RTOG 0924: ANDROGEN DEPRIVATION THERAPY AND HIGH DOSE RADIOTHERAPY WITH OR WITHOUT WHOLE-PELVIC RADIOTHERAPY IN UNFAVORABLE INTERMEDIATE OR FAVORABLE HIGH RISK PROSTATE CANCER: A PHASE III RANDOMIZED TRIAL

Fast Facts

PATIENT SELECTION
Conditions for Patient Eligibility

1. Histologic proven diagnosis of prostatic adenocarcinoma within 180 days of registration at moderate to high risk for recurrence as determined by one of the following combinations:
    a. Gleason score 7-10 + T1c-T2b (palpation) + PSA < 50 ng/ml (includes intermediate and high risk patients);
    b. Gleason score 6 + T2c-T4 (palpation) + PSA < 50 ng/ml or Gleason score 6+ ≥ 50% (positive) biopsies + PSA < 50 ng/ml;
    c. Gleason score 6 + T1c-T2b (palpation) + PSA > 20 ng/ml.
2. History/physical examination (to include at a minimum digital rectal examination of the prostate and examination of the skeletal system and abdomen) within 90 days prior to registration.
3. Clinically negative lymph nodes as established by imaging (pelvic ± abdominal CT or MR), (but not by nodal sampling, or dissection) within 90 days prior to registration.
    a. Patients with lymph nodes equivocal or questionable by imaging are eligible if the nodes are ≤ 1.5 cm.
4. No evidence of bone metastases (M0) on bone scan within 120 days prior to registration (Na F PET/CT is an acceptable substitute).
    a. Equivocal bone scan findings are allowed if plain films (or CT or MRI) are negative for metastasis.
5. Baseline serum PSA value performed with an FDA-approved assay (e.g., Abbott, Hybritech) within 120 days prior to registration.
    a. Study entry PSA should not be obtained during the following time frames: (1) 10-day period following prostate biopsy; (2) following initiation of hormonal therapy; (3) within 30 days after discontinuation of finasteride; (4) within 90 days after discontinuation of dutasteride.
6. Zubrod Performance Status 0-1(unless otherwise specified);
7. Age ≥ 18;
8. CBC/differential obtained within 60 days prior to registration on study, with adequate bone marrow function defined as follows:
    a. Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3;
    b. Platelets ≥ 100,000 cells/mm3;
    c. Hemoglobin ≥ 8.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8.0 g/dl is acceptable.);
9. **Patient must be able to provide study specific informed consent prior to study entry.**

Conditions for Patient Ineligibility

1. Prior invasive (except non-melanoma skin cancer) malignancy unless disease-free for a minimum of 3 years (1095 days) not in the pelvis. (For example, carcinoma in situ of the oral cavity is permissible; however, patients with prior history of bladder cancer are not allowed). Prior hematological (e.g., leukemia, lymphoma, myeloma) malignancy not allowed.
2. Previous radical surgery (prostatectomy) or cryosurgery for prostate cancer
3. Previous pelvic irradiation, prostate brachytherapy, or bilateral orchiectomy
4. Previous hormonal therapy, such as LHRH agonists (e.g., leuprolide, goserelin, buserelin,triptorelin) or LHRH antagonist (e.g. degarelix), anti-androgens (e.g. flutamide, bicalutamide, cyproterone acetate), estrogens (e.g., DES), or surgical castration (orchiectomy) Refer to section 7.1.1 for ADT timing.

   a. Prior pharmacologic androgen ablation for prostate cancer is allowed only if the onset of androgen ablation is ≤ 45 days prior to the date of registration.
5. Use of finasteride within 30 days prior to registration
6. Use of dutasteride or dutasteride/tamsulosin (Jalyn) within 90 days prior to registration
7. Previous or concurrent cytotoxic chemotherapy for prostate cancer; note that prior chemotherapy for a different cancer is allowable. See Section 3.2.1.
8. Prior radiotherapy, including brachytherapy, to the region of the study cancer that would result in overlap of radiation therapy fields
9. Severe, active co-morbidity, defined as follows:
   a. Unstable angina and/or congestive heart failure requiring hospitalization within the last 6 months
   b. Transmural myocardial infarction within the last 6 months
   c. Acute bacterial or fungal infection requiring intravenous antibiotics at the time of registration
   d. Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of registration
   e. Hepatic insufficiency resulting in clinical jaundice and/or coagulation defects or severe liver dysfunction
   f. Acquired immune deficiency syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive. Protocol-specific requirements may also exclude immuno-compromised patients.
10. Patients who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.
11. Prior allergic reaction to the hormones involved in this protocol
12. Patients status post a negative lymph node dissection are not eligible
13. Blood collection is mandatory for patients who provided consent for the QOL portion of this study.
    Note: The QOL component closed to new patient accrual on 3/9/15.

Required Evaluations That Do Not Affect Eligibility

1. Any patient undergoing brachytherapy must have transrectal ultrasound confirmation of prostatic volume <60 cc within 60 days of registration. This may be performed before or after study enrollment. If a patient is thought to be a poor brachytherapy candidate based on anatomy at the time of ultrasound, he may still participate in the study but must receive EBRT only per protocol guidelines. If a patient is deemed an inadequate brachytherapy candidate after he has already been enrolled on the protocol, he will no longer be eligible for study participation.
2. AST or ALT <2 x the upper limit of normal within 60 days prior to registration
3. Prior testosterone administration must have been last administered at least 90 days prior to registration.

Pre-Study Parameters

1. Pathology slides for Central Review
2. History and physical with DRE
3. Pelvic +/- abdominal CT
4. Bone scan
5. Transrectal ultrasound
6. CBC w/ diff
7. AST or ALT
8. PSA
9. Research specimens (optional)

SCHEMA

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<td>Risk Group
1. GS 7-10 + T1c-T2b + PSA < 50 ng/ml

2. GS 6 + T2c-T4 or > 50% biopsies + PSA < 50 ng/ml

3. GS 6 + T1c-T2b + PSA > 20 ng/ml</td>
<td rowspan="3">R
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<td>Arm 1:
Neoadjuvant androgen deprivation therapy
+ prostate & seminal vesicle RT
+ boost to prostate & proximal seminal vesicles</td>
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<tr>
<td>Type of RT Boost
1. IMRT
2. Brachytherapy (LDR using PPI or HDR)</td>
<td rowspan="2">Arm 2:
Neoadjuvant Androgen Deprivation Therapy
+ whole-pelvic RT
+ boost to prostate & proximal seminal vesicles</td>
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<tr>
<td>Duration of Androgen Deprivation Therapy
1. Short Term (6 months)
2. Long Term (32 months)*</td>
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* 32 months chosen because RTOG 9202 used 28 months and EORTC used 36 months = avg 32 months

Note: As this protocol allows for treatment with exclusively EBRT or EBRT + brachytherapy (at the discretion of the treating physician), this must be specified at the time of study enrollment. Should a patient who was originally intended to receive brachytherapy be found, post enrollment, to be a poor brachytherapy candidate based on transrectal ultrasound examination, he will no longer be eligible for participation in this study. Therefore, it is strongly recommended to obtain ultrasound assessment of prospective brachytherapy patients before enrollment on this study.