BC Cancer Clinical Pharmacy Guide

Laboratory Test Interpretation

Contents

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BC Cancer protocols list the standard and diagnostic laboratory tests required at baseline to meet protocol eligibility, and those required before each drug treatment to enable ongoing monitoring for safety and efficacy.

Standard Laboratory Tests

Pharmacists are involved in interpreting protocol required lab tests, such as hematology, liver and renal function, endocrine function, INR and electrolytes. These results are used to monitor toxicity, optimize doses and ensure that patients have adequate organ function to safely proceed with treatment as ordered. In certain cases, pharmacists may order lab tests per ST Policy III-100 Laboratory Tests: Ordering by Pharmacists.

Interpretation of these lab tests is not always a straight forward process. Most lab tests are not specific to one organ and abnormal results may reflect a variety of disease processes. It is necessary to look at both the pattern of lab test results and the clinical picture of the patient when determining the cause of abnormal results and the necessary action. Factors to consider when reviewing lab tests include:

- False positive and negative results can occur; therefore, a single abnormal lab result may require further investigation.
- The treatment intent for the patient should be considered when adjusting doses based on abnormal lab results. It may be reasonable to push ahead with full doses of cancer drugs when the treatment intent is curative; whereas, in the palliative setting, it is often preferable to reduce the dose or delay treatment rather than risk unacceptable toxicity.
- Dose modification recommendations in the setting of organ dysfunction are largely empiric; most of the clinical trials that support these modifications exclude patients with organ dysfunction and they were derived from clinical data obtained prior to the widespread use of colony-stimulating factors.
- Elevations in lab test results can be caused by the cancer itself. For example, liver cancer (primary or metastatic) can cause elevations in liver function tests (LFTs). The oncologist may choose to give full doses of cancer drugs, since treating the liver cancer may improve the LFT results. Some protocols have different dose adjustment recommendations for patients with liver metastases compared with patients without liver metastases (e.g., BRAVTAX).

More information on the various standard lab tests will be covered in the rest of Module 3.

Biomarker Tests

Cancer biomarker testing can look at DNA, RNA, protein or metabolite profiles that are specific to a tumour. Tests for biomarkers play an important role in diagnosing and treating cancer when used in addition to other diagnostic testing such as imaging or biopsy.

Biomarkers can be used in:

- diagnosis and classification of an individual's cancer
- estimation of prognosis
- analysis of appropriate treatment options
- evaluation of response to treatment
- detection of a recurrence after treatment discontinuation

The terms "Biomarker" and "Tumour Marker" are often used interchangeably, depending on which resource is used. For the purposes of this introduction, we have divided this section into where these tests are conducted and reported.

Genetic Test Reporting

Genetic testing is growing at a very rapid rate. With the increased technological advances around genetic testing comes the increased use of targeted therapy for individual cancer patients. Genetic testing can be used to evaluate changes and mutations in genes, chromosomes or proteins.

BC Cancer laboratory's diagnostic services include cancer genetics and screening blood, specimen and biopsy samples. Within these services, the Cancer Genetics and Genomics Laboratory (CGL) at BC Cancer provides molecular genetic diagnostics and cytogenetic testing for patients with cancer in British Columbia. Protocol choice and efficacy monitoring is guided by these results. Descriptions of some of these types of tests are listed below. The results of these tests are found under **Genetics** in BC Cancer Cerner and in the pathology section of CAIS.

These routine genetic tests do not determine the origin of variants. Those patients with suspicious variants that could be inherited, may be referred to the BC Cancer Hereditary Cancer Program for germline (inherited) mutation testing.

Molecular Genetics

Molecular-based RNA or DNA tests vary and can look at changes to a single gene (single gene testing) or many genes (panel testing). Technologies include sequencing and polymerase chain reaction-based assays (PCR).

- DPYD genotyping is an example of a PCR assay test that can alter initial dosing. DPYD is a gene that codes for the DPD (dihydropyrimidine dehydrogenase) enzyme. A number of DPYD gene variants are associated with decreased DPD enzyme activity. The DPD enzyme is the primary route by which capecitabine and fluorouracil are metabolized and inactivated, and DPD deficiency is linked to the accumulation of their active metabolites. The prediction of DPD activity by DPYD genotyping alerts clinicians to alter initial dosing or avoid the use of the two drugs in select patients. More information is available in the Cancer Drug Manual chart Fluorouracil and Capecitabine Dosing Based on DPYD Activity Score.

- Oncotype DX testing (United States) is available for BC Cancer patients with early stage hormone receptor positive, HER2 negative breast cancer. This test assesses the expression of 21 different genes in a patient's tumour and calculates a recurrence-risk score (Recurrence Score®) between 0 to 100 to help identify patients who would benefit from the addition of adjuvant chemotherapy. Women with scores of 26 or over are considered at high-risk of recurrence and most likely to benefit from chemotherapy. Women with lower scores, and depending on age and tumour factors, may be able to receive hormone therapy alone. More information is available at http://www.oncotypedx.com.

- OncoPanel testing by the Cancer Genetics and Genomics Laboratory is an example of a panel test using a sequencing assay that can guide treatment decisions. The OncoPanel, available for select solid tumour types, screens specific genes for DNA changes (variants). The clinical significance of the variant or variant combinations is then interpreted. Genes targeted by OncoPanel include KRAS, BRCA1 and BRCA2, BRAF and EGFR.

- Tumour sequencing panels detect certain gene variants strongly associated with inherited cancer predisposition syndromes (e.g., BRCA1), but do not distinguish between somatic (acquired) and germline (inherited) origin. Individuals with these

suspicious variants, and their family members, may be referred to the BC Cancer Hereditary Cancer Program for germline mutation testing.

Cytogenetics

Cytogenetics is the examination of chromosomes to determine chromosome abnormalities. Karyotyping is one method which detects structural and numerical abnormalities such as deletions, duplications, insertions, inversions and translocations. Fluorescence in situ hybridization (FISH) is a method that detects chromosome abnormalities by targeting **specific** genetic sequences using complementary DNA probes labelled with fluorescent dye. FISH is used in select hematological and solid tumour testing.

- The diagnosis and monitoring of Chronic Myeloid Leukemia (CML) is an example of how a combination of genetic tests is used to influence treatment options. FISH and karyotype analysis are used to diagnose and stage CML and results are reported in a cytogenetics report. FISH looks at the specific translocation of chromosomes 9 and 22 and karyotype analysis is used for disease staging purposes. Once CML is initially diagnosed and staged, molecular-based PCR testing is used to determine baseline molecular burden and preferred type of PCR test for monitoring, depending on the CML variant present. Once treatment has started, PCR monitoring for response to treatment is initially indicated every 3 months as per protocol LKCMLI.

Specific Tumour Marker Reporting

Immunohistochemistry (IHC) and flow cytometry are examples of tests that use antibodies to detect a target antigen in a cell or tissue sample. In IHC, the results are viewed under a light or fluorescent microscope. Flow cytometry uses a flow cytometer and laser beam to detect antigens and the analysis is performed using a computer.

Circulating Tumour Marker

Circulating tumour markers can be found in the blood, urine, stool or other body fluids. Circulating tumour markers cannot be used alone for diagnosis, as noncancerous conditions can sometimes also increase their level. Additionally, not all who have a particular cancer will have increased levels associated with that cancer. However, they are often used to determine effectiveness of treatment or progression of disease.

- CA 15-3 (breast cancer), CA-125 (ovarian cancer), beta-2-microglobulin (hematologic cancers), and prostate-specific antigen (PSA) (prostate) are examples of circulating tumour markers that are followed during cancer treatment to determine the effectiveness of the regimen. Lab results are found under **Tumour Marker** tests in BC Cancer Cerner and CAIS and also in CareConnect.

Tumour Tissue Marker

Tumour tissue markers are found in the tumour and sometimes in blood as "liquid biopsies". They are used to help diagnose, stage, and classify cancer, estimate prognosis and select appropriate treatment such as targeted therapy.

- ER and PR status are breast biomarkers indicating the presence of estrogen and progresterone receptors on breast cancer cells to which the hormones can bind and cause cancer cell growth. ER/PR status is measured from a biopsy sample and if the results are positive, the patient can be treated with hormone therapy (e.g., BRAJTAM). Results of breast biomarker tissue analysis are found in BC Cancer Cerner and in CAIS under pathology results as a **Histopathology** test.

Using Multiple Tests to Diagnose and Monitor an Individual Patient with Cancer

Some patients require regular complex monitoring of their disease and effectiveness of treatment using a variety of biomarker tests.

Multiple Myeloma

Multiple myeloma is an accumulation of malignant plasma cells (malignant white blood cells) in the bone marrow. Often these malignant cells secrete identical abnormal antibody proteins (myeloma immunoglobulins) that crowd out healthy antibodies (normal immunoglobulins). Multiple myeloma is a complex disease and patients can experience increasing risk of immunodeficiency, osteolytic bone lesions, anemia and kidney impairment based on a number of factors. These proteins may be whole immunoglobulins (heavy chain portion and light chain portion), or partial immunoglobulins (light chain portion only) and can be used as surrogate biomarkers for disease activity. A number of serum and urine tests for protein are used to help diagnose and monitor multiple myeloma treatment. All of these tests provide insight into the effectiveness of the individual's treatment and are monitored routinely in

patients with multiple myeloma. These results are found in CareConnect and under **General Chemistry** in Cerner.

- Immunoglobulin panel tests measure the amount of whole antibodies (IgA, IgG, IgM immunoglobulins) in the urine or blood. In multiple myeloma, when the cancer protein level is up, the normal antibody levels are down. In BC Cancer Myeloma protocols, these tests are not mandatory after baseline bloodwork.

- Serum free light chain assay measures the amount of partial free light chain portions of antibodies in the blood (kappa and lambda). A higher level of one or the other may be seen with multiple myeloma. In BC Cancer Myeloma protocols, these tests are usually ordered at baseline and on a regular basis.

- Protein Electrophoresis, serum (SPE) or urine (UPE), uses an electrical field to separate the proteins in the sample into groups: albumin, alpha-1 globulin, alpha-2 globulin, beta-1 globulin, beta-2 globulin and gamma globulin. Most patients with multiple myeloma will show a large amount of one abnormal immunoglobulin protein (M-spike). SPE or UPE can identify the specific type of protein which can then be monitored throughout the disease. In BC Cancer Myeloma protocols, these tests are usually ordered at baseline and on a regular basis.