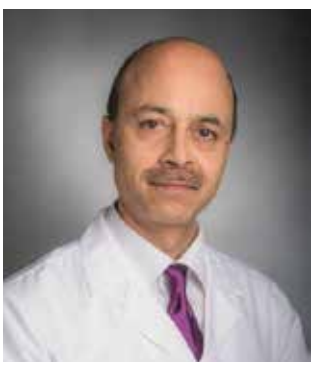
In the recent few years, we have witnessed multiple advances in the multidisciplinary therapy of bladder cancer. These advances have arrived across the spectrum of diagnosis, surgery, radiotherapy and systemic therapy. Blue light cystoscopy has improved the sensitivity of detection of malignancy, although further studies are ongoing to evaluate efficacy and cost effectiveness to justify universal adoption. Baseline clinical staging of muscle invasive bladder cancer and upper tract urothelial carcinoma requires advances. In this context, multiparametric (mp)-magnetic resonance imaging (MRI) and fluoro-deoxy-glucose (FDG)-positron emission tomography (PET) imaging may be a step in this direction to fulfill an unmet need in this setting. Therapy for non-muscle invasive bladder cancer has enjoyed much-needed advances with the arrival of systemic pembrolizumab for BCG-unresponsive high-risk disease and mitomycin gel for low-grade upper tract urothelial carcinoma. Moreover, promising intraluminally delivered agents are emerging such as nadofaragene firadenovec and vicinium for high-risk BCG-unresponsive disease. Enhanced recovery after surgery (ERAS) protocols are emerging in the setting of radical cystectomy and their universal adoption may improve the quality of life of patients. Moreover, the emergence of intensity-modulated radiation therapy (IMRT) and use of MRI to plan radiotherapy may improve the therapeutic index of radiotherapy for muscle-invasive bladder cancer.

The therapeutic landscape for metastatic urothelial carcinoma has been transformed with the advent of multiple PD1/L1 inhibitors in the post-platinum and first-line cisplatin-ineligible space. However, durable responses with PD1/L1 inhibitors are observed in only 15% to 25% of patients. More recently, the landmark Javelin Bladder-100 phase III trial demonstrated that firstline switch-maintenance avelumab PD-L1 inhibitor therapy following responding or stable disease on platinum-based chemotherapy improved survival significantly and is considered practice-changing. Unfortunately, adjuvant atezolizumab did not improve outcomes following radical cystectomy for high risk muscle invasive disease in one phase III trial (IMvigor-010), although efforts to evaluate other PD1 inhibitors and incorporate PD1/L1 inhibitors in bladder preserving trimodal chemoradiation approaches are ongoing. Disappointingly, the combination of PD1/L1 inhibitors with platinum-based chemotherapy (KEYNOTE361, IMvigor130) or CTLA-4 inhibitors (DANUBE) for metastatic disease has not been successful in improving survival in recent trials. Enfortumab Vedotin, a Nectin-4 targeting antibody drug conjugate, and erdafitinib, an oral FGFR inhibitor for ~15% of patients have provided advances in the salvage setting. As ongoing efforts attempt to develop novel combinations incorporating these agents in the firstline setting (EV-302 trial), efforts to refine the optimal sequencing of these agents need investigation. Despite these advances in therapy, it is important to not lose sight of the fact that metastatic disease is generally incurable and clinical trials should be considered a standard of care for all settings of the disease.

The most important step toward improvement of therapies and outcomes is the understanding of tumor biology. Never has the collaboration between specialists from medical oncology, urology, radiation oncology, pathology and basic science been more critically important. Knowledge of the enormous heterogeneity of tumor biology is now emerging. Specifically, dynamic changes in tumor and microenvironment following therapy need to be understood for insights into resistance and new therapeutic targets. While tumor PD-L1 expression and FGFR3/2 activating genomic alterations are already in the clinic, precision medicine leveraging molecular information from other platforms may be necessary for optimal patient selection. In this context, DNA damage repair alterations and gene expression subtypes of tumor are associated with pathologic response to neoadjuvant chemotherapy. Finally, capitalizing on non-invasive molecular monitoring is important and early data from cell-free DNA profiling studies utilizing plasma and urine are encouraging.

This book provides a valuable collection of new information in the understanding of tumor biology and multimodality therapy for bladder cancer that has been recently published in *Translational Andrology and Urology*. Some of the key opinion leaders have been involved in this textbook, which readers will find informative. I am honored to write the preface to this textbook.



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