Letter to the Editor

Adjuvant chemotherapy or immunotherapy for completely resected stage IB non-small cell lung cancer: still a grey zone?

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We read with interest a prospective, phase II study by Park and colleagues investigating the efficacy of adjuvant pemetrexed plus cisplatin after completely resected stage IB to IIIA lung adenocarcinoma in South Korea (1). The authors reported that adjuvant chemotherapy with pemetrexed plus cisplatin (N=105) improve the 2-year disease-free survival (DFS) rate [78.1%, 95% confidence interval (CI): 70.6–86.4%] compared to historical control group. Nevertheless, we still have some concerns about the adjuvant chemotherapy for completely resected stage IB non-small cell lung cancer (NSCLC) patients in the new era of immunotherapy.

Recently, the interim analysis of the randomised, phase III PEARLS/KEYNOTE-091 study demonstrated that adjuvant pembrolizumab (N=590), a programmed death 1 (PD-1) inhibitor, significantly improved DFS [hazard ratio (HR) 0.76, 95% CI: 0.63–0.91] compared with placebo (N=587) in completely resected, stage IB (≥4 cm size tumors) to IIIA NSCLC. The HR for DFS in the stage IB was 0.74 (95% CI: 0.47–1.37) in subgroups of the overall population (2).

Another randomised, phase III IMpower010 study also indicated that atezolizumab (N=507), an anti-PD-L1 inhibitor, significantly improved DFS (HR 0.79, 95% CI: 0.64–0.96) versus best supportive care (n=498) after adjuvant chemotherapy in patients with completely resected stage II–IIIA NSCLC (3). The HR for DFS in the stage IIA was 0.68 (95% CI: 0.46–1.00), however, the concerning DFS in the stage IB was not been fully reported.

In a cohort study of 50,814 patients with NSCLC, Pathak and colleagues suggested that high-risk pathologic features (visceral pleural invasion, lymphovascular invasion, and high-grade histologic findings) and tumor size should be simultaneously evaluated in the setting of adjuvant chemotherapy for patients with early-stage, including stage IB NSCLC (4).

In view of these issues, the survival benefits of adjuvant chemotherapy for completely resected stage IB NSCLC with or without high-risk pathologic features should be carefully considered in the APICAL trial by Park and colleagues (1). We appreciate the insights of Park *et al.* and also look forward to more details regarding the role of adjuvant chemotherapy or immunotherapy for completely resected stage IB NSCLC in the ongoing trials.

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