PD-L1 IHC in lung cancer: Interlaboratory concordance and challenges in clinical application
Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2016:

<table>
<thead>
<tr>
<th>Name of the enterprise / Nature of the interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS, MSD, Roche, QuIP, NordiQC</td>
</tr>
</tbody>
</table>
**Immunotherapy, biomarkers**

Checkpoint (PD-L1/2, ...)

**Neoantigenes, Tumor Mutational Burden**

PD-L1 IHC:
- Biggest evidence
- Clinically validated

Do not score (currently):
- PD-1
- PD-L2
- TILs

PD-L1 immunohistochemistry ('IHC')

**PD-L1, physiological**
- Immune tolerance
- Tissue protection

**PD-L1, pathological**
- Immune escape
- T-cell anergy

**PD-L1 immunohistochemistry ('IHC'):**
May be predictive for
- anti-PD-1
- anti-PD-L1
PD-L1 IHC: Pro & Contra

☑️ Advantages IHC:
- Well-established, robust technique
- Available in most labs
- Fast results (1 - 2 days)
PD-L1 IHC: Pro & Contra

**Advantages IHC:**
- Well-established, robust technique
- Available in most labs
- Fast results (1 - 2 days)

**Challenges IHC:**
- Standardisation
- Staining
- Interpretation
- Nonlinear; semi-quantitative
- PD-L1: 5 different assays
Assay vs. LDT

"Assay" (aka 'kit')
- Validated in clinical trials
- IVD-certified
- "All-in-one-box"

"Laboratory developed test" (LDT) aka "Homebrew"
- Anything that deviates from IVD-protocol, i.e.
  - reagents / suppliers
  - devices
  - protocol
Assay vs. LDT

"Assay" (aka 'kit')
- Validated in clinical trials
- IVD-certified
- "All-in-one-box"

"Laboratory developed test" (LDT) aka "Homebrew"
- Anything that deviates from IVD-protocol, i.e.
- reagents / suppliers
- devices
- protocol

☑️ Advantages of Assays
- Standardized
- Easy to use

❗ Challenges of Assays
- Expensive
- Limited to specific equipment
- 'One-fits-all'

☑️ Advantages of LDTs
- More flexible (equipment, ...)
- Cheaper

❗ Challenges of LDTs
- More expertise required
- Calibration required
- More likely to deviate from validation-trial
Step-wise approach

Predictive value

- Biological significance
- Technical aspects
Step-wise approach

Predictive value

- Biological significance
- Technical aspects
  - Material
  - Assays
  - Scoring
1. **Internal ring trial** (DGP\textsuperscript{1}) -

   Gain experience; identify challenges
   - 1a, Scoring: Observer-concordance
   - 1b, Staining: Laboratory-concordance
   - Assays: Comparisons

2. **Open ring trial** (QuIP GmbH\textsuperscript{2}) -

   Quality assessment
   - Workshop
   - Open ring trial

---

1 'DGP' = German Association for Pathology
   https://www.pathologie-dgp.de/

2 'QuIP' = 'Quality-Initiative Pathology'
   = German EQA Institution
   http://www.quip-ringversuche.de
1) Internal ring trial

PD-L1 IHC harmonisation trial

Pathologists:
- Reinhard Büttner
- Gustavo Baretton
- Manfred Dietel
- Lukas Heukamp
- Korinna Jöhrens
- Thomas Kirchner
- Iver Petersen
- Simone Reu
- Josef Rüschoff
- Andreas Scheel
- Hans-Ulrich Schildhaus
- Peter Schirmacher
- Markus Tiemann
- Arne Warth
- Wilko Weichert

Industry partners:
- BMS
- MSD
- Roche
- AstraZeneca
- Ventana
- Dako / Agilent
- Targos Molecular Pathology

10 pathological institutions
1a) Internal ring trial: Scoring

1a: Internal ring trial, PD-L1 Scoring
### PD-L1 Scoring

<table>
<thead>
<tr>
<th>Name</th>
<th>Assay, Antibody</th>
<th>Cell Type</th>
<th>Negative</th>
<th>Low/Weak</th>
<th>Medium</th>
<th>High/Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nivolumab (α-PD1; BMS)</td>
<td>Dako 28-8</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-5%</td>
<td>5-10%</td>
<td>≥10%</td>
</tr>
<tr>
<td>Pembrolizumab (α-PD1; MSD)</td>
<td>Dako 22C3</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-5%</td>
<td>1-50%</td>
<td>≥50%</td>
</tr>
<tr>
<td>Atezolizumab (α-PD-L1; Roche)</td>
<td>Ventana SP142</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-5%</td>
<td>5-10%</td>
<td>≥50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immune</td>
<td>0-1%</td>
<td>1-5%</td>
<td>1-50%</td>
<td>≥10%</td>
</tr>
<tr>
<td>Durvalumab (α-PD-L1; AstraZeneca)</td>
<td>Ventana SP263</td>
<td>Tumor</td>
<td></td>
<td>1-25%</td>
<td></td>
<td>≥25%</td>
</tr>
<tr>
<td>Avelumab (α-PD-L1; Pfizer + Merck)</td>
<td>Dako 73-10</td>
<td>Tumor</td>
<td>0-1%</td>
<td></td>
<td></td>
<td>?</td>
</tr>
</tbody>
</table>

- Various cut-off criteria (assays; line of treatment)

### PD-L1 Scoring

<table>
<thead>
<tr>
<th></th>
<th>Assay, Antibody</th>
<th>Cell Type</th>
<th>Negative</th>
<th>Low/Weak</th>
<th>Medium</th>
<th>High/Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nivolumab</strong></td>
<td>Dako 28-8</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-5%</td>
<td>5-10%</td>
<td>≥10%</td>
</tr>
<tr>
<td><strong>Pembrolizumab</strong></td>
<td>Dako 22C3</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-50%</td>
<td></td>
<td>≥50%</td>
</tr>
<tr>
<td><strong>Atezolizumab</strong></td>
<td>Ventana SP142</td>
<td>Tumor</td>
<td>0-1%</td>
<td>1-5%</td>
<td>5-50%</td>
<td>≥50%</td>
</tr>
<tr>
<td></td>
<td>Immune</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Durvalumab</strong></td>
<td>Ventana SP263</td>
<td>Tumor</td>
<td></td>
<td>1-25%</td>
<td></td>
<td>≥25%</td>
</tr>
<tr>
<td><strong>Avelumab</strong></td>
<td>Dako 73-10</td>
<td>Tumor</td>
<td>0-1%</td>
<td></td>
<td></td>
<td>?</td>
</tr>
</tbody>
</table>

### B

<table>
<thead>
<tr>
<th>Proportion-Score</th>
<th>Negative</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category:</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cut-Off:</td>
<td>&lt;1%</td>
<td>≥1%</td>
</tr>
<tr>
<td>Intervall:</td>
<td>0-1%</td>
<td>≥1%</td>
</tr>
</tbody>
</table>

- Various cut-off criteria (assays; line of treatment)
- Criteria can be integrated into 6-step score
- Currently most important:
  - ≥50% and ≥1% stained tumor cells (TC)

1a) Internal ring trial: Scoring

1\textsuperscript{st} round, 'Training Set':
- 15 cases NSCLC
- Central staining
- 2 LDTs
- 9 Observer

2\textsuperscript{nd} round, 'Validation Set':
- 15 cases NSCLC
- Central staining
- 4 Assays
- 9 Observer
### Interobserver-Concordance (TCs)

- **6-step score:** $\kappa \approx 0.5$
- **Cut-offs:** $\kappa \approx 0.6 - 0.8$
- **Interobserver-Concordance comparable between assays, LDTs**

#### Table: Light's kappa [95% CI], Tumor cell proportions

<table>
<thead>
<tr>
<th>PD-L1 IHC</th>
<th>6-step score</th>
<th>Proportion cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\geq 1%$</td>
</tr>
<tr>
<td><strong>Training Set</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lab dev. Tests</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=15 cases NSCLC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E1L3N on Leica</td>
<td>0.50 [0.37 - 0.64]</td>
<td>0.73 [0.60 - 0.88]</td>
</tr>
<tr>
<td>SP142 on Leica</td>
<td>0.49 [0.34 - 0.66]</td>
<td>0.61 [0.41 - 0.85]</td>
</tr>
<tr>
<td><strong>Validation Set</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assays</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=15 cases NSCLC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dako 28-8</td>
<td>0.49 [0.36 - 0.63]</td>
<td>0.79 [0.58 - 0.95]</td>
</tr>
<tr>
<td>Dako 22C3</td>
<td>0.47 [0.34 - 0.63]</td>
<td>0.74 [0.44 - 0.94]</td>
</tr>
<tr>
<td>Ventana SP142</td>
<td>0.47 [0.35 - 0.62]</td>
<td>0.72 [0.53 - 0.89]</td>
</tr>
<tr>
<td>Ventana SP263</td>
<td>0.47 [0.34 - 0.63]</td>
<td>0.59 [0.39 - 0.73]</td>
</tr>
</tbody>
</table>

#### Interpretation of kappa’s coefficient:

- $\kappa < 0$: poor
- $\kappa = 0 - 0.2$: slight
- $\kappa = 0.21 - 0.4$: fair
- $\kappa = 0.41 - 0.6$: moderate
- $\kappa = 0.61 - 0.8$: substantial
- $\kappa = 0.81 - 1.0$: (almost) perfect


Landis JT, Koch GG. *Biometrics* 1977. 33(1);159-174
1a) Scoring: Cell-type

IHC: PD-L1

TC: 1-5%
IC: >10%

200μm

IHC: CD163
1a) Scoring: Low intensity
1b) Internal ring trial: Staining

1b: Internal ring trial,
PD-L1 Staining
1b) Internal ring trial: Staining

- NSCLC-TMA, 2mm cores, n=21
- Sections cut at central lab
- Staining and scoring at local labs
  - 10 institutes
  - 4 PD-L1 assays
    (22C3, 28-8, SP263, SP142)
  - 11 lab-developed tests (LDTs)
  - Total: 27 stained sections
- Central review of stainings
- Controls: Cell-lines; Tonsil
## 1b) Interlaboratory-Concordance

<table>
<thead>
<tr>
<th>IHC: PD-L1</th>
<th>Sites (n)</th>
<th>Readable TMA-cores</th>
<th>Light’s kappa (±SD), Tumor proportion score</th>
<th>Proportion cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>6-step score</td>
<td>3-step score</td>
</tr>
<tr>
<td>22C3, Kit</td>
<td>3</td>
<td>90% (57/63)</td>
<td>0.69 (±0.09)</td>
<td>0.83 (±0.09)</td>
</tr>
<tr>
<td>28-8, Kit</td>
<td>3</td>
<td>94% (59/63)</td>
<td>0.66 (±0.17)</td>
<td>0.80 (±0.15)</td>
</tr>
<tr>
<td>SP263, Kit</td>
<td>4</td>
<td>81% (68/84)</td>
<td>0.66 (±0.22)</td>
<td>0.89 (±0.18)</td>
</tr>
<tr>
<td>SP142, Kit</td>
<td>6</td>
<td>90% (114/126)</td>
<td>0.63 (±0.16)</td>
<td>0.73 (±0.11)</td>
</tr>
<tr>
<td>LDTs</td>
<td>11</td>
<td>82% (189/231)</td>
<td>0.43 (±0.15)</td>
<td>0.50 (±0.18)</td>
</tr>
</tbody>
</table>

*#High SD because most samples were ≥1%

### Interlab-Concordance (TCs)
- 6-step score: \( \kappa \approx 0.66 \)
- Cut-offs: \( \kappa \approx 0.71 - 1.0 \)
- Interobserver-Concordance comparable between assays
- LDTs slightly lower

---

*Scheel AH et al. Histopathology 2017, accepted*
1b) Internal ring trial: Interassay

1b, Interassay-Comparison
NSCLC-TMA, assays

Scheel AH et al. *Histopathology* 2017, accepted
LDTs: QC+ and QC-

n=11 TMA-sections stained with LDTs

Employed Abs:
- 22C3 n=4
- 28-8 n=3
- SP263 n=2
- E1L3N n=1
- QR1 n=1

Manual review

Staining similar to 22C3 / 28-8 pharmDx = QC+ , n=6

Employed Abs:
- 22C3 n=1
- 28-8 n=1
- SP263 n=2
- E1L3N n=1
- QR1 n=1

Staining divergent = QC- , n=5

Employed Abs:
- 22C3 n=3
- 28-8 n=2

Image-analysis / quantitation

Scheel AH et al. *Histopathology* 2017, accepted
# NSCLC-TMA, LDTs

<table>
<thead>
<tr>
<th>Lab-dev. test</th>
<th>Site 03 28-8 (QC+)</th>
<th>Site 04 E1L3N (QC+)</th>
<th>Site 06 28-8 (QC-)</th>
<th>Site 04 22C3 (QC-)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Core B2</strong></td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
</tr>
<tr>
<td><strong>Core B1</strong></td>
<td><img src="image5" alt="Image" /></td>
<td><img src="image6" alt="Image" /></td>
<td><img src="image7" alt="Image" /></td>
<td><img src="image8" alt="Image" /></td>
</tr>
<tr>
<td><strong>Tonsil</strong></td>
<td><img src="image9" alt="Image" /></td>
<td><img src="image10" alt="Image" /></td>
<td><img src="image11" alt="Image" /></td>
<td><img src="image12" alt="Image" /></td>
</tr>
</tbody>
</table>
Quantitation by image-analysis

IHC: PD-L1

- Per core: analysis of 0.46mm² @ 200x
- Invasive carcinoma manually selected
- Color-deconvolution
- Read-outs: Hem. intensity, DAB-area relative to area of invasive carcinoma
**Image-analysis**

- Bars: Mean of sites; antennae: SD
- QC+: Similar to 28-8 / 22C3; QC-: Less DAB

Scheel AH et al. *Histopathology* 2017, accepted
IHC: Nonlinearity
IHC: Nonlinearity

See also: Cheung CC, Appl Immunohistochem Mol Morphol 2016

Staining A: TPS ≥50%

Staining B: TPS ≥50%
Low limit of detection (LLOD)

Staining A: TPS ≥50%
Staining B: TPS <1%

Staining B: TPS ≥50%
See also: Cheung CC, Appl Immunohistochem Mol Morphol 2016
Summary internal ring trial

1. Reproducible PD-L1 scoring is achievable
   - Scoring challenges: Cell-type; low intensity

2. Reproducible PD-L1 staining is achievable
   - Assays ('Kits') quite reliable
   - LDTs possible, calibration critical
   - Different primary antibody possible:
     28-8, 22C3, SP263, E1L3N, others

Results match other studies, in particular
Adams J., / InCA-Network; WCLC 2016, Vienna
2.) Open ring trial / QuIP#

# 'QuIP' = 'Quality-Initiative Pathology'
= German EQA Institution
http://www.quip-ringversuche.de
Open ring trial; work-flow

Case selection
- 3 lead institutes
- 14 cases
- Resection specimens

Case verification
- 5 panel institutes
- IHC: Assays and LDTs
- Concordance ≥ 7/8

Ring trial
- 10 NSCLC cases
- 2 unstained slides / case
- Participants: n=87
Open ring trial; evaluation

Per case
- Correct score 2 points
- Not evaluable 1 point

Total
- Optimal 20 points
- 'Successful' $\geq 18$ points

Optional
- Return of stained slides for review

QuIP GmBH, used with permission
Open ring trial; cases, results

Composition

- NSCLC resection specimens, 9 cases
  (One case excluded; 'equivocal')
- Category 0, TC < 1%: 2 cases
- Category 1, TC 1%-49%: 2 cases
- Category 2, TC 50-100 %: 5 cases
- Results-form: Category, not percentage

Results

- Returned scores: 83
- participated successful: 60 (72%)
- participated: 23 (28%)
## Employed clones

<table>
<thead>
<tr>
<th>Clone</th>
<th>Participants (%)</th>
<th>participated successful</th>
<th>participated</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1L3N</td>
<td>25 (30%)</td>
<td>22 (88%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>28-8</td>
<td>20 (24%)</td>
<td>13 (65%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>22C3</td>
<td>13 (16%)</td>
<td>9 (69%)</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>QR1</td>
<td>6 (7%)</td>
<td>4 (67%)</td>
<td>2 (33%)</td>
</tr>
<tr>
<td>SP263</td>
<td>5 (6%)</td>
<td>2 (40%)</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>Cal10</td>
<td>4 (5%)</td>
<td>3 (75%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>ZR3</td>
<td>3 (4%)</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>SP142</td>
<td>2 (2%)</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>n.a.</td>
<td>5 (6%)</td>
<td>2 (40%)</td>
<td>3 (60%)</td>
</tr>
</tbody>
</table>
Deviating scores, stainings

## A

<table>
<thead>
<tr>
<th>Clone</th>
<th>Score compared to reference</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Higher</td>
<td></td>
</tr>
<tr>
<td>E1L3N</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>28-8</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>22C3</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>QR1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SP263</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Cal10</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>ZR3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SP142</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td><strong>19</strong></td>
<td><strong>22</strong></td>
<td></td>
</tr>
</tbody>
</table>

## B

- Slide-sets returned: n=18
- Correct staining / score: n=1
- Scoring incorrect: n=4
- Staining incorrect: n=13

QuIP GmBH, used with permission
QuIP - summary

- 87 participants, 83 results (95%), 60 successful (72%)
- Success possible with Assays and LDTs
- LDTs: Different clones may be used
  (E1L3N particularly successful)
- Deviating results: calibration > interpretation

- QuIP: 2nd open ring trial PD-L1 in NSCLC completed;
  n=97 participants; results to be published
Control TMA: Baseline performance

- TMA: 11 cell-lines (Horizon Discovery)
- Defined PD-L1 expression
- Core-diameter: 2mm

- Analysis of baseline assay performance:
  1. ) Qualitative analysis
  2. ) Quantitative analysis by
     whole-slide-scanning (4px/µm)
     and image-analysis (ImageJ)
Control-TMA: Assays; cores A1, A4

22C3 assay, reference

28-8 assay, reference

SP263 assay, reference

SP142 assay, reference
Control-TMA: LDTs, core A4

QC+  
22C3, Site07  28-8, Site03  SP263, Site08  SP263, Site09  E1L3N, Site04  QR1, Site10

QC-  
22C3, Site01  22C3, Site04  28-8, Site05  28-8, Site06
Control-TMA: Image-analysis

DAB-stained area in selected cores

<table>
<thead>
<tr>
<th>High proportion</th>
<th>Moderate proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AB</strong></td>
<td><strong>DAB, mean area</strong></td>
</tr>
<tr>
<td></td>
<td>(A1, A2, A3)</td>
</tr>
<tr>
<td>22C3 Kit</td>
<td>61.3%</td>
</tr>
<tr>
<td>28-8 Kit</td>
<td>61.0%</td>
</tr>
<tr>
<td>SP142 Kit</td>
<td>73.5%</td>
</tr>
<tr>
<td>SP263 Kit</td>
<td>63.1%</td>
</tr>
<tr>
<td>LDAs, QC+</td>
<td>65.4%</td>
</tr>
<tr>
<td>LDAs, QC-</td>
<td>49.4%</td>
</tr>
<tr>
<td></td>
<td><strong>DAB, mean area</strong></td>
</tr>
<tr>
<td></td>
<td>(A5, B2, B3)</td>
</tr>
<tr>
<td>22C3 Kit</td>
<td>11.1%</td>
</tr>
<tr>
<td>28-8 Kit</td>
<td>14.6%</td>
</tr>
<tr>
<td>SP142 Kit</td>
<td>1.1%</td>
</tr>
<tr>
<td>SP263 Kit</td>
<td>15.0%</td>
</tr>
<tr>
<td>LDAs, QC+</td>
<td>15.8%</td>
</tr>
<tr>
<td>LDAs, QC-</td>
<td>15.4%</td>
</tr>
</tbody>
</table>

Student's t-test

| 22C3 Kit vs 28-8 Kit | 0.895 |
| 22C3 Kit vs SP142 Kit | 0.000 |
| 28-8 Kit vs SP142 Kit | 0.000 |
| 28-8 Kit vs SP263 Kit | 0.227 |
| SP142 Kit vs SP263 Kit | 0.000 |
| LDAs, QC+ vs. 22C3 Kit | 0.323 |
| LDAs, QC- vs. 22C3 Kit | 0.000 |

| 22C3 Kit vs 28-8 Kit# | 0.082 |
| 22C3 Kit vs SP142 Kit | 0.000 |
| 28-8 Kit vs SP142 Kit# | 0.000 |
| 28-8 Kit vs SP263 Kit | 0.174 |
| SP142 Kit vs SP263 Kit | 0.005 |
| LDAs, QC+ vs. 22C3 Kit | 0.323 |
| LDAs, QC- vs. 22C3 Kit | 0.436 |

DAB-stained area:
- 22C3 assay \(\triangleq\) 28-8 assay
- 28-8 assay \(\triangleq\) SP263 assay
- SP142 is distinct
  (High: more DAB,
   Medium: less DAB)
- LDTs, QC+ \(\triangleq\) 22C3 assay
- LDTs, QC- \(\neq\) 22C3 assay

(# 28-8 Kit Site 01 excluded because of high background)
LDT-calibration with cell-lines

- TMAs of PD-L1\(^+\) cell-lines:
  (Horizon Discovery; HistoCyte) tools for LDT-calibration

- Here:
  Reference (22C3 assay),
  LDT, assay-analogue (QC+),
  LDT, divergent (QC-)

- Reference stainings:
  www.pdl1.de \((\text{free})\)

Scheel AH et al. Histopathology 2017, accepted
Summary

Internal ring trials
- Reproducible PD-L1 scoring and staining possible
- Assays: Reliable;
  \[22C3 \approx 28-8 \approx SP263; \neq SP142\]
- LDTs: LDTs \approx 22C3/28-8 possible;
  6/11 protocols successful;

Open ring trial
- 60/83 successful (72%)
- Success possible with PD-L1 assay or LDT
- LDTs: Different antibodies possible

Challenges
- Scoring: Cell type; low intensity
- LDT-calibration
Thank you for your attention!