From the Editor

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This issue of *AJHO* contains a concise and timely review on renal cell carcinoma (RCC), one of the less-common types of malignancies, but one for which medical oncology approaches have developed very quickly. The mainstay for therapy had been surgery, which is usually curative for very-early-stage disease; even in advanced disease, nephrectomy is associated with a better outcome for reasons that remain obscure. RCC is an immunogenic cancer, probably not as much as melanoma, but a few long-term responses have been seen with interleukin-2 therapy. This provides a rationale for using this approach in suitable patients since newer therapies do not generally provide durable responses.

The long list of contemporary treatments outlined in this review by Drs Sadeghi and Quinn are based on an interesting biological hallmark of RCC: Many RCCs have a defect in the von Hippel-Lindau (VHL) pathway, which serves as a hypoxia sensor and response mechanism. These cancers compensate for this by a variety of responses that include a robust angiogenic drive, which accounts for the "tumor blush" reported in older literature when angiography was used to make a diagnosis. Today, antiangiogenic therapies therefore are a mainstay of therapy, as detailed in this article's summary. Since the mammalian target of rapamycin complex 1 (mTORC1) is a key mediator of this pathway as well, mTOR inhibitors also are effective therapies for RCC. The clinical dilemmas regarding which drug to use and when, and how to best sequence therapies upon progression, are addressed in this article. These algorithms are based on risk stratification and evidence from key randomized studies, but illustrate how modern oncology practice is tied to the way in which pivotal trials were designed, with the primary aim of meeting US Food and Drug Administration approval requirements.

The revolution in cancer immunology is fueled by a greater understanding of immune checkpoints that prevent hyperactivity and autoimmunity. Disabling these checkpoints—CTLA-4 and PD-1/PD-L1—has yielded responses in melanoma, with early promising results seen in triple-negative breast cancer and lung cancer—notably in squamous cell cancers. In RCC, also a relatively immunogenic cancer, promising results are being seen in advanced disease, and immune approaches may also be the most amenable as adjuvant therapy.