Asco guidelines her2

American Society of Clinical Oncology / American College of Pathologists guidelines for human epidermal growth factor receptor ironer2 testing in breast cancer. Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, Dowsett M, Fitzgibbons PL, Hanna WM, Langer A, McShane LM, Paik S, Pegram MD, Perez EA, Press MF, Rhodes A, Sturgeon C, Taube SE, Tubbs R, Vance GH, van de Vijver M, Wheeler TM, Hayes DF; American Society of Clinical Oncology; American College of Pathologists. Wolff AC, et al. J Clin Oncol. 2007 January 1;25(1):118-45. doi: 10.1200/JCO.2006.09.2775. Epub 2006 December 11. J Clin Oncol. 2007. PMID: 17159189 Her2 tahsin verification, sample fixation, proficiency testing and accreditation checklist requirements related to the use of ASCO/CAP scoring criteria to report results are included in the anatomical pathology (ANP), cytogenetics (CYG) and molecular pathology (MOL) checklists. CAP accredited laboratories can access these checklists through the e-LAB Solutions Suite. CAP-accredited laboratories can purchase these checklists by non-CAP approved laboratories through order form bananas. Meet PT requirements by ordering the appropriate HER2 PT program. Call cap customer contact center at 1-800-323-4040. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guide update. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, Allred DC, Bartlett JM, Bilous M, Fitzgibbons P, Hanna W, Jenkins RB, Mangu PB, Paik S, Perez EA, Press MF, Spears PA, Van GHce, Viale G, Hayes DF; American Society of Clinical Oncology; American College of Pathologists. Wolff AC, et al. J Clin Oncol. 2013 November 1;31(31):3997-4013. doi: 10.1200/JCO.2013.50.9984. Epub 2013 October 7. J Clin Oncol. 2013. PMID: 24101045 Skip Nav Destination PDF Split View Article content Figures and tables Video Audio Additional Data 2018 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) human epidermal growth factor receptor 2 (HER2) guide-oriented update revises HER2 scoring criteria. We evaluated the effect on HER2 rates in breast cancer diagnosed in our center. In a series of breast seed biopsy retrospectives diagnosed with invasive carcinoma (n = 1,350) between 2014 and 2017, her2 status was classified according to the 2013 and 2018 ASCO/CAP guidelines and changes in her2 state were determined. In the 2018 guidelines, HER2 status of 6% of patients was reclassified. Most were changed from HER2 equivalent status (equivalent to immunohistokimya and fluorescent in on-site hybridization under 2013 guidelines) to HER2-negative status (2018 guidelines). Her2-positive rate decreased by 0.4%. 2018 guidelines to reduce the rate of HER2 positive breast cancer and reduce HER2 testing again on excretion samples. Approximately 0.4% of patients are newly eligible for anti-HER2 the future is the future Human epidermal growth factor receptor 2 (HER2) is an estimate and prognostic biomarker that over-expresses between 15% and 20% of invasive breast carcinomas.1 Her2 condition is critical in clinical decision-making because it report the use of systemic chemotherapy and anti-HER2 targeted therapy. In 2018, the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) revised every 2 guideline recommendations and interpretation criteria for both immunohistokimya (IHC) and fluorescent in situ hybridization (FISH) assays.2 Compared to the 2013 ASCO/CAP HER2 guideline (2013 2013 guidelines),3 2018 ASCO/CAP HER2 guide-oriented update (2018 guidelines) further improve HER2 assessment algorithms by addressing tumors with rare HER2 in situ hybridization (ISH) amplification patterns of ambiguous biological and clinical importance.2 Furthermore, 2018 guidelines, Increases the emphasis on coordination between IHC and ISH results, Class 3 tumors are initially found to be HER2 negative to soften recommendations for HER2 testing again, raise thresholds to stop the option to use the alternative probe HER2 FISH for clinical HER2 evaluation and categorize the patient as HER2 positive. As a result, the 2018 guidelines have the potential to reca categorize the HER2 status of some patients by eliminating final results, reducing the rate of HER2-positive results, and reducing the number of cases exposed to repeat the HER2 test. While the 2018 guidelines2 estimate that 5% of cases can be reclassified as ISH results, the true impact of the 2018 guidelines on HER2 rates is unknown. According to the 2018 guidelines, tumors with rare HER2 ISH amplification pathers are subjected to a more complex study that requires review with HER2 IHC. If the IHC result is final, it is required to use the HER2 IHC slide to guide the selection of the region of the tumor to re-score a blind ISH recession HER2. According to the 2018 guidelines, both IHC and FISH must be done in the same institution to ensure parallel examination and quality.2 One of the biggest advantages of HER2 IHC and ISH integration is that this approach better handles tumors with intratuumural heterogeneity for HER2 expression, which can result in a potentially inadbal negative result. In our study, we investigated the potential impact of 2018 guidelines on HER2 ratios in primary invasive breast carcinomas diagnosed in our center. Between 2014 and 2017, we conducted a retrospective search of breast nucleus needle biopsy (CNB) samples diagnosed with primary invasive breast carcinoma in our institution. The standard HER2 test protocol used in our institution during this period closely follows the test algorithm provided in the 2018 guidelines in various key aspects. Simultaneous testing of Her2 using both IHC and dual probuLU ISH has been routinely performed and interpreted in parallel at least 90 tumor cells are evaluated per case. The HER2 IHC slide was used to direct the choice of tumor region to her2 ISH in all cases with intratuumural heterogeneity. Therefore, using the 2018 guidelines, we were able to re-score all cases and analyze the impact on HER2 rates in our institution. Following the approval of the Corporate Review Board on Materials and Method Case Selection, we conducted a retrospective search of our pathology database to determine all breast CNB diagnosed as primary invasive breast carcinoma from January 1, 2014 to December 31, 2017 at Ohio State University Comprehensive Cancer Center (OSUCCC). Non-CNB cases examined in our institution where her2 studies were carried out in an external laboratory are excluded. Cases other than cnb where HER2 studies were conducted at OSUCCC were included. Data collected from electronic medical records and pathology reports for each case include the date of procedure, the age of the patient at the time of the procedure, histological sub-type, tumor rating (1, 2 or 3), estrogen receptor (ER) and progesterone receptor (PR) status (positive or negative and positive dyeing percentage of tumor nuclei), HER2 IHC (score 0, 1+, 2+, 3+) and HER2 FISH (positive, negative, clear, ambiguous, HER2/centromere numbering probe 17 [CEP17], and average HER2 copy number/core). All cases were first scored according to 2013 guidelines.3 Hormone receptor (HR) status for tumor was assessed as positive if tumor ER and/or PR positive (>1% nuclear reactivity), HR negative if tumors were clinically negative for both ER and PR (<1% nuclear reactivity). Formalin-hard paraffin embedded (FFPE) tissue er and PgR 636 clone (DAKO) USING SP1 clone (Spring Bioscience) for PR and Leica/Bond or DAKO autostainer Leica/Bond polymer detection system was evaluated by immunoohistochemistry ER and PR IHC. In our institution, all CNB with invasive carcinoma is tested at the same time using both HER2 IHC (4B5, Ventana), a Ventana autostainer and HER2 FISH (PathVysion HER2 DNA Probe Kit). Interfaz FISH HER2 gene amplification was collected with the FFPE tissue section containing invasive tumor selected by the relevant surgical pathologist. The FISH section/slide was analyzed by a licensed medical technologist using a Food and Drug Administration-approved, verified semi-automatic scanning imaging workstation (BioView Image Analysis System) and related analytics software. This scanner detects nonoverlapping nuclei of at least 90 interphase invasive carcinomas in three different areas at ×60 high power magnification. The software is then determined by technology control to calculate the average HER2/CEP17 ratio, the number of HER2 and CEP17 signals in each cell. The interpretation pathologist then reviewed the FISH section/slide and viewed the data generated by BioView manually Olympus is under fluorescent microscope. The pathologist further evaluated the section/slide for tumor auffability, fluorescent dye quality and confirming internal and external control tissue pathers. As a standard practice in our institution, her2 IHC stained slide and corresponding H&E stained slide are reviewed together with HER2 FISH in all cases with intratuumural heterogeneity for HER2 IHC expression and the corresponding H&E stained slide is reviewed together with HER2 FISH and the analyzer focuses on the site of the tumor showing intensive HER2 IHC coloring. Alternative probe HER2 FISH data was not used in the analysis of this study. Data Analysis The general HER2 status of each case was determined according to the 2013 guidelines,3 and 2018 guidelines were re-recorded.2 Cases of two-week diseases were recorded separately. The highest (most positive) HER2 condition was recorded in multifocal ipsilateral disease cases that differed between foci or HER2 intratuural heterogeneity of her2 condition. 2013 General HER2 Status Classification Positive: any positive result (IHC and/or FISH)Negative: Negative results for both IHC and FISH or lack of second testing or net equivocalEquivocal: a single net result or a single net result when no final results or second tests are performed for both IHC and FISH. The 2018 General HER2 Status Classification 2018 guidelines were used to categorize each HER2 FISH result 1-5 to the appropriate ISH groups, and the 2018 overall HER2 status was determined using her2 IHC and FISH results in each case: ISH Group 1 HER2/CEP17 ratio ≥2.0 and average HER2 signals/cell ≥4.0 copy number HER2 FISH positive. The 2018 overall HER2 situation was assessed positively regardless of the relevant HER2 IHC result. In cases with ISH Group 2 HER2/CEP17 ratio ≥2.0 and average HER2 copy number <4.0), the 2018 overall HER2 status was determined according to the relevant HER2 IHC result. If the IHC result was considered positive (score 3+), the overall HER2 status would be considered positive. If the IHC result was final (score 2+), the overall HER2 status was considered negative. If the IHC result was negative (score 0 -1+), the overall HER2 status was considered negative. In cases with ISH Group 3 HER2/CEP17 ratio <2.0 and average HER2 copy number ≥6.0, the general HER2 status of 2018 was determined according to the relevant HER2 IHC result. If the IHC result was positive (score 3+), the overall HER2 status was considered positive. If the IHC result was final (score 2+), the general HER2 condition was considered positive. If the IHC result was negative (score 0 -1+), the overall HER2 status was considered negative. In cases with ISH Group 4 HER2/CEP17 ratio <2.0 and average HER2

copy number ≥ 4.0 and <6.0, the overall HER2 status of 2018 was determined according to the relevant HER2 IHC result. General HER2 status if IHC result was considered positive (score 3+) Positive. If the IHC result was final (score 2+), the overall HER2 status was considered negative. If the IHC result was negative (score 0 -1+), the overall HER2 status was considered negative. ISH Group 5 Cases with RATIO <2.0 to HER2/CEP17 were considered ISH negative with average HER2 copy number <4.0 signals/cell. The 2018 general HER2 situation was determined according to the relevant HER2 IHC result. If the IHC result was positive (score 3+), the overall HER2 status was considered positive. If the IHC result was final (score 2+), the overall HER2 status was considered negative. If the IHC result was negative (score 0 -1+), the overall HER2 status was considered negative. Statistical Analysis HER2 recategorization rate was determined by comparing the overall HER2 status of each case according to the 2013 and 2018 guidelines. Concordato cases are defined as having the same overall HER2 state result under both sets of guidelines (positive/positive or negative/negative). Dysordant cases are defined as having different general HER2 statuses according to the instructions used (positive/negative). The change in the HER2 state is defined as having different general HER2 statuses under each set of guides (positive/negative or negative or net/positive). The concordato was reported as a percentage and evaluated by Cohen's coefficient of λ. Statistical analysis using categorical variables was performed and summarized using frequency. The importance of ISH group vs degree was evaluated using t test and Pearson 2 test was used to assess the importance of HR status with Ish group. Continuous variables were evaluated using average and range as applicable. Results Patient Demographics We detected 1,350 CNB samples with invasive breast carcinoma and HER2 test performed in our institution between 2014 and 2017. The average patient age during biopsy was 59 (distribution, 23-96 years). Histological subseques were duktal (84%), lobes (11%), mixed duktal/lobuler (4%), metaplastic (1%), musinous < (1%), low-grade adenosquamous (%<1), small cell (%<1), and invasive papillary (%<1). Of the majority (46%) tumors, 2% were grade 2, 28% were grade 3 and 26% were grade 1. Table 1 Comparison of The Sample Number of Each Histological Sub-Type by Degree, Hormone Status, and HER2 IHC and FISH Result. Class. Hormone Status . HER2 IHC . HER2 Fish . . 1 . 2 . 3 . Positive. Negative. 0-1+. 2+ . 3+ . Group 1 . Group 2 . Group 3 . Group 4 . Group 5 . Ductal NOS 276 507 352 908 226 793 209 133 153 4 12 123 843 Lobular 51 86 7 139 5 122 12219 3 5 0 1 4 134 Mixed type 17 27 5 45 40 8 1 3 1 1 2 43 Metaplastic 0 1 11 11 11 10 2 0 1 0 0 0 1 00 0 0 9 Mücinous 2 5 0 7 0 6 1 0 0 0 0 7 LGAS 1 0 0 1 0 0 0 0 0 0 0 0 0 0 small cell 0 0 1 1 0 0 0 0 0 0 papils 0 1 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 1 0 0 0 0 0 1 1 1 1 1. (%) 347 (26) 627 (46) 376 (28) 1,102 (82) 247 (18) 973 (72) 240 (18) 137 (10) 162 (12) 4 (0.3) 14 (1) 131 (10) 1.038 (77) HER2 FISH RESULTS In the 2013 guidelines, 180/1,350 (13%) her2 FISH positive, 131/1,350 (10%) FISH equivocal and 1,039/1,350 (77%) FISH negative. According to 2018 guidelines, 162/1,350 (12%) ISH group 1, It was 4/1,350 (0.3%), ISH was in group 2, 14/1,350 (1%) in ISH group 3, 131/1,350 (10%) ish group 4 and 1,039/1,350 (77%) in ISH group 5. ISH groups 2-4 calculated 11% of HER2 FISH results up to table 2. Table 2 Using the 22 DISTRIBUTION of FISH Result 2013 Guidelines and 2018 Guidelines . FISH Result . . Group 1 . Group 2 . Group 3 . Group 4 . Group 5 . HER2 status Rate ≥2.0, Copy No. ≥4.0 Ratio ≥2.0, Copy No. <4.0 Ratio <2.0, Copy No. ≥6.0 Ratio <2.0, Copy No. ≥4.0 and <6.0 Ratio <2.0, Copy No. <4.0 2013 guides Positive Positive Positive Positive Positive 2018 guidelines Positive Additional work Additional work Additional work Additional work Negative No. General HER2 Status under directives 162 (12) 4 (0.3) 14 (1) 131 (10) 1.039 (77) 2013, 180/1,350 (13%) HER2 positive, 78/1,350 (6%) her2 and 1,092/1,350 (81%) HER2 negative. According to 2018 guidelines, 174/1,350 (13%) HER2 positive and 1,176/1,350 (87%) were HER2 negative Tables 3. Cases in ISH groups 2 and 4 were not HER2 IHC positive, and therefore all of these were categorized as negative in the overall HER2 situation according to the 2018 guidelines. The majority (86%) of ISH group 3 cases had a HER2 score of 2+ or 3+, and therefore the overall HER2 status was positively categorized according to 2018 guidelines. No cases in ISH group 5 were HER2 IHC positive, and all were categorized as general HER2 status negative regardless of 2018 guidelines. Total 84/1,350 (6%) cases changed overall HER2 status, with majority (78/1,350, 6%) The overall HER2 state is precise (under the 2013 guidelines) due to general HER2 state negative (under 2018 guidelines) transitions. Of the 78 cases that changed her2 status from HER2 to negative, all were double net with FISH results (2013 guidelines)/ISH group 4 (2018 guidelines) and a HER2 IHC score of 2+. The discord rate was 6/1,350 (0.4%), and all six cases vary from general HER2 status positive (according to 2013 guidelines) to general HER2 state negative (according to 2018 guidelines). Most (four) disadsed cases were in ISH group 2 Image 1, Image 2 and Image 3, and two separate cases in ISH group 3 were in negative HER2 IHC Table 4 and Figure 4. Table 3 Comparison of General HER2 Status That Benefits from 2013 Guidelines and 2018 Guidelines. HER2 Status . It's negative. Equivocal. Positive. 2013 guides, No. (%) 1.092 (81) 78 (6) 180 (13) 2018 guide, No. (%) 1.176 (87) 0 (0) 174 (13) Difference +6% – 6%– 0.4% Table 4 Comparison of HER2 IHC Result for each ISH Groupa. FISH Result . . . Group 1 . Group 2 . Group 3 . Group 4 . Group 5 . . HER2 IHC Result . Rate ≥2.0, Copy No. ≥4.0 . Rate ≥2.0, Copy No.<4.0 . Rate <2.0, Copy No. ≥6.0 . Rate <2.0, Copy No. ≥4.0 and . Rate <2.0, Copy No. <4.0 . Total. 0 - 1+, No. (%) 4 (2) 3 (75) 2 (14) 53 (40) 911 (88) 973 (72) 2+, No. (%) 24 (15) 1 (25) 9 (64) 78 (60) 128 (12) 240 (18) 3+, No. (%) 134 (83) 0 (0) 3 (21) 0 (0) 0 (0) 0 (0) 0 (0) 137 (10) Total 162 4 14 131 1,039 1,350 New tabDownload slideA, Breast seed needle biopsy from a 30-year-old woman with duktin carcinoma, grade 3 (H&E, ×20). The tumor was estrogen receptor negative (0%). and progesterone receptor negative (0%). B, Human epidermal growth factor receptor 2 (HER2) immunohistochemistry×20 core needle biopsy was equal (score 2+). Her2 fluorescent in situ hybridization (FISH) result was positive under 2013 guidelines, with a ratio of 2.30 HER2/CEP17 and a copy number of 3.60 HER2. Using the 2018 guidelines, it will fall below ISH group 2 as a result of HER2 FISH, and the tumor is classified as HER2 negative. OpenopenSlideA in the new tabA, breast seed needle biopsy from a 60-year-old woman with invasive duktal carcinoma with mucinous properties, grade 2 (H&E ×20). The tumor estrogen receptor was positive (100%) and progesterone receptor positive (2%). B, Human epidermal growth factor receptor 2 (HER2) immunohistochemistry×20 core needle biopsy was equal (score 2+). Her2 fluorescent in situ hybridization (FISH) result was positive in the 2013 guidelines with a ratio of 2.47 HER2/CEP17 and a number of 2.95 HER2 copies. Using the 2018 guidelines, it will fall below ISH group 2 as a result of HER2 FISH, and the tumor is classified as HER2 negative. New tabA openOpenSlideA, invasive duktal carcinoma, breast core needle biopsy from a 56-year-old woman with class 1 (H&E ×20). The tumor estrogen receptor was positive (100%) and the progesterone receptor was positive (85%). B, Human epidermal growth factor receptor 2 (HER2) immunohistochemistry×20 core needle biopsy was negative (score 1+). HER2 fluorescent in situ hybridization (FISH) result was positive in 2013 guidelines with a ratio of 2.20 HER2/CEP17 and a copy number of 3.80 HER2. Using the 2018 guidelines, this HER2 FISH result goes below ISH group 2 and the tumor is classified as HER2 negative. OpenopenSlideA in the new tabA, breast seed needle biopsy from a 95-year-old woman with invasive duktal carcinoma, grade 2 (H&E ×20). The tumor estrogen receptor was positive (95%) and the progesterone receptor was positive (70%). B, Human epidermal growth factor receptor 2 (HER2) immunohistochemistry×20 core needle biopsy was negative (score 1+). HER2 fluorescent in situ hybridization (FISH) result was positive with a her2/CEP17 ratio of 1.29 in 2013 guidelines and 6.40 copies of HER2. Using the 2018 guidelines, this HER2 FISH result enters ISH group 3 and the tumor is classified as HER2 negative. Comparison of ISH Groups ISH group and her2 number of copies associated with histological class Table 5. Tumors in ISH group 1 are highest 2.5 rating (average 1.9, P < .00001), which is significantly higher than ish group 5. Tumors in ISH group 3 and ISH group 4 had histological second and third highest average grades of 2.5 (P = .002) and 2.3 (P< .00001), respectively (Table 5). HR status is significantly associated with the ISH group (P < .0001). ISH group 1 61% (P< .0001) Compared to ISH group 5, HR positivity, which had the highest HR positive rate of 86% Table 6, showed a significantly lower rate. Table 5 Average Grade for Each In Situ Hybridization Group . Group 1Oran≥2.0, Copy No. ≥4.0 . Group 2Oran ≥2.0, Copy No. <4.0 . Group 3Oran <2.0, Copy No. ≥6.0 . Group 4Oran <2.0, Copy No. ≥4.0, and <6.0 . Group 5Oran <2.0, Copy No. <4.0 . Average class 2.5 1.7 2.5 2.3 1.9 Table 6 Comparison of Hormone-Positive Ratio (HR+) for Each In Situ Hybridization Group. Group 1 Ratio ≥2.0, Copy No. ≥4.0 . Group 2 Ratio ≥2.0, Copy No. <4.0 . Group 3 Ratio <2.0, Copy No. ≥6.0 . Group 4 Ratio <2.0, Copy No. ≥4.0, and <6.0 . Group 5 Ratio <2.0, Copy No. <4.0 . Total. HR+, No. (%) 99 (61) 3 (75) 10 (71) 100 (77) 891 (86) 1,102 (82) HR–, No. (%) 63 (39) 1 (25) 4 (29) 30 (23) 148 (14) 247 (18) Total 162 4 14 130a 1.039 1.349 According to our Discussion Information, This is the first study to analyze the potential impact on HER2 rates with the 2018 ASCO/CAP HER2 guide-driven update. In our analysis, we observed that the 2018 guidelines will predominantly affect patients whose ish groups are between 2 and 4, because the new guidelines will recay the overall HER2 condition of the majority of these patients. In our research, it was determined that ISH groups of 2 to 4 constituted 11% of ISH results, twice as much as the 2018 guidelines predicted.2 For institutions that performed ISH first, this represents a relatively large number of cases requiring reflex HER2 IHC. More importantly, the 2018 guidelines suggest that a higher-than-expected percentage of patients may recategorize her2 status. The 2018 guidelines will have a clear negative impact on the HER2 situation. This will occur in three basic ways: (1) reduced need to re-test patients in ISH group 4 (formerly classified as ISH under 2013 guidelines); (2) Reclassation of patients in ISH group 2 (high HER2/CEP17 ratio/low HER2 copy number) and a subset of ISH group 3 (low HER2/CEP17 ratio/high HER2 copy number) to HER2-negative status (classified as HER2 positive in old 2013 guidelines); and (3) reduced mandatory re-testing of patients who were initially HER2 negative and grade 3. In our series, we observed a total of 6% of cases that would change the overall HER2 state, the majority of which in ish group 4 (low HER2/CEP17 ratio/borderline HER2 copy number) (under 2013 guidelines) changed to negative status (under 2018 guidelines). According to 2013 guidelines, officially 6% of patients with HER2 would be re-tested for . it would have been. The exastension sample and a subset of these patients are converted back to her2-positive state according to the test results. Previously, under the 2013 guidelines, we reported a positive conversion rate of 6% from re-tests on exasperation samples in patients with HER2 IHC and ISH double equivocal initially in CNB.4 Other published studies will likely be overlooked under the 2018 guidelines under the 2018 guidelines. Since all ISH group 4 cases in our series are classified as HER2 negative under the 2018 guidelines, no mandatory requirement is specified for additional re-testing.We estimate that the HER2-positive rate will decrease by at least 0.4% in the 2018 guidelines due to the fact that the Her2-positive ratio in 2222 is directly reclassified from HER2-positive to HER2-positive status in accordance with the 2013 guidelines. The majority of positive and negative recategorizations were classified as HER2 IHC negative or deficit in ISH group 2 cases and therefore HER2 final status negative under 2018 guidelines. Patients in a small subset (15%) ISH group 3 will also be categorized as negative for their last HER2 status using the 2018 guidelines. This 0.4% of patients will become eligible for new anti-HER2 treatment in the transition from 2013 guidelines to 2018 guidelines. It should be taken into account that the 0.4% decrease in the HER2-positive rate we observed was probably underestimated, and that softening the 2018 guideline requirement for mandatory re-testing (for example, 3rd degree tumors found to be HER2 negative in the first test) would have a practical effect on further reducing the volume of re-testing on excion samples. Two studies showed that class 7.8 3 initially detected 3% of cases with incompatible (re-positive) HER2 results on mandatory re-test exastension of HER2-negative tumors. Many of these discosters were linked to intratueural heterogeneity for HER2 expression. Although the prevalence of intratuural heterogeneity of HER2 expression in primary breast cancer appears low, it is estimated at 6% in a series.9 If mandatory repeat testing is reduced in the 2018 guidelines, fewer cases of intratuminal heterogeneity are likely to be detected, and therefore additional patients (false negative on CNB) may be missed, which could potentially benefit from anti-HER2 targeted therapy. While the 2018 guidelines increase the threshold for classifying patients as HER2 positive and will have a net negative impact on HER2-positive rates, it is not fully understood whether revised cuts under the 2018 guidelines are supported by clinical results data. Findings from the latest NSABP-B47 experiment targeted her2 of patients with her2 over-expression that could not be strengthened by ISH (in accordance with 2013 guidelines) Similarly, while re-analysis of BCIRG 005 and 00611 studies provides clinical evidence to support new categorization algorithms, there is also the specialization that result data is limited in some subsets (especially ISH group 4). The study by Sneige et al12 reveals that patients in ISH group 4 (deviation of HER2 according to 2013 guidelines) were not shown a health disadvantage compared to HER2-negative patients. Overall, current published data suggests that 2018 guidelines will prevent ineffective, costly and potentially harmful treatment from being offered to patients unlikely to benefit from HER2 targeted treatment. While the 2018 guidelines undoubtedly increase the complexity of her2 test interpretation for pathologists (the need for HER2 ISH results to be grouped into five different outcome groups, reviewed with the IHC, and blind ISH recount of additional cells), the advantage of revision is that it will clearly simplify the management of patients. This will be achieved by eliminating the HER2 equivocal category. In some series, the incidence of definitive HER2 ISH results under the 2013 guidelines has increased to 10%.4.5 This is the case, it caused a large number of patients with unresolved HER2 status, increased reflex and re-testing, as well as the controversial use of the alternative probe HER2 FISH test.13-15 In our series, we observed that all cases that appeared as ISH in accordance with 2013 guidelines (ISH group 4) were turned into HER2 negatives under the 2018 guidelines. Therefore, we note that one of the biggest practical effects of the 2018 guidelines will be the elimination of the HER2 equivocal category, resulting in a significant reduction (6%). Absolute volume in cases requiring mandatory repeat HER2 testing under 2013 guidelines. In addition, we estimate that the 2018 guidelines will reduce the total volume of every two tests that need to be performed on excion samples, as a much smaller number of patients will need additional tests to resolve or confirm the condition of HER2 (initially HER2-negative/grade 3 tumors). Our work had its strengths. Our institution's standardized protocols for HER2 assessment have effectively enabled the evaluation of the impact of 2018 guidelines on HER2 rates. In our institution, routine binary testing by HER2 IHC and FISH has allow us to detect potential changes in HER2 rates using 2018 guidelines and minimize the potential selection bias that can occur when HER2 FISH is performed only as a reflex test. In addition, this potential inter-laboratory analytical variability was eliminated, as all tests were completed at home. Only a single sample type (CNB) was studied, so the potential for preanalytic deviation was very small due to prolonged cold iskemia time or insufficient formalin fixation time (as is more common in exassemia samples). Our standard HER2 FISH protocol The accompanying examination of 2.3 HER2 IHC and HER2 FISH from 90 cells, which is higher than the first issue of 20 cells required in the 2013 and 2018 guidelines, is conducted in all intratueural heterogeneity cases for HER2 expression. While we agree that this approach is not the same as the 2018 guidelines requirement for a 2018 guideline recount, the first oversuming method used in our study provides a reasonably accurate assessment of ISH grouping under the 2018 guidelines. Finally, our study covers a large series of consecutive CNB (n = 1,350), which provides sufficient statistical strength to our research. As a result, the 2018 ASCO/CAP HER2 guide addresss rare HER2 ISH amplification patterned cases that were previously difficult to classify under 2013 guidelines representing an important source of discussion and clinical uncertainty. At this limit, we observed that the diagnostic approach of the 2018 guidelines to cases facilitated clinical decision-making by re-categorizeing the majority of these cases as HER2 negative. However, the 2018 guidelines also have a treating decision-making effect for a subset of patients that will lower her2-positive rates and become newly eligible for targeted treatment. The majority of patients (66%) were previously classified as HER2 positive (2013 guidelines) and reclassified as HER2 negative (2018 guidelines) as a result of HER2 FISH ISH group 2 (HER2/CEP17 rate > 2.0, A minority (33%) positive (2013 guidelines) negative (2018 guidelines) reclassifications occurred in patients with ISH group 3 (HER2/CEP17 ratio < 2.0, HER2 copie count > 6.0) and negative HER2 IHC result her2 FISH result while HER2 copy number < 4.0) and negative HER2 IHC result. Continuous studies are needed to verify the clinical validity of this latest version of the ASCO/CAP HER2 guideline recommendations. This study was supported in part by the Ohio State University School of Medicine Roessler Research Fellow at A.G. References 1. , , , and others. The National Cancer Institute (NCI) Surveillance, Epidemiology and Final Results (SEER) program is a feasibility study for the collection of HER2 data by central cancer records. 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Class 3 breast carcinoma HER2 test re-and on-site analysis at excision using reflex immunohistochemistly: HER2 benefits from refined core needle biopsy parameters in diskordancy frequency and case selection. ;:-.8. , , , and others. Human epidermal growth factor receptor 2 test in invasive breast cancer: should histological class, type and estrogen receptor status affect the decision to re-ignite test? ;:-.9. , , , , and arc. HER2 heterogeneity affects trastuzumab responses and health in patients with her2-positive metastatic breast cancer. ;:-.10. , , , , and others. NSABP B-47 (NRG oncology): adriamicin (A) and cyclophosphamide (C) →-week paklitaksel (WP) or adjuvant chemotherapy with docetaxel (T) and C Phase III randomized study comparing or node positive or high risk node-negative invasive breast cancer (IBC) with iHC 1 + or 2 + negative FISH (HER2-Low IBC) expressing her2 dyeing intensity in women without a year of trastuzumab (H). . ;():Abstract -.11. , , , , , , et al. her2 gene amplification test situ hybridization by fluorescent (FISH): Comparison of ASCO-College of American Pathologists guidelines with FISH scores used for registration in clinical trials of the international research group on breast cancer. ;:-.12. , , , , and others. Results of equivocal human epidermal growth factor receptor 2 in patients with invasive breast cancer and the prognostic importance of clinical benefit of alternative chromosome 17 genes: a cohort study. ;:-.14.15. , , et al. 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