Study validates clinical utility of pan-tumor predictive biomarker for checkpoint inhibitor immunotherapy benefit

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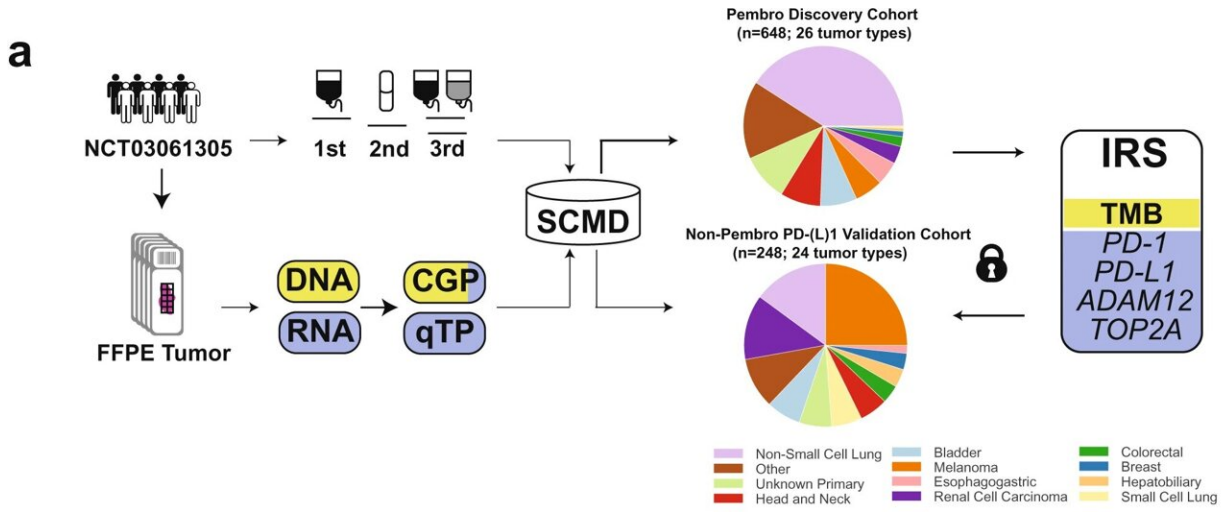

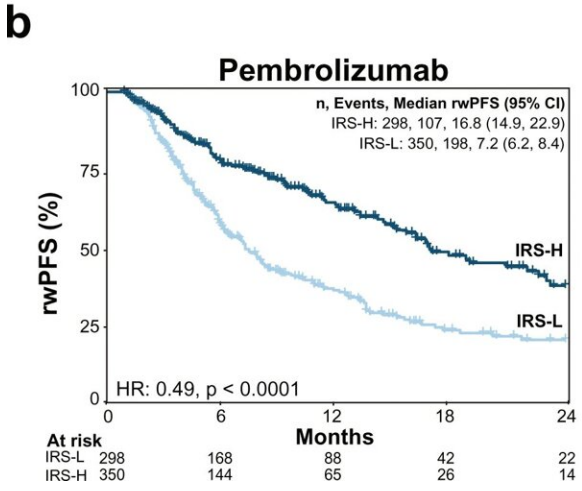

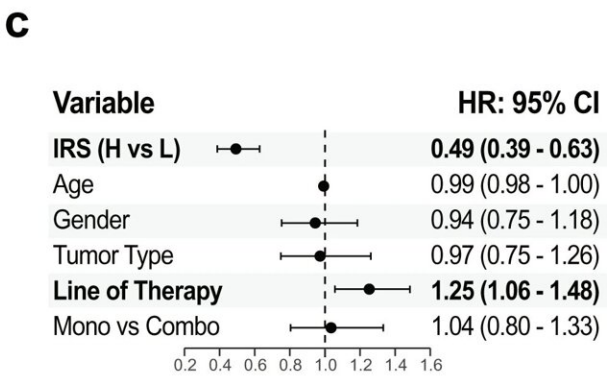

Development of an integrative immunotherapy response score (IRS) model to

stratify PD-(L)1 therapy benefit in patients with advanced solid tumors. **a** Real-world treatment and molecular profiling data from formalin fixed paraffin embedded (FFPE) tumor tissue from patients enrolled in the StrataTrial (NCT03061305) are collected in the Strata Clinical Molecular Database (SCMD). Molecular data from both DNA (yellow) and RNA (blue) include both comprehensive genomic profiling (CGP) with both DNA and RNA components, and in-parallel quantitative transcriptional profiling (qTP) comprised of RNA from analytically and clinically validated tests. To develop an integrative predictor of PD-(L)1 therapy benefit, we identified a cohort of 648 patients (from 26 tumor types) with available molecular information who were treated with a pembrolizumab (pembro; PD-1) containing systemic therapy line of treatment. Lasso-penalized Cox proportional hazards modeling with five-cross validation was used to develop the IRS model for predicting real world progression free survival (rwPFS; by time to next therapy), which includes tumor mutation burden (TMB; from CGP) and expression of *PD-1*, *PD-L1*, *ADAM12* and *TOP2A* (from qTP). The locked IRS model and threshold to assign patients to IRS-Low [L] or IRS-High [H; increased benefit] was then applied to an independent validation cohort of 248 patients (from 24 tumor types) treated with non-pembrolizumab PD-[L]1systemic monotherapy. Pie charts for the development and validation cohorts show tumor type distributions for the 11 most common tumor types and other tumor types. **b** IRS stratifies pembrolizumab rwPFS in the development cohort. Pembrolizumab rwPFS in the development cohort stratified by IRS groups is shown by Kaplan Meier analysis with the adjusted hazard ratio (HR) and *p* value (adjusted by variables shown in (**c**) for IRS-H vs. IRS-L. The number (*n*) of patients, events, and median rwPFS (with 95% confidence intervals [CI]) for each group are shown. **c** IRS is robust to potential confounders in the development cohort. Forest plot of variables included in the adjusted Cox proportional hazards model used to evaluate the ability of IRS to stratify pembrolizumab rwPFS. Adjusted hazard ratios with 95% CIs are shown for each variable with statistically significant variables bolded. *n* = 648 patients (from 26 tumor types). Credit: *Communications Medicine* (2023). DOI: 10.1038/s43856-023-00243-7

A new study validating the clinical utility of a proprietary pan-solid

tumor predictive biomarker for anti-PD-1/PD-L1 checkpoint inhibitor monotherapy benefit—called Immunotherapy Response Score (IRS)—was published in *Communications Medicine*.

Strata Oncology developed IRS using treatment data and comprehensive, clinically validated genomic and transcriptomic profiling of tumor tissue from the Strata Trial, an ongoing observational clinical trial evaluating the impact of molecular profiling for patients with advanced solid tumors. The biomarker algorithm, which was validated in an independent cohort of trial patients, captures the biology of the tumor and its microenvironment by combining tumor mutation burden (TMB) with quantitative expression of PD-L1, PD-1, ADAM12 and TOP2A.

"Our Immunotherapy Response Score meets a significant unmet medical need for an integrative diagnostic test that better predicts likelihood of benefit from anti-PD-1/PD-L1 checkpoint inhibitor monotherapy, across solid tumor types," said Scott Tomlins, M.D., Ph.D., Strata Oncology co-founder and Chief Medical Officer. "Current pan-tumor biomarkers for these treatments identify only a fraction of responsive patients, meaning far too many people who could benefit from these therapies are not being identified."

Tomlins continued, "Additionally, immunotherapy is now often combined with chemotherapy. Our exploratory data in non-small cell lung cancer indicate that IRS may be a useful tool to help determine which patients can achieve similar benefit without the toxic effects of chemotherapy."

Key findings from the study include:

- IRS predicted real-world progression-free survival and overall survival in anti-PD-1/PD-L1 monotherapy treated patients across tumor types

- IRS-high status predicted similar duration of benefit as tumor mutational burden (TMB)-high status across tumor types, but identified twice as many patients who may benefit from checkpoint inhibitor treatment as TMB
- In non-small cell lung cancer (NSCLC) patients who were IRS-high, there was no significant benefit of combination therapy (pembrolizumab + chemotherapy) compared to monotherapy (pembrolizumab)

"Immunotherapy has transformed cancer care and now with IRS we have the ability to predict benefit across tumor types," said Dan Rhodes, Ph.D., Strata Oncology co-founder and Chief Executive Officer. "We are excited to put this novel biomarker into the hands of physicians to help them ensure every patient gets their best possible therapy."

More information: Scott A. Tomlins et al, Development and validation of an integrative pan-solid tumor predictor of PD-1/PD-L1 blockade benefit, *Communications Medicine* (2023). DOI: 10.1038/s43856-023-00243-7

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