The Oncotype DX® Breast Cancer Assay:

- Predicts the magnitude of chemotherapy benefit
- Quantifies the likelihood of breast cancer recurrence
- Provides clinical experience for multiple patient populations

Continuous, quantitative HER2 score captures a wide range of expression

- Interpreting the HER2 Result:
  - Negative: < 10.7
  - Equivocal: ≥ 10.7 to < 11.5
  - Positive: ≥ 11.5
The Oncotype DX® Breast Cancer Assay Report to Include a Quantitative HER2 Score

Although the Recurrence Score remains the best tool for assessing prognosis and prediction of chemotherapy benefit, HER2 is an important marker for therapeutic decision-making for patients with breast cancer, and its measurement may significantly impact the chosen course of treatment.

- **Quantitative HER2 Information:**
  - The HER2 Score by the Oncotype DX Breast Cancer Assay is another measure for clinicians and patients to determine HER2 status, and it provides further insight into individual patients’ breast cancer tumor biology together with the Recurrence Score.
  - **Highly Concordant with IHC and FISH:** The HER2 score’s concordance with IHC and FISH meets or exceeds the ASCO/CAP guidelines requirement of 95% for determination of HER2 status.
  - **Added Clinical Information:** Many clinicians who rely on the Oncotype DX Breast Cancer Assay for treatment planning have requested that Genomic Health also report the quantitative HER2 Score as this is already a component of the Recurrence Score.
    - To provide further clarification especially in cases of equivocal IHC and/or FISH results or discordance between FISH and IHC.
  - **Addressing a Limitation with Current Testing:** The impact of preanalytical variability can be minimized by “normalization” strategies used in quantitative gene expression assessment as performed by quantitative RT-PCR by Oncotype DX.

**Concordance with IHC:**

<table>
<thead>
<tr>
<th>HER2 Expression by Central RT-PCR &amp; Central IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>27 (22%) IHC+ cases were negative by RT-PCR</td>
</tr>
<tr>
<td>4 (1%) IHC negative cases were positive by RT-PCR</td>
</tr>
</tbody>
</table>

**Concordance with FISH:**

<table>
<thead>
<tr>
<th>HER2 Expression by Central RT-PCR &amp; Central FISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>8 (7%) IHC+ cases were negative by RT-PCR</td>
</tr>
<tr>
<td>1 (1%) IHC negative cases were positive by RT-PCR</td>
</tr>
</tbody>
</table>

- **Summary:**
  - **E2197 Study**
    - N = 755 patients
    - The overall range of HER2 expression is approximately 1,000-fold
    - Range of HER2 expression for HER2 positive is approximately 16-fold
  - **Kaiser Study**
    - N = 568 patients
    - The overall range of HER2 expression is approximately 500-fold
    - Range of HER2 expression for HER2 positive is approximately 16-fold

* Spearman rank-order correlation

**Concordance:**

- **HER2 Central IHC vs Oncotype DX (Current ASCO/CAP Guidelines)**
  - Concordance: 95%
  - 95% CI (92%,96%)

- **HER2 Central FISH vs Oncotype DX (Current ASCO/CAP Guidelines)**
  - Concordance: 97%
  - 95% CI (96%,99%)

- **FISH output using Vysis**

- **IHC analysis using HercepTest®**