Inter-reader Reliability of Programmed Death Ligand-1 (PD-L1) Scoring Using the VENTANA PD-L1
(SP263) Assay in Non-Small Cell Lung Cancer (NSCLC)

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Background

• Significant repositioning is targeting the immune checkpoint programmed cell death-1 (PD-1) programmed cell death-1 (PD-1) pathway for the treatment of patients with various cancers, including non-small cell lung cancer (NSCLC) and oesophageal adenocarcinoma (EAC).
• Clinical data from multiple studies across several indications have demonstrated that PD-L1 expression levels can be used to select patients for treatment with anti-PD-L1 agents.
• The VENTANA PD-L1 (SP263) Assay is an immunohistochemical diagnostic assay for anti-PD-L1 immune checkpoint inhibition.
• It is approved by the US FDA as a complementary diagnostic for NSCLC.

Methods

• Six expert pulmonary pathologists from different European sites independently scored 520 NSCLC tumour samples using the VENTANA PD-L1 (SP263) Assay.
• Statistical analyses were performed using STATA 13.1 (StataCorp, Texas, USA).
• Agreement between pathologists was determined by two observers - each observer scored 250 tumour samples.

Results

Table 1. Overall agreement between pathologists for PD-L1 TC scores across cutoffs

| PD-L1 cut-off | OPA | GPA | OA | ACA | RR
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<tr>
<td>TC ≥1%</td>
<td>98.5% (98.5–99.1)</td>
<td>98.5% (98.3–99.1)</td>
<td>99.0% (98.8–99.2)</td>
<td>99.0% (98.8–99.2)</td>
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<td>TC ≥25%</td>
<td>95.0% (94.3–95.8)</td>
<td>95.0% (94.3–95.8)</td>
<td>95.0% (94.3–95.8)</td>
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<td>TC ≥50%</td>
<td>94.3% (93.5–95.2)</td>
<td>94.3% (93.5–95.2)</td>
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Table 2. ICC for reliability of scores between pathologists

| Class    | ICC (95% CI) | Interpretation lower bound
|----------|-------------|---------------------------|
| OPA      | 0.89 (0.87–0.91) | Excellent
| GPA      | 0.81 (0.78–0.84) | Good
| OA       | 0.78 (0.75–0.80) | Good
| ACA      | 0.76 (0.73–0.79) | Good
| RR       | 0.75 (0.72–0.78) | Good

Table 3. ICC for reliability of scores between pathologists for PD-L1 IC scores across cutoffs

| IC cut-off | OPA | GPA | OA | ACA | RR
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<tr>
<td>IC ≥5%</td>
<td>92.5% (92.1–92.9)</td>
<td>92.5% (92.1–92.9)</td>
<td>93.0% (92.6–93.4)</td>
<td>93.0% (92.6–93.4)</td>
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<td>IC ≥25%</td>
<td>90.0% (89.3–90.7)</td>
<td>90.0% (89.3–90.7)</td>
<td>90.0% (89.3–90.7)</td>
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<tr>
<td>IC ≥50%</td>
<td>88.3% (87.5–89.1)</td>
<td>88.3% (87.5–89.1)</td>
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Conclusions

• Assessment of IC scores by expert pathologists was highly reproducible in NSCLC tumour samples using the VENTANA PD-L1 (SP263) Assay, building confidence in the performance of this assay in patient selection for anti-PD-L1 therapy.
• PD-L1 staining on ICs is not included in the assays that aim to identify patients eligible for immuno-oncology monotherapy treatment in NSCLC.
• PIC and IC scoring were not reproducible in NSCLC tumour samples, suggesting that the assay methodology is unsuitable for this tumour type and assay.
• The results for NSCLC are in contrast with those for UC, where inter-laboratory reproducibility studies have shown strong agreement in both TC and IC scoring.
• Further studies are required to investigate this difference in the pathology of tumour types.

References

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