NCCN Clinical Practice Guidelines in Oncology
(NCCN Guidelines®)

Breast Cancer

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**SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-NEGATIVE DISEASE**

**Postmenopausal Patients with pT1–3 and pN0 or pN+ Tumors**

- **Tumor ≤0.5 cm and pN0**
  - Consider adjuvant endocrine therapy\(^z\) (category 2B)
  - Adjuvant chemotherapy\(^{bb,cc}\) followed by endocrine therapy\(^z\) (category 1)
  - Adjuvant endocrine therapy\(^z\)

- **Tumor >0.5 cm or pN1mi (≤2 mm axillary node metastases) or pN1 (1–3 positive nodes)**
  - Strongly consider 21-gene RT-PCR assay if candidate for chemotherapy (category 1)\(^{\text{hi,ij}}\)
  - Recurrence score <26
    - Adjuvant chemotherapy\(^{bb,cc}\) followed by endocrine therapy\(^z\) (category 1)
  - Recurrence score ≥26
    - Adjuvant chemotherapy\(^{bb,cc}\) followed by endocrine therapy\(^z\) (category 1)

- **pN2/pN3 (≥4 ipsilateral metastases >2 mm)**\(^{hh}\)
  - Not done

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\(^d\) See Principles of Biomarker Testing (BINV-A).
\(^q\) See Special Considerations for Breast Cancer in Men (Sex Assigned Male at Birth) (BINV-J).
\(^i\) According to WHO, carcinoma of NST encompasses multiple patterns including medullary pattern, cancers with neuroendocrine expression, and other rare patterns.
\(^y\) Although patients with cancers with 1%–100% ER IHC staining are considered ER-positive and eligible for endocrine therapies, there are more limited data on the subgroup of cancers with ER-low–positive (1%–10%) results. The ER-low–positive group is heterogeneous with reported biologic behavior often similar to ER-negative cancers; thus individualized consideration of risks versus benefits of endocrine therapy and additional adjuvant therapies should be incorporated into decision-making. See Principles of Biomarker Testing (BINV-A).
\(^g\) See Definition of Menopause (BINV-O).

\(^bb\) Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with RT is acceptable. See Adjuvant Endocrine Therapy (BINV-K) and Preoperative/Adjuvant Therapy Regimens (BINV-L).

\(^cc\) There are limited data to make chemotherapy recommendations for those ≥70 y of age. See NCCN Guidelines for Older Adult Oncology.

\(^\text{hi,ij}\) Other prognostic gene expression assays may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy. See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).

\(^hh\) There are few data regarding the role of gene expression assays in those with ≥4 ipsilateral axillary lymph nodes. Decisions to administer adjuvant chemotherapy for this group should be based on clinical factors.

\(^z\) Consider adjuvant bisphosphonate therapy in patients with natural or induced menopause.

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**SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-NEGATIVE DISEASE**

**PREMENOPAUSAL**

**PATIENTS with pT1–3 AND pN0 TUMORS**

- **Tumor ≤0.5 cm and pN0**
  - Strongly consider 21-gene RT-PCR assay if candidate for chemotherapy (category 1)
  - Recurrence score ≤15
  - Not done
  - Consider adjuvant endocrine therapy

- **Tumor >0.5 cm and pN0**
  - pN1–pN3
  - See BINV-8

- **Not done**
- **Recurrence score 16–25**
  - Adjuvant endocrine therapy ± ovarian suppression/ablation
  - Adjuvant chemotherapy followed by endocrine therapy

- **Recurrence score ≥26**
  - Adjuvant chemotherapy followed by endocrine therapy

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**See Special Considerations for Breast Cancer in Men (Sex Assigned Male at Birth) (BINV-J).**

**See Definition of Menopause (BINV-O).**

**See Principles of Biomarker Testing (BINV-A).**

**See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).**

Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with RT is acceptable. See Adjuvant Endocrine Therapy (BINV-K) and Preoperative/Adjuvant Therapy Regimens (BINV-L).

Other prognostic gene expression assays may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy. See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).

Patients with T1b tumors with low-grade histology and no lymphovascular invasion should be treated with endocrine monotherapy as the TAILORx trial did not include patients with such tumors.

In premenopausal patients with RS <26, the addition of chemotherapy to endocrine therapy was associated with a lower rate of distant recurrence compared with endocrine monotherapy, but it is unclear if the benefit was due to the ovarian suppression effects promoted by chemotherapy.
SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-NEGATIVE DISEASE
PREMENOPAUSAL\textsuperscript{99} PATIENTS with pT1–3 AND pN+ TUMORS

- Ductal/NST\textsuperscript{1}
- Lobular
- Mixed
- Micropapillary

\begin{itemize}
  \item pN1mi (≤2 mm axillary node metastasis) or pN1 (1–3 positive nodes)
  \item pN2/pN3 (≥4 ipsilateral metastases >2 mm)\textsuperscript{ll}
\end{itemize}

\textbf{Not a candidate for chemotherapy}

Assess to determine if candidate for chemotherapy

If candidate for chemotherapy consider gene expression assay to assess prognosis\textsuperscript{kk,mm}

\begin{itemize}
  \item Adjuvant endocrine therapy + ovarian suppression/ablation\textsuperscript{zz,aa,kk}
  \item Adjuvant chemotherapy\textsuperscript{bb} followed by endocrine therapy\textsuperscript{zz,aa,kk}
  \item Adjuvant endocrine therapy + ovarian suppression/ablation\textsuperscript{zz,aa,kk}
  \item Adjuvant chemotherapy\textsuperscript{bb} followed by endocrine therapy\textsuperscript{zz,aa (category 1)}
\end{itemize}

\textbf{Adjuvant endocrine therapy + ovarian suppression/ablation}\textsuperscript{zz,aa,kk}

Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with RT is acceptable. See Adjuvant Endocrine Therapy (BINV-K) and Preoperative/Adjuvant Therapy Regimens (BINV-L).

See Definition of Menopause (BINV-O).

In premenopausal patients with RS <26, the addition of chemotherapy to endocrine therapy was associated with a lower rate of distant recurrence compared with endocrine monotherapy, but it is unclear if the benefit was due to the ovarian suppression effects promoted by chemotherapy.

There are few data regarding the role of gene expression assays in those with ≥4 ipsilateral axillary lymph nodes. Decisions to administer adjuvant chemotherapy for this group should be based on clinical factors.

See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).

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\textsuperscript{zz} See Definition of Menopause (BINV-O).
\textsuperscript{kk} In premenopausal patients with RS <26, the addition of chemotherapy to endocrine therapy was associated with a lower rate of distant recurrence compared with endocrine monotherapy, but it is unclear if the benefit was due to the ovarian suppression effects promoted by chemotherapy.
\textsuperscript{ll} There are few data regarding the role of gene expression assays in those with ≥4 ipsilateral axillary lymph nodes. Decisions to administer adjuvant chemotherapy for this group should be based on clinical factors.
\textsuperscript{aa} Evidence suggests that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal patients with HR-positive breast cancer is similar to that achieved with CMF alone. See Adjuvant Endocrine Therapy (BINV-K).
\textsuperscript{mm} See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).
**WORKUP PRIOR TO PREOPERATIVE SYSTEMIC THERAPY**

**CLINICAL STAGE**

A2T2\(rr\) or cN+ and M0

- Considering preoperative systemic therapy\(pp\) (see criteria for preoperative systemic therapy on [BINV-M, 1 of 2](#))

**ADDITIONAL WORKUP\(a\)**

- Axillary assessment with exam
  - Consider ultrasound
  - Percutaneous biopsy of suspicious nodes\(qq\)
- CBC
- Comprehensive metabolic panel, including liver function tests and alkaline phosphatase

**Additional tests to consider:**

- Chest diagnostic CT with contrast
- Abdominal pelvic diagnostic CT with contrast or MRI with contrast
- Bone scan or sodium fluoride PET/CT\(ss\) (category 2B)
- FDG PET/CT\(tt\) (optional)
- Breast MRI\(b\) (optional), with special consideration for mammographically occult tumors, if not previously done

**For operable breast cancers:** See [Breast and Axillary Evaluation Prior to Preoperative Systemic Therapy (BINV-13)](#)

**For inoperable breast cancers:** See [Preoperative Systemic Therapy (BINV-15)](#)

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\(a\) For tools to aid optimal assessment and management of older adults, see [NCCN Guidelines for Older Adult Oncology](#).

\(b\) Breast MRI may be useful for characterizing axillary and/or internal mammary nodal disease. See [Principles of Dedicated Breast MRI Testing (BINV-B)](#).

\(h\) Routine systemic staging is not indicated for non-metastatic (M0) cancer in the absence of signs or symptoms. If metastatic disease is suspected, see Workup on [BINV-18](#).

\(pp\) See [Principles of Preoperative Systemic Therapy (BINV-M)](#).

\(qq\) At the time of axillary node sampling, a clip or tattoo should be placed to permit verification that the biopsy-positive lymph node has been removed at the time of definitive surgery.


\(ss\) Bone scan or sodium fluoride PET/CT may not be needed if FDG PET/CT is performed and clearly indicates bone metastasis, on both the PET and CT component.

\(tt\) FDG PET/CT may be performed at the same time as diagnostic CT, and may be helpful in situations where standard staging studies are equivocal or suspicious. FDG PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard staging studies.

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<table>
<thead>
<tr>
<th>Assay</th>
<th>Predictive</th>
<th>Prognostic</th>
<th>NCCN Category of Preference</th>
<th>NCCN Category of Evidence and Consensus</th>
<th>Recurrence Risk and Treatment Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-gene (Oncotype Dx) (for pN0)</td>
<td>Yes</td>
<td>Yes</td>
<td>Preferred</td>
<td>1</td>
<td>BINV-N (2 of 5)</td>
</tr>
<tr>
<td>21-gene (Oncotype Dx) for pN1 (1–3 positive nodes)</td>
<td>Yes</td>
<td>Yes</td>
<td>Postmenopausal: Preferred</td>
<td>1</td>
<td>BINV-N (2 of 5)</td>
</tr>
<tr>
<td>21-gene (Oncotype Dx) for pN1 (1–3 positive nodes)</td>
<td>Not determined</td>
<td>Yes</td>
<td>Other</td>
<td>1</td>
<td>BINV-N (3 of 5)</td>
</tr>
<tr>
<td>70-gene (MammaPrint) for pN0 and pN1 (1–3 positive nodes)</td>
<td>Not determined</td>
<td>Yes</td>
<td>Other</td>
<td>2A</td>
<td>BINV-N (3 of 5)</td>
</tr>
<tr>
<td>50-gene (Prosigna) for pN0 and pN1 (1–3 positive nodes)</td>
<td>Not determined</td>
<td>Yes</td>
<td>Other</td>
<td>2A</td>
<td>BINV-N (3 of 5)</td>
</tr>
<tr>
<td>12-gene (EndoPredict) for pN0 and pN1 (1–3 positive nodes)</td>
<td>Not determined</td>
<td>Yes</td>
<td>Other</td>
<td>2A</td>
<td>BINV-N (3 of 5)</td>
</tr>
<tr>
<td>Breast Cancer Index (BCI)</td>
<td>Predictive of benefit of extended adjuvant endocrine therapy</td>
<td>Yes</td>
<td>Other</td>
<td>2A</td>
<td>BINV-N (4 of 5)</td>
</tr>
</tbody>
</table>

a Gene expression assays provide prognostic and therapy-predictive information that complements T,N,M and biomarker information. Use of these assays is not required for staging. The 21-gene assay (Oncotype Dx) is preferred by the NCCN Breast Cancer Panel for prognosis and prediction of chemotherapy benefit. Other prognostic gene expression assays can provide prognostic information but the ability to predict chemotherapy benefit is unknown.

b See Special Considerations for Breast Cancer in Men (Sex Assigned Male at Birth) (BINV-J).

c In the overall study population of the RxPONDER trial, 10.3% had high grade disease and 9.2% had 3 involved nodes.

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<thead>
<tr>
<th>Assay</th>
<th>Recurrence Risk</th>
<th>Treatment Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-gene (Oncotype Dx) for postmenopausal patients with pN0 and pN1 (1–3 positive nodes)(^c)</td>
<td>&lt;26</td>
<td>Patients with T1b/c–2, pN0, HR-positive, HER2-negative tumors, with risk scores (RS) between 0–10 have a risk of distant recurrence of &lt;4% and those with RS 11–25, derived no benefit from the addition of chemotherapy to endocrine therapy in the prospective TAILORx study.(^1) Postmenopausal patients with pT1–3, pN1, HR-positive, HER2-negative, with RS ≤26 derived no benefit from the addition of chemotherapy to endocrine therapy in the prospective RxPONDER study.(^2)</td>
</tr>
<tr>
<td></td>
<td>≥26</td>
<td>In postmenopausal patients with pT1–3, HR-positive, HER2-negative, and pN0 and pN1 (1–3 positive nodes) tumors and an RS ≥26, the addition of chemotherapy to endocrine therapy is recommended.(^1,2)</td>
</tr>
<tr>
<td>21-gene (Oncotype Dx) (for premenopausal patients: pN0)</td>
<td>≤15</td>
<td>Premenopausal patients with T1b/c –2, pN0, HR-positive, HER2-negative tumors with RS ≤16 derived no benefit from the addition of chemotherapy to endocrine therapy in the prospective TAILORx study.(^1)</td>
</tr>
<tr>
<td></td>
<td>16–25</td>
<td>In premenopausal patients with RS between 16–25, a small benefit from the addition of chemotherapy could not be ruled out, but it is unclear if the benefit was due to the ovarian suppression effect promoted by chemotherapy in premenopausal patients.(^1,2) For this group, consider chemotherapy followed by endocrine therapy or alternatively, ovarian function suppression combined with either tamoxifen or an AI.</td>
</tr>
<tr>
<td></td>
<td>≥26</td>
<td>In premenopausal patients with HR-positive, HER2-negative, and pN0 tumors and an RS ≥26, the addition of chemotherapy to endocrine therapy is recommended.(^1,2)</td>
</tr>
<tr>
<td>21-gene (Oncotype Dx) (for premenopausal patients with 1–3 positive nodes)(^c)</td>
<td>&lt;26</td>
<td>In premenopausal patients with pT1–3 and pN1 (1–3 positive nodes) tumors and an RS &lt;26, the addition of chemotherapy to endocrine therapy was associated with a lower rate of distant recurrence compared with endocrine monotherapy(^2) but it is unclear if the benefit was due to the ovarian suppression effects promoted by chemotherapy. For this group of patients, consider chemotherapy followed by endocrine therapy or alternatively, ovarian function suppression combined with either tamoxifen or an AI.</td>
</tr>
<tr>
<td></td>
<td>≥26</td>
<td>In premenopausal patients with HR-positive, HER2-negative, pT1–3 and pN1 (1–3 positive nodes) tumors and an RS ≥26, the addition of chemotherapy to endocrine therapy is recommended.(^2)</td>
</tr>
</tbody>
</table>

\(^a\) Gene expression assays provide prognostic and therapy-predictive information that complements T,N,M and biomarker information. Use of these assays is not required for staging. The 21-gene assay (Oncotype Dx) is preferred by the NCCN Breast Cancer Panel for prognosis and prediction of chemotherapy benefit. Other prognostic gene expression assays can provide prognostic information but the ability to predict chemotherapy benefit is unknown.

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<tr>
<th>Assay</th>
<th>Recurrence Risk</th>
<th>Treatment Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>70-gene (MammaPrint) (for pN0 and 1–3 positive nodes)</strong></td>
<td>Low</td>
<td>With a median follow-up of 5 years, among patients at high clinical risk and low genomic risk, the rate of survival without distant metastasis in this group was 94.7% (95% CI, 92.5%–96.2%) among those who did not receive adjuvant chemotherapy. Among patients with 1–3 positive nodes, the rates of survival without distant metastases were 96.3% (95% CI, 93.1–98.1) in those who received adjuvant chemotherapy vs. 95.6 (95% CI, 92.7–97.4) in those who did not receive adjuvant chemotherapy. Therefore, the additional benefit of adjuvant chemotherapy may be small in this group. In a subset analyses, the benefit of chemotherapy was mostly seen in patients under 50 years of age. The absolute difference in distant metastasis-free survival at 8 years in those receiving chemotherapy for patients ≤ 50 years was 5.4% ± 2.8% versus 0.2% ± 2.3% for those &gt;50 years. It is not known whether the benefit of chemotherapy observed in women ≤ 50 years is related to chemotherapy-induced ovarian function suppression.</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 50-gene (Prosigna) (for pN0 and 1–3 positive nodes) | Node negative: Low (0–40) | For patients with T1 and T2 HR-positive, HER2-negative, pN0 tumors, a risk of recurrence score in the low range, regardless of T size, places the tumor into the same prognostic category as T1a–T1b,N0,M0. |
| Node negative: Intermediate (41–60) | | |
| Node negative: High (61–100) | | |
| Node positive: Low (0–40) | In patients with HR-positive, HER2-negative, pN+ tumors (1–3 positive lymph nodes) with low risk of recurrence score, treated with endocrine therapy alone, the distant recurrence risk was less than 3.5% at 10 years and no distant recurrence was seen at 10 years in the TransATAC study in a similar group. |
| Node positive: High (41–100) | | |

| 12-gene (EndoPredict) (pN0 and 1–3 positive nodes) | Low (≤3.3) | For patients with T1 and T2 HR-positive, HER2-negative, and pN0 tumors, a 12-gene low-risk score, regardless of T size, places the tumor into the same prognostic category as T1a–T1b,N0,M0. In ABCSG 6/8, patients in the low-risk group had risk of distant recurrence of 4% at 10 years and in the TransATAC study, patients with 1–3 positive nodes in the low-risk group had a 5.6% risk of distant recurrence at 10 years. The assay is prognostic in endocrine and chemo-endocrine treated patients. |
| High (>3.3) | | |

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References

BINV-N

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<table>
<thead>
<tr>
<th>Assay</th>
<th>Recurrence Risk/ Predictive Result</th>
<th>Treatment Implications</th>
</tr>
</thead>
</table>
| **Breast Cancer Index (BCI)** | BCI (H/I) Low | • For patients with T1 and T2 HR-positive, HER2-negative, and pN0 tumors, a BCI (H/I) in the low-risk range (0–5), regardless of T size, places the tumor into the same prognostic category as T1a–T1b, N0,M0.  
• Patients with BCI (H/I) low demonstrated a lower risk of distant recurrence (compared to BCI [H/I] high) and no significant improvement in DFS or OS compared to the control arm in terms of extending endocrine therapy duration.9 |
| | BCI (H/I) High | • For patients with T1 HR-positive, HER2-negative, and pN0 tumors, a BCI (H/I) high (5.1–10) demonstrated significant rates of late distant recurrence.  
• In secondary analyses of the MA.17, Trans-aTTom, and IDEAL trials, patients with HR-positive, T1–T3, pN0 or pN+ who had a BCI (H/I) high demonstrated significant improvements in DFS when adjuvant endocrine therapy was extended, compared to the control arm.9-12  
• In contrast, BCI (H/I) low patients derived no benefit from extended adjuvant therapy.9 |

*Gene expression assays provide prognostic and therapy-predictive information that complements T,N,M and biomarker information. Use of these assays is not required for staging. The 21-gene assay (Oncotype Dx) is preferred by the NCCN Breast Cancer Panel for prognosis and prediction of chemotherapy benefit. Other prognostic gene expression assays can provide prognostic information but the ability to predict chemotherapy benefit is unknown.*

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**References**
GENE EXPRESSION ASSAYS FOR CONSIDERATION OF ADJUVANT SYSTEMIC THERAPY

References

2. Kalinsky K, Barlow WE, Meric-Bernstam F, et al. First results from a phase III randomized clinical trial of standard adjuvant endocrine therapy (ET) +/- chemotherapy (CT) in patients (pts) with 1-3 positive nodes, hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer (BC) with recurrence score (RS) < 25: SWOG S1007 (RxPonder). SABCS 2021:81(4): Abstract GS3-00.

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**Table 4. Pathological Prognostic Stage (continued)**

<table>
<thead>
<tr>
<th>TNM</th>
<th>Grade</th>
<th>HER2</th>
<th>ER</th>
<th>PR</th>
<th>Stage</th>
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<tbody>
<tr>
<td>T4 N0 M0</td>
<td>T4 N1*** M0</td>
<td>T4 N2 M0</td>
<td>Any T N3 M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>IIIA</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>Negative</td>
<td>IIIB</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
1. For cases with lymph node involvement with no evidence of primary tumor (e.g. T0 N1 etc.) or with breast ductal carcinoma in situ (e.g. Tis N1 etc.), the grade, HER2, ER and PR information from the tumor in the lymph node should be used for assigning stage group.
2. For cases where HER2 is determined to be “equivocal” by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, HER2 “negative” category should be used for staging in the Pathological Prognostic Stage Group.
3. The prognostic value of these Prognostic Stage Groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

**Table 5. Genomic Profile for Pathologic Prognostic Staging**

When Oncotype DX Score is Less than 11...

<table>
<thead>
<tr>
<th>TNM</th>
<th>Grade</th>
<th>HER2</th>
<th>ER</th>
<th>PR</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 N0 M0</td>
<td>T2 N0 M0</td>
<td>Any</td>
<td>Negative</td>
<td>Positive</td>
<td>Any</td>
</tr>
</tbody>
</table>

**Notes:**
1. Obtaining genomic profiles is NOT required for assigning Pathological Prognostic Stage. However, genomic profiles may be performed for use in determining appropriate treatment. If the OncotypeDx® test is performed in cases with a T1N0M0 or T2N0M0 cancer that is HER2-negative and ER-positive, and the recurrence score is less than 11, the case should be assigned Pathological Prognostic Stage Group IA.
2. If OncotypeDx® is not performed, or if it is performed and the OncotypeDx® score is not available, or is 11 or greater for patients with T1–2 N0 M0 HER2–negative, ER-positive cancer, then the Prognostic Stage Group is assigned based on the anatomic and biomarker categories shown above.
3. OncotypeDx® is the only multigene panel included to classify Pathologic Prognostic Stage because prospective Level I data supports this use for patients with a score less than 11. Future updates to the staging system may include results from other multigene panels to assign cohorts of patients to Prognostic Stage Groups based on the then available evidence. Inclusion or exclusion in this staging table of a genomic profile assay is not an endorsement of any specific assay and should not limit appropriate clinical use of any genomic profile assay based on evidence available at the time of treatment.

***N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1 and T4 N1, respectively.

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