482 DECIPHERING THE HETEROGENEITY OF B-CELL CHECKPOINT INHIBITORS WITHIN TERTIARY LYMPHOID STRUCTURES: IMPLICATIONS FOR LUNG CANCER IMMUNOTHERAPY

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Background Tertiary lymphoid structures (TLS) are ectopic lymphoid formations and sites of local immune response, where B-cells, among other immune cells, play critical roles.[1] [2] In the tumor microenvironment TLS play pivotal roles in the orchestration of immune responses in lung cancer. However, the spatial distribution of B-cell checkpoint inhibitors within these structures remains poorly understood.[3] Understanding these interactions could lead to more effective use of checkpoint inhibitors and the development of novel therapeutic strategies for lung cancer, thereby improving clinical outcomes.[4–6] This study aims to elucidate this complex spatial interface and its implications for therapy response.

Methods Retrospectively collected surgically resected NSCLC tumors treated with checkpoint inhibitors therapy were used. Using multiplexed immunohistochemistry and comprehensive spatial analytics, we analyzed the distribution, density, and interaction of B-cell checkpoint inhibitors, including PD-1 and CTLA-4, within the TLS. This technique allowed for an in-depth analysis of the protein expression patterns and spatial relationships at the single-cell level, providing an opportunity to explore correlations between spatial distribution of B-cell checkpoint inhibitors and therapy response.

Results Preliminary findings showed a distinct heterogeneity in the spatial localization of these inhibitory markers, suggestive of a complex interplay between the B-cell subsets, checkpoint expression, and tumor characteristics. Additionally, we identified distinct spatial signatures correlating with patients' responses to checkpoint blockade therapies. Our results suggested that the spatial distribution of B-cell checkpoint inhibitors within TLS may serve as a novel biomarker for predicting immunotherapy responses in lung cancer patients.

Conclusions Our data enriches the understanding of the tumor-immune interface in lung cancer, and we propose novel strategies for tailoring immunotherapies based on the spatial distribution of B-cell checkpoint inhibitors within TLS. We anticipate this research to stimulate further discussion on optimizing lung cancer treatment strategies and identifying patients who are most likely to benefit from B-cell checkpoint blockade therapies.

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http://dx.doi.org/10.1136/jitc-2023-SITC2023.0482