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Disclosures

- None

Learning Objectives

- 5 clinical questions for 2018 Focused Update addressed by ASCO/CAP Expert Panel
- 5 categories of in situ hybridization (ISH) results
- Additional work-up required for 3 less common ISH categories

Nuclear DNA: HER2 (ERBB2) gene amplification

Cell surface: HER2 overexpression

Monoclonal antibody (trastuzumab) binding to HER2 protein

Negatives
- Negative 0
- Negative 1+
- Equivocal 2+
- Positive 3+

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Table 2

Histopathologic Features Suggestive of Possible HER2 Test Discordance

<table>
<thead>
<tr>
<th>Criteria to Consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>New HER2 test should not be ordered if the following histopathologic findings occur and the initial HER2 test was negative:</td>
</tr>
<tr>
<td>Infiltrating ductal or lobular carcinoma, ER and PgR positive</td>
</tr>
<tr>
<td>Mucinous (at least 50% pure)</td>
</tr>
<tr>
<td>Cribriform (at least 50% pure)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma (10% pure) and other triple negative</td>
</tr>
</tbody>
</table>

Similarly, a new HER2 test should be ordered if the following histopathologic findings occur and the initial HER2 test was positive:

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If the initial HER2 test result in a core needle biopsy specimen of a primary breast cancer is negative, a new HER2 test must be ordered on the excision specimen if one of the following is observed:

<table>
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<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor grade 3</td>
</tr>
<tr>
<td>Amount of invasive tumor in the core biopsy is small</td>
</tr>
<tr>
<td>Resection specimen contains high-grade carcinoma that is morphologically distinct from that in the core</td>
</tr>
<tr>
<td>Core biopsy result is equivocal for HER2 after testing by both IHC and FISH</td>
</tr>
</tbody>
</table>

There is discord in the assessment of HER2 status by IHC and FISH in a core biopsy using different dilutions of antibody. The test result is considered positive or negative on the basis of testing using a 1:500 dilution.

Abbreviations: ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IHC, in situ hybridization; PgR, progesterone receptor.

Criteria to consider if there are concerns regarding discordance with apparent histopathologic findings and possible false negative or false positive HER2 test result.

HER2/CEP17 ratio ≥ 2.0

Group 1
Positive

Average HER2 copy number ≥ 4.0 signals/cell

Group 2

Average HER2 copy number < 4.0 signals/cell

Group 3

Average HER2 copy number ≥ 6.0 signals/cell

Group 4

Average HER2 copy number ≥ 4.0 and < 6.0 signals/cell

Group 5
Negative

Additional work up required (immunohistochemistry)

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Average HER2/cell: 3.2
Average cen/cell: 1.3
HER2/cen ratio: 2.5

“Group 2”

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Average HER2/cell: 6.5
Average 17 cen/cell: 5.0
HER2/cen ratio: 1.3

“Group 3”


Average HER2/cell: 5.2
Average 17 cen/cell: 4.3
HER2/cen ratio: 1.2

“Group 4”

Summary

- 5 clinical questions for 2018 Focused Update were addressed by the ASCO/CAP Expert Panel
- 5 categories of in situ hybridization (ISH) results
  - Groups 1, 2, 3, 4, and 5
  - Additional work-up (IHC) required for Groups 2, 3, and 4
References

