# Tumor Markers

Tumor markers are molecules that can often be detected in higher than normal amounts in the blood, urine or body tissues of some patients with certain types of cancer. Tumor markers are produced either by the tumor itself or by the body in response to the presence of cancer or certain benign (noncancerous) conditions. Measurements of tumor marker levels can be useful when used along with X-rays or other tests in the detection and diagnosis of disease and monitoring of treatment. They can also help predict the stage of the disease, since the higher the tumor marker level, the greater the likelihood that the disease is aggressive or has metastasized (spread). However, measurements of tumor marker levels alone are not sufficient to diagnose cancer. With a few exceptions tumor makers are not widely used to screen or diagnose disease because noncancerous conditions can sometimes produce a positive result.

Some tumor marker levels are measured on the surgical specimen before treatment to help physicians plan appropriate therapy. An example would be the tumor marker HER2 or estrogen receptor (ER), progesterone receptors (PR) or a genomic profile of a tumor like Oncotype DX®. Knowing the levels of these characteristics help determine treatment options.

Tumor marker levels may also be measured during treatment to monitor a patient's response to the treatment. A decrease or return to normal levels of a tumor marker may indicate that the cancer has responded favorably to therapy. If the tumor marker level rises, it may indicate that the cancer is growing. Finally, measurements of tumor marker levels may be used after treatment is complete as a part of follow-up care to check for recurrence. Tumor markers after treatment will be considered along with the patient's history, physical exam and other lab tests by the physician to determine further treatment.

## Studies on Initial Cancer Specimen

### Estrogen (ER) and Progesterone (PR) Receptors

Estrogen and progesterone receptors are recommended to be measured on every newly diagnosed breast cancer patient. It is also recommended that testing of levels be performed on metastatic lesions if biopsy is possible and the results would influence treatment planning. In both premenopausal and postmenopausal patients, ER/PR hormone receptor status is used to identify patients most likely to benefit from hormonal types of cancer therapy. Hormonal therapies include:

- Tamoxifen (Nolvadex®, Soltamox®)
- Aromatase Inhibitors (AIs), which include anastraozole (Arimidex®), letrozole (Femara®) and exemestane (Aromasin®)
- Fulvestrant (Faslodex®)

Estrogen and progesterone receptors are relatively weak predictors of disease-free survival and are not recommended to be used alone to assign patients to prognostic groupings.

## HER2/ neu Gene

HER2/neu gene is another tumor marker that may be increased in some tumors. Amplification or over-expression is the determining factor for the use of the drugs Herceptin or Tykerb® as recommended chemotherapy drugs. Hormonal therapies designed to block HER2 include:

- Trastuzumab (Herceptin®)
- Pertuzumab (Perjeta®)
- Lapatinib (Tykerb®)
- Neratinib (Nerlynx®)
- Ado-trastuzumab emtansine or T-DM1 (Kadcyla®)

## Ki-67 Tumor Marker

Ki-67 is a cancer antigen that is found in growing and dividing cells. It is absent in the resting phase of cell growth when no cell division is occurring. Rate of cell growth may be determined by the testing for Ki-67. This test is done on a sample of tumor tissue and reports how rapidly the tumor is growing which determines aggressiveness.

## Urokinase Plasminogen Activator (uPA); Plasminogen Activator Inhibitor (PAI-1)

Higher than normal levels of these tumor markers in the cancer tissue may mean that the cancer is more aggressive (faster growing). These tumor markers may be used to guide the use of chemotherapy after surgery for patients with node-negative breast cancer (no cancer found in the lymph nodes).

## Genomic Testing

Genomics is the study of how an individual's genes behave in their cancer cells. Genomic tests study genes to help determine what is causing the cancer to grow. The information derived from a genomic test can help physicians determine treatment options.

- **Oncotype DX®** has two genomic tests, one for DCIS and one for invasive breast cancer.
  - **In Situ (DCIS):** The in situ (DCIS) study is for ER-positive lumpectomy patients. The test studies 12 genes associated with aggressiveness and returns a score that predicts 10-year risk of local recurrence or invasive breast cancer. A low Recurrence Score for Stage 0 (in situ cancer) may allow a patient to avoid radiation therapy.
  - **Invasive Breast Cancer:** The invasive breast cancer study measures 21 genes known to be associated with aggressive breast cancer. The test is approved for patients with invasive breast cancer who are ER positive, HER2 negative, diagnosed in stages I-IIIa, and have 1 – 3 positive nodes. The test returns a Recurrence Score on a scale from 0 – 100. Low scores indicate that chemotherapy will not likely be of benefit.
- **Breast Cancer Index (BCI)** is a genomic study for estrogen positive women who have taken an endocrine medication for 4 – 5 years. The study determines if the patient may benefit by continuing to take endocrine therapy for an additional five years. The study is performed on the original pathology slides and reports whether the patient has a low to high risk of breast cancer recurrence. Low risk patients are unlikely to benefit from additional therapy and can confidently stop endocrine therapy after five years. High risk women will benefit from continuing to take endocrine therapy.
- **MammaPrint®** is a genomic study offered to women under the age of 61 with ER-positive or ER-negative carcinomas with negative lymph nodes. An analysis of 70 different gene RNA profiles help identify women with a higher risk of recurrence. This analysis helps a physician make treatment decisions.
- **Other Genomic Testing Labs** may include: Prosigna®, EnoPredict®, Mammostrat® and IHC4®.

### Proteomic Studies

Another newer approach is called proteomics which studies the pattern of all the proteins in the blood instead of looking at an individual protein. This new testing method allows physicians to study the proteins in the body looking for increases in the proteins associated with cancer. This test is also used to help determine aggressiveness of disease.

### Blood Markers After Treatment

After treatment tumor blood markers may be used along with a patient's history and physical exam to monitor response to treatment.

### CEA (Carcinoembryonic Antigen)

CEA belongs to a family of cell-surface glyco-proteins with increased expression found in a number of cancers, including breast cancer. CEA is not recommended alone for screening, diagnosis, staging or routine surveillance of breast cancer patients following primary therapy. However in the absence of other readily measurable disease tests, an increasing CEA level may suggest treatment failure.

### CA 15-3 and CA 27.29

CA 15-3 and CA 27.29 are tumor markers that may be used to help healthcare professionals make decisions regarding therapy for metastatic breast cancer. Baseline levels of the tumor markers are taken before treatment and monitored. Early increases may occur when treatment begins because dying cells may spill their contents into the bloodstream. However, rising levels after six weeks may indicate that treatment is insufficient and may be used as a guide for treatment adjustment.

There are numerous tests for other markers that may be performed on a tumor. Ask your physician which tumor markers will be ordered to evaluate your tumor and follow-up care.

### *Additional Information:*

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