Baseline higher neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios are associated with less durable radiographic response to immune checkpoint inhibitors in non-small cell lung cancer.

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Background

- Immune checkpoint inhibitors (ICI) are the standard of care in the treatment of non-small cell lung cancer (NSCLC). There are no reliable predictive markers that determines the response and its durability.
- Recruitment of the inflammatory cells in the tumor microenvironment (TME) can determine the response to ICIs and an increased inflammatory state can be a poor prognostic factor[1].
- Peripheral inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can reflect the inflammatory changes within the TME[2].
- We aim to study the effect of high NLR and PLR on the radiographic response and its durability in NSCLC patients treated with ICIs.

Methods

- We conducted a retrospective analysis on 178 NSCLC patients treated with ICIs either alone or in combination with chemotherapy.
- Radiographic response, and the duration of radiographic response (date of best response to radiographic progression), NLR, and PLR were calculated at baseline and 8 weeks since the start of ICI.

$$NLR = \frac{Neutrophil\ count}{Lymphocyte\ count} \qquad PLR = \frac{Platelet\ count}{Lymphocyte\ count}$$

- High NLR and PLR was defined as greater than the median NLR and PLR values.

Results

- The objective response rate was 45.1%. The disease control rate was 75.8%.
- The baseline odds ratio (OR) of response in the high NLR and high PLR group was 0.73 (P = 0.5, 95% CI 0.36–1.64) and 0.63 (P = 0.2, 95% CI 0.32–1.23), respectively.
- The odds to respond to ICI decreased significantly in patients with high NLR (OR = 0.16, P = 0.0001, 95% CI 0.06–0.43) and high PLR (OR = 0.27, P = 0.005, 95% CI 0.1–0.6) at 8 weeks.

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Results-continued

Features	Low NLR N= 76 (44.2%)	High NLR N= 96 (55.1%)	P-value	Low PLR N=91 (54.5%)	High PLR N=76 (45.5%)	P-Value
Male	30(39.5%)	46(60.5%)		30(40.5%)	44(59.5%)	
Female	46(47.9%)	50(52.1%)	P=0.2	46(49.5%)	47(50.5%)	P=0.2
Median Age at Diagnosis (years)	67.5	67.5		66.5	69	
ICIs						
Ipilimumab/Nivolumab	0 (0%)	1 (100%)	P=0.3	0(0%)	1(100%)	P=0.3
Pembrolizumab, Nivolumab	67(73.1%)	88(56.8%)	P=0.4	68(45.3%)	82(54.6%)	P=0.8
Atezolizumab	8 (53.3%)	7 (46.7%)	P=0.4	7 (46.7%)	8(53.3%)	P=0.9
ICI as Second Line	28(43.1%)	37(56.9%)	P=0.7	27(42.2%)	37(57.8%)	P=0.9
Radiation Therapy	27(31.0%)	60(69%)	P=0.001	31 (36%)	55(64%)	P=0.01
Metastatic Sites						
Skeletal	23(40.4%)	34(59.6%)	P=0.4	17(30.9%)	38(69.1%)	P=0.008
Hepatic	15(48.4%)	16(51.6%)	P=0.8	14(43.7)	18(56.3)	P=0.4
Brain	28(53.8%)	24(46.2%)	P=0.09	23(46%)	27(54%)	P=0.9
Adrenal Gland	9 (31%)	20(69%)	P=0.1	11(37.9%)	18(62.1%)	P=0.3
Any Immune Related Adverse Events	18(46.2%)	21(53.8%)	P=0.7	16(43.2%)	21(56.8%)	P=0.6
ECOG-PS						
0	15(20.8%)	14(14.9%)		15(20.3%)	14(15.6%)	
1	48(66.7%)	55(58.5%)	P=0.09	52(70.3%)	50(55.6%)	P=0.03
2	8 (11.1%)	23(24.5%)		7(9.5%)	23(25.6%)	
3	0 (0%)	2 (2.1%)		0(0)	2(2.2%)	
Progressed	48(37.8%)	79(62.2%)	P=0.002	52(41.3%)	74(58.7%)	P=0.05
Dead	36(35.3%)	66(64.7%)	P=0.005	36(35.6%)	65(64.4%)	P=0.001

***Table 1**: Patient demographics.*

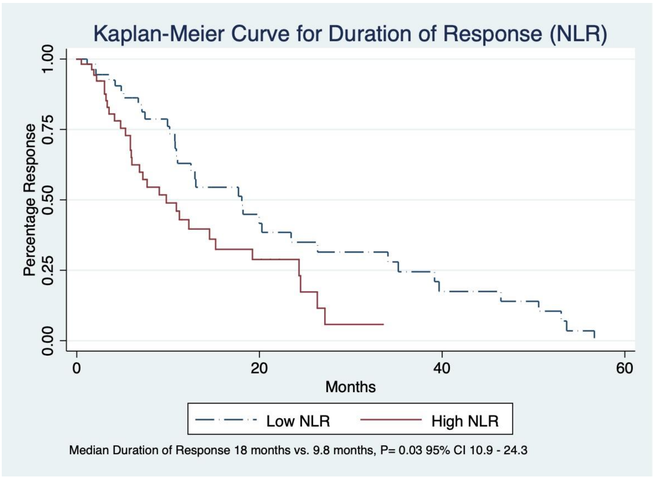

***Figure 1**: Duration of response associated with NLR. Median duration of response 18 months vs 9.8 months. P=0.03*

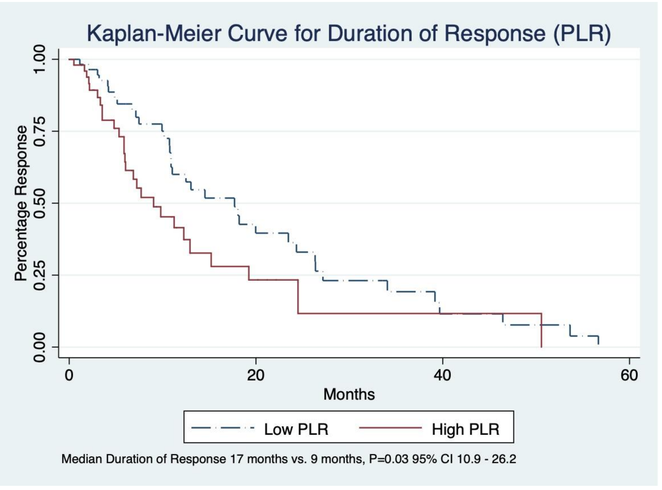

***Figure 2**: Duration of response associated with PLR. Median duration of response 17 months vs 9 months. P=0.03*

Conclusions

- NLR and PLR may be reliable surrogate markers determining the durability of response to ICIs in NSCLC patients.
- Standard imaging studies and serial monitoring of these indices may help to track the response to ICIs.
- Prospective studies are needed to develop predictive and prognostic models utilizing these indices.

References

1. Wu P, Wu D, Zhao L, Huang L, Chen G, Shen G, Huang J, Chai Y. Inverse role of distinct subsets and distribution of macrophage in lung cancer prognosis: a meta-analysis. Oncotarget. 2016 Jun 28;7(26):40451-40460.
2. Katayama Y, Yamada T, Chihara Y, Tanaka S, Tanimura K, Okura N, et al. Significance of inflammatory indexes in atezolizumab monotherapy outcomes in previously treated non-small-cell lung cancer patients. Sci Rep. 2020 Dec;10(1):17495.