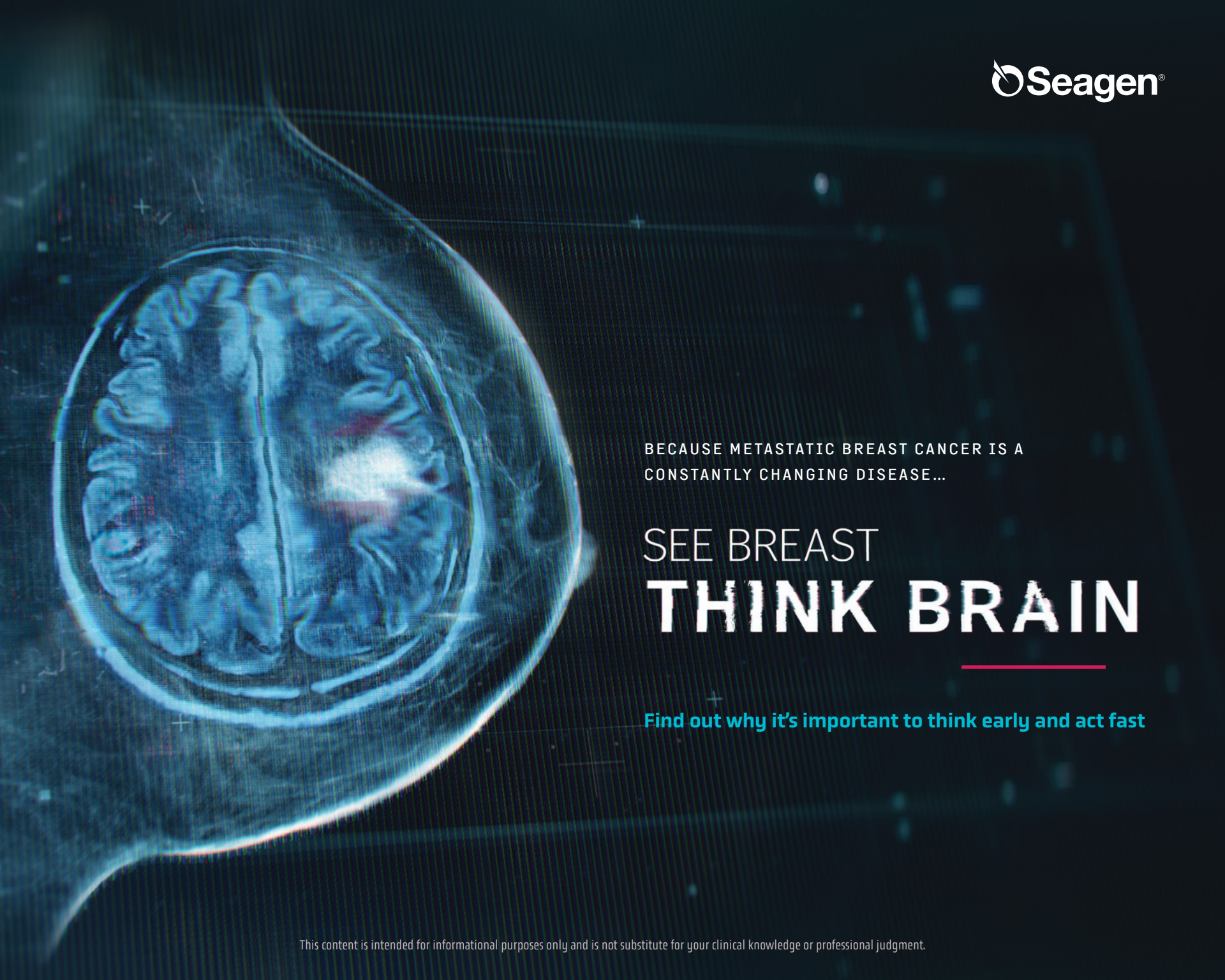
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BECAUSE METASTATIC BREAST CANCER IS A CONSTANTLY CHANGING DISEASE…
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Find out why it's important to think early and act fast
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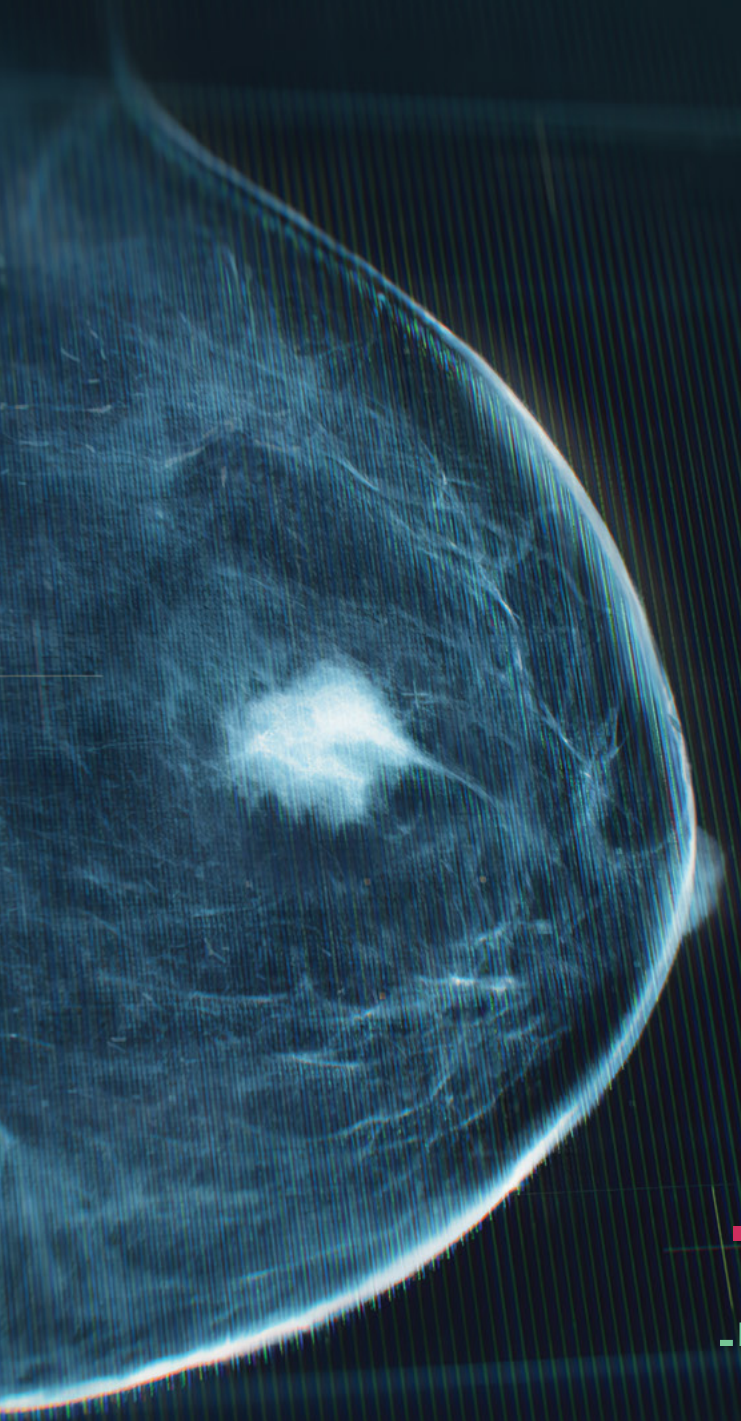


THE INCIDENCE OF BRAIN METASTASES IN PATIENTS WITH MBC IS HIGH AND CONTINUES TO RISE[1–5]

Breast cancer is the second-most common cause of brain metastases[1,2]

- Up to 30% of patients with MBC develop brain metastases during the course of disease[2–5]
- A 44% increase in the risk of hospital admittance with brain metastases was observed among patients diagnosed in 2004–2006 compared with 1998–2000, according to a Swedish registry of 50,528 patients with breast cancer[6]
- The extended survival that has accompanied MBC treatment advances may give brain metastases more time to develop[7,8]
- Advancements in imaging technology may contribute to increased identification of brain metastases[7,8]

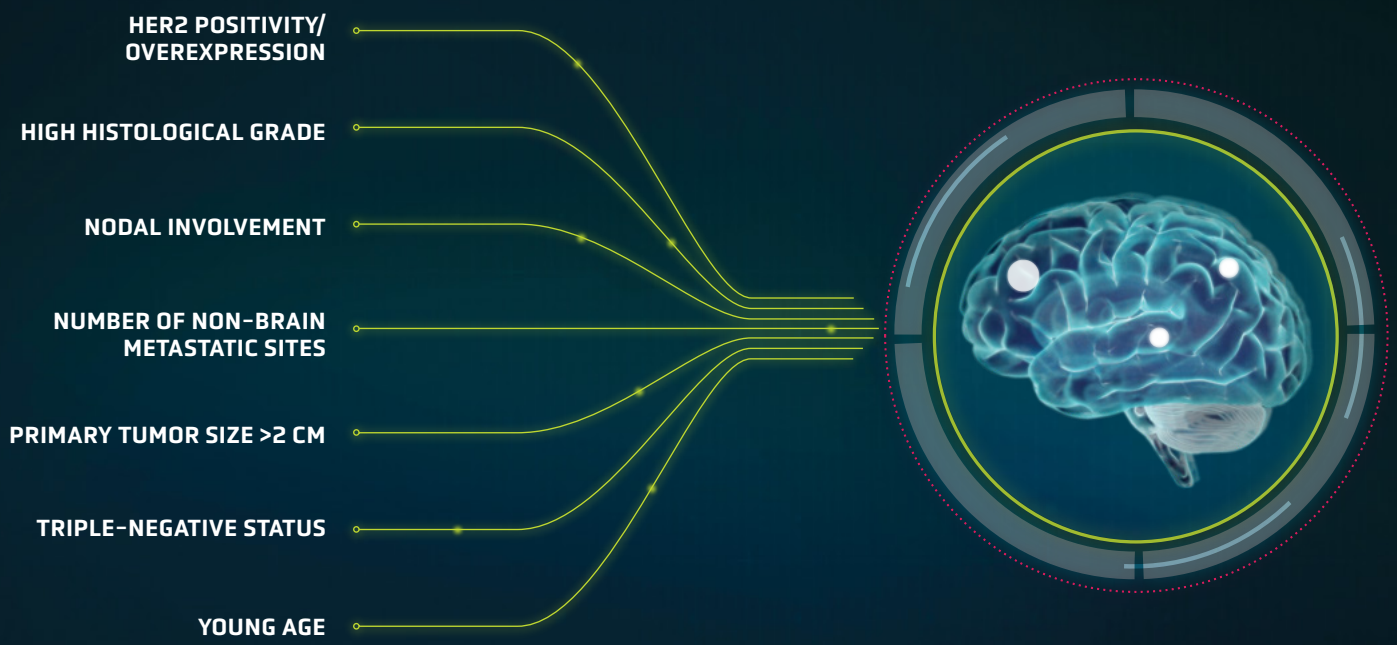
Brain metastases are often a cause of death in patients with MBC[2,8,9]

- In a Japanese multicenter, retrospective study from 2001 to 2012, of 1256 patients with MBC who had brain metastases, more than half of patients (695/1256) died as a direct result of brain metastases[8]

IS THE POTENTIAL FOR BRAIN METASTASES GETTING THE ATTENTION IT DESERVES IN PATIENTS WITH MBC?

MBC = metastatic breast cancer.

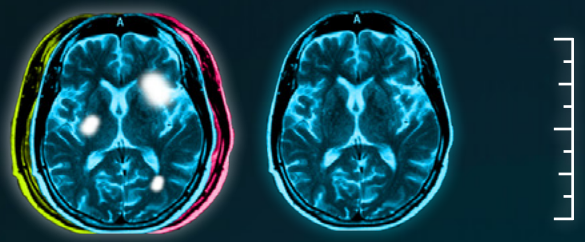
MULTIPLE RISK FACTORS FOR BRAIN METASTASES HAVE BEEN IDENTIFIED IN PATIENTS WITH MBC[7,10]★



HOW DO YOU CURRENTLY ASSESS THE RISK OF BRAIN METASTASES IN YOUR PATIENTS WITH MBC?

*Factors listed were shown to contribute to a higher risk of brain metastases in 5 or more studies.[10]
HER = human epidermal growth factor receptor.

HER2 POSITIVITY IS ONE OF THE GREATEST RISK FACTORS FOR BRAIN METASTASES IN PATIENTS WITH BREAST CANCER[5,7,10–13]



Almost **1 in 2 patients with HER2+ MBC** will develop brain metastases over the course of their disease[11,13]

- Retrospective data show that patients with tumors overexpressing HER2 develop brain metastases at a higher rate than most patients with HER2–negative tumors, including those with the TN subtype[5,14]
- Brain metastases in patients with HER2+ MBC, as identified by IHC or ISH, can occur even in patients who are otherwise responding to treatment or who have stable disease at other sites[15,16]

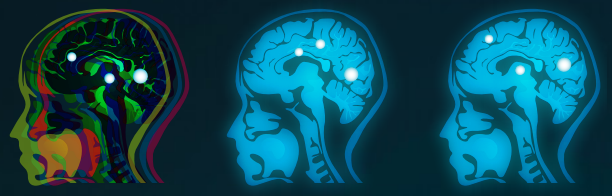
ARE ENOUGH MEASURES BEING TAKEN TO DETECT BRAIN METASTASES IN PATIENTS WITH HER2+ MBC?

IHC = immunohistochemistry; ISH = in situ hybridization; TN = triple negative.

In patients with HER2+ MBC

BRAIN METASTASES, DESPITE THEIR FREQUENT OCCURRENCE, CAN GO UNDETECTED[17,18]

Brain metastases can occur without identifying symptoms[17,18]



Up to **1 in 3 patients** with brain metastases may be neurologically asymptomatic[17,18]

- Current ASCO guidelines do not recommend proactive imaging in asymptomatic patients[19]
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend imaging only as clinically indicated and not for all patients[20]

Some brain metastases symptoms are similar to treatment-related side effects or are also symptoms of other conditions[21-28]

ARE THE CURRENT METHODS USED FOR DETECTING BRAIN METASTASES IN PATIENTS WITH HER2+ MBC SUFFICIENT?

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ASCO = American Society of Clinical Oncology; NCCN = National Comprehensive Cancer Network.

In patients with HER2+ MBC

BRAIN METASTASES CAN DEVELOP QUICKLY AND CAN SIGNIFICANTLY REDUCE OVERALL SURVIVAL[29-31]

>HALF at or before 2L

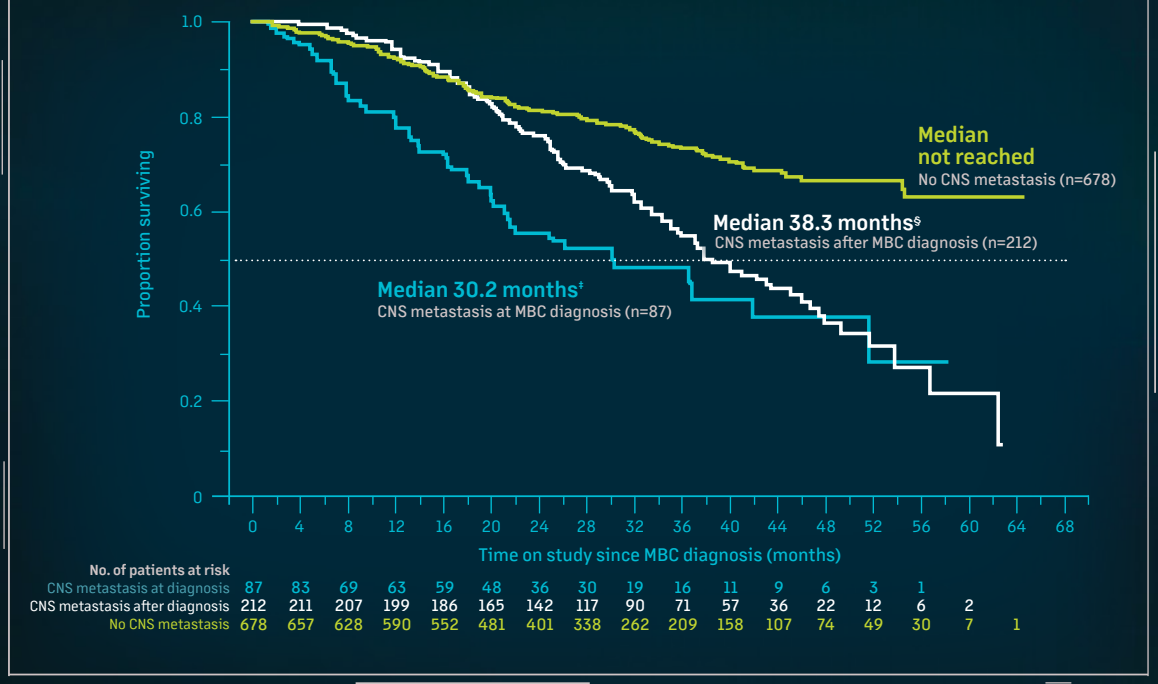
More than half of patients with HER2+ MBC who develop brain metastases may do so at or before the **second line** of therapy[29]★

~1YR

Median time to brain metastases after initial MBC diagnosis: **~1 year**[30]†

The presence of CNS metastases either at or after MBC diagnosis significantly reduces OS and PFS[31]

Overall survival of patients with HER2+ MBC by presence of CNS metastases[31]



No. of patients at risk																
CNS metastasis at diagnosis	87	83	69	63	59	48	36	30	19	16	11	9	6	3	1	
CNS metastasis after diagnosis	212	211	207	199	186	165	142	117	90	71	57	36	22	12	6	2
No CNS metastasis	678	657	628	590	552	481	401	338	262	209	158	107	74	49	30	7	1

- Patients with CNS metastasis also progress more quickly than those without, requiring a faster transition to the next line of therapy[31]
  - Median PFS in patients with CNS metastases at MBC diagnosis: 9.2 months; HR = 2.49 (95% CI: 1.93–3.20); *P* <0.0001
  - Median PFS in patients with CNS metastases after MBC diagnosis: 9.9 months; HR = 2.52 (95% CI: 2.13–2.99); *P* <0.0001
  - Median PFS in patients with no CNS metastases: 19.1 months

★Based on a retrospective review of electronic medical records from 86 of 165 patients with HER2+ MBC with brain metastases.[29]

†In 226 patients with HER2+ MBC who developed initial brain metastases after MBC diagnosis.[30]

‡Median OS in patients with CNS metastasis at diagnosis vs no CNS metastasis at any time: 30.2 months vs not reached; HR = 2.86 (95% CI: 2.05–4.00); *P* <0.0001[31]

§Median OS in patients with CNS metastasis after diagnosis vs no CNS metastasis at any time: 38.3 months vs not reached; HR = 1.94 (95% CI: 1.52–2.49); *P* <0.0001[31]

2L = second line; CI = confidence interval; CNS = central nervous system; HR = hazard ratio; OS = overall survival; PFS = progression-free survival.

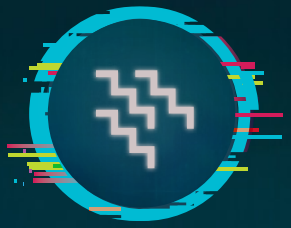
Adapted from Clinical Cancer Research, 2019, Volume 25, Issue 8, 2433–2441, Hurvitz, Central Nervous System Metastasis in Patients with HER2-Positive Metastatic Breast Cancer: Patient Characteristics, Treatment, and Survival from SystHERs, with permission from AACR.
Data from the SystHERs study, a real-world analysis of 977 patients with HER2+ MBC.[31]

CAN MORE BE DONE EARLIER TO GET THE MOST OUT OF YOUR APPROACH TO BRAIN METASTASES?

In patients with HER2+ MBC

THE EFFECTS OF BRAIN METASTASES ARE WIDE-RANGING AND DEVASTATING [22,23]

DIZZINESS



SEIZURES

ATAXIA

HEADACHE

ALTERED MENTAL STATUS

VISUAL IMPAIRMENT

NAUSEA/ VOMITING

ALTHOUGH LOCAL TREATMENT FOR BRAIN METASTASES HAS ADVANCED, LIMITATIONS REMAIN[32–37]

Recurrence is a common threat, even when brain metastases are stabilized with local treatments[32,33]

IN A STUDY OF 84 PATIENTS

with newly diagnosed HER2–amplified breast cancer brain metastases who underwent SRS[32]:

~50% of patients

developed new brain metastases within

12 MONTHS

of SRS treatment

IN A STUDY OF 57 PATIENTS

with breast cancer with brain metastases who underwent SRS, of which 28 had HER2+ disease[33]:

50% (14/28) of patients

with HER2+ MBC required salvage radiation therapy, including SRS (5/14) and WBRT (5/14)

A trend toward increased intracranial relapse in HER2+ patients vs HER2– patients was observed

Both SRS and WBRT may have serious side effects that negatively impact patient quality of life[34–37]

Side effects of SRS include[34,35]:

- [X] **FATIGUE**
- [X] **HEADACHE**
- [X] **HEARING IMPAIRMENT**
- [X] **NAUSEA**
- [X] **COGNITIVE ISSUES**
- [X] **RADIONECROSIS**

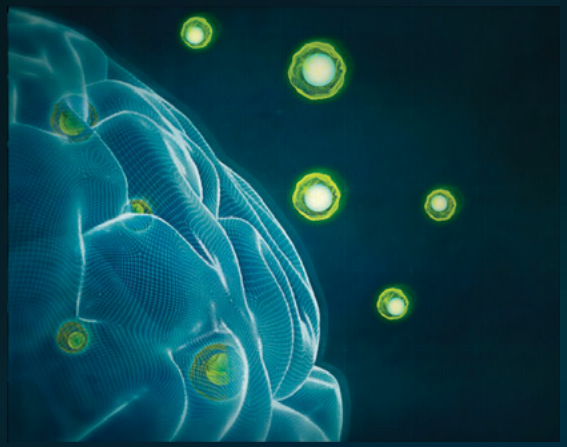
WBRT may cause serious, progressive, and irreversible side effects[36,37]

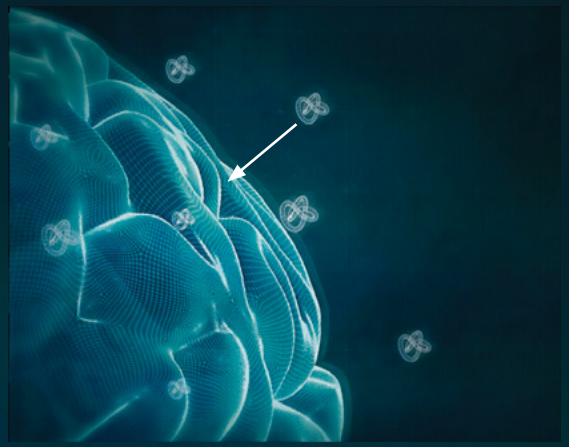
- Side effects may include inattention, confusion, memory loss, emotional dysfunction, coma, vascular injury/risk of stroke, and dementia
- Side effects may occur from months to years after treatment

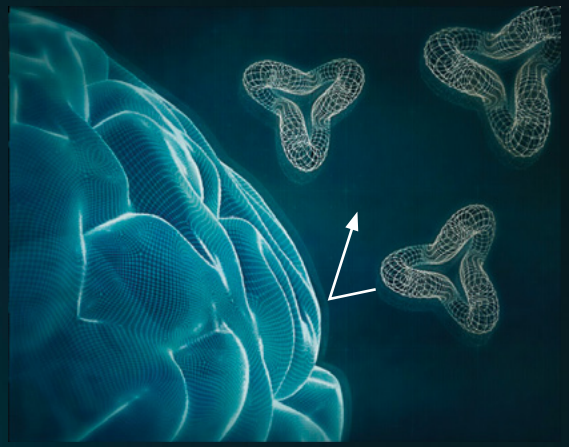
SRS = stereotactic radiosurgery; WBRT = whole brain radiation therapy.

THE BLOOD-BRAIN BARRIER IS AN IMPORTANT FACTOR IN THE DEVELOPMENT AND TREATMENT OF BRAIN METASTASES[1,38-41]

The selective permeability of the BBB may make the brain a sanctuary site for metastases[38,39]







Images are for illustrative purposes only and are not to scale.

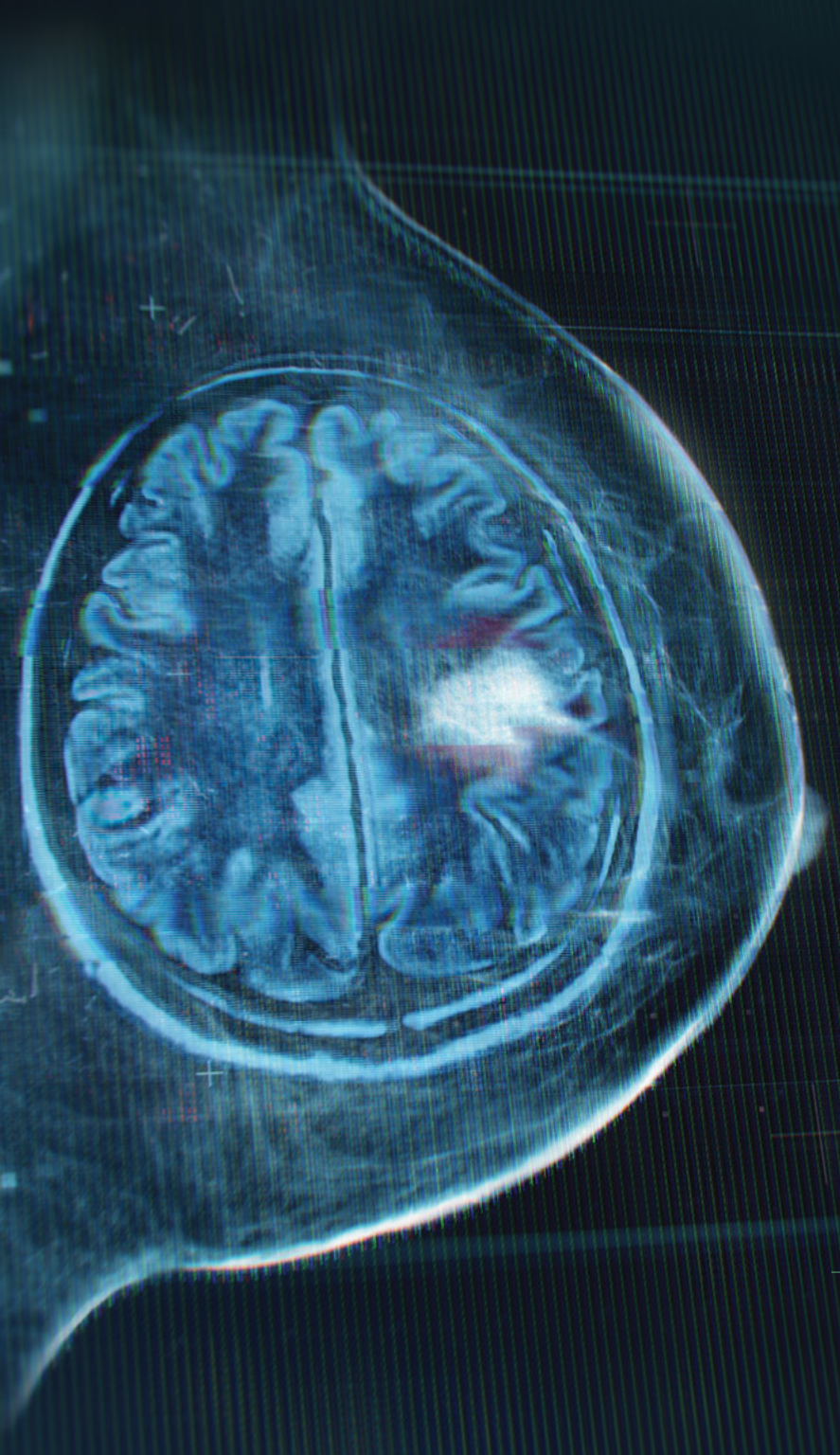
1 | Cancer cells infiltrate the brain through an intact BBB via the process of extravasation, enabling the development of micrometastases.[1,38,39]

2 | Tight junctions may restrict paracellular transport through an intact BBB.[1,38,40]

3 | Large molecules may not cross an intact BBB due to their size.[40]

DO YOU CONSIDER THE CHALLENGES OF THE BBB IN YOUR CLINICAL APPROACH FOR YOUR PATIENTS WITH BREAST CANCER?

BBB = blood-brain barrier; Da = dalton.



SEE BREAST
THINK BRAIN

The diagnosis of HER2+ MBC should come with the anticipation of possible brain metastases

- The incidence of brain metastases in patients with MBC is high and continues to rise[1-5]
- HER2 positivity is one of the greatest risk factors for brain metastases in patients with MBC[5,7,10-13]
- Brain metastases are often asymptomatic and can go undetected[17,18]
- Brain metastases can significantly reduce survival[22,23,31]
- Local treatments have serious side effects and do not eliminate the threat of recurrence[33,34]
- The brain can be a sanctuary site for metastases in patients with HER2+ MBC, making the BBB an important factor in the development and treatment of brain metastases[38,39]

CONSIDER THE POTENTIAL IMPACT OF BRAIN METASTASES IN PATIENTS WITH HER2+ MBC IN YOUR PRACTICE

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