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EDITORIAL

The Year in Review for Renal Cancer

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The treatment of kidney cancer has made some remarkable strides over the last few years. Two regimens received Food and Drug Administration (FDA) approval, multiple biomarkers were reported to show promise, and further enhancement and refinement of the prognostic characteristics occurred. The combinations of anti-angiogenic tyrosine kinase inhibitors with immune checkpoint inhibitors have rapidly become the preferred therapies in the front-line setting of advanced renal cancer.

The combinations of axitinib with either avelumab or pembrolizumab have received FDA approval in all risk groups of advanced renal cancer. In the backdrop of immune checkpoint combination therapy of ipilimumab and nivolumab being approved for intermediate and poor-risk RCC, three options of therapy for the initial management of advanced renal cancer have been proposed. Multiple other trials of combinations of cabozantinib and nivolumab, and lenvatinib and pembrolizumab, and triplet regimens, involving cabozantinib and ipilimumab and nivolumab, are likely to continue to revolutionize the landscape of RCC therapeutics. Recently, the 42-month overall survival was reported for the CheckMate 214 trial, with the long-term remission results being upheld.

Renal Cancer therapeutics has come a long way from witnessing nephrectomy make a small survival benefit or waiting for interleukin 2 to show a response in a chosen few, to doubling of median survival within the clinical trial patient population. We have gradually been able to impact specific subtypes, such as sarcomatoid RCC, but remain far behind in customizing therapies to the individual patient. The expansion into the area of combinations of local therapies and synergy with systemic therapies has added a new dimension to the management of oligometastatic disease. These approaches are very expensive and not without toxicities—both acute and chronic—and are currently lacking randomized evidence. In select patients, the results appear promising, but real-world vetting is required. In comparison with systemic therapy alone, the incremental benefit was disappointingly small.

Every patient is a complex clinical trial, with N = 1

The future will bring profiling of each patient to determine therapy; however, specific biomarkers guiding therapy remain elusive. Currently, in RCC, biomarkers have shown their utility in predicting prognosis alone but not in guiding therapies. The year 2020 will likely bring multiple therapeutic regimens, such as lenvatinib and pembrolizumab and cabozantinib and nivolumab, which will represent therapeutic advances. S1500, the papillary renal cancer study, will likely establish a baseline therapy and clinical outcome in this rare disease for future clinical trial development. Along with this comes the responsibility of clinical application of results to the community and real-world population. Systemic therapy should be the mainstay of management in metastatic RCC, and the role of cytoreductive nephrectomy should be carefully considered. The next randomized trial will address the comparison of deferred cytoreductive nephrectomy and whether that has a survival impact on the control arm of systemic therapy alone.

The sobering truth is that in spite of exciting advances, we are not currently curing more than half of the kidney cancer patients. A well-known adage states, "Celebrate your successes and learn from our failures." However, in the era of genomics, we cannot just rest on our laurels but need to learn even more from our successes to help streamline therapies for future patients. The microbiome studies are an example of how the responding patients can help contribute to improve outcomes in others less fortunate. We should continue the teamwork between patient advocates and basic science researchers and clinicians toward the mission of beating kidney cancer.

For the last 2 years, Nobel prizes in medicine have made a deep impact on kidney cancer management. Both the immune checkpoint and the hypoxia inducible factor pathways reflect the pathophysiology of the majority of clear cell RCC and have been harnessed for therapeutic purposes. Specific

populations, such as patients with synchronous metastatic disease, patients with autoimmune diseases, renal transplant patients, dialysis patients, and patients presenting with locoregionally advanced disease, have been underrepresented in clinical trials, and further studies focusing on them are required. Future challenges lie in optimizing current therapies and identifying novel targets and therapies to improve outcomes.