Internal request:
Comment to consider updating the systemic adjuvant treatment recommendations for HR-positive – HER2-negative disease based on the update RxPonder trial data.

The panel consensus was to revise and reorganize the adjuvant therapy recommendations by the following settings:

- **Postmenopausal patients with pT1-3 and pN0 or pN+ tumors (BINV-6)**
  - The panel consensus supported a category 1 recommendation for postmenopausal patients with pT1-3 and pN0 or pN1 (1-3 positive nodes) tumors
    - Recurrence score < 26: Adjuvant endocrine therapy
    - Recurrence score ≥ 26: Adjuvant chemotherapy followed by endocrine therapy

- **Premenopausal Patients with pT1-3 and pN0 Tumors (BINV-7)**
- **Premenopausal patients with pT1-3 and pN+ tumors (BINV-8)**

**BINV-N**
The panel consensus supported changing the 21-gene (Oncotype Dx) assay from a category 2A to a category 1, preferred option for postmenopausal patients with pN1 tumors (1-3 positive nodes). This is a category 2A, other recommended option for premenopausal patients.

**References:**
- 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.

<table>
<thead>
<tr>
<th>Guideline Page and Request</th>
<th>Panel Discussion/References</th>
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<td>BINV-6/BINV-7/BINV-8/BINV-N</td>
<td>The panel consensus was to revise and reorganize the adjuvant therapy recommendations by the following settings:</td>
<td>YES</td>
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| Internal request: | - Postmenopausal patients with pT1-3 and pN0 or pN+ tumors (BINV-6)  
  - The panel consensus supported a category 1 recommendation for postmenopausal patients with pT1-3 and pN0 or pN1 (1-3 positive nodes) tumors  
    - Recurrence score < 26: Adjuvant endocrine therapy  
    - Recurrence score ≥ 26: Adjuvant chemotherapy followed by endocrine therapy | 31 | 0 | 0 | 0 |
| | - Premenopausal Patients with pT1-3 and pN0 Tumors (BINV-7) | | | | |
| | - Premenopausal patients with pT1-3 and pN+ tumors (BINV-8) | | | | |
| **BINV-N** | The panel consensus supported changing the 21-gene (Oncotype Dx) assay from a category 2A to a category 1, preferred option for postmenopausal patients with pN1 tumors (1-3 positive nodes). This is a category 2A, other recommended option for premenopausal patients. | 31 | 0 | 0 | 0 |
**Internal request:**

In response to the FDA approval of margetuximab-cmkb + chemotherapy for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, the panel considered the addition of margetuximab-cmkb + chemotherapy for this indication.

Based on a review of the data in the noted reference, the panel consensus was to include margetuximab-cmkb + chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) as an option in third line and beyond for the treatment of patients with recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease. This is a category 2A, other recommended regimen.


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**Comment to consider reorganizing the systemic therapy options for HER2-positive recurrent unresectable (local or regional) or stage IV (M1) disease by setting/line of therapy.**

The panel consensus supported reorganizing the systemic therapy options for HER2-positive recurrent unresectable (local or regional) or stage IV (M1) disease by setting/line of therapy.