SURVIVAL RATES IN STAGE IV MELANOMA PATIENTS TREATED WITH RADIATION AND IMMUNOTHERAPY DIFFER DEPENDING ON AGE AND RADIATION TREATMENT SITE

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Background Melanoma is difficult to treat due to its propensity of evading the immune system. Radiation can be combined with immune checkpoint inhibitors to potentially prolong survival. Radiation has been shown to reduce tumor sizes both at the site of radiation and at non-irradiated lesions, also known as the abscopal effect. However, the interaction of immunotherapy and radiation treatment in melanoma cancer is not well-defined. This study seeks to better characterize factors influencing survival in Stage IV melanoma patients treated with both radiation and immunotherapy.

Methods Retrospective data was collected from melanoma patients receiving both radiation and immunotherapy within 6 months of each other between 2008–2021 at our institution. Patient and treatment characteristics were examined for their influence on overall survival and progression-free survival using the log-rank test on Kaplan Meier survival curves. Radiographic response was assessed according to PERCIST/RECIST criteria and analyzed against patient/treatment characteristics using the Mann-Whitney U Test. For the abscopal effect, the percent changes both before and after radiation treatment were subtracted in non-irradiated lesions to produce a "delta-delta" percent change to reflect the rate of change in tumor response to radiation treatment.

Results Younger patients trended towards worse overall ($p=0.141$) and progression free ($p=0.06$) survival as well as less favorable PERCIST/RECIST response to radiation ($p=0.0562$) compared to older patients. Combination CTLA-4 and PD-1 inhibition therapy tended to produce better PERCIST/RECIST tumor response ($p=0.09$), but it did not significantly affect survival times. In addition, there was some lower overall ($p=0.22$) and significantly lower progression free ($p=0.012$) survival among patients with intracranial irradiated lesions. However, no difference was found in PERCIST/RECIST response in the irradiated lesions between the intra- or extracranial groups. Non-irradiated lesions in patients with extracranial irradiated lesions had a pattern of less favorable rate of change in tumor size ($p=0.16$).

Conclusions Lower survival times in younger patients is unexpected and may reflect differences in immunotherapy response in patients receiving both radiotherapy and immunotherapy, which requires further investigation. Combination CTLA-4 and PD-1 inhibition therapy correlating with better tumor response confirms the effect is still present in this cohort receiving radiotherapy. The lower survival times among intracranial lesion patients is most likely due to lower expectancy of brain metastasized patients; however, it could also be the brain is less responsive to immunotherapy. Further research in a larger cohort is needed for deeper analysis, but this series is still comparable in size to other published series.

Ethics Approval This retrospective review was approved by the University IRB, UMCIRB 15-001726. Consent of participants was waived due to the retrospective nature of this review.

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