A Comparative Analysis of TAR and NLR in Patients with triple negative breast cancer treated with as KEYNOTE-522 trial : Distinct Predictors of Pathologic Response and Survival

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Background

- Pathologic complete response (pCR) :
a surrogate marker for relevant outcomes in breast cancer patients undergoing neoadjuvant treatment.

- Some patients achieving pCR still experience recurrence, suggesting that pCR and survival outcomes such as event-free survival (EFS) may represent distinct biological endpoints from different processes.

- This study investigated whether the tumor-aorta ratio based on Hounsfield units (TAR) and the neutrophil-to-lymphocyte ratio (NLR) function as distinct predictive biomarkers for pCR and EFS in TNBC patients treated with the KEYNOTE-522 regimen.

Materials and Methods

- Patients with TNBC who received neoadjuvant systemic therapy according to the KEYNOTE-522 regimen were included.

Results_01

- Initial TAR was significantly associated with pCR (p = 0.022), supporting its role as a predictive biomarker for immediate tumor response. In contrast, EFS was more strongly associated with post-treatment NLR, a systemic immune marker ($p < 0.001$).

Table 1. Analysis of TAR and NLR based on pCR and events.

	pCR (n=82)	non-pCR (=58)	P value	Event-free (n=130)	Event (n=10)	p value
initial TAR	**0.55±0.14**	**0.62±0.19**	**0.02**	0.58±0.16	0.55±0.15	0.56
TAR at competion noeadjuvant TX	**0.29±0.15**	**0.41±0.29**	**0.02**	0.36±0.25	0.30±0.16	0.53
delta TAR	-0.28±0.20	-0.21±0.29	0.18	-0.25±0.26	-0.20±0.18	0.59
initial NLR	2.10±0.87	1.92±0.87	0.25	2.00±0.85	2.26±1.05	0.35
NLR at completion neoadjuvatn TX	2.71±3.37	2.04±1.71	0.16	2.50±2.88	1.22±0.46	0.16
delta NLR	0.61±3.59	0.11±2.16	*0.783	**0.50±3.13**	**-1.05±1.32**	***0.047**

Results_02

- Changes in Tumor-to-Aorta Ratio (TAR) and Neutrophil-to-Lymphocyte Ratio (NLR) measured before and after neoadjuvant treatment in breast cancer patients, grouped by pathologic complete response (pCR) status. Both TAR and NLR show changes in the same direction (decrease or increase) regardless of achieving pCR (Figure1).
- Changes in TAR and NLR before and after treatment, grouped by the presence or absence of subsequent clinical events (event-free survival). While TAR consistently decreases after treatment in both groups, NLR decreases only in patients with subsequent events but increases in event-free patients, indicating an opposite pattern of change between the two biomarkers with respect to event outcomes (Figure 2).

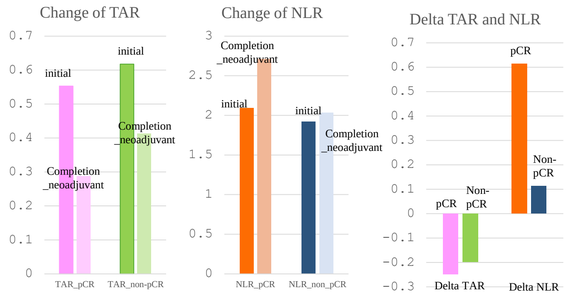


Figure 1. Change or TAR (A), NLR (B), and delta TAR and NLR based on pCR status

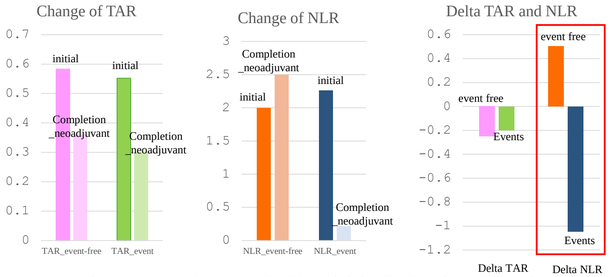


Figure 2. Changes in TAR (A), NLR (B), and delta TAR and NLR based on Event-Free Survival

Discussion

In this uniform cohort of TNBC patients treated with an identical neoadjuvant regimen, an increase in NLR —driven primarily by increased neutrophil counts — was associated with better prognosis. While it contradicts traditional interpretations of high NLR as a negative prognostic marker, this finding may represent context-specific immune shift, where pembrolizumab might reprogram neutrophils (possibly into N1 anti-tumor phenotypes) and/or reflect a robust systemic immune activation post-therapy, rather than suppression. Further retro-translational research regarding functional reprogramming of neutrophils by pembrolizumab is warranted.

Conclusion

Changes TAR and NLR parallel each other after therapy regardless of pCR status. However, when stratified by EFS, TAR consistently decreases while NLR trends diverge, increasing in event-free cases but decreasing in those with adverse events. These findings suggest that pCR and event occurrence may be regulated by distinct biological mechanisms. Different biomarkers may thus be needed to predict pCR and adverse events in breast cancer patients, optimizing clinical decision-making.

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