

Preface

Current Landscape of Advanced and Metastatic Renal Cell Carcinoma Management



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Editors

The first decade of the new millennium witnessed a revolution in the management of advanced renal cell carcinoma (aRCC), thanks to the approval of therapeutic agents targeting the VEGF and mTOR pathways. These targeted therapies transformed the treatment landscape of aRCC and highlighted the success of translational medicine. The arrival of the following decade brought with it clinical trials demonstrating efficacy of immunoncology (IO) agents in metastatic renal cell carcinoma (mRCC). These trials led to the establishment of second-/third-line roles of IO in mRCC, first as monotherapy and, later, as combinations with other IO agents blocking various immune pathways (ipilimumab/nivolumab). Finally, as the decade came to an end, further successes were achieved through the approval of additional targeted and IO agents and the combination of these therapies resulting in a first line indication across all risk groups with pembrolizumab and axitinib (pembrolizumab/axitinib).

All of these treatment advances have resulted in a redefining of the traditional roles of urologists, medical oncologists, and radiation oncologists. Therefore, we have decided to kick-off this issue of *Urologic Clinics* with an article by Kim

and colleagues summarizing the evolving role urologist in this new era.

Significant advances have also been made not only on the treatment but also in the evaluation and assessment of patients with aRCC. In the article by Vig and colleagues, the authors examined the evolution of different imaging modalities for diagnosis and staging of aRCC and provide insight on new imaging modalities currently under development.

With the approval of new therapies comes a revision of risk stratification, treatment indications, and patient selection. In the article written by Atalla and colleagues, the authors review the current methods of risk stratification utilizing clinical parameters and discuss the future development of biomarkers that will help identify patients most likely to benefit from these novel therapies.

Changes in indications and sequencing of these drugs continue to change at a dizzying pace. The article by Dizman and colleagues helps clear the confusion by explaining the fundamentals of these agents, providing easy-to-use algorithms, and discussing how gene expression models may play in the near future.

There remain, of course, many unanswered questions in this new landscape. Some of these questions revolve around the utilization of these new therapies in patients with non-clear cell histology and how these therapies can be incorporated into use in the perioperative setting. Filppot and colleagues discuss the successes and shortcomings of treating patients with non-clear cell aRCC in their article. Westerman and colleagues elaborate on both completed and ongoing clinical trials in the neoadjuvant setting in their article, while Wood and colleagues discuss the current role of adjuvant therapy and also explore ongoing clinical trials on this subject.

Thanks to the success of these novel therapies, the role of surgery in aRCC continues to be redefined. Biles and colleagues tackle the increasingly controversial question of cytoreductive nephrectomy in lieu of the seminal findings noted in the CARMENA and SURTIME trials. The benefits of lymphadenectomy and metastasectomy in this era are elegantly discussed and assessed by Unadkat and colleagues and Hall and colleagues, respectively. The articles discussing surgery in aRCC are concluded in a chapter by Becher and colleagues discussing the role of minimally invasive surgery and how the wide acceptance of robotic platforms in the urologic community has impacted the surgical treatment of this disease.

Although much of the focus in advances in the treatment of aRCC revolves around systemic and surgical therapies, other treatment options have continued to evolve as well. RCC has

classically been categorized as a radioresistant tumor. However, the advent of higher dose-per-fraction systems has enabled investigators to reevaluate the role of radiotherapy in both localized and mRCC. Miccio and colleagues elaborate on the growing body of evidence behind the rationale for the use of radiation as a beneficial treatment modality in advanced and metastatic RCC.

It has truly been a privilege for us to be guest editors of this issue of *Urologic Clinics*. We feel indebted to all the authors who contributed their knowledge and wisdom as they are the preeminent thought-leaders in this field. It is our wish that this issue will serve in this unprecedented time as a road map for not only urologists, but all health care providers tasked with treating patients with advanced and metastatic RCC.

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