Clinical Case Conference

Intermediate-risk prostate cancer
08/06/2014

Long Pham
Clinical Case

- 64 yo man was found to have elevated PSA of 8.65.
- TRUS-biopies were negative.
- Surveillance PSA was 7.2 in 3 years later.
- Repeat biopsy year 3 → small focus of atypical glands in right lobe and benign prostatic tissue in left lobe.
- Repeat biopsy year 4 → 1/5 cores in the right lobe positive for adenocarcinoma, GS 3+3, 10% of core involved.
- He decided to go with active surveillance.
- PSA was noted to rise to 11.44 at year 5.
- Repeat biopsy in year 5 showed prostate adenocarcinoma, GS 3+4, 3/6 cores positive of the left lobe in up to 80% tissue involved, 0/6 cores positive on the right lobe.
Clinical Case

- **Clinical sx:**
  - Sensation of weak stream
  - Incomplete emptying
  - Post-void dribbling
  - Urinary frequency
  - Nocturia x 3 daily
  - IPSS of 20.
  - No erectile dysfunction nd his SHIM score was 24.

- **Exam:**
  - DRE: no nodularity or induration.
Clinical Case

- **PMHx:**
  - HLP, meningioma s/p cyberknife tx
- **PSHx:**
  - None
- **Allergy:**
  - NKDA
- **Medications:**
  - Pravastatin, Aspirin
- **FamHx:**
  - No family Hx of cancer
- **Social Hx:**
  - Former smoker with remote 5 pack-year hx
Epidemiology – Prostate Cancer

- Estimated 233,000 new cases in 2014
  - 27% of new cancer cases in men
- Prostate-cancer death: 29,480 in 2014.
- PSA Screening – Stage Migration
  - Locally advanced/metastatic disease → clinically nonpalpable disease.
- 2 large prostate cancer registries:
  - CaPSURE: Cancer of the Prostate Strategic Urologic Research Endeavor
    - High risk disease:
      - Stage T1:
        - 16.9% (1990-1994) → 49.4% (2004-2007)
  - DoD CPDR: Center for Prostate Disease Research
    - T1c: 0% (1988) → 47.8% (1998)
Clinical Presentation – Prostate Cancer

- Asymptomatic
- Lower Urinary Tract Symptoms:
  - Nocturia
  - Urinary frequency and/or urgency
  - Decrease flow
  - Incomplete voiding
  - Intermittent flow
  - Urinary hesitancy
- Difficulty of passing stool
- Bloody stool
Risk Factors – Prostate Cancer

- Hormonal factors
- Dietary factors
- Familial factors
- Genetic and Molecular factors
- Chronic and recurrent inflammation of prostate/prostatitis
## TNM Staging – Prostate Cancer

### Primary tumor (T)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor incidental histologic finding in ≤ 5% of tissue</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor incidental histologic finding in &gt; 5% of tissue</td>
</tr>
<tr>
<td>T1c</td>
<td>Tumor identified by needle biopsy (e.g., elevated PSA)</td>
</tr>
<tr>
<td>T2a/pT2a</td>
<td>Unilateral, up to one-half of one side</td>
</tr>
<tr>
<td>T2b/pT2b</td>
<td>Unilateral, involving more than one-half of one side</td>
</tr>
<tr>
<td>T2c/pT2c</td>
<td>Tumor involves both lobes (i.e., bilateral involvement)</td>
</tr>
<tr>
<td>T3a/pT3a</td>
<td>Extraprostatic extension or microscopic invasion of bladder neck</td>
</tr>
<tr>
<td>T3b/pT3b</td>
<td>Tumor invades seminal vesicle(s)</td>
</tr>
<tr>
<td>T4/pT4</td>
<td>Tumor is fixed and invades adjacent structures other than seminal vesicles (such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall)</td>
</tr>
</tbody>
</table>

### Regional lymph nodes (N)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
</tbody>
</table>

### Distant metastasis (M)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Distant metastasis to non-regional lymph nodes</td>
</tr>
<tr>
<td>M1b</td>
<td>Distant metastasis to skeletal system</td>
</tr>
<tr>
<td>M1a</td>
<td>Distant metastasis to additional sites with or without skeletal metastasis</td>
</tr>
</tbody>
</table>
Risk Classification – Prostate Cancer

  - Low-risk
    - T1c-T2a, PSA<10, **AND** Gleason score ≤ 6
  - Intermediate-risk
    - T2b or T2c, PSA 10-20, OR Gleason score 7
  - High-risk
    - T3a, PSA > 20, OR Gleason score 8-10

- Widely used and basis for NCCN guidelines
- 2010 AJCC includes grouping system to include PSA and Gleason’s score

- D’Amico, et al. IJROBP 2001; 49(3)
  - Independent prognostic capabilities of percentage of positive biopsy cores [PPC] (# of positive cores/# total cores biopsied) of PSA control.
  - Intermediate-risk disease:
    - PPC <34% : similar outcomes as low-risk pts
    - PPC >50% : similar outcomes as high-risk pts
Clinical stage, PSA, GS → predicting

OC = Organ confined
EPE = Extraprostatic extension
SV+ = Seminal vesicle involvement
LN+ = Lymph node involvement

http://urology.jhu.edu/prostate/partintables.php
Risk Classification – Kattan Nomograms

- [http://nomograms.mskcc.org/Prostate/index.aspx](http://nomograms.mskcc.org/Prostate/index.aspx)
- 4 nomograms
  - **Pre-treatment nomogram**
    - Progression free probability after radical prostatectomy or brachytherapy
  - **Post-radical prostatectomy nomogram**
    - Probability of recurrence after radical prostatectomy (rising PSA after prostatectomy)
  - **Salvage Radiation Therapy**
    - Probability that recurrence after radical prostatectomy can be successfully treated with salvage radiation therapy.
  - **Hormone Refractory**
    - Survival probability in one or two years for patients with hormonal refractory metastatic prostate cancer.
Risk Classification – Roach’s Formula

- **Extracapsular Extension**
  \[ \frac{3}{2} \times PSA + [(GS - 3) \times 10] \]

- **Seminal Vesicle Involvement**
  \[ PSA + [(GS - 6) \times 10] \]
  - (<13% → actual risk 7%)
  - (≥ 13% → actual risk 37%)

- **Lymph Node Involvement**
  \[ \frac{2}{3} \times PSA + [(GS - 6) \times 10] \]
  - (<15% → actual risk 6%)
  - (≥ 15% → actual risk 40%)
Risk Classification – CaPRA Score

- **UCSF-CaPRA score:** 0-10
  - **Age at diagnosis**
    - <50 = 0
    - ≥50 = 1
  - **PSA at diagnosis**
    - ≤6 = 0
    - 6.1-10 = 1
    - 10.1-20 = 2
    - 20.1-30 = 3
    - >30 = 4
  - **Gleason score**
    - no 4 or 5 = 0
    - secondary pattern 4 or 5 = 1
    - primary pattern 4 or 5 = 3
  - **Clinical stage (T stage)**
    - T1 or T2 = 0
    - T3a = 1
  - **Percent of biopsy cores positive**
    - < 34% = 0
    - ≥ 34% = 1

- **Low Risk:** 0-2
- **Intermediate Risk:** 3-5
- **High Risk:** 6-10
Prostate Cancer

RISK GROUP

EXPECTED PATIENT SURVIVAL

INITIAL THERAPY

ADJUVANT THERAPY

RP\textsuperscript{h} + PLND if predicted probability of lymph node metastasis \geq 2%\

\begin{cases}
\text{Intermediate:} & \text{d} \\
T2b-T2c or Gleason score 7 or PSA 10-20 ng/mL
\end{cases}

\begin{cases}
\text{\geq 10 y} \\
\text{< 10 y}
\end{cases}

\begin{cases}
\text{Observation} \text{j} \\
\text{RT}^g \pm \text{ADT}^k (4-6 \text{ mo}) \pm \text{brachytherapy or brachytherapy alone} \text{d}
\end{cases}

\begin{cases}
\text{Adverse features:} \text{i} \\
\text{RT}^0 \text{ or Observation} \text{j}
\end{cases}

\begin{cases}
\text{Lymph node metastasis: ADT}^k (\text{category 1}) \pm \text{RT (category 2B)} \text{ or Observation (category 2B)} \text{i}
\end{cases}

\begin{cases}
\text{Undetectable PSA or nadir} \rightarrow \text{See Monitoring (PROS-6)} \\
\text{PSA failure} \rightarrow \text{See Radical Prostatectomy Biochemical Failure (PROS-7)} \\
\end{cases}

\text{See Radiation Therapy Recurrence (PROS-8)}
Intermediate-risk Prostate Cancer – Treatment Decision

- ADT?
- Pelvic Radiotherapy?
The role of ADT in intermediate-risk prostate cancer
The role of ADT in intermediate-risk prostate cancer

- **Most common forms of ADT**
- **Surgical castration**
  - Orchietomy
- **Chemical castration**
  - LHRH agonists/GnRH agonists
    - Goserelin (Zoladex)
    - Leuprolide (Lupron, Eligard)
    - Triptorelin (Trelstar)
  - LHRH antagonists/GnRH antagonists
    - Degarelix (Firmagon)
- **Anti-androgen therapy – Androgen receptor blocker**
  - Bicalutamide (Casodex)
  - Flutamide (Eulexin, Flutamin, Cytomid)
  - Nilutamide (Nilandron)
  - Enzalutamide (Xtandi)
The role of ADT in intermediate-risk prostate cancer

- D’Amico et al., JAMA 2004 and D’Amico et al., JAMA 2008.
- 1995-2001: Prospective randomized control trial
- 206 pts
  - TNM: T1b-T2b Nx M0
  - PSA: 10-40
  - GS: at least 7
  - Endorectal coil MRI evidence of ECE or SV invasion for low-risk pts.
  - Negative bone scan & negative pelvic node by MRI or CT within 6 mos.
- Arm 1: EBRT alone (70 Gy 3D-CRT) [104 pts]
- Arm 2: EBRT + 6-month AST
- RT: (1.8 Gy x 25)+(2 Gy x 11) \( \rightarrow \) 67 Gy normalized to 95% \( \rightarrow \) 70.35 Gy (4-field 3D-CRT) \( \rightarrow \) Prostate and SV in initial radiation field.
- AST: Leuprolide or Goserelin + Flutamide
- Median F/U: 4.52 yrs and 7.6 yrs

D’Amico et al. JAMA. 2004 Aug 18;292(7):821-7  
The role of ADT in intermediate-risk prostate cancer

- Study designed to detect a difference in freedom from biochemical progression between 2 treatment groups with 80% power.

D'Amico et al. JAMA. 2004 Aug 18;292(7):821-7

The role of ADT in intermediate-risk prostate cancer

Figure 2. Overall Survival for 3D-CRT vs 3D-CRT Plus AST

Figure 3. Cumulative Incidence of Prostate Cancer and Non-Prostate Cancer-Specific Mortality for 3D-CRT vs 3D-CRT Plus AST

D'Amico et al. JAMA. 2004 Aug 18;292(7):821-7
The role of ADT in intermediate-risk prostate cancer

OS at 8yrs was 74% with RT + AST vs. 61% with RT alone.
-RT + AST also had less prostate cancer specific mortality than RT alone (HR 4.1).

Conclusions:
- RT + AST (6 mos) → increase OS in men (without moderate or severe co-morbidity) with localized but unfavorable-risk prostate cancer.

D'Amico et al. JAMA. 2004 Aug 18;292(7):821-7
The role of ADT in intermediate-risk prostate cancer

- **RTOG 94-08**
- 1994-2001
- Prospective RCT of 1979 men with Prostate CA <T2b AND PSA <20
- Arm 1: EBRT alone
- Arm 2: EBRT + 4 months ADT (2 mos before RT + 2 mos after RT)
- RT was 46.8 Gy to the whole pelvis with cone-down to the prostate up to 66.6 Gy.
  - Omission of pelvic LN treatment in pts with negative LN dissections or PSA < 10 AND GS <6.
- ADT was goserelin or leuprolide (GnRH agonists) + Flutamide (ARB) initially.
- Median F/U was 9.1 yrs
- Primary end point: OS
- Secondary end points: Disease-specific mortality, distant metastasis, biochemical failure, rate of (+) findings on repeat bx

Jones et al. NEJM 2011; 365: 107-18
The role of ADT in intermediate-risk prostate cancer

- Trial design to provide 90% power to detect a 7% absolute difference in the 8-yr survival rate.

Jones et al. NEJM 2011; 365: 107-18
The role of ADT in intermediate-risk prostate cancer

Overall Survival

RT+ADT vs RT
10-yr OS: 62% vs 57%

Figure 2. Kaplan–Meier Estimates of Overall Survival.
ADT denotes androgen-deprivation therapy. Panels B, C, and D show post hoc analyses.
The role of ADT in intermediate-risk prostate cancer

Disease-Specific Mortality

RT + ADT  RT
10 yr rate: 4% vs 8%

Jones et al. NEJM 2011; 365: 107-18
The role of ADT in intermediate-risk prostate cancer

RTOG 0815

A Phase III Prospective Randomized Trial of Dose-Escalated Radiotherapy With or Without Short-Term Androgen Deprivation Therapy for Patients With Intermediate-Risk Prostate Cancer

SCHEMA

<table>
<thead>
<tr>
<th>Number of Risk Factors*</th>
<th>Arm 1</th>
<th>Arm 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. One risk factor</td>
<td>Dose-escalated RT alone</td>
<td>Dose-escalated RT combined with short-term (6 months) androgen blockade (LHRH agonist + antiandrogen)</td>
</tr>
<tr>
<td>2. Two or 3 risk factors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comorbidity Status**

1. ACE-27** grade ≥ 2
2. ACE-27 grade < 2

RT Modality

1. Dose-escalated EBRT
2. EBRT + LDR brachytherapy boost
3. EBRT + HDR brachytherapy boost

*Intermediate risk factors: Gleason Score 7***; PSA >10 but ≤20; T-Stage T2b-T2c. Patients with all three intermediate risk factors and ≥ 50% of their sampled biopsy cores involved will not be eligible for this study. Note: The percentage of biopsy cores involved will only be considered with respect to eligibility for those patients with all 3 of the above risk factors (i.e., patients with one or two of the above risk factors are eligible irrespective of the percentage of biopsy cores involved).

**The “untreated malignancy” section of the ACE-27 form is to be disregarded with respect to the patient’s newly diagnosed, untreated prostate cancer.

08/2014
Target Accrual: 1520  Current Accrual: 1222
Status: Open to Accrual
The role of pelvic RT in intermediate-risk prostate cancer

- GETUG-01 (French)(1998-2004)
- Randomized, multicenter, open phase III design
- 444 pts; T1b-T3, N0 pNx, M0
- Stratification of nodal involvement risk
  - Low risk: T1-2 and GS ≤ 6 and PSA < 3X the upper normal limit (4 ng/ml) [21%]
  - High risk: T3 and/or GS ≥ 7 and/or PSA ≥ 3X the upper normal limit (4 ng/ml) [79%]
  - Short-term ADT (6 mos) allowed for high-risk group.
- Arm 1 – Prostate + Pelvic RT
- Arm 2 – Prostate RT only
- RT dose
  - Pelvis: 46 Gy
  - Prostate: 66-70 Gy
- Median F/U: 3.5 years
- 5-year outcome: PFS 66% vs. 65% (NS); high risk PFS 63% vs. 60% (NS); low risk PFS 75% vs. 84% (NS)
- Toxicity: Pelvic arm small but nonsignificant late GI toxicity
- Conclusion: no benefit to pelvic radiotherapy

The role of pelvic RT in intermediate-risk prostate cancer

- Trial design to detect an absolute difference in PFS of 15% at 5 years with a power of 80% and a unilateral significance level of 5% (60→75% increase in PFS in favor of pelvic RT).

The role of pelvic RT in intermediate-risk prostate cancer

- **2x2 factorial design**

### RTOG 94-13

A Phase III Trial Comparing Definitive Whole Pelvic Irradiation Followed by a Conedown Boost to Boost Irradiation Only and Comparing Neoadjuvant to Adjuvant Total Androgen Suppression (TAS)

#### Stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>1. T1c, T2a</th>
<th>2. T1b, T2b</th>
<th>3. T2c-T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. ≤ 30</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>2. &gt; 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gleason Score</td>
<td>1. &lt; 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 7-10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Arm 1:** Neoadjuvant TAS 2 months before and during RT to the whole pelvis followed by a prostate boost.

**Arm 2:** Neoadjuvant TAS 2 months before and during RT. RT to prostate only.

**Arm 3:** RT to include whole pelvis followed by a boost to the prostate and then by 4 months of TAS.

**Arm 4:** RT to the prostate only followed by 4 months of TAS.

**Radiation:**

Patients on Arms 1 and 3 will receive whole pelvic irradiation to 50.4 Gy (1.8 Gy/day five times a week x 28 fractions) followed by a 19.8 Gy boost (1.8 Gy/day,five times a week x 11 fractions) to a total dose of 70.2 Gy to the prostate.

Total: 39 fractions in 8 weeks

Patients on Arms 2 and 4 will receive RT to prostate only (1.8 Gy/day,five days a week x 39 fractions) to a total dose of 70.2 Gy.

Total: 39 fractions in 8 weeks

**Total Androgen Suppression (TAS):**

Patients on Arms 1 and 2 will receive Flutamide (two 125 mg capsules t.i.d., p.o.) and Zoladex (3.6 mg s.c. monthly x four months) or Lupron, beginning 2 months before RT and continuing until RT is completed.

Patients on Arms 3 and 4 will receive Flutamide and Zoladex (or Lupron) for four months beginning at completion of RT.

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The role of pelvic RT in intermediate-risk prostate cancer

- Study design to detect a 10% difference in 5-year PFS rates with a significance level of 0.025 and a statistical power of 0.80.

4-yr PFS: 54.2% (WPRT) vs 47% (Prostate only RT)  
P=0.022
The role of pelvic RT in intermediate-risk prostate cancer

**Table 5. 4-Year Outcomes: All Patients Radiation Field and Hormone Timing**

<table>
<thead>
<tr>
<th>End Point</th>
<th>WP RT + N &amp; CHT (n = 319)</th>
<th>PO RT + N &amp; CHT (n = 316)</th>
<th>WP RT + AHT (n = 322)†</th>
<th>PO RT + AHT (n = 322)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>95% CI</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>Progression-free survival</td>
<td>59.6</td>
<td>53 to 66</td>
<td>44.3</td>
<td>38 to 51</td>
</tr>
<tr>
<td>Biochemical failure</td>
<td>30.3</td>
<td>24 to 36</td>
<td>42.8</td>
<td>36 to 49</td>
</tr>
</tbody>
</table>

Abbreviations: WP RT + N & CHT, whole-pelvic radiotherapy and neoadjuvant hormonal therapy; PO RT + N & CHT, prostate-only radiotherapy and neoadjuvant hormonal therapy; WP RT + AHT, whole-pelvic radiotherapy and adjuvant hormonal therapy; PO RT + AHT, prostate-only radiotherapy and adjuvant hormonal therapy; CI, confidence interval.

*P value is from either the log-rank test (progression free) or Gray’s test (biochemical failure) for comparing the four survival curves.

†One patient is excluded from the progression-free survival analysis because disease status is unknown (n = 321).

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**Fig 3.** Four-year progression-free advantage for whole pelvic (WP) radiotherapy (RT) and neoadjuvant and concurrent hormonal therapy (NCHT) compared with prostate only (PO) RT and NCHT, and WP RT or PO RT and adjuvant hormonal therapy (AHT; 60 vs 44%, 49% and 50% respectively, P = .008).

**Fig 4.** Prostate-specific antigen (PSA) control favors whole pelvic (WP) radiotherapy (RT) and neoadjuvant and concurrent hormonal therapy (NCHT) compared with prostate only (PO) RT and NCHT, and WP RT or PO RT adjuvant hormonal therapy (AHT; P = .048).
The role of pelvic RT in intermediate-risk prostate cancer

Conclusion:
1. WP RT + NCHT improves the freedom from progression compared with PO RT + NCHT, PO RT + AHT and WP RT + AHT in pts with a risk of LN involvement of more than 15% (Roach’s formula)


Table 6. 4-Year Progression-Free Survival: Intermediate-Risk Patients
(PSA < 30 & GS = 7-10 or PSA ≥ 30 & GS = 2-6)

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Failures</th>
<th>n</th>
<th>%</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>WP RT + N &amp; CHT</td>
<td>64</td>
<td>198</td>
<td>63.9</td>
<td>56 to 72</td>
<td>.014</td>
</tr>
<tr>
<td>PO RT + N &amp; CHT</td>
<td>91</td>
<td>196</td>
<td>46.4</td>
<td>38 to 55</td>
<td>—</td>
</tr>
<tr>
<td>WP RT + AHT</td>
<td>88</td>
<td>197</td>
<td>48.9</td>
<td>41 to 57</td>
<td>—</td>
</tr>
<tr>
<td>PO RT + AHT</td>
<td>88</td>
<td>196</td>
<td>49.3</td>
<td>41 to 58</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: PSA, prostate-specific antigen; CI, confidence interval; WP RT + N & CHT, whole-pelvic radiotherapy and neoadjuvant hormonal therapy; PO RT + N & CHT, prostate-only radiotherapy and neoadjuvant hormonal therapy; WP RT + AHT, whole-pelvic radiotherapy and adjuvant hormonal therapy; PO RT + AHT, prostate-only radiotherapy and adjuvant hormonal therapy.

*P value from log-rank test for comparing the four survival curves.
The role of pelvic RT in intermediate-risk prostate cancer

- RTOG 94-13 - Update

WP RT vs PO RT

N-CHT vs AHT

Fig. 1. Progression-free survival for neoadjuvant hormonal therapy (NHT) vs. adjuvant hormonal therapy (AHT) using (a) protocol definition of biochemical failure and (b) Phoenix definition of biochemical failure.

Fig. 2. Progression-free survival for whole pelvis radiotherapy (WPRT) vs. prostate only radiotherapy (PORT) (a) protocol definition of biochemical failure and (b) Phoenix definition of biochemical failure.
The role of pelvic RT in intermediate-risk prostate cancer

- RTOG 94-13 - Update

### Table 2. Progression-free survival*

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>n</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>WPRT + NHT</td>
<td>198/320</td>
<td>0.065</td>
</tr>
<tr>
<td>PORT + NHT</td>
<td>210/316</td>
<td></td>
</tr>
<tr>
<td>WPRT + AHT</td>
<td>220/319</td>
<td></td>
</tr>
<tr>
<td>PORT + AHT</td>
<td>199/320</td>
<td></td>
</tr>
</tbody>
</table>

Pairwise comparison
- WPRT + NHT vs. PORT + NHT 0.066
- WPRT + NHT vs. WPRT + AHT 0.022
- WPRT + NHT vs. PORT + AHT 0.75
- WPRT + AHT vs. PORT + AHT 0.69
- WPRT + AHT vs. PORT + AHT 0.15
- WPRT + AHT vs. PORT + AHT 0.057

Abbreviations as in Table 1.
* p value is from the Log–rank for comparing progression-free survival curves.

### Table 3. Overall survival

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>n</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>WPRT + NHT</td>
<td>104/320</td>
<td>0.027*</td>
</tr>
<tr>
<td>PORT + NHT</td>
<td>99/316</td>
<td></td>
</tr>
<tr>
<td>WPRT + AHT</td>
<td>130/319</td>
<td></td>
</tr>
<tr>
<td>PORT + AHT</td>
<td>101/320</td>
<td></td>
</tr>
</tbody>
</table>

Pairwise comparison
- WPRT + NHT vs. PORT + NHT 0.9629
- WPRT + AHT vs. PORT + AHT 0.019
- PORT + NHT vs. WPRT + AHT 0.80
- PORT + NHT vs. PORT + AHT 0.019
- WPRT + AHT vs. PORT + AHT 0.86
- WPRT + AHT vs. PORT + AHT 0.01

Abbreviations as in Table 1.
* Log–rank test for comparing overall survival curves.
† p value is from the log rank for comparing overall survival curves.

Study is not powered to compare the four arms separately.
The role of pelvic RT in intermediate-risk prostate cancer

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

**Schema**

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Arm 1: Neoadjuvant androgen deprivation therapy + prostate &amp; seminal vesicle RT + boost to prostate &amp; proximal seminal vesicles</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. GS 7-10 + T1c-T2b + PSA &lt; 50 ng/ml</td>
<td><strong>Randomize</strong> Neoadjuvant androgen deprivation therapy + prostate &amp; seminal vesicle RT + boost to prostate &amp; proximal seminal vesicles</td>
</tr>
<tr>
<td>2. GS 6 + T2c-T4 or &gt; 50% biopsies + PSA &lt; 50 ng/ml</td>
<td><strong>STRATIFY</strong> Neoadjuvant androgen deprivation therapy + prostate &amp; seminal vesicle RT + boost to prostate &amp; proximal seminal vesicles</td>
</tr>
<tr>
<td>3. GS 6 + T1c-T2b + PSA &gt; 20 ng/ml</td>
<td><strong>RANDOMIZE</strong> Neoadjuvant androgen deprivation therapy + prostate &amp; seminal vesicle RT + boost to prostate &amp; proximal seminal vesicles</td>
</tr>
</tbody>
</table>

| Type of RT Boost | **STRATIFY** IMRT, Brachytherapy (LDR using PPI or HDR) |

| Duration of Androgen Deprivation Therapy | **STRATIFY** Short Term (6 months), Long Term (32 months)* |

* 32 months chosen because RTOG 9202 used 28 months and EORTC used 36 months = avg 32 months
Clinical Case

• Definitive EBRT
  • 180 cGy x 45 to 8100 cGy to prostate and proximal vesicle.
Thank you