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A precision, personalized approach to the management of bladder cancer

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Treating urinary bladder cancer is highly demanding. Among the major urologic neoplasms, bladder cancer has seen the least amount of progress in recent years, with no breakthroughs comparable to robotic surgery in prostate cancer or antiangiogenic therapy in renal cell carcinoma.

Yet, despite daunting obstacles to progress, we are making strides in understanding the basic mechanisms of bladder cancer tumorigenesis. More importantly, we are seeing improvements in prognostic stratification, which is paramount in clinical management as differential therapies, such as bladder-sparing approaches vs. radical cystectomy or perioperative chemotherapies, have a tremendous impact on functional and oncological outcomes. We have also come to understand that no simple scoring system can take every tumor-related and patient-related parameter into account. Quite simply, the future of treatment for bladder cancer patients is personalized, precision medicine.

Precision medicine is the leading edge in cancer treatment. It employs genomic pathology derived from genetic sequencing and molecular profiling to classify subsets of patients as candidates for potential therapies [1]. While precision medicine identifies subpopulations of patients, personalized medicine focuses on defining treatment strategies for individual patients, based on classifications such as sex, age, prior treatments, lifestyle, genetic subtypes and alterations, and immune system status. In contrast to the ‘one-size-fits-all’ mindset common among oncologists, practitioners of personalized medicine tailor therapies and treatment strategies based on multiple biological and social factors. It is the ideal practice approach for patients with complex neoplasms such as bladder cancer.

Bladder cancer is a collection of biologically heterogeneous cancers with different molecular and histopathologic subtypes and variable responses to therapy and, thus, variable clinical outcomes [2]. Genetic profiling has revealed bladder cancer tumors’ very high mutational burden [3], indicating their complex molecular profile. Managing this disease becomes even more complex when patients are elderly and have numerous comorbidities. These are the

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patients who may derive the most benefit from a personalized approach to disease management.

In this edition of *Current Opinion in Oncology*, we have invited internationally renowned experts in bladder cancer to present an overview of their research and clinical work, focusing on individual patient factors that may affect bladder cancer treatment and clinical outcomes. Matthias May reports on the impact of sex on bladder cancer outcomes, outlining emerging data suggesting that men fare better than women despite imbalances in incidence favoring women. Matt Milowsky focuses on age as a factor and the complexities of managing elderly patients with muscle-invasive bladder cancer. David McConkey outlines the genetic subtypes of muscle-invasive bladder cancer that can affect treatment decisions, especially in the absence of detailed histopathologic differentiation in muscle-invasive stages. Andrea Apolo details the latest findings on whether local and distant radiologic imaging can help in defining clinical pathways.

Bladder preservation in high-risk nonmuscle-invasive bladder cancer almost always requires bacillus Calmette-Guérin (BCG) treatment. Bas van Rhijn (pp. 427–435) discusses the complex mechanisms of this immunotherapy, as well as the wide range of host responses to BCG. Armin Pycha demonstrates how a personalized approach may reduce the need for urinary diversion in patients for whom radical surgery is the best option. Radical cystectomy is still the gold standard for muscle-invasive bladder cancer. However, Romain Matthieu (pp. 476–482) discusses whether trimodal therapy involving radiotherapy, local resection, and chemotherapy may provide outcomes equal to radical cystectomy.

Two particularly challenging issues in clinical care are the management of tumor recurrence and treatment of advanced-stage disease. Piyush Agarwal (pp. 468–475) presents options for management of noninvasive recurrence after definitive treatment for muscle-invasive bladder cancer or high-grade upper-tract urothelial carcinoma, and Agnes Maj Hes, Maria DeSantis, and Andrea Apolo review and discuss whether novel immunotherapies offer hope for patients with advanced disease (later issue).

We hope these articles will enlighten and inspire our efforts to improve the treatment for bladder cancer. We must build on the modest progress that has been made, while realizing that the key to success lies in personalized care for bladder cancer patients.

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