with good performance (c-index$_{model}$ = 0.652, $p_{c\text{-}index}$ = 0.0290).

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

REFERENCE

1. Mariathasan S, Turley S, Nickles D, *et al*. TGFβ attenuates tumour response to PD-L1 blockade by contributing to exclusion of T cells. *Nature* 2018;**554**:544–548.

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663 CORRELATION BETWEEN EARLY ENDPOINTS AND OVERALL SURVIVAL IN NON-SMALL-CELL LUNG CANCER: A TRIAL-LEVEL META-ANALYSIS

[1]Shameer Khader*, [1]Youyi Zhang, [1]Daniel Jackson, [1]Kirsty Rhodes, [1]Imran Khan Anwer Neelufer, [1]Sreenath Nampally, [2]Andrzej Prokop, [1]Emmette Hutchison, [1]Jiabu Ye, [1]Feng Liu, [1]Antony Sabin, [1]James Weatherall, [1]Cristina Duran, [1]Renee Iacona, [1]Faisal Khan, [1]Pralay Mukhopadhyay. *[1]AstraZeneca, Gaithersburg, MD, USA; [2]AstraZeneca Pharma Poland, Warsaw, MD, Poland*

Background In clinical trials that assess novel therapeutic agents in patients with non-small-cell lung cancer (NSCLC), early endpoints (e.g. progression-free survival [PFS] and objective response rate) are often evaluated as indicators of biological drug activity, and are used as surrogate endpoints for overall survival (OS). Compiling trial-level data could help to develop a predictive framework to ascertain correlation trends between treatment effects for early (e.g. odds ratio [OR] for PFS at 6 months) and late endpoints (e.g. hazard ratio [HR] OS).

Methods A dataset was compiled, which included 81 randomized, controlled trials (RCTs; Phase II–IV) of NSCLC (Stages I–IV), with 35 drugs and 156 observations. The dataset was collected from multiple source databases, including Citeline, TrialTrove, clinicaltrials.gov, and PubMed. We applied random-effects meta-analysis to correlate a variety of treatment effects for early endpoints with HR OS. We performed meta-regression analyses across different data-strata, stratified by the mechanism of action (MoA) of the investigational product (programmed death protein-1/programmed death-ligand 1 [PD-1/PD-L1], epidermal growth factor receptor [EGFR], vascular endothelial growth factor receptor, and DNA damage response).

Results Low (Spearman's rho 0.3–<0.5) to moderate (rho 0.5–<0.7) correlations were observed between HR OS and (1) HR PFS, (2) OR PFS 4 months, and (3) OR PFS 6 months for PD-1/PD-L1 trials, EGFR trials, and all trials combined (Random-effects meta-regression; P<0.05). Similar correlations were observed between each of the early endpoint treatment effects and HR OS. For example, the moderate correlation observed between OR PFS 4 months and HR OS (rho-0.579; 95% confidence interval [CI]-0.800,-0.274; meta-regression R2= 72.5%) was similar to that between OR PFS 6 months and HR OS (rho-0.633; 95% CI-0.802, -0.383; R2=86.1%) for PD-1/PD-L1 trials. Note, the reported rho values are negative as a HR<1, and an OR>1, indicate benefit with the investigational product.

Conclusions Using a comprehensive summary data set in the NSCLC space, we observed low-to-moderate correlations between treatment effects for early endpoints and HR OS across RCTs of agents with different MoAs, including trials of PD-1/PD-L1 checkpoint inhibitors. Exploration of additional endpoints, beyond RECIST, is required to identify other early indicators of efficacy that might predict HR OS. By incorporating additional trial-level parameters and building composite biomarkers using machine intelligence methods, in collaboration with innovative trial design efforts, we envisage to improve the prediction of HR OS from early endpoints.

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

Sarah Kolitz*, Yoonjeong Cha, Sailaja Battula, Rebecca Kusko, Benjamin Zeskind, Howard Kaufman. *Immuneering Corporation, Cambridge, MA, USA*

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 subsets 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 Immuneering 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