Interlaboratory variation in PD-L1 positivity in histological and cytological material of non-small cell lung cancer patients

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Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2018:

Name of the enterprise / Nature of the interest

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<th>Enterprise</th>
<th>Interest</th>
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<td>AstraZeneca, MSD and Roche Diagnostics:</td>
<td>receival of research grants.</td>
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In non-small cell lung cancer (NSCLC) immunohistochemical expression of PD-L1 predicts likelihood of response to PD-(L)1 checkpoint inhibitors. Clinically relevant cut-offs are 1% (Durvalumab) and 50% (Pembrolizumab). Other studies with real-world clinical data have shown considerable interlaboratory variation in histologic grading and immunohistochemical scoring. Variation in PD-L1 testing:
- Different standardised assays and laboratory-developed tests (LDTs);
- Inter-pathologist variation.
Management of many patients with advanced NSCLC is based on cytology instead of histology:
- PD-L1 testing on cytology not validated;
- Differences between laboratories in processing of cytological material.
Study aim

To study interlaboratory variation in PD-L1 positivity in *histological* and *cytological* material of NSCLC patients in the Netherlands, using real-world clinical pathology data.
Methods

- PALGA Foundation: nationwide network and registry of histo- and cytopathology in the Netherlands
- Pathology reports of all Dutch NSCLC patients tested for PD-L1 between July 2017 – December 2018
- 42 pathology laboratories / 32 performed PD-L1 testing

Analysis:
- Proportion of reported PD-L1 positive patients per laboratory (≥20 PD-L1 tests) (based on 1% and 50% cut-offs)
- Comparison between laboratories by creating funnel plots with 95%-confidence intervals (corrected for case mix)
- Separate analysis of histology and cytology
Results

- Inclusion thus far: July 2017 – October 2018 (inclusion ongoing)
- 7688 NSCLC patients tested for PD-L1

Use of histological or cytological material per PD-L1 test

- Cytology; 24.7%
- Histology; 75.3%
Results Histology: 5634 patients, 30 labs

❖ 3/30 (10.0%) labs differ significantly from mean
❖ Maximum variation 18.3%

❖ 8/30 (26.7%) labs differ significantly from mean
❖ Maximum variation 33.6%
Results Cytology: 1637 patients, 23 labs

- 50% cut-off
- 1% cut-off

- 4/23 (17.4%) labs differ significantly from mean
- Maximum variation 32.3%
- 7/23 (30.4%) labs differ significantly from mean
- Maximum variation 42.3%
Conclusions

- Interlaboratory variation of PD-L1 positivity is greater when using a 1% cut-off compared to a 50% cut-off.

- Amount of variation is smallest when using a 50% cut-off and histological material.

- Interlaboratory variation is greater in cytological material compared to histological material.

→ Hypothesis: due to greater differences in processing of cytology, with use of some fixatives resulting in lower PD-L1 immunostaining.
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