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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

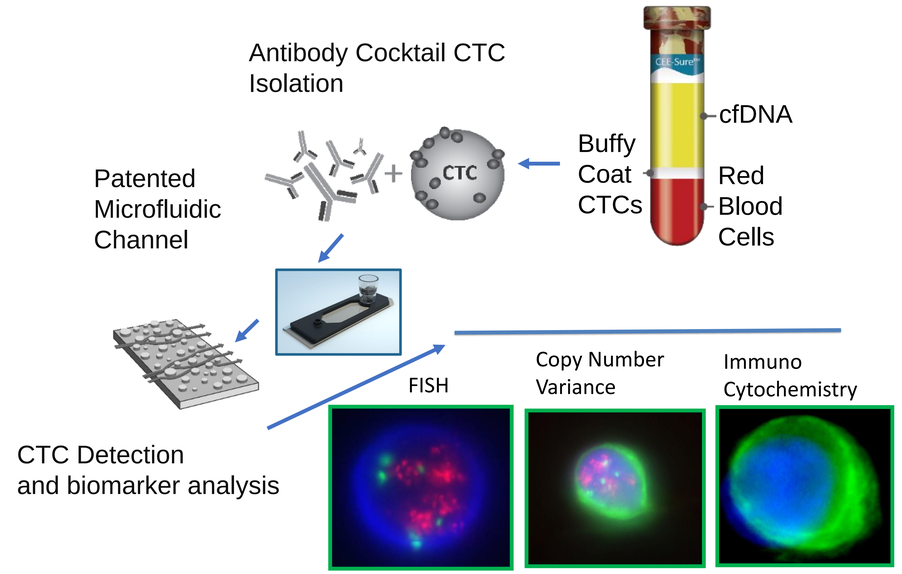
- Despite improvements in early detection, 1 in 8 women in the US (12%) will develop invasive breast cancer over the course of her lifetime.
- Approximately 20% of breast cancer is HER2 positive (1).
- During treatment and at disease progression in the metastatic setting, HER2 conversion may occur (from 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.

Circulating Tumor Cell Capture Workflow

Figure 1. Workflow of Target Selector™ CTC isolation and biomarker Expression platform



HER2 amplification of CTCs compared to tissue at different time points throughout treatment

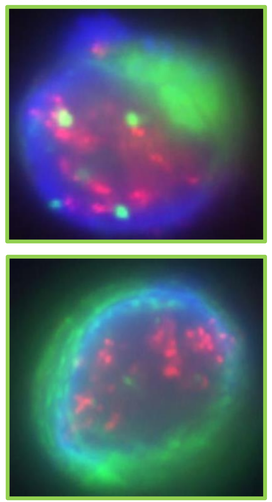
Table 1. HER2 concordance CTC to tissue < 10 weeks of tissue biopsy

Study	Results (N=15)
Accuracy (15 cases)	93 %
Specificity (15 cases)	93 %
Positive Predictive Value	100 %
Negative Predictive Value	100 %

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

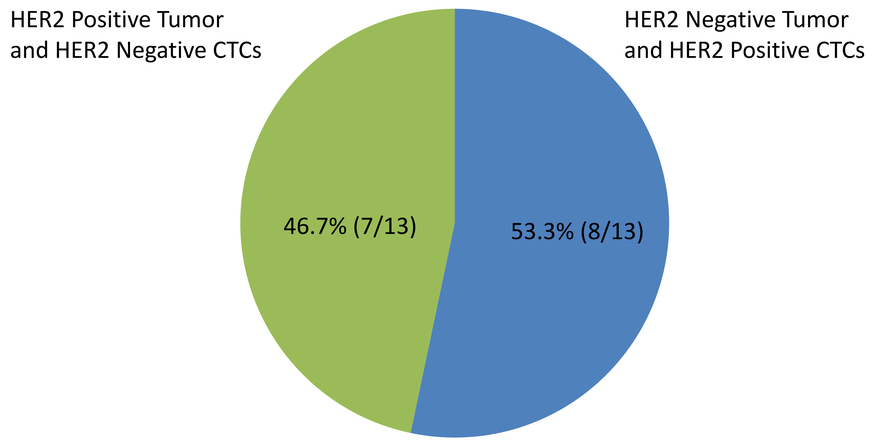
Study	Results (N = 85)
Accuracy (65 cases)	76.5%
Specificity (79 cases)	79.7%
Positive Predictive Value	11.1%
Negative Predictive Value	94.4%

Figure 2. Representative images of HER2 FISH on the CTCs



Frequency of HER2 switches between tumor and CTCs

Figure 3. HER2 status switch between tumors and CTCs throughout treatment (N=13 unique patients), Independent of elapsed time between tissue biopsy and CTC analysis



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 anti-HER2 therapy and those on anti-HER2 therapy who may not benefit optimally and for whom additional therapeutic options may warrant consideration.

References

1. Chun Wang Et Al. Prognostic value of HER2 status on circulating tumor cells in advanced-stage breast cancer patients with HER2- negative tumors. Breast Cancer Research and Treatment (2020)