No conflict of interest related to the following presentations:
• PSA screening, diagnosis and staging classification
• Role of surgery and other local treatments
• Active surveillance
• Surgery in high-risk prostate cancer patients
• cN1 should be treated by surgery
• Rising PSA after local treatment.
This house believes that high-risk localized prostate cancer should be treated with radiotherapy and ADT AGAINST
<table>
<thead>
<tr>
<th>Definition</th>
<th>Low-risk</th>
<th>Intermediate-risk</th>
<th>High-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-risk</strong></td>
<td>PSA &lt; 10 ng/mL and GS &lt; 7 (ISUP grade 1) or GS 7 (ISUP grade 2/3) and cT1-2a</td>
<td>PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b</td>
<td>PSA &gt; 20 ng/mL or GS &gt; 7 (ISUP grade 4/5) or cT2c</td>
</tr>
<tr>
<td><strong>Localised</strong></td>
<td></td>
<td></td>
<td>Locally advanced</td>
</tr>
</tbody>
</table>
High-risk localised disease/locally advanced disease

Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.

2a Strong
STAGING

A
12/2014
PSA 387.06 ng/mL
150 MBq $^{68}$Ga-PSMA11 PET/CT (MIP) 1 h p.i.

B
12/2014
PSA 387.06 ng/mL
6 GBq $^{177}$Lu-PSMA617 Planar scan (GM) 20 h p.i.

C
02/2015
PSA 9.21 ng/mL
6 GBq $^{177}$Lu-PSMA617 Planar scan (GM) 20 h p.i.

04/2015
PSA 1.98 ng/mL
6 GBq $^{177}$Lu-PSMA617 Planar scan (GM) 20 h p.i.

06/2015
PSA 1.08 ng/mL
700 MBq $^{99m}$Tc-MIP1427 Planar scan (GM) 3 h p.i.
# EAU - ESTRO - ESUR - SIOG Guidelines on Prostate Cancer

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Strength rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use individual life expectancy, health status, and comorbidity in PCa management.</td>
<td>Strong</td>
</tr>
<tr>
<td>Systematically screen the health status of older men (&gt; 70 years) diagnosed with PCa.</td>
<td>Strong</td>
</tr>
<tr>
<td>Use the Geriatric-8 and mini-COG tools for health status screening.</td>
<td>Strong</td>
</tr>
<tr>
<td>Perform a full specialist geriatric evaluation in patients with a G8 score ≤ 14.</td>
<td>Strong</td>
</tr>
<tr>
<td>Consider standard treatment in frail patients with reversible impairments (after resolution of geriatric problems) similar to fit patients, if life expectancy is &gt; 10 years.</td>
<td>Weak</td>
</tr>
<tr>
<td>Offer adapted treatment to patients with irreversible impairment.</td>
<td>Weak</td>
</tr>
<tr>
<td>Offer palliation to patients with poor health status.</td>
<td>Weak</td>
</tr>
</tbody>
</table>
Benefits of radical prostatectomy for high-risk PCa?

- Pathologic staging of the primary cancer and of the regional lymph nodes

- Pathologic downgrading and downstaging at RP may potentially spare patients from receiving adjuvant therapy

- Possible post-treatment avoidance of additional therapy

- Expectation and significance of a nondetectable PSA

RRP for high-risk prostate cancer
Gleason score 8-10

- 238 patients with biopsy Gleason 8-10
- Down grading: 45% of patients had GS ≤7 in RRP specimen
- Other studies suggest that 1/3 of high-risk patients with GS ≥8 are down graded
Outcome and Specimen Confined Status

**BR-free survival stratified according to specimen confined disease**

**CSS survival stratified according to specimen confined disease**

100% CSS in specimen confined disease!!
CSS after RRP in cT3/high-risk prostate cancer

<table>
<thead>
<tr>
<th>Combination of RRP +/- EBRT ( +/- ADT)</th>
<th>CSS 5 year</th>
<th>CSS 10 year</th>
<th>CSS 15 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>85-99%</td>
<td>72-92%</td>
<td>76-84%</td>
</tr>
</tbody>
</table>
Duration of Androgen Suppression in the Treatment of Prostate Cancer

Surgery or EBRT for high-risk prostate cancer?

- No prospective randomized trials
- Retrospective evidence comes from high volume centers
- High rates of multimodal treatments
- Recent shift towards modern treatment approaches (high dose EBRT, ePLND)

Why not EBRT and ADT?
Androgen Deprivation Therapy Increases Cardiovascular Morbidity in Men With Prostate Cancer
Saigal et al Cancer 110:1493-1500, 2007

22,816 patients: 4,810 ADT for 36 months
18,006 no ADT
in conjunction with RRP/EBRT

At 5 year significant difference in CV events (p <0.001)
ADT: 1.2 times increased risk of CV death
Androgen deprivation therapy in prostate cancer and cardiovascular risk: a science Advisory from the American Heart Association, American Cancer Society, and American Urological association: endorsed by the American Society for Radiation Oncology

**SUMMARY**

- Proven impact on standard CV risk factor
- Proven impact on CV events
- Disputable effect of CV death

Levine et al *Circulation* 121:833-840, 2010
Secondary Cancer After Radiotherapy for Prostate Cancer: Should We Be More Aware of the Risk?


• Acute GU and GI toxicity

**Conclusion:** Although the incidence of secondary cancers after prostate cancer radiotherapy is not dramatically different from the overall population, **patients should be informed about this risk.** Other treatment modalities should be considered for patients with long life expectancy and for patients with additional risk factors.
Rectal cancer:
Relative risk after EBRT, Brachy, and EBRT/Brachy, compared with RRP: 1.26, 1.08, and 1.21, respectively

Bladder cancer:
Increased risk after EBRT with a risk ratio of approximately 1.5
Long-Term Functional Outcomes after Treatment for Localized Prostate Cancer

• Need for ADT
• Early and late radiotoxicity
• Risk of second cancer
• Functionally not better at long term
Comparative effectiveness of radical prostatectomy and radiotherapy in prostate cancer: observational study of mortality outcomes

Sooriakumaran et al BMJ 2014

34,515 men: radical prostatectomy n=21,533 radiotherapy n=12,982

Risk group
Age
Charlson score

<table>
<thead>
<tr>
<th>Risk categories</th>
<th>Clinical stage</th>
<th>Prostate specific antigen (ng/mL)</th>
<th>Biopsy Gleason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (low risk)</td>
<td>T1-2 N0/Nx M0/Mx</td>
<td>≤10</td>
<td>≤6 or WHO 1</td>
</tr>
<tr>
<td>Group 2 (intermediate risk)</td>
<td>10-20</td>
<td></td>
<td>7 or WHO 2</td>
</tr>
<tr>
<td>Group 3 (high risk)</td>
<td>T3 N0/Nx M0/Mx</td>
<td>20-50</td>
<td>≥8 or WHO 3</td>
</tr>
<tr>
<td>Group 4 (metastatic)</td>
<td>T4 N+ M+</td>
<td>&gt;50</td>
<td>—</td>
</tr>
</tbody>
</table>
Conclusions This large observational study with follow-up to 15 years suggests that for most men with non-metastatic prostate cancer, surgery leads to better survival than does radiotherapy. Younger men and those with less comorbidity who have intermediate or higher risk localised prostate cancer might have a greater benefit from surgery.
How to approach high-risk prostate cancer?

>T2 and GS >7 and high PSA

• Good imaging
• The tumour must be operable
• Involve the patient
• Discuss possible adjuvant treatments
## EAU - ESTRO - ESUR - SIOG Guidelines on Prostate Cancer Surgery

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength rating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radical Prostatectomy (RP)</strong></td>
<td>Strong</td>
</tr>
<tr>
<td>Offer RP to patients with high-risk localised PCa and a life expectancy of &gt; ten years only as part of multi-modal therapy.</td>
<td></td>
</tr>
<tr>
<td><strong>Extended pelvic lymph node dissection (ePLND)</strong></td>
<td>Strong</td>
</tr>
<tr>
<td>Perform an ePLND in high-risk disease.</td>
<td></td>
</tr>
</tbody>
</table>
Why surgery for locally advanced prostate cancer?

- Good results in experienced centers
- Pathological down grading and staging
- No ADT
- Possibility to individualize adjuvant treatment