**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 242**

**MONITORING MDSC – A HURDLE TO IMMUNE CHECKPOINTS INHIBITORS**


**Background** Certain cell subsets have been identified to have a negative impact on cancer immunotherapies by promoting angiogenesis and immunosuppression in the tumor microenvironment. One of these cell subsets is a heterogeneous population of immature myeloid cells that have been named Myeloid Derived Suppressor Cells (MDSC). MDSC are increased in states of cancer and their numbers have been shown to inversely correlate with a positive clinical outcome. These findings have prompted the measurement of MDSC in order to predict clinical outcome during treatment with immunotherapies. In this study, flow cytometry was used to measure M-MDSC in frozen PBMC samples and hence predict medical outcome in melanoma patients treated with an anti-CTLA-4 drug (ipilimumab).

**Methods** M-MDSC were measured in frozen PBMC from 20 healthy donors and 68 patients with melanoma treated with ipilimumab. M-MDSC were enumerated using a Lin-CD14+CD11b+HLA-DRlow/- phenotype. In order to prevent subjectivity during gating, caused by the lack of bi-modality with HLA-DR staining, a computational algorithm was used. As distinct HLA-DR spread can be observed in the different subjects, measuring the CV (a ratio between GMFI and SD) of this spread allows to calculate a standardized ad hoc quantitative measure of MDSC frequency in cancer patients. This measurement enables identification of M-MDSC in an objective manner and was used to determine whether the percentage of M-MDSC in patients could be linked with overall survival.

**Results** The relative frequency of M-MDSC was determined in 68 melanoma patients treated with two different doses of ipilimumab. By comparing the percentage of M-MDSC at baseline (pre-treatment) and after two doses of ipilimumab with the overall survival data and applying log-rank statistics, a cut-off was defined allowing the separation of ‘high’ and ‘low’ M-MDSC expressers. Patients with ‘low’ M-MDSC were associated with improved overall survival with a hazard ratio of 0.35.

**Conclusions** The reliable measurement of immune suppressive cells such as MDSC gives the ability to predict the clinical outcome of cancer treatments. In turn, these measurements will permit the design of patient-specific treatments as inhibitors to these cell subsets become available, making personalized medicine a reality in contemporaneous cancer treatment. The identification of specific phenotypes and activation markers for MDSC may improve the prediction ability of the test described in this study. These results highlight the importance of linking the frequency of immune suppressive cells with clinical outcome.

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**Abstract 243**

**REAL WORLD EXPOSURE SURVIVAL RELATIONSHIP OF PEMBROLIZUMAB IN METASTATIC MELANOMA**


Conclusions The reliable measurement of immune suppressive cells such as MDSC gives the ability to predict the clinical outcome of cancer treatments. In turn, these measurements will permit the design of patient-specific treatments as inhibitors to these cell subsets become available, making personalized medicine a reality in contemporaneous cancer treatment. The identification of specific phenotypes and activation markers for MDSC may improve the prediction ability of the test described in this study. These results highlight the importance of linking the frequency of immune suppressive cells with clinical outcome.

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**REFERENCE**

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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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.

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.

REFERENCES

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