

DATE:	6 August 2024
TO:	Pathologists, lung oncologists, and thoracic surgeons, provincially
FROM:	Anatomic and Molecular Pathology
RE:	Lung non-small cell carcinoma (NSCLC) biomarker testing in Alberta

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Key Message

- Ordering of biomarkers in lung non-small cell carcinoma (NSCLC) has increased in complexity with newly indicated testing for resected early-stage lung adenocarcinoma / adenosquamous carcinoma. This document intends to clarify the procedures and indications for lung biomarker testing in NSCLC. Different tests are required for patients with stage IIIB and higher (late-stage) adenocarcinoma / adenosquamous carcinoma, late-stage squamous cell carcinoma, and stage II-III A (early-stage), fully-resected NSCLC.

Background

- The treatment of NSCLC depends on stage and histology. Different biomarkers are required to qualify patients for stage- and histology-specific therapies depending on the patient's situation. As the number of indications has increased, biomarker ordering complexity has increased. Currently, in Alberta, there are three pathways for lung carcinoma biomarker testing in patients with NSCLC, depending on the patient's presentation. This document clarifies the ordering pathways for these indications.
- All patients with adenocarcinoma or adenosquamous carcinoma (or reasonable suspicion of an adenocarcinoma component) who are late-stage at diagnosis should receive reflexive pathologist-initiated comprehensive testing for driver mutations ("Lung Carcinoma Mutation Analysis") and staining with the 22C3 clone of PD-L1 for palliative immunotherapy. Patients with squamous cell carcinoma who are late-stage at diagnosis should receive reflexive pathologist-initiated PD-L1 performed using the 22C3 clone only. Patients with NSCLC (histology not specified) who have been entirely resected, are stage II-III A and are being considered for atezolizumab or osimertinib adjuvant therapy should receive the lung carcinoma DNA evaluation by massarray ("Lung Carcinoma MassArray Early Stage"), ALK immunohistochemistry, and PD-L1 immunohistochemistry using the SP263 clone. This latter application is ONLY to be ordered by oncologists and only on resection specimens.

How this will impact you

- Pathology will continue to offer reflexive comprehensive testing of late-stage lung adenocarcinoma and PD-L1 testing of late-stage squamous cell carcinoma. Oncology and Surgery will initiate testing of early-stage cases (only on resection specimens).

Action Required

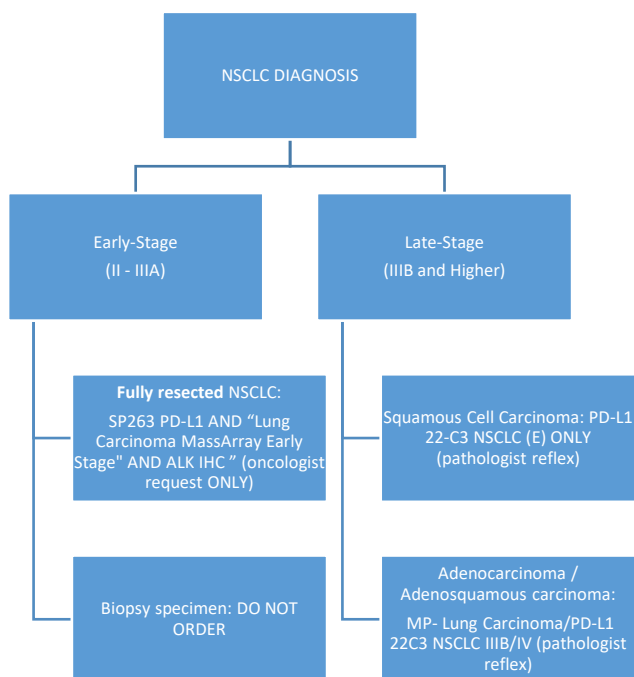
- For pathologists: If the patient has either definitive or likely late-stage lung adenocarcinoma / adenosquamous carcinoma (defined as positive N2-N3 lymph nodes, compelling imaging findings, or definite biopsy of a metastatic site), please order MP- Lung Carcinoma/PD-L1 22C3 NSCLC IIIB/IV in EPIC CaseBuilder on your biopsy or resection specimen.



- In Calgary, lung mutation analysis may be ordered on a CytoLyt-exposed specimen, but only if a suitable biopsy or resection specimen with >5% tumour percentage is not available. CytoLyt-exposed samples yield poorer quality nucleic acids and have a higher chance of molecular test QC failure. CytoLyt-exposed samples are not suitable for PD-L1 testing. This limitation does not apply to Cytopathology samples in Edmonton since CytoLyt-exposed samples are not standard.
- If the patient has definite/likely late-stage squamous cell carcinoma, please order PD-L1 22-C3 NSCLC in Epic Case Builder on the biopsy or resection specimen. Please note that ordering early-stage biomarkers is restricted to oncologist/surgeon requests.
- For oncologists or thoracic surgeons: In patients with complete resection of a stage II-IIIa NSCLC and atezolizumab or osimertinib therapy is being considered, please request the SP263 clone of PD-L1, ALK IHC, and “Lung Carcinoma MassArray Early Stage” testing using the “Additional Testing on Pathology Specimens” function in EPIC (see below for details). It is imperative that “early-stage” be specified on that request. If molecular testing has been missed on an adenocarcinoma / adenosquamous carcinoma patient for whom late-stage testing is indicated, please order “Lung Carcinoma Mutation Analysis” and PD-L1 22C3 using the “Additional Testing on Pathology Specimens” function in EPIC, specifying “late-stage.”

Please see the following for additional ordering information:

Disease	Testing Performed	How to request
NSCLC-Squamous	PD-L1 biomarker testing performed	<p>In Epic: Use “Request for Additional Testing for Pathology Samples” Select: PD-L1 as test Select: Correct stage (Advanced vs Early)</p> <p>Requisition: Forward to Edmonton Zone IHC Lab. Fax: 780-429-2819</p>
NSCLC-Non-squamous (Adenocarcinoma)	EGFR/ALK-5A4/PD-L1 biomarker testing algorithm is performed	<p>In Epic: Use “Request for Additional Testing for Pathology Samples” Select: Lung Carcinoma Mutation Analysis (MP-C,E) as test Select: Correct stage (Stages IIIB/IV vs. Adjuvant therapy Stage II/IIIA)</p> <p>Requisition: Forward to Edmonton Molecular Pathology Lab: Fax:780-407-8599 Forward to: Calgary Consult Desk: Fax 403-944-4748</p>



Effective August 6, 2024

Questions/Concerns

- PD-L1 indications and requests:
 - Dr. Gilbert Bigras, Immunohistochemistry Lead North Sector, gilbert.bigras@albertaprecisionlabs.ca
- Molecular testing questions:
 - Drs. Adrian Box, Scientific/Medical Director Molecular Pathology , adrian.box@albertaprecisionlabs.ca or Cheryl Mather, Molecular Pathology Clinical Lead North Sector, cheryl.mather@albertaprecisionlabs.ca
- Anatomic pathology-related questions:
 - Drs. Angela Franko, Thoracic SG Lead South Sector, angela.franko@albertaprecisionlabs.ca or Sebastiao Nunes Martins Filho, Thoracic SG Lead North Sector, sebastiao.martins@albertaprecisionlabs.ca

Approved by

- Dr. Erik Nohr, Acting Medical/Scientific Director, Molecular Pathology Program
- Mark Douesnard, Operations Director, Genetics & Genomics / Molecular Pathology
- Dr. Carolyn O'Hara, Chief Medical Laboratory Officer (Interim), Alberta Precision Laboratories

Effective September 1, 2023, APL has become the sole provider of all public lab services in Alberta. As a result, community lab services formally provided by DynaLIFE Medical Labs will become the responsibility of Alberta Precision Labs (APL). This change impacts all zones.