

**Ethics Approval** The study was approved by Neogenomics Institution's Ethics Board and external IRB, approval number 420160280.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0240>

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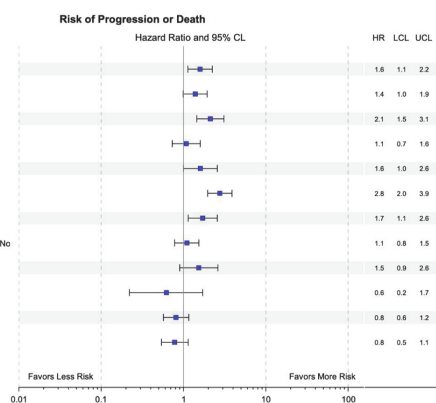
**CLINICAL OUTCOMES OF METASTATIC MELANOMA PATIENTS WITH LIVER METASTASES TREATED WITH ANTI-PD-1 MONOTHERAPY VERSUS COMBINATION IPIIMUMAB/NIVOLUMAB**

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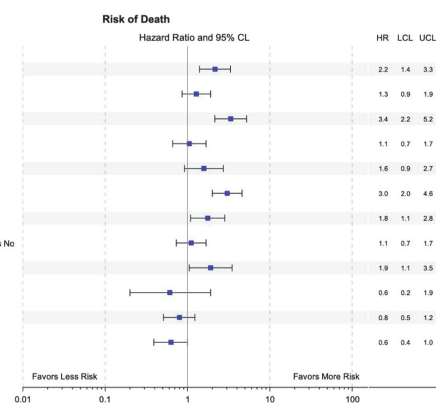
**Background** Recent studies report of liver metastases (LM) as a poor prognostic factor in patients treated with immune checkpoint inhibitors (ICIs),<sup>1</sup> but clinical outcomes associated with different ICI regimens remains uncertain. In this study, we investigate melanoma patients with and without LM and assess differential treatment outcomes associated with anti-PD-1 monotherapy and combination ipilimumab/nivolumab (I/N).

**Methods** We conducted a single-center, retrospective review of advanced stage melanoma patients with and without LM treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) or I/N between 2012 and 2018. Overall survival (OS) and progression free survival (PFS) were measured from the first dose of treatment to date of death and clinical or radiographic progression, respectively. Univariate and multivariate analysis were performed using Cox proportional hazard (CPH) models and logistic regression models. Inverse probability of treatment weighting using propensity scores in CPH models was used to account for the following baseline covariates: age, ECOG performance status, BRAF status, pre-treatment LDH level, prior therapy status, and number and sites of metastases.

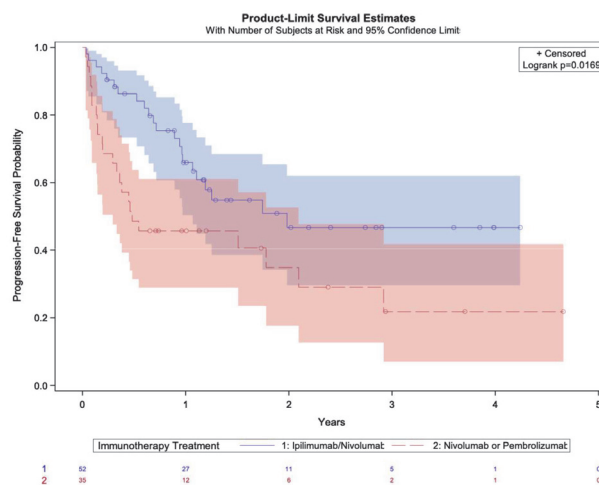
**Results** 327 patients were identified, 87 with LM and 240 without LM. Patients with LM was associated with worse PFS [HR: 2.1, 95% CI, 1.5 – 3.1] (figure 1) and OS [HR: 3.4, 95% CI, 2.2 – 5.2] (figure 2). Respective 3-year PFS and OS estimates associated with anti-PD-1 monotherapy were 21.8% and 28.7% in patients with LM (figure 3, figure 4); and 36.5% and 57.6% without LM (figure 5, figure 6). Respective 3-year PFS and OS estimates associated with I/N were 46.7% and 56.7% in patients with LM; and 58.0% and 74.4% without LM.



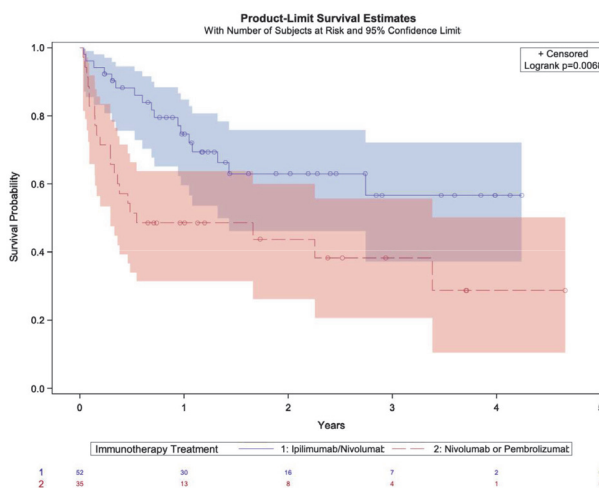
**Abstract 241 Figure 1** Forest plot for progression free survival in all advanced stage (unresectable or metastatic) melanoma patients treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) or combination ipilimumab/nivolumab (Ipi/Nivo). n = 327



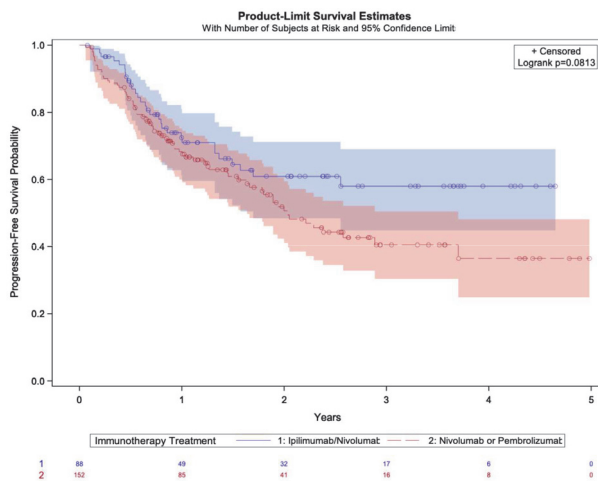
**Abstract 241 Figure 2** Forest plot for overall survival in all advanced stage (unresectable or metastatic) melanoma patients treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) or combination ipilimumab/nivolumab (Ipi/Nivo). n = 327



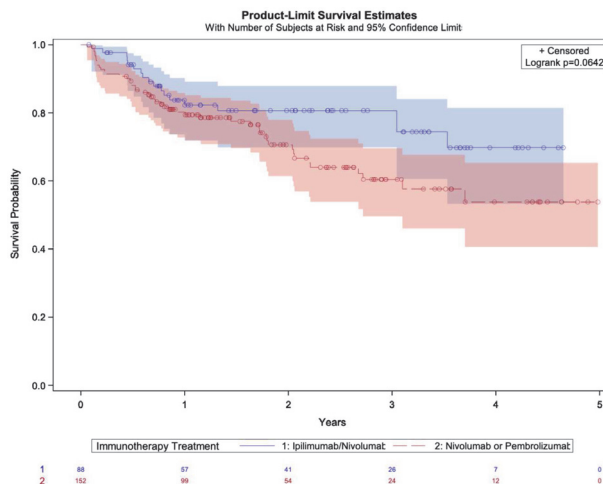
**Abstract 241 Figure 3** Kaplan-Meier curves comparing advanced stage melanoma patients with liver metastases treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) versus ipilimumab/nivolumab by progression free survival. n = 87



**Abstract 241 Figure 4** Kaplan-Meier curves comparing advanced stage melanoma patients with liver metastases treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) versus ipilimumab/nivolumab by overall survival. n = 87



**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



**Abstract 241 Figure 6** Kaplan-Meier curves comparing advanced stage melanoma patients without liver metastases treated with anti-PD-1 monotherapy (nivolumab or pembrolizumab) versus ipilimumab/nivolumab by overall 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

1. Bilen MA, Shabto JM, Martini DJ, *et al.* Sites of metastasis and association with clinical outcome in advanced stage cancer patients treated with immunotherapy. *BMC Cancer* 2019; **19**(1):857.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0241>

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

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**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.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0242>

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

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