Quantitative measurement of HER2 levels by multiplexed mass spectrometry from FFPE tissue predicts survival in patients treated with anti-HER2 based therapy

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Background

Approximately 20% of breast cancer patients overexpress HER2 and are treated with anti-HER2 therapies. However, there is a great deal of disparity of HER2 levels in the patients that are classified as HER2 positive (IHC+). Techniques like FISH or IHC do not allow for HER2 quantification and a significant proportion of patients are wrongly classified as HER2 positive. Liquid Tissue-Selected reaction monitoring (LT-SRM) is a multiplexed mass spectrometric technique that can objectively quantify levels of HER2 and other targets (e.g. EGFR, HER3 etc) simultaneously from formalin fixed paraffin embedded (FFPE) samples. Accurate quantification of the expression levels of HER family proteins and knowledge of its impact on response to anti-HER2 therapies may be beneficial for clinicians to better personalize the treatment to the patient.

Study population

Quantitative HER2 level distribution by IHC groups

Tumor cell identification Laser microdissection Liquid Tissue® standardizes protein

Tissue with internal standards

Analysis and reporting

Quantitative Multiplex Mass Spec Assay

Survival analyses

<table>
<thead>
<tr>
<th>Time to Progression (TTP)</th>
<th>HR</th>
<th>CI 95% (HR)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>TTP non-HER2</td>
<td>0.20</td>
<td>0.07-0.57</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Conclusions

- Quantification of HER2 protein by SRM (>740 amol/µg) accurately predicts HER2 expression status compared to standard IHC (3+)/ISH (≥2.0) in 277 FFPE samples.
- High HER2 protein levels (>2200 amol/µg) predict DFS (HR = 0.22; p = 0.014) and OS (HR = 0.16; p = 0.013) benefit with HER2 targeted therapy in the adjuvant setting.
- Patients who highly express HER2 protein (>2200 amol/µg) also have significant OS benefit (HR = 0.20; p < 0.001) from HER2 targeted therapy in the metastatic setting.
- The OncoPlex test can identify HER2 moderate expressors (740 to 2200 amol/µg) who may not receive complete therapeutic benefit from anti-HER2 therapy. These moderate expressors may benefit from co-treatment with targeted therapies based on coexpressed targets.
- Upfront multiplex SRM testing will reveal what these options are and support physicians in making informed treatment decisions.