1168P Tumor PD-L1 predicts the outcome of PD-1-based immunotherapy in metastatic melanoma depending on the type of tissue examined

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Background: PD-1-based immune checkpoint inhibition (ICI) is the major backbone of current melanoma therapy. Tumor PD-L1 expression represents one of few biomarkers predicting ICI therapy outcome. Here, we systematically investigated whether the type of tumor tissue examined for PD-L1 expression has an impact on ICI therapy outcome prediction.

Methods: Pre-treatment tumor tissue obtained before 1st ICI therapy for non-resectable stage III/IV metastatic melanoma was prospectively collected within the DeCOG multicenter study Tissue Registry in Melanoma. Stratified by tissue type, best overall response (BOR), progression-free survival (PFS), and overall survival (OS) were correlated with tumor PD-L1 expression (cutoff $\geq$5%).

Results: Of 448 patients, tumor PD-L1 was determined on 95 primary tumors (PT; 36.8% positivity), 153 skin (34.0% positivity), 115 lymph node (LN; 50.4% positivity), and 85 organ (40.8% positivity) metastases. Skin metastases were significantly more often classified as PD-L1 negative than LN metastases (OR=0.751; 95%CI=0.599-0.956; P=0.007). PD-L1 positivity was predictive for BOR if determined on LN (CR/PR 37.5% versus 16.1%; OR=0.319; 95%CI=0.138-0.76; P=0.010), but not on skin metastases (CR/PR 36.0% versus 28.0%; OR=0.778; 95%CI=0.379-1.554; P=0.49), translating into favorable survival for PD-L1 positivity determined on LN metastases (median PFS 22.0 versus 3.5 months, HR=0.490; 95%CI=0.310-0.775; P=0.002; median OS 68.9 versus 16.6 months, HR=0.519; 95%CI=0.307-0.880P=0.014). PD-L1 positivity determined on PT (PFS= HR=0.757; 95%CI=0.467-1.226; P=0.27; OS= HR=0.528; 95%CI=0.305-0.913; P=0.032) was predictive to a lesser extent. No relevant survival differences were detected by PD-L1 determined on skin metastases. Multivariate analysis revealed tumor PD-L1 determined on LN metastases as independent predictive factor for PFS (HR=0.43; 95%CI=0.24-0.75; P=0.003) and OS (HR=0.51; 95%CI=0.27-0.96; P=0.037).

Conclusions: For outcome prediction of PD-1-based immunotherapy in melanoma, tumor PD-L1 determined on LN metastases was more reliable than that assessed on PT. PD-L1 determined on skin metastases showed no predictive value and cannot be recommended for clinical use.

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