Baseline Systemic Inflammatory Immune Index May Predict Overall Survival and Progression-Free Survival in Patients with Non-Small Cell Lung Cancer Patients on Immune Checkpoint Inhibitors.

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Background

- Increased systemic inflammatory state and increased inflammation within tumor micro-environment (TME) have been associated with a worse prognosis and lower responsiveness to immune checkpoint inhibitors (ICI).
- Systemic inflammatory immune index (SII) reflects the changes in the systemic inflammatory matrix.
- Studies have shown the association of SII with cancer survival and treatment outcomes.
- We aim to study the effect of SII on treatment outcomes in non-small cell lung cancer (NSCLC) patients being treated with ICI.

Methods

- We conducted a retrospective analysis on 178 NSCLC patients treated with ICIs (pembrolizumab, nivolumab, ipilimumab/nivolumab or atezolizumab) alone or in combination with chemotherapy.
- SII is defined as:

$$SII = \frac{(platelets)\,(neutrophils)}{lymphocytes}$$

- Baseline and 8-week SIIs were obtained.
- Radiographic response, duration of radiographic response (date of best response to radiographic progression), overall survival (OS), and progression-free survival (PFS) were evaluated.
- A high SII was defined as a value greater than the median SII.
- Cox regression univariate and multivariate analyses were performed. Logistic regression, t-test, and Chi-square tests were applied.

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Results

Features	Low SII at baseline N= 62 (26.9%)	High SII at baseline N= 106 (63.1%)	P-value
Sex			
Male	27 (43.5%)	48 (45.3%)	P=0.8
Female	35 (56.5%)	58 (54.7%)	
Median Age at Diagnosis (years)	74	68	
Immune Checkpoint Inhibitors			
Ipilimumab/Nivolumab	0 (0%)	1 (100%)	P=0.4
Pembrolizumab, Nivolumab	53 (35.1%)	98 (64.9%)	P=0.1
Atezolizumab	9 (6%)	6 (40%)	P=0.0.05
ICI as Second Line Therapy	25 (39.1%)	39 (60.9%)	P=0.6
Radiation Therapy	23 (26.7%)	63 (73.3%)	P=0.005
Metastatic Sites			
Skeletal	16 (29.1%)	39 (70.9%)	P=0.1
Hepatic	11 (34.4%)	21 (65.6%)	P=0.7
Brain	21 (41.2%)	30 (58.8%)	P=0.4
Adrenal Gland	7 (24.1%)	22 (75.9%)	P=0.1
Any Immune Related Adverse Events	17 (44.7%)	$SII = \frac{(platelets)(neutrophils)}{lymphocytes}$	
ECOG-PS			
0	13 (21.7%)	16 (15.4%)	
1	40 (66.7%)	62 (59.6%)	P=0.2
2	7 (11.7%)	23 22.1%)	
3	0 (0%)	2 (1.9%)	
Progressed	41 (32.5%)	85 (67.5%)	P=0.02
Dead	29 (28.7%)	72 (71.3%)	P=0.004

Table 1: Demographics of the study

Progression-free Survival

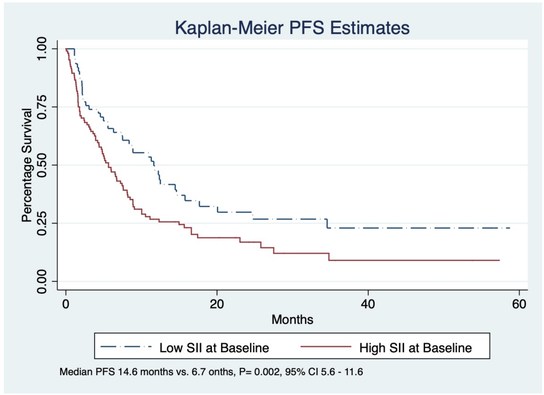

Figure 1: PFS associated with baseline SII

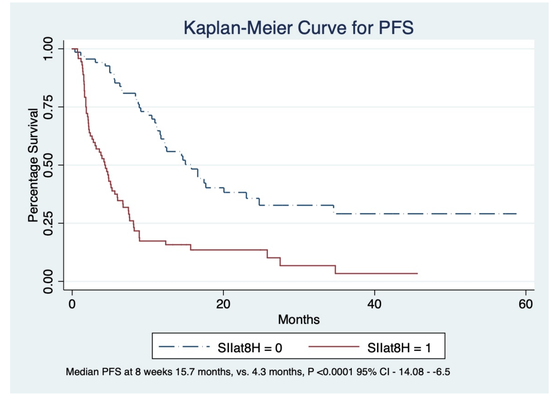

Figure 2: PFS associated with SII at 8 weeks

Overall Survival

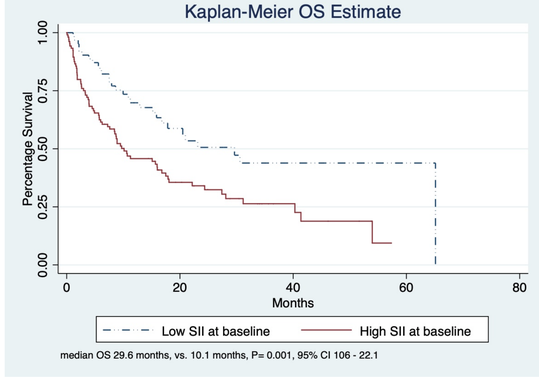

Figure 3: OS associated with baseline SII

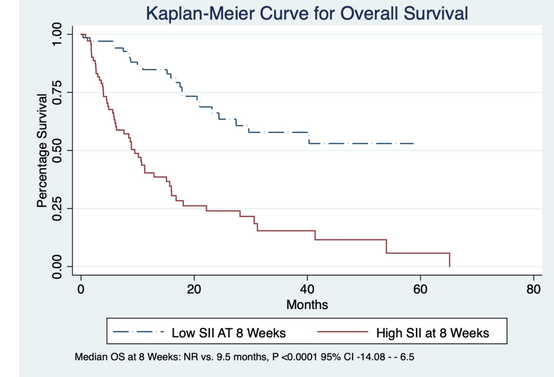

Figure 4: OS associated with SII at 8 weeks

- The objective response rate (ORR) was 45.1%. The disease control rate was 75.8%. The ORR was 51% in patients receiving ICI first-line compared to 35% in those who received ICI as a second-line therapy.
- At baseline, there was no difference in the mean SII between responders and non-responders (2146.2 vs. 1917.5, P= 0.5); however, at 8 weeks, the mean SII was significantly lower in responders compared to non-responders (1198.8 vs. 2880.2, P= 0.02).
- A total of 15 (10.9%) patients were found to have pseudoprogression or mixed response on follow-up imaging. Among these, 11(73.3%) patients had low SII at 8 weeks (P=0.04).

Conclusion

- SII may have significant impact on PFS and OS and could be serially monitored to assess the response to ICI.
- A low SII at 8 weeks exhibited improved survival, suggesting serial SII monitoring could provide meaningful clinical value.
- A low SII may help to differentiate pseudoprogression vs. true progression. Prospective studies are needed to validate these findings.
- It will be interesting to see if SII could be incorporated into predictive models to determine the duration of cytotoxic therapy in selected patients.