/1.8 Gy/fraction

Plus

Androgen Deprivation Therapy:*
LHRH Agonist/antagonist
Plus
Non-Steroidal Anti-androgen
6 months duration

Arm 2

External Beam Radiation:
Starting 8 weeks after initiation of ADT
68.4 Gy/1.8 Gy/fraction

Plus

Androgen Deprivation Therapy:*
LHRH Agonist/antagonist
Plus
Non-Steroidal Anti-androgen
6 months duration
Plus
Docetaxel starting 4-6 weeks after completion of radiation
Day 1 of each 21-day cycle x 6 cycles**