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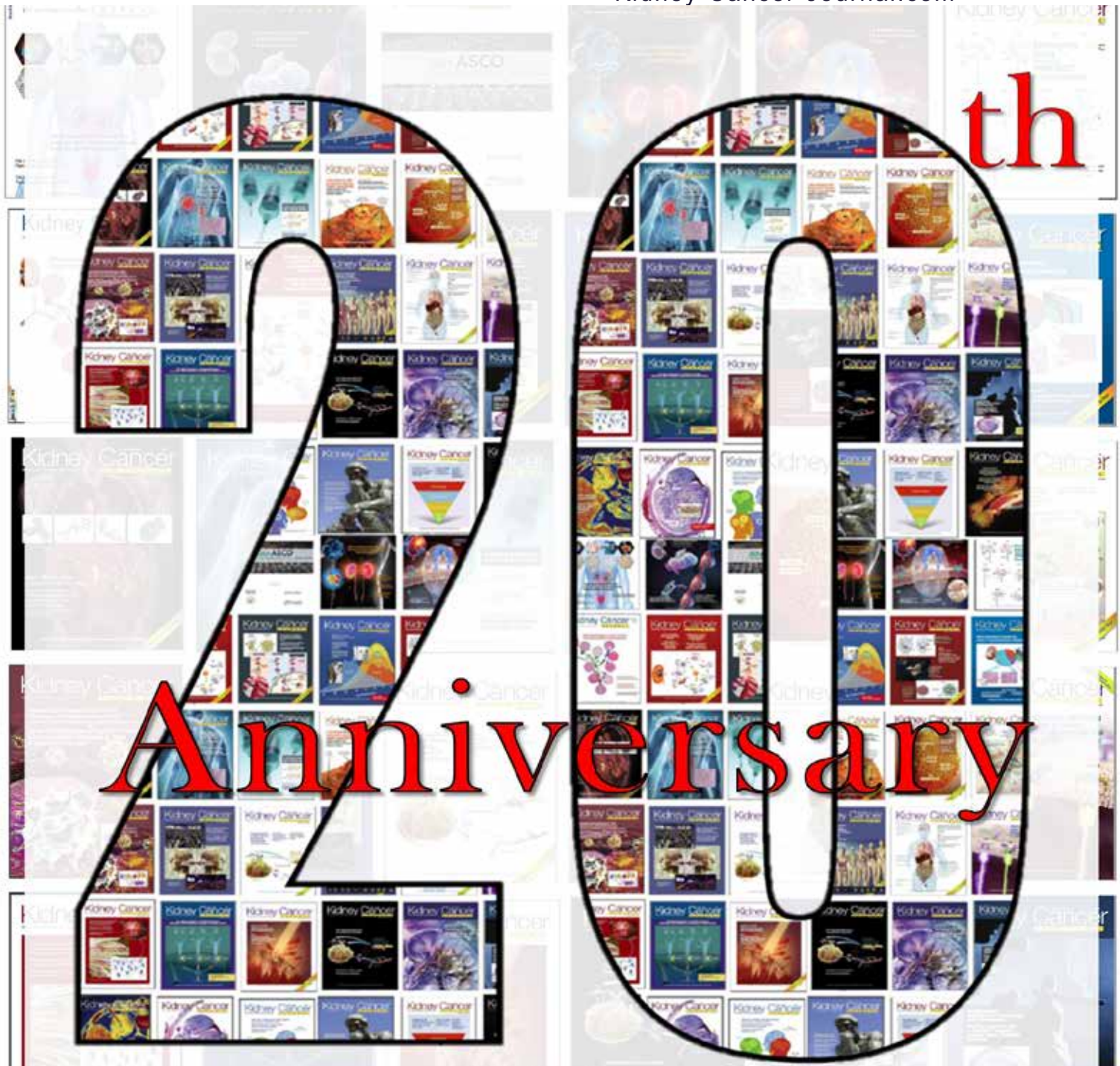

ASCO GU22 Special

An Educational Service for Medical Oncologists, Hematologist-Oncologists, and Urologists

A 20-Year Retrospective of Kidney Cancer Journal: 2003-2022

These 20 years of the Kidney Cancer Journal's journey encapsulate the most dramatic advances ever achieved in the management of RCC. This Q&A with Editor-in-Chief Robert A. Figlin, MD, reflects on the last two decades of the journey, and significant milestones in the evolution of strategies and optimized outcomes.

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KCJ: For the last 20 years, the Kidney Cancer Journal has kept clinicians on the leading edge of the evolution in therapy and the journal's contents have closely paralleled advances in cancer care. As the editor for the last two decades, to what extent does the peer-reviewed contents of the journal influence your overall perspective and rationale on cancer management?

The decision to launch our *Kidney Cancer Journal* two decades ago was to inform and educate clinicians who care for kidney cancer patients about caring for, and future options for patient care. Most cancer physicians do not see many kidney cancer patients and we felt that it is important to have a journal that is completely aligned with kidney cancer research and its translation. Little did we know that when we launched the journal, the next two decades would be the most dynamic two decades in the history of kidney cancer research with the approval of multiple drugs alone or in combination, groundbreaking research, and dramatic improvement in patient outcomes over the last two decades. We believe that our journal has been a trusted resource and has received a wonderful reception from the kidney cancer community, the Kidney Cancer Association, doctors, patients, and nurses who care for kidney cancer patients.

KCJ: Do you think we are at an inflection point such that in the next few years we can expect a paradigm-shifting advance comparable to the introduction of targeted therapy or checkpoint inhibition or is it more likely that we will continue incremental progress by building on the current combination and sequential treatment algorithms?

Over the last two decades, there have been multiple inflection points. I think these inflection points have almost always parallel scientific discoveries and translational investigation from novel therapies into the clinic. There was only interferon 20 years ago and interleukin-2, then the era of targeted therapy, and now the era of the checkpoint inhibitors. Each of those was inflection points as defined by giving patients better options, better outcomes, and improved quality of life. If you ask me whether it's an inflection point currently, I think with the current checkpoint inhibition trials, in combination or alone, we are making incremental progress. I'm hopeful that the future kidney cancer science will continue to provide us with groundbreaking discoveries that can offer kidney cancer patients further inflection points, whether that is through HIF2 inhibition, CAR-T cell therapy, or other as yet to be defined as pathways that can influence treatment strategies in patients. We hope that there'll be discovered over the next few years.

KCJ: Aside from the VHL-HIF pathway, are there additional directions in identifying molecular, genetic models that could yield prognostic and therapeutic value? What innovative therapies currently under investigation are likely to emerge as candidates for first or second-line strategies?

It takes me back to the 1990s when I was invited by the FDA on two separate occasions to review for the approval of interleukin-2. The challenge of IL-2 therapy was its route of administration and the associated morbidity and potential mortality. Currently, there are emerging next-generation interleukin-2 molecules that delivered alone or in combination with checkpoint inhibition may offer the opportunity to convert cold tumors to hot tumors and then be able to deliver promising outcomes. I also look forward to seeing these outcomes as well as further integration of VHL pathway-based discoveries in the kidney cancer space. These agents targeting metabolic pathways such as glutaminase inhibitors are worthy to mention. However, these agents have not proven to be as effective as we had hoped, but such areas of research are largely unexplored.

KCJ: What is your perspective about the validation of reliable biomarkers in the renal cancer space?

I look at biomarkers through several lenses. For example, when I was at UCLA, my colleague Arie Belldegrun and I developed the UCLA integrated staging system with defined clinical parameters that predict outcomes for surgically resectable patients and had been fully integrated into all prospective adjuvant trials. The most recent KEYNOTE trial which demonstrated survival benefit using pembrolizumab was based on the original biomarker evaluation in the clinical setting and selection of patients from decades ago. In other cancers, actionable mutations, or checkpoint status can be developed as biomarkers. However, in the advanced kidney cancer setting, the quest is still on for developing biomarkers that are associated with outcomes to identify the patients that immediately benefit, reliable biomarkers development remains an elusive goal

KCJ: Have studies during the last 5 years definitively resolved controversies surrounding the use of nephrectomy and if not, what issues are still unsettled and need to be elucidated?

That's an excellent question. I think that what we know is that nephrectomy has not been associated with an outcome that is entirely predictive in the setting of 25 to 30% of patients who present with metastatic disease. Having said that, however, a subset of patients seems to benefit from nephrectomy. There's an ongoing argument that in the era of checkpoint inhibition when you need tumor antigens to be able to stimulate the immune system, having an intact kidney may be more important than removing that kidney, especially in the setting of metastatic disease. So, I think that the tide is turned to where routine nephrectomy in the setting of metastatic disease is no longer needed. We still need to understand the contribution of that primary tumor to the immunologic milieu to see how patients benefit from those therapies. Certainly, more work is to be done.

KCJ: What is your perspective about health disparities and equity in clinical trials and cancer care? Can you share your thoughts about the recent initiatives for equity and diversity in cancer care and new programs and resources that address health equity issues in cancer care?

We do not do a good enough job as a cancer community, making sure that all patients who suffer from kidney cancer are treated comparably whether they're underinsured, minimally insured, or uninsured. Most of the clinical trial paradigms are driven primarily by a population of patients that do not adequately address health disparities and the diversity issues in both kidney cancer care and overall cancer care. I think we need to have enhanced commitments to health equity in the kidney cancer environment, especially for those populations of patients that may have poor outcomes because of their economic circumstances. It is unacceptable that we have strived so hard to develop potential therapies over the last few decades, yet we do not make all therapies equally distributed across all patients.