Programmed death-ligand 1 (PD-L1) Characterization of Circulating Tumor Cells (CTCs) and White Blood Cells in Muscle Invasive and Metastatic Bladder Cancer Patients

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PD-L1 immune checkpoint therapies have demonstrated durable responses in a subset of metastatic cancer patients including those with melanoma, non-small cell lung cancer (NSCLC), and bladder cancer. Recent clinical studies have observed improved progression free survival (PFS) after treatment with PD-L1-directed therapy in patients with higher expression of PD-L1 protein in tumor sections in addition to the magnitude of PD-L1 expression on tumor infiltrating T-cells being investigated as a potential biomarker. Currently, fresh solid tumor biopsy is required for these assays, which can be difficult to access, lead to patient morbidity, and miss relevant subpopulations reflective of tumor heterogeneity.

We have developed an assay to quantify PD-L1 expression on circulating tumor cells (CTCs) and white blood cells (WBCs) detected using the Epic CTC Platform. Here, we present data on the incidence, morphology, and PD-L1 expression of CTCs and WBCs detected from the venous circulation of 17 muscle invasive and metastatic bladder cancer patients prior to initiation of PD-L1 immune checkpoint therapy.

Background

Blood was drawn from 17 muscle invasive and metastatic bladder cancer patients, just prior to PD-L1 immune checkpoint therapy, and sent to Epic Sciences for processing with the Epic CTC PD-L1 assay.

Methods

Blood was drawn from 17 muscle invasive and metastatic bladder cancer patients, just prior to PD-L1 immune checkpoint therapy, and sent to Epic Sciences for processing with the Epic CTC PD-L1 assay.

Bladder Cancer CTC Subtype Heterogeneity

Assessment of PD-L1 assay sensitivity and specificity: Left: A monoclonal antibody against PD-L1 was tested using high (H920, medium (H920), low (DU-145)) and negative (Lo2, U937) PD-L1-expressing cell lines to determine assay sensitivity and specificity. As the optimal antibody concentration, mean H920/PD-L1 expression was determined to be 0.4% higher than mean background staining in negative controls. Right: Representative images.

CTCs w/ no abnormalities

CTCs w/ at least 1 abnormality

CTCs w/ all abnormalities

Total CTCs (PD-L1(-)) w/ normal

Total CTCs (PD-L1(+)) w/ normal

Recent studies indicate that the presence of PD-L1(+) WBCs in solid tumors is a potential PD-1 immune checkpoint therapy response biomarker, both as a univariate biomarker or as part of a multivariate panel.

Conclusion

- The Epic CTC Platform can detect PD-L1(+) CTCs in bladder cancer patients.
- Bladder cancer CTCs expressing PD-L1 are frequently CK(-) and show genetic abnormalities consistent with malignant origin and PD-L1 localization consistent with established literature.
- Bladder cancer patients frequently have higher PD-L1(+)ICD45(+) WBC counts.
- Correlation with treatment response is necessary to determine if the presence of PD-L1(+) CTCs or high PD-L1(+) WBC counts may be used for patient selection and as early pharmacodynamic biomarkers of response to PD-1/PD-L1 directed therapy.