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Update in Breast Cancer Staging and Reporting

Patrick L. Fitzgibbons, MD
St. Jude Medical Center
Fullerton, CA 92887
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Breast Cancer Staging Update

- Changes to AJCC 8th edition
- Clarifications from AJCC 7th edition
- Prognostic stage group system
- CAP breast cancer and biomarker reporting

Disclosure

Dr. Fitzgibbons has no conflict(s) of interest or relevant financial relationships to disclose.

Breast Cancer Staging Update

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Changes to AJCC 8th edition

- LCIS no longer included in pTis category
  - Removed because it is not treated as cancer
  - Pleomorphic LCIS not included as pTis due to insufficient evidence for definitive treatment recommendations

Changes to AJCC 8th edition

- For tumor size, round up or down to the nearest mm

EXCEPT for tumors between 1 and 2 mm

  - All tumors between 1 and 2 mm are rounded up to 2.0 mm to avoid misclassifying those between 1.0 and 1.5 mm as microinvasive (T1mi)
    - 1.0 mm = pT1mi
    - >1.0 mm = pT1a

Changes to AJCC 8th edition

- (f) modifier added to N category
  - Denotes confirmation of metastasis by fine needle aspiration or needle biopsy with NO further resection of nodes.
  - Usually applies to cN staging before definitive resection or neoadjuvant therapy

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Clarifications from AJCC 7th edition

Staging multiple tumors

- If in same breast:
  - T category is based on single largest tumor focus (not highest grade)
  - Use (m) modifier
  - Don’t include adjacent satellite foci when measuring tumor size
  - If multiple foci of microinvasion, report the # of foci and the size of the largest focus (don’t combine)

- If bilateral:
  - Stage each side separately

Clarifications from AJCC 7th edition

Use imaging findings if necessary to assign correct pT category

- Applies when tumor is present in multiple pieces/specimens
- For small tumors diagnosed by core biopsy, reporting only the size in the excision may understage the tumor
- If no residual tumor in excision, use information from previous core biopsy (don’t categorize as pTX)

Clarifications from AJCC 7th edition

Example:

8 mm spiculated mass; 4 mm invasive focus in needle biopsy

- 4 mm focus of residual carcinoma in excision
  - categorize as pT1b (not pT1a)

- No residual cancer in excision
  - categorize as pT1b (not pTX)

Clarifications from AJCC 7th edition

Skin involvement

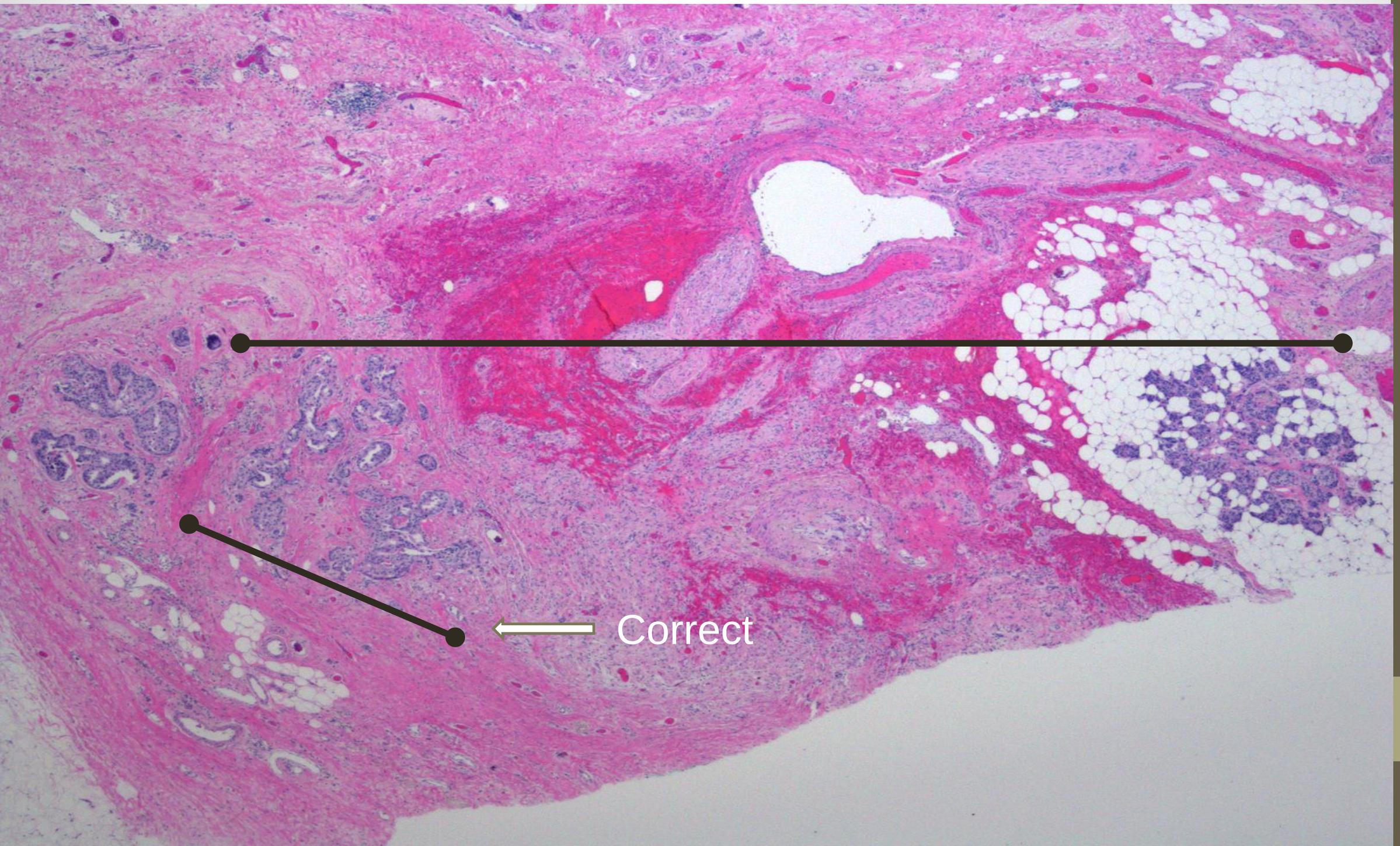
- Satellite skin foci (pT4b) must be separate from the primary tumor (not contiguous) AND macroscopically identified
- Direct extension into skin and skin involvement only identified microscopically are categorized based on tumor size
- Dermal lymphatic tumor emboli are NOT categorized as pT4d unless there are clinical findings of inflammatory carcinoma (erythema and edema involving 1/3 of breast skin)

Clarifications from AJCC 7th edition

Assessment following neoadjuvant therapy

- ypT is based on largest single focus of residual invasive carcinoma

- Treatment-related fibrosis around residual tumor is NOT included in the ypT dimension (don't measure tumor bed)


Correct

Clarifications from AJCC 7th edition

Assessment following neoadjuvant therapy

- Cases with no residual invasive tumor are categorized as ypT0 or ypTis (not ypTX)
- Pathologic complete response (pCR) is defined as no residual invasive cancer in breast, lymphatics or nodes – ypT0 N0 or ypTis N0
- Cases with intralymphatic tumor only are classified as ypT0 (not pCR)

Clarifications from AJCC 7th edition

Assessment following neoadjuvant therapy

- Use the (m) modifier when multiple foci of residual tumor are present

- Cases categorized as M1 before neoadjuvant therapy stay that way (i.e. they remain Stage IV even if there is pCR)

Clarifications from AJCC 7th edition

Assessment of N category

- The following are regional lymph nodes and reported in the N category:
  - Axillary
  - Intramammary
  - Interpectoral
  - Supraclavicular
  - Ipsilateral internal mammary
- Metastases to other nodes are categorized as pM1:
  - Cervical
  - Contralateral internal mammary
  - Contralateral axillary nodes

Clarifications from AJCC 7th edition

Assessment of N category

- Invasive tumor nodules in axillary fat without apparent nodal tissue are classified as regional lymph node metastases (pN)

Clarifications from AJCC 7th edition

Assessment of N category

- Nodes with isolated tumor cells (ITCs) are not included in the overall count of positive nodes

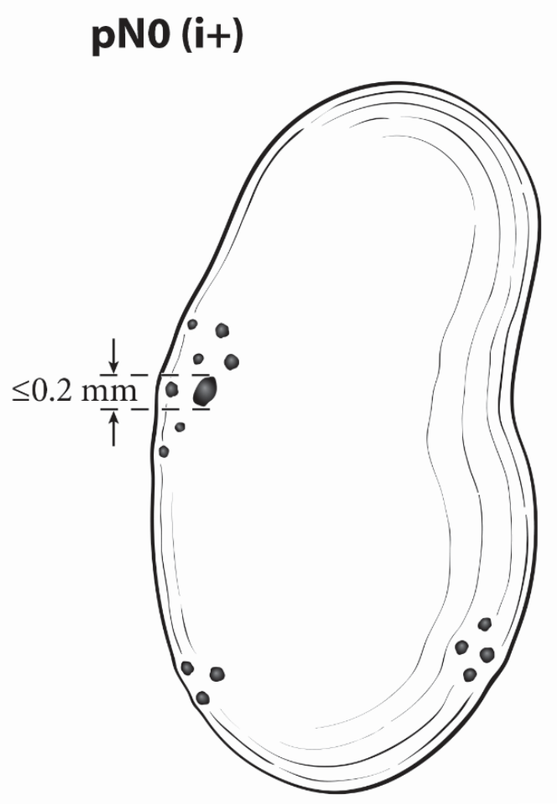
Example:

- 10 nodes: 2 with macromets; 2 with ITCs
- No. of positive nodes is 2/10 = pN1a (not 4/10 = pN2a)

Clarifications from AJCC 7th edition

Assessment of N category

- When measuring ITCs, report size of largest contiguous focus (NOT the overall area in which the ITCs are found)



Clarifications from AJCC 7th edition

Assessment of N category

- The (sn) modifier is not restricted to sentinel nodes

- The modifier is used when 2 things occur:
    1. SLN biopsy procedure is performed (using either dye or tracer)
    2. Fewer than six nodes are removed (sentinel and nonsentinel)

- Don’t use when a node or two is found in a simple mastectomy

Clarifications from AJCC 7th edition

Assessment of N category

- If axillary dissection is done following previous SLN, combine the two to determine the pN category

  Example:

  - SLN done two weeks ago with 1 positive node
  - Axillary dissection reveals 12 lymph nodes, 3 with metastases
  - Correct N category is pN2a (4/13)

Clarifications from AJCC 7th edition

Assessment of M category

- pM category is reported only when documenting metastasis in that specimen
- M category is not assigned when a biopsy of a possible metastatic lesion is negative
- Microscopic disseminated tumor clusters (DTCs)
  - Tumor deposits ≤0.2 mm found unexpectedly (e.g. prophylactic oophorectomy)
  - In the absence of clinical findings of metastatic disease, DTCs alone are classified as cM0(i+), not pM1

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Anatomic Stage Grouping

- T, N, M only
- Unchanged in 8th edition

T	N	M	Stage Group
Tis	N0	M0	0
T1	N0	M0	IA
T0, T1	N1mi	M0	IB
T0, T1	N1	M0	IIA
T2	N0	M0	
T2	N1	M0	IIB
T3	N0	M0	
T0, T1, T2	N2	M0	IIIA
T3	N1, N2	M0	
T4	N0, N1, N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

Prognostic Stage Grouping

- New in 8th edition
- Used for all cancer patients in the U.S.
- Combines tumor grade and biomarkers with T, N, M
- Includes multigene panels when done
- Currently over 120 combinations

Anatomic Stage IA

TNM	Grade	HER2	ER	PgR	Pathologic Prognostic Stage Group
	2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
T1 N0 M0				Negative	IB
	3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB

Anatomic Stage IIB

TNM	Grade	HER2	ER	PgR	Pathologic Prognostic Stage Group
	1	Positive	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
T2 N1 M0				Negative	IIB
	3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIA

Anatomic Stage IIIA

T	Grade	HER2	ER	PgR	Pathologic Prognostic Stage Group
T1, N2, M0	2	Negative	Negative	Negative	IIIB
T2, N2, M0	2	Negative	Negative	Negative	IIIB
T3, N2, M0	2	Negative	Negative	Negative	IIIB

Multigene Panels

- Not required for staging
- Only applies to patients with T1 or T2, N0, ER(+) and HER2(-) tumors
  - Patients with Oncotype Dx score <11 are in same prognostic category as T1a or T1b, N0, M0.
  - Stage IA even if >2 and <5 cm
- Mammaprint, PAM50, EndoPredict are not yet included in the Prognostic Stage Group system

If Oncotype DX score <11:

T	Grade	HER2	ER	PgR	Pathologic Prognostic Stage Group	
					Oncotype score <11	No multigene panel
T2, N0, M0	1	Negative	Positive	Negative	IA	IB
T2, N0, M0	2, 3	Negative	Positive	Negative	IA	IIA

Prognostic Stage Grouping

- Improves grouping patients with similar prognosis
- More than 35% of patients reassigned to a different stage group
- Patient should still be assigned anatomic stage even if prognostic staging is done

Prognostic Stage Grouping

New issue

- How to assign stage for microinvasive carcinomas (no stage assignment possible without a grade)

- AJCC working on administrative solution

Responsibility for Stage Assignment

- Stage assignment requires assessment of
  - Patient history and physical exam
  - Imaging findings
  - Pathology information
  - Biochemical, molecular and genetic data

- “Only the managing physician can assign the patient’s stage because only (s)he has access to all pertinent information…”

AJCC 8th edition (page 4)

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CAP Cancer Protocols

- Updated to include AJCC 8th edition
- Inclusion of cover pages
- Stage groups removed from all protocols

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Protocol for the Examination of Specimens From Patients With Invasive Carcinoma of the Breast

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Excision less than total mastectomy	Includes specimens designated excision, segmental resection, lumpectomy, quadrantectomy, and segmental or partial mastectomy, with or without axillary contents
Total Mastectomy	Includes skin-sparing and nipple–sparing mastectomy, with or without axillary contents
Tumor Type	**Description**
Invasive breast carcinoma of any type, with or without ductal carcinoma in situ (DCIS)	Includes microinvasive carcinoma and carcinoma with neuroendocrine features

This protocol is NOT required for accreditation purposes for the following:

Procedure
Needle, incisional or skin biopsies
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Additional excision performed after the definitive resection (eg, re-excision of surgical margins)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Ductal carcinoma in situ (consider the Breast DCIS protocol)
Paget disease of the nipple not associated with invasive breast carcinoma (consider the Breast DCIS protocol)
Encapsulated (solid) papillary carcinoma (consider the Breast DCIS protocol)
Phyllodes tumor
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

Authors
Patrick L. Fitzgibbons, MD*; Shikha Bose, MD; Yunn-Yi Chen, MD, PhD; James L. Connolly, MD; Monica E. de Baca, MD; Mary Edgerton, MD; Daniel F. Hayes, MD; Kalisha A. Hill, MD; Celina Kleer, MD; Susan C. Lester, MD, PhD; Frances P. O'Malley, MD; David L. Page, MD; Jean F. Simpson, MD; Ross Simpson, MD; Barbara L. Smith, MD, PhD; Lee K. Tan, MD; Donald L. Weaver, MD; Eric Winer MD

CAP Breast Cancer Protocol

2018 update

- pN0(i-) removed (has no meaning)
- Treatment effect – changed from optional to conditionally required
- LCIS removed from DCIS protocol
- Added many notes

CAP Breast Biomarker Template

2018 update

- For ER & PgR: Average intensity now required
- Percent of cells with complete membrane staining for HER2 no longer applies to Score 0 and 1+

Next update

- Minor changes to HER2 by IHC section
- Major changes to HER2 by ISH section

Future update

- ASCO/CAP ER/PgR guideline update in progress

HER2 by ISH (dual-probe assay)

Result	Criteria
Positive	Group 1
	Group 2 AND concurrent IHC 3+
	Group 3 AND concurrent IHC 2+ or 3+
	Group 4 AND concurrent IHC 3+
Negative	Group 2 AND concurrent IHC 0-1+ or 2+
	Group 3 AND concurrent IHC 0-1+
	Group 4 AND concurrent IHC 0-1+ or 2+
	Group 5

Group 1	HER2/CEP17 ratio ≥2.0; ≥4.0 HER2 signals/cell
Group 2	HER2/CEP17 ratio ≥2.0; <4.0 HER2 signals/cell
Group 3	HER2/CEP17 ratio <2.0; ≥6.0 HER2 signals/cell
Group 4	HER2/CEP17 ratio <2.0; ≥4.0 and <6.0 HER2 signals/cell
Group 5	HER2/CEP17 ratio <2.0; <4.0 HER2 signals/cell

HER2 by ISH (single-probe assay)

Result	Criteria
Positive	≥6.0 HER2 signals/cell
	≥4.0 and <6.0 HER2 signals/cell AND concurrent IHC 3+
	≥4.0 and <6.0 HER2 signals/cell AND concurrent dual probe Group 1
Negative	<4.0 HER2 signals/cell
	≥4.0 and <6.0 HER2 signals/cell AND concurrent IHC 0 or 1+
	≥4.0 and <6.0 HER2 signals/cell AND concurrent dual probe Group 5