The Association between Early Changes in Neutrophil-Lymphocyte Ratio and Survival in Patients Treated with Immunotherapy

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INTRODUCTION

- Dynamic changes in the blood-based biomarkers could reflect the changes in the immune machinery in response to immune checkpoint inhibitors (ICIs) and could be used as a prognostic biomarker in patients treated with ICIs.
- However, the studies evaluating the prognostic role of baseline NLR and early NLR changes are limited in ICI-treated patients.
- Therefore, we evaluated the association between NLR and early NLR changes with survival in ICI-treated patients.
- Additionally, we created an NLR-based compound prognostic score (NLR2-CEL score) and tested the efficacy of this score in a cohort of two institutions.

METHODS

- Following variables were recorded: patient age, sex, Eastern Cooperative Oncology Group (ECOG) performance score, baseline height and weight, baseline and the fourth-week NLR, Charlson Comorbidity Index (CCI), immunotherapy line, metastatic sites at the start of ICIs, the best response to ICIs, and progression-free (PFS) and overall survival (OS).
- Univariate and multivariate survival analyses were conducted with Kaplan–Meier curves and Cox regression analyses. Hazard ratios with 95% confidence intervals (CIs) were reported.
- The predictive performance of the NLR-based composite score for OS was assessed as receiver operating characteristic (ROCs) curves.

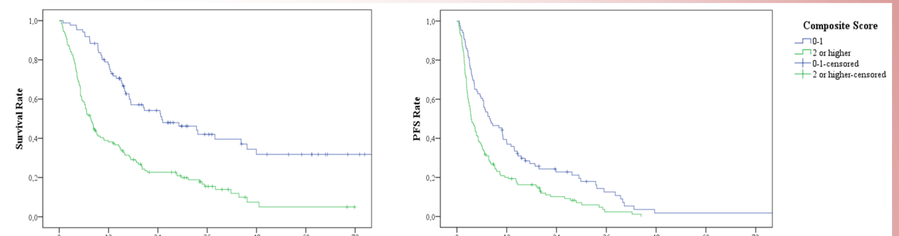
RESULTS

- A total of 231 patients were included and the median age was was 61 (IQR 51-67). The most common diagnoses were RCC and melanoma. In the fourth-week evaluation, 97 patients (42%) had a 10% or higher increase in NLR levels compared to baseline values.
- The median OS and PFS of the cohort were 13.5 (95% CI = 10.10–16.90) and 4.98 (95% CI = 3.57–6.02), respectively.
- In multivariate analyses, **a higher NLR at baseline** (HR = 1.743, p = 0.002), **10% or over NLR increase in the fourth week of treatment** (HR: 1.807, p = 0.001), **higher ECOG performance score** (HR: 1.552, p = 0.006), **higher LDH levels** (HR: 1.454, p = 0.017), and **higher CCI** (HR: 1.400, p = 0.041) were associated with decreased OS.
- In the prognostic model created by these parameters, compared to patients with the lowest scores, patients in the highest score group had significantly lower OS (HR = 7.967, 95% CI = 3.531–17.979, p < 0.001) and PFS (HR = 2.971, 95% CI = 1.570–5.620, p = 0.001).
- The composite score had moderate success for OS prediction with AUC of 0.702 (95% CI = 0.626–0.779, p < 0.001).

CONCLUSION

- We observed significantly lower in patients with higher baseline NLR levels and increased NLR values under treatment. Additionally, our proposed model, including these parameters, had a moderate predictive power for OS.

Figure-1. Kaplan–Meier analyses of overall survival and progression-free survival according to NLR-based compound prognostic score.



0	12	24	36	48	60	72
86	65	35	19	12	9	3
145	52	27	12	3	2	0

0	12	24	36	48	60	72
86	32	15	7	1	1	1
145	27	11	2	0	0	0

Figure-2. ROC analyses of the NLR-based composite score for survival prediction.

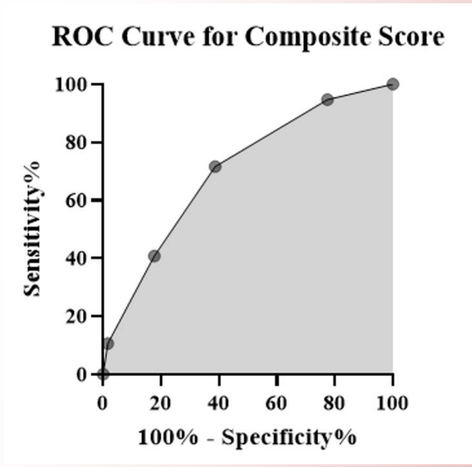


Table-1. The association between clinical factors with OS and PFS in multivariate analyses.

	Progression-Free Survival			Overall Survival		
	Hazard Ratio	95% CI*	P Value	Hazard Ratio	95% CI*	P Value
CCI (<9 vs. ≥9)	1.193	0.890-1.600	0.238	1.400	1.014-1.932	0.041
Baseline NLR (<5 vs. ≥5)	1.354	0.997-1.839	0.053	1.743	1.227-2.476	0.002
Fourth-week NLR increase (<10% vs. ≥10%)	1.544	1.152-2.068	0.004	1.807	1.294-2.524	0.001
ECOG (0 vs. ≥1)	1.401	1.061-1.848	0.017	1.552	1.134-2.123	0.006
LDH (N vs. ≥ULN)	1.219	0.926-1.605	0.158	1.454	1.069-1.976	0.017

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Conflicts of Interest: None to declare. **E-mail:** denizcguven@hotmail.com