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PD-L1 expression heterogeneity in NSCLC: accuracy and reliability of using primary lung tumour versus metastatic lymph node deposits.

Background:

Assessing expression of PD-L1 on tumour cell membranes by immunochemistry is an important complementary or crucial companion diagnostic test to guide the use of immune modulating drugs (IMs) in the treatment of non-small cell lung cancer (NSCLC). Difficulties in ascertaining an accurate and precise PD-L1 score are due in part to the heterogeneity of PD-L1 expression and questions over suitability of specimens for testing. Primary tumour tissue and metastatic tissue reflect different tumour microenvironments, and the question of which may provide a more reliable and accurate substrate for PD-L1 analysis is an area of ongoing debate.

Method:

61 cases of resected NSCLC had PD-L1 expression assessed on two blocks of matched primary tumour and 35 cases of resected NSCLC had multiple matched nodal deposits of tumour assessed for PD-L1 using the Roche-Ventana SP263 antibody and expressed as the tumour proportion score (TPS%). 122 blocks of primary tumour and 85 blocks of involved nodes were assessed.

Result:

Of the 61 matched primary cases, 6 (10%) showed a discrepancy of PD-L1 score based on a clinical threshold cut-off of TPS ≥25% or ≥50%. Of the 35 matched nodal deposit cases, 4 were N1 and the remainder were N2. Of these, 6 (17%) showed a discrepancy of PD-L1 score based on clinical thresholds of TPS at ≥1% ≥25% or ≥50%.

Discussion:

Difficulties in ascertaining a precise PD-L1 score due to expression heterogeneity is compounded by the use of small specimens that do not provide accurate representation of the entire tumour/nodal deposit. Primary blocks of tumour show less intra-tumoural variation than cases comparing matched metastatic deposits, but the amount of tissue required for fair representation is far greater. Therefore, small specimens from lymph node deposits may, relative to overall metastases, provide a fairer representation of the true PD-L1 score, but the most precise result may require testing multiple lymph node deposits for PD-L1 expression.