E-Mail: aurelia.noske@tum.de

Institute of Pathology
Technical University of Munich

13P Comparison study of different programmed death-ligand 1 (PD-L1) assays, readers and scoring methods in triple-negative breast cancer (TNBC)

A. Noske[1], D.-C. Wagner[2], K. Schwamborn[1], S. Foersch[2], K. Steiger[1], M. Kiechle[3], S. Karapetyan[4], D. Oettler[5], A.Hapfelmeier[4,6], W. Roth[2], W. Weichert[1]

[1]Institute of Pathology, TUM, Munich, Germany, [2]Institute of Pathology, Johannes Gutenberg University Mainz, Germany, [3]Dept. of Gynaecology, Klinikum Rechts der Isar - TUM, Munich, Germany, [4]General Practice and Health Services Research, TUM, Munich, Germany, [5]Medical Affairs, MSD Sharp & Dohme GmbH, Haar, Germany, [6]Medical Informatics, Statistics and Epidemiology, TUM, Munich, Germany.

Background

Different immunohistochemical programmed death-ligand 1 (PD-L1) assays and scoring methods in triple-negative breast cancer (TNBC) have been reported to yield variable results.

Aims of the study

We compared the analytical concordance and interobserver variability of four clinically developed PD-L1 IHC assays assessing immune cell (IC) score, tumour proportion score (TPS), and combined positive score (CPS) in TNBC.

Methods

Archival primary TNBC resection specimens were stained for PD-L1 using VENTANA SP142, VENTANA SP263, DAKO 22C3 and DAKO 28-8. PD-L1 expression was scored by four trained readers according to guidelines for IC-score, TPS, and CPS on whole slide images by virtual microscopy.

Results

PD-L1 staining of 99 TNBC was evaluable. In Figure 1 the positivity for IC-score and CPS across all readers of each assay and sample is shown. The SP263 assay showed a higher positivity rate with both scorings as compared to the other three assays.
The mean PD-L1 positivity ranged between 53%-74% for IC-score ≥1% and CPS ≥1 and was similar for SP142, 22C3, and 28-8 but higher for SP263. When applying CPS ≥10, the positivity with SP263 was even higher as compared to the other assays. TPS showed similar levels for 22C3 and 28-8 but only low levels for SP142 and highest for SP263 (Figure 2).

We further compared the percentage overlap of positive and negative cases between IC-score ≥1% and CPS ≥1 and CPS ≥10 cut-off, respectively for each assay across all readers (Figure 3A, B). We found a high concordance (above 90%) for PD-L1-IC-positivity ≥1% and CPS ≥1 for each assay. In contrast, the overlap between IC-score ≥1% and CPS ≥10 was below the concordance level (<90%).

Inter-assay-agreement was tested for pair-wise assay combinations for each score. ICCs for 22C3 vs. 28-8 showed a good to excellent agreement but SP142 vs. 22C3/ 28-8 only for the IC-score. Kappa values for 22C3 vs. 28-8 revealed a good agreement, while SP142 vs. 22C3/28-8 was only good for IC 1% and CPS 1.

Results

Figure 1 PD-L1 positivity according to IC-score (A) and CPS (B) for each case and assay averaged over four readers.

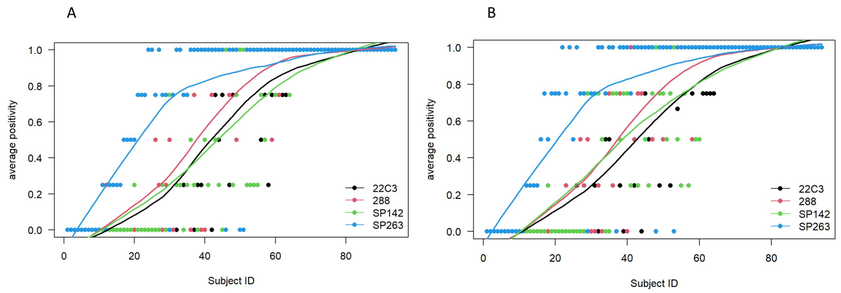
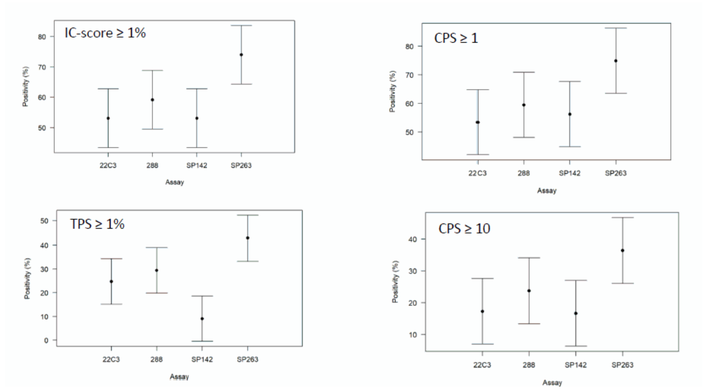


Figure 2 Adjusted mean percentages of PD-L1 positivity for each assay and different scorings across the four readers are depicted with CI 95%.



Results

Figure 3A Concordance between IC-score ≥1% and CPS ≥1 across all readers for each assay

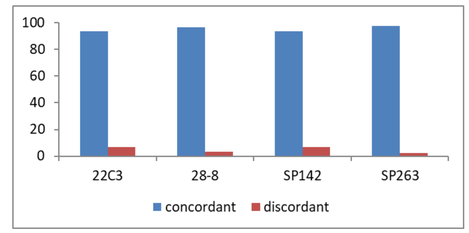
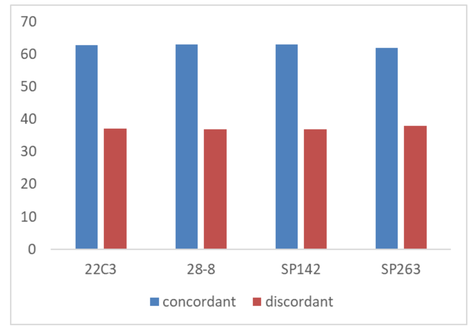


Figure 3B Concordance between IC-score ≥1% CPS ≥10 across all readers for each assay



Inter-assay agreement between SP263 and the other three assays was poor to fair in almost all scenarios.
Inter-reader agreement (ICCs and kappa statistics) for each assay and score revealed an overall good reproducibility.

Conclusions

SP142, 22C3, and 28-8 show comparable PD-L1 positivity rates, while SP263 identifies more positive cases

Overall good assay concordance between 22C3, 28-8, and SP142 at IC-score 1% cut-off

Overall good assay concordance between 22C3 and 28-8 at both CPS 1 and 10 cut-offs, while SP142 is only concordant at CPS 1 but less at CPS 10

Low positivity of tumour cells with SP142 might render SP142 as a less optimal antibody for CPS assessment in TNBC, specifically at higher cut-offs

SP263 assay is not interchangeable with the other three PD-L1 assays

Overall good reproducibility for all scorings and each assay among the pathologists

Disclosure (first author): Aurelia Noske has no conflict of interest to declare.

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