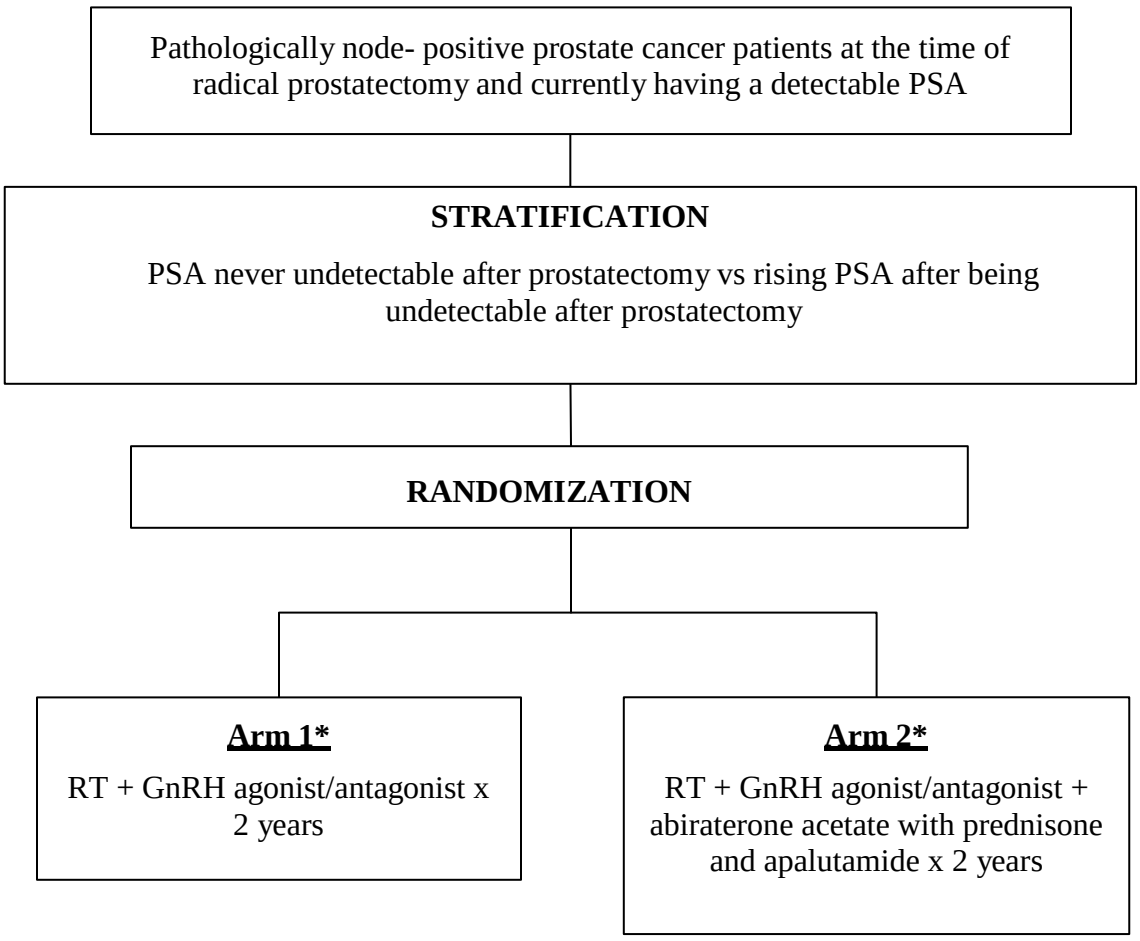
NRG-GU008
SCHEMA



***** See Section 5.1 for drug treatment details and Section 5.2 for radiation therapy details.

3. ELIGIBILITY AND INELIGIBILITY CRITERIA

Note: Per NCI guidelines, exceptions to inclusion and exclusion criteria are not permitted. For questions concerning eligibility, please contact the Biostatistical/Data Management Center (see protocol cover page). For radiation therapy-related eligibility questions, please contact RTQA (see protocol cover page).

Inclusion of Minorities

NIH policy requires that members of minority groups and their subpopulations be included in all NIH-supported biomedical and behavioral research projects involving NIH-defined clinical research unless a clear and compelling rationale and justification establishes to the satisfaction of the funding Institute & Center (IC) Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. Exclusion under other circumstances must be designated by the Director, NIH, upon the recommendation of an IC Director based on a compelling rationale and justification. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Please see http://grants.nih.gov/grants/funding/phs398/phs398.pdf

3.1 Eligibility Criteria

A patient cannot be considered eligible for this study unless ALL of the following conditions are met.

3.1.1 Pathologically (histologically) proven diagnosis of prostate adenocarcinoma. Any type of radical prostatectomy is permitted, including retropubic, perineal, laparoscopic or robotically assisted;

3.1.2 Any T-stage is eligible (AJCC 8th ed);

3.1.3 Appropriate stage for study entry based on Fluciclovine F-18 PET scan (FACBC, Axumin) within 90 days prior to registration that is negative for distant metastatic (M1a, M1b, M1c) disease (see Appendix IV for molecular imaging guidelines); [Note that though every effort should be made to obtain a Fluciclovine F-18 PET (FACBC, Axumin) scan, if the patient has already had a recent Ga-68 PSMA PET scan or C-11 or F-18 Choline PET scan within 90 days prior to registration (to include scan report) then repeat molecular imaging with a Fluciclovine F-18 PET (FACBC, Axumin) scan will not be required.]

3.1.4 Pathologically node positive disease with nodal involvement only in the pelvis in the prostatectomy specimen (including external iliacs, internal iliacs, and/or obturator nodes);

3.1.5 History/physical examination within 90 days prior to registration;

3.1.6 Age ≥ 18;

3.1.7 ECOG Performance Status of 0-1 within 90 days prior to registration;

3.1.8 Detectable PSA after radical prostatectomy. Detectable PSA is defined as serum PSA >0 ng/mL at least 30 days after prostatectomy and within 90 days of registration and before start of GnRH agonist/antagonist (see Section 3.1.9).

3.1.9 Patients who have already started on post-prostatectomy GnRH agonist/antagonist for ≤ 45 days prior to registration are eligible (Note: patients who started on an oral antiandrogen are eligible if started ≤ 45 days and stopped prior to registration);

3.1.10 Adequate hematologic function within 90 days prior to registration defined as follows:

- Hemoglobin **≥**9.0 g/dL, independent of transfusion and/or growth factors
- Platelet count ≥100,000 x 10^9/µL independent of transfusion and/or growth factors

3.1.11 Serum potassium ≥3.5 mmol/L within 90 days prior to registration;

3.1.12 Adequate renal function within 90 days prior to registration defined as follows:

- Creatinine Clearance (CrCl) ≥30 mL/min estimated by Cockcroft-Gault (please use actual weight for calculation unless greater than 30% above ideal body weight then use the adjusted body weight)

$$\text{Creatinine Clearance (mL/min)} = \frac{[140\text{-Age (years)}] \times \text{Weight (kg)}}{72 \times \text{serum creatinine (mg/dL)}}$$

3.1.13 Adequate hepatic function within 90 days prior to registration defined as follows:

- Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (Note: In subjects with Gilbert's syndrome, if total bilirubin is >1.5 × ULN, measure direct and indirect bilirubin and if direct bilirubin is ≤1.5 × ULN, subject is eligible)
- AST(SGOT) or ALT(SGPT) ≤2.5 × institutional ULN
- Serum albumin ≥3.0 g/dL

3.1.14 Discontinue or substitute concomitant medications known to lower the seizure threshold at least 30 days prior to registration (see list under prohibited medications in Section 5.3).

3.1.15 The patient must agree to use a condom (even men with vasectomies) and another effective method of birth control if he is having sex with a woman of childbearing potential or agree to use a condom if he is having sex with a woman who is pregnant while on study drug and for 3 months following the last dose of study drug.

3.1.16 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy (didanosine (DDI) is not permitted see 3.2.5) with undetectable viral load within 6 months are eligible for this trial and have a CD4 count ≥ 200 cells/microliter within 30 days prior to registration. Note: HIV testing is not required for eligibility for this protocol.

3.1.17 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy within 30 days prior to registration, if indicated. Note: HBV viral testing is not required for eligibility for this protocol.

3.1.18 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 within 30 days prior to registration.

3.1.19 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. Note: Any patient with a cancer (other than keratinocyte carcinoma or carcinoma in situ) who has no evidence of disease for < 3 years must contact the Principal Investigator, Ron Chen, MD.

3.1.20 The patient or a legally authorized representative must provide study-specific informed consent prior to study entry.

3.2 Ineligibility Criteria

Patients with any of the following conditions are NOT eligible for this study.

3.2.1 Definitive radiologic evidence of metastatic disease ((M1a, M1b or M1c) on molecular imaging (e.g. Fluciclovine F-18 PET, PSMA, F-18 choline 11);

3.2.2 Prior systemic chemotherapy for the study cancer; note that prior chemotherapy for a different cancer is allowed (completed > 3 years prior to registration);

3.2.3 Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields;

3.2.4 Current use of 5-alpha reductase inhibitor. NOTE: if the alpha reductase inhibitor is stopped prior to randomization the patient is eligible.

3.2.5 Didanosine (DDI) antiretroviral therapy is not permitted;

3.2.6 History of any of the following:

- Seizure or known condition that may pre-dispose to seizure (e.g. prior stroke within 1 year prior to registration, brain arteriovenous malformation, Schwannoma, meningioma, or other benign CNS or meningeal disease which may require treatment with surgery or radiation therapy)
- Severe or unstable angina, myocardial infarction, arterial or venous thromboembolic events (eg, pulmonary embolism, cerebrovascular accident including transient ischemic attacks), or clinically significant ventricular arrhythmias within 6 months prior to registration
- New York Heart Association Functional Classification III/IV (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.)

- History of any condition that in the opinion of the investigator, would preclude participation in this study

3.2.7 Current evidence of any of the following:

- Known gastrointestinal disorder affecting absorption of oral medications
- Active uncontrolled infection
- Presence of uncontrolled hypertension (persistent systolic blood pressure [BP] ≥160 mmHg or diastolic BP ≥100 mmHg). Subjects with a history of hypertension are allowed, provided that BP is controlled to within these limits by anti-hypertensive treatment.
- Any chronic medical condition requiring a higher dose of corticosteroid than 10 mg prednisone/prednisolone once daily
- Baseline moderate and severe hepatic impairment (ChildPugh Class B & C)
- Inability to swallow oral pills
- Any current condition that in the opinion of the investigator, would preclude participation in this study

3.2.8 Patients must not plan to participate in any other therapeutic clinical trials while receiving treatment on this study.

3.2.9 Patients with inflammatory bowel disease.