Poor Outcome to Pembrolizumab in Lung Adenocarcinoma with High PD-L1 and STK11/KRAS co-mutations

경희대학교 의과대학 호흡기내과

신정하, 이정미, 손경희, 곽원건, 황재준, 강성욱, 장복순, 최혜숙, 김이형, 최천웅, 박명재, 이승현

Background : Although the PD-L1 expression is a positive predictive biomarker for immunotherapy in lung cancer, it is not sufficient to predict the best response to ICIs. Tumor mutational burden (TMB) and concurrent genetic alterations are emerging as novel biomarkers for ICIs. Here, we report a case with poor response to frontline pembrolizumab monotherapy in a lung adenocarcinoma patient with high PD-L1 expression and STK11/KRAS co-mutation.

Case: A 70-year-old male visited our outpatient clinic due to a chronic cough. A chest computed tomographic (CT) scan showed a huge mass at the left lower lobe (LLL), diagnosed with invasive mucinous lung adenocarcinoma. The staging work-up revealed multiple bones and lymph nodes metastasis, suggesting stage IV disease. Studies for EGFR, ALK, and ROS1 were all negative, while PD-L1 expression (22C3) was 100%. Thus, we started the pembrolizumab monotherapy as first-line treatment. Chest CT taken after the third cycle of treatment showed stable disease. However, the follow-up CT and PET taken after the ninth cycle of treatment showed markedly increased LLL mass and new metastatic lymphadenopathies. Next-generation sequencing (NGS) revealed mutations at the STK11 (p.Y36fs* frameshift) and the KRAS (p.G12V missense) genes, associated with the poor response to ICIs in previous studies. Despite subsequent chemotherapy with cisplatin and pemetrexed, he expired after the second cycle of treatment.

Discussion: High PD-L1 expression has been a promising signal to choose ICIs as optimal therapy. However, the predictive power remains debatable. Studies have demonstrated that TMB and certain genetic alterations are associated with poor prognosis in patients treated with ICIs. Especially, STK11/KRAS co-mutation has been recently identified as a predictor of dismal clinical outcome as shown in our case. Our case emphasizes that NGS should be routine clinical practice before the commencement of ICIs, and that studies are essentially required to establish an optimal therapeutic strategy for those harboring such genetic alterations.