Abstract 241 Figure 5  Kaplan-Meier curves comparing advanced stage melanoma patients without liver metastases treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) versus ipilimumab/nivolumab by progression free survival. n = 240

Conclusions In melanoma patients treated with PD-1 inhibitor-based regimens, the presence of LM leads to poorer survival outcomes. Our study suggests the poor prognosis associated with LM can be substantially mitigated by treatment with combination I/N over anti-PD-1 monotherapy. Further studies are warranted to investigate the anti-immunotherapy effect associated with LM.

Ethics Approval The study was approved by the University of Michigan institutional ethical guidelines and patients' consents were waived following Institutional Review Board protocol review (HUM00156014).

REFERENCE

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Abstract 243 Figure 1  OS Kaplan-Meier survival curves stratified for the group with the 50% highest trough concentrations (red) and 50% lowest trough concentrations (blue). The median OS for high pembrolizumab exposure group was not reached, which was significantly longer than the low pembrolizumab exposure median of 48 months (p=0.021)

Abstract 243 Figure 2  PFS Kaplan-Meier survival curves stratified for the group with the 50% highest trough concentrations (red) and 50% lowest trough concentrations (blue). The mean PFS for the high pembrolizumab exposure group was 49.2 months, which was not significantly longer than low pembrolizumab exposure mean PFS of 37.9 months. The median PFS was not reached in either group.

Background Despite the paradigm shift heralded by immune checkpoint blockade (ICB), only a small proportion of patients have a meaningful response. Dose selection of ICB agents was significantly based on in-silico modelling.1 Trial data has shown that clearance of these agents varies over time, with a reduction in clearance associated with improved best overall response (BOR).2, 3 Real world data has shown patients with higher exposure to ICB, manifested as higher plasma trough concentrations, experience improved BOR and longer survival.4 This study aimed to determine the relationship between longitudinal ICB exposure and BOR, progression free survival (PFS) and overall survival (OS) in patients with metastatic melanoma receiving pembrolizumab monotherapy.

Methods 28 patients with metastatic melanoma receiving weight based pembrolizumab (2 mg/kg Q3w) had serial pharmacokinetic trough draws prior to their next scheduled dose, up to a maximum of 22 cycles. BRAF mutation positive patients were pre-treated with BRAFi/MEKi therapy, otherwise pembrolizumab was given first line. Plasma trough levels were determined using the Abcam® pembrolizumab ELISA kit. The cohort was split by best overall response (BOR), determined by iRECIST. No statistically significant differences were determined, using one-way ANOVA. The cohort was stratified into high versus low pembrolizumab trough concentrations, split by the median. Trough is an established surrogate for drug exposure.5 Kaplan-Meier survival analysis for progression-free and overall survival was performed based on pembrolizumab drug exposure groups.

Results Median follow up was 32.5 months. Complete responders (CR) (n=11) had 29.8% higher geometric mean pembrolizumab trough levels (90.8 mcg/mL) than partial responders (PR) (n=9) (63.7 mcg/mL, p=ns). CR patients had 16.1% higher trough levels than patients with progressive disease (PD) (n=6) (76.2 mcg/mL, p=ns). 2 patients with stable disease had mean trough pembrolizumab levels of 106.4 mcg/mL. The high pembrolizumab exposure group experienced significantly longer median OS (not reached versus 48 months, p=0.021) (figure 1), than the low exposure group. No significant difference was found in mean PFS between the groups (49.2 versus 37.9 months, p=ns) (figure 2). The median PFS was not reached in either group.

Conclusions A positive exposure survival relationship for pembrolizumab in metastatic melanoma is described in a real world setting. Whether this relationship indicates a true causal effect of variation in drug exposure on clinical outcomes remains to be determined. Further pharmacokinetically driven dosing studies are required to identify whether therapeutic drug monitoring of pembrolizumab in the clinic is a necessity.

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Ethics Approval This study was approved by the Hunter New England Health Local Health District (14/12/10/4.02) and University of Newcastle Human Research Ethics Committee institutional review board (H-2018-0159).

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

REFERENCES

NOVEL RESPIRABLE ANTISENSE OLIGONUCLEOTIDE (RASON) APPROACH TO PRIMARY AND METASTATIC HUMAN LUNG CANCER: PRELIMINARY RESULTS IN A MODEL SYSTEM EMPLOYING SPONTANEOUS LUNG TUMORS IN DOGS

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Background Antisense oligonucleotides function by targeting the messenger RNA coding for a target protein, rather than the protein itself. This laboratory previously introduced Respirable Antisense Oligonucleotides (RASONS) into human clinical