

Prediction of irAEs with hematologic markers in patients receiving 1L ICI-based therapy in mRCC (IUC26666-91)



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Background

- ICI-based therapies are standard-of-care for first-line mRCC treatment¹⁻³
- Frequency of irAEs is high at 44% for any grade⁴
- G≥2 irAEs warrant active treatment
- Prediction of irAEs in mRCC remains a challenge

Methods

- Patients with mRCC treated with 1L ICI-ICI or ICI-TKI regimens between 2015 – 2025 were included from the City of Hope national database
- We collected data on baseline neutrophils, eosinophils, lymphocytes and platelets to calculate baseline NER, NLR, PLR and SII
- Patients were stratified into high and low groups for baseline hematologic ratios using recursive partitioning
- We applied logistic regression on baseline hematologic ratios and G≥2 irAEs

Results

	ICI-ICI (N = 100)		ICI-TKI (N = 93)	
	Grade 2	Grade 3-4	Grade 2	Grade 3-4
Any event	18 (18.0%)	20 (20.0%)	5 (5.4%)	14 (15.1%)
ALT/AST increased	5 (5.0%)	6 (6.0%)	1 (1.1%)	6 (6.5%)
Colitis and diarrhea	2 (2.0%)	2 (2.0%)	1 (1.1%)	1 (1.1%)
Arthralgia	2 (2.0%)	2 (2.0%)	1 (1.1%)	1 (1.1%)
Adrenal insufficiency	2 (2.0%)	2 (2.0%)	0 (0.0%)	2 (2.2%)
Pneumonitis	2 (2.0%)	0 (0.0%)	1 (1.1%)	2 (2.2%)

Table 1: Most common G≥2 irAEs

Baseline hematologic markers	Cut-off value	Multivariate analysis	
		OR (95% CI)	P value
NER	19	0.46 (0.21-0.99)	0.047
NLR	2.8	2.26 (1.09-4.65)	0.028
PLR	186	3.02 (1.40-6.53)	0.005
SII	892	2.67 (1.28-5.59)	0.009

Tables 2 & 3: Association of baseline hematologic ratios with G≥2 irAEs in overall cohort and by ICI backbone

Conclusions

- Frequency of G≥2 irAEs is higher in ICI-ICI treated patients
- Baseline hematologic ratios appear as predict biomarkers for G≥2 irAEs
- Potential selective roles of baseline hematologic ratios based on ICI backbone
- Early patient irAE risk stratification would personalize monitoring and intervention
- Prospective validation of these baseline hematologic ratios is merited

Baseline hematologic markers	ICI-ICI (N = 100)		ICI-TKI (N = 93)	
	OR (95% CI)	P value	OR (95% CI)	P value
NER	0.37 (0.13-1.04)	0.058	0.63 (0.16-2.43)	0.501
NLR	1.63 (0.58-4.55)	0.354	2.42 (0.81-7.25)	0.115
PLR	2.52 (0.90-7.09)	0.079	3.80 (1.10-13.11)	0.034
SII	3.30 (1.17-9.33)	0.024	1.50 (0.44-5.12)	0.518

References
1. Motzer, et al. N Engl J Med. 378:1277–1290 (2018). 2. Motzer, et al. N Engl J Med. 384:1289–1300 (2021). 3. Choueiri, et al. N Engl J Med. 384:829–841 (2021). 4. Zhang Y, et al. Cancer Treat Rev. 129:102787 (2024)
Abbreviations
NER, neutrophil-to-eosinophil ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune inflammation index