Programmed Death-1 Ligand (PD-L1) Expression on Circulating CD45(-) Cells is an Independent Prognostic Factor for Overall Survival in Patients with Lung Cancer

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Background

Lung cancer patients currently require invasive tissue biopsies to diagnose and profile tumors prior to treatment. There is a need for tumor profiling from circulating biomarkers to avoid invasive and complicated procedures. PD-L1 is an immune-suppressor via interaction with its receptor, PD-1, expressed on activated T- and B-cells. PD-L1 upregulation in cancer cells enables evasion of immune surveillance by the inhibition of immune cell activation. PD-L1 expression in lung cancer is associated with increased tumor invasiveness and worse overall survival.

PD-L1 expression on lung cancer biopsy specimens correlates with efficacy of immune checkpoint therapy. However, the expression of PD-L1 on circulating cells has not been fully characterized, limiting their ability to guide therapy. Using the Epic Sciences PD-L1 assay, we sought to correlate patient outcome with PD-L1(+ circulating CM45(-) cells, as a prerequisite to prospective evaluation as a predictive biomarker in a prospective, multicenter cohort.

Methods

145 peripheral blood samples were collected from suspected lung cancer patients at three clinical sites prior to diagnostic biopsy, or at follow-up and shipped to Epic Sciences. All nucleated cells were plated on glass slides and subjected to immunofluorescence (IF) staining and CTC identification by fluorescent scanners and algorithms analysis. CTCs, defined as traditional (CK, CD45) with intact morphology and distinct DAPI nuclei, appendage (CK, CD68, non-stainable nuclei) or CD45(-, intact and distinct nuclei) were identified. Samples were stained and characterized with the CST antibody PD-L1 (11F1L3) XP® Rabbit mAb #66864 to assess protein expression.

PD-L1 Protein Assay Development (cont.)

Figure 3: Scatter Plot of Circulating CD45(-) Cells, showing patient distribution by PD-L1 burden and Kaplan-Meier survival analysis.

PD-L1 Expression is a Prognostic Factor for Overall Survival at Diagnosis and Follow-Up

Figure 7: PD-L1(+) CTCs is a Prognostic Factor for Overall Survival at Diagnosis and Follow-Up. Kaplan-Meier estimates of overall survival from baseline date and multivariate estimate comparison to AICC staging (B). Follow-up NCI-CTC estimates (C) of overall survival from baseline date and multivariate estimate comparison to AICC staging (D). 

Conclusions

- In a prospectively enrolled, multicenter cohort, PD-L1(+) cell burden prognosticated OS in univariate and multivariate settings, independent to AICC staging in pre-biopsy and follow-up samples.
- This lays the groundwork for PD-L1(+)-circulating cells to be prospectively assessed as a predictive biomarker to immune checkpoint inhibitors in lung cancer.