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PD-L1 expression in resected non-small cell lung cancer: variation between primary tumour and nodal metastases

Introduction:
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). Heterogeneity of PD-L1 expression is a major challenge to accurate assessment of PD-L1 status and specimens
of metastatic disease in regional lymph nodes are often the only or most contemporary material available for testing. Concordance between the metastasis and primary tumour remains an important but unknown factor.

Methods: PD-L1 expression was assessed in 107 resected NSCLCs and their stage N1 and N2 nodal metastases using the Roche-Ventana SP263 antibody and expressed as the tumour proportion score (TPS%). 107 blocks of primary tumour and 157 blocks of involved lymph nodes were assessed.

Results: Metastases were present in 157 lymph nodes from the 107 tumours studied; N1 disease in 63 and N2 in the remainder. In 32 cases (30%), there was discrepancy in PD-L1 expression between the primary and its metastases based on cut-offs at ≥1%, ≥25% or ≥50%. In 21 cases, expression was greater in lymph nodes than in the primary tumour, and in 11 it was less.

Conclusion: Heterogeneity of PD-L1 expression is unlikely to be random and probably reflects the complex dynamics between the tumour and its immune environment, which is clearly likely to differ between primary growth in the lung and growth secondarily established in lymphoid tissue. It is suggested that the discrepancy described here is a consequence of these different immune environments. Until more is unknown about this biology, it is impossible to know which component of a disseminated tumour is likely to be most predictive of response to IMs. In the absence of certainty, however, the importance of sampling as generously and as widely as possible is clear.