Background

Biological factors, such as HER2 signaling activity, may be important in addition to expression and amplification of HER2 when selecting patients eligible for HER2-based therapies. HER2 gene amplification and/or protein overexpression is commonly identified in approximately 10%-20% of breast cancers and is associated with more aggressive disease progression, sensitivity to anti-HER2 therapy, and worse clinical outcomes. However, clinical trials have indicated a weak correlation between HER2 expression or amplification and HER2 targeted therapy benefits.

New methods for determining HER2 expression and/or HER2 targeted treatment benefits were identified as needed to improve treatment decisions. The CELx MP test was developed to determine real-time HER2 and HER3 signaling activity in live breast cancer cells as a result of stimulation with HGF, NRG1, and EGF. The CELx MP test is characterized by the following:

- The CELx MP test measures an on-time real-time HER2 and HER3 signaling score.
- The CELx MP test can be used to determine if the HER2 and HER3 signaling score is consistent with the HER2 protein expression or amplification and/or HER2 targeted therapy benefits.
- The CELx MP test further differentiates patients with dysfunctional c-Met signaling who will respond to these therapies.

Using primary breast cancer cell samples with hyperactive HER2 and HER3 signaling activity and the CELx MP test, the current study set to evaluate the CELx MP test scores and determine if these scores are concordant to the patients’ standard clinical HER2 evaluations.

Methods

Cell Culture: Methods to de-identify a de-identified set of primary breast cancer samples for analysis were developed.

Pan-HER and c-Met Inhibitors: Identification of pan-HER and c-Met inhibitors was achieved by testing a panel of pan-HER and c-Met inhibitors against HER2-negative cell samples with HER2 signaling activity levels above a previously determined cut-off value of 250 signaling units.

References