Nintedanib Effect in Osimertinib-Induced Interstitial Pneumonia

To the Editor:

Osimertinib is an oral, potent, irreversible third-generation EGFR tyrosine kinase inhibitor (TKI) approved for the treatment of EGFR-positive NSCLC patients. Although osimertinib has shown significant efficacy in EGFR-mutant patients with NSCLC, severe adverse events such as interstitial lung disease (ILD) have been reported in a few patients and even case deaths.1,2 Currently, the underlying pathogenesis of EGFR TKI-induced ILD remains unclear. Common treatments encompass targeted therapy discontinuation and hormone therapy. However, there are limited therapies for patients unsuitable for hormone therapy. Herein, we report the first successful treatment of nintedanib in an EGFR L858R-mutant NSCLC patient who was diagnosed as osimertinib-induced interstitial pneumonia.

An 84-year-old Chinese female ex-smoker presented with a pulmonary mass in the left lobe discovered on computed tomography (CT) scan. Biopsy on pleural effusions and subsequent amplification-refractory mutation system – polymerase chain reaction for EGFR analysis led to the diagnosis of advanced lung adenocarcinoma with EGFR L858R mutation. The patient started osimertinib 80 mg once daily as first-line therapy and achieved partial response. However, she developed deteriorating chest distress and shortness of breath after 5 months of osimertinib treatment. A CT scan of the chest revealed extensive patchy shadows in both lungs. Therefore, the patient discontinued osimertinib immediately and received 1 week of empirical antibiotic treatment at local hospital. Simultaneous laboratory test did not identify pathogens. CT scans after antibiotic therapy did not show improvement (Fig. 1A). Considering that no pathogen was detected and CT manifestation was consistent with osimertinib-induced ILD, osimertinib-induced interstitial pneumonia was diagnosed. Because the patient was gerontic with a history of diabetes, hormone therapy was not considered in case of hyperglycemia and infection. Nintedanib has been approved for treatment of idiopathic pulmonary fibrosis.3 Given its antifibrotic activity, nintedanib 150 mg twice daily was prescribed. CT scans after 2 weeks of nintedanib monotherapy showed obvious improvement in both lungs without tumor progression (Fig. 1A). The patient felt better overall and remained on nintedanib treatment. CT scans after 4 weeks of nintedanib commencement still showed stable disease control (Fig. 1A). Because the overall condition had improved, the patient withdrew nintedanib and started gefitinib monotherapy with good tolerance.

Severe ILD has been reported in patients with targeted therapy including osimertinib, gefitinib, and crizotinib.4,5 There is no optional treatment for patients who are diagnosed with targeted therapy–related interstitial pneumonia and are unsuitable for hormone therapy. Herein, our case preliminarily shows dramatic effect of nintedanib in a patient with osimertinib-induced interstitial pneumonia. Although osimertinib was discontinued immediately after the diagnosis of pneumonia, the patient did not experience cancer progression within 1 month of nintedanib treatment. To the best of our knowledge, this case is the first to provide evidence of nintedanib effect in patients with interstitial pneumonia induced by EGFR TKIs.

In conclusion, this case initially proves nintedanib effective in EGFR TKI–induced interstitial pneumonia, providing a new promising strategy for a subset of patients with targeted therapy–induced pneumonia, especially for those unsuitable for hormone therapy.

References

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**References**


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**Figure 1.** Computed tomography scan of chest and depiction of clinical course of the patient. A, Computed tomography during the clinical course. B, Timeline of the clinical course. PR, partial response.