PD-L1 Testing of Patients With Lung Cancer for Immunooncology Therapies Guideline in Collaboration with American Society of Clinical Oncology (ASCO), Association for Molecular Pathology (AMP), International Association for the Study of Lung Cancer (IASLC), Pulmonary Pathology Society (PPS), and LUNGevity Foundation

Draft Statements with Strength of Recommendations

Statement 1
Strong Recommendation: In patients with advanced non-small cell lung cancer (NSCLC), clinicians should use a validated PD-L1 immunohistochemical (IHC) expression assay, in conjunction with other targetable genomic biomarker assays where appropriate, to optimize selection for treatment with immune checkpoint inhibitors.
Statement 2
Conditional Recommendation: Clinicians should test for PD-L1 expression using the best available specimen.   *Note:* Laboratories should ensure appropriate validation has been performed on all specimen types and fixatives. Specific validation requirements are out of scope with this guideline and laboratories should refer to the CAP's IHC Validation Guideline for details on how to validate IHC specimens.
Statement 3
Conditional Recommendation: When feasible, laboratorians should use clinically validated PD-L1 IHC assays as intended.
Statement 4
Strong Recommendations: Laboratories that choose to use laboratory developed tests (LDTs) for PD-L1 expression should validate according to the requirement of their accrediting body.   *Note:* Specific validation requirements are out of scope with this guideline and laboratories should refer to the CAP's IHC Validation Guideline for details on how to validate IHC specimens.
Statement 5
Conditional Recommendation: Laboratorians should report PD-L1 immunohistochemistry results using a percent expression score.
Statement 6
Conditional Recommendation: Clinicians should not use tumor mutation burden alone to select patients with advanced NSCLC for immune checkpoint inhibitors based on insufficient evidence in this population.

Aggregate Certainty of Evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[1] system was used to determine the aggregate certainty of evidence for each outcome, or group of related outcomes, informing Key Questions. GRADE defines a body of evidence in relation to how confident guideline developers can be that the estimate of effects as reported by that body of evidence is correct. Evidence is categorized as high, moderate, low, and very low, and assessment is based on the aggregate risk of bias for the evidence base, plus limitations introduced as a consequence of inconsistency, indirectness, imprecision and publication bias across the studies. Upgrading of evidence is possible if the body of evidence indicates a large effect or if confounding would suggest either spurious effects or would reduce the demonstrated effect.

Grades for Certainty of Evidence (CoE)

Designation	Description
High	There is high confidence that the true effect lies close to that of the estimate of effect.
Moderate	There is moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different
Low	There is limited confidence in the estimate of effect. The true effect may be substantially different from the estimate of effect.
Very Low	There is very little confidence in the estimate of effect. The true effect is likely to be substantially different from the estimate of effect.

[1]

STRENGTH OF RECOMMENDATIONS

Strength of Recommendation (SOR) were determined using the GRADE Evidence to Decision (ETD)[2] framework. The ETD framework includes the COE plus balance of benefits and harms and considered judgements by the EP around values and preferences in relation to outcomes, resources, health equity, acceptability, and feasibility.

Grades for Strength of Recommendations (SOR)

Designation	Recommendation Language	Rationale
Strong Recommendation	Recommend for or against a particular practice (can include 'must' or 'should' as the obligatory verb)	Supported by high or moderate certainty ofevidence and clear benefit that outweighs any harms or clear harms to patients if the opposite action was performed
Conditional Recommendation	Recommend for or against a particular practice (can include 'should' or 'may' as the obligatory verb)	Some limitations in certainty of evidence (moderate to very low certainty), possible balance of benefits and harms, values, or costs, but Expert Panel concludes there is sufficient evidence and/or benefit to inform a recommendation

[3]

References

1. Guyatt G, Oxman AD, Akl EA et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383-394.
2. Alonso-Coello P, Schünemann HJ, Moberg J et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *BMJ* 2016;353:i2016-i2016.
3. Andrews JC, Schünemann HJ, Oxman AD et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. *J Clin Epidemiol*. 2013;66(7):726-735.