March 31, 2023

Re: Changes in Early Stage Lung Cancer Testing

Dear colleagues,

This is an update regarding planned changes to molecular testing for early-stage non-small cell lung cancer (NSCLC) at the Cancer Genetics and Genomics Laboratory (CGL) at BC Cancer. As of April 1st completely resected (R0) stage IB to stage IIIA NSCLC patients are eligible for the next generation sequencing (NGS) testing with the Illumina Focus Panel.[1] This change in testing coincides with provincial funding for osimertinib as adjuvant therapy for NSCLC patients (surgical resected stage IB to IIIB) with *EGFR* exon 19 or L858R mutation-positive tumours.[2,3]

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How has testing changed?

Previously completely resected (R0) stage IB to stage IIIA NSCLC patients were eligible for molecular testing performed by single gene Idylla EGFR testing that was funded by AstraZeneca (ALTER program). As of April 1st NSCLC patients (with surgical resected stage IB to IIIA)[1] are eligible to receive Illumina NGS Focus Panel testing. This test can detect variants including SNVs, indels in over 50 genes as well as fusions and CNVS. Additional details including the list of genes and regions that are tested by Focus Panel can be found on CGL's website: http://cancergeneticslab.ca/genes/focus-panel/

What is the expected turn-around time (TAT) for results?

The anticipated TAT for Focus Panel testing is ≤ 14 days from receipt of sample at CGL.

Who qualifies for testing?

NSCLC patients diagnosed with adenocarcinoma stage IB to IIIA that have or plan to have surgical resection. Note that NSCLC patient diagnosed with later stage (IIIB to IV) continue to be eligible for Focus Panel NGS testing.

How is the test ordered?

For CST-Cerner sites

- **Sunquest 10.0 Code:** FPMGIB
- **Cerner test name:** Focus Panel Molecular Genetic Test Tissue
  - Complete "BC Cancer – Cancer Genetics Laboratory Solid Tumour Testing – Molecular Requisition"

For non CST-Cerner sites:

- **A copy of the requisition can be found here:** http://cancergeneticslab.ca/requisitions/
  - Complete "BC Cancer – Cancer Genetics Laboratory Solid Tumour Testing – Molecular Requisition"

How can I access the clinical report results of a Focus panel test for my patient?

For CST-Cerner sites

- Test results will be received through the CERNER message center, posted to the patient's electronic medical record (only Cerner and CAIS) and mailed (paper copy via Canada Post).

For non CST-Cerner sites:

- Test results will be posted to the patient's electronic medical record (only Cerner and CAIS) and mailed (paper copy via Canada Post).

How does this impact future molecular testing options for NSCLC patients with disease progression from early stage (IB to IIIA) to stage IIIB to IV?

NSCLC patients diagnosed with later stage (IIIB to IV) lung cancer that have not had any molecular testing will continue to be eligible for testing by Focus Panel
For NSCLC patients initially diagnosed with early stage (IB to IIIA) that have previously molecular testing the criteria for additional molecular testing is:

- Any patients that had negative result by the single gene Idylla *EGFR* testing for early stage (IB to IIIA) and have disease progression to stage IIIB to IV will be eligible for Focus Panel NGS testing.
- Patients that had Focus Panel NGS or single gene Idylla EGFR testing for early stage (IB to IIIA) where an *EGFR* exon 19 or L858R mutation was identified and had adjuvant treatment with osimertinib and subsequent disease progression to stage IIIB to IV will be eligible for Focus Panel NGS testing

Note: Patients with previous Focus Panel testing that do not meet the eligibility criteria listed above, do not qualify for a second Focus Panel test (regardless of stage). Should the physician believe that there is clinical justification for a repeat test; approval from the medical director or designate is required.

What will the common results be and how should these be interpreted?

Variants are interpreted and categorized based on their clinical impact using AMP/ASCO/CAP guidelines (PMID: 27993330)[3] as follows:

- Tier I: variants with strong clinical significance (level A and B evidence)
- Tier II: variants with potential clinical significance (level C and D evidence)
- Tier IIIA: variant with uncertain clinical significance
- Tier IIIB: variants with uncertain function
- Tier IV: variants deemed benign or likely benign

References:

1 Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR, Winchester DP. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017 Mar;67(2):93-99. doi: 10.3322/caac.21388. Epub 2017 Jan 17. PMID: 28094848.

2 BC Cancer Protocol Summary for Adjuvant Treatment of Epidermal Growth Factor Receptor (EGFR) Mutation-Positive NonSmall Cell Lung Cancer (NSCLC) with Osimertinib. http://www.bccancer.bc.ca/chemotherapy-protocols-site/Documents/Lung/LUAJOSI_Protocol.pdf (Accessed March 27, 2023)

3 Wu YL, Tsuboi M, He J, John T, Grohe C, Majem M, et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. N Engl J Med. 2020;383(18):1711–23. https://www.nejm.org/doi/full/10.1056/NEJMoa2027071

4 Li MM, Datto M, Duncavage EJ, Kulkarni S, Lindeman NI, Roy S, Tsimberidou AM, Vnencak-Jones CL, Wolff DJ, Younes A, Nikiforova MN. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23. doi: 10.1016/j.jmoldx.2016.10.002. PMID: 27993330; PMCID: PMC5707196.