Abstract

Background: Recent data indicate a promising response to immune checkpoint inhibition in patients with metastatic TNBC. Ample research showed that PD-L1, a PD-1 ligand, is expressed in multiple tumor types, including TNBC, and may be a predictor of response to PD-1/PD-L1 blockade. Quantification of the tumor composition, particularly PD-1 and PD-L1 expression, continues to be controversial in its relationship to immune checkpoint inhibition in several cancer types, and it remains unclear whether PD-L1 expression is necessary to predict response. Here, we aimed to determine the distribution of PD-1 and PD-L1 in a large set of centrally ascertained specimens of TNBC.

Methods: The study cohort consisted of 993 tumor samples (both primary and metastatic TNBC) analyzed for either PD-1 or PD-L1 expression in one laboratory (Caris Life Sciences; Phoenix, AZ). Estrogen receptor (ER) and progesterone receptor (PR) status was determined by immunohistochemistry (IHC). HER2/Neu expression or amplification was assessed by either IHC or in-situ hybridization. PD-1 and PD-L1 expression were confirmed using IHC with validated antibodies. For PD-L1, clone SP142 (Roche Diagnostics) was utilized and a sample was considered positive if there was ≥ 5% membranous staining of tumor cells. For PD-1, clone H1L11 (BD Biosciences) was used. Tumor infiltrating lymphocytes (TILs) expressing PD-L1 were counted and a sample was considered positive if there was at least one PD-1 positive TIL per 40x microscope field.

Results: The median age in this cohort was 56 years (range: 22-88). A total of 963 TNBC specimens were tested for PD-1 via IHC. One hundred fifty eight (158; 43.5%) were negative for PD-1 expression. Two hundred five (205; 56%) were positive for PD-1. Of those that were PD-1 positive, 116 (56.6%), were in samples from a primary site (breast) and 89 (43.4%) from metastatic sites (28/324, and 28/306, respectively). Based on our threshold, we showed that 8.89% of TNBCs are PD-L1 positive. These results are slightly lower than the Sun et al. study,2 which showed 11% positive rate PD-L1 positive rate in TNBC using the SP142 antibody. This 116 (56.6%), were in samples from a primary site (breast) and 89 (43.4%) from metastatic sites (28/324, and 28/306, respectively).

Conclusions: PD-L1 expression was shown in 56.4% of our TNBC cohort, consistent with recently published I-SPY-1 study. • Based on our threshold, we showed that 8.89% of TNBCs are PD-L1 positive. • These results are slightly lower than the Sun et al. study, which showed 11% positive rate PD-L1 positive rate in TNBC using the SP142 antibody. This 116 (56.6%), were in samples from a primary site (breast) and 89 (43.4%) from metastatic sites (28/324, and 28/306, respectively). • Based on our threshold, we showed that 8.89% of TNBCs are PD-L1 positive. These results are slightly lower than the Sun et al. study, which showed 11% positive rate PD-L1 positive rate in TNBC using the SP142 antibody. This 116 (56.6%), were in samples from a primary site (breast) and 89 (43.4%) from metastatic sites (28/324, and 28/306, respectively).

References