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***™

Improved ability to identify who needs a biopsy

Stratification Advancements

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

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

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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

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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?

Classification	Nonseminoma	Seminoma
Good risk	Gonadal or retroperitoneal primary tumor No nonpulmonary visceral metastases Good tumor markers (AFP <1,000 μg/l and hCG <5,000 IU/l and LDH <1.5×*N**)	Any primary site No nonpulmonary visceral metastases Normal AFP, any hCG, and any LDH
Intermediate risk	Gonadal or retroperitoneal primary tumor No nonpulmonary visceral metastases Intermediate tumor markers (AFP 1,000–10,000 μg/l or hCG 5,000–50,000 IU/l or LDH 1.5–10×*N**)	Any primary site Nonpulmonary visceral metastases Normal AFP, any hCG, and any LDH
Poor risk	Mediastinal primary tumor *or* Nonpulmonary visceral metastases *or* Poor tumor markers (AFP >10,000 μg/l or hCG >50,000 IU/l or LDH >10×*N**)	NA

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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

Department of Urology

"Embracing and advancing innovation in urologic care, research, and education."

— Mission Statement 2014

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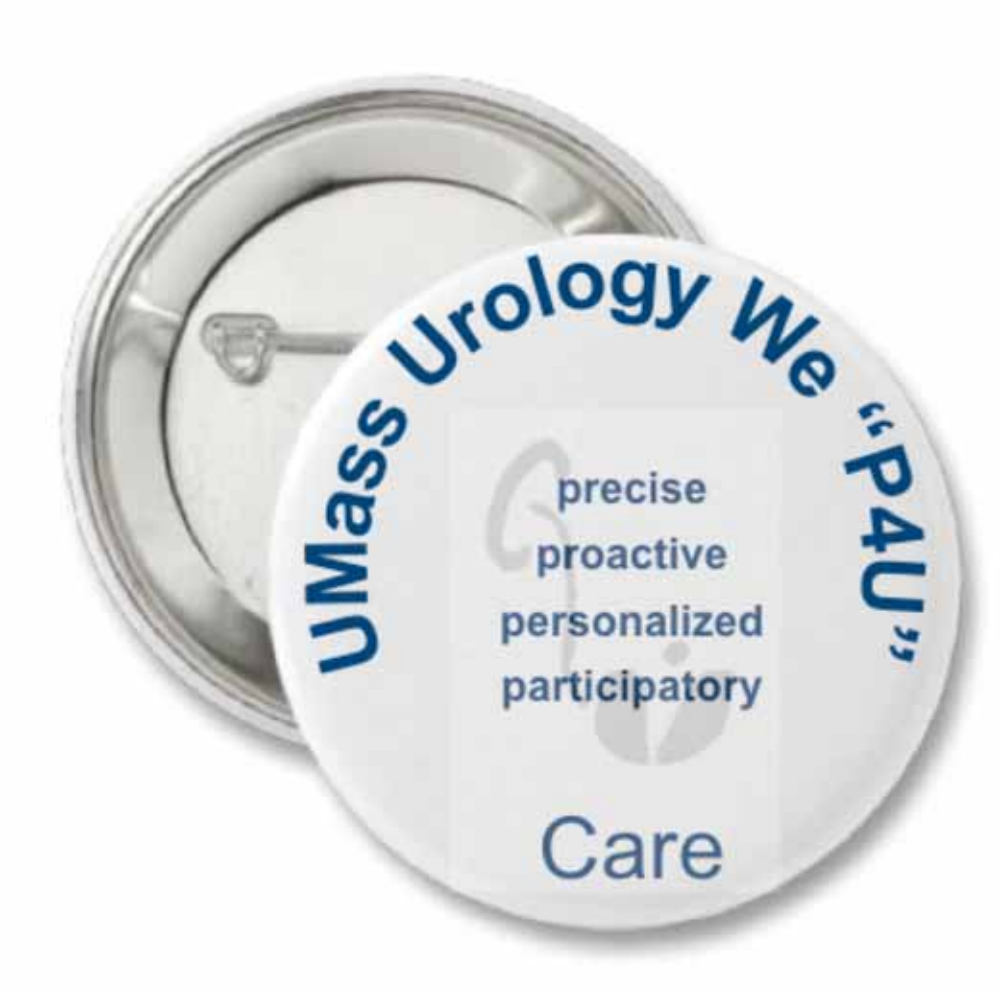
UMass Urology Starts with U



Members of the Department of Urology. Front row (from left): Drs. Yates, Sokoloff, Bellin, and Steiger. Back row (from left): Drs. Bamberger, Berry, and Ellsworth. Missing: Drs. Bernhard and Rampello