JMSR
Journal of Medical and Surgical Research

Mini Review

ISSN: 2351-8200

JMSR 2016, Vol III; N°2: 265-266

UPDATE OF THE RECOMMENDATIONS FOR HER2 STATUS DETERMINATION IN BREAST CANCERS: ASCO/CAP 2013 AND GEFPICS 2014.

H. Chahdi, M. Allaoui, A. Boudhas, M. Tbouda, M.R. El Ochi, A. Damiri, A. Al Bouzidi, M. Oukabli
Department of Pathology, Mohammed V[th] Military Hospital. Rabat, Morocco.
Medical School of Rabat, Mohammed V[th] University, Rabat, Morocco.

ABSTRACT

International guidelines on HER2 determination in breast cancer have just been updated by the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP), on the basis of more than 10 years practice, results of clinical trials and concordance studies. The "Groupe d'Etude des Facteurs Pronostiques et Immunohistochimiques dans le Cancer du Sein" (GEFPICS), a group of pathologists experts in breast cancer, presents these guidelines, adapted to the French routine practice. These recommendations highlight the possible diagnosis issues facing HER2 status determination, such as intra-tumor heterogeneity, special histological subtypes and biomarker reevaluation during metastatic relapse. Pre-analytical data and updated scoring criteria (especially for equivocal cases) are detailed, in order to optimize diagnosis and reduce the possibility of false negative results. In the era of personalized medicine, the quality of oncotheranostic biomarkers evaluation is a major element for pathologist, clinical practitioner and patient.

Keywords: HER2; Breast cancer; Immunohistochemistry; In situ hybridization; Guidelines

Corresponding Author:
Prof. Hafsa Chahdi, MD.
Address: Department of Pathology, Mohammed V[th] Military Hospital. Rabat, Morocco.
Email: h_chahdi@hotmail.com

INTRODUCTION

The latest guidelines of the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) and GEFPICS to test Human Epidermal Growth Factor Receptor 2 (HER2) in breast cancer after being revised in 2008 underwent a second modification in October 2013. The modification includes changes in cut-offs: 10% strong membranous staining for score 3+ on immune-histochemistry (IHC) (previously 30%) and using the ratio of >2 or absolute gene-copy-number (6 or more) alone or in combination with each other by in-situ-hybridization technology (previously >2.2 and average copy-number of 6 or more) [1 - 4].
Hereby we addressed the question, which impact the modified cut-offs had on overall HER2-positivity in a single institution.

DISCUSSION

At least one tumor sample from all patients with breast cancer (early-stage or metastatic disease) should be tested for either HER2 protein expression (IHC assay) or *HER2* gene expression (ISH assay) using a validated HER2 test.

In the United States, the ASCO/CAP Guidelines recommend use of an assay that has received FDA approval, although a CLIA-certified laboratory may use a laboratory-developed test; the analytic performance of the laboratory-developed test must be prospectively validated in the same clinical laboratory that will perform it and the test must have documented analytic validity. Bright-field ISH assays must be initially validated by comparing them with an FDA-approved fluorescence in situ hybridization (FISH) assay [1, 3 - 5].
The HER2 test result must be reported as *positive* if it is: (a) IHC 3+ positive; or (b) ISH positive using either a single-probe ISH or dual-probe ISH.
Recommendations in case of positive, equivocal and negative results all support that there is no apparent histopathologic discordance reported by the pathologist [1, 2, 5 - 7].
The HER2 test result must be reported as "*equivocal*" and a reflex test is recommended on the same specimen (unless there are concerns about the specimen) using the alternative test if the result is: (a) IHC 2+ equivocal; or (b) ISH equivocal using single-probe ISH or dual-probe ISH. Some rare breast cancers (eg. gland-forming tumors,

JMSR
Journal of Medical and Surgical Research

Mini Review

ISSN: 2351-8200 JMSR 2016, Vol III; N°2: 265-266

micropapillary carcinomas) show IHC 1+ staining that is intense but incomplete (basolateral or U shaped) and are found to be *HER2* amplified. The pathologist should classify these specimens as equivocal and order reflex testing using the alternative test [1, 4].

The HER2 test result must be reported as "*negative"* if a single test (or all tests) performed in a tumor specimen show: (a) IHC 1+ negative or IHC 0 negative results; or (b) ISH-negative results using single-probe ISH or dual-probe ISH.

The HER2 test result must be reported as "*indeterminate"* if technical issues prevent one or both of IHC and ISH from being reported as positive, negative, or equivocal. Another specimen should be requested for testing and a comment should mention the intended action in the pathology report [1].

Bright-field ISH should be interpreted on the basis of a comparison between patterns in normal and tumor cells of the breast, because artifactual patterns may occur that are difficult to interpret. If the tumor cell pattern is neither normal nor clearly amplified, an expert opinion is recommended. When performing HER2 testing, the specimen should undergo the fixation process quickly (time to fixative within 1 hour) and be fixed in 10% neutral buffered formalin for 6 to 72 hours; routine processing and staining should follow the standardized analytically validated protocols. [3] The testing laboratory should conform to standards of CAP accreditation or an equivalent accreditation authority, including initial test validation, ongoing internal quality assurance, ongoing external proficiency testing, and routine periodic performance monitoring [1 - 3, 7 - 10].

If an apparent histo-pathologic discordance is observed in any testing situation, the pathologist should consider ordering additional HER2 testing and conferring with the oncologist and should document the decision-making process and results in the pathology report. The pathologist may also pursue additional HER2 testing without conferring with the oncologist [3, 4].

CONCLUSION

The recent updated guideline recommendations published by the joint ASCO/CAP expert panel represent an important step on the way towards high-quality personalized medicine. This update contains more detailed recommendations on key points relating to HER2 testing methodology, testing algorithms, interpretation of results, and the potential need for retesting.

REFERENCES

1. Penault-Llorca F, Vincent-Salomon A, MacGrogan G, Roger P, Treilleux I. and al. Mise à jour 2014 des recommandations du GEFPICS pour l'évaluation du statut HER2 dans les cancers du sein en France. Annales de pathologie (2014) 34, 352—365.
2. Penault-Llorca F, Vincent-Salomon A, Bellocq JP, Matthieu MC, Grogan GM, Treilleux I and al. Mise à jour des recommandations du GEFPICS pour l'évaluation du statut HER2 dans les cancers du sein en France. Ann Pathol 2010; 30:357—73.
3. MacGrogan G.; M.C Mathieu; B. Poulet; F. Penault-Llorca. Recommandations du GEFPICS concernant la phase pré-analytique pour l'évaluation de HER2 et des récepteurs hormonaux dans le cancer du sein : mise à jour 2014. Annales de pathologie (2014).
4. Rakha E.A, Starczynski J, Lee A.H, Ellis I.O. The updated ASCO/CAP guideline recommendations for HER2 testing in the management of invasive breast cancer: a critical review of their implications for routine practice. Histopathology 2014, 64, 609–615.
5. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, Allison KH, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol 2013; 31: 3997—4013.
6. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol 2010; 28: 2784—95.
7. Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. J Clin Oncol 2007; 25: 118—45.
8. Bellocq JP, Arnould L, Chenard MP, Chetritt J, Petit T, Egele C, and al. HER France, observatoire national des pathologistes sur HER2, RO-RP et Ki-67 dans le cancer du sein — Bilan à un an sur 14 000 entrées. Acquis et limites en sénologie/Assets and limits in breast diseases. In: 34e Journées de la Société française de sénologie et de pathologie mammaire. Paris: Springer Eds.; 2013. p. 497—9.
9. Lakhani SR, Ellis IO, Schnitt SJ, et al. WHO Classification of Tumours. IARC WHO Classification of Tumours,4th edition;2012: 22—3.
10. Hanna WM, Rüschoff J, Bilous M, Coudry RA, Dowsett M, Osamura RY, et al. HER2 in situ hybridization in breast cancer: clinical implications of polysomy 17 and genetic heterogeneity. Mod Pathol 2014; 27: 4—18.