PD-L1 Profiling of Circulating Tumor Cells is a Viable Companion Diagnostic for Checkpoint Inhibitor Therapy in Lung Cancer.

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Background

Selection of Checkpoint Inhibitor therapies in several cancers are based on PD-L1 expression in tumor tissue determined by IHC. Invasive biopsy to obtain tumor tissue is associated with procedural risks, sequelae and expenses. Though PD-L1 profiling of Circulating Tumor Cells (CTCs) has been attempted previously, limitations arise due to low yields of CTCs in conventional means. We describe a novel approach for harvesting sufficient CTCs that can be used for PD-L1 profiling by Immunocytochemistry (ICC).

Methods

15 ml peripheral blood was collected from 95 patients with histopathologically confirmed diagnosis of lung cancer. Peripheral Blood Mononuclear Cells (PBMCs) were isolated by centrifugation. CTCs were enriched from PBMCs via an epigenetically acting stabilization process which induces apoptosis in normal (non-cancerous) cells while simultaneously conferring survival privilege on apoptosis-resistant cells of tumorigenic origin (CTCs). Surviving CTCs were confirmed by immunostaining for EpCAM and pan-CK. CTCs were further profiled for Napsin and TTF-1 (Lung-specific), p40 (Squamous Cell Carcinoma specific), CK7 (Adenocarcinoma specific), Synaptophysin and Chromogranin (Neuroendocrine carcinoma specific) and PD-L1 (22c3).
Results

Viable CTCs could be enriched and harvested in all 95 samples regardless of treatment status and extent of disease (metastatic status). Deep ICC profiling including all organ- and subtype-specific markers as well as PD-L1 could be conducted in 71 out of the 95 samples (74.7%). Among the 71 samples which were evaluable, PD-L1 positivity was observed in 33 samples (46.5%). PD-L1 expression in these 33 samples was quantitatively estimated and assigned as ‘Low’, ‘Moderate’ or ‘High’. Among the 33 PD-L1 positive samples, 25 (75.8%) had low PD-L1 expression, 7 (21.2%) had moderate expression, and 1 (3%) had high expression.

Conclusion

ICC profiling of CTCs is a viable approach for determining suitability of patients for checkpoint inhibitor treatments. Quantitative determination of PD-L1 expression is possible using this method and appears to have clinical relevance in determining the probability of favourable response to checkpoint inhibitor treatment.