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A PHASE II STUDY EVALUATING LOW DOSE IPILIMUMAB IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH MELANOMA BRAIN METASTASES

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Background: Among all solid tumors, melanoma has the highest likelihood of metastases to the central nervous system (CNS) and up to 60% of patients of stage IV are diagnosed with melanoma brain metastases (MBM) during their disease course. Combination checkpoint inhibitors (CPI) at the standard dose of ipilimumab (3mg/kg) and nivolumab (1mg/kg) is established as the standard treatment for newly diagnosed and asymptomatic patients with MBM, and has demonstrated intracranial response rate (ICRR) in more than half and ongoing benefit in 87% of patients who achieved an initial response. Unfortunately, grade 3 and 4 toxicities are seen in over half of these patients and nearly 25% discontinue treatment related to toxicities. Prior studies have demonstrated combining low dose ipilimumab (1mg/kg) with pembrolizumab preserves efficacy while reducing toxicity but patients with untreated MBM were not evaluated.

Methods: We conducted a phase II study (NCT03873818) evaluating the safety and efficacy (ICRR by modified RECIST) of ipilimumab 1mg/kg in combination with pembrolizumab for asymptomatic patients with MBM.

Results: 20 patients with anti-PD-1 treatment naïve MBM were enrolled. Median age was 65, and 55% were male. The median number of lesions at time of enrollment was 3 (range 1-20) and the median size of the largest lesion was 7.5mm (5.0-28.0). After a median follow up of 21.6 months (0.5 – 50.7), the ICRR was 56%, and the median duration of the IC response was 9 months. Median progression free survival was 5.2 months (95% CI: 1.3, NE), median overall survival has not been reached, and 70% of patients were still

alive at 12 months. Treatment related grade 3 or 4 adverse events were experienced in 25% of patients and included encephalopathy, rash, intracranial hemorrhage, anorexia/colitis, and elevated LFTs.

Conclusion: Low dose ipilimumab as part of a combination CPI regimen for patients with untreated MBM represents a promising approach to maximize benefit while reducing treatment related toxicities but further investigation should be considered.