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PD-L1 Expression in EBUS-Guided Cytology Specimens of Non-Small Cell Lung Cancer is Not Affected by Type of Fixation: A Study of Matched Pairs

Background: No previous trials of immune modulators (IMs) to treat non-small cell lung cancer (NSCLC) have included 'cytology' specimens, dispersed cells aspirated from a tumour deposit or body cavity, for immunochemical assessment of PD-L1, a useful complementary or compulsory companion diagnostic test. This has led to the widely-held view that, in the absence of such 'validation', cytology specimens cannot be used to assess it. In many centres, endobronchial ultrasound (EBUS)-guided aspiration of the tumour or intra-thoracic lymph nodes is the preferred means of diagnosis and staging of NSCLC and such specimens account for the majority received for analysis. Failure to assess them has serious implications for appropriate management and might deny patients effective therapy. Much of this reluctance centres on the alleged effect of fixation in alcohol-based fixatives, the preferred method of cytopathologists, rather than formalin, the standard fixation medium for tissue specimens, on the expression of PD-L1 on the cell surface.

Method: We compared expression of PD-L1 in 50 paired specimens of NSCLC, one fixed in an alcohol-based fixative and one in neutral-buffered formalin, taken from the same tumour deposit or lymph node during the same procedure. All were spun down and formed into a cell block before assessment for PD-L1 expression, which was by two appropriately-trained pathologists with extensive experience in its interpretation.

Result: In none of the 50 pairs studied was there any significant difference, qualitative or quantitative, in the pattern or extent of PD-L1 expression and, in the great majority, it was identical irrespective of fixation.

Conclusion: There is no evidence from this study that the use of alcohol-based fixatives has any effect on the expression of PD-L1 or its interpretation. Notwithstanding the general challenges in accurately assessing such expression, which are common to specimens of tissue as well as dispersed cells, pathologists should feel able to interpret cytology specimens with confidence and clinicians able to rely on the results.