Survival outcomes predicted by irAEs on $^{18}$F-FDG-PET in response to PD-1 antibody therapy in metastatic melanoma

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Background: PD-1 antibody therapy has revolutionised the landscape of metastatic cutaneous melanoma treatments and outcomes. The aim of our study is to investigate whether immune related adverse events (irAEs) or granulomatous/reactive nodal changes visible on $^{18}$F-FDG-PET during treatment with PD-1 antibody therapy for metastatic cutaneous melanoma predicts improved overall survival.

Methods: Patient demographics, treatment regimes, toxicity profiles and $^{18}$F-FDG-PET scans were collected for patients who underwent treatment at Alfred Health in Melbourne, Victoria between 2015 and 2019 for advanced melanoma. Data were extracted from each patient's electronic medical record. Patients were included if they were treated with 1st line PD-1 antibody +/- CTLA-4 antibody therapy for unresectable stage III or stage IV metastatic cutaneous melanoma.

Patients were excluded if an $^{18}$F-FDG-PET was not performed both during and prior to commencement of immunotherapy. Two blinded-nuclear medicine physicians reviewed $^{18}$F-FDG-PET imaging at baseline and following immunotherapy. The review criteria included granulomatous/reactive changes and PET detected irAEs. Clinically reported irAEs were also collected. Statistical analysis was performed using IBM SPSS software.

Results: A total of 103 patients (68% male) met the inclusion criteria for the study. The largest proportion of individuals had M1c disease (26.2%) followed by unresectable stage III (25.2%), M1b (21.4%), M1a (16.5%) and M1d (10.7%) respectively. Most individuals received single agent anti-PD-1 (71.6%) whereas a smaller proportion received combination therapy with CTLA4 antibody therapy (28.4%).

The median follow up period for survivors was 4.78 years. Patients with irAEs visible on $^{18}$F-FDG-PET during treatment had improved survival (Figure 1) (p=0.014). Granulomatous or reactive nodal changes visible on $^{18}$F-FDG-PET did not have any significant impact on survival outcomes (p=0.86) nor did clinically reported irAEs (p=0.71).

Conclusion: This study demonstrates that irAEs visible on $^{18}$F-FDG-PET during PD-1 antibody therapy for metastatic melanoma predicts improved overall survival.

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