COMPUTATIONAL PATHOLOGY DELIVERS OBJECTIVE AND QUANTITATIVE PD-L1 EXPRESSION ANALYSIS FOR ENRICHMENT OF RESPONDERS TO DURVALUMAB IN NON-SMALL CELL LUNG CANCER (NSCLC)

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Background The pathologist’s visual assessment of tumor proportion score (TPS) with 25% cutoff on PD-L1 stained tissue samples is an established method to select metastatic NSCLC patients that are likely to respond to an anti-PD-L1 monotherapy. However, manual scoring is often subject to subjectivity in human perception and there remains a critical need for more objective and quantitative methods to assess PD-L1 expression in immuno-oncology.

Methods We used deep learning (DL) based image analysis (IA) to generate a novel PD-L1 Quantitative Continuous Score (QCS) in tumor cells. PD-L1 QCS consists of two DL models to first segment epithelial regions and second detect membranes, cytoplasm and nuclei of each tumor cell in PD-L1 immunohistochemically (IHC) stained tissue slides. The PD-L1 expression of each tumor cell compartment was estimated by the respective optical density (OD) of DAB, and tumor cells with a membrane OD greater than ODmin are considered as PD-L1-positive. A slide comprising at greater percentage of PD-L1-positive tumor cells than a cutoff value (CoV) is considered QCS-positive. The ODmin and CoV parameters were linked to patient overall survival (OS), by minimizing the Kaplan Meier log-rank p-values and keeping at least 50% prevalence in the QCS-positive subgroup. Fully supervised QCS-IA models were extensively trained using pathologists’ annotations and the performance was validated on unseen data to ensure its generalization and robustness. The QCS IA was locked and blindly applied on clinical trial data (NCT01693562, durvalumab-treated late-stage NSCLC cohort) without further refinement.

Results Data analytics techniques were used to determine optimal PD-L1 QCS parameters for the clinical trial cohort of N=162 late-stage NSCLC patients. A PD-L1 QCS algorithm (ODmin=8, CoV=57%) is able to stratify durvalumab-treated NSCLC patients at a higher prevalence and more significant log rank p-value (64%, p=0.0001) for OS (figure 1) compared to pathologist TPS (59%, p=0.01). Median OS times of (19.2 months vs 7.9 months) was observed in the QCS-positive vs negative subgroups, respectively. The box plots (figure 2) indicate an overall good agreement (72% concordance) of the fully automated QCS with the pathologists TPS, which quantitatively supports the positive visual assessment of the cell segmentation accuracy.

Conclusions The novel Quantitative Continuous Scoring (QCS) provides an objective way of correlating a quantitative estimate of PD-L1 IHC expression on tumor cells with survival of durvalumab-treated NSCLC patients. This data establishes a first proof-of-concept demonstrating the potential utility of PD-L1 QCS towards precision medicine in immuno-oncology.

REFERENCES

Abstract 365 Figure 1 Kaplan Meier (KM) curves for OS stratification. KM curves for Overall Survival (OS) stratification with (left) manual PD-L1 TPS score (25% cutoff), and (right) automated QCS (57% cutoff).

Abstract 365 Figure 2 QCS scores within TPS positive and negative groups. Box plot indicating percent positive cells (OD>8) as measured by PD-L1 QCS within the PD-L1 high (red) and low (blue) groups as per pathologist assessment by TPS.
Ethics Approval Clinical study NCT01693562, from which data in this report were obtained, was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol, amendments, and participant informed consent document were approved by the appropriate institutional review boards.

http://dx.doi.org/10.1136/jitc-2021-SITC2021.365