Immune checkpoint inhibitor for melanoma

Immune checkpoint inhibitor is used to treat melanoma of the skin. It is also being studied for use against other cancers.

Robin et al., retrospectively identified all consecutive cases of newly diagnosed melanoma brain metastases (MBM) treated with Gamma Knife radiosurgery at a single institution between 2012 and 2017, and included only patients that initiated CPIs within 8 weeks before or after radiosurgery.

Thirty-eight patients were included with a median follow-up of 31.6 months. Two-year local control was 92%. Median time to out-of-field CNS and extra-CNS progression were 8.4 and 7.9 months, respectively. Median progression-free survival (PFS) was 3.4 months and median overall survival (OS) was not reached (NR). Twenty-five patients (66%) received anti-CTLA4 and 13 patients (34%) received anti-PD-1+/-anti-CTLA4. Compared with anti-CTLA4, patients that received anti-PD-1+/-anti-CTLA4 had significant improvements in time to out-of-field CNS progression ($p = 0.049$), extra-CNS progression ($p = 0.015$), and PFS ($p = 0.043$), with median time to out-of-field CNS progression of NR vs. 3.1 months, median time to extra-CNS progression of NR vs. 4.4 months, and median PFS of 20.3 vs. 2.4 months. Six patients (16%) developed grade ≥ 2 CNS toxicities (grade 2: 3, grade 3: 3, grade 4/5: 0).

Excellent outcomes were observed in patients that initiated CPIs within 8 weeks of undergoing radiosurgery for newly diagnosed MBM. There appears to be an advantage to anti-PD-1 or combination therapy compared to anti-CTLA4 [1].

Immune checkpoint inhibitors have demonstrated remarkable benefits in cancer patients. However, concern regarding toxicity in the setting of stereotactic radiosurgery (SRS) is often raised. In this study, we characterize radiation necrosis (RN) following immunotherapy and SRS. Melanoma patients treated with SRS and anti-CTLA-4 and/or anti-PD-1 at our institution from January 2006 to December 2015 were retrospectively reviewed. Overall survival (OS) and time to RN were assessed using Kaplan-Meier analysis. Logistic regression and Cox proportional hazards analyses were performed to identify predictors of radiation necrosis-free survival (RNFS) and RN risk. One-hundred thirty-seven patients with 1094 treated lesions over 296 SRS sessions were analyzed. Median follow-up was 9.8 months from SRS. Rate of RN was 27% of patients with median time to RN of 6 months. Median OS from SRS treatment was 16.9 months. RNFS at 6 months, 1 and 2 years was 92.7, 83.0, and 81.2%. Treatment with chemotherapy within 6 months of SRS was associated with worse RNFS at 1 year (78.4 vs. 87.5%, $p = 0.017$). On multivariate analysis, chemotherapy within 6 months and increased number of lesions treated were predictive of increased RN risk (HR 2.20, 95% CI 1.22-3.97, $p = 0.009$; HR 1.09, 95% CI 1.03-1.15, $p = 0.002$), whereas immunotherapy type and targeted therapy were not predictive. Median target volume of lesions that developed RN was greater than that of lesions that did not ($p < 0.001$). Concurrent treatment with chemotherapy, larger size and number of lesions treated were predictive of RN. Immunotherapy type and timing proximity to SRS were not associated with RN risk [2].

Case reports

Miki K, Hata N, Kawano Y, Michiwaki Y, Nakamizo A, Uchino K, Iihara K. [A Case of Metastatic

Malignant Melanoma with Symptomatic Hemorrhage Developing after Treatment with Immune Checkpoint Inhibitors and Radiotherapy]. No Shinkei Geka. 2018 Nov;46(11):1021-1025. doi: 10.11477/mf.1436203858. Japanese. PubMed PMID: 30458440.

1)

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2)

Fang P, Jiang W, Allen P, Glitza I, Guha N, Hwu P, Ghia A, Phan J, Mahajan A, Tawbi H, Li J. Radiation necrosis with stereotactic radiosurgery combined with CTLA-4 blockade and PD-1 inhibition for treatment of intracranial disease in metastatic melanoma. J Neurooncol. 2017 Jul;133(3):595-602. doi: 10.1007/s11060-017-2470-4. Epub 2017 May 12. PubMed PMID: 28500560.