FOR A LOCALLY ADVANCED LESION, THE PREFERRED LOCAL TREATMENT (COMBINED WITH A SYSTEMIC ONE) IS EBRT OR SURGERY?

For Surgery

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ESMO PRECEPTORSHIP PROGRAMME
PROSTATE CANCER
DISCLOSURE SLIDE

Honorarium: Astellas, Astrazeneca, Janssen, Takeda, Bayer, Sanofi
Research grant: Astellas, Takeda, Sanofi
Treatments for High risk localized PC
From current guidelines

• High risk PC patients were recommended **RP or radiotherapy (RT) plus ADT.** (Grade A) ¹

• RP combined with an extended nodal dissection (ePLND) is a reasonable first step in a multimodal approach. ²

• The high risk of relapse outside the irradiated volume makes it mandatory to use a combined modality approach, consisting of dose-escalated IMRT, possibly including the pelvic lymphatics and long-term ADT, generally for 2 to 3 yr.²

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¹ AUA/ASTRO/SUO Guideline. Part I 2018
² EAU-ESTRO-SIOG Guidelines Part 1 2017
Surgery Versus Radiotherapy for Clinically-localized Prostate Cancer: A Systematic Review and Meta-analysis

- Systematic Reviews and Meta-Analysis and Meta-analysis of Observational Studies in Epidemiology guideline.
- To compare efficacy data on overall and prostate cancer-specific survival among patients treated with RP or RT for clinically-localized PC.
- 19 studies of low to moderate risk of bias were selected and up to 118830 patients were pooled.
Overall mortality

- Patients treated with RT experienced an increased risk of overall mortality compared with those treated with RP.
- They found a similar direction of effect when examined patients with low risk PC, intermediate risk PC, or high risk PC.
Cancer-specific mortality

- Patients treated with RT had an increased risk of cancer-specific mortality compared with those treated with RP.
The Role of Radical Prostatectomy and Radiotherapy in Treatment of Locally Advanced Prostate Cancer: A Systematic Review and Meta-Analysis

Omar Fahmy, et al. Urologia Int. 2017

- Systematic Review and Meta-Analysis.
- total of 14 studies, 17,869 patients.
- LAPC was defined as stage ≥ T3, or any T-stage with LN+.

<table>
<thead>
<tr>
<th></th>
<th>RP</th>
<th>RT</th>
<th>HT</th>
<th>p-value</th>
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<tbody>
<tr>
<td>5-years OS rate</td>
<td>86.4(78.2-94.5)</td>
<td>81(69.5-92.6)</td>
<td>57.3(44.0-70.6)</td>
<td>0.005</td>
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<tr>
<td>10-years OS rate</td>
<td>70.7(61.3-80.2)</td>
<td>65.8(48.1-83.3)</td>
<td>22.6(4.9-40.3)</td>
<td>0.001</td>
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<tr>
<td>5-years DSS rate</td>
<td>94.2(89.8-98.6)</td>
<td>95.7(88.2-103.3)</td>
<td>78.5(69.2-87.8)</td>
<td>0.0149</td>
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<tr>
<td>10-years DSS rate</td>
<td>84.1(75.1-93.2)</td>
<td>89.4(70.1-108.6)</td>
<td>50.4(31.2-69.6)</td>
<td>0.012</td>
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RP: radical prostatectomy  RT: radiotherapy  HT: hormonal therapy
OS: overall survival  DSS: disease-specific survival
Best survival outcome for patients presented with non-metastatic LAPC

- These results displayed clear superiority of both RP and RT over HT as the primary treatment for LAPC.
- RP could significantly improve survival outcomes when compared to any other modality not including RP.
- Based on these results, both RP plus adjuvant RT or primary RT plus adjuvant HT are suggested to provide the best survival outcome for patients presented with non-metastatic LAPC.

Omar Fahmy, et al. Urologia Int. 2017
This study compared survival outcomes and adverse effects in SEER-Medicare data associated with RP plus RT versus RT plus ADT in LAPC (cT3-T4N0M0 or cT3-T4N1M0).

Propensity score methods were used to balance cohort characteristics between the treatment arms.

13,856 men (≥65 years old) were diagnosed with LAPC: 6.1% received RP plus RT, and 23.6% received RT plus ADT.

<table>
<thead>
<tr>
<th>Tumor stage</th>
<th>RP + adjuvant XRT</th>
<th>XRT + ADT</th>
</tr>
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<tbody>
<tr>
<td>T3a-bN0-xM0</td>
<td>64.2</td>
<td>48.3</td>
</tr>
<tr>
<td>T3a-bN1M0</td>
<td>44.3</td>
<td>40.5</td>
</tr>
<tr>
<td>T4N0-xM0</td>
<td>49.6</td>
<td>34.9</td>
</tr>
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</table>

10-y prostate cancer specific survival Adjusted survival (%)
RP plus RT versus RT plus ADT in LAPC

- Regardless of the tumor stage or the Gleason score, the adjusted 10-year prostate cancer-specific survival and 10-year overall survival favored men who underwent RP plus XRT over men who underwent XRT plus ADT.
- The theoretical benefits of RP as first-line treatment are tumor volume reduction and optimal local control.
- Men who underwent RP plus RT had higher rates of erectile dysfunction (28% vs 20%), higher rates of urinary incontinence (49% vs 19%) in comparison with those who underwent RT plus ADT.

Thomas L. Jang, et al. Cancer. 2018
Nine-year overall survival and prostate cancer-specific survival were estimated using the Kaplan-Meier method.

Locally advanced (cT3-T4 or N1 and M0) (272 men) or metastatic (M1) (314 men)
The 9-year prostate cancer-specific survival rate for ADT group was 67% versus 78% and 89%, respectively, for those receiving RT and RP.

This study noted a clear survival advantage with aggressive prostate-directed therapies in patients with LAPC versus ADT, with a trend toward an advantage for RP over RT.

Figure 1. Prostate cancer-specific survival by treatment in patients with locally advanced prostate cancer.

Marc A. Dall’Era, et al. Cancer. 2018
Surgery for locally advanced prostate cancer (LAPC)?

• Recent evidence suggested that radical prostatectomy (RP) can improve outcomes for patients with LAPC within the framework of a multimodal setting.

• The advantage of surgery has an option of adjuvant XRT according to the pathology.