May 5th, 2021

Re: Launch of Focus Panel NGS testing at CGL

Dear all,

This letter is to inform you that the Cancer Genetics and Genomics Laboratory (CGL) at BC Cancer will be commencing panel- based next generation sequencing (NGS) or "Focus Panel" testing starting May 2021. This testing has received Full Accreditation for Molecular Diagnostics – Next Generation Sequencing (NGS) by the Diagnostic Accreditation Program (DAP) at the College of Physicians and Surgeons of British Columbia. The AmpliSeq for Illumina Focus Panel enables rapid and accurate assessment of genomic variants in 52 genes with known clinical relevance in solid tumors. DNA and RNA obtained from the same tumor formalin- fixed paraffin-embedded (FFPE) specimen are analyzed concurrently to detect alterations including single nucleotide variants (SNVs), insertion/deletions (indels), and copy number variants (CNVs) in DNA, or gene fusions in RNA. Identified variants will be reported out based on their clinical impact using AMP/ASCO/CAP guidelines.[1]

Stephen Yip, M.D., Ph.D., FRCPC
Medical director – Cancer Genetics & Genomics Laboratory
Medical director (Interim)– Centre for Clinical Genomics

What variants are detected by the Focus Panel?

The AmpliSeq for Illumina Focus Panel is an amplicon-based targeted resequencing assay designed to detect recurrent somatic single nucleotide variants (SNVs), small insertion and deletions (indels), copy number variants (CNVs) and fusions, putative fusions and other aberrant splicing events in genes that are clinically relevant to solid tumors. Further details of the methods and the genes and regions covered by Focus Panel can be found on CGL website http://cancergeneticslab.ca/panels/focus-panel/

What patients/indications qualify for Focus Panel testing?

Focus Panel testing will be a new option and/or replace testing for several indications that are currently approved and funded at CGL including:

- Lung Cancer (Stage IIIB/IV Non-Squamous, Non-Neuroendocrine)
- Lung Cancer (Treated, progression for *EGFR* T790M) – For tissue biopsies only
- Low grade infiltrating glioma
- Melanoma (Non-Resectable/Metastatic)

Note: Colorectal Cancer (Metastatic) or Gastrointestinal Stromal Tumour (GIST) patient specimens that have insufficient material (DNA) for the requested Oncopanel test may be reflexed to Focus Panel.

New indications that are funded by Roche under the PREDiCTm study include:

- Biliary Tract
- Pancreatic
- Sarcoma (NOS)
- Salivary gland carcinoma
- Head and Neck squamous cell carcinoma (HNSCC)
- Thyroid carcinoma
- Other indications (approval required)

Additional information on the PREDiCTm study, including confirmation of eligibility for Focus Panel testing can be obtained by contacting Dr. Stephen Yip (SYip-02@bccancer.bc.ca) or Dr. Deepu Alex (deepu.alex@bccancer.bc.ca).

In addition Focus Panel testing is being funded by Novartis for advanced-stage or metastatic hormone-receptor-positive, HER2-negative breast cancer that has progressed after treatment with hormonal therapy in postmenopausal women and men. The goal of this testing is to identify mutations in the *PIK3CA* gene, that may allow these patients to qualify for targeted therapy with the PIK3CA inhibitor Alpelisib (Piqray ®). Please contact Dr. Sean Young (SYoung@bccancer.bc.ca) for inquiries and confirmation of patient eligibility.

How is the test ordered?

Requisitions for currently funded indications as well as for the pharma sponsored testing can be found on the CGL website http://cancergeneticslab.ca/requisitions/

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)[1] 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.

How can I access the clinical report results of the Focus Panel for my patient?

The report will be generated using the CGL SHIRE platform that has formed the basis of all CGL molecular reporting and will be uploaded in the BC Cancer CAIS database and CST Cerner (post June 19).

References:

1. 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.