A RANDOMIZED PHASE III TRIAL OF HYPOFRACTIONATED POST-PROSTATECTOMY RADIATION THERAPY (HYPORT) VERSUS CONVENTIONAL POST-PROSTATECTOMY RADIATION THERAPY (COPORT)

SCHEMA

STEP 1 REGISTRATION
Completion of the Step 1 eligibility checklist then completion of the Step 1 registration process

↓

STEP 2 RANDOMIZATION
Completion and submission of the Expanded Prostate Composite Index (EPIC)

Completion and submission of the step 2 eligibility checklist

STRATIFY

1. Baseline EPIC score group (A vs. B vs. C vs. D)
   A = high bowel and urinary scores
   B = high bowel and low urinary scores
   C = low bowel and high urinary scores
   D = low bowel and urinary scores†

2. Androgen Deprivation Therapy (Yes vs. No)

↓

ARM I (COPORT)
Radiation Therapy:*  
66.6 Gy in 37 fractions of 1.8 Gy to the prostate bed;  
EQD$_2$ (1.5 Gy) = 63 Gy

ARM II (HYPORT)
Radiation Therapy:*  
62.5 Gy in 25 fractions of 2.5 Gy to the prostate bed;  
EQD$_2$ (1.5 Gy) = 71 Gy

*ADT is allowed and if given, no more than 6 months will be administered  
**Lymph node RT is not permitted.  
†High bowel score > 96, low bowel score ≤ 96, high urinary score > 84, low urinary score ≤ 84  
Accrual goal = 282
3.1 Patient Selection Guidelines
Although the guidelines provided below are not inclusion/exclusion criteria, investigators should consider these factors when selecting patients for this trial. Investigators also should consider all other relevant factors (medical and non-medical), as well as the risks and benefits of the study therapy, when deciding if a patient is an appropriate candidate for this trial.

3.1.1 Patients must have the psychological ability and general health that permits completion of the study requirements and required follow up, including all quality of life surveys through 5 years of follow-up.

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

Prior to Step 1 Registration
3.2.1 Adenocarcinoma of the prostate treated primarily with radical prostatectomy
   • Any type of radical prostatectomy will be permitted, including retropubic, perineal, laparoscopic or robotically assisted. There is no time limit for the date of radical prostatectomy.

3.2.2 One of the following pathologic T-classifications: pT2 or pT3.
   • Patients with positive surgical margins are eligible.

3.2.3 One of the following pathologic N-classifications: pN0, pNX.
   • If a lymph node dissection is performed, the number of lymph nodes removed per side of the pelvis and the extent of the pelvic lymph node dissection (obturator vs. extended lymph node dissection) should be noted whenever possible.

3.2.4 No clinical evidence of regional lymph node metastasis.
   • CT (with contrast if renal function is acceptable; a noncontrast CT is permitted if the patient is not a candidate for contrast), MRI, nodal sampling, or dissection of the pelvis within 120 days prior to Step 1 registration.
   • Patients with pelvic lymph nodes equivocal or questionable by imaging are eligible if the nodes are ≤ 1 cm in the short axis.

3.2.5 A post-radical prostatectomy study entry PSA ≥45 days after prostatectomy and within 30 days prior to Step 1, < 2.0 ng/mL.

3.2.6 No evidence of a local recurrence in the prostate fossa based on a digital rectal examination (DRE) within 60 days prior to Step 1 registration.
   • Patients with equivocal or questionable DRE findings should have an MRI of the pelvis to exclude the presence of a prostate fossa mass.
   • Patients with equivocal or questionable exam findings by DRE or MRI are eligible if a biopsy of the lesion is negative for tumor.

3.2.7 No evidence of bone metastases (M0) on bone scan (Na F PET/CT is an acceptable
substitute) within 120 days prior to Step 1 registration.
  • Equivocal bone scan findings are allowed if plain films and/or MRI are negative for metastasis.

3.2.8 Zubrod Performance Status 0-1 within 60 days prior to Step 1 registration.
3.2.9 Age ≥ 18
3.2.10 The patient or a legally authorized representative must provide study-specific informed consent prior to Step 1 registration.
3.2.11 Willingness and ability to complete the Expanded Prostate Cancer Index Composite (EPIC) questionnaire (see Section 11.2.1).
3.2.12 Only English and French-speaking patients are eligible to participate as these are the only language the EPIC has been validated in.

**Prior to Step 2 Registration**

3.2.13 The EPIC must be completed in full and entered within 10 business days after Step 1 registration. NRG Oncology Statistical and Data Management Center has 3 business days to score the results and send a notification to the site to proceed to Step 2 Randomization.

3.3 Ineligibility Criteria

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

3.3.1 A post-prostatectomy PSA nadir ≥ 0.2 ng/mL AND Gleason ≥ 7 (Considered for NRG-GU002, PI: Hurwitz).
3.3.2 pT2 with a negative surgical margin and PSA < 0.1 ng/mL
3.3.3 Androgen deprivation therapy started prior to prostatectomy for > 6 months (180 days) duration. *Note: The use of finasteride or dutasteride (tamsulosin) for longer periods prior to prostatectomy is acceptable.*
3.3.4 Androgen deprivation therapy started after prostatectomy and prior to Step 1 registration for > 6 weeks (42 days).
3.3.5 Neoadjuvant chemotherapy before or after prostatectomy.
3.3.6 Prior invasive (except non-melanoma skin cancer) malignancy unless disease-free for a minimum of 3 years and not in the pelvis. (For example, carcinoma in situ of the oral cavity is permissible if disease free for a minimum of 3 years; however, patients with prior history of bladder cancer are not allowed no matter the disease free duration). Prior hematological (e.g., leukemia, lymphoma, myeloma) malignancy is not allowed.
3.3.7 Previous chemotherapy for any other disease site if given within 3 years prior to Step 1 (see Section 3.3.6).
3.3.8 Prior radiotherapy, including brachytherapy, to the region of the study cancer that would result in overlap of radiation therapy treatment volumes.
3.3.9 Severe, active co-morbidity, defined as follows:
  • 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 or precluding study therapy at the time of Step 1 registration
- Severe hepatic disease, defined as a diagnosis of Child-Pugh Class B or C hepatic disease
- 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 registration. Note also that HIV testing is not required for eligibility for this protocol.
- End-stage renal disease (ie, on dialysis or dialysis has been recommended)

3.3.10 Prior allergic reaction to the study drugs involved in this protocol
3.3.11 History of inflammatory bowel disease, prior bowel surgeries (or colostomy) for any reason, or prior partial/radical cystectomy for any reason