Trans-Pacific Variation in Outcomes for Men Treated With Primary Androgen Deprivation Therapy For Localized Prostate Cancer

Matthew R. Cooperberg\textsuperscript{1)}, Shiro Hinotsu\textsuperscript{2)}, Mikio Namiki\textsuperscript{3)}, Peter R. Carroll\textsuperscript{1)}, and Hideyuki Akaza\textsuperscript{4)}

\textsuperscript{1)} University of California, San Francisco, \textsuperscript{2)} Kyoto University, \textsuperscript{3)} Kanazawa University, \textsuperscript{4)} The University of Tokyo
Background

- Primary androgen deprivation therapy (PADT) for clinically localized prostate cancer is not endorsed by the AUA, NCCN, or EAU guidelines, except in rare cases.

- However, PADT is described as an option for localized disease by the NCCN Asia Consensus and JUA guideline, and is used commonly in practice on both Japan and US.

- The origin of this discrepancy and its appropriateness are not clear. We aimed to determine survival outcomes for men undergoing PADT in two large cohorts, one in the U.S. (CaPSURE) and one in Japan (J-CaP).
Patients

- **J-CaP**: men treated in Japan for prostate cancer (any stage) at one of 384 participating practices, capturing ~50% of all patients in Japan from 2001 to 2003 (95% of PADT patients), N=16,300.

- **CaPSURE**: men diagnosed with prostate cancer in the U.S. at one of 45 participating practices, primarily community-based. Analyses performed on men treated with PAD. N=1934.
Methods

- Risk assessed using validated **J-CAPRA** score, measured on a 0-12 scale.
- Prostate cancer-specific mortality estimated using Kaplan Meier Method and a Cox model adjusting for type of PADT, age, J-CAPRA, year of treatment, comorbidity count, and registry (CaPSURE vs. J-CaP).
Results

• Age distribution (mean ± SD)

   CaPSURE: 72.7 ± 8.5
   J-CaP:    75.0 ± 7.2

• Patients treated with PADT in J-CaP were older than those in CaPSURE
J-CAPRA score distribution

- CaPSURE: 2.1 ± 2.3
  - J-CaP: 3.0 ± 3.6

- Patients in J-CaP had higher risk of disease
Cancer-specific survival in each cohort by J-CAPRA score

- Patients in J-CaP had better cancer-specific survival than patients treated with PADT in CaPSURE

![Graphs showing cancer-specific survival by J-CAPRA score](image)
### Multivariate analysis of cancer-specific mortality

Adjusting for multiple factors in the table, patients treated with PADT in Japan compared to the US have 3-fold lower Cancer-specific mortality.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00 (0.99 – 1.01)</td>
<td>0.350</td>
</tr>
<tr>
<td>J-CAPRA</td>
<td>1.43 (1.40 – 1.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Year of dx</td>
<td>1.04 (1.00 – 1.08)</td>
<td>0.042</td>
</tr>
<tr>
<td>LHRH</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Orchieotomy</td>
<td>1.43 (1.08 – 1.89)</td>
<td>0.01</td>
</tr>
<tr>
<td>CAB</td>
<td>0.85 (0.71 – 1.02)</td>
<td>0.08</td>
</tr>
<tr>
<td>Academic v. community</td>
<td>1.09 (0.91 – 1.32)</td>
<td>0.35</td>
</tr>
<tr>
<td>Comorbidity count</td>
<td>1.08 (1.00 – 1.15)</td>
<td>0.04</td>
</tr>
<tr>
<td>J-CaP v. CaPSURE</td>
<td>0.36 (0.27 – 0.48)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Discussion

- Large differences observed in cancer-specific mortality for PADT patients in the U.S. compared to Japan.
- Patients treated with PADT in Japan had far greater survival than patients with same disease risk categories in the U.S.
- Guidelines on both US and Japan therefore seem appropriate.
- The etiology of these differences is unclear.
- Possible explanations include differences in
  - Genetics
  - dietary / lifestyle / environmental exposures
  - differences in risk incompletely captured by the J-CAPRA (potential confounding factors unmeasured)
Conclusions

• Survival outcomes are substantially different in these two cohorts of CaPSURE and J-CaP.
• Understanding these differences is likely to yield novel insights into interactions among these endogenous and exogenous factors in men with prostate cancer worldwide.