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High Risk of Acute Exacerbation of Interstitial Lung Disease In Relapsed Small Cell Lung Cancer Treated With Amrubicin

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Abstract:

Background: The safety and efficacy of chemotherapy for relapsed small cell lung cancer (SCLC) with interstitial lung disease (ILD) is uncertain. ILD is a risk factor for acute exacerbation (AE)-ILD.

Keywords: Small cell lung cancer; Interstitial lung disease; Acute exacerbation; Amrubicin

Introduction:

Lung cancer is the leading cause of death from cancer worldwide. Small cell lung cancer (SCLC) accounts for 15% to 20% of lung cancer. SCLC is characterized by a high rate of invasion and rapid cell proliferation. The SCLC also shows a high sensitivity to chemotherapy and radiotherapy; however, the duration of the response is relatively short. The standard chemotherapy regimen for SCLC patients is a combination of platinum and etoposide agents or platinum agents plus irinotecan, which is the most frequently used combination and gives a median survival period of approximately 9 to 12 months in clinical trials.

Interstitial lung disease (ILD) is characterized by damage to the lung parenchyma through inflammation and fibrosis. Preexisting ILD is a risk factor for acute exacerbation (AE) for chemotherapy-related ILD (AE-ILD). AE-ILD can cause death. Chemotherapy is possible for patients with SCLC with ILD remains unclear, since patients with ILD have been excluded from most prospective clinical trials. In clinical practice, patients with SCLC with ILD have been carefully treated with cytotoxic chemotherapy.

Patients with advanced SCLC with ILD treated with etoposide and chemotherapy combined with platinum agents have advantages, with safety equivalent to that observed in patients without ILD. For second-line chemotherapy, nogitecan (NGT) or paclitaxel (PTX) is effective in treating patients with relapsed SCLC. However, the safety and effectiveness of chemotherapy for patients with relapsed SCLC with ILD have not been clarified, while a previous study found that results from computed tomography (CT) were associated with AE -HE D.

We conducted a retrospective study to assess the safety and efficacy of chemotherapy for the treatment of patients with SCLC relapsing with ILD. In addition, we retrospectively analyzed CT before treatment and studied the clinical course of patients with SCLC relapsing with ILD.

METHODS:

The medical records of patients with SCLC with ILD treated with cytotoxic chemotherapy at Nagoya Medical Center between January 2009 and December 2017 were retrospectively reviewed. The primary endpoint of this study was to evaluate the incidence of AE-ILD for relapsed SCLC with ILD with each agent. Secondary endpoint was to evaluate the overall survival (OS) of the patients with SCLC with ILD who received second-line chemotherapy; in short, to find an optimal drug and whether the patients obtained survival benefit.

The clinical characteristics, treatment outcomes and survival of these patients were analyzed using data obtained from their medical records. ILD was diagnosed from the patients' medical histories, physical examinations and radiological abnormalities that were consistent with

the characteristics of bilateral lung fibrosis, such as ground-glass opacity and consolidation, with or without reticular shadow. In patients with ILD, usual interstitial pneumonia (UIP) and other types of pneumonia were diagnosed based on CT features defined by the International Consensus Statement of the European Respiratory Society. We excluded patients with apparent pulmonary infection, pulmonary embolism, or heart failure.

Results:

A total of 266 consecutive patients were diagnosed with SCLC at our institution. Twenty-one of these patients had ILD and 16 received second-line chemotherapy.

Of the 16 patients with SCLC with ILD, six (38%) developed AE- ILD. Table 2 summarizes the treatment outcomes of chemotherapy for relapsed SCLC with ILD. Eleven patients received amrubicin (AMR), six received paclitaxel (PTX), two received nanoparticle albumin-bound PTX (nab-PTX), three received Topotecan (TOP), and two received platinum agents plus ETP (re-challenge). AE-ILD was observed in 46% (5/11) and 33% (1/3) of patients treated with AMR and TOP, respectively. The patients with AE-ILD are summarized in Table 2. Two of six patients had UIP patterns (33%). Treatment for AE-ILD was administered to one patient. The other patients improved with corticosteroid therapy. The median OS from the day second- line chemotherapy started was 131 days [95% confidence interval (CI): 67–195 days] and 165 days [95% CI: 63–267 days] for patients with and without AE-ILD, respectively (Figure 1). No statistically significant difference in OS was observed between the AE-ILD and non-AE-ILD groups (p=0.324). Moreover, one patient was excluded from the Kaplan-Meier curve because AE-ILD developed after third- line chemotherapy (Table 3, patient 3). The disease control rates of each chemotherapeutic regimen were 27%, 17%, 50%, 33% and 100%, respectively.

Conclusion:

Relapsed SCLC patients with ILD with AMR had a higher risk of developing AE-ILD even for patients with a non-UIP pattern. Chemotherapy containing PTX or nab-PTX for relapsed SCLC patients with ILD may be safe for relapsed SCLC with ILD.

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