

# Impact of the New American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) Guidelines on the Determination of Breast Cancer HER2 Status

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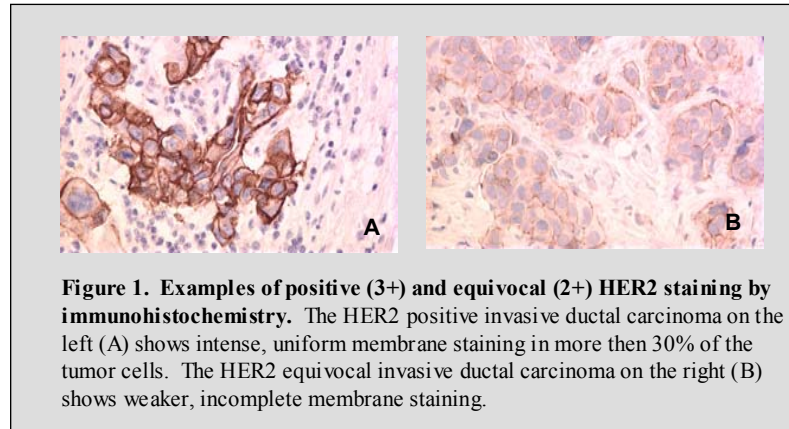


## BACKGROUND

- ◆ In clinical practice, HER2 status of breast cancers is most often determined by immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH)
- ◆ Recently, ASCO and CAP jointly issued new guidelines to improve the accuracy of HER2 testing
- ◆ In these new guidelines:
  - ◆ For IHC testing:
    - A positive (3+) test result is defined as uniform, intense membrane staining of >30% of invasive tumor cells (in comparison with the original scoring criteria which required that >10% of tumor cells show uniform, intense membrane staining) (Fig. 1)
    - IHC test results of 2+ are scored as “equivocal” (Fig. 1)
    - IHC test results of 0 or 1+ are scored as “negative”
  - ◆ For FISH testing using the PathVysion (Vysis) dual probe system:
    - A test result is considered “positive” for HER2 gene amplification when the HER2/CEP17 ratio is >2.2, “equivocal” for gene amplification when the ratio is 1.8-2.2, and “negative” for gene amplification when the ratio is <1.8
  - ◆ The aim of our study was to assess the impact of these scoring guidelines on:
    - The proportion of cases scored as HER2 positive by IHC
    - The IHC-FISH concordance rate

## METHODS

- ◆ Between January 2007 and December 2007, all invasive breast cancers diagnosed at our institution were assessed for HER2 status by both IHC and FISH
- ◆ HER2 analysis was performed in our laboratory by IHC using Dako rabbit polyclonal antibody A085. Cases were scored using both the old (>10%) and the new (>30%) thresholds for positivity
- ◆ The paraffin block on which IHC was performed was then sent to a reference laboratory (US Labs, Irvine, CA) for HER2 FISH analysis using the PathVysion HER2 DNA Probe Kit (Vysis)
- ◆ Results of the two HER2 testing methods were compared using both the old and new IHC cut-offs for positivity
- ◆ 353 cases were available for analysis



## RESULTS

- ◆ By IHC, 251 cases were negative (0–1+), 60 were equivocal (2+), and 42 cases were positive (3+) when uniform, intense membrane staining in >10% of tumor cells was used as the threshold for a positive result (See Figure 2)
- ◆ Of note, all 42 cases scored as 3+ by IHC using the >10% cut-off remained 3+ using the new cut-off of >30%. Therefore, IHC-FISH concordance was not influenced by the new cut-off of >30%
- ◆ In 274 of 284 (96.5%) cases with positive or negative IHC results there was concordance with FISH results (97% for IHC negative results; 93% for IHC positive results) (Table 1)
- ◆ Among 60 cases that were equivocal (2+) by IHC, 44 (73%) were negative for HER2 gene amplification by FISH, 12 (20%) were positive for HER2 gene amplification, and 4 (7%) were equivocal for HER2 gene amplification

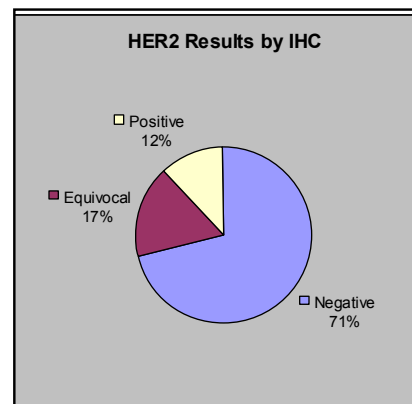


Figure 2. Distribution of IHC HER2 Results in 353 Invasive Breast Carcinomas

Table 1. Comparison of the HER2 status of 353 cases of invasive breast carcinoma using both IHC and FISH.

		FISH		
		Not Amplified <1.8	Equivocal 1.8 – 2.2	Amplified >2.2
IHC	Negative (0-1+)	236	8	7
	Equivocal (2+)	44	4	12
	Positive (3+)	3	1	38

## CONCLUSIONS

- ◆ All cases scored as IHC positive (3+) when uniform, intense membrane staining was seen in >10% of invasive tumor cells remained positive using the new ASCO/CAP guidelines which raise the threshold for positivity to uniform, intense membrane staining in >30% of tumor cells.
- ◆ We observed a 97% concordance rate with FISH results among 284 cases scored as HER2 positive or negative by IHC, whether or not the new ASCO/CAP guidelines were used.
- ◆ The results of this study suggest that the new ASCO/CAP guidelines are unlikely to have a substantial impact on the proportion of cases scored as HER2 positive (3+) by IHC or, in turn, on the level of concordance between IHC and FISH among IHC positive and negative cases.