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## ***Test Update***

*From Your Laboratory Service Provider, PathGroup Labs*

### **CellSearch™ Circulating Tumor Cells, Breast Cancer**

#### **Overview**

PathGroup Labs is now offering CellSearch™ technology. This unique, recently FDA approved test detects and enumerates circulating tumor cells (CTC) from peripheral blood in metastatic breast cancer patients.

It is well known that malignant cells circulate in the bloodstream of patients with solid tumors [1, 2]. Most recent findings have shown that presence of CTC in the peripheral blood of patients with solid malignancies correlates with clinical outcome[3]. Indeed, some clinical studies indicate that the assessment of CTCs can assist physicians in monitoring and predicting cancer progression and in evaluating response to therapy in patients with metastatic cancer[4, 5].

Detection and enumeration of CTC from patient's blood with stage IV breast cancer has been shown to be a significant predictor of progression-free survival (PFS) and overall survival (OS) [5-7].

In a recent study by Cristofanilli et al, patients undergoing treatment for metastatic breast cancer with greater than 5 CTC per 7.5 mL whole blood had shorter median PFS (2.7 months vs 7.0 months, P<0.001) and shorter OS (10.1 months vs >18 months, P<0.001) than patients having less than 5 CTC per 7.5 mL blood. Moreover, a decrease in the number of CTCs to less than 5 from baseline to first follow-up (4-5 weeks after initiation of new therapy) was also found to be predictive of PFS and OS. These results suggest that the number of CTCs is a useful prognostic guide for patients with metastatic breast cancer and can reliably estimate disease progression and survival earlier (4-5 weeks vs 8-12 weeks, respectively) than traditional imaging methods[6].

The CellSearch™ Circulating Tumor Cell technology detects and enumerates CTC of epithelial origin that are CD45 negative, EpCAM positive, and cytokeratins 8, 18, and 19 positive [8].

#### **Clinical Utility:**

Predict progression-free survival (PFS) and overall survival (OS) in patients with stage IV breast cancer[6]

Potential use in monitoring treatment of metastatic cancer[7]

Disease management[7]

#### **Candidate for testing:**

Patients with stage IV breast cancer, prior to a new course of therapy and at follow-up

#### **Method:**

CellSearch™ technology (Veridex LLC). Immunomagnetic sample enrichment using antibodies targeting epithelial cell adhesion molecule (EpCAM) and cell labeling with fluorescent nucleic acid dye (DAPI).

Epithelial cells distinguished from leukocytes using fluorescent labeled monoclonal antibodies specific for leukocytes (CD-45) and epithelial cells (cytokeratins 8,18, and 19)[8].

Results reported as number of CTCs/7.5 mL of whole blood.

Analytical sensitivity: 1 CTC/7.5 mL whole blood[8].

Analytical specificity: 99.7%[8]



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*Note: Antibodies used in the CellSearch assay are targeted at cell markers (EpCAM and cytokeratins 8, 18, and 19) expressed by adenocarcinomas.<sup>9-12</sup> CTCs that do not express these markers will not be detected by the CellSearch assay, whereas CTCs from non-breast malignancies expressing these markers may be detected. CellSearch test results should be interpreted in conjunction with other clinical and laboratory findings.*

**Ordering Information:**

**Specimen Collection and Storage:**

**NOTE: PathGroup Labs will only accept specimens collected on the following days of the week: Mondays, Tuesdays, and Wednesdays. Specimens collected on other days will be rejected due to time sensitive specimen processing.**

Collect 2 -10 ml CellSave Preservative Tube™ (7.5 mL minimum) provided by PathGroup Labs.

Whole blood specimen – invert tubes 8 times to prevent clotting.

Maintain specimens at **ROOM TEMPERATURE**.

Samples may be collected prior to therapy and at first follow-up visit (4-5 weeks after initiation of new therapy).

Specimen is to be kept at room temperature during all phases: collection, shipping, testing process and final storage.

Specimen must be tested within 72 hours of collection. **DO NOT REFRIGERATE**.

*Note: because doxorubicin inhibits the assay, allow at least 7 days after administration of doxorubicin (adriamycin) before sample collection.*

**CPT Codes:** 88346 x3, 88361, 86316

**Reference Range:**

Less than 5 CTCs/7.5 mL whole blood

**Interpretation of results:**

CTC count  $\geq 5/7.5$  mL prior to therapy or at first follow-up is predictive of shorter PFS and OS. A decrease in the number of CTCs to  $<5/7.5$  mL from baseline to first follow-up is associated with longer PFS and OS[6, 7].

**Turnaround Time:** Preliminary report will be available 48 hours after testing completed.

**References:**

1. Mocellin, S., et al., *Circulating tumor cells: the 'leukemic phase' of solid cancers*. Trends Mol Med, 2006. **12**(3): p. 130-9.
2. Allard, W.J., et al., *Tumor cells circulate in the peripheral blood of all major carcinomas but not in healthy subjects or patients with nonmalignant diseases*. Clin Cancer Res, 2004. **10**(20): p. 6897-904.
3. Hayes, D.F., et al., *Circulating tumor cells at each follow-up time point during therapy of metastatic breast cancer patients predict progression-free and overall survival*. Clin Cancer Res, 2006. **12**(14 Pt 1): p. 4218-24.
4. Aquino, A., et al., *A novel method for monitoring response to chemotherapy based on the detection of circulating cancer cells: a case report*. J Chemother, 2002. **14**(4): p. 412-6.
5. Weigelt, B., et al., *Marker genes for circulating tumour cells predict survival in metastasized breast cancer patients*. Br J Cancer, 2003. **88**(7): p. 1091-4.
6. Cristofanilli, M., et al., *Circulating tumor cells, disease progression, and survival in metastatic breast cancer*. N Engl J Med, 2004. **351**(8): p. 781-91.



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7. Cristofanilli, M., et al., *Circulating tumor cells: a novel prognostic factor for newly diagnosed metastatic breast cancer*. J Clin Oncol, 2005. **23**(7): p. 1420-30.
8. Cai, Q.Q., et al., *Detection and clinical significance of circulating tumor cells in peripheral blood of breast cancer patients*. Ai Zheng, 2005. **24**(7): p. 837-41.