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Treatment of Metastatic HER2-Positive Breast Cancer [1]

To help doctors give their patients the best possible care, the American Society of Clinical Oncology (ASCO) asks its medical experts to develop evidence-based recommendations about specific topics in cancer care. These recommendations are for the treatment of human epidermal receptor 2 (HER2)-positive breast cancer that has spread beyond the breast. This guide for patients and caregivers is based on ASCO's recommendations.

Key Messages:

- Several treatments are currently available that can help women with HER2-positive breast cancer continue to live and function well after diagnosis, even if it has spread.
- Treatment of HER2-positive breast cancer that has spread to organs other than the brain usually includes drugs called HER2-targeted therapies, which are intended to slow or stop cancer growth by blocking HER2.
- Surgery and radiation therapy are usually used alone or in combination for HER2-positive breast cancer that has spread to the brain to shrink or temporarily eliminate cancer from the brain.
- Treatments to manage the symptoms of metastatic breast cancer and the side effects of treatment are also an important part of each patient?s treatment plan.
- Clinical trials are also a treatment option to consider at any time during cancer care.

Background

Metastatic breast cancer is cancer that has spread from the breast to another part of the body or has come back in another distant location. This area of spread is called a metastasis, or metastases if there are multiple areas of spread. Breast cancer most commonly spreads to the bone, lungs, liver, and brain. It is important to remember that breast cancer that spreads to these other organs is still considered breast cancer and treated similarly.

Some women are diagnosed with metastatic breast cancer after having received treatment for early-stage breast cancer. For others, the first diagnosis of breast cancer is when it has already spread.

Treatment options for metastatic breast cancer depend on several factors, including where the cancer has spread, the patient?s overall health, and the levels of hormone receptors and HER2

in the tumor. Both hormone receptors and HER2 are specialized proteins. Hormone receptors are found inside breast cells and HER2 is found on the surface of breast cells. Cancers with high levels of hormone receptors, called hormone receptor-positive, use the hormones estrogen and progesterone to grow and spread. When a breast cell has abnormally high levels of the *HER2* gene or the HER2 protein, it is called HER2- positive.

About 15% to 20% of patients with invasive breast cancer have abnormally high levels of HER2. These cancers tend to be more likely to spread than other types of breast cancer, particularly to the brain. HER2-positive metastatic breast cancer will spread to the brain in up to half of patients.

Drugs that specifically block HER2 to stop the growth of cancer cells are called HER2-targeted therapies. Examples of these drugs include trastuzumab (Herceptin), lapatinib (Tykerb), pertuzumab (Perjeta), and ado-trastuzumab emtansine (Kadcyla), commonly referred to as T-DM1. Some of these drugs may be used together with chemotherapy. Unfortunately, these drugs are not usually able to reach the brain as easily as they can reach the rest of the body, with lapatinib being a possible exception. Therefore, when cancer spreads to the brain it is usually treated with surgery and/or radiation therapy.

In addition to treatment to slow, stop, or eliminate the cancer, an important part of cancer care, particularly for those with metastatic cancer, is relieving the symptoms and side effects. This is called supportive or palliative care [2], and it includes supporting the patient with his or her physical, emotional, and social needs.

Recommendations for cancer that has spread to parts of the body other than the brain

In general, HER2-targeted therapy should be added to treatment for HER2-positive breast cancer that has spread. The drugs used depend on the treatments already given and whether the cancer is hormone receptor-positive. The first set of drugs used for metastatic disease is called first-line treatment. If the cancer worsens or comes back, another regimen may be used, called second-line treatment. Below are the treatment recommendations for first-line, second-line, and third-line or higher treatment.

First-line treatment

- Treatment is usually a combination of pertuzumab, trastuzumab, and a type of chemotherapy called a taxane.
- If the cancer is hormone receptor-positive, treatment may be a combination of hormonal therapy plus HER2-targeted therapy with either trastuzumab or lapatinib. Hormonal therapy may also be given alone if the cancer has not spread widely, a patient has other health conditions that could be worsened with HER2-targeted therapies, or the cancer has recurred after a long time.
- Chemotherapy is generally given for at least four to six months or until the patient experiences too many severe side effects, or the disease worsens. For patients with hormone receptor-positive cancer, HER2-targeted therapy and hormonal therapy usually continue after chemotherapy ends.

Second-line treatment

- For patients with early-stage breast cancer who had the cancer spread during initial treatment with trastuzumab or return within 12 months after stopping treatment with trastuzumab, second-line treatment is used.
- The preferred second-line treatment is the drug T-DM1.

Third-line or higher treatment

- T-DM1 is a treatment option for patients who have not already received it.
- Pertuzumab is also an option for patients who have not already received it, and it is usually given in combination with trastuzumab.
- For patients who have already received T-DM1 and pertuzumab, other options include lapatinib with capecitabine (Xeloda), other combinations of chemotherapy with HER2-targeted therapy, or hormonal therapy when appropriate.

Recommendations for cancer that has spread to the brain

Routine screening with imaging tests, such as brain magnetic resonance imaging (MRI), are not recommended for patients who do not have symptoms or a history of HER2-positive breast cancer spreading to the brain. However, if a patient develops any symptoms that suggest that the cancer has spread to the brain, such as headaches, memory problems, and/or weakness or numbness in the arms and legs, a brain MRI is recommended.

The treatment of HER2-positive breast cancer that has spread to the brain usually involves combinations of surgery and/or different types of radiation therapy, depending on the size and location of the tumor(s) in the brain, and the symptoms they are causing, as well as the patient?s general health.

Surgery. Surgery is the removal of the tumor and surrounding tissue during an operation. Usually, surgery to remove brain metastases is done by a neurosurgeon, a doctor who specializes in surgery on the brain. Learn more about surgery [3].

Radiation therapy. Radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. Several different types of radiation therapy are used to treat brain metastases, including whole brain radiation, stereotactic radiosurgery, and fractionated stereotactic radiotherapy. Whole brain radiation therapy is directed at the entire brain. Stereotactic radiosurgery is the use of a single, high dose of radiation given directly to the tumor to avoid harming the surrounding healthy tissues. Fractionated stereotactic radiation therapy is similar to stereotactic radiosurgery but divided into small daily doses called fractions that are given over multiple days or weeks, in contrast to the one-day radiosurgery. Learn more about radiation therapy [4].

Below is a general summary of when and how the above treatment options are used to treat brain metastases:

- Patients with a good chance of recovery and a single brain metastasis or two to four brain metastases generally receive surgery, followed by some type of radiation therapy.
- Treatment for patients with a poorer chance of recovery and/or cancer that has spread widely throughout the brain usually includes whole brain radiation therapy plus palliative care.

- For patients whose cancer in the brain is worsening even after receiving radiation therapy, additional treatment options depend on the initial treatment and include surgery, the types of radiation therapy discussed above, and/or a drug that can affect the whole body, such as HER2-targeted therapy.
- Patients who also have metastatic HER2-positive breast cancer in parts of the body other than the brain usually continue their treatment regimen if the disease outside the brain is not worsening. If the disease is worsening, a HER2-targeted therapy may be added/changed based on the recommendations for HER2-positive cancer that has spread to parts of the body other than the brain (see further above).

What This Means for Patients

For most patients, a diagnosis of metastatic cancer is very stressful and, at times, difficult to bear. It is important to remember that people with an advanced cancer such as metastatic breast cancer continue to have treatment options and can maintain a good quality of life for months or even years. The development of HER2-targeted therapies has helped lengthen the lives of many patients with metastatic breast cancer.

Each person?s chance of recovery depends on many factors, including how widespread the cancer is and what treatments have already been used. Be sure to talk with your doctor about the goals of treatment, the next steps if the cancer worsens, and the best options to help maintain your quality of life. It may also help to talk about the way you are feeling with doctors, nurses, social workers, other members of the health care team, or a support group.

Questions to Ask the Doctor

If you have metastatic breast cancer, consider asking your doctor the following questions:

- Where has the cancer spread?
- What is the HER2 status of the cancer? What does it mean?
- What is the hormone-receptor status of the cancer? What does it mean?
- What is my prognosis (chance of recovery)?
- What treatments have I already received?
- What are my treatment options?
- What are the benefits and risks of each option?
- What clinical trials are open to me? Where are they located, and how do I find out more about them?
- What treatment plan do you recommend? Why?
- What is the goal of each treatment? Is it to eliminate the cancer, help me feel better, or both?
- What are the next steps if the cancer worsens or comes back?
- What side effects of the treatments are most common?
- How can the symptoms and side effects be managed?
- How will treatment of brain metastases affect how my brain functions?

More Information

Read the entire clinical practice guidelines at www.asco.org/guidelines/treatHER2pos [5] and www.asco.org/guidelines/her2brainmets [6].

Guide to Breast Cancer [7]

HER2 Testing for Breast Cancer [8]

When the First Treatment Doesn't Work [9]

Advanced Cancer Care Planning [10]

Links:
[1] http://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-her2-positive-breast-cancer
[2] http://www.cancer.net/node/25282
[3] http://www.cancer.net/node/30689
[4] http://www.cancer.net/node/30687
[5] http://www.asco.org/guidelines/treatHER2pos
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