Recommendations on Disease Management for Patients with Advanced HER2-Positive Breast Cancer and Brain Metastases

Clinical Tools and Resources

Clinical Practice Guideline

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Introduction

• Survival has improved for patients with both early stage-breast cancer and metastatic breast cancer
• HER2-positivity is a known risk factor for the development of brain metastases
• Up to 50% of patients with HER2-positive metastatic breast cancer develop brain metastases over time
• Paucity of guidance for patients in this setting
Guideline Methodology: Formal Consensus

• An Expert Panel completed a systematic review and analysis of the medical literature through May 2013
  ✓ Medline

• None of the results met pre-specified inclusion criteria

• ASCO switched to its formal Expert Consensus process (Modified Delphi) for these recommendations

• Assembly of Consensus Ratings Group
  • Two rounds of consensus ratings completed
  • Consensus agreement reached pre-defined criteria (≥75%)
Clinical Questions

What is the appropriate course of treatment for patients with HER2-positive advanced breast cancer and brain metastases?

Four sub-questions:
(1) Does the approach to local therapy of brain metastases differ in patients with HER2-positive breast cancer?

(2) How should systemic therapy be managed in patients with HER2-positive brain metastases (including how to manage systemic therapy when the brain is the only site of progression versus when progression in both brain and elsewhere)?

(3) Is there a role for systemic therapy specifically to treat brain metastases in HER2-positive breast cancer?

(4) Should patients with HER2-positive breast cancer be screened for development of brain metastases?
Recommendations
Favorable Prognosis - Single Metastasis

- If a patient has a favorable prognosis for survival and a single brain metastasis, then he/she should be evaluated by an experienced neurosurgeon for discussion of the option of surgical resection, particularly if the metastasis is >3-4 cm and/or if there is evidence of symptomatic mass effect.
- See next slide for additional recommendations in this setting.
Favorable Prognosis - Single Metastasis

**Symptomatic?**

**Asymptomatic?**

**Large**

>3-4cm

- **Symptomatic?**
  - Resection + postoperative radiotherapy for large symptomatic, resectable metastasis

- **Asymptomatic?**
  - Surgery, SRS, WBRT+/-SRS, or FSRT depending on location, size, need for tissue diagnosis, and operative risk

**Small**

<3-4cm

- **Symptomatic?**
  - Resection + postoperative radiotherapy for small symptomatic, resectable metastasis

- **Asymptomatic?**
  - SRS +/- WBRT; consider surgery if tissue diagnosis needed

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stereotactic radiosurgery (SRS), whole brain radiotherapy (WBRT), fractionated stereotactic radiotherapy (FSRT)

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Favorable Prognosis - Single Metastasis

- After treatment, serial imaging every 2-4 months may be used to monitor for local and distant brain failure
Favorable Prognosis 2-4 Metastases

Treatment Options

Large
>3-4cm

Symptomatic

Resection for large symptomatic lesion(s) + postoperative radiotherapy; SRS for additional smaller lesions

Asymptomatic

WBRT+/- SRS, SRS+/- WBRT, FSRT

Small
<3-4cm

Symptomatic

Resection + postoperative radiotherapy for symptomatic lesions; SRS for additional asymptomatic lesions

Asymptomatic

SRS +/- WBRT

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Favorable Prognosis \(\geq 5\) Metastases
(not diffuse)

\[
\begin{align*}
\geq 5 \text{ metastases} & \quad \rightarrow \quad \text{WBRT*} \\
\text{Symptomatic leptomeningeal metastasis in the brain} & \quad \rightarrow \quad \text{WBRT}
\end{align*}
\]

* In select cases, patients may be considered for systemic therapy, SRS, or treatment on clinical trial depending on tumor size, symptomatology and systemic disease status.

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Poor Prognosis

Brain metastases

- WBRT (symptomatic patients)
- Best Supportive Care/Palliative Care
Progressive Intracranial Disease Despite Initial Therapy

Limited Progression/Favorable Prognosis

Post-WBRT

- SRS
- Surgery
- Trial of systemic therapy
- Clinical trial
- Re-SRS /FSRT, WBRT

Post-SRS

- Surgery
- Trial of systemic therapy
- Clinical trial
Progressive Intracranial Disease Despite Initial Therapy

Diffuse Progression/Unfavorable Prognosis

Post-WBRT

- Re-WBRT*
  - * ≥ 6 months post initial WBRT
- Trial of systemic therapy
- Best supportive care
- Clinical trial

Post-SRS

- Trial of systemic therapy
- Best supportive care
- Clinical trial
Systemic Therapy

• For a patient who receives standard surgical or radiotherapy-based approaches to treat brain metastases and are receiving anti-HER2 based therapy and whose systemic disease is not progressive at the time of brain metastases diagnosis, clinicians should not switch the systemic therapy.
Systemic Therapy

• For a patient who receives standard surgical and/or radiotherapy-based approaches to treatment of brain metastases and 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.
Screening

• If a patient does not have a known history of or symptoms of brain metastases, then clinicians should not perform routine surveillance with brain MRI.

• Clinicians should have a low threshold to perform diagnostic brain MRI testing in the setting of any neurologic symptoms suggestive of brain involvement, such as new onset headaches, unexplained nausea/vomiting, or change in motor/sensory function.
Patient and Clinician Communication

• Present the statistics in this guideline in a format tailored to the patient/caregiver’s learning style. Discussions with patients should include key subjects, such as:
  • Explanation of metastatic breast cancer and the objectives of treatment (prolonging life versus curative)
  • Treatment options, including clinical trials, with potential benefits, side effects and risks
  • The availability of supportive care
  • Importance of considering chronic conditions such as congestive heart failure in choosing treatments
  • Explanation of treatment failure and lines of treatment, including for patients with brain metastases
  • The multiple members of the clinical team who may implement these recommendations, including oncology nurses, radiation oncologists, neurosurgeons, palliative care clinicians, psychosocial professionals, etc.
Limitations and Future Directions

• Lack of specific data on patients with HER2-positive disease and brain metastases in general
• Specific issues
  • The benefits/risks of lapatinib alone or with capecitabine
  • Data on “long term" toxicities of radiation therapy
  • How to measure efficacy, efficacy of various chemotherapy agents
• The Panel strongly urges researchers to conduct robust comparative studies
The Bottom Line

- **Interventions**
  - Radiation therapy (SRS, WBRT, FSRT), surgery, HER2-targeted therapy

- **Target Population**
  - Individuals with advanced HER2-positive breast cancer and brain metastases

- **Target Audience**
  - Medical, surgical, and radiation oncologists; neurosurgeons, oncology nurses and physician assistants; and patients/caregivers

- **Methods**
  - Formal Expert Consensus using a modified-Delphi method

- **Additional Information**
  - Background in Guideline and Data Supplement
  - Data Supplements and Clinical Tools and Resources at [www.asco.org/guidelines/her2brainmets](http://www.asco.org/guidelines/her2brainmets)
  - Patient information is available at [http://www.cancer.net](http://www.cancer.net)
Additional Resources

• This guideline, as well as its companion on treating patients with HER2+ metastatic breast cancer with non-brain metastases in patients with is available at www.asco.org/guidelines/breast-cancer

• This guideline, a methodology supplement, data supplements, and a patient guide are available at www.asco.org/guidelines/her2brainmets

• The patient guide is also available at http://www.cancer.net
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[Cont’d on next slide]
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