## 508 GENERALIZABILITY OF PREDICTIVE VERSUS PROGNOSTIC INDICATORS FROM PUBLISHED TRANSCRIPTOMIC ASSOCIATIONS WITH TUMOR RESPONSE TO IMMUNE CHECKPOINT INHIBITION

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**Background** Clinically actionable biomarkers of immune checkpoint inhibitor (ICI) response are currently limited to specific mutation profiling, immunohistochemistry staining for PD-L1, and tumor mutational burden. Use of the latter two are challenging, as they are incompletely predictive and lack accepted standards for measurement and interpretation. Transcriptomic associations with response have been reported and may add critical information to an integrated biomarker strategy. There is a need for better understanding of the performance of potential biomarkers across multiple datasets and tumor tissue types.

**Methods** RNA sequencing FASTQ data files from 12 ICI trials [1-13] and 29 solid tumors in The Cancer Genome Atlas (TCGA)[14] were processed using a standardized bioinformatics workflow for quality control, mapping, generation of gene expression matrices, and extraction of immunogenomics features. We evaluated 18 [2, 15-22] immunogenomics features that have been published or proposed to associate with clinical response to ICI therapy for correlation with response and survival across these datasets, estimating predictive information from the ICI trials and prognostic information from TCGA dataset results.

**Results** The MIRACLE score was associated with response and survival in most ICI studies, both overall and within melanoma trials (figures 1). Other immunogenomics features had both lower effect sizes of outcome associations and fewer cohorts in which their outcome associations were statistically significant. Features that were associated with outcome in the ICI studies were generally associated with survival in TCGA as well, whether evaluating all tumor tissue types (figure 2) or melanoma only (figure 3). In melanoma, the TIDE score was associated with response to ICIs, but not with overall survival in TCGA, though the effect size was small. Gene expression signatures built from responders versus non-responders in each trial did not yield generalizable associations with response across other trials. Harmonized gene expression data and immunogenomics features extracted in this project are available for review and further analysis in the CRI iAtlas platform (https://cri-iatlas.org/).

**Conclusions** The MIRACLE score performed best in both effect size and frequency of studies where its association with outcome was statistically significant. No features gave substantial predictive rather than prognostic information. We expect that integration of transcriptomic features with clinical features and DNA alterations will be required to provide predictive (rather than just prognostic) information. Methods that train models on prioritization of predictive information and generalizability across studies may be required for optimal biomarker development.

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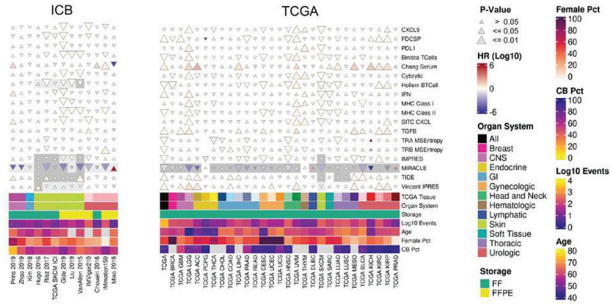
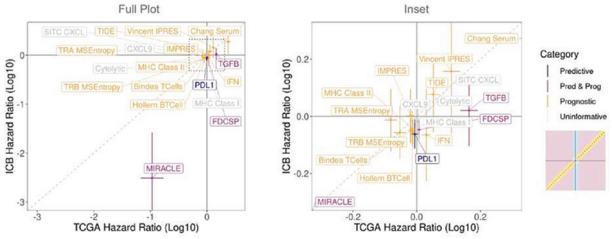
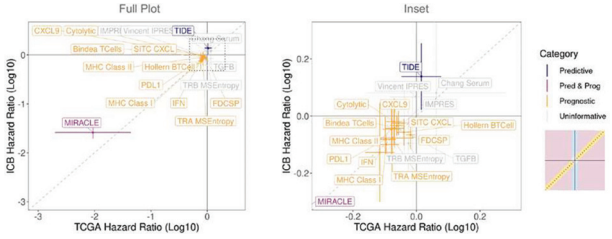



**Abstract 508 Figure 1** Overall survival associations of selected immunogenomics features. Rows represent selected immunogenomics features and columns represent individual datasets. Results from ICI trials are shown in the left panel, and results from TCGA datasets are shown in the right panel. Row/column intersections represent effect size (triangle direction and color) and statistical significance (triangle size) of associations with overall survival. Column-side colorbars show various dataset features for comparison




**Abstract 508 Figure 2** Predictive versus prognostic information content of selected immunogenomics features. X-axis represents the log10 hazard ratio with 95% confidence interval derived from TCGA data, and Y-axis represents log10 hazard ratio with 95% confidence interval derived from ICI data.




**Abstract 508 Figure 3** Predictive versus prognostic information content of selected immunogenomics features, melanoma trials only. X-axis represents the log10 hazard ratio with 95% confidence interval derived from TCGA data, and Y-axis represents log10 hazard ratio with 95% confidence interval derived from ICI data.

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