Breast Complete™

Each year there are over 230,000 new cases of invasive breast cancers and over 60,000 of *in situ* breast cancers diagnosed in the U.S. In 2014, there were more than 2.8 million women living in the U.S. with a history of breast cancer. Millions of women are surviving this disease as a result of advancements in diagnosis and clinical management. Breast cancer subtyping is critical in determining appropriate targeted therapy options and predicting treatment response. By offering the most comprehensive testing panel available, CGI's Breast Complete™ Program can help in determining the best personalized course of action for the patient.

Empowering Personalized Medicine

Clinicians have long known that patients respond differently to treatment. Genomics is now helping them in apprehending each patient's unique genetic make-up and the probable outcome of their disease. Testing patients for specific biomarkers can provide insight into diagnosis, prognosis, and the patient's likelihood of responding to certain treatments.

Tests being offered in the Complete™ Programs include biomarkers that rely on various methodologies and that have diagnostic and prognostic significance for each patient.

List of Breast Complete™ Tests

Physicians can order tests individually or allow CGI pathologists and directors to determine a panel evaluation as determined necessary.

IHC & ISH

Histological Evaluation (IHC)

The Histological evaluation provides critical information for confirmation and subtyping breast cancer as breast primary, ductal vs. lobular, invasive vs. *in situ* carcinoma, usual hyperplasia vs. atypical hyperplasia, and basal-like carcinoma. Markers commonly utilized include CK7, CK20, GCDFP-15, mammaglobin, E-cadherin, p63, SMMHC, Calponin-1, CK 5/6, CK 903 (34βE12), and CD 117 (c-KIT).

Breast cancer therapeutic and prognostic biomarker studies are listed below.

Hormonal Receptor ER/PR (IHC)

ER and PR expression predicts increased response rates to endocrine therapy in breast cancer patients. Patients with ER and/or PR-positive early stage breast cancer undergoing tamoxifen or other endocrine therapy have substantially lower risk for recurrence and death across all age groups. ER and PR testing is also used to predict response to endocrine therapy in the metastatic setting. Higher amounts of ER have been positively correlated with increased response rates to tamoxifen treatment.

EGFR (IHC)

EGFR is involved in regulating cell growth in breast cancers. Overexpression of EGFR is associated with adverse disease characteristics and poor clinical outcome.

HER2 [Pathway®] (IHC) (FDA Approved)

The Pathway® IHC assay is intended to determine the HER2 status of breast cancer and aid in predicting disease-free and overall survival in breast cancer cases. This assay is also indicated as an aid in the assessment of patients for whom Herceptin® (trastuzumab) or other HER2-targeted treatment is being considered.

HER2 [INFORM®] (Dual ISH) (FDA Approved)

The INFORM® HER2 Dual ISH DNA Probe Cocktail Assay is a chromogenic *in situ* hybridization assay and intended to determine HER2 gene status as an aid in the assessment of patients for whom Herceptin® (trastuzumab) treatment is being considered.

Ki-67 (IHC)

Ki-67 expression is used to assess tumor cell proliferation and assists in prognosis of breast cancers.

p53 (IHC)

p53 expression assists in the prognosis of breast cancers.

FISH

HER2/neu [PathVysion®] (FDA Approved)

The PathVysion® Probe Kit is designed to detect amplification of the HER-2/neu gene via FISH in formalin-fixed paraffin-embedded (FFPE) human breast cancer tissue specimens. This test aids in predicting disease-free and overall survival in patients with stage II, node-positive breast cancer who have been treated with adjuvant cyclophosphamide, doxorubicin and 5-fluorouracil (CAF) chemotherapy. The test is also indicated as an aid in the assessment of patients for whom Herceptin® (trastuzumab) treatment is being considered.

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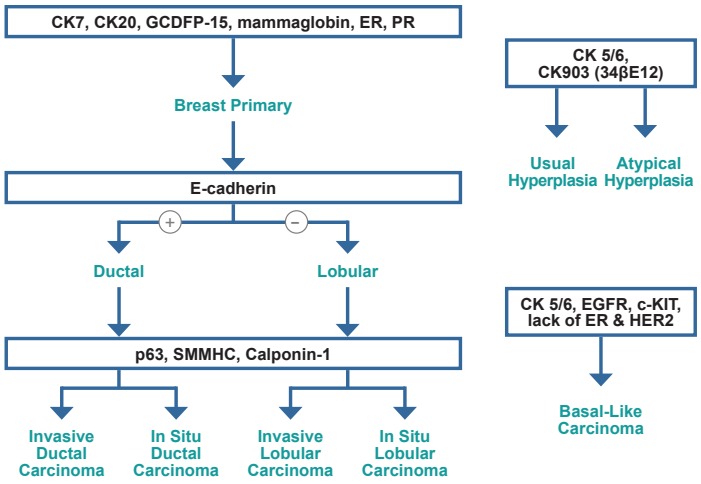
CANCER GENETICS®

Empowering Personalized Cancer Treatment

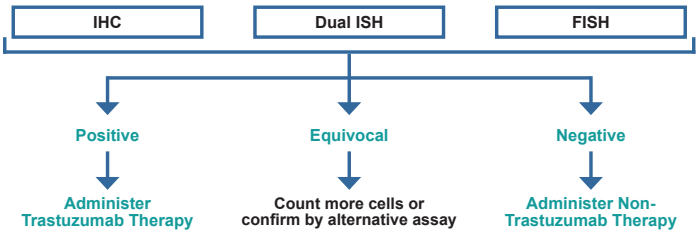
Breast COMPLETE

Work Up for Breast Complete™

Histological Evaluation - Diagnosis



HER2 Testing



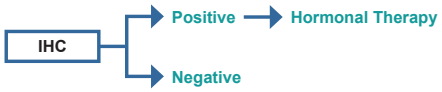
Reference Range: HER2 by IHC

0, Negative	no staining or incomplete faint staining in ≤10% cells
1+, Negative	incomplete faint membrane staining in >10% cells
2+, Equivocal	incomplete, weak/moderate staining in >10% cells or complete intense staining in ≤10% cells
3+, Positive	complete intense staining in >10% cells

Reference Range: HER2 by Dual ISH or FISH

Negative	HER2/CEP17 ratio <2.0, with avg. HER2 copy no. <4.0
Equivocal	HER2/CEP17 ratio <2.0, with avg. HER2 copy no. ≥4.0 and <6.0
Positive	HER2/CEP17 ratio ≥2.0 or avg. HER2 copy no. ≥6.0

ER/PR Testing



Reference Range: ER/PR by IHC

Negative	< 1%
Positive	≥ 1%

This work up is intended as a guide for the comprehensive suite of diagnostic tests included in Breast Complete™ to diagnose and monitor breast cancers. Physicians can order tests individually or allow CGI pathologists and directors to determine a panel evaluation as determined necessary. Tests offered through CGI's Complete™ Programs are also available via Digital Pathology.

Specimen Requirements

	Test	TAT (Mon.-Fri.)	Tissue	Shipping Requirements
IHC & ISH	Histological Evaluation (IHC)	1-2 days	FFPE block/H&E slide	Room temperature
IHC & ISH	ER/PR (IHC)	2-4 days	FFPE block or Ten 4-5 µm thick unstained sections on positively coated slides	Room temperature
IHC & ISH	EGFR (IHC)			
IHC & ISH	HER2 Pathway® (IHC)			
IHC & ISH	HER2 INFORM® (Dual ISH)			
IHC & ISH	Ki67 (IHC)			
IHC & ISH	p53 (IHC)			
FISH	HER2/neu PathVysion®	5-7 days	Three 4 µm thick unstained sections on positively coated slides or FFPE tissue block	Room temperature
Breast Complete™ Panel		5 - 7 days	Fifteen 4-5 µm thick FFPE unstained sections on positively coated slides or FFPE tissue block	Room temperature

FFPE: formalin-fixed paraffin-embedded

CGI Laboratory Licensure

CAP (Laboratory #: 7191582, AU-ID: 1434060), CLIA (Certificate #: 31D1038733), New Jersey (CLIS ID #: 0002299), New York State (PFI: 8192), Pennsylvania (031978), Florida (800018142), Maryland (1395), California (COS 800558).

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