Impact of Infections in Patients with Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) Receiving Pembrolizumab-Based Therapies

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Background Immune checkpoint inhibitor (ICI) therapy has improved outcomes in patients with NSCLC, particularly with the programmed death-1 inhibitor pembrolizumab. However, this therapy is not benign and while immune related toxicities are well-described, infections, a common cause of morbidity and mortality amongst patients with solid organ malignancies, are seldom studied. Herein, we investigate the incidence, risk factors, and impact of infections in patients receiving pembrolizumab regimens for NSCLC.

Methods Patients receiving pembrolizumab regimens for advanced/metastatic NSCLC from January 2017 through August 2021 across a seven-hospital network were retrospectively identified and dichotomized into infection and non-infection cohorts. Covariates included age, gender, race, comorbidities, ECOG, chronic infections, line of therapy, monotherapy/combination therapy, anti-infectives at ICI initiation, and growth factor use. Outcomes included all-cause emergency department (ED), inpatient, or intensive care unit (ICU) visits, median number of treatment cycles, overall survival (OS), and progression free survival (PFS). Univariable and multivariable analysis with reported odds ratio (OR) and 95% confidence intervals (CI) evaluated risk of developing infection, and OS/PFS was assessed via Kaplan-Meier methodology. P-value <0.05 was considered statistically significant.

Results Among 243 patients, 111 (45.7%) had ≥1 reported infection, with median time to first infection of 1.9 (0-48.8) months. Demographics were similar between cohorts. Compared to non-infected, infected patients had more ED [37 (33.3%) vs 26 (19.7%), p=0.016], hospital [87 (78.4%) vs 53 (40.1%), p<0.001], and ICU [31 (27.9%) vs 5 (3.8%), p<0.001] visits. During course of infection, there were treatment delays and discontinuation in 56 (50.4%) and 28 (25.2%) patients. Median treatment cycles received by infected and non-infected was 5 (2-13) and 8 (4-12) (p=0.057), respectively. Median OS and PFS in infected and non-infected patients was 11 (95% CI 6.4-16.7) and 21 (95% CI: 14.7-24.2) (p=0.023), and 13.03 (95% CI: 10.03-19.73) and 9.7 (95% CI: 7.13-12.83) (p=0.54) months, respectively. Anti-infective therapy (OR 3.32, [95% CI: 1.26-8.76], p=0.015) and ECOG of 2 (OR 5.79, [95% CI 1.72-19.47], p=0.005) at ICI initiation had higher associations with infection; no other covariates were significant. At last evaluation, 74 (66.7%) infected and 70 (53.0%) non-infected died (p=0.031). Of these, infection caused death in 11 (14.9%) and 4 (5.7%) patients (p=0.041), respectively.

Conclusions Infections are common in NSCLC patients receiving pembrolizumab regimens and associated with greater morbidity, treatment interruptions, and poorer survival. Risk factors included poorer baseline ECOG status and anti-infective therapies at ICI initiation. Prospective studies assessing infectious process prevention and anti-infective stewardship programs may be valuable to augment ICI benefit.

Ethics Approval This retrospective study was an institutional review board approved study (Approval ID: PRO00028635). Informed consent was not obtained due to the retrospective nature of this study.