Therapy of lung cancer in China: introducing the special collection

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Lung cancer remains the leading cause of cancer incidence and mortality.[1] Non-small-cell lung cancer (NSCLC) and small cell lung cancer (SCLC), the two most frequent histologic subtypes, account for approximately 85% and 13–17% of lung cancer cases in China. The treatment landscape of NSCLC and SCLC has advanced rapidly in the past decade. The prognosis of lung cancer patients differs in different clinical scenarios. These papers published as part of this Research Topic provide a snapshot of the current treatment paradigm and the clinical research efforts for our patients with lung cancer in China.

Anti-programmed cell death-1 (PD-1)/anti-programmed cell death ligand-1 (PD-L1) protein expression in tumor samples, as measured by immunohistochemistry analysis, has emerged as the main predictive biomarker for response to immunotherapy.[2] The relationship between major driver mutations and PD-L1 expression remains controversial. Li *et al.*[3] explored the association between PD-L1 expression and the mutation status of nine major cancer-related genes using Ventana SP142 antibody in a large cohort of Chinese NSCLC patients. They found that expression of PD-L1 was found to be more common in patients harboring no driver mutations. PD-L1 expression in tumor cells was less frequent in patients harboring EGFR and HER2 mutations. Conversely, PD-L1 expression was high in the presence of KRAS, BRAF, PICK3A, and MET mutations and ROS1/RET translocations.

Carboxyamidotriazole (CAI) is known to inhibit angiogenesis and aberrant tumor cell growth by suppressing inositol triphosphate synthesis, nitric oxide formation, and Ca2+-dependent VEGF-A production.[4] Si *et al.*[5] conducted a multicenter, double-blind, randomized phase III trial demonstrating that adding CAI to platinum-based chemotherapy could prolong progression-free survival [median, 134 days *versus* 98 days with a hazard ratio (HR) of 0.6900, $p = 0.0030$] comparing with chemotherapy alone in the Chinese patients with NSCLC with manageable adverse effects.

Neo-angiogenesis promotes cancer cells' growth and metastasis, which depends on the activation of vascular endothelial growth factor (VEGF) signaling pathway.[6] Apatinib is a latest oral small-molecule angiogenesis inhibitor that selectively targets VEGFR2.[7] Liang *et al.*[8] performed a retrospective analysis of 70 patients with advanced NSCLC to evaluate the clinical efficacy of apatinib treatment after second-line or later treatment and found that median overall survival (OS) in the apatinib group was significantly longer than that in the control group (9.6 *versus* 3.8 months; $p < 0.0001$). There were no differences in adverse reactions between the patients of treatment and control groups.

Nomograms have been accepted as reliable tools to quantify risk by incorporating and illustrating important factors for oncologic prognoses, thus helping to select patients who may benefit from the considered treatment.[9] A prognostic nomogram and heat map for patients with stage I NSCLC after complete resection established by Cao *et al.*[10] showed that sex (adjusted HR = 0.5570, $p < 0.0010$), age (adjusted HR = 1.853, $p < 0.0010$), tumor size (adjusted HR = 1.3910, $p < 0.0010$), and pleural invasion (adjusted HR = 1.4660, $p = 0.0100$) were significantly associated with prognosis, which was in accordance with the results previous published by Liang *et al.*[11]

Specific immune markers (CD3, CD8, and CD45RO) of tumor infiltrating lymphocytes

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(TILs) were regarded as significant prognostic immune components.[12] Feng *et al.*[13] assessed the immune score of 288 patients with pathologically confirmed stage IIIA (N2) NSCLC who underwent complete resection, based on TIL type, density, and distribution within tumor center (CT) and invasive margin (IM).[13] The results of analysis demonstrated that the density of CD45RO+ TILs in the IM was a significant prognostic factor for clinical outcome [distant metastasis-free survival (DMFS) and OS], a high density of CD8+ TILs in the CT was associated with prolonged survival but did not reach statistical significance and the density of CD3+ TILs was associated with neither DMFS nor OS.

Immune checkpoint inhibitors (ICIs) in lung cancer have become the latest and novel treatment modalities in the decade following the introduction of the targeted therapy. Patents in China have benefited a lot from immunotherapy recently. The review in this issue,[14] 'Research progress of immune checkpoint inhibitors for lung cancer in China', summarizes current research and ongoing trials of various ICIs for relevant indications in China.

We would like to thank all the authors for their contributions to this special issue and are confident it will help improve the Chinese clinicians' decisions in lung cancer. We believe that with the gradual deepening of research, treatment and decisions for lung cancer will surely develop rapidly along a positive path.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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