PIK3CA Genetic Testing for Consideration of Use of PIK3CA Inhibitors (alpelisib) in Breast Cancer – Specimen Requirements and Shipping Guidelines

April 8, 2021

Role of PIK3CA gene testing in Breast Cancer:

Genes within the phosphatidylinositol-3-kinase (PI3K) pathway can become mutated in breast and other cancers, leading to pathway activation that plays a key role in cancer cell proliferation and survival. In breast cancer, activating mutations in the PIK3CA gene is present in up to 40% of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancers. Patient with advanced or metastatic breast cancer whose tumor tissue is HR-positive, HER2-negative and have PIK3CA mutations may benefit from treatment with PIK3CA inhibitors (SOLAR-1 clinical trial).

PIK3CA Testing and Reporting:

The UHN Genome Diagnostics Laboratory at Toronto General will be offering testing of formalin fixed, paraffin-embedded (FFPE) tumor tissue from breast cancer patients for PIK3CA mutations (testing funded by Novartis). Testing will be done using a next-generation sequencing panel that has been validated to detect multiple mutations within the PIK3CA gene.

This test is eligible to postmenopausal women, and men, with hormone receptor-positive, HER2-negative, advanced or metastatic breast cancer that are ongoing on treatment on an endocrine-based regimen in combination with CDK4/6 inhibitor or had this combination of treatment as last line of therapy before progression.

Patients must be:

- Medically fit to receive alpelisib
- Ongoing treatment with aromatase inhibitor +/- CDK 4/6i
- HR+ and HER2- on last biospecimens available
- One line of prior chemotherapy in aBC allowed
- No diabetes mellitus type I or uncontrolled type II
- Not in visceral crises
- No prior Fulvestrant
- No prior Everolimus

Specimen Requirements:

- When possible, the FFPE block is preferred; a ~3mm area will be cored from the block. If a block cannot be sent, please send tissue sections on uncoated air-dried slides shipped at room temperature (8 unstained sections at 7μm). For small biopsies, please contact the laboratory for instructions. For core biopsies, the entire block is required.
- Tumour cellularity must be $\geq$ 20% tumor cells for accurate test results.
- PLEASE NOTE: tumour cellularity must be indicated on the requisition
- EXTERNAL pathology review and corresponding circled H&E slide required prior to sending block.
- For all tissue sections, we require 2 H&E stained sections, one cut before cutting slides from the block and one cut after serial sectioning

Shipping Requirements:

Samples should be appropriately labelled and shipped according to these instructions:

- The slides must be shipped to reach the laboratory immediately after sectioning, preferably in an airtight container.
- Each slide must be labelled with the patient's name, date of birth and MRN#
- Complete the UHN Cytogenetics and Molecular Diagnostics 'Somatic Tumour Testing' requisition form
- Place the slides in an appropriate protective package
- Insert the package in a biohazard plastic bag
- Place the biohazard bag, and completed requisition, into an appropriate outer container for shipping and label the outer container with a biohazard label
- Send to the following address using appropriate methods (FedEx, courier or similar):

The current UHN UHN Cytogenetics and Molecular Diagnostics 'Somatic Tumour Testing' requisition form is available at:
https://www.uhn.ca/LMP/Pages/services_physicians.aspx

Shipping Address: (address is also on requisition)
Genome Diagnostics, Department of Clinical Laboratory Genetics
Toronto General Hospital
Eaton Wing 11th floor, Room 11-444
200 Elizabeth Street Toronto, Ontario, M5G 2C4
Phone: (416) 340-4800 ext. 5170

All Specimens That DO NOT MEET the above specimen and shipping requirements will be REJECTED.