**HER2DX**

**SUMMARY**

<table>
<thead>
<tr>
<th>HER2DX</th>
<th>RELAPSE RISK</th>
<th>pCR LIKELIHOOD SCORE</th>
<th>ERBB2 EXPRESSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>14</td>
<td>61</td>
<td>65</td>
</tr>
<tr>
<td>Result</td>
<td>Low</td>
<td>Medium</td>
<td>High</td>
</tr>
<tr>
<td>Description</td>
<td>97% disease-free survival at 5-years when treated with chemotherapy and trastuzumab</td>
<td>42% pCR rate when treated with trastuzumab-based chemotherapy</td>
<td>High response to T-DM1</td>
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**TEST DESCRIPTION**

HER2DX in HER2+ breast cancer measures the expression of 27 genes tracking immune infiltration (14 genes), tumor cell proliferation (4 genes), luminal differentiation (5 genes) and the HER2 amplicon (4 genes, including ERBB2).

The information from the 4 gene signatures is combined with tumor stage and nodal stage into 2 single scores (ranging from 0 to 100).

**HER2DX predicts 2 clinical endpoints in each patient:**
1) Long-term risk of relapse following trastuzumab-based chemotherapy.
2) The probability of achieving a pathological complete response (pCR) following neoadjuvant anti-HER2-based therapy.

In addition, HER2DX provides ERBB2 mRNA expression levels within HER2+ breast cancer.
The HER2DX prognostic score correlates with the probability of distant relapse-free survival (DRFS) in 434 patients with early stage HER2+ breast cancer who received trastuzumab (9 weeks or 12 months) and chemotherapy in the Short-HER phase III clinical trial. A single cut-off from the final HER2DX risk score was selected to split patients into low- and high-risk groups.

The prognostic value of HER2DX was evaluated in an external validation cohort, where 268 patients with Early stage HER2+ cancer received local therapy and anti-HER2-based treatment (96% received chemotherapy, 56% received dual HER2 blockade in the neoadjuvant setting, and 0% received adjuvant T-DM1). All patients in the validation cohort received 1-year of trastuzumab.
The HER2DX pCR score correlates with the probability of achieving a pCR following neoadjuvant anti-HER2-based therapy. The HER2DX pCR score was derived from a cohort of 120 patients with HER2+ breast cancer treated with neoadjuvant anti-HER2-based chemotherapy. The pCR groups (low, medium, and high) are based on tertiles obtained from the training HER2+ neoadjuvant dataset. The association of the HER2DX pCR score with pCR was evaluated in 2 independent validation cohorts:

- The first validation cohort was composed of 67 patients treated with trastuzumab-based chemotherapy (72% with trastuzumab only and 28% with trastuzumab in combination with pertuzumab).
- The second validation cohort was composed of 91 patients treated with neoadjuvant lapatinib and trastuzumab (and endocrine therapy if hormone receptor-positive) without chemotherapy from the SOLT-1114 PAMELA phase II trial.
The HER2DX ERBB2 mRNA score reflects the expression in a given sample within HER2-negative and HER2-positive breast cancer.

Previous studies in HER2+ breast cancer have linked ERBB2 mRNA expression at diagnosis with a higher likelihood to respond to anti-HER2-based therapy, including T-DM1. Changes in ERBB2 mRNA expression during anti-HER2 therapy have also been linked to treatment response.

Three ERBB2 groups (i.e., low, medium and high) have been defined according to the following criteria:

The low group was defined as the optimal ERBB2 cutoff to identify HER2 status according to the ASCO/CAP guidelines.

The medium group was assigned as the lowest tertile of ERBB2 expression in HER2+ breast cancer.

The high group was determined as the medium and high tertiles of ERBB2 expression within HER2+ breast cancer (i.e., top 66%).