Abstract #5358

Digital SP263 PD-L1 tumor cell scoring in non-small cell lung cancer achieves comparable outcome prediction to manual pathology scoring

Hen Prizant[1*], John Shamshoian[2*], John Abel[2], Andrew Beck[2], Laura Chambre[2], Stephanie Hennek[2], Hartmut Koeppen[1], Daniel Ruderman[1], Meghna Das Thakur[1], Michael Montalto[2], Ben Trotter[2], Ilan Wapinski[2], Wei Zou[1], Minu K. Srivastava[1#], Jennifer M. Giltnane[1#]

[1]Genentech, Inc, South San Francisco, CA, USA; [2]PathAI, Boston, MA USA; *Co-first author, #Co-senior author

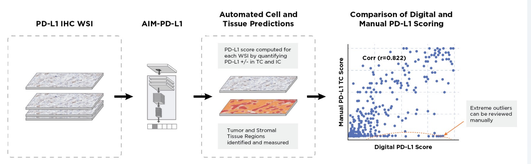
INTRODUCTION

- Tumor cell (TC) PD-L1 expression is predictive of response to PD-L1-targeted therapy, and accurate scoring is crucial for treatment selection. TC scoring, a quantitative assessment of the proportion of tumor cells expressing PD-L1, relies on manual assessment of immunohistochemically labeled tissue which can be variable due to subjective pathologist assessment.
- As a digital alternative, a clone-agnostic AI-based model for PD-L1 quantification in non-small cell lung cancer (AIM-PD-L1 NSCLC) was developed[1].
- AIM-PD-L1 was deployed on whole slide images (WSI) from a front-line Phase 3 study of anti-PD-L1 atezolizumab combination with carboplatin and paclitaxel, and/or bevacizumab in metastatic NSCLC (IMpower150; NCT02366143). Digital and manual SP263 PD-L1 TC scores were compared and interrogated for their respective potential to predict response to atezolizumab combination treatments.

PATIENTS AND METHODS

AIM-PD-L1 automatically identifies and quantifies tissue areas (cancer epithelium, cancer stroma, necrosis, and normal), and cells (cancer cells, lymphocytes, macrophages, and other cells) in digitized images of tumor tissue, as well as PD-L1 positivity in cancer and immune cells[1] (**Figure 1, Figure 2**).

Figure 1. Deployment of AIM-PD-L1



AIM-PD-L1 deployment in PD-L1 WSI yields model prediction and quantification of cells and tissues that show strong agreement with pathologist manual scoring. Outlier scores can be identified and assessed manually.

AIM-PD-L1 was deployed on IMpower150 whole slide images (n=768) digitized from SP263-labeled slides with available manual pathologist TC scores to quantify tissue regions and individual TCs.

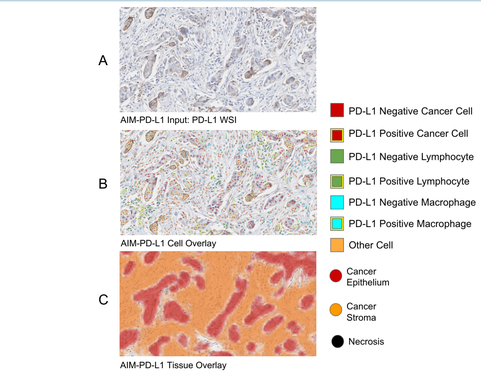
PD-L1 expression status was determined for each TC and a slide-level (digital) TC score was generated by computing the proportion of TCs expressing PD-L1.

Overall survival (OS) and progression free survival (PFS) analyses of patients at selected cutoffs of 1%, 50%, and across a continuum of cutoffs from 0% to 100% PD-L1 TC by digital and manual methods were conducted, comparing groups treated with or without atezolizumab in combinations with carboplatin and paclitaxel, and/or bevacizumab.

Digital and manual scores were compared using agreement rates, Lin's concordance and Spearman's correlation coefficients, and hazard ratios (HRs) were calculated for OS and PFS analysis.

RESULTS

Figure 2. AIM-PD-L1 Cell and Tissue Overlays

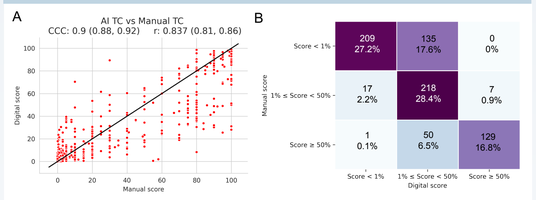


Example of AIM-PD-L1 deployment in IMpower150. Input shows a region of interest of a SP263 PD-L1 WSI (A), and cell (B) and tissue (C) overlay outputs

At the slide level, overall correlation between continuous digital and manual scores was high (r 0.84 [95% CI 0.81-0.86]; **Figure 3A**).

At the 1% cutoff, digital assessment of PD-L1 positivity identified more positive patients than manual scoring (70% vs. 55% prevalence, respectively; **Figure 3B**).

Figure 3. Comparison of Manual and Digital PD-L1 Scoring



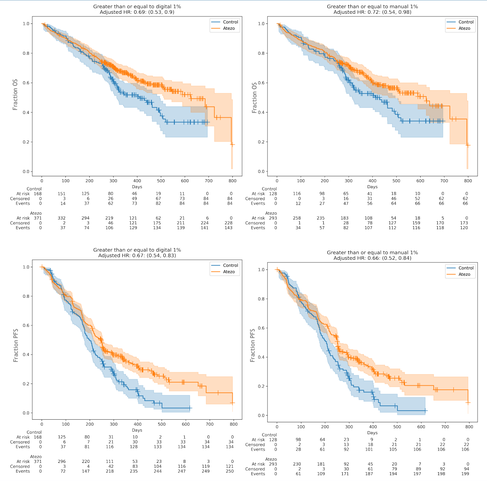
Concordance between digital and manual PD-L1 scoring across continuous cutoffs (A), and above and below the 1% and 50% cutoffs (N/% of total patients selected from cohort) (B)

Treatment benefit was assessed for the groups of PD-L1 positive patients identified by digital and manual methods, at the 1% and 50% cutoffs (**Figures 4 and 5**).

Both OS and PFS effect sizes were comparable for digitally and manually-selected patients at the 1% cutoff: OS digital HR 0.69 (95% CI 0.53-0.9) and manual HR 0.72 (95% CI 0.54-0.98); PFS digital HR 0.67 (95% CI 0.54-0.83), and manual HR 0.66 (95% CI 0.52-0.84) (**Figure 4**).

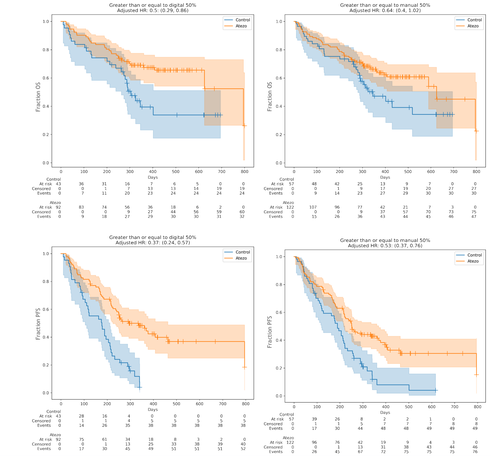
At the ≥50% PD-L1 TC cutoff (**Figure 5**), numerical improvement was observed in OS and PFS by digital scoring compared to manual (digital OS HR 0.5 [0.29-0.86] compared to manual OS HR 0.64 [0.4-1.02], and digital PFS HR 0.37 [0.24-0.57], compared to manual PFS HR 0.53 [0.37-0.76]).

Figure 4. OS and PFS at 1% PD-L1 Positive Cutoff by Digital and Manual Scoring



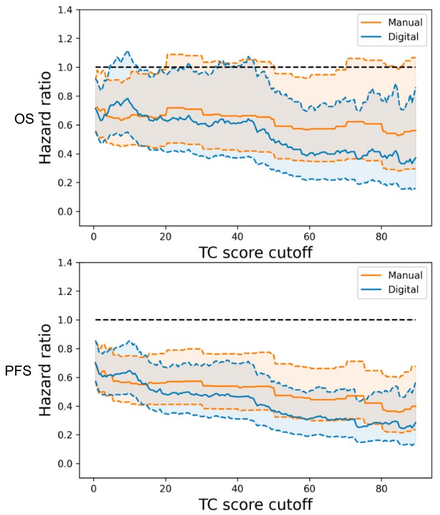
Benefit of Atezolizumab in combination with carboplatin and paclitaxel, and/or bevacizumab (Atezo) in comparison to carboplatin and paclitaxel, and bevacizumab (Control) treatment in patients with PD-L1 positivity at the 1% cutoff by digital and manual scoring

Figure 5. OS and PFS at 50% PD-L1 Positive Cutoff by Digital and Manual Scoring



Benefit of Atezolizumab in combination with carboplatin and paclitaxel, and/or bevacizumab (Atezo) in comparison to carboplatin and paclitaxel, and bevacizumab (Control) treatment in patients with PD-L1 positivity at the 50% cutoff by digital and manual scoring

Figure 6. OS and PFS with Atezolizumab in Combination with Carboplatin and Paclitaxel, and/or Bevacizumab Across Continuous Digitally and Manually Scored Cutoffs



Benefit of Atezolizumab in combination with carboplatin and paclitaxel, and/or bevacizumab treatment in patients with PD-L1 positivity across a continuous range of cutoffs by digital and manual scoring. Solid colored lines indicate HR, which are bounded by same-colored dashed lines that indicate confidence interval upper and lower bounds; dashed black line indicates a constant HR of 1 as reference.

For OS and PFS, continuous digital PD-L1 TC scores showed that treatment benefit improved in a continuous manner for patients with scores ≥50% compared to manual scoring (**Figure 6**).

CONCLUSIONS

- AIM-PD-L1 scoring was as effective at predicting outcomes as manual using the ≥1% SP263 PD-L1 TC expression, and at the ≥50% TC cutoff digital scoring identified a subgroup with enriched efficacy compared to manual.
- Notably, treatment benefit was seen in patients identified as PD-L1 positive by digital scoring across all cutoffs, in line with previous observations.[2]
- Continuous improvement was seen in HRs across all cutoffs in patients identified by digital pathology, a trend not seen in patients selected by manual scoring.
- Further evaluation of the accuracy and reproducibility of PD-L1 scoring by digital pathology as well as its potential use for patient enrollment or stratifications in clinical trials is needed.

AUTHOR EMAIL

Minu K. Srivastava
(srivastava.minu@gene.com)
Jennifer M. Giltnane
(giltnane.jennifer@gene.com)

REFERENCES

1.Griffin et al., Proceedings of the American Association for Cancer Research Annual Meeting 2022 Cancer Res 2022;82(12_Suppl)

2.Baxi et al. (2022) Modern Pathology 35 (11), 1529-1539.

ACKNOWLEDGMENTS

•The patients and their families
•The study was funded by Genentech
•Third-party writing assistance was provided by Health Interactions

DISCLOSURES

H.P., H.K., D.R., M.D.T., W.Z., M.K.S., and J.M.G. are employees of and hold stock or stock options in Genentech, Inc.

J.S., J.A., A.B., L.C., S.H., M.M., B.T., and I.W. are employees of and hold stock or stock options in PathAI, Inc.