

Impact of Smoking Status on Efficacy of Checkpoint Inhibitors in Advanced NSCLC: Meta-analysis

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Background/Aims: Although smoking status has potential as a biomarker for checkpoint blockade in advanced non-small cell lung cancer (NSCLC), its clinical significance remains obscure. This meta-analysis aims to assess the impact of the smoking status on the efficacy of first-line immunotherapy and to find better treatment in never-smoker and ever-smoker patients.

Methods: We searched the MEDLINE, EMBASE, and Cochrane database for trials comparing immunotherapy with conventional chemotherapy as front-line treatment for advanced NSCLC. Random-effects models were used to pool estimates of hazard ratios (HRs) for overall survival with 95% confidence intervals (CIs). Predefined subgroup analysis was performed to investigate the difference in the efficacy between the single checkpoint blockade and checkpoint inhibitor plus chemotherapy combination in the never-smokers and current/former smokers.

Results: Twelve trials involving 6,446 patients were included in the analysis. An overall survival benefit of immunotherapy was found for combination with chemotherapy (HR, 0.64; 95% CI, 0.43-0.94) but not for monotherapy (HR, 1.05; 95% CI, 0.81-1.37) in the never-smoker group, and there was a significant subgroup difference between combination and monotherapy ($p=0.04$). However, this difference was not observed in the current/former smoker group; both combination therapy (HR, 0.75; 95% CI, 0.63-0.90) and monotherapy (HR, 0.71; 95% CI, 0.59-0.85) showed a better outcome than chemotherapy (p for subgroup difference= 0.67). Similarly, there was a significant difference in efficacy of monotherapy between the current/former smoker and never-smoker group ($p=0.01$), but the efficacy of the combination treatment was comparable between the two groups ($p=0.45$).

Conclusions: Smoking status, which is easily available information, could be used as a guide in clinical practice to choose better treatment in the front-line setting for advanced NSCLC patients.

