

Supplementary Table S8. HER2 status by dual-probe in situ hybridization based on the 2018 ASCO/CAP guidelines [3]

HER2 ISH status	Definition
ISH positive	<p><i>HER2</i>/<i>CEP17</i> ratio ≥ 2.0 and average <i>HER2</i> copy number ≥ 4.0 (ISH group 1)</p> <p><i>HER2</i>/<i>CEP17</i> ratio ≥ 2.0 and average <i>HER2</i> copy number < 4.0 (ISH group 2) with concurrent IHC 3+</p> <p><i>HER2</i>/<i>CEP17</i> ratio < 2.0 and average <i>HER2</i> copy number ≥ 6.0 (ISH group 3) with concurrent IHC 2^{+a} or 3+</p> <p><i>HER2</i>/<i>CEP17</i> ratio < 2.0 with average <i>HER2</i> copy number ≥ 4.0 and < 6.0 (ISH group 4) with concurrent IHC 3+</p>
ISH negative	<p><i>HER2</i>/<i>CEP17</i> ratio < 2.0 with average <i>HER2</i> copy number < 4.0 (ISH group 5)</p> <p><i>HER2</i>/<i>CEP17</i> ratio ≥ 2.0 and average <i>HER2</i> copy number < 4.0 (ISH group 2) with concurrent IHC 2^{+b}</p> <p><i>HER2</i>/<i>CEP17</i> ratio < 2.0 with average <i>HER2</i> copy number ≥ 4.0 and < 6.0 (ISH group 4) with concurrent IHC 2^{+b}</p> <p>ISH group 2, 3 and 4 with concurrent IHC 0 or 1+</p>

HER2, human epidermal growth factor receptor type 2; ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; ISH, in situ hybridization; *CEP17*, centromere on chromosome 17; IHC, immunohistochemistry.

^aAn additional observer blinded to previous result recounts ISH. If the repeated ISH result is categorized to the same group, it is finally regarded as HER2 positive; ^bAn additional observer blinded to previous result recounts ISH. If the repeated ISH result is designated to same ISH group, it is finally regarded as HER2 negative.

References

1. WHO Classification of Tumours Editorial Board. WHO classification of tumours: breast tumours. 5th ed. Lyon: International Agency for Research on Cancer, 2019.
2. Hortobagyi GN, Connolly JL, D'Orsi CJ, et al. Breast. In: Amin MB, Edge S, Greene F, et al., eds. AJCC cancer staging manual. 8th ed. New York: Springer, 2017; 589-636.
3. Wolff AC, Hammond MEH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline focused update. J Clin Oncol 2018; 36: 2105-22.