Breast cancer diagnostic solutions
Deliver diagnostic confidence
Breast cancer remains a significant scientific, clinical and societal challenge. Everyone’s cancer diagnosis is as distinct as the person it affects. Breast cancer is heterogeneous in nature and has distinct biological, pathological and genetic diversity. Biomarkers can help identify patient subgroups most likely to benefit from a specific treatment. Diagnostic and prognostic descriptions of subtypes, guided by biomarker results, have become increasingly more sophisticated over the past decades.
**Precision medicine: The right test at the right time facilitates differential diagnosis**

Evidence supports that breast cancer tumors can be grouped into subtypes with distinct clinical profiles and treatment options. Understanding the diversity in breast cancer allows for stratification of patient subgroups. Individual biomarkers (or panels of biomarkers) characterize subtypes, confirm origin of tissue, differentiate primary from metastatic tumor and provide prognostic and predictive information.

- Biomarkers play an important role in the detection and management of patients
- Biomarkers are the most precise way of identifying intrinsic subtypes
- Failure to correctly stratify a patient can lead to unnecessary and costly exposure to therapeutics, prevent the delivery of the most beneficial treatment and may reduce the degree of positive outcomes

**Three reasons to choose Roche Tissue Diagnostic’s Solutions**

Our breast cancer diagnostics deliver on three key benefits that are valued by pathology professionals:

1. **Clinical utility**
   With proven accuracy, our breast cancer diagnostic assays help you identify patients other assays can miss — so you can deliver the right test, with clinical confidence in the shortest possible time.

2. **Analytical performance**
   Specific and sensitive rabbit monoclonal antibodies, best-in-class probes, and powerful detection systems help you diagnose precisely and confidently.

3. **Testing efficiency**
   Our comprehensive breast cancer workflow solution delivers fully automated assays on market-leading platforms, with digital pathology and workflow solutions that free resources, reduce labor costs, and reduce time to results.

---

*Our mission is to improve the lives of all patients afflicted with cancer. We are committed to empowering you in your quest to elevate the standard of care.*
Biomarker status helps to identify patient groups most likely to respond to a specific treatment

HER2 overexpression accounts for 15% to 20% of all breast cancers. Tumors that overexpress the HER2 gene are associated with more rapid growth compared to HER2 negative tumors.6,10,12

Estrogen Receptor (ER) and Progesterone Receptor (PR) positive tumors account for approximately 74% of all breast cancer tumors. Dual positive hormone receptor tumors are usually slow growing and less aggressive.5

Luminal A tumors have favorable short-term prognosis and show favorable response to hormonal therapy.5 Luminal B tends to be more aggressive and higher grade than Luminal A.5

In early breast cancer, moderate to strong PR expression is an aid to differentiate between Luminal A and B tumors.12

Classifications of IHC subtypes: St. Gallen Consensus12

<table>
<thead>
<tr>
<th>Erb-B2 overexpression (non-luminal)</th>
<th>Luminal A</th>
<th>Luminal B (Her2 +)</th>
<th>Luminal B (Her2 -)</th>
<th>Basel like (Ductal, TN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 + Overexpressed or amplified</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ER -</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>PR -</td>
<td>+</td>
<td>Any</td>
<td>Negative or low</td>
<td>-</td>
</tr>
<tr>
<td>Ki-67 Low</td>
<td>Any</td>
<td>High</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key**

+ positive
- negative
TN triple negative

This chart is not for diagnostic use. It represents staining patterns that are associated with breast cancers based on St. Gallen Expert Consensus, 2013.12
Pathology assessments play a critical role in breast cancer management

Breast cancer management is complex and biomarkers play an integral role in determining the status of the tumor. IHC and ISH biomarkers help facilitate decision-making for subsequent therapeutic options.\(^3,6,10\)

The benefit of chemotherapy is dependant on multiple factors: Tumor size, lymph node involvement and the presence of biomarkers.\(^5\)

Multiple tests used to determine treatment\(^{11}\)

Breast cancer histology

- **Hormone receptor status**
  - ER+ and/or PR+
  - ER- and/or PR-

**HER2 status**

- HER2+
  - Targeted therapy*
  - Hormone therapy * and targeted therapy

- HER2-
  - Hormone therapy *
  - Targeted therapy*

**Treatment decision**

- Non-targeted therapy*

Source: Diagram is developed based on NCCN Guideline for Invasive Breast Cancer\(^{11}\)

* Targeted therapy can include chemotherapy with trastuzumab for HER2 positive patients, hormone therapy is for ER and/or PR positive patients, non-targeted therapy refers to chemotherapy for patients with triple negative status.
Provide confidence in your lab with Roche Tissue Diagnostics HER2 testing

INFORM HER2 Dual ISH DNA Probe cocktail
INFORM HER2 Dual ISH DNA Probe cocktail is designed to detect amplification of the HER2 gene and is indicated as an aid in the assessment of patients for whom Herceptin treatment is being considered.13

Results are easily scored using brightfield microscopy — in-house with familiar technologies
- HER2 gene amplification assessment over the entire slide — not just a pre-selected area — facilitates scoring and identification of heterogeneity
- Simultaneous morphological assessment independent of H&E stain
- Archivable results allow for easy maintenance and simplifies consults in difficult cases
- Enhanced technical support tools — including clear, consolidated guidance on best practices and streamlined training

ISH utilized as a reflex for IHC equivocal (2+) results

Patient breast tissue sample
- Standardized and validated test platforms
- Adequate (formalin) fixation (6-72h)

H&E stain
- Primary staining shows morphologic changes

IHC
- Controls passed
- No significant staining in normal epithelium

<table>
<thead>
<tr>
<th>ISH</th>
<th>IHC</th>
<th>Patient breast tissue sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0+</td>
<td>No faint or partial staining^</td>
</tr>
<tr>
<td>1+</td>
<td></td>
<td>Weak complete staining^</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Greater than 10%</td>
</tr>
<tr>
<td>2+</td>
<td></td>
<td>Intense &quot;complete&quot; staining^</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Greater than 10%</td>
</tr>
</tbody>
</table>

Report as HER2 positive oncologist for HER2-targeted therapies
In a recent publication assessing the socioeconomic impact of inaccurate HER2 breast cancer testing, laboratory-developed in vitro diagnostic (IVD) were compared to U.S. Food and Drug Administration-approved IVD, found a cost benefit in using an approved IVD test.

**HER2/neu (4B5)* Rabbit Monoclonal Primary Antibody**

The use of pre-diluted PATHWAY HER2 (4B5), in combination with the fully automated BenchMark IHC/ISH slide staining instrument, standardizes all IHC processes from baking through staining, and reduces the possibility of human error. It also minimizes inherent variability resulting from individual reagent dilution and other processes found in manual and semi-automated IHC methods.

The PATHWAY HER2 (4B5) Primary Antibody empowers you to:

- Achieve consistently high proficiency assessment scores with HER2 (4B5) antibody, compared to other clones
- Employ the most widely adopted and reliable HER2-IHC primary antibody
- High concordance with HER2 FISH

**HER2 (4B5): Consistent high performance***

*Data refers to PATHWAY and VENTANA products. Based on 5 years of data from a leading external quality assessment scheme. Retrieved from http://www.nordiqc.org/epitopes.htm
Provide an aide in the management, prognosis and prediction of therapy outcomes of breast cancer

CONFIRM anti-Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody and CONFIRM anti-Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody

ER is a powerful predictor of response to hormone therapy (such as Tamoxifen) and clinical outcome of breast cancer patients. PR status can add additional prognostic and predictive value to ER status by providing an independent and significant tool for predicting hormone therapy response and clinical outcome.  

- Indicated as an aid in patient management, prognosis, and the prediction of therapy outcomes in breast cancer
- Rapid and consistent results delivered through fully automated platforms and digital pathology solutions
- ER (SP1) is a significant predictor of disease-specific survival
- Achieve consistently high proficiency assessment scores with ER (SP1) antibody, compared the other clones
- PR (1E2) antibody provides significant value as a prognostic factor and response prediction of hormone therapy, even in ER negative patients

ER (SP1): Consistent high performance

*Based on 5 years of data from a leading external quality assessment scheme. Retrieved from http://www.nordiqc.org/epitopes.htm
CONFIRM anti-Ki-67 (30-9) Rabbit Monoclonal Primary Antibody
CONFIRM Ki-67 (30-9) Antibody is directed against C-terminal portion of Ki-67 antigen. Staining for Ki-67 can be used to aid in assessing the proliferative activity of normal and neoplastic tissue. With intense nuclear staining and no adipose (K2) or cell membrane staining (MIB-1), CONFIRM Ki-67 (30-9) rabbit monoclonal antibody can help deliver a confident assessment of tumor aggressiveness.22,23

Uncontrolled proliferation is a hallmark of malignancy. The 2013, St Gallen Expert Consensus12 found that the degree of proliferative activity in breast cancer helped differentiate Luminal A from Luminal B tumors.

VENTANA anti-E-cadherin (36) Mouse Monoclonal Primary Antibody
VENTANA E-cadherin (36) antibody is directed against the cytoplasmic domain of the human transmembrane protein E-cadherin expressed as a part of the cell–cell adhesion complex in epithelial tissues.24 Reduction or loss of expression is associated with invasive carcinoma and possibly metastasis in a variety of carcinomas. This antibody may be used to aid in the differentiation of in-situ and/or invasive lobular carcinoma from in situ and/or invasive ductal carcinoma of the breast.

CONFIRM p53 (DO-7) Primary Antibody
CONFIRM p53 (DO-7) is used in conjunction with VENTANA Companion Algorithm p53 (DO-7) image analysis application using the VENTANA iScan Coreo Au scanner and VIRTUOSO software.25

GATA3 (L50-823) Mouse Monoclonal Primary Antibody
Use of this antibody is indicated as an aid in the identification of breast carcinomas within the context of an antibody panel, clinical history and a qualified pathologist.26 GATA3 expression is primarily seen in breast carcinoma and urothelial carcinoma and only rarely found in tumors from other organs.26

Mammaglobin (31A5) Rabbit Monoclonal Antibody
Use of this antibody is indicated as an aid in the identification of metastatic breast carcinomas within the context of an antibody panel, clinical history and a qualified pathologist.27 When combined with other breast-restricted markers such as GCDFP-15, an overall sensitivity for breast carcinoma of 84% has been achieved.27
Digital pathology: Virtual consultation, image analysis and education

Roche Digital Pathology is transforming the practice of pathology by developing innovative technologies that deliver medical value, inform decision making and improve cancer care. The integrated solution consists of high-quality scanners, image analysis software, image and workflow management software and education applications, all working together globally to optimize laboratories. Digital pathology enables more efficient and informed treatment decisions for patients — enchanting care by eliminating the boundaries of time and distance.

Your benefit

Virtual consultation
• Maximize pathologist time
• Enable flexibility for tumor boards, case sharing and collaboration
• Enable fast turnaround time for expert opinions
• Provide access to sub-specialists

Image analysis
• Build clinical confidence with US and CE-IVD validated Companion Algorithm image analysis software
• Facilitate consistent, objective interpretations for breast IHC — verified by a pathologist — for every patient

Education
• Enrich and accelerate learning in a collaborative environment
• Allow students to review material anywhere, anytime, from the device of their choice

Product features

VENTANA Virtuoso image and workflow management software
• Anytime, anywhere access to slide images
• Optimize digital workflow and decision-making environment
Web-based application to support remote consults and image analysis

VENTANA Companion Algorithm image analysis software
• US and CE-IVD validated image analysis algorithms for the full breast panel: HER2, ER, PR, Ki-67 and p53
• Semi-quantitative scores for markers requiring cell counts
• Fully validated as part of a systems approach — includes reagents, staining platforms, scanners and software

VENTANA iScan Coreo slide scanner
• Intended for low- to mid-volume scanning sites
• Brightfield scanning capability (160 slide capacity) at various magnifications — 4x, 10x, 20x, 40x
• Live mode (remotely controlled microscope)

VENTANA iScan HT slide scanner
• Intended for high-volume scanning sites
• Brightfield scanning capability (360 slide capacity) at various magnifications — 20x, 40x
• Continuous random access and STAT processing — with no workflow interruption

VENTANA Vector education and collaboration software
• Support education and collaboration with digital images
• Standardize content and eliminate sharing resources (slides or microscopes)
• Allow students to review material anywhere, anytime, from the device of their choice (mobile-capable on iOS and Android devices)

Breast cancer diagnostic solutions
## World-class antibodies to stratify breast cancer

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Catalog no.</th>
<th>Ordering code</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA-125 (OC125) Mouse Monoclonal Antibody</td>
<td>760-2610</td>
<td>05267269001</td>
<td>50</td>
</tr>
<tr>
<td>Calponin-1 (EP798Y) Rabbit Monoclonal Antibody</td>
<td>760-4376</td>
<td>05435684001</td>
<td>50</td>
</tr>
<tr>
<td>E-cadherin (36) Mouse Monoclonal Primary Antibody, VENTANA</td>
<td>790-4447</td>
<td>05985290001</td>
<td>50</td>
</tr>
<tr>
<td>E-cadherin (EP700Y) Antibody</td>
<td>760-4440</td>
<td>05973872001</td>
<td>50</td>
</tr>
<tr>
<td>Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody, CONFIRM</td>
<td>760-4324</td>
<td>05278406001</td>
<td>50</td>
</tr>
<tr>
<td>Estrogen Receptor (ER) (SP1) Rabbit Monoclonal Primary Antibody, CONFIRM</td>
<td>790-4325</td>
<td>05278414001</td>
<td>250</td>
</tr>
<tr>
<td>FOXA1 (2F83) Mouse Monoclonal Primary Antibody</td>
<td>760-4937</td>
<td>07292848001</td>
<td>50</td>
</tr>
<tr>
<td>GATA3 (L50–823) Mouse Monoclonal Primary Antibody</td>
<td>760-4697</td>
<td>07107749001</td>
<td>50</td>
</tr>
<tr>
<td>GCDFP-15 (EP1582Y) Rabbit Monoclonal Antibody</td>
<td>760-4386</td>
<td>05463530001</td>
<td>50</td>
</tr>
<tr>
<td>GLIAL Fibrillary Acidic Protein (EP672Y) Rabbit Monoclonal Antibody</td>
<td>760-4345</td>
<td>05269784001</td>
<td>50</td>
</tr>
<tr>
<td>Growth Hormone (polyclonal)</td>
<td>760-2804</td>
<td>05268257001</td>
<td>50</td>
</tr>
<tr>
<td>Human Placental Lactogen (hPL) (polyclonal)</td>
<td>760-4443</td>
<td>05973830001</td>
<td>50</td>
</tr>
<tr>
<td>HER2 Dual ISH DNA Probe Cocktail, INFORM</td>
<td>780-4422</td>
<td>05586840001</td>
<td>50</td>
</tr>
<tr>
<td>HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody, PATHWAY</td>
<td>790-2991</td>
<td>05278368001</td>
<td>50</td>
</tr>
<tr>
<td>Her-2/neu (4B5) Rabbit Monoclonal Primary Antibody, VENTANA</td>
<td>790-4493</td>
<td>05999570001</td>
<td>50</td>
</tr>
<tr>
<td>Ki-67 (30–9) Rabbit Monoclonal Primary Antibody, CONFIRM</td>
<td>790-4286</td>
<td>05278384001</td>
<td>50</td>
</tr>
<tr>
<td>Memmoglobin (31A5) Rabbit Monoclonal Antibody</td>
<td>760-4263</td>
<td>05269253001</td>
<td>50</td>
</tr>
<tr>
<td>P53 (BPS3-11) Primary Antibody</td>
<td>760-2542</td>
<td>05267102001</td>
<td>50</td>
</tr>
<tr>
<td>P53 (DO-7) Primary Antibody, CONFIRM</td>
<td>800-2912</td>
<td>05278775001</td>
<td>50</td>
</tr>
<tr>
<td>P57 (Kp10) Mouse Monoclonal Primary Antibody</td>
<td>760-4617</td>
<td>06523897001</td>
<td>50</td>
</tr>
<tr>
<td>p63 (AA4) Mouse Monoclonal Primary Antibody, VENTANA</td>
<td>790-4509</td>
<td>05867061001</td>
<td>50</td>
</tr>
<tr>
<td>P120 CATENIN (98) Mouse Monoclonal Primary Antibody, VENTANA</td>
<td>790-4517</td>
<td>05867088001</td>
<td>50</td>
</tr>
<tr>
<td>PAX8 (MRQ-50) Mouse Monoclonal Primary Antibody</td>
<td>760-4618</td>
<td>06523927001</td>
<td>50</td>
</tr>
<tr>
<td>PLAP (NB10)</td>
<td>760-2664</td>
<td>05267757001</td>
<td>50</td>
</tr>
<tr>
<td>Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody</td>
<td>790-2223</td>
<td>05277990001</td>
<td>50</td>
</tr>
<tr>
<td>Progesterone Receptor (PR) (1E2) Rabbit Monoclonal Primary Antibody</td>
<td>790-4296</td>
<td>052783920001</td>
<td>250</td>
</tr>
<tr>
<td>PTEN (SP218) Rabbit Monoclonal Primary Antibody</td>
<td>790-5097</td>
<td>07970200001</td>
<td>50</td>
</tr>
<tr>
<td>Topoisomerase IIo (JS548) Rabbit Monoclonal Primary Antibody</td>
<td>790-4371</td>
<td>05479339001</td>
<td>50</td>
</tr>
</tbody>
</table>

Experience the power and confidence that comes from bringing VENTANA breast cancer diagnostics to your practice—and patients—today. For more information, contact your local Account Manager or visit us at www.ventana.com/breast
References


13. INFORM HER2 Dual ISH DNA Probe Cocktail Assay Package Insert.


