New Data Highlight Acute Kidney Injury Associated with Immune Checkpoint Inhibitors

By Mitchell H. Rosner

The past decade has seen a revolution in the treatment of patients with cancer with novel therapies that harness the power of the immune system to kill tumor cells (1). This has been achieved by removing checkpoints on the immune system that typically are exploited by tumor cells that allow for proliferation and growth. Two classes of immune checkpoint inhibitors are available: drugs that act against checkpoint proteins programmed death 1 (PD-1) or cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) or both (2). An expected side effect of these drugs is the occurrence of immune-related adverse events (irAEs) that manifest as autoimmunity affecting a wide range of organ systems, including the development of acute kidney injury (AKI), usually due to immune-related interstitial nephritis (3).

A large observational study by Gupta and colleagues (4) adds to our understanding of the risks and presentation of immune-related AKI associated with these novel agents. This is a study of over 400 patients at 30 clinical sites, features that should make their findings more generalizable.

What are the key takeaway messages? In those patients who had a kidney biopsy, tubulointerstitial nephritis was the most common lesion (82.7%) seen, but other lesions, such as glomerulonephritis, were also encountered. AKI was more common in patients with higher baseline serum creatinine values, although 71% of AKI cases occurred in patients with an estimated glomerular filtration rate (eGFR) > 60 mL/min/m^2. Nearly one-half of patients with AKI experienced no renal irAEs, and the presence of prior or coexisting irAEs was associated with a twofold higher risk of AKI. Interestingly, the use of proton pump inhibitors (PPIs), drugs independently associated with the development of interstitial nephritis, was also associated with the development of AKI from immune checkpoint inhibitors. Importantly for clinicians, the timing of AKI was variable, occurring at a median of 16 weeks after therapy, but was seen as early as 8 weeks and as late as 1 year after therapy. Outcomes of AKI associated with immune checkpoint inhibitors demonstrated that approximately two-thirds of patients had renal recovery, and this was associated with early initiation of corticosteroids. Last, and somewhat surprising, was that rechallenge of patients who had AKI with immune checkpoint inhibitors was only associated with recurrent AKI in less than 20% of cases.

The findings from this study will greatly influence our thinking about immune checkpoint inhibitor AKI. For instance, PPIs should be used with caution in these patients, and the presence of extra-renal irAEs and AKI should raise suspicion that the mechanism of AKI is related to immune checkpoint inhibitor therapy. However, the study did not identify any clinical features that were so reliable that they clearly pointed to a diagnosis of an immune-related kidney injury over other etiologies, and thus there remains an important role for kidney biopsy to obtain a definitive diagnosis and guide appropriate therapy. In addition, more data are needed regarding dosing and duration of corticosteroid therapy as well as outcomes from this therapy, including risks on progression of the underlying cancer. Still, the authors should be congratulated for bringing together an international group to shed additional light on this evolving area. ■

Mitchell H. Rosner, MD, is the Henry B. Mulholland Professor of Medicine and Chair, Department of Medicine, Division of Nephrology, with University of Virginia Health, Charlottesville.

The author reports no conflicts of interest.

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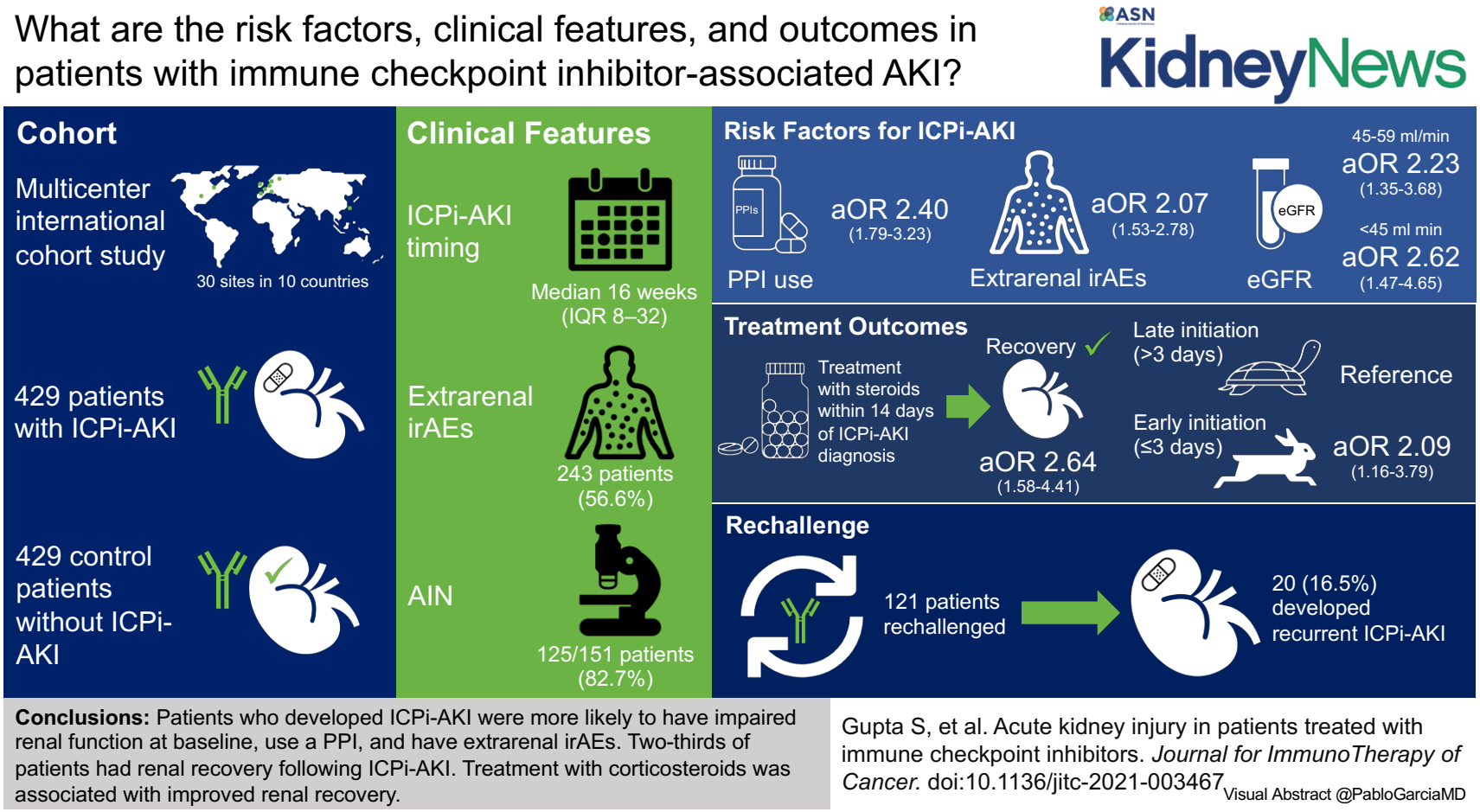

ICPi-AKI, immune checkpoint inhibitor-associated AKI; AIN, acute interstitial nephritis; IQR, interquartile range; aOR, adjusted odds ratio.