HER2 Expression in Matched Metastatic Tumor and Circulating Tumor Cells (CTCs) In Breast Cancer: Implications for profiling and monitoring of HER2 status

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Introduction

- Despite improvements in early detection, 1 in 8 women in the US (12%) will develop invasive breast cancer over the course of her lifetime.
- Approximately 20% of breast cancer is HER2 positive (1).
- During treatment and at disease progression in the metastatic setting, HER2 conversion may occur (from positive to negative or negative to positive).
- Serial biopsies from metastatic tumors are challenging.
- Biomarker expression results from metastatic biopsies may have limited accuracy due to factors including inter-tumoral and intra-tumoral heterogeneity.
- A liquid biopsy is a non-invasive and cost-effective method that allows for collection and analysis of tumor material and includes circulating tumor cells (CTCs) or circulating tumor DNA (ctDNA).
- We compared prospectively the amplification of HER2, or HER2 expression in metastatic tumors to Her2 amplification expression in CTCs.

Methods

- Thirty-six patients with metastatic breast cancer enrolled in the Individualized Molecular Analyses Guide Efforts in Breast Cancer (IMAGE) II Study (NCT02965755) were included.
- All patients had received at least one line of appropriate therapy.
- We analyzed tumor biopsies obtained 0-43 months (mean 7.3 months) prior to enrolling in IMAGE, and CTCs isolated from peripheral blood (PB) within 10 weeks of tissue biopsy (eighty-five samples).
- CTCs were captured by Target Selector™ (Biocept) and analyzed for HER2 amplification by FISH (Figure 1).
- The biomarker expression profile on the metastatic tumor and CTCs were compared for each patient.
- Concordance of HER2 expression between CTCs and the metastatic tumor tissue was analyzed using McNemar’s test.

Results

- HER2 amplification results from metastatic tumor tissue was analyzed using CTCs isolated from peripheral blood (PB) within 10 weeks of tissue biopsy (eighty-five samples).
- CTCs were captured by Target Selector™ (Biocept) and analyzed for HER2 amplification by FISH (Figure 1).
- The biomarker expression profile on the metastatic tumor and CTCs were compared for each patient.
- Concordance of HER2 expression between CTCs and the metastatic tumor tissue was analyzed using McNemar’s test.

Table 1. HER2 concordance CTC to tissue < 10 weeks of tissue biopsy

<table>
<thead>
<tr>
<th>Study</th>
<th>Results (N=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy (15 cases)</td>
<td>93 %</td>
</tr>
<tr>
<td>Specificity (15 cases)</td>
<td>93 %</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>100 %</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>100 %</td>
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</tbody>
</table>

Table 2. HER2 concordance CTC to tissue independent of CTC collection time point

<table>
<thead>
<tr>
<th>Study</th>
<th>Results (N = 85)</th>
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<tbody>
<tr>
<td>Accuracy (65 cases)</td>
<td>76.5%</td>
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<tr>
<td>Specificity (79 cases)</td>
<td>79.7%</td>
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<tr>
<td>Positive Predictive Value</td>
<td>11.1%</td>
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<tr>
<td>Negative Predictive Value</td>
<td>94.4%</td>
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Conclusions

- Target Selector™ demonstrates high accuracy of HER2 amplification on CTCs at baseline and within 10 weeks of treatment compared to HER2 in tumor tissue.
- Target Selector™ may provide a sensitive and specific mechanism to monitor for receptor change a well-established phenomenon.
- The ability to monitor HER2 status has the potential to identify patients who may benefit from the addition of antiHER2 therapy and those on anti-HER2 therapy who may not benefit optimally and for whom additional therapeutic options may warrant consideration.

References