Unlocking new treatment options for Patients with Metastatic Breast Cancer

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Recommend Molecular Testing in Breast Cancer

1 Therapeutic options are available for amplified and/or mutated ERBB2 (HER2)

2 Testing for germline BRCA1 and BRCA2 mutations should be considered in patients with HER2- metastatic breast cancer under consideration for chemotherapy

3 Assess for PIK3CA mutation with tumor or liquid biopsy if patient has HR+/HER2-metastatic breast cancer

4 For patients with metastatic triple-negative breast cancer (TNBC) assess PD-L1 biomarker status

Our portfolio of tests analyzes guideline recommended genes for relevant alterations in patients with breast cancer including ERBB2 (HER2), BRCA1/2*, and PIK3CA and offer a supplemental IHC-test for PD-L1.

Value of Comprehensive Genomic Profiling with Foundation Medicine:

- Our tests detect additional alterations in genes known to be relevant in breast cancer, such as NTRK, ESR1, AKT1, as well as alterations in genes involved in the cell cycle pathway and the PI3K-AKT-mTOR and HER2/FGFR pathways.

- Conveniently order supplemental PD-L1 testing that is the companion diagnostic for atezolizumab with your comprehensive tissue-based test all from one partner.

- Breast cancer patients from all sub-types who have TMB ≥9 may benefit from cancer immunotherapy independent of their PD-L1 status or prior therapies.

Advancing Therapy Options in Breast Cancer

FDA-Approved therapies3, including the bolded therapies for which FoundationOne CDx is the companion diagnostic

<table>
<thead>
<tr>
<th>BIOMARKER</th>
<th>FDA-APPROVED THERAPY</th>
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<tbody>
<tr>
<td>ERBB2 (HER2) amplification</td>
<td>Herceptin® (trastuzumab) Perjeta® (pertuzumab) Kadcyla® (ado-trastuzumab-emtansine)</td>
</tr>
<tr>
<td>PIK3CA alterations</td>
<td>Piqray® (alpelisib)</td>
</tr>
<tr>
<td>HER2- and BRCA1/2+</td>
<td>Lynparza® (olaparib) Talzenna® (talazoparib)</td>
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<tr>
<td>MSI-H</td>
<td>Keytruda® (pembrolizumab)</td>
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<tr>
<td>NTRK fusions</td>
<td>Vitrakvi® (larotrectinib) Rozlytrek® (entrectonib)</td>
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<tr>
<td>PD-L1 expression4</td>
<td>Tecentriq® (atezolizumab) in combination with Abraxane®</td>
</tr>
<tr>
<td>TMB ≥ 10 mutations per megabase</td>
<td>Keytruda® (pembrolizumab)</td>
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* Foundation Medicine detects both somatic and germline alterations but does not differentiate between the two on reports.
Growing Therapy Options in Breast Cancer
Genomic alterations and relevance for clinical trials with novel therapies

<table>
<thead>
<tr>
<th>MOLECULAR ALTERATION</th>
<th>SUBTYPE CONSIDERATION</th>
<th>DRUG CLASS</th>
</tr>
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<tbody>
<tr>
<td>ERBB2 mutation</td>
<td>2%–4% breast cancer</td>
<td>HER2 Tyrosine kinase inhibitors (TKI)</td>
</tr>
<tr>
<td>AKT1 mutation</td>
<td>2%–5% breast cancer</td>
<td>AKT inhibitor, mTor inhibitor</td>
</tr>
<tr>
<td>ESR1 mutation</td>
<td>30%–40% ER+/HER2- after aromatase inhibitors (AI)</td>
<td>Selective estrogen receptor degrader</td>
</tr>
<tr>
<td>TMB ≥9</td>
<td>8–12% breast cancers²</td>
<td>Immune checkpoint inhibitor</td>
</tr>
</tbody>
</table>

FDA-approved portfolio of tests to help identify more treatment options:

**TISSUE BIOPSY**

FoundationOne CDx is FDA-approved and includes Medicare coverage for qualifying patients³.

- Analyzes 324 genes
- Reports TMB and MSI

**LIQUID BIOPSY**

FoundationOne Liquid CDx is FDA-approved and includes Medicare coverage for qualifying patients⁶.

- Analyzes 324 genes³
- bTMB, MSI-High, and tumor fraction⁴

◊ FoundationOne Liquid CDx is FDA-approved to report substitutions and indels in 311 genes, including rearrangements and copy number losses only in BRCA1/2. Comprehensive results across all 324 genes, including bTMB, MSI-H status, and tumor fraction are reported in the professional services section of the report.

For the complete label, including companion diagnostic indications and important risk information, please visit www.F1CDxLabel.com and www.F1LCDxLabel.com.

**REFERENCES**:

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.5.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed July 29, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.


3. Herceptin®, Perjeta®, and Kadcyla® are registered trademarks of Genentech, Inc. Lynparza® is a registered trademark of the AstraZeneca group of companies. Talzenna® is a registered trademark of Pfizer Inc. Brontyza® is a registered trademark of Novartis. Keytruda® is a registered trademark of Merck Sharp & Dohme Corp. a subsidiary of Merck & Co., Inc. Vitrakvi® is a registered trademark of Bayer. Pitrax® is a registered trademark of Novartis.

4. VENTANA PD-L1 (SP142) assay is the companion diagnostic for atezolizumab and can be ordered a supplemental test to tissue-based testing with Foundation Medicine.


6. The Centers for Medicare & Medicaid Services (CMS) Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R) see Appendix B

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