High Risk Urologic Cancers

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Prostate Cancer

• What is “high risk” prostate cancer?
  • PSA>20ng/ml, GS 8-10, cT2c/T3
  • represents 10-20% of screened men
  • expand to include nodes, SVs, or mets?

• What issues in high risk PC need addressing?
  • earliest and best identification of patients; most effective treatment
  • improved therapies to prevent and/or treat progression/recurrence
Identification of High Risk Patients

• Screening tests have improved, but…
  • need to move beyond a PSA platform

• Molecular assays have enhanced stratification
  • genetic signature-based biomarkers
Biggest Problem is Perception

- Perception Problem
  - “prostate cancer is not harmful”
Screening Advancements

- PSA density
- PSA velocity
- Free/total PSA
- PHI (Prostate Health Index)
- 4K
- PCA-3 (± TMPRSS)
- Confirm-MDX™

Stratification Advancements

- Oncotype™ and Prolaris™
- Decipher™
- Multivariate Risk Stratification
- Imaging (Future Potential?)

Improved ability to identify who needs a biopsy

Improved ability to identify who is at risk for death or progression once diagnosed

Improvements

- We have witnessed improvements in
  - screening appropriate population
  - prognosticating significance of disease in men diagnosed with prostate cancer
  - treatment for those who need it

- We have made conscious effort to address concerns of over-treatment: to separate diagnosis from treatment
Biggest Problem is Perception

- We need to change the conversation
PC: Identification of High Risk Patients

- Screening tests have improved, but...
  - need to move beyond a PSA platform
- Molecular assays have enhanced stratification
  - genetic signature-based biomarkers
  - situation is better but still imperfect
- Need the ability to identify which men/cancers will respond best to which specific treatments
  - use genomics to identify best therapeutic targets
PC: Management of High Risk Patients

- Local versus distant failure
  - more extensive local therapy/treatment of oligometastatic disease
  - early addition of multimodality and systemic therapies
  - use genomics to optimize treatment with therapies that are target-specific
Kidney Cancer

• What is “high risk” kidney cancer?
  • recurrent disease after treatment

• RCC has many successes
  • surgical therapy for localized disease
  • systemic therapy for early metastatic disease

• What issues in RCC need addressing?
  • early identification of metastatic disease
  • improved treatment of metastatic disease
RCC: Needs

- Tumor-based predictive biomarkers
- Mechanisms of immune escape
- Additional downstream targets
- RNA based discovery and therapeutics
RCC: Approaches

• Have we exhausted adjuvant therapy? Have we exhausted immunotherapy?
  • look at specific genetic profiles
  • fresh look at autologous vaccines and immunotherapy
Approaches

• Promising approaches for metastatic disease?
  • checkpoint inhibitors (PD-1, CTLA-4)
  • programmed death ligand (PD-L1)
  • HIF-2α inhibitors
  • chimeric antigen T-cell (CAR-T cell)
  • addressing co-existent medical conditions
**Testis Cancer**

- What is “poor risk” testis cancer?

<table>
<thead>
<tr>
<th>Classification</th>
<th>Nonseminoma</th>
<th>Seminoma</th>
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<tbody>
<tr>
<td>Good risk</td>
<td>Gonadal or retroperitoneal primary tumor</td>
<td>Any primary site</td>
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<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>No nonpulmonary visceral metastases</td>
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<tr>
<td></td>
<td>Good tumor markers (AFP &lt;1,000µg/l and hCG &lt;5,000 IU/l and LDH &lt;1.5×N*)</td>
<td>Normal AFP, any hCG, and any LDH</td>
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<tr>
<td>Intermediate risk</td>
<td>Gonadal or retroperitoneal primary tumor</td>
<td>Any primary site</td>
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<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>Nonpulmonary visceral metastases</td>
</tr>
<tr>
<td></td>
<td>Intermediate tumor markers (AFP 1,000–10,000 µg/l or hCG 5,000–50,000 IU/l or LDH 1.5–10×N*)</td>
<td>Normal AFP, any hCG, and any LDH</td>
</tr>
<tr>
<td>Poor risk</td>
<td>Mediastinal primary tumor or Nonpulmonary visceral metastases or Poor tumor markers (AFP &gt;10,000µg/l or hCG &gt;50,000 IU/l or LDH &gt;10×N*)</td>
<td>NA</td>
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Testis Cancer

• What issues in TC need addressing?
  • early identification of metastatic disease
  • treatment of recurrent chemo-resistant advanced disease
    • new genetic/molecular targets
  • limiting toxicity of chemotherapy
    • reduce chemotherapy dose
  • new genetic/molecular targets for (presumed) less toxic therapies
“Embracing and advancing innovation in urologic care, research, and education.”

— Mission Statement 2014
UMass Urology Starts with U