### STAGE IV MELANOMA PATIENTS TREATED WITH RADIATION AND IMMUNOTHERAPY: SURVIVAL RATES AND ANALYSIS OF ABSCOPEL EFFECT

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#### INTRODUCTION

Skin cancer is the leading cause of cancer in USA: melanoma carries the highest mortality rate of all skin cancers.

- Immune checkpoint inhibitors have been highly effective in the treatment of systemic melanomas cancers by blocking immune regulators (PD-1 and CTLA-4) and amplifying immune response.
- Radiation therapy can be combined with immunotherapies to potentially prolong survival, perhaps by stimulating antigen release and increasing response to immunotherapy; although little is understood about the best dose and timing of combination.
- Metastasized melanoma lesions have been shown to display different treatment responses according to their location; suggesting certain tissues may be more responsive to immunotherapy.
- The abscope1 effect describes the reduction in non-treated tumor sizes when another lesion is treated with radiation.
- Little is known about the mechanism behind the abscope1 effect, but it has been postulated to be mediated by immune stimulation. The hope is that immunotherapy can be enhanced through the abscope1 effect.
- Our goal is to better characterize survival in Stage IV melanoma patients treated with both radiation therapy and immunotherapy and aid clinicians in the treatment of melanoma and other systemic cancers.

#### MATERIALS & METHODS

- Institutional Retrospective Review (between 2008-2021)
  - Criteria: included melanoma diagnosis + radiation treatment within 6 months of RT + 20 total patients selected, 7 of which had multiple tumor lesions to follow
- Patient characteristics including age at RT, gender, and comorbidities
- Immunotherapy treatment type, timing in accordance to RT, and number of cycles
- Radiation treatment dose, trajectory, biologically effective dose
- Endpoints include survival status, disease progression status, and radiographic response of lesions treated with radiation therapy and those not treated with radiation therapy that can be measured with abscopal response.
- Extracranial or intracranial melanoma index tumor lesions pre- and post radiation treatment measured according to RECIST or PERCIST criteria.
- Kaplan-Meier survival curves for both overall and progression-free survival using log-rank test
- Mann-Whitney U test analysis against PERCIST/RECIST response to radiation-treated index tumor values.

#### RESULTS

- **Overall Survival**
  - Younger patients displayed lower overall survival and progression free survival times than older patients treated with radiation.
- **Age of Radiation Treatment**
  - Younger patients had worse survival.
  - Kaplan-Meier survival curves for both overall and progression-free survival using log-rank test.
- **Age of Radiation Treatment**
  - Younger patients displayed lower overall survival and progression free survival times than older patients treated with radiation.
- **Immunotherapy Administration Type**
  - Patients receiving combination PD-1 and CTLA-4 inhibitors displayed better PERCIST/RECIST tumor responses than those only receiving only PD-1 or CTLA-4 inhibitors.
  - Patients who received both PD-1 and CTLA-4 inhibitors did not display significant differences in overall or progression free survival times compared to patients receiving either PD-1 or CTLA-4 inhibitors.

#### DISCUSSION/CONCLUSIONS

- Younger patients had worse survival as well as less favorable PERCIST/RECIST response to RT compared to older patients. This was an unexpected, novel finding not seen in patients receiving immunotherapy alone. This may reflect differences in immunotherapy response in patients receiving both radiotherapy and immunotherapy that needs to be further investigated.
- Combination CTLA-4 and PD-1 therapy was correlated with better PERCIST/RECIST tumor response, but did not significantly affect survival times, and further research is needed to understand the interaction of immunotherapy and radiation.
- There was significantly lower survival among intracranial lesion patients. This is most likely explained by lower expectancy in brain metastasis compared to other metastasized sites. No difference was found in PERCIST/RECIST response in the irradiated lesions between the groups. One possible explanation is that there is worse immunogenic response in the brain.
- However, the trend of our patients with irradiated intracranial lesions exhibiting a more favorable delta-delta in un-irradiated tumors challenges the understanding as the brain a less immunogenic tissue. Further research in larger cohorts and better tools to radiographically assess abscopal response is needed.

#### REFERENCES