Tertiary lymphoid structure predicts major pathological response in resectable non-small cell lung cancer patients with neoadjuvant chemotherapy

Wenhua Cai¹, Miao Jing¹, Jiaxin Wen¹, Yajun Gu², Xiaochen Zhao², Zhiqiang Xue¹,²
¹Department of Thoracic Surgery, The First Medical Center of Chinese PLA General Hospital, Beijing, P.R. China. ²The Medical Department, 3D Medicines Inc., Shanghai, P.R. China.
#Corresponding to Zhiqiang Xue (xuezhiqiang301@126.com)

BACKGROUND

The induction of tertiary lymphoid structure (TLS) in solid tumors has been associated with a favorable prognosis. However, the role of TLS in pathological response remains to be further elucidated, especially in patients with resectable non-small cell lung cancer (NSCLC) receiving neoadjuvant chemotherapy.

METHODS

NSCLC patients with neoadjuvant chemotherapy, resectable stage I–III, age ≥18 years, ECOG performance status 0–1 were recruited in the study. Hematoxylin and eosin (H&E) staining of surgical resection was applied for assessing histopathologic responses. The definition of MPR involved showing no more than 10% residual viable tumor cells, while a pCR referred to no residual tumor cells. Fluorescent multiplex immunohistochemistry (mIHC), which allows the simultaneous detection of multiple markers on a single tissue section was performed by the automated quantitative pathology imaging system. The TLS consists of T cell (CD3⁺) and B cell (CD20⁺) rich regions.

RESULTS

Thirty-one patients were enrolled and received neoadjuvant chemotherapy, including pCR (n=4) and MPR (n=12). The TLS was significantly higher in patients with MPR than non-MPR (counts per mm²: p=0.0063; μm² per mm²: p=0.0044). The area under the curve (AUC) of TLS to predict MPR was 0.7873 (counts per mm²) and 0.7982 (μm² per mm²), respectively. The optimal cutoff value for TLS were found to be 0.5550 and 32114 at the unit of counts per mm² and μm² per mm², respectively. The sensitivity and specificity could reach up to 83% for predicting MPR in patients with NSCLC.

CONCLUSIONS

Higher TLS value indicates better efficacy of neoadjuvant chemotherapy in resectable patients with NSCLC.