Management of HER2 Equivocal Breast Cancer

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Introduction

• The benefits of HER2 targeted therapy in the treatment of human epidermal growth factor receptor 2 (HER2) positive breast cancer have been well studied.
• Large clinical trials such as NSABP B47 are attempting to analyze the potential benefit of this therapy even for HER2 negative breast cancers.
• There is currently no standard of care in the treatment of HER2 equivocal breast cancers.
• The goal of this study is to compare differences in therapy for those patients diagnosed with HER2 equivocal breast cancer on initial core biopsy needle to our institution from 2014 through 2017.

Methods and Materials

• Retrospective review of all HER2 equivocal core biopsies diagnosed and treated at Levine Cancer Institute from 2014 through 2017.
• HER2 equivocal specimens were defined using standards set forth by the 2013 ASCO/CAP guidelines: IHC 2+, single-probe FISH average HER2 copy number ≥4.0 and <6.0 signals/cell, or dual-probe HER2/CEP17 ratio <2.0 with an average HER2 copy number ≥4.0 and <6.0 signals/cell.
• Exclusion criteria included: positive or negative reflex test, positive or negative repeat test on a different core biopsy from the same specimen, patients with metastatic disease, patients not considered for surgery or chemotherapy for varying reasons, and biopsy at a site other than the breast.

Results

Table 1: Chart illustrating different patient characteristics of each treatment group.

<table>
<thead>
<tr>
<th>HER2 Targeted NAC</th>
<th>Non-HER2 Targeted NAC</th>
<th>Upfront Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=4</td>
<td>n=5</td>
<td>n=40</td>
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<tr>
<td>44%</td>
<td>56%</td>
<td>82%</td>
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Figure 1: Flow chart illustrating the treatment patterns of the cohort of patient’s with HER2 equivocal diagnosed on core biopsy.

**NAC = Neoadjuvant chemotherapy.**

49 HER2 equivocal core biopsies were identified.
• 82% (n=40) patients underwent upfront surgery.
• 18% (n=9) patients underwent NAC.
• 44% (n=4) of patients undergoing NAC underwent HER2 targeted NAC.

Surgical pathology for the group that received upfront surgery demonstrated:
• HER2 positive = 45% (n=9)
• HER2 negative = 55% (n=11)
• HER2 equivocal = 50% (n=20)

78% (n=7) patients with HER2 positive surgical specimen received adjuvant HER2 targeted therapy. 22% (n=2) of patients with HER2 positive surgical specimen did not receive HER2 targeted therapy: 1 patient was diagnosed with T1a disease, 1 patient refused treatment.

• 20% (n=4) of upfront surgery patients with HER2 equivocal surgical specimen received adjuvant HER2 targeted therapy.
• No patients with HER2 negative surgical specimen received adjuvant HER2 targeted therapy.

Conclusions

• Offering upfront surgery enabled our institution to better select patients that would benefit from HER2 targeted therapy and prevented the overtreatment of patients who would not. In those who remained equivocal few received HER2 targeted therapy.
• Factors such as locally advanced tumors or node positive disease may necessitate NAC instead of upfront surgery. NCCN Guidelines should be utilized in these decisions.

References: