UMC Utrecht

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

Enterprise | Interest

AstraZeneca, MSD and Roche Diagnostics: receival of research grants.

Background

- In non-small cell lung cancer (NSCLC) immunohistochemical expression of PD-L1 predicts likelihood of response to PD-(L)1 checkpoint inhibitors[1].

- Clinically relevant cut-offs are 1% (Durvalumab)[2] and 50% (Pembrolizumab)[3].

- Other studies with real-world clinical data have shown considerable interlaboratory variation in histologic grading[4,5] and immunohistochemical scoring[6].

- 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[7]:
  - PD-L1 testing on cytology not validated;
  - Differences between laboratories in processing of cytological material[8].

1. Reck et al. *N Engl J Med* 2016;375(19):1823-33.
2. Planchard et al. ESMO Guideline. *Ann Oncol* 2018;29(Supplement_4):iv192-iv237.
3. EMA. Imfinzi (Durvalumab) 2018. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/imfinzi.
4. Kuijpers et al. *Am J Surg Pathol* 2016;40(8):1100-1108.
5. Dooijeweert van et al. *Int J Cancer* 2019;00:00-00.
6. Dooijeweert van et al. *Breast Cancer Res Treat* 2019;175(2):487-497.
7. Skov et al. *Apmis* 2015;123(2):108-15.
8. Nambirajan A, Jain D. *Cytopathology* 2018;29(6):505-24.

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

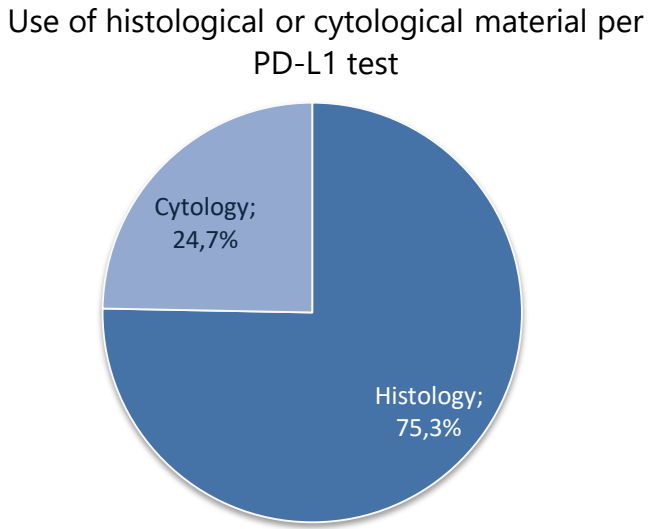
- PALGA Foundation: nationwide network and registry of histo- and cytopathology in the Netherlands
- Pathology reports of all Dutch NSCLC patients tested for PD-L1 between July 2017 – December 2018
- 42 pathology laboratories / 32 performed PD-L1 testing

Analysis:

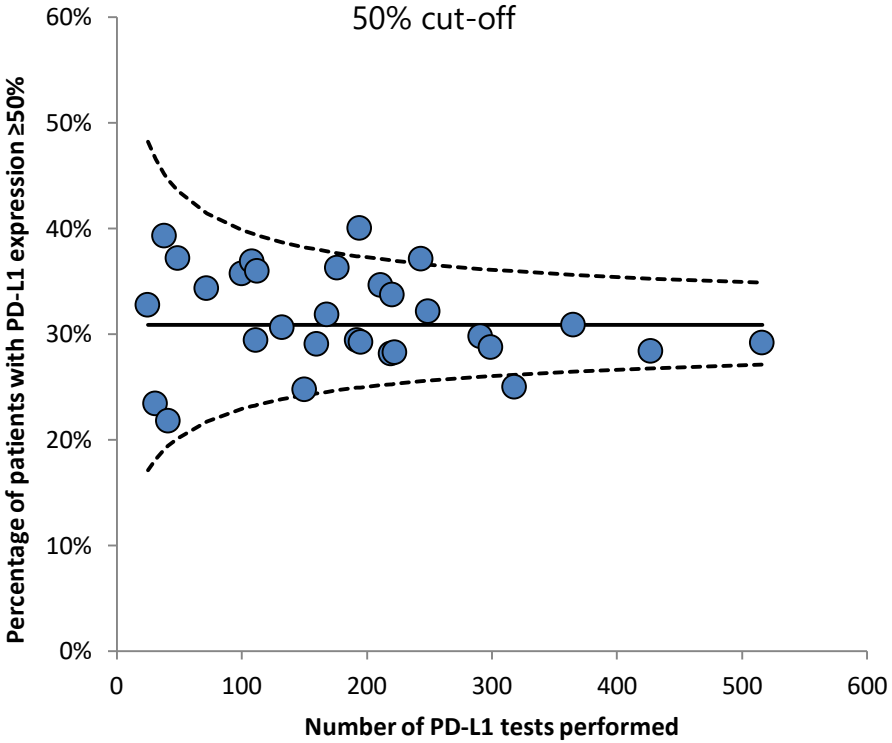
- Proportion of reported PD-L1 positive patients per laboratory (≥20 PD-L1 tests) (based on 1% and 50% cut-offs)
- Comparison between laboratories by creating funnel plots with 95%-confidence intervals (corrected for case mix)
- Separate analysis of histology and cytology

Results

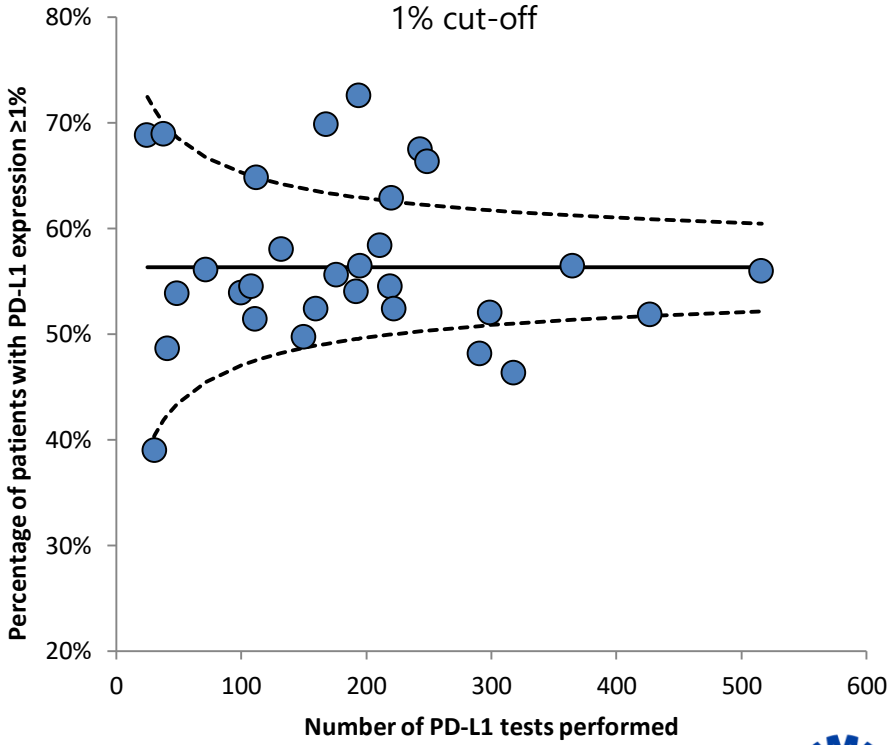
- Inclusion thus far: July 2017 – October 2018 (inclusion ongoing)
- 7688 NSCLC patients tested for PD-L1



Results Histology: 5634 patients, 30 labs

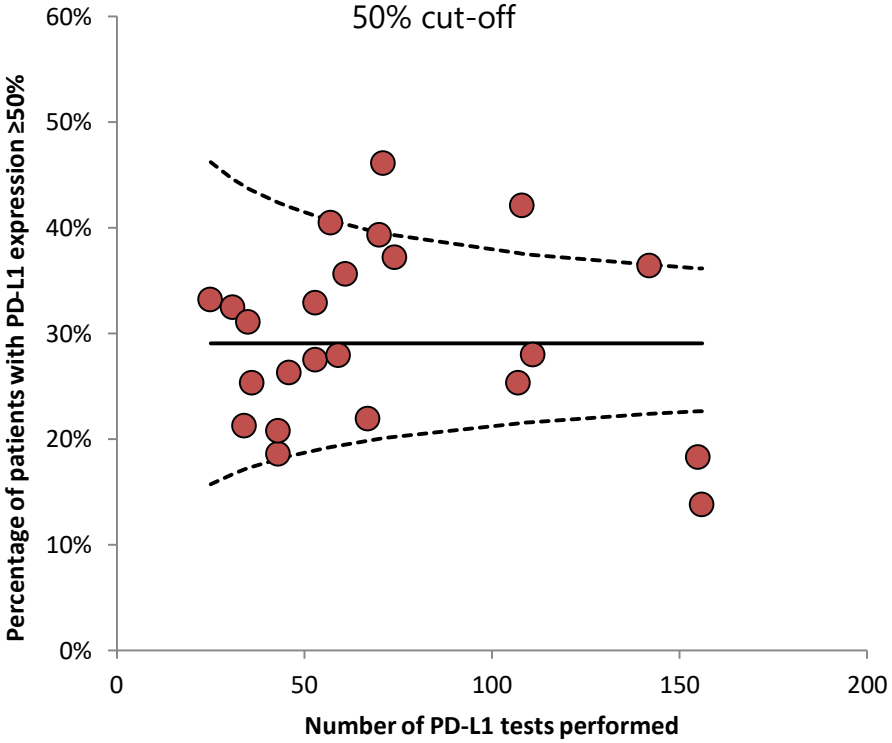


- 3/30 (10.0%) labs differ significantly from mean
- Maximum variation 18.3%

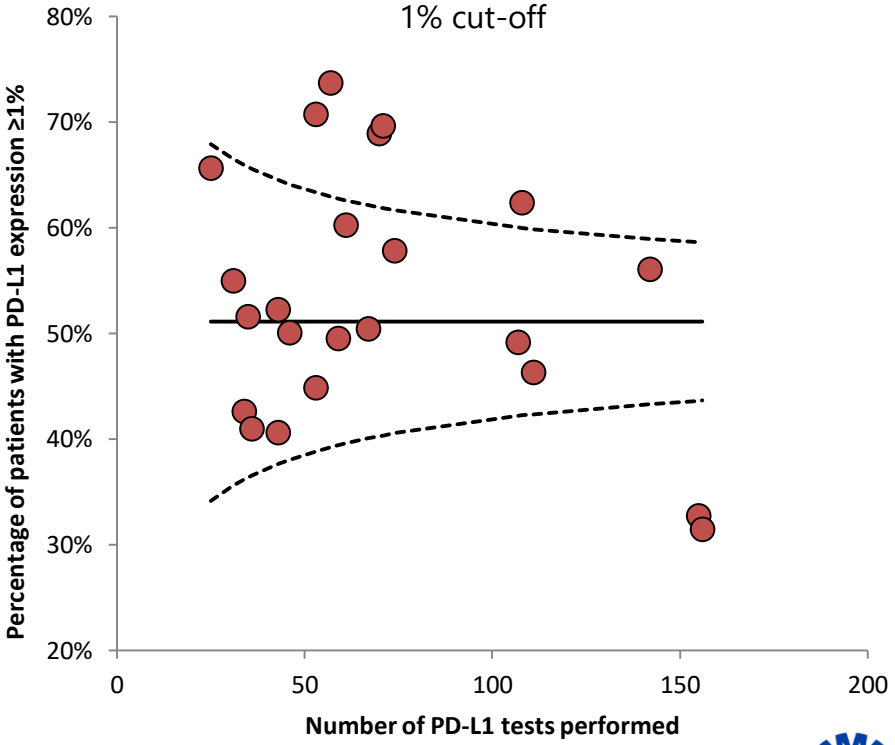


- 8/30 (26.7%) labs differ significantly from mean
- Maximum variation 33.6%

Results Cytology: 1637 patients, 23 labs



- 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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