INTEGRATION OF MOLECULAR CANCER CLASSIFICATION AND NEXT-GENERATION SEQUENCING TO IDENTIFY METASTATIC PATIENTS ELIGIBLE FOR IMMUNE CHECKPOINT INHIBITORS

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Background: Immune checkpoint inhibitors (ICIs) have improved patient outcomes and are a new standard of care for treating a variety of cancers. Eligibility for ICIs is established through determination of tumor type and use of predictive biomarkers. PD-L1, microsatellite instability (MSI), and tumor mutation burden (TMB) are FDA-approved predictive biomarkers for ICIs. However, the validity of these biomarkers remains controversial, as studies have shown a failure to predict ICI response in many cancer types. The 92-gene assay (CancerTYPE ID) is a validated gene expression classifier of 50 tumor types and subtypes for metastatic patients with ambiguous diagnoses. CancerTYPE ID provides critical cancer type identification to guide ICI treatment eligibility and selection. In the current study, analyses integrating tumor type with multimodal biomarker testing for PD-L1 and TMB were evaluated to identify patients for ICI eligibility.

Methods: MOSAIC (Molecular Synergy to Advance Individualized Cancer Care) is an IRB-approved, de-identified database of CancerTYPE ID results from 2572 patients with tumor-specific multimodal biomarker testing by next-generation sequencing for TMB and immunohistochemistry for PD-L1. The Cochran-Mantel-Haenszel test was used to evaluate the relationship between PD-L1 and TMB across tumor types.

Results: Tumor type was determined in 2377 of 2572 cases (92.4%), comprising 27 different tumor types including 14 tumor types with FDA-approved ICI therapies. Among the top 20 tumor types, PD-L1 was present in a larger proportion of tumors (weighted mean=78.9%, range=58.3%-100%) versus TMB (20.9%, 0%-72.7%) (figure 1). Varying expression levels of PD-L1 and TMB were noted across tumor types (Figure 1), and no relationship between PD-L1 and TMB (P=0.15) was observed. Prevalence of high TMB in melanoma (42.9%) and lung adenocarcinoma (38.9%), which are more likely to respond to ICI treatment, are consistent with published data; however, prevalence of high TMB in mesothelioma (20.0%), sarcoma (23.6%) and prostate adenocarcinoma (33.3%), which are not likely to respond to ICI treatment, are higher than previously reported.

Conclusions: Tumor type classification and cellular context are critical for ICI eligibility. CancerTYPE ID successfully differentiated 14 ICI-eligible tumor types from 13 non-ICI-eligible tumor types. Further, since there is no relationship between PD-L1 and TMB for different tumor types, accurate tumor type identification is necessary to select the most appropriate biomarker. This highlights the clinical utility of CancerTYPE ID combined with multimodal biomarker testing to guide ICI treatment and predict response based on tumor type identification, which may improve outcomes in patients with metastatic cancer.

REFERENCES

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