THE ROLE OF COMBINATION IMMUNE CHECKPOINT INHIBITORS AS SALVAGE THERAPY FOR PD-1/PD-L1-RESISTANT MERKEL CELL CARCINOMA

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Background Merkel cell Carcinoma (MCC) is a rare but aggressive cutaneous neuroendocrine malignancy that often presents as locally advanced or metastatic disease. MCC has a high risk of relapse, morbidity, and mortality that can be challenging to manage. The PD-1/PD-L1 inhibitors, pembrolizumab and avelumab, have recently been shown to benefit approximately 50% of metastatic MCC patients, indicating that a significant fraction of these patients are in need of alternative therapeutic options. There is currently no standard salvage treatment regimen for anti-PD-1-refractory MCC patients. We sought to explore our clinical experience at Duke University with combination immune checkpoint inhibitors (ICIs), ipilimumab and nivolumab, after progression on PD-1/ PD-L1 inhibitors for patients with metastatic or locally advanced MCC.

Methods A comprehensive electronic database search was conducted for all metastatic and locally advanced MCC patients that were treated with PD-1/PD-L1 therapies between years 2015 and 2022, at Duke University. Patients that were treated with combination ICIs were included. Patients treated with surgery, radiation, and chemotherapy were not excluded. The primary outcome was objective response rates (ORR), as assessed by utilizing Response Evaluation Criteria in Solid Tumors (RECISTv1.1) as well as immune-related Response Evaluation Criteria in Solid Tumors (irRECIST). Secondary outcomes were progression free survival (PFS), overall survival (OS), and immune-related adverse events (irAEs) at the longest follow-up.

Results Our search yielded 6 patients with metastatic or locally advanced MCC that were treated with ipilimumab and nivolumab after progression on PD-1/PD-L1 inhibitor therapies. The patients’ mean age was 69.6 years with a male percentage of 66.66%. ORR was 50%, where 2 patients had a complete response and one had a partial response. Of the other 50% of patients, 2 patients had progression of disease and one had stable disease at their week 12 restaging scans. Mortality rate was 50% and all deaths were cancer-related. Median PFS was 7 months and median OS was 13 months. 50% of patients suffered an irAE while 33% experienced a grade 3 or higher irAE.

Conclusions Our study highlights that the use of combination ICIs with ipilimumab and nivolumab as salvage therapy for patients with metastatic or locally advanced MCC resistant to PD-1/PD-L1 therapy can be effective and is relatively well-tolerated. These data indicate that this treatment regimen is worthy of further exploration in a larger cohort of MCC patients.