Patient selection for clinical trials eliminating surgery in HER2-positive breast cancer treated with neoadjuvant systemic therapy

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Introduction

• High rates of pCR for HER2 positive breast cancer highlight potential omission of surgery after neoadjuvant systemic therapy

• How do we identify patients with pCR who may be candidates for ongoing MD Anderson Multicenter and other clinical trials assessing the safety of non-operative treatment?
  – Multimodality imaging lacks in sensitivity/specificity in predicting pCR
  – Multimodality imaging with vacuum assisted biopsy
    • Accuracy: 98%
    • False negative rate: 5%
    • NPV: 95%

van la Parra and Kuerer, BCR 2016
Kuerer et al, ANN SURG 2018

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Methods and Purpose

• Inclusion criteria
  – HER2 positive
  – cT1-T2, cN0-N1
  – Treated with neoadjuvant HER2 targeted regimens

• Surgical resection and axillary surgery

• Purpose
  – Identify clinicopathologic characteristics associated with residual disease in HER2 positive breast cancer after neoadjuvant therapy
  – Assess effectiveness of neoadjuvant therapy on invasive disease and DCIS
Overall key breast pathologic outcome measures following neoadjuvant systemic therapy in HER2-positive cancer treated with neoadjuvant systemic therapy

T1/T2 HER2+ N=280

- pCR invasive = 55.4%
- pCR invasive & DCIS; ypT0 = 37.5%
- Residual DCIS alone; ypTIS = 17.9%

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Effect of neoadjuvant therapy on the DCIS component in HER2-positive invasive breast cancer

DCIS identified on initial biopsy, N=129 (46.1%)

DCIS eradicated, N=46 (35.7%)

Presence of DCIS on biopsy associated with higher proportion of patients with residual disease compared to those without DCIS on initial biopsy (69% vs 57%; p=0.04)
Effect of hormone receptor status of HER2 positive cancer on response to NST

Hormone receptor positive status predictive of residual disease on multivariate analysis (OR 2.7, p<0.0001)
Multimodality imaging response and pathologic response after NST

<table>
<thead>
<tr>
<th>Measure</th>
<th>Breast</th>
<th>Lymph Nodes</th>
<th>Breast and lymph nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>96.5 (94.3-98.7)</td>
<td>66.3 (57.9-74.6)</td>
<td>97.1 (95.1-99.1)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>13.3 (9.2-17.3)</td>
<td>40.9 (32.3-49.6)</td>
<td>12.2 (8.33-16.2)</td>
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<tr>
<td>Positive-predictive value, %</td>
<td>66 (60.3-71.7)</td>
<td>67.1 (58.8-75.4)</td>
<td>65.9 (60.2-71.5)</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>68.4 (62.9-74.0)</td>
<td>40.0 (31.4-48.6)</td>
<td>70.6 (65.1-76.0)</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% CIs

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Summary and Conclusions NST in HER2+ Disease

• NST can eradicate the DCIS component of HER2+ breast cancer
  – Associated with decreased rate of pCR
  – For no surgery trials, need eradication of invasive and DCIS components of disease to avoid nidus for carcinoma in the future

• Hormone receptor positive tumors associated with residual disease

• Multimodality imaging not reliable in identifying pCR
  – Image guided percutaneous biopsy required to safely select patients for inclusion in ongoing and future elimination of surgery clinical trials