Abstract 662 Figure 1 Elastic Net Logistic Regression with Monte Carlo Cross-Validation to Predict Response to Atezolizumab in Urothelial Cancer. (A) Predictive variables with beta coefficient 95% confidence intervals that exclude 0, derived from Monte Carlo cross-validation. (B) Confusion matrix of actual vs. predicted response data in the validation set. (C) Total response proportions of actual and predicted response data in the validation set

Abstract 662 Figure 2 Elastic Net Cox Proportional-Hazards Regression with Monte Carlo Cross-Validation to Predict Survival. (A) Predictor variables with beta coefficient 95% confidence intervals that exclude 0, derived from Monte Carlo cross-validation. (B) Predictions vs. survival outcomes in the validation set. (C) Loess fit of predictions vs. survival outcomes in the validation set. 95% confidence interval indicates strength of fit.
with good performance ($c-index_{\text{model}} = 0.652$, $p_{c-index} = 0.0290$).

**Conclusions** Models incorporating clinical metadata and immunogenomic signatures can predict response and survival for uveal melanoma patients treated with atezolizumab. Among predictors in those models, baseline performance status is the greatest and most positive predictor of response and survival.

**REFERENCE**

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**664 APPLYING ADVANCED DATA ANALYSIS TO IMMUNOTHERAPY DRUG DISCOVERY FOR UVEAL MELANOMA**

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**Background** Uveal melanoma is a rare variant of melanoma associated with monosomy 3, present high risk for metastatic disease, and has been resistant to all therapeutic approaches. We sought to use a novel advanced big data approach to identify potential new immunotherapy targets for the treatment of uveal melanoma.

**Methods** Comprehensive multiplatform analysis of 80 primary uveal melanoma specimens in the TCGA gene expression database were evaluated. There were four previously reported [Robertson et al, Cancer Cell, 2017] molecularly distinct subgroups consisting of two high-risk, largely disomy 3 (N=38 after data QC) and two low-risk, largely monosomy 3 (N=40) patterns predictive of metastatic progression. RNA sequencing data for these subsets were analyzed at Immuneneering to obtain differential expression signatures associated with prognosis. QC was performed, including principal component analysis to identify outlier samples, and gene expression changes were determined by limma-voom analysis and organized by magnitude of change and statistical significance, using Benjamini-Hochberg multiple hypothesis correction. Pathway enrichments were conducted by GSEA. Prognosis-associated genomic signatures were evaluated using an advanced big data platform to identify relevant biological perturbations in each subgroup using two- and four-subset analyses.

**Results** Large differences in gene expression were identified in high-risk vs. low-risk uveal melanoma samples. Volcano plots identified several independent genes differentially expressed in good vs. poor risk uveal melanoma. The most positively enriched gene expression pathways associated with poor prognosis related to innate and adaptive immune processes. This included genes associated with MHC expression, antigen processing and presentation, regulation of T cell responses, leukocyte chemotaxis, antigen binding and type I interferon responses. Transcriptomic perturbation analysis identified several associations of which the top included genes associated with overexpression of interferon-gamma and interferon-beta 1, and interferon-gamma ligand stimulation. Another major family identified was RAB31, which coordinate small GTPases involved in intracellular membrane trafficking. Prognosis-associated immune perturbations were far more highly enriched among a subset of patients, indicating differing underlying biology in a patient subset that could be relevant for treatment.

**Conclusions** Our data identified numerous potential therapeutic targets, many associated with tumor-immune system interactions in high-risk uveal melanoma samples. Advanced big data analysis platforms may be leveraged to identify...