

ASCO[®] Guidelines

Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: ASCO-CAP Guideline Update

Supplement

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Data Supplement 1. Guideline Development Methodology

GUIDELINE QUESTIONS

This clinical practice guideline update addresses two overarching clinical questions: (1) What is the optimal testing algorithm for the assessment of HER2 status; and (2) What strategies can help ensure optimal performance, interpretation, and reporting of established assays?

GUIDELINE UPDATE PROCESS

PubMed was searched (January 1, 2018, through July 13, 2022) for randomized controlled trials (RCTs) and prospective studies of novel HER2 assays that demonstrate accuracy in determining HER2 status and benefit from anti-HER2 therapy. The search terms were those that were used for the 2018 guideline. A multidisciplinary Expert Panel which included a patient representative and an ASCO guidelines staff member with health research methodology expertise (Appendix Table A1, online only), reviewed the abstracts that were identified for signals that would suggest the need to change a previous recommendation. The Expert Panel corresponded via electronic mail to consider the evidence. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of the guideline, which was then circulated for external review, and submitted to the *Journal of Clinical Oncology* and the *Archives of Pathology & Laboratory Medicine* for editorial review and consideration for publication. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Evidence Based Medicine Committee (EBMC) before publication. An independent review panel, masked to the Expert Panel and vetted through the CAP conflicts of interest COI process, recommended approval by the CAP Council on Scientific Affairs.

The ASCO Guidelines Methodology Manual available at www.asco.org/guideline-methodology provides additional information about the guideline update process. All funding for the administration of the project was provided by ASCO.

LITERATURE SEARCH RESULTS

A total of 173 hits were identified in the two literature searches, 67 from the prospective studies search and 106 from the RCTs search. After applying the eligibility criteria, five abstracts remained. After careful review of the identified publications, the Expert Panel concluded that there were no results that would substantially change the 2013 and 2018 guideline recommendations for standard, anti-HER2 therapies other than trastuzumab-deruxtecan.

Data Supplement 2. Literature Search Strategy String and Dates

Literature Search String for Search for Prospective Studies

Dates of search: January 1, 2018 to July 13, 2022

Limits: The search was restricted to articles published in English and to humans.

Databases searched: PubMed

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((("Immunohistochemistry"[MeSH] OR immunohistochemistry[tiab] OR immunocytochemistry[tiab] OR "IHC"[tiab] OR "In Situ Hybridization, Fluorescence"[MeSH] OR "fluorescence in situ hybridization"[tiab] OR "fluorescence in-situ hybridization"[tiab] OR "FISH"[tiab] OR (chromogenic[tiab] AND hybridization[tiab]) OR "CISH"[tiab] OR ((gold-facilitated[tiab] OR autometallographic[tiab] OR "bright field"[tiab] OR bright-field[tiab]) AND hybridization[tiab]) OR "GOLDFISH"[tiab]) AND (Genes, erbB- 2[MeSH] OR Receptor, erbB-2[MeSH] OR "Her-2"[tiab] OR "Her2"[tiab] OR "HER2"[tiab] OR "HER-2"[tiab] OR "erbB-2"[tiab] OR "erbB2"[tiab] OR "epidermal growth factor receptor- 2"[tiab] OR "epidermal growth factor receptor 2"[tiab] OR receptor, epidermal growth factor[mh] OR epidermal growth factor receptor-neu receptor[nm]) AND (Breast neoplasms[MeSH] OR "breast neoplasm*" [tiab] OR "breast cancer*" [tiab] OR "breast tumor*" [tiab] OR "breast tumour*" [tiab])) AND ("prospective studies"[MeSH Terms] OR ("prospective"[All Fields] OR "prospective studies"[All Fields])) NOT (animals [mh] NOT human [mh]) AND English[la] AND ("2018/01/01"[PDat]: "2022/07/13"[PDat])
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Literature Search String for Search for Phase III Randomized Clinical Trials

Dates of search: January 1, 2018 to July 13, 2022

Limits: The search was restricted to articles published in English and to humans.

Databases searched: PubMed

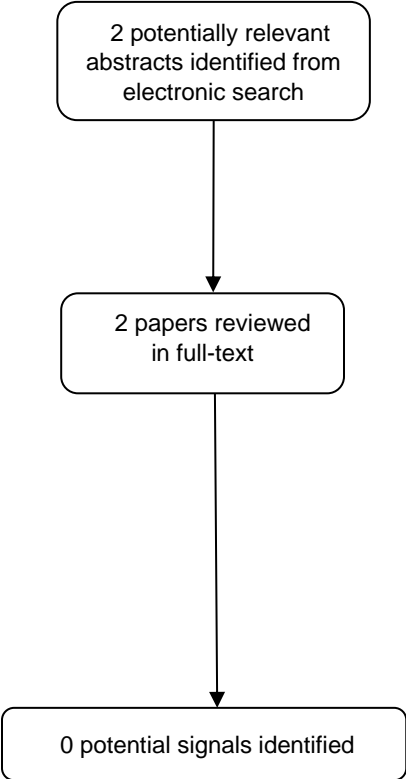
((("Immunohistochemistry"[MeSH] OR immunohistochemistry[tiab] OR immunocytochemistry[tiab] OR "IHC"[tiab] OR "In Situ Hybridization, Fluorescence"[MeSH] OR "fluorescence in situ hybridization"[tiab] OR "fluorescence in-situ hybridization"[tiab] OR "FISH"[tiab] OR (chromogenic[tiab] AND hybridization[tiab]) OR "CISH"[tiab] OR ((gold-facilitated[tiab] OR autometallographic[tiab] OR "bright field"[tiab] OR bright-field[tiab]) AND hybridization[tiab]) OR "GOLDFISH"[tiab]) AND (Genes, erbB- 2[MeSH] OR Receptor, erbB-2[MeSH] OR "Her-2"[tiab] OR "Her2"[tiab] OR "HER2"[tiab] OR "HER-2"[tiab] OR "erbB-2"[tiab] OR "erbB2"[tiab] OR "epidermal growth factor receptor- 2"[tiab] OR "epidermal growth factor receptor 2"[tiab] OR receptor, epidermal growth factor[mh] OR epidermal growth factor receptor-neu receptor[nm]) AND (Breast neoplasms[MeSH] OR "breast neoplasm*" [tiab] OR "breast cancer*" [tiab] OR "breast tumor*" [tiab] OR "breast tumour*" [tiab])) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized controlled trials[MeSH] OR randomized controlled trials as topic[MeSH] OR clinical trials, phase III as topic[MeSH] OR clinical trial, phase III[pt] OR design[TIAB])) NOT (case reports[pt] OR case report[TIAB]) NOT (animals[MeSH] NOT humans[MeSH])) AND English[la] AND ("2018/01/01"[PDat]: "2022/07/13"[PDat])

Data Supplement 3. Bibliography of the Results of the Updated Literature Review

Year	Bibliography
2020	Rüschhoff J, Lebeau A, Sinn P, Schildhaus HU, Decker T, Ammann J, Künzel C, Koch W, Untch M. Statistical modelling of HER2-positivity in breast cancer: Final analyses from two large, multicentre, non-interventional studies in Germany. <i>Breast</i> .;49:246-253.
2022	Xu K, Bayani J, Mallon E, Pond GR, Piper T, Hasenburg A, Markopoulos CJ, Dirix L, Seynaeve CM, van de Velde JH, Rea DW, Bartlett JMS. Discordance between Immunohistochemistry and Erb-B2 Receptor Tyrosine Kinase 2 mRNA to Determine Human Epidermal Growth Factor Receptor 2 Low Status for Breast Cancer. <i>J Mol Diagn</i> . Jul;24(7):775-783.
2020	Clifton GT, Hale D, Vreeland TJ, Hickerson AT, Litton JK, Alatrash G, Murthy RK, Qiao N, Philips AV, Lukas JJ, Holmes JP, Peoples GE, Mittendorf EA. Results of a Randomized Phase IIb Trial of Nelipepimut-S + Trastuzumab versus Trastuzumab to Prevent Recurrences in Patients with High-Risk HER2 Low-Expressing Breast Cancer. <i>Clin Cancer Res</i> . Jun 1;26(11):2515-2523.
2019	Perez EA, de Haas SL, Eiermann W, Barrios CH, Toi M, Im YH, Conte PF, Martin M, Pienkowski T, Pivot XB, Burris HA 3rd, Stanzel S, Patre M, Ellis PA. Relationship between tumor biomarkers and efficacy in MARIANNE, a phase III study of trastuzumab emtansine ± pertuzumab versus trastuzumab plus taxane in HER2-positive advanced breast cancer. <i>BMC Cancer</i> . May 30;19(1):517.
2022	Tarantino P, Jin Q, Tayob N, et al: Prognostic and Biologic Significance of ERBB2-Low Expression in Early-Stage Breast Cancer. <i>JAMA Oncol</i> 8:1177-1183.

Data Supplement 4. QUOROM Diagrams

A. Prospective Studies Search Yield



B. Phase III RCT Search Yield

