A 27-gene IO assay to capture the tumor immune microenvironment is associated with response in metastatic and primary tumors

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Introduction

- ICIs have radically altered standard of care for NSCLC patients, yet only a fraction of patients respond. Thus, there is an urgent need for biomarkers to aid in clinical decision making.
- Current biomarkers rely on therapeutic target assessment (PDL-1 IHC) or tumor antigenicity (TMB), but do not assess the surrounding tumor immune microenvironment (TIME).
- New biomarkers capable of assessing the immune phenotypes of either the primary or metastatic site might expand access and improve response rates to ICIs.
- The CLIA-validated 27-gene immuno-oncology (IO) assay was developed to assess both inflammatory effector cell and surrounding cancer associated fibroblasts phenotypes in the TIME.
- The 27-gene assay has been previously validated as associated with response to ICI treatment in TNBC, renal, urothelial and NSCLC tumor types.
- The aim of this study was to assess the potential redundancy of phenotypic assessment of the stromal versus tumor infiltrated TIME, and the association of the 27-gene IO assay with ICI response measured in primary tumor and metastatic sites.

Methods

- Archival NSCLC samples were macro-dissected to enrich the tumor from the surrounding stromal tissue (Figure 1).
- RNA was extracted from the macro-dissected samples as well as from NSCLC samples obtained from either primary or metastatic sites. RNA was then processed through the 27-gene IO assay workflow to obtain IO scores.
- Spearman correlation was used to assess the relationship between whole tissue samples and macro-dissected samples.
- Kaplan-Meier curves were fitted to estimate the association between 1-year PFS and IO score in the subset of patient samples obtained from primary tissue versus patients with a metastatic site biopsy.

Tumor Cell Content

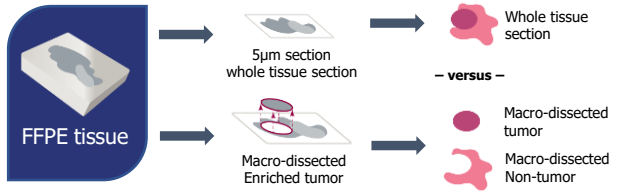

Figure 1: Macro-dissection of tumor or non-tumor tissue from archival FFPE tissue

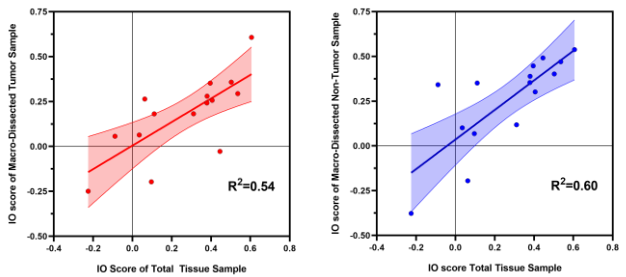

Figure 2: The IO scores obtained from macro-dissected A) tumor and B) non-tumor tissue from archival FFPE specimens are correlated with the IO score of the total tissue specimen.

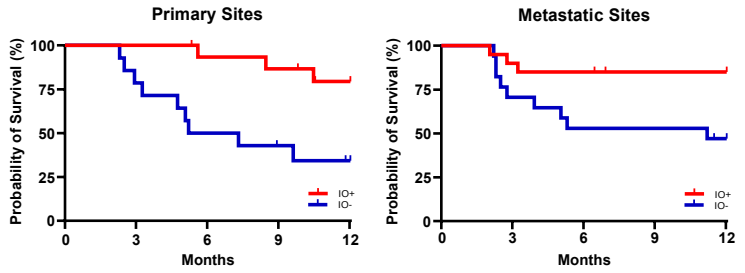

Figure 3: The IO scores obtained from A) primary or B) metastatic tumor sites are associated with 1-year PFS. Primary sites HR=0.238, p=0.02, n=37. Metastatic sites HR=0.281, p=0.02, n=33.

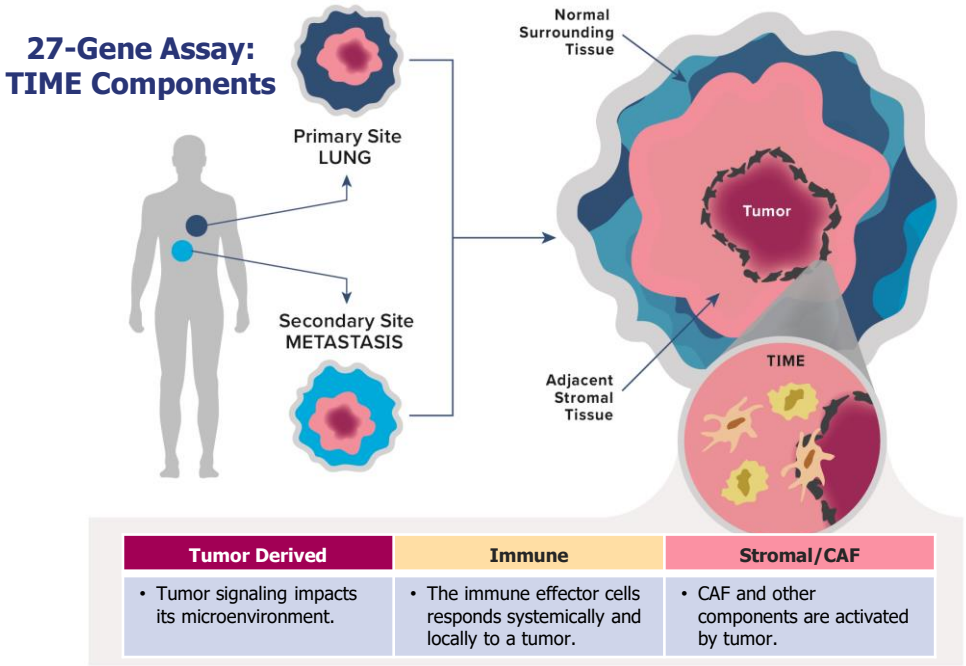

Figure 4: Schematic relationship between TIME and a tumor in either its primary or metastatic site. The 27-gene IO assay has demonstrated an ability to capture an underlying TIME signature regardless of its primary or metastatic location despite different surrounding tissues. CAF, Cancer Associated Fibroblast

Discussion

The genes used in the IO score measure three components of the TIME, which is distributed throughout the tumor and adjacent non-tumor tissue. This data shows that the IO scores from both macro-dissected tumor tissue, or adjacent non-tumor tissues are both correlated with the IO score from the whole sample. This suggests some redundancy in tumor versus surrounding tissue derived phenotypic signal, and supports previous observations that the IO score is tolerant of small samples (core biopsies) with differing representation of tissue compartments.

As an extension of this observation, we sought to determine whether the IO scores from either primary and or metastatic tumor sites were associated with PFS. The data support that IO scores obtained from tissue sampled from either primary tumors or metastatic tumors sites are adequate for assessment of association with outcome.

Conclusion

The 27-gene IO assay derives phenotypic information from both the TIME intermixed with tumor cells and the TIME in surrounding stroma. Association with ICI response was found in either primary or metastatic samples. This suggest that this assay is unusually tolerant of potentially confounding normal tissue elements and stochastic sampling differences that may confound assays that rely upon inflammatory phenotypes alone.

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Presenter DISCLOSURES

Ineligible Company (formerly: Commercial Interest)	**Relationship(s)**
Matthew G. Varga	Employee

The 27-gene IO assay highlights the key, universal, activities of the TIME such that its implementation can be used across indications for informing clinical decision making pertinent to immune checkpoint inhibitors.