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# Recommendations on Disease Management for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer and Brain Metastases: ASCO Clinical Practice Guideline Update

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Editor's note: This American Society of Clinical Oncology (ASCO) 2018 Clinical Practice Guideline update reaffirms and summarizes the recommendations that were previously published in 2014; the 2014 recommendations remain current as of April 2018. Additional information, including an abbreviated Data Supplement with new studies, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at http://www.asco.org/breast-cancer-guidelines.

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## ABSTRACT

### Purpose
To update the formal expert consensus-based guideline recommendations for practicing oncologists and others on the management of brain metastases for patients with human epidermal growth factor receptor 2–positive advanced breast cancer to 2018.

### Methods
An Expert Panel conducted a targeted systematic literature review (for both systemic treatment and CNS metastases) and identified 622 articles. Outcomes of interest included overall survival, progression-free survival, and adverse events. In 2014, the American Society of Clinical Oncology (ASCO) convened a panel of medical oncology, radiation oncology, guideline implementation, and advocacy experts, and conducted a systematic review of the literature. When that failed to yield sufficiently strong quality evidence, the Expert Panel undertook a formal expert consensus–based process to produce these recommendations. ASCO used a modified Delphi process. The panel members drafted recommendations, and a group of other experts joined them for two rounds of formal ratings of the recommendations.

### Results
Of the 622 publications identified and reviewed, no additional evidence was identified that would warrant a change to the 2014 recommendations.

### Recommendations
Patients with brain metastases should receive appropriate local therapy and systemic therapy, if indicated. Local therapies include surgery, whole-brain radiotherapy, and stereotactic radiosurgery. Treatments depend on factors such as patient prognosis, presence of symptoms, resectability, number and size of metastases, prior therapy, and whether metastases are diffuse. Other options include systemic therapy, best supportive care, enrollment in a clinical trial, and/or palliative care. Clinicians should not perform routine magnetic resonance imaging to screen for brain metastases, but rather should have a low threshold for magnetic resonance imaging of the brain because of the high incidence of brain metastases among patients with HER2-positive advanced breast cancer. Additional information is available at www.asco.org/breast-cancer-guidelines.

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## INTRODUCTION

The goal of this update is to provide oncologists, other health care practitioners, patients, and caregivers with recommendations regarding guidance for optimal management of patients with human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer and brain metastases. The American Society of Clinical Oncology (ASCO) first published two evidence-based clinical practice guidelines on optimal management of patients with HER2-positive metastatic breast cancer in 2014.[1,2] The goal of this 2018 guideline update is to provide oncologists and other clinicians with current recommendations regarding the treatment of patients with HER2-positive metastatic breast cancer and brain metastases. The current 2018 update assesses

ASSOCIATED CONTENT

Appendix
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Data Supplement
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## THE BOTTOM LINE

### Recommendations on Disease Management for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer and Brain Metastases: ASCO Clinical Practice Guideline Update

#### *Guideline Question*

What is the appropriate course of treatment of patients with human epidermal growth factor receptor (HER2)–positive advanced breast cancer and brain metastases?

#### *Target Population*

Individuals with advanced HER2-positive breast cancer and brain metastases.

#### *Target Audience*

Medical oncologists, radiation oncologists, neurosurgeons, oncology nurses, patients/caregivers.

#### *Methods*

A systematic review of the literature was performed and relevant evidence was evaluated for inclusion in this updated clinical practice guideline using the signals approach.

#### *Recommendations*

- For patients with a favorable prognosis for survival and a single brain metastasis, treatment options include surgery with postoperative radiation, stereotactic radiosurgery (SRS), whole-brain radiotherapy (WBRT; ± SRS), fractionated stereotactic radiotherapy (FSRT), and SRS (± WBRT), depending on metastasis size, resectability, and symptoms. After treatment, serial imaging every 2 to 4 months may be used to monitor for local and distant brain failure.
- For patients with a favorable prognosis for survival and limited (two to four) metastases, treatment options include resection for large symptomatic lesion(s) plus postoperative radiotherapy, SRS for additional smaller lesions, WBRT (± SRS), SRS (± WBRT), and FSRT for metastases > 3 to 4 cm. For metastases < 3 to 4 cm, treatment options include resection with postoperative radiotherapy. In both cases, available options depend on resectability and symptoms.
- For patients with diffuse disease/extensive metastases and a more favorable prognosis and those with symptomatic leptomeningeal metastasis in the brain, WBRT may be offered.
- For patients with poor prognosis, options include WBRT, best supportive care, and/or palliative care.
- For patients with progressive intracranial metastases despite initial radiation therapy, options include SRS, surgery, WBRT, a trial of systemic therapy, or enrollment in a clinical trial, depending on initial treatment. For patients in this group who also have diffuse recurrence, best supportive care is an additional option.
- For patients whose systemic disease is not progressive at the time of brain metastasis diagnosis, systemic therapy should not be switched.
- For patients whose systemic disease is progressive at the time of brain metastasis diagnosis, clinicians should offer HER2-targeted therapy according to the algorithms for treatment of HER2-positive metastatic breast cancer.
- If a patient does not have a known history or symptoms of brain metastases, routine surveillance with brain magnetic resonance imaging should not be performed.
- Clinicians should have a low threshold for performing diagnostic brain magnetic resonance imaging testing in the setting of any neurologic symptoms suggestive of brain involvement.

(continued on following page)

## THE BOTTOM LINE (CONTINUED)

### *Additional Resources*

More information, including a Data Supplement with additional evidence tables, a Methodology Supplement with information about evidence quality and strength of recommendations, slide sets, and clinical tools and resources, is available at www.asco.org/breast-cancer-guidelines. Patient information is available at www.cancer.net

**ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.**

whether the 2014 recommendations remain valid. A complete list of previous recommendations is available at www.asco.org/breast-cancer-guidelines and in Data Supplement 1.

## METHODS

### *Guideline Update Process*

ASCO uses a signals[3] approach to facilitate guideline updating. This approach is intended to identify new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on routine literature searching and the expertise of ASCO guideline panel members to identify signals. The Methodology Supplement available at http://www.asco.org/breast-cancer-guidelines provides additional information about the signals approach.

PubMed and the Cochrane Library were searched for randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines for the period from March 8, 2012, to overlap with searches for the previous guidelines, through August 7, 2017. The disease and intervention search terms were those that were used for the 2014 guideline. An Expert Panel (members listed in Appendix Table A1, online only), formed in accordance with the ASCO Conflict of Interest Management Procedures for Clinical Practice Guidelines, reviewed the abstracts that were identified for predefined signals that would suggest the need to change a previous recommendation. Additional information about the results of the updated literature search (Data Supplement 2) and 2017 search strategy string and results (Data Supplement 3), as well as a discussion of the ASCO signals approach to guideline updating, are available at www.asco.org/breast-cancer-guidelines and in the 2018 Data Supplement and 2018 Methodology Supplement, respectively. A QUOROM (Quality of Reporting of Meta-Analyses) diagram of the updated search and the clinical questions are provided in Data Supplements 4 and 5, respectively.

The Expert Panel communicated via telephone and e-mail to consider the evidence for each of the 2018 recommendations. This systematic review-based guideline product was developed by a multidisciplinary Expert Panel, which included two patient representatives and an ASCO guidelines staff member with health research methodology expertise. The guideline was circulated in draft form to the Expert Panel. ASCO's Clinical Practice Guidelines Committee leadership reviewed and approved the final document. All funding for the administration of the project was provided by ASCO.

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This is the most recent information as of the publication date. For the most recent information, and to submit new evidence, please visit www.asco.org/breast-cancer-guidelines.

*Guideline and Conflicts of Interest.* The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

## RESULTS

A joint search for both guidelines yielded 622 publications. After careful review of the identified publications, the Expert Panel concluded that there were no results that would change the 2014 guideline recommendations. A bibliography of the results of the updated literature search is provided in Data Supplement 2.

## RECOMMENDATIONS

The 2018 recommendations are listed in the Bottom Line Box. These recommendations are consistent with the previous (2014) recommendations. ASCO believes that cancer clinical trials are

  

vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate.

### Related ASCO Guidelines

- Systemic Therapy for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer[4] (http://ascopubs.org/doi/10.1200/JCO.2018.79.2697)
- Integration of Palliative Care Into Standard Oncology Care[5](http://ascopubs.org/doi/10.1200/JCO.2016.70.1474)
- Patient-Clinician Communication[6] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)
- American Cancer Society/ASCO Breast Cancer Survivorship Care[7] (http://ascopubs.org/doi/10.1200/JCO.2015.64.3809)

## ADDITIONAL RESOURCES

More information, including Data and Methodology Supplements, slide sets, and clinical tools and resources, is available at www.asco.org/breast-cancer-guidelines. Patient information is available at www.cancer.net.

## AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

## AUTHOR CONTRIBUTIONS

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## REFERENCES


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## Appendix

**Table A1.** Recommendations on Disease Management for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer and Brain Metastases Expert Panel Membership

| Name (and designation) | Affiliation/Institution | Role/Area of Expertise |
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Abbreviation: PGIN, Practice Guidelines Implementation Network.