62. Urinary Bladder

Authors

Emerging Prognostic Factors for Clinical Care

Molecular Phenotype
Bladder cancers are biologically heterogeneous with variable response to treatment and clinical outcomes. Molecular studies have demonstrated significant differences in the genetic alterations associated with the two major clinical entities of bladder cancer: non-invasive, low-risk disease (characterized by FGFR3, KRAS alterations) and high-grade, or invasive, disease (characterized by retinoblastoma and p53 pathway alterations). Whole-genome mRNA expression profiling and unsupervised hierarchical cluster analyses recently have identified two to three distinct subtypes of muscle invasive bladder cancer similar to subtypes in breast cancer. The basal subtype is characterized by p63 activation, squamous differentiation, and aggressive disease at presentation. The luminal subtype is characterized by active PPAR-γ and estrogen receptor transcription and enriched with activating FGFR3 mutations. The p53-like subtype is characterized by resistance to neoadjuvant chemotherapy.

Risk Assessment Models
The AJCC recently has established guidelines that will be used to evaluate published statistical prediction models for the purpose of granting endorsement for clinical use. Although this is a monumental step toward the goal of precision medicine, this work was published only very recently. For this reason, the existing models that have been published or that may be in clinical use have not yet been evaluated for this cancer site by the Precision Medicine core of the AJCC. In the future, the statistical prediction models for this cancer site will be evaluated, and those that meet all AJCC criteria will be endorsed.

Recommendations for Clinical Trial Stratification
Important considerations for patient selection and stratification in the design of clinical trials in the perioperative front line and refractory settings include cisplatin eligibility (including renal function and presence of peripheral neuropathy) and performance status.

For perioperative trials, stratification should consider not only staging, but also the aforementioned clinical prognostic variables as well as molecular phenotype.
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Therapy for metastatic urothelial cancer failing initial systemic therapy is particularly challenging and represents a substantial unmet need. These patients should be categorized separately from patients who have no prior systemic therapy. A retrospective analysis of pooled prospective phase II trials (n = 570) in the second line setting has shown that baseline performance status (PS), hemoglobin, presence or absence of liver metastases, and time since prior chemotherapy were significant prognostic factors. More recently, serum albumin also has been validated as a prognostic factor in the second-line setting.7

Bibliography