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Prediction of immune-related adverse events (irAEs) with hematologic markers in patients receiving first-line immune checkpoint inhibitor (ICI)-based therapy in metastatic renal cell carcinoma (mRCC)

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Background

First-line therapies with combinations of ICI-ICI and ICI-tyrosine kinase inhibitor (TKI) are commonplace in mRCC. Frequency of irAEs in patients receiving first-line ICI-based therapies is high, with grade ≥ 2 (G≥ 2) typically warranting active management. Although prognostication based on irAEs has been demonstrated, prediction of irAE occurrence in mRCC remains a challenge. We investigated the role of baseline hematologic markers to predict G≥ 2 irAE occurrence with first-line ICI-based therapies in mRCC.

Methods

We used the City of Hope database (encompassing 5 centers across 4 states) to retrospectively identify mRCC patients treated with first-line ICI-based therapies from September 2015 to September 2025. Baseline patient demographics, including age, gender, Karnofsky Performance Status (KPS), pre-existing autoimmune condition, IMDC risk group and first-line ICI-based regimen were collected. We stratified baseline hematologic markers, including neutrophil-to-lymphocyte ratio (NLR), neutrophil-to-eosinophil ratio (NER), platelet-to-lymphocyte ratio (PLR) and systemic inflammatory index (SII) into high and low levels using recursive partitioning, and evaluated their association with occurrence of first-line ICI-related G≥ 2 irAEs.

Results

A total of 198 patients with mRCC were treated with first-line ICI-based therapy, of which 5 were excluded due to insufficient data. Of the 193 evaluable patients, the median age was 64.2, 131 patients (67.9%) were male, 100 patients (51.8%) received ICI-ICI and 93 patients (48.2%) received ICI-TKI. G≥2 irAEs were observed in 55 patients (28.5%), requiring systemic steroid use in 32 patients (16.6%) and treatment discontinuation in 30 patients (15.5%). The most common G≥2 irAE was ALT/AST elevations, seen in 18 patients (9.3%). Of the baseline hematologic markers studied, increased PLR and SII were most strongly associated with occurrence of G≥2 irAEs ($P<0.005$ for each).

Conclusions

Our results point to a novel potential role of PLR and SII as predictive biomarkers of G≥2 irAEs, with ICI-based therapies in mRCC, meriting further validation in prospective studies.