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Title: Impact of KRAS Mutation Status on the Efficacy of Immunotherapy in Lung Cancer Brain Metastases

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Immune checkpoint inhibitors (ICI) have resulted in improved outcomes in non-small cell lung cancer (NSCLC) patients. However, data demonstrating the efficacy of ICI in NSCLC brain metastases (NSCLCBM) is limited. We analyzed overall survival (OS) in patients with NSCLCBM treated with ICI within 90 days (ICI-90) and compared them patients who never received ICI (no-ICI). We reviewed 800 patients with LCBM who were diagnosed between 2010 and 2019 at a major tertiary care institution. OS from BM was compared between the ICI-90 and no-ICI groups using the Log-Rank test, and Cox proportional hazards model. Additionally, the impact of KRAS mutational status on the efficacy of ICI was investigated. After accounting for known prognostic factors, ICI-90 led to significantly improved overall survival (12.5 months vs 9.1, $p<0.001$) in patients with LCBM. In the 109 patients that had both a known PD-L1 expression and KRAS status, 80.4% of patients with KRAS mutation had PD-L1 expression vs 61.9% in wild-type KRAS patients ($p=0.04$). In patients without a KRAS mutation, there was no difference in OS between the ICI-90 vs no-ICI cohort with a one-year survival of 60.2% vs 54.8% ($p=0.84$). However, in patients with a KRAS mutation, ICI-90 led to a one-year survival of 60.4% vs 34.1% ($p=0.004$). Patients with NSCLCBM that received ICI-90 had improvement in OS compared to no-ICI patients. Additionally, this benefit appears to be observed primarily in patients with KRAS mutations that may drive the overall benefit, which should be taken into account in the development of future trials.