ORIGINAL ARTICLE

PD-L1 Immunohistochemistry Comparability Study in Real-Life Clinical Samples: Results of Blueprint Phase 2 Project

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ABSTRACT

Objectives: The Blueprint (BP) Programmed Death Ligand 1 (PD-L1) Immunohistochemistry Comparability Project is a pivotal academic/professional society and industrial collaboration to assess the feasibility of harmonizing the clinical use of five independently developed commercial PD-L1 immunohistochemistry assays. The goal of BP phase 2 (BP2) was to validate the results obtained in BP phase 1 by using real-world clinical lung cancer samples.

Methods: BP2 were conducted using 81 lung cancer specimens of various histological and sample types, stained with all five trial-validated PD-L1 assays (22C3, 28-8, SP142, SP263, and 73-10); the slides were evaluated by an international panel of pathologists. BP2 also assessed the reliability of PD-L1 scoring by using digital images, and samples prepared for cytological examination. PD-L1 expression was assessed for percentage (tumor proportional score) of tumor cell (TC) and immune cell areas showing PD-L1 staining, with TCs scored continuously or categorically with the cutoffs used in checkpoint inhibitor trials.

Results: The BP2 results showed highly comparable staining by the 22C3, 28-8 and SP263 assays; less sensitivity with the SP142 assay; and higher sensitivity with the 73-10 assay to detect PD-L1 expression on TCs. Glass slide and digital image scorings were highly concordant (Pearson correlation >0.96). There was very strong reliability among pathologists in TC PD-L1 scoring with all assays (overall intraclass correlation coefficient [ICC] = 0.86–0.93), poor reliability in IC PD-L1 scoring (overall ICC = 0.18–0.19), and good agreement in assessing PD-L1 status on cytological cell block materials (ICC = 0.78–0.85).

Conclusion: BP2 consolidates the analytical evidence for interchangeability of the 22C3, 28-8, and SP263 assays and lower sensitivity of the SP142 assay for determining tumor proportion score on TCs and demonstrates greater sensitivity of the 73-10 assay compared with that of the other assays.

Keywords: Immunooncology; Checkpoint inhibitors; Companion diagnostics; Complementary diagnostics; Cytology; Pathology

Introduction

Immune checkpoint inhibitor therapies targeting the programmed death 1/programmed death ligand 1 (PD-L1) pathway have become part of the standard of care in oncology.[1] At least five inhibitors (nivolumab, pembrolizumab, atezolizumab, durvalumab, and avelumab) have been approved by drug regulatory bodies in one or more countries for the treatment of several tumor types and for various indications. For patients with advanced NSCLC without driver mutations (e.g., *EGFR,* ALK receptor tyrosine kinase gene [*ALK*], *ROS1*, and *BRAF*) that are treatable by approved targeted therapies, nivolumab, pembrolizumab, and atezolizumab are all available as second-line treatment with (for pembrolizumab) or without (for nivolumab and atezolizumab) biomarker selection. Pembrolizumab is available for first-line monotherapy but only in patients with high PD-L1 expression,[2,3] and in some countries, for use in combination with chemotherapy without any biomarker selection. Importantly, almost all clinical trials involving these inhibitors have demonstrated consistent correlation between their response rates and outcomes and the tumor cell (TC) PD-L1 expression levels, as measured by PD-L1 immunohistochemistry (IHC). Therefore, despite the fact that only pembrolizumab requires a PD-L1 IHC