THE EFFECT OF IMMUNOSUPPRESSION DURING ANTI-PD-1 TREATMENT FOR STAGE III MELANOMA

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Background Anti-PD-1 therapy improves recurrence-free survival in patients with resectable Stage III/IV melanoma. Immune-related adverse events (irAEs) represent a challenge for patient care especially in the setting of adjuvant management and may serve as a predictor for therapeutic benefit. We sought to evaluate the incidence of immune related adverse events (irAEs) in melanoma patients receiving adjuvant anti-PD-1 therapy and assess the impact of corticosteroid and non-corticosteroid-based therapy on recurrence-free and overall survival at the University of Pittsburgh Medical Center (UPMC) cohort.

Methods This retrospective, single-center study reviewed adult patients undergoing treatment for Stage III melanoma between 1996 and 2021 who received either pembrolizumab or nivolumab. Patients were further excluded if they did not receive adjuvant treatment with anti-PD-1 therapy, had prior exposure to immunotherapy or BRAF inhibitors, or did not have sufficient follow-up to allow necessary data collection. The resulting 231 patients were stratified into two cohorts – those treated with >10mg prednisone equivalent for longer than two weeks during anti-PD-1 therapy, and those who were not.

Results Of 231 patients reviewed, 123 (53%) developed an irAE of any grade; 57 patients required systemic steroids during adjuvant therapy, with 11 (5%) patients that received steroids and another immunosuppressing agent. Use of steroids did not reduce OS (HR = 1.037, 95% CI 0.4517, 2.381; p=0.93) or RFS (HR = 1.026, 95% CI 0.6198, 1.699; p=0.92). Development of irAEs was associated with improved OS (HR = 0.3698, 95% CI 0.1682, 0.8127; p=0.010), and melanoma specific survival (HR 0.3608, 95% CI: 0.145, 0.8974; p=0.022), but not RFS (HR = 0.8908, 95% CI 0.5659, 1.402; p=0.62). In a multivariable analysis adjusting for age, sex, and stage development of irAEs remained significantly associated with increased overall survival (HR = 0.4079, 95% CI 0.1826, 0.9112; p=0.0288).

Conclusions IrAEs are common in patients treated with adjuvant anti-PD-1 and frequently require treatment with systemic corticosteroids. The development of irAEs during adjuvant therapy is associated with improved OS, but not RFS. Exposure to systemic steroids during adjuvant therapy did not have an impact on OS or RFS. These results provide reassurance that the use of systemic steroids during adjuvant treatment of fully-resected stage III melanoma does not have a negative impact on disease recurrence or survival.

Ethics Approval Approved by the University of Pittsburgh Institutional Review Board under Study ID: STUDY21080074.