Comparison of continuous measures across diagnostic PD-L1 assays using image analysis

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Background: Tumour programmed cell death ligand-1 (PD-L1) expression is a key biomarker in identifying patients who may have an enhanced response to non-small cell lung cancer treatment using anti-PD-L1 (e.g. nivolumab and pembrolizumab) or anti-PD-L1 (e.g. atezolizumab and durvalumab). Each treatment is currently used in conjunction with an individual PD-L1 diagnostic immunohistochemistry (IHC) assay and it is unclear whether immunolabelling parameters determined by pathologists are comparable across assays. We extended previous studies (Ratcliffe et al Clin Cancer Res 2017; Ratcliffe et al ASCO-SITC 2017 (abstr 7)) by performing image analysis (IA) with a customised PD-L1 scoring solution to permit a quantitative comparison of the 4 PD-L1 IHC assays.

Methods: We developed an IA scoring algorithm that enabled us to quantify the percentage of positive tumour cells on a whole slide image for 4 PD-L1 assays (Ventana SP263, Ventana SP142, Dako 28-8, Dako 22C3). The analysis was applied to 473 commercially available NSCLC cases (180 cases with SP142). We co-registered the consecutive slides per case and harmonised tumour and exclusion annotations to ensure that readouts of identical areas were compared per case.

Results: In agreement with previous reports, IA results showed concordance between 3 assays, whereas the SP142 assay was discordant. Moreover, high correlation was observed between IA results and pathologist ratings. This correlation could be further improved by matching the information the pathologist received to the same information used in the IA solution: blinding against the assay, scoring on digital scans and masking of non-comparable image regions. The remaining differences represent the differing sensitivity profiles of the assay protocols.

Conclusions: The results of our objective IA suggest differences in sensitivity between the analysed assays. Importantly, despite the observed differences, we confirm previous findings indicating concordance between 22C3, 28-8 and SP263. In addition, our analysis provides a continuous distribution of PD-L1 measurements allowing deeper characterisation of the samples. Tobias Wiestler and Moritz Widmaier are joint first authors.

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