What's Next for Onconephrology? Key Takeaways From Kidney Week 2024

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The interplay between nephrology and oncology continues to evolve as advanced cancer therapies highlight the delicate balance of safeguarding kidney health while optimizing therapeutic outcomes. ASN Kidney Week 2024 showcased key findings that shed light on nephrotoxic risks and advancements in biomarker-based diagnostics. Seven groundbreaking studies presented at the meeting underscore the need for multidisciplinary approaches and innovative strategies to enhance patient outcomes in this intersectional field.

Infliximab in steroid-dependent immune checkpoint inhibitor-acute interstitial nephritis

Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy but carry a 3%–5% risk of acute interstitial nephritis (ICI-AIN), with some cases exhibiting steroid dependence. A study presented at Kidney Week (1) detailed three patients with biopsy-confirmed ICI-AIN treated with infliximab as a steroid-sparing agent. All patients initially showed elevated biomarkers, including urine CXCL9, tumor necrosis factor-α, RNA-binding protein, serum interleukin-2 receptor, and C-reactive protein, which decreased following therapy. Infliximab enabled steroid tapering while preventing significant serum creatinine rise in all cases. The relapse-associated rise in biomarkers underscores their potential as indicators for monitoring disease activity. These findings highlight the promise of infliximab in managing steroid-dependent ICI-AIN, although larger studies are needed to validate these biomarkers and therapeutic strategies.

Risk stratification for chronic kidney disease postnephrectomy

Nephrectomy for renal cell carcinoma increases the risk of chronic kidney disease (CKD), and risk stratification tools are critical for early intervention. The Australian risk stratification score for CKD (ARSC) was assessed in a Brazilian cohort of 349 patients with renal cell carcinoma undergoing nephrectomy (2). While ARSC demonstrated satisfactory discrimination (area under the concentration time curve, 0.70), it overestimated CKD risk in higher-risk categories. These findings emphasize the need for external validation of risk scores across diverse populations. Tailored follow-up strategies for patients at risk for CKD can mitigate CKD progression, making accurate risk-stratification tools an indispensable part of postnephrectomy care.

Glucagon-like peptide-1 receptor agonists and acute kidney injury in oncology

The safety of glucagon-like peptide-1 receptor agonists (GLP-1RAs) in patients with cancer has been debated due to reports of acute kidney injury (AKI). A retrospective analysis of over 14,000 patients treated with anticancer therapies revealed no significant association between GLP-1RA use and increased AKI risk (3). Despite exposure to nephrotoxic chemotherapies, patients treated with GLP-1RAs showed similar AKI rates compared with those not receiving these agents. These findings reassure clinicians about the safety of GLP-1RAs on the kidneys and suggest that their potential cardiovascular and metabolic benefits can be safely extended to patients with cancer.

Magnesium's role in preventing cisplatin-induced AKI

Cisplatin, a cornerstone in cancer treatment, poses a significant risk of nephrotoxicity. A multicenter cohort study evaluated the effect of intravenous magnesium (Mg) administration in over 13,000 patients receiving cisplatin (4). Mg administration was associated with a significant reduction in the risk of moderate to severe cisplatin-associated AKI (adjusted odds ratio, 0.73). These findings align with preclinical evidence suggesting that Mg reduces cisplatin uptake by renal tubular cells. With no currently established standard of care to prevent cisplatin nephrotoxicity, these results lay the groundwork for prospective trials to confirm the nephroprotective role of Mg.

The role of sodium-glucose cotransporter-2 inhibitors during cisplatin therapy

Sodium-glucose cotransporter-2 inhibitors (SGLT2is) are well known for their nephroprotective benefits in CKD and heart failure, but their role in acute settings remains unclear. A retrospective study of 300 patients assessed the safety of SGLT2i use during cisplatin therapy (5). Over 1 year, SGLT2i users and nonusers experienced similar declines in kidney function, and no significant differences were observed in AKI or major adverse kidney events, including mortality or dialysis initiation. While these findings are promising, they emphasize the need for prospective studies to explore whether SGLT2is can offer protective benefits during cisplatin therapy.

Advancing biomarker-based diagnostics for ICI-AIN

The limitations of kidney biopsy in diagnosing immune-related kidney injuries have fueled efforts to develop noninvasive biomarkers. Researchers used Nucleic Acid Linked Immuno-Sandwich Assay (NULISA) to assess 203 proteins in urine and plasma from patients treated with ICI (6). A novel two-protein urine signature emerged as a highly accurate tool for diagnosing ICI-AIN, achieving an area under the concentration time curve of 0.94. This represents a significant improvement over traditional biomarkers such as CXCL9. By enabling an earlier and a less-invasive diagnosis, these findings could revolutionize the management of ICI-AIN, improving outcomes for patients receiving life-saving ICIs.

Single-cell analysis illuminates ICI-AIN pathogenesis

Building on the biomarker findings, another study used single-cell RNA sequencing to map the cellular landscape of ICI-AIN (7). The study identified $CD8^+$ T cells as key mediators of disease by analyzing kidney and urine samples from patients with biopsy-confirmed ICI-AIN. These cells, conserved across kidney tissue and urine, exhibited gene-expression patterns consistent with interferon-gamma signaling. The findings provide mechanistic insights into ICI-AIN and reinforce the feasibility of using urine samples for noninvasive diagnostic testing. This innovative approach paves the way for targeted therapies and improved diagnostic tools in immune-mediated kidney injuries.

Implications for clinical practice and research

Together, these studies highlight the growing complexity of nephrology in oncology. The potential of infliximab to manage steroid-dependent ICI-AIN, the promise of Mg and SGLT2is in mitigating chemotherapy-associated AKI, and the development of cutting-edge biomarkers all underscore the importance of nephrologists in cancer care. At the same time, the limitations of existing tools like ARSC emphasize the need for robust, externally validated strategies to guide clinical decision-making.

ASN Kidney Week has once again demonstrated the power of multidisciplinary collaboration in advancing patient care. The intersection of oncology and nephrology is a challenging yet promising field, in which innovative approaches are essential to address nephrotoxicity risks while preserving the efficacy of cancer therapies. As research continues to evolve, nephrologists are uniquely positioned to lead these efforts, improving the lives of patients navigating both cancer and kidney diseases. ■

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