Role of Radiotherapy in High-risk Prostate Cancer

Current status in 2018

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Instructor, Duke-NUS Graduate Medical School, Singapore

ESMO Advanced Course on Prostate Cancer,
21-22 Sep 2018, Singapore
Disclosures

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GenomeDx Biosciences, Ferring Singapore, Varian, MedLever Inc.

Speakers’ fees/Honorarium:
Varian, AstraZeneca, Janssen

Advisory/Consultancy roles:
Varian
Emergence of a new disease paradigm
- High-risk to Oligometastastic state (N+, limited M1)

Key advances in RT in this space
- GS 9-10: Role of HDR brachytherapy – dose escalation to distant mets control
- Treatment of N+ disease – efficacy of pelvic RT

Combination with novel anti-androgens
- cN+ disease state
- Optimising outcomes of salvage RT
Locally Advanced

*(High risk of occult metastases)*

**Clinical:** cT3-4; GS 8-10; PSA>20-50; N+; *biochemical recurrent PCa post-RadP*

**Molecular:** Genomic instability; SChLAP1+ve

**Treatment:** Long-term androgen deprivation (ADT) + Radiotherapy *(IGRT vs IGRT + Brachytherapy boost)*; Radical Prostatectomy +/- Pelvic nodal dissection
Radiotherapy of Prostate Cancer in 2018

Low
cT1-T2a
PSA <10
GS ≤6

Intermediate
cT2b-T2c
PSA 10-20
GS 7

High
cT3-4
PSA >20
GS 8-10

Active surveillance

Favourable
RadP vs IGRT

Unfavourable
IGRT + ADT

RadP +/- IGRT
IGRT + LTAD

IGRT (image-guided RT)
• SBRT – 36.25 Gy/5#
• Mod hypofract – 60 Gy (3 Gy/#)
• Conv fract – 74-78 Gy (2 Gy/#)
Brachy – LDR (seeds) vs HDR mono

IGRT (image-guided RT)
• SBRT – 37-40 Gy/5#
• Conv fract – 74-78 Gy (2 Gy/#) over mod hypofract
• RT to Pelvis???
Brachy – HDR boost

IGRT (image-guided RT)
• SBRT – 37-40 Gy/5#
• Conv fract – 74-78 Gy (2 Gy/#) + 50-54 Gy to Pelvis
Brachy – HDR boost

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Radiotherapy of Prostate Cancer in 2018

Low
- cT1-T2a
- PSA <10
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Favourable
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Unfavourable
- IGRT + ADT

RadP +/- IGRT
- IGRT + LTAD

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IGRT (image-guided RT)
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- RT to Pelvis??

Brachy – HDR boost

Brachy – HDR boost

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HDR brachytherapy boost as an effective dose intensification strategy

ASCENDE-RT Ph III trial
(Morris et al., IJORBP, 2017)

Control arm
46 Gy EBRT to Pelvis
+ 32 Gy to Prostate
+ 12-mo ADT

Experimental arm
46 Gy EBRT to Pelvis
+ LDR 110 Gy to Prostate
+ 12-mo ADT
HDR brachytherapy boost as an effective dose intensification strategy
Contemporary data with HDR brachy boost

UK MVCC Ph III (Hoskin et al., 2012)
Int-high-risk Prostate Cancers
55 Gy/20# vs
37.5 Gy/15# + 8.5 Gy x 2 HDR

Beaumont (Martinez et al., 2011)
Int-high-risk Prostate Cancers
46 Gy/23# to Pelvis ->
<8.5 Gy x 2 HDR vs >9 Gy x 2 HDR
HDR boost in **GS 9-10** high-grade disease

*More than just dose escalation??*

**UCLA (Kishan et al., Eur Urol, 2016)**

High-risk GS 9-10 Prostate Cancers
HDR boost in **GS 9-10** high-grade disease

*More than just dose escalation??*

**Improved distant metastasis control as a result of dose escalation!!!**
HDR boost in **GS 9-10** high-grade disease

*More than just dose escalation??*

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**JAMA** | **Original Investigation**

Radical Prostatectomy, External Beam Radiotherapy, or External Beam Radiotherapy With Brachytherapy Boost and Disease Progression and Mortality in Patients With Gleason Score 9-10 Prostate Cancer 2018

**Journal of Clinical Oncology** | **Original Report**

Brachytherapy-Based Radiotherapy and Radical Prostatectomy Are Associated With Similar Survival in High-Risk Localized Prostate Cancer

Ronald D. Ennis, Liangxuan Hu, Shannon N. Ryemon, Joyce Lin, and Madhu Mazumdar 2018

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**Radiotherapy patients**

- Equivalent dose in 2-Gy fractions, median (range), Gy
  - 74.3 (65-81.4) 91.5 (75.8-131.4)
- Initial androgen deprivation therapy
  - 657 (89.5) 403 (92.4)
- Duration of androgen deprivation therapy, median (range), mo
  - 21.9 (1-160) 12.0 (1-100)
- Pelvic nodal irradiation
  - 299 (40.7) 320 (73.4)

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HDR boost in **GS 9-10** high-grade disease

*More than just dose escalation?*

---

**Obs #1**

<table>
<thead>
<tr>
<th>Equivalent dose in 2-Gy fractions, median (range), Gy</th>
<th>74.3 (65-81.4)</th>
<th>91.5 (75.8-131.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial androgen deprivation therapy</td>
<td>657 (89.5)</td>
<td>403 (92.4)</td>
</tr>
<tr>
<td>Duration of androgen deprivation therapy, median (range), mo</td>
<td>21.9 (1-160)</td>
<td>12.0 (1-100)</td>
</tr>
<tr>
<td>Pelvic nodal irradiation</td>
<td>299 (40.7)</td>
<td>320 (73.4)</td>
</tr>
</tbody>
</table>

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**Obs #2**

---

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Node-positive prostate cancers are **INCURABLE**

- Node-positive prostate cancers are staged as N1 regardless of the number involved
- Is 1 pN+ = 2 pN+ = 3 pN+ = >4 pN+??
- “Undisputed dogma: Patients with lymph node metastasis are affected by a systemic disease (M1a).”
Node-positive prostate cancers are **INCURABLE**
- Node-positive prostate cancers are staged as N1 regardless of the number involved
- Is 1 pN+ = 2 pN+ = 3 pN+ = >4 pN+??
- “Undisputed dogma: Patients with lymph node metastasis are affected by a systemic disease (M1a).”

**Role of local treatment for a systemic disease unproven**
- Against additional toxicities of RT or RadP
Node-positive prostate cancers are **INCURABLE**

- Node-positive prostate cancers are staged as N1 regardless of the number involved
- Is 1 pN+ = 2 pN+ = 3 pN+ = >4 pN+??
- “Undisputed dogma: Patients with lymph node metastasis are affected by a systemic disease (M1a).”

**Role of local treatment for a systemic disease unproven**

- Against additional toxicities of RT or Surgery

**Watch and Wait vs Early systemic treatment**

- Trials are inconclusive about early ADT
- **Only 1 positive study** – Messing et al., NEJM, 1999; Small study (N = 100); Clinically heterogeneous (no. of +ve nodes ranged from 1-20!!!!)
- Preceding VA study negative
“Contemporary” concepts of N+ CaP

- Number of non-level 1 evidence have shown that surgery alone in 1-2 node+ CaP leads to long-term survivors –

Emerging practice of extended lymph node dissection

N = 369; Single institution; RadP + ELND; NO ADT
“Contemporary” concepts of N+ CaP

- Number of non-level 1 evidence have shown that surgery alone in 1-2 node+ CaP leads to long-term survivors
- Better molecular imaging and genomics have allowed for better clinical stratification
  -> Identification of truly oligo-/limited metastatic occult mets
PSMA-PET as an ultrasensitive modality

Pattern of nodal relapses detected by PSMA matched RT lymph node CTV contouring consensus

Janice Tan, Chua, et al, in review

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Clinical evidence for local RT for N+

MDACC data (Zagars et al., 2001)
- N = 255
- ADT (indefinite) vs ADT+RT for pN+
- RT – Pelvis + Prostate

Freedom From Disease

Overall Survival

2x improvement!!
Clinical evidence for local RT for N+

MDACC data (Zagars et al., 2001)
- N = 255
- ADT (indefinite) vs ADT+RT for pN+
- RT – Pelvis + Prostate

RTOG 96-08
ADT (indefinite) vs ADT+RT to Pelvis + Prostate
50.4 Gy Pelvis + 70.2 Gy to Prostate
Closed due to poor accrual!
Clinical evidence for local RT for N+

UK-STAMPEDE (James et al., 2015)
- Subgroup analysis of 324 M0 patients
- High-risk locally advanced N0 and N+
- ADT (indefinite) vs ADT+RT
- RT – Pelvis (46-50 Gy) + Prostate (74 Gy)

N0: N = 167
N+: N = 157

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Clinical evidence for local RT for N+

**UK-STAMPEDE (James et al., 2015)**

- Subgroup analysis of 324 M0 patients
- High-risk locally advanced N0 and N+
- ADT (indefinite) vs ADT+RT
- RT – Pelvis (46-50 Gy) + Prostate (74 Gy)

**Graphs**

![Graph A](image1)

**Graph A**

- N0M0 subcohort
- HR = 0.48
- Majority were treated with conv fract 2 Gy/#

![Graph B](image2)

**Graph B**

- N+M0 subcohort
- HR = 0.35!!

James et al., JAMA Oncol, 2015

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Clinical evidence for local RT for N+

<table>
<thead>
<tr>
<th>Source</th>
<th>Data Type</th>
<th>Population</th>
<th>Deaths, No./Patients, No.</th>
<th>Radiotherapy Effect, HR (95% CI)</th>
<th>Treatment Groups</th>
<th>Estimates Progression</th>
<th>Estimates Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPCG-7, 2009</td>
<td>R</td>
<td>Low risk, NOMO</td>
<td>116/875</td>
<td>0.16 (0.12-0.20)</td>
<td>ADT only</td>
<td>10-y PSA-FS, 25%</td>
<td>10-y OS, 61%</td>
</tr>
<tr>
<td>NCIC PR.3/MRC P.07, 2011/2015</td>
<td>R</td>
<td>NOMO</td>
<td>465/1205</td>
<td>0.31 (0.25-0.39)</td>
<td>ADT only</td>
<td>10-y PFS, 74%</td>
<td>10-y OS, 49%</td>
</tr>
<tr>
<td>National Cancer Database, 2015</td>
<td>NR</td>
<td>High-risk MO</td>
<td>?/636c</td>
<td>0.50 (0.37-0.67)</td>
<td>ADT only</td>
<td>Not given</td>
<td>5-y OS, 53%</td>
</tr>
<tr>
<td>STAMPEDE, 2015</td>
<td>NR</td>
<td>NOMO</td>
<td>16/180</td>
<td>0.25 (0.13-0.49)</td>
<td>ADT only</td>
<td>5-y FFS, 38%</td>
<td>5-y OS, 86%</td>
</tr>
<tr>
<td>STAMPEDE, 2015</td>
<td>NR</td>
<td>N+MO</td>
<td>22/177</td>
<td>0.35 (0.19-0.65)</td>
<td>ADT only</td>
<td>5-y FFS, 39%</td>
<td>5-y OS, 82%</td>
</tr>
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Lin, et al., JNCI, 2015

James et al., JAMA Oncol, 2015
Clinical evidence for local RT for N+ 

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<td></td>
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<td></td>
<td>Progression</td>
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<tr>
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<td>R</td>
<td>Low risk, NOMO</td>
<td>116/875</td>
<td>0.16 (0.12-0.20)</td>
<td>ADT only</td>
<td>10-y PSA-FS, 25%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ADT+RT</td>
<td>10-y PSA-FS, 74%</td>
</tr>
<tr>
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<td>R</td>
<td>NOMO</td>
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<td>ADT only</td>
<td>10-y PFS, 46%</td>
</tr>
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<td></td>
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<td></td>
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<td>ADT+RT</td>
<td>10-y PFS, 74%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ADT+RT</td>
<td>5-y FFS, 76%</td>
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<td></td>
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<td></td>
<td></td>
<td>ADT+RT</td>
<td>5-y FFS, 65%</td>
</tr>
</tbody>
</table>

Lin, et al., JNCI, 2015

James et al., JAMA Oncol, 2015

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Pelvic RT to N+ CaP

One size fits all approach???

Mayo and Milan cohorts
Abdollah, et al., JCO, 2014

Novel RPA risk stratification tool

<table>
<thead>
<tr>
<th>Gleason score 2–6 (n = 133; 12%)</th>
<th>Entire Cohort</th>
<th>aHT Alone</th>
<th>aRT + aHT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>98.4 (95.4 to 100)</td>
<td>100 (100 to 100)</td>
<td>.7</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>pT2/pT3a and negative SM (n = 131; 11.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
</tr>
<tr>
<td>96.8 (93.2 to 100)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>pT3b/pT4 or positive SM (n = 552; 49.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Int</td>
</tr>
<tr>
<td>84.2 (79.7 to 89.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Positive nodes = 3–4 (n = 160; 14.5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
</tr>
<tr>
<td>78.8 (69.7 to 89.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Positive nodes &gt; 4 (n = 131; 11.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high</td>
</tr>
<tr>
<td>72.0 (60.9 to 85.2)</td>
</tr>
</tbody>
</table>

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Pelvic RT to N+ CaP

One size fits all approach???

Mayo and Milan cohorts
Abdollah, et al., JCO, 2014
Pelvic RT to N+ CaP

One size fits all approach???

Rusthoven et al., JCO, 2015
Validation in SEER data
N = 1707

Benefit only observed in intermediate-risk

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**Table 1. Overall Survival With Adjuvant Radiotherapy for pN1M0 Prostate Cancer in SEER, With Complete Data Sets for Risk Group Assessment (2004-2009)**

<table>
<thead>
<tr>
<th>Risk Category*</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>No. of Patients</th>
<th>No. of Events</th>
<th>Univariable Analysis†</th>
<th>Multivariable Analysis†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Adjuvant Radiotherapy</td>
<td>No. of Events</td>
<td>No. of Patients</td>
<td>HR‡</td>
<td>95% CI</td>
</tr>
<tr>
<td>All patients</td>
<td>1,707</td>
<td>206</td>
<td>420</td>
<td>41</td>
<td>0.714</td>
<td>0.507 to 1.005</td>
</tr>
<tr>
<td>Very low risk</td>
<td>41</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>7.746</td>
<td>0.484 to 124.0</td>
</tr>
<tr>
<td>Low risk</td>
<td>451</td>
<td>42</td>
<td>70</td>
<td>5</td>
<td>0.731</td>
<td>0.287 to 1.860</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>910</td>
<td>108</td>
<td>271</td>
<td>24</td>
<td>0.624</td>
<td>0.396 to 0.982</td>
</tr>
<tr>
<td>High risk</td>
<td>181</td>
<td>26</td>
<td>42</td>
<td>7</td>
<td>0.987</td>
<td>0.412 to 2.368</td>
</tr>
<tr>
<td>Very high risk</td>
<td>124</td>
<td>27</td>
<td>32</td>
<td>4</td>
<td>0.472</td>
<td>0.163 to 1.367</td>
</tr>
</tbody>
</table>

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**Multivariable Analysis**

<table>
<thead>
<tr>
<th>Group</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low risk*</td>
<td>0.01</td>
<td>&lt;0.01 to &gt; 99.9</td>
<td>.9</td>
</tr>
<tr>
<td>Low risk†</td>
<td>0.63</td>
<td>0.22 to 1.82</td>
<td>.4</td>
</tr>
<tr>
<td>Intermediate risk‡</td>
<td>0.42</td>
<td>0.25 to 0.70</td>
<td>.001</td>
</tr>
<tr>
<td>High risk§</td>
<td>0.32</td>
<td>0.12 to 0.83</td>
<td>.02</td>
</tr>
<tr>
<td>Very high risk‖</td>
<td>0.59</td>
<td>0.28 to 1.28</td>
<td>.2</td>
</tr>
</tbody>
</table>
Pelvic RT to N+ CaP

Take home message: Very high-risk patients may not benefit from local intensification

Impact of Adjuvant Radiotherapy in Node-positive Prostate Cancer Patients: The Importance of Patient Selection

Firas Abdollah a,*, Deepansh Dalela a, Akshay Sood a, Jacob Keeley a, Shaheen Alanee a, Alberto Briganti b, Francesco Montorsi b, James O. Peabody a, Mani Menon a

N = 5,500

<table>
<thead>
<tr>
<th>Risk groups</th>
<th>Treatment</th>
<th>aRT + ADT (n)</th>
<th>ADT only (n)</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td>6</td>
<td>13</td>
<td>1.46 (0.13–16.21)</td>
<td>~</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td>405</td>
<td>546</td>
<td>0.72 (0.60–0.87)</td>
<td>0.75 (0.62–0.91)</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td>1536</td>
<td>1740</td>
<td>0.55 (0.36–0.83)</td>
<td>0.57 (0.38–0.86)</td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
<td>289</td>
<td>531</td>
<td>0.88 (0.58–1.35)</td>
<td>0.92 (0.61–1.41)</td>
</tr>
</tbody>
</table>

Group 1: patients with one to two positive nodes and pathological Gleason score 2–6.
Group 2: patients with one to two positive nodes, pathological Gleason score 7–10, pT2/pT3a disease, and negative surgical margins.
Group 3: patients with one to two positive nodes, pathological Gleason score 7–10, pT3b/pT4 disease, or positive surgical margins.
Group 4: patients with three to four positive nodes.
Group 5: patients with more than four positive nodes.
Precision matching: targeting nodal mets

PSMA-PET
Contouring

RT plan
Boost

Daily matching – transverse

Coronal

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Combination of novel anti-androgens in cN+

James and STAMPEDE investigators, ESMO 2017

![Graph showing survival rates and outcomes](Image)

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My approach for high-risk oligo-cN+ PC

cN+
- Comprehensive clinical staging – MRI +/- PSMA-PET

- Discuss LTAD KIV indefinite
  - *Emerging evidence to combine with 18-24 mo of Zytiga (James, et al., ESMO 2017)*

- 3-6-mo neoadjuvant ADT to downsize nodal disease
  - If EI/II/obturator, these regions are usually safe to target with IGRT matching
  - If CI or multiple, then might downsize with ADT first and repeat imaging

- If CR, 54 Gy to eradicate microscopic disease
- If PR, 54 Gy to whole pelvis; **60-66 Gy in 27# simultaneous boost to gross node** (*EQD2 64-74 Gy*)
Salvage RT in biochemically recurrent disease

Assessing the Optimal Timing for Early Salvage Radiation Therapy in Patients with Prostate-specific Antigen Rise After Radical Prostatectomy

Nicola Fossati, R. Jeffrey Karnes, Cesare Cozzarini, Claudio Fiorino, Giorgio Gandaglia, Steven Joniau, Stephen A. Boorjian, Gregor Goldner, Wolfgang Hinkelbein, Karin Haustermans, Bertrand Tombal, Shahrokh Shariat, Pierre I. Karkkiewicz, Francesco Montorsi, Hein Van Poppel, Thomas Wiegel, Alberto Briganti

2016

Rule of thumb: The sooner the better

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Pathologic stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>1.00</td>
<td>Ref.</td>
<td>–</td>
</tr>
<tr>
<td>pT3a</td>
<td>2.11</td>
<td>1.40–3.17</td>
<td>0.0004</td>
</tr>
<tr>
<td>pT3b or higher</td>
<td>2.07</td>
<td>1.22–3.52</td>
<td>0.007</td>
</tr>
<tr>
<td>Pathologic Gleason score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6</td>
<td>1.00</td>
<td>Ref.</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>1.69</td>
<td>1.10–2.59</td>
<td>0.02</td>
</tr>
<tr>
<td>≥8</td>
<td>2.69</td>
<td>1.60–4.53</td>
<td>0.0002</td>
</tr>
<tr>
<td>Surgical margin status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>1.00</td>
<td>Ref.</td>
<td>–</td>
</tr>
<tr>
<td>Positive</td>
<td>0.40</td>
<td>0.27–0.59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PSA at eSRT, ng/ml</td>
<td>4.89</td>
<td>1.40–22.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Addition of systemic HT to salvage

Radiation with or without Antiandrogen Therapy in Recurrent Prostate Cancer


Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

Christian Carrie, Ali Hasbini, Guy de La Rochef, Pierre Richard, Stéphane Guerif, Igor Latster, Stéphane Sipio, Mathieu Bosset, Jean-Léon Lagrange, Véronique Beckendorf, François Lesanier, Bernard Dubray, Jean-Philippe Wagner, Tan Dat N Guyen, Jean-Philippe Suchard, Gilles Cribange, Nicolas Barbier, Murid Habibian, Céline Ferlay, Philippe Fournet, Alain Ruffion, Sophie Dussart

Hazard ratio, 0.77 (95% CI, 0.59–0.99)
P = 0.04

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Addition of systemic HT to salvage

Radiation with or without Antiandrogen Therapy in Recurrent Prostate Cancer


Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

Hazard ratio, 0.45 (95% CI, 0.25–0.81)
P=0.007
Addition of systemic HT to salvage

Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial

2016

2017

64 vs 34 deaths
Which subgroup to combine?

A Systematic Review and Framework for the Use of Hormone Therapy with Salvage Radiation Therapy for Recurrent Prostate Cancer


2017

RTOG 9601

GETUG-16

Pre-RT PSA
Pre-RT PSA
Surgical margins
T stage
Persistently positive PSA
Gleason score

<0.3 vs ≥0.3 ng/ml
<0.7 vs ≥0.7 ng/ml
Negative vs positive
T2 vs T3 disease
No vs Yes
6-7 vs 8-10
Which subgroup to combine?

A Systematic Review and Framework for the Use of Hormone Therapy with Salvage Radiation Therapy for Recurrent Prostate Cancer

NRG-GU-005

Prognostic biomarker of recurrence:
- Pre-RT PSA: <0.7 ng/ml vs ≥0.7 ng/ml

Predictive biomarker of ADT response:
- PAM50 molecular subtypes: Basal, Liminal A, Liminal B

RT alone for everyone? RT + ADT for everyone?

RTOG 9601 GETUG-16

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Which subgroup to combine?

A Systematic Review and Framework for the Use of Hormone Therapy with Salvage Radiation Therapy for Recurrent Prostate Cancer

NRG-GU-005

Eligibility
PSA recurrent post-RP with PSA ≥0.1 and ≤1.0 ng/mL and at least one of the following risk features:
- Gleason score 4+3 or greater
- Persistent PSA elevation after RP
- Pathologic pT3 disease

Stratification
1. One vs. multiple risk features
2. Molecular subtype (Luminal B vs non-Luminal B)

Randomize
Arm 1
Salvage RT + 6 months of placebo

Arm 2
Salvage RT + 6 months of apalutamide

Trial PIs: F Feng & D Spratt

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Thank you!

Questions