Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care
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Long-term Kidney Outcomes After Immune Checkpoint Inhibitor Therapy Compared with Conventional Chemotherapy

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Objectives : Immune checkpoint inhibitors (ICIs) have become a standard therapy for various cancers. Although ICIs improve survival, they may cause immune-related adverse events, including acute kidney injury. However, their long-term renal outcomes compared with conventional chemotherapy remain unclear.
Methods : Data were obtained from the electronic health records of two tertiary referral centers (2015–2024). Among 19,668 patients initiating first-line systemic anticancer therapy, propensity score matching on 12 covariates was performed, yielding a matched cohort (N=2,172; 1,086 pairs).
Results : In the matched cohort, the mean age was 65.5 years, 70.8% were male, and the mean baseline eGFR was 93.3 mL/min/1.73 m²; The median follow-up was 11.1 months (IQR 4.7–21.0) in the ICI group and 10.4 months (IQR 4.7–22.2) in the non-ICI group. The ICI group experienced a significant early decline within the first 6 months (Δslope −0.352 mL/min/1.73 m²/month, p<0.001), followed by a significant attenuation in the rate of decline during months 6–12 (Δslope +0.227, p=0.002), after which no between-group difference remained (Δslope +0.028, p=0.22). The risk of ≥30% eGFR decline showed a statistically significant but modest association with ICI therapy (HR 1.16, 95% CI 1.02–1.31, p=0.019), which was attenuated after competing risk adjustment. In contrast, de novo overt proteinuria was consistently associated with ICI: stratified Cox HR 1.84 (95% CI 1.37–2.47, p<0.001). Subgroup analysis by ICI class revealed that anti-PD-1 therapy was associated with both eGFR decline and proteinuria, whereas anti-PD-L1 therapy showed no eGFR decline but a markedly elevated risk of proteinuria (HR 3.12, 95% CI 1.66–5.89, p<0.001). All-cause mortality was higher in the ICI group (HR 1.49, 95% CI 1.30–1.70, p<0.001).
Conclusions : ICI therapy was associated with an early decline in eGFR followed by partial recovery and an increased risk of proteinuria.

figure1_ICI.jpg

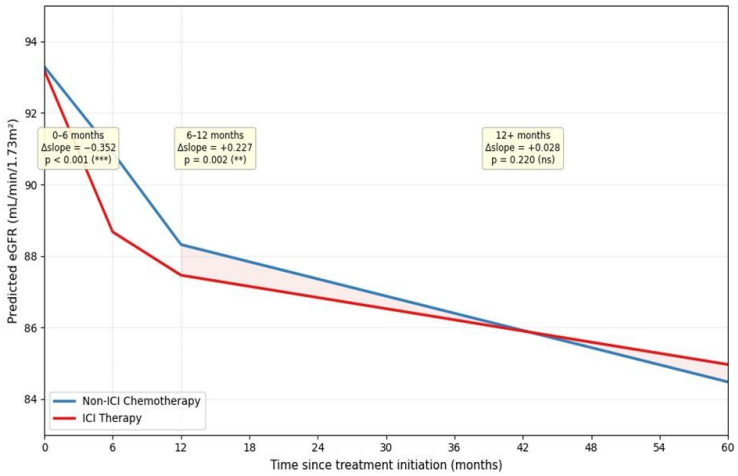

Figure 1. Predicted eGFR trajectories by treatment group using a piecewise linear mixed-effects model (knots at 6 and 12 months, follow-up ≤60 months; N=2,172). Δslope represents the difference in eGFR slope between the ICI and non-ICI groups within each time segment. The shaded area indicates the residual eGFR deficit between groups from 12 months onward.

figure1_ICI.jpg

Table 1. Association between ICI therapy and kidney outcomes across competing risk analytical frameworks

Endpoint	Stratified Cox	Fine-Gray SHR	IPCW
eGFR ≥30% decline	1.16 (1.02 - 1.31)*	1.09 (0.95 - 1.25)	1.11 (0.98 - 1.27)
eGFR ≥40% decline	1.14 (0.99 - 1.32)	1.14 (0.97 - 1.33)	1.11 (0.95 - 1.29)
Proteinuria ≥1+	1.41 (1.20 - 1.65)*	1.30 (1.11 - 1.52)*	1.23 (1.05 - 1.45)*
Proteinuria ≥2+	1.84 (1.37 - 2.47)*	1.53 (1.16 - 2.03)*	1.54 (1.12 - 2.12)*
All-cause mortality	1.49 (1.30 - 1.70)*	-	1.61 (1.37 - 1.89)*

Values are hazard ratios (95% confidence intervals). eGFR decline defined as single measurement below threshold; proteinuria defined as two consecutive dipstick results ≥1+ or ≥2+ among patients with negative or trace baseline.*p<0.05.