Editorial

Emerging new evidence for the treatment of pulmonary sarcomatoid carcinoma

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Lung cancer is a leading cause of cancer-related mortality, accounting for 1.8 million people worldwide in 2020 (1). Pulmonary sarcomatoid carcinoma (PSC) is a rare type of non-small cell lung cancer (NSCLC), characterized by poorly differentiated carcinoma with components of sarcoma or sarcoma-like differentiation. The most recent classification of PSC includes pleomorphic carcinoma, giant cell carcinoma, spindle cell carcinoma, pulmonary blastoma, and carcinosarcoma (2). Owing to the rapid advancement in cancer treatment and elucidation of disease mechanisms, the outcomes of lung cancer have drastically improved over the last decade. However, the prognosis of PSC is still poor compared to other forms of NSCLC (3,4). There is limited data regarding the standard treatment strategy, clinical characteristics, and prognostic factors due to the rarity of the disease. Therefore, this necessitates the accumulation of evidence for PSC.

In a recent study, Zhao *et al.* reported the long-term follow-up data of 119 patients with PSC in a single cancer center in China (5). The authors described the data regarding the main features of patients with PSC and disease prognosis, including median survival and 1-, 3-, and 5-year overall survival based on patient characteristics. In addition, they elucidated that the TNM stage, especially T staging and M staging, was associated with the prognosis of PSC. These data were consistent with previous studies (4,6,7).

Interestingly, more than 90% of patients underwent surgery in this study, and this proportion was substantially greater, despite the small number of stage IV patients. Since surgical resection is the only known curative treatment for PSC, the relatively good overall survival in this study may be partly attributed to a proactive surgical treatment strategy (6). As emphasized by the authors, complete resection of a tumor should be targeted based on the patient's condition. However, mixed results exist on the effectiveness of chemotherapy in combination with surgery, and this study did not provide a definite conclusion regarding this point (4,6,8). Since a majority of the patients received adjuvant or neoadjuvant chemotherapy in current and previous studies, future studies focusing on the combination of chemotherapy and surgery are warranted (5,6).

To date, there is no standard treatment regimen for management of advanced-stage PSC. A previous study on a French cohort showed that platinum-based chemotherapy modestly improved the outcomes of patients with PSC (9). However, patients with PSC tend to develop chemotherapy resistance at an early stage, thereby resulting in less efficacy. Therefore, similar to other NSCLCs, other treatment strategies, such as molecular-targeted drugs and immune checkpoint inhibitors, may play an important role in the treatment of advanced-stage PSC. The current study showed that 8/18 (44%) patients with PSC were positive for mutations in genes such as *KRAS*, *EGFR*, and *ALK*. In addition, some PSC patients harbored the *MET* mutation, and *MET* and *KRAS* mutations were associated with poor prognosis (10,11). Although the effectiveness of molecular-

targeted drugs for PSC has not been elucidated, a previous report showed that MET-TKI was effective in patients with *MET* exon 14 mutations (12). Patients with other driver gene mutations may also benefit from molecular-targeted treatment. Therefore, whole genome sequencing analysis might help in selection of an appropriate treatment regimen and improvement in the outcomes of PSC.

Similarly, since programmed death ligand-1 (PD-L1) expression tends to be high in PSC, patients with PSC may benefit from immunotherapy (13,14). A recent study confirmed that the patients treated with immune-checkpoint inhibitors as second-line treatment achieved a 40% response rate, which is significantly higher than conventional chemotherapy (15). Additionally, the combination of chemotherapy and immune checkpoint inhibitors was reported to be effective on a case-report basis (16,17).

In conclusion, multimodality treatment, including surgery, cytotoxic chemotherapy, tyrosine kinase inhibitors, and immune checkpoint inhibitors, is essential for effective management of PSC owing to its poor prognostic nature. The current study provided new insights into PSC; however, further prospective studies with a larger sample size are needed to fully elucidate the characteristics of PSC and the efficacy of emerging treatments such as molecular-targeted agents and immune checkpoint inhibitors.

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