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

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**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.

**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.

Presented at ESMO Breast Cancer Congress, 5-8 May 2021